The assessment and management of venous thromboembolism

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Summary

This article examines venous thromboembolism (VTE) and offers guidance on its prevention. VTE is a potentially fatal condition, which can be prevented using both pharmacological and mechanical methods. Nursing staff should be aware of the risk factors that predispose patients to venous thromboembolism and ensure that high-risk patients receive the prophylaxis they require.

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Keywords

Deep vein thrombosis; Thrombosis; Vascular disorders

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Aims and intended learning outcomes

This article aims to provide an update and overview of venous thromboembolism (VTE) and its clinical presentation. It discusses management strategies and how to recognise at-risk patients to initiate prophylactic measures in hospital. After reading this article you should be able to:

- Outline the clinical manifestation of VTE.
- Recognise the signs and symptoms of deep vein thrombosis (DVT) and pulmonary embolism (PE).
- Summarise the pathophysiology associated with the formation of VTE.
- List the risk factors that predispose patients to VTE.
- Identify which patients will benefit from prophylactic measures.
- Discuss the treatment options and nursing interventions available to patients with VTE.

Time out 1

Before reading on, summarise what you know already about VTE. How does it present in practice, and which patients are most at risk?

Introduction

In March 2005, the House of Commons Health Committee published a critical report on the prevention of VTE. The report states that more than 25,000 patients in England die each year from VTE, which is more than the combined total of deaths from breast cancer, acquired immune deficiency syndrome and road traffic injuries (House of Commons Health Committee 2005).

Many of these deaths are preventable. By recognising high-risk patients, and starting them on what is proven to be a safe and cost-effective prophylactic treatment, lives can be saved. At present, no national guidelines exist to ensure that health professionals consider the risk of VTE, but the National Institute for Health and Clinical Excellence (NICE) has been commissioned to address this problem and a report is expected to be published in May 2007 (House of Commons Health Committee 2005). In the meantime, it is important that nurses can recognise patients at risk from VTE and implement prophylaxis.

Pathophysiology

Venous thrombosis is a condition in which a blood clot (thrombus) forms in a vein. This

manifests clinically as DVT, commonly in the deep veins of the legs, thighs and pelvis; and PE if the clot breaks off from the site in which it was created and lodges in the lung vessels (House of Commons Health Committee 2005). DVT and PE are collectively known as VTE (Box 1).

Thrombus formation is a result of an imbalance between the anticoagulant and procoagulant systems in the blood (Enders *et al* 2002). Three pathological processes, known collectively as Virchow's triad, have been shown to promote this imbalance (United Kingdom (UK) Venous Thromboembolism Registry (VERITY) 2004). Patients with venous trauma (problems with the vessel wall), venous stasis (problems with blood flow) or hypercoagulability (problems with the blood's clotting components) are predisposed to VTE formation (Box 2).

Clotting Clot formation is a complex process in which fibrinogen, a soluble protein in blood, is converted to a fibrin clot by the action of thrombin. This process is important in reducing blood loss when vessels are damaged or ruptured (Kumar and Clark 2002). Injury to vessel walls exposes collagen and releases tissue factor, a protein expressed by cell surfaces. This leads to a complex cascade of reactions in which various coagulation factors activate one another (Enders *et al* 2002). Although this process is important in the repair of damaged vessels, the clotting cascade can be initiated in high-risk patients, resulting in thrombus formation and causing symptoms of VTE (Kumar and Clark 2002).

Time out 2

What clinical signs and symptoms would lead you to suspect a DVT or PE?

Deep vein thrombosis

DVT usually begins when small deposits of fibrin collect in the deep veins of the thigh or calf as a result of slow blood flow and local activation of the clotting cascade. DVT can be asymptomatic, but the classic symptoms of calf pain, swelling, increased skin temperature, superficial venous dilation and (occasionally) pitting oedema usually occur when a thrombus becomes large enough to cause blood outflow problems (Gorman *et al* 2000). Complete occlusion of a vein is rare, but can lead to a cyanotic discoloration of the limb and severe oedema, which can develop into venous gangrene (Kumar and Clark 2002).

Venous thrombosis usually occurs around the cusp of a venous valve (Sevitt 1974). This can cause irreversible valve damage, leading to chronic venous insufficiency or post-thrombotic syndrome, which increases the risk of recurrent VTE (Geerts *et al* 2004). DVT can resolve completely without causing patients any ill effects, but its prevention and treatment are important, since it can lead to a fatal PE.

Time out 3

Reflect on the investigations you have seen carried out on a patient with suspected DVT or PE and make a list of these.

Investigations Clinical diagnosis of DVT is often unreliable, so combinations of diagnostic investigations are usually performed. The gold standard for establishing a diagnosis of DVT is contrast venography, but since this procedure is invasive and expensive it is rarely used (Tovey and

BOX 1

Glossary

Deep vein thrombosis (DVT): venous thrombosis that occurs in the 'deep veins' of the legs, thighs or pelvis.

Post-thrombotic (post-phlebitic) syndrome: chronic pain and swelling and occasional ulceration of the skin, occurring as a consequence of previous venous thrombosis.

Pulmonary embolism (PE): a blood clot that breaks off from the deep veins and travels round the circulation to block the pulmonary arteries. Most deaths arising from DVT are caused by PE. A 'massive' PE is one so severe as to cause circulatory collapse.

Venous thromboembolism (VTE): the blocking of a blood vessel by a clot dislodged from its site of origin. It includes both DVT and PE.

Venous thrombus: a condition in which a blood clot (thrombus) forms in a vein.

(British Thoracic Society (BTS) 2003, House of Commons Health Committee 2005)

BOX 2

Virchow's triad

1. Venous trauma

Trauma or damage to vascular endothelium as a result of infection can lead to the release of tissue factor which initiates the extrinsic clotting cascade leading to clot formation.

2. Venous stasis

Vessel compression by enlarged lymph nodes, bulky tumours, or previous thromboses can lead to venous stasis, as can immobility or confinement to bed – one of the main reasons that hospital inpatients are at increased risk of venous thromboembolism (VTE).

3. Hypercoagulability

Genetic conditions such as thrombophilia, which affects one in 20 of the United Kingdom population and causes the blood to clot more easily than it should, increasing the chances of thrombus formation. Cancers, particularly adenocarcinomas and metastatic cancers, and oestrogens, found in oral contraceptives and hormone replacement therapy, can also activate the clotting system, increasing the risk of VTE.

(Enders *et al* 2002, Turpie *et al* 2002a, House of Commons Health Committee 2005)

Wyatt 2003). In practice, ultrasonography combined with a d-dimer blood test (Box 3) is usually carried out. Ultrasound is not 100 per cent reliable, and those patients who are clinically suspected of having a DVT but have a negative ultrasound result should ideally have the test repeated a week later (Turpie *et al* 2002a).

Treatment DVT and PE are treated similarly. Low molecular weight heparin (LMWH) is given to patients with suspected VTE and, once diagnosis is confirmed, patients are started on oral anticoagulation with warfarin. Box 4 summarises why LMWH has replaced unfractionated heparin as the treatment of choice.

Warfarin is the most widely used oral anticoagulant and works by antagonising the effects of vitamin K. It is teratogenic (may cause serious embryonic or fetal malformation) and should not be given in the first trimester of pregnancy. It is known to interact with a number of drugs including alcohol (British National Formulary (BNF) 2005). The anticoagulant effects of warfarin take at least 48 to 72 hours to develop fully, so it is important that heparin is given concomitantly (BNF 2005). The usual starting dose of warfarin is 10mg daily for two days and the subsequent maintenance dose varies between patients and depends on the prothrombin time, which is reported universally as the international normalised ratio (INR). A target INR range of 2-3 is standard for treatment of VTE, and patients should be monitored for signs of bleeding (Turpie *et al* 2002b). The INR should be measured daily in the early days of treatment, then at longer intervals depending on the response (BNF 2005).

BOX 3

D-dimer blood test

D-dimers are protein derivatives of fibrin found in plasma and produced when fibrin is degraded by plasmin (also known as fibrin degradation products). Plasma concentrations of d-dimers are therefore raised in patients with venous thromboembolism (VTE). A positive diagnosis of VTE cannot be made using a d-dimer blood test alone, since levels can also be raised during infection, malignancy, pregnancy and after an operation. D-dimers have a high negative predictive value, so if a patient with suspected VTE has a normal d-dimer blood test, the diagnosis can be ruled out. D-dimer testing is not indicated in patients with a high clinical probability of pulmonary embolism, since the test is almost certainly going to be positive and adds little to the clinical picture.

(BTS 2003, Tovey and Wyatt 2003)

BOX 4

Unfractionated heparin vs low molecular weight heparin

In the past, unfractionated heparin was the initial treatment for venous thromboembolism (VTE) and was administered by continuous infusion. This method required daily monitoring of activated partial thromboplastin time (APTT) with adjustment of dose according to the response of each patient. Heparin use for more than six days is also associated with an increased risk of thrombocytopenia (a reduction in the number of platelets in the blood).

Low molecular weight heparin (LMWH) has a more predicable relation between dose and response based on a patient's body weight, so does not require such close monitoring. It is associated with a lower risk of thrombocytopenia, no excess bleeding and can be administered by patients at home. For these reasons, LMWH has largely replaced the use of unfractionated heparin.

(Turpie *et al* 2002b)

Heparin treatment should continue alongside warfarin therapy for at least five days or until the INR is greater than 2 (Turpie *et al* 2002b). Anticoagulation with warfarin should continue for at least three months, although longer treatment regimens are recommended in certain patients (Box 5).

Pulmonary embolism

PE occurs when a thrombus or other foreign substance lodges in a pulmonary blood vessel and obstructs circulation to the lung tissue. Classic symptoms include breathlessness and tachypnoea, pleuritic chest pain and occasionally haemoptysis. In the instance of a massive PE, leading to cardiac arrest, patients may collapse, become hypotensive and hypoxic and may show signs of engorged neck veins and a right ventricular gallop (a loud, additional heart rhythm) (BTS 2003).

Investigations Patients with suspected PE should have initial routine investigations including chest X-ray, electrocardiogram (ECG) and arterial blood gases to exclude other causes. A negative d-dimer blood test can reliably exclude diagnosis in patients considered low probability for PE, and further imaging is not required in such patients. Patients with a high clinical probability of PE (that is, multiple risk factors and ECG changes suggestive of PE), and those with low to intermediate probability but with a positive d-dimer blood test should have further investigations. Isotope lung scanning (commonly known as a ventilation-perfusion or 'V/Q' scan) is usually the initial investigation implemented, but has been found to generate a significant number of false positive results. It is also unreliable in patients with chronic cardiac or respiratory disease. In these cases, patients go on to have a computed tomographic pulmonary

angiography (CTPA), which is quicker to perform, rarely needs to be followed by other imaging and may provide the correct diagnosis if PE is excluded. Ideally this should be the first-line investigation used, but current resources make this impractical (BTS 2003). Since 70 per cent of patients with proven PE have proximal DVT, ultrasound scanning of the legs has also been suggested as the initial imaging test to confirm VTE (BTS 2003).

A clinically massive PE can be reliably diagnosed with CTPA and echocardiography. Such imaging should be performed within one hour of presentation and within 24 hours in non-massive PE (BTS 2003).

Treatment Supportive therapy with oxygen and analgesia should be initiated as indicated. In patients with massive PE where cardiac arrest is imminent, thrombolysis with a bolus of 50mg alteplase is recommended, although this should not be used as a first-line treatment in non-massive PE (BTS 2003). Invasive approaches, that is, inferior vena caval filter insertion or thrombus fragmentation, should be considered where the facilities and expertise are readily available (BTS 2003).

Anticoagulation therapy for patients with PE is the same as described above for treatment of DVT.

Complications The majority of PEs are reabsorbed spontaneously and cause no ill effects once treated. The altered blood flow and impaired gas exchange caused by a massive PE, however, result in decreased pulmonary compliance or even pulmonary infarction, leading to haemodynamic compromise which can be fatal. Patients who survive may have increased pulmonary vascular resistance which can lead to pulmonary hypertension and heart failure (Enders *et al* 2002).

Risk factors

Surgery and acute myocardial infarction (MI) are well-recognised major risk factors for VTE and, as a consequence, these groups of patients are routinely provided with prophylaxis (Anderson and Spencer 2003). General medical patients are also at risk. Post-mortem studies estimate that 10 per cent of hospital deaths can be attributed to PE; 70 per cent of these occurring in medical patients and three quarters of which were unrecognised before post-mortem (Gerotziafas and Samama 2004).

Factors that promote venous stasis, hypercoagulability or vascular damage contribute to the risk of VTE. Table 1 shows factors that increase this risk, as agreed by the American College of Chest Physicians (ACCP) and the Thromboembolic Risk Factors Consensus Group (THRIFT 1992).

The more risk factors a person has, the greater his or her risk of developing VTE (Anderson *et al* 1992). Prophylaxis in hospitalised patients is extremely important since they often have multiple risk factors (THRIFT 1992, Verstraete 1997, Geerts *et al* 2004).

BOX 5

Duration of anticoagulation therapy for venous thromboembolism (VTE)

Three to six months: patients with first event VTE with reversible or time-limited risk factors.*

More than six months: patients with idiopathic VTE (first event).

One year to life:

- Patients with first event VTE with cancer (until resolved), anticardiolipin antibody, antithrombin deficiency.
- Patients with recurrent events – idiopathic or with thrombophilia.

* Reversible or time-limited risk factors include surgery, trauma, immobilisation and oestrogen use.

(Hirsh 1995, Turpie *et al* 2002b)

Long-haul travel The risk of VTE in people travelling on long-haul flights has been widely publicised, but the actual risk of death from flight-related VTE is estimated at one per two million passengers arriving from a flight (Kelman *et al* 2003). It is thought that the immobility, low atmospheric pressure and dehydration associated with prolonged air travel may increase the risk of developing VTE (Kelman *et al* 2003), and the greater the distance travelled, the more at risk patients become (Lapostolle *et al* 2001). Despite this, long-haul travel as a risk factor for VTE in its own right still remains to be proven conclusively (Hirsh and O'Donnell 2001).

The ACCP recommends that travellers on flights lasting six hours or more should ensure adequate hydration, avoid constrictive clothing and stretch their calf muscles frequently. Those at risk of VTE may benefit from properly fitted below-knee compression stockings or a dose of LMWH, but aspirin is not recommended because there is not enough evidence supporting its use in VTE prevention (Geerts *et al* 2004).

Evidence for prevention

The NICE guidelines on VTE prophylaxis, due to be published in 2007, will only outline interventions for thromboprophylaxis in surgical patients (House of Commons Health Committee 2005). There is evidence to suggest that medical inpatients are at as much risk as those undergoing surgery, and that guidelines should be in place throughout the UK to ensure medical patients are protected against VTE (Geerts *et al* 2004).

The UK national venous thromboembolism registry recorded 2,720 cases of VTE between

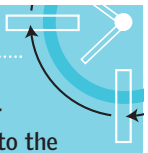
December 2001 and November 2003. Twelve per cent (n=323) of these cases had recently had a hospital stay as a medical inpatient compared to the 10 per cent (n=265) who had undergone recent surgery, suggesting that acute medical illness is an independent risk factor for VTE (UK VERITY 2004). In the United States, it has been recommended that all medical inpatients with one or more risk factor for VTE should receive thromboprophylaxis (Geerts *et al* 2004), and computer-alert programmes are being instituted to remind practitioners of this (Poller *et al* 1998, Kucher *et al* 2005).

Patients with contraindication to heparin prophylaxis, or those at high risk of bleeding are advised to use mechanical prophylaxis such as graduated compression stockings (Geerts *et al* 2004).

Pharmacological prophylaxis

The ACCP recommends pharmacological prophylaxis with either unfractionated heparin or LMWH in all acutely ill medical patients who have one or more risk factors for VTE (Geerts *et al* 2004). Surgical patients should also continue to be given prophylaxis on admission since LMWH prophylaxis reduces the risk of VTE in general surgery patients by more than 70 per cent compared with placebo (Mismetti *et al* 2001). A meta-analysis carried out by Mismetti *et al* (2000) showed that unfractionated heparin and LMWH are equally effective at reducing the incidence of VTE, but LMWH is safer with a 52 per cent lower risk of bleeding. The MEDENOX (Samama *et al* 1999) and PREVENT (Leizorovicz *et al* 2004) randomised controlled trials investigated the efficacy of LMWH. Both found the incidence of DVT to be reduced.

Time out 4



Consider the following scenarios. Should prophylactic low molecular weight heparin (LMWH) be given to the following patients:

- **A fully mobile 31-year-old female smoker admitted to the acute medical admissions unit with a severe chest infection?**
- **A 40-year-old male with a body mass index of 35 (obese), who is usually fit and well and has presented to hospital with gastroenteritis?**

According to the ACCP guidelines, both patients have risk factors for VTE, and should be given LMWH. Do you agree and if so, why?

LMWHs have a longer duration of action than unfractionated heparins, allowing for once daily subcutaneous dosage and the standard prophylactic regimen does not require

TABLE 1

Risk factors for venous thromboembolism

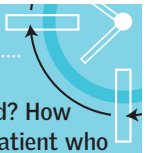
Background factors	Disease or surgical procedure
Activated protein C resistance	Behçet's disease
Age more than 40 years	Central venous catheterisation
High-dose oestrogens	Heart failure
Homocystinaemia (an amino acid disorder that causes an excess of homocystine in the blood)	Inflammatory bowel disease
Immobility (bed rest more than four days)	Malignancy, especially pelvic or abdominal
Phospholipid antibody or lupus anticoagulant	Nephrotic syndrome
Pregnancy and postpartum	Paralysis of lower limb(s)
Previous deep vein thrombosis or pulmonary embolism	Paraproteinaemia (the presence of abnormal proteins in the blood)
Puerperium	Paroxysmal nocturnal haemoglobinuria (a disorder characterised by blood in the urine because of an abnormality of the red cell membrane)
Severe obesity	Polycythaemia (increase in haemoglobin content of blood)
Smoking	Recent myocardial infarction
Thrombophilia: deficiency of antithrombin III, protein C, protein S	Respiratory failure
Varicose veins	Severe infection
	Trauma or surgery, especially of pelvis, hip, and lower limb

(THRIFT 1992, Verstraete 1997, Geerts *et al* 2004)

monitoring (BNF 2005). Several types of LMWH are licensed for use in VTE prevention, but protocols remain to be established for exact prophylactic dose regimens. Table 2 outlines the typical recommended doses available.

LMWH is given via subcutaneous injection, a procedure with which nursing staff should be familiar. Box 6 provides practical information on administering a subcutaneous injection.

Time out 5



For which patients should antiembolism stockings be avoided? How would you assess and care for a patient who requires antiembolism stockings?

Nursing interventions

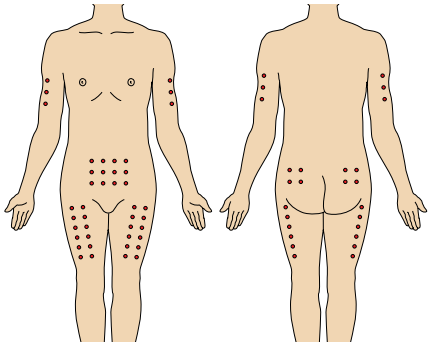
All patients should be assessed for risk of VTE on admission to hospital, remembering that medical patients can be at as much risk as surgical patients. Methods of prophylaxis are aimed at targeting the three predisposing factors (venous stasis, venous trauma and hypercoagulability), using pharmacological and mechanical interventions.

Antiembolism stockings have been found to prevent venous dilation (Coleridge Smith *et al* 1991) and improve blood flow by stimulating fibrinolytic activity within blood vessels (Arcelus *et al* 1995). The use of compression stockings has also been found to significantly reduce post-thrombotic syndrome (Brandjes *et al* 1997). Nurses should assess all patients for any contraindications to antiembolism stockings, avoiding their use in patients with arterial impairment or leg ulcers.

Many stockings contain latex, so alternate brands should be used for patients with a latex allergy. All patients should be measured to ensure that they receive the correct size of stocking, and should be given information on how to wear and care for their antiembolism stockings (Box 7).

FIGURE 1

Anatomical sites for subcutaneous injection



BOX 6

Practical information on subcutaneous injection

- After explaining the procedure to the patient, checking the correct drug, dose, date and time of administration, start by choosing an appropriate injection site and clean the area with an alcohol swab. Sites used for subcutaneous injection are shown in Figure 1.
- Using the non-dominant hand, gently pinch the skin over the site. Insert the needle into the skin at a 45˚ angle, releasing the skin once the needle is in position to reduce discomfort and ensure the drug is delivered into the subcutaneous tissue.
- Withdraw the piston of the syringe. If any blood is drawn up, then withdraw the needle and start the procedure again at a different site. This ensures the drug is not injected directly into a blood vessel.
- If no blood is withdrawn, inject slowly then withdraw the needle quickly. Apply pressure to any bleeding, document administration and ensure all sharps are disposed of correctly.

(Mallett and Dougherty 2000)

BOX 7

Fitting antiembolism stockings

Nurses should refer to manufacturer's literature when measuring and fitting patients for antiembolism stockings. The general procedure shown on the following website and taken from Kendall's TED antiembolism stocking product packing, should apply to most brands:
www.newlook.com.sg/info.asp?key=TED%20ApplyThB
(Last accessed: March 7 2006.)

Patients should be told the following information:

- Stockings should be smooth when fitted.
- The toe hole should lie underneath the toes.
- The heel patch should be in the correct position.
- The thigh gusset should be on the inner thigh.
- Rolling down the stockings may have a tourniquet effect.

(Bonner 2004)

TABLE 2

Typical recommended doses of low molecular weight heparin (LMWH)

	Subcutaneous injection once daily	
LMWH preparation	Low to moderate risk	High risk
Enoxaparin	2,000 iu	4,000 iu
Tinzaparin	3,500 iu	4,500 iu
Dalteparin	5,000 iu	5,000 iu

(Geerts *et al* 2004, BNF 2005)

Skin integrity should be regularly checked, and patients should be advised to report any feelings of tingling or numbness. Early mobilisation should be encouraged and nurses can teach patients leg and breathing exercises to stimulate the calf muscle pump and aid venous return (Bonner 2004).

Conclusion

VTE is a potentially fatal condition, which can be prevented using both pharmacological and mechanical methods. LMWH for VTE prophylaxis is underused in the UK at present, despite evidence that it is effective. It is important that nurses are aware of the risk factors of patients in their care, and ensure that high-risk patients are receiving the prophylaxis they require **NS**

Time out 6

Now that you have completed this article, you might like to consider writing a practice profile. Guidelines are on page 68.

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