

*ABC of arterial and venous disease***Swollen lower limb—1: General assessment and deep vein thrombosis**

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The most common cause of leg swelling is oedema, but expansion of all or part of a limb may be due to an increase in any tissue component (muscle, fat, blood, etc). A correct diagnosis requires consideration of whether the swelling is acute or chronic, symmetrical or asymmetrical, localised or generalised, and congenital or acquired. Chronic swelling, particularly if asymmetrical, is usually a sign of chronic oedema arising from venous or lymphatic disease, whereas symmetrical lower limb swelling suggests a systemic or more central cause of oedema, such as heart failure or nephrotic syndrome. Oedema develops when the rate of capillary filtration (lymph formation) exceeds lymphatic drainage, either because of increased capillary filtration, inadequate lymphatic flow, or both. Extracellular fluid volume is controlled principally by the lymphatic system, which normally compensates for increases in capillary filtration. Most oedemas arise because filtration overwhelms the lymph drainage system. Increased capillary filtration may occur because of raised venous pressure, hypoalbuminaemia, or increased capillary permeability due to local inflammation. The two main causes of a swollen lower limb are deep vein thrombosis and lymphoedema (a failure of the lymph drainage system). This article concentrates on deep vein thrombosis and next week's article on lymphoedema.

Deep vein thrombosis

Thrombosis usually develops as a result of venous stasis or slow flowing blood around venous valve sinuses; extension of the primary thrombus occurs within or between the deep and superficial veins of the leg and the propagating clot causes venous obstruction, damage to valves, and possible thromboembolism. Deep vein thrombosis is often asymptomatic.

Assessment and investigation

Various clinical features suggest deep vein thrombosis, but the findings of physical examination alone are notoriously unreliable. Deep vein thrombosis is confirmed in only one out of every three cases suspected clinically. Confirmation of a suspected deep vein thrombosis requires use of one or more investigations, and the confirmation rate rises with the number of clinical risk factors. Identification of an underlying cause, if any, will guide both the treatment and the approach to secondary prevention.

Clinical features of acute deep vein thrombosis

- Calf pain or tenderness, or both
- Swelling with pitting oedema
- Swelling below knee in distal deep vein thrombosis and up to groin in proximal deep vein thrombosis
- Increased skin temperature
- Superficial venous dilatation
- Cyanosis can occur with severe obstruction

The standard investigation is contrast venography, but this invasive procedure is painful, often technically difficult and time consuming, and occasionally complicated by thrombosis and

Causes of swelling of lower limb**Acute**

- Deep vein thrombosis
- Cellulitis
- Superficial thrombophlebitis
- Joint effusion or haemarthrosis
- Haematoma
- Baker's cyst
- Torn gastrocnemius muscle
- Arthritis
- Fracture
- Acute arterial ischaemia
- Dermatitis

Chronic*Congenital vascular abnormalities*

- Haemangioma
- Klippel-Trenaunay syndrome

Venous disease

- Post-thrombotic syndrome
- Lipodermatosclerosis
- Chronic venous insufficiency
- Venous obstruction

Lymphoedema

- Cancer treatment
- Infection
- Tumour
- Trauma
- Pretibial myxoedema

Other

- Heart failure
- Reflex sympathetic dystrophy
- Idiopathic oedema of women
- Hypoproteinaemia, such as cirrhosis, nephrotic syndrome
- Armchair legs
- Lipoedema



Colour duplex scan of deep vein thrombosis in common femoral vein adjacent to artery

Risk factors for deep vein thrombosis

- Age > 40 years
- Underlying malignancy
- Obesity
- Presence of varicose veins
- Personal or family history of deep vein thrombosis or pulmonary embolism
- Any surgical procedure lasting more than 30 minutes—especially orthopaedic, neurosurgical, urological, and gynaecological surgery
- Paralysis or immobility—for example, recent stroke
- Combined contraceptive pill
- Hormone replacement therapy
- Pregnancy and puerperium
- Serious illness—for example, heart failure, myocardial infarction, sepsis, inflammatory bowel disease
- Presence of hypercoagulable disorders

extravasation of contrast. Recent developments in non-invasive testing mean that venography is now unnecessary in most cases, particularly in suspected first proximal vein thrombosis.

The accuracy of non-invasive techniques varies with the clinical circumstances. For example, compression ultrasonography and impedance plethysmography are accurate for detecting symptomatic proximal (ileofemoral) deep vein thrombosis, but both techniques are less satisfactory in asymptomatic patients and for detecting distal (calf vein) thrombosis. Compression ultrasonography has become the preferred first line investigation (see *BMJ* 2000;320:698-701).

Imaging techniques are generally much less satisfactory in patients with suspected recurrent deep vein thrombosis, when confirmation of the diagnosis requires evidence of new thrombus formation—for example, the appearance of a new non-compressible venous segment on ultrasonography or a new intraluminal filling defect on venography.

Measurement of circulating D-dimer concentrations (a byproduct of fibrin production) is a useful adjunct to ultrasonography, with 98% sensitivity for deep vein thrombosis and a high negative predictive value. The sensitivity of the test is lower for smaller calf vein thrombi. However D-dimer concentrations rise as a non-specific response to concomitant illness, not just thrombosis, so D-dimer testing can be misleading in patients admitted to hospital for other reasons.

A combination of diagnostic approaches—for example, compression ultrasonography coupled with clinical pretest probability scoring or D-dimer measurements, or both, gives better diagnostic accuracy than any single investigation. Lensing et al have recently shown that the combination of compression ultrasonography and D-dimer measurement is an efficient diagnostic approach, with a rate of subsequent thromboembolism less than 1% in patients with false negative results who were not treated with heparin. A robust investigational algorithm has been devised that does not include routine use of venography.

Complications

The main complications of deep vein thrombosis are pulmonary embolism, post-thrombotic syndrome, and recurrence of thrombosis. Proximal thrombi are a major source of morbidity and mortality. Distal thrombi are generally smaller and more difficult to detect non-invasively, and their prognosis and clinical importance are less clear. However, a fifth of untreated newly developing calf vein thrombi extend proximally, and a quarter are associated with long term symptoms of post-thrombotic syndrome; it is therefore appropriate to treat proved significant calf vein thrombosis.

Post-thrombotic syndrome develops as a result of high venous pressure due to thrombotic damage to valves. It complicates 50-75% of deep vein thromboses, and there is a strong association with ipsilateral recurrence. Clinical features include pain, swelling, dermatitis, and ulceration. Proximal deep vein thrombosis is associated with a higher frequency and greater severity of post-thrombotic syndrome, but the risk is halved by use of graded compression stockings after deep vein thrombosis.

Prevention

Patients at significantly increased risk of deep vein thrombosis—for example, those having major pelvic or abdominal surgery for cancer or those with a history of pulmonary embolism or deep vein thrombosis who have

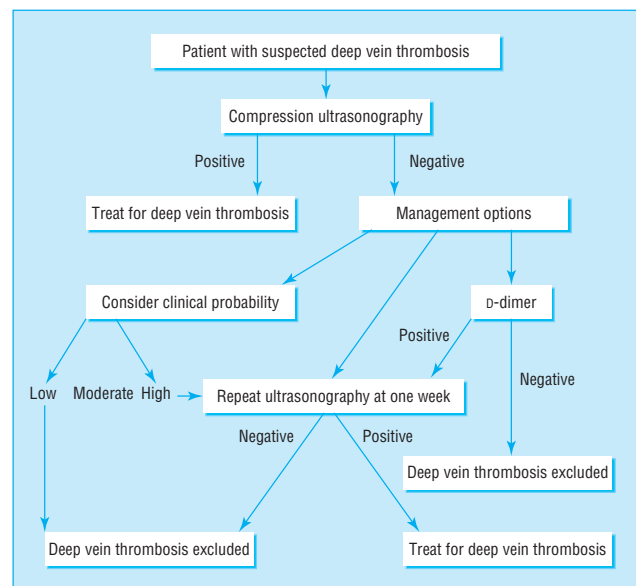


Venogram showing thrombus in lower leg

Right ileofemoral deep vein thrombosis

Clinical model to determine pretest probability of deep vein thrombosis (3 points=high risk, 1 or 2=moderate, 0=low)

	Score
Active cancer (treatment ongoing, or within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the legs	1
Recent immobilisation > 3days or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling > 3 cm than asymptomatic side (measured 10 cm below tibial tuberosity)	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Alternative diagnosis equally or more likely than deep vein thrombosis	-2



Algorithm for investigation of deep vein thrombosis

Absolute risks of venous thrombotic complications in procedures or conditions of low, moderate, and high risk

Risk level	Risk (%)			Examples
	Deep vein thrombosis	Proximal deep vein thrombosis	Fatal pulmonary embolism	
Low	< 10	< 1	0.01	Minor surgery, trauma, or medical illness Major surgery at age < 40 with no other risk factors
Moderate	10-40	1-10	0.1-1	Major surgery with another risk factor Major trauma, medical illness, or burns Emergency caesarean section in labour Minor surgery with previous deep vein thrombosis, pulmonary embolism, or thrombophilia Lower limb paralysis
High	40-80	10-30	1-10	Major pelvic or abdominal surgery for cancer Major surgery, trauma, or illness with previous pulmonary embolism, deep vein thrombosis, or thrombophilia

serious trauma or illness or are having major surgery—should be given prophylaxis. Early mobilisation and graduated compression stockings are effective, and antiplatelet drugs such as aspirin provide additional protection.

Pneumatic compression devices have been proved effective when used perioperatively and in some groups of medical patients. Low dose unfractionated heparin (5000 units two hours before surgery and 8-12 hourly postoperatively) given by subcutaneous injection reduces the rate of postoperative thromboembolism in general surgical patients by 65%, with little increase in the risk of serious bleeding. Low molecular weight heparins are effective and have some advantages over unfractionated heparin, particularly in high risk patients such as those having hip replacement.

Treatment

Treatment is aimed at reducing symptoms and preventing complications. Elevation of the leg with some flexion at the knee helps reduce swelling, early mobilisation is beneficial, and use of graded compression stockings achieves a 60% reduction in post-thrombotic syndrome.

It is important to establish effective anticoagulation rapidly. Patients are usually given an initial intravenous heparin bolus of 5000 units followed by unfractionated or low molecular weight heparin for at least five days. With unfractionated heparin an intravenous constant infusion and subcutaneous injection twice daily are equally effective. A heparin algorithm should be used to adjust the dose. The activated partial thromboplastin time should be checked six hourly until the target is reached and then daily to maintain the international normalised ratio at 1.5-2.5. The platelet count should be checked at the start of treatment and on day 5 to exclude thrombocytopenia. Warfarin should be started on day 1, with the dose determined by a warfarin algorithm. The target ratio is 2-3, and heparin can be stopped when the target ratio is maintained for more than 24 hours.

Patients with deep vein thrombosis who do not need to be in hospital (around 35%) can be treated with subcutaneous low molecular weight heparin in the community. This can be administered subcutaneously once or twice daily. Low molecular weight heparin has the advantages of a slightly lower rate of haemorrhage and thrombocytopenia and more reliable absorption after injection, and anticoagulation monitoring is not required routinely. Warfarin should be started on day 1, and the duration of treatment guided by the risk profile.

Other approaches

Inferior vena cava filters reduce the rate of pulmonary embolism but have no effect on the other complications of deep



Pneumatic compression devices

Duration of anticoagulation in patients with deep vein thrombosis

- Transient cause and no other risk factors: 3 months
- Idiopathic: 3-6 months
- Ongoing risk—for example, malignancy: 6-12 months
- Recurrent pulmonary embolism or deep vein thrombosis: 6-12 months
- Patients with high risk of recurrent thrombosis exceeding risk of anticoagulation: indefinite duration (subject to review)

Indications for insertion of an inferior vena cava filter

- Pulmonary embolism with contraindication to anticoagulation
 - Recurrent pulmonary embolism despite adequate anticoagulation
- Controversial indications:*
- Deep vein thrombosis with contraindication to anticoagulation
 - Deep vein thrombosis in patients with pre-existing pulmonary hypertension
 - Free floating thrombus in proximal vein
 - Failure of existing filter device
 - Post pulmonary embolectomy



Vena cavagram showing umbrella delivery device inserted into the inferior vena cava through the jugular vein. The filter has been released just below the renal veins. Inferior vena cava filters help prevent pulmonary embolism but not other complications of deep vein thrombosis, including recurrent thrombosis

vein thrombosis. Thrombolysis should be considered in patients with major proximal vein thrombosis and threatened venous infarction. Surgical embolectomy is restricted to life threatening proximal thrombosis where all else has failed.

Pregnancy

Anticoagulating doses of heparin are given for deep vein thrombosis in pregnancy. It is essential to confirm the presence of a thrombus objectively. This is usually done by compression ultrasonography (serially if necessary).

Unfractionated heparin or low molecular weight heparin (which has a better risk profile but is not licensed in United Kingdom for this indication) should then be continued throughout the pregnancy and stopped temporarily before delivery. Anticoagulation should be restarted in the puerperium and continued for six weeks to three months. Warfarin is usually contraindicated during pregnancy because it is teratogenic and increases risk of maternal and fetal haemorrhage perinatally. It can be restarted 48 hours after delivery.

Further reading and useful references

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Deep vein thrombosis in pregnancy and puerperium and in women taking contraceptive pill or hormone replacement therapy

- Normal pregnancy is a hypercoagulable state
- Deep vein thrombosis occurs antepartum in 0.6/1000 women aged < 35 years and 1.2/1000 women > 35 and postpartum in 0.3/1000 and 0.7/1000 respectively
- Age, operative delivery, personal or family history, and thrombophilia are particular risks
- Heparin does not cross the placenta and is not secreted in breast milk
- Prolonged heparin therapy raises concerns about osteoporosis, heparin-induced thrombocytopenia, and allergy
- The combined contraceptive pill increases the relative risk of deep vein thrombosis by 3-4 times
- Hormone replacement therapy also increases the relative risk of deep vein thrombosis by 3-4 times but is associated with a 10 fold higher absolute risk because of the older age group

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The ABC of arterial and venous disease is edited by Richard Donnelly, professor of vascular medicine, University of Nottingham and Southern Derbyshire Acute Hospitals NHS Trust (richard.donnelly@nottingham.ac.uk) and Nick J M London, professor of surgery, University of Leicester, Leicester (sms16@leicester.ac.uk). It will be published as a book later this year.

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A book that changed me Understanding today's Joads

Like all great books *The Grapes of Wrath* by John Steinbeck absorbs and entertains but also alters your perspective on life. Its principal theme is intolerance; its uncomfortable lesson is that prejudice lies beneath the surface of us all; its optimistic conclusion is the courage of the human spirit and the kernel of good that remains when all else is stripped away. The poetic style and vernacular dialogue take time at first, but once it hooks you it won't let go.

It is the story of the Joad family. They are Oklahoma farmers whose lives are ruined by the Dust Bowl of the 1930s; forced from their land and fuelled by the American Dream of opportunity they travel west to California. They endure dreadful hardship on the way, and when they arrive their optimistic hopes and dreams are shattered by the hostility they encounter.

Steinbeck's greatest skill is showing us how the Joads engender this hostility, prickling our own innate prejudices. They are crude, crassly naive, violent, and hypocritical—they seem unable to make the link that they are being driven from the land as their forefathers drove the native Indians from it. Yet once you get to know them, feel the pathos of their humanity, and share their experience you become so deeply attached that you are appalled not only at the treatment they receive but also at your own initial prejudicial reaction.

I have just reread the book after 20 years, and its relevance persists. The homeless, the travellers in their caravans next to our busy dual carriageways, the asylum seekers and refugees in Dover

bedsits or imprisoned in detention centres—these are all today's Joads.

Throughout the novel Steinbeck parodies faith that has no moral depth; he uses many biblical themes and images, and some passages of the book are written in a quasiscriptural tone. The Bible developed out of a collective human need to give life context, meaning, and a moral structure, but Steinbeck suggests that this message has been lost along with its contemporary relevance. In a secular, multicultural age *The Grapes of Wrath* shows us that storytelling remains (second only to life itself) the pre-eminent form in teaching us about ourselves and our world. It is a book that teaches empathy, compassion, and tolerance, but perhaps its greatest lesson is that these things need to be taught, and constantly retaught, to us all.

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We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.