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placebo effect.

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When people are unwell, they will often begin to recover just as soon as they receive medical attention., but before the treatment could have any direct effect and even when the treatment is a sham. Mere belief that recovery is coming can by itself bring the recovery about.

This is the placebo effect (named in the middle-ages after the professional mourners at a funeral who were paid to sing vespers for the dead, beginning "Placebo Domino . .) . The essayist Michel de Montaigne, writing in 1572, noted that 'there are men on whom the mere sight of medicine is operative', and he went on to describe what would now be considered a textbook case:

> [There was] a man who was sickly and subject to [kidney] stone who often resorted to enemas, which he had made up for him by physicians, and none of the usual formalities was omitted. . . Imagine him then, lying on his stomach, with all the motions gone through except that no application has been made! This ceremonial over, the apothecary would retire, and the patient would be treated just as if he taken the enema; the effect was the same as if he actually had . . . When, to save the expense, the patient's wife tried sometimes to make do with warm water, the result betrayed the fraud; this method was found useless and they had to return to the first.

Recent scientific studies, comparing placebo with no-placebo, as Montaigne did here, have confirmed the reality of the phenomenon. The effects appear to be strongest and most reliable in the treatment of pain, where in both clinical and laboratory settings placebos of all kinds – sugar pills, cold creams, saline injections, fake ultrasound, even mere words, when convincingly presented as medical pain-killers – have been found to bring significant relief. But placebos can also be effective in the treatment of a range of other illnesses: including, stomach ulcers, heart disease, depression, and Parkinson's disease. As Robert Buckman has summed it up: 'Placebos are extraordinary drugs. They seem to have some effect on almost every symptom known to mankind, and work in at least a third of patients and sometimes in up to 60%. They have no serious side-effects and cannot be given in overdose. In short they hold the prize for the most adaptable, protean, effective, safe and cheap drugs in the world's pharmacopoeia.'

Still, much remains to be discovered about how and why placebos work. What exactly is the message the placebo gives the patient, and by what perceptual routes does it arrive? How does this message and the meaning that's attached to it affect the patient's specific expectations and/or general mood? How do these changes in what the patient thinks (particularly) or feels (more generally) about his ailment activate the physiological mechanisms that lead to recovery? And, then, the deeper question about evolutionary design: what biological advantage can there be in having the mind control the body's healing systems in this way?

People rely on a variety of sources of information for foretelling the future. It is clear that the placebo's message – to the effect that 'this treatment will soon make you better' – can be conveyed by any or all of them: learned associations, explicit instruction, rational argument, magical reasoning, trust in authority, and, of particular importance, subtle social cues of the kind called 'bedside manner' (so that, for example, the same placebo pill may work consistently better when administered by one doctor than another). But, by whatever route the message comes, the patient must have the right mind-set to receive it. There are large cross-cultural differences in placebo responsiveness, which, though little understood, promise to throw light on how local attitudes to medicine and the symbolism of the body may enable or disable the 'meaning response'(Moerman 2002). For example, placebo medicine works powerfully for the treatment of stomach ulcers in Germany (60% healing rate), but hardly at all in Brazil (7%); yet for the treatment of hypertension, placebo medicine is less effective in Germany than elsewhere.

Placebo treatments tend to have results specific to the particular ailment and the part of the body to which they are applied (for example placebo pain-relieving cream applied to the left hand does not relieve pain on the right). So the effects cannot be being mediated entirely through changes in the patient's general mood. Rather, the patient's expectations that the treatment will work (like a real medicine) to help with the particular problem it addresses must be being channelled into a relatively narrow and 'appropriate' response.

How does the mind talk to the body's healing systems in such specific ways? Recent research in neuro-immunology has uncovered intimate links between the central nervous system and the immune system, with several kinds of neurotransmitters doubling as signallers for immune activation and vice-versa. (Evans 2003). There is therefore plenty of scope for cross-talk. However one chemical pathway in particular – the endogenous opiates – very likely plays a central role: for it has been found that placebo treatments for pain become completely ineffective if the patient is also given the drug, naloxone, which blocks endogenous opiates from working. What is more, endogenous opiates are known also to be involved in the regulation of inflammation, nausea, wound-healing and antibody production. So

it is possible – but as yet unproved – that endogenous opiates are responsible for mediating placebo effects across the board: indeed that they provide a kind of lingua franca for mind-body interaction in relation to healing.

No doubt we shall soon have answers to these questions about how placebos work, but there will remain the larger question: why.

When people recover from illness as a result of placebo treatments, it is of course their own healing systems that are doing the job. Placebo cure is self-cure. But if the capacity for self-cure is latent, then why is it not used immediately? If people can get better by their own efforts, why don't they just get on with it as soon as they get sick – without having to wait, as it were, for outside permission? Why should the mind be allowed to have such influence, when the net result is, if anything, to put a brake on healing?

This paradox has to be resolved by considering the placebo effect in a broader evolutionary context (Humphrey 2002).

Long before medicines or doctors came on the scene, human beings had already developed a fine capacity for looking after their own health: by mounting defences such as pain and fever, by actively attacking infections, by repairing bone and tissue damage, by indulging in sickness behaviours, and so on. However none of these measures is free of cost (immune resources are expensive, pain is debilitating, acting-sick is time-wasting, etc.). So it has been essential to have some kind of internal 'health management system' in place, to ensure that the way the body responds to any particular threat is nearly optimal.

Sometimes, for example, it would be best for a sick person to get well as rapidly as possible, throwing off defences such as pain and mounting a full-scale immune response; but at other times it might be more prudent to remain unwell and out of action and to conserve resources for later use. As a general rule (and of crucial importance for the story of placebos): the brighter the prospects for a rapid recovery, the less to be gained from playing safe and remaining sick.

But this has meant that the health management system has needed to take account, so far as possible, of any intelligence available to the sick person about what the future holds. Relevant information would include the nature of the threat, the costs of the defensive measure, the prospects for spontaneous remission, evidence of how other people are faring, the presence of social support, and so on. The mind therefore has had to become an adjunct to the healing system – precisely so as to gather this intelligence.

In the past all kinds of environmental information would be brought to bear. And no doubt they still are. But today, the medicalisation of sickness has changed the picture. For it means there will often be a novel and even overriding piece of information to take into account. People have learned – their culture has taught them – that nothing is a better

predictor of how things will turn out when they are sick (whether the pain will ease, whether the infection will abate, whether they will be nursed back to health . .) than the presence of doctors, medicines, and so on.

Yet human beings remain tied to their evolutionary heritage. And so, today, the very prospect of medical attention – the patient's belief in it – works its magic for the simple reason, stemming from the general rule above, that for most of human history, once a sick person has had cause to think that he will soon be safe and well, he has had just the excuse he needs to bring on his own recovery as fast as possible.

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