INTRODUCTION

Chronic venous insufficiency (CVI) of the legs is a condition characterised by ambulatory venous hypertension, involving either the superficial venous system or both the deep and superficial systems, and invariably associated with skin changes within the lower leg, leading to venous ulceration.

Chronic venous disease of the lower limbs is one of the most common conditions affecting humankind, with a prevalence of 30-50%, if varicose veins are included. CVI affects approximately 5%, and chronic leg ulcer approximately 1% of the adult population of developed countries. Characterised by chronicity and relapse, it gives rise to massive healthcare expenditure amounting, in the UK, to around £400 million per annum (1990-91 prices), and consumes 1.5-2.0% of the healthcare budgets of European countries.

The diagnosis of CVI is usually clear from the history and clinical examination, and can be confirmed by simple non-invasive testing with Duplex ultrasound. Doppler examination can also confirm the presence of arterial insufficiency in the lower limbs which, if significantly reduced, can influence treatment choice. Although drug treatment can have beneficial effects in CVI, compression therapy is the mainstay of treatment in this condition. The majority of patients will also benefit from superficial venous surgery.

CLINICAL PRESENTATION OF CVI

Varicose veins are the most common feature in CVI. These may range from a submalleolar venous flare to various degrees of vessel dilatation. Progressive skin changes occur and include a reddish brown discoloration particularly over the skin at the medial ankle (Figure 1). In more advanced cases the skin may have small erosions with weeping and excoriations due to scratching. There may be crusting which can be aggravated by sensitisation to applied topical medications. With sufficient chronicity, patients may develop lipodermatosclerosis, a fibrosing panniculitis of the leg. This can be felt as a firm induration at the medial ankle, and in the most advanced cases found to extend circumferentially up to the mid calf (Figure 2). The skin overlying the panniculitis is heavily pigmented and bound down to the subcutaneous tissues. Fibrosis may be so extensive and constrictive as to girdle the lower third of the leg resulting in a brawny oedema above the fibrosis and on the foot below. These advanced changes resemble an inverted champagne bottle. Within the areas of heavy pigmentation are 2-5mm macules of depigmentation, atrophic blanche which represent avascular, fibrotic skin and are thought to predispose to ulcer formation (Figure 2). Venous ulcers tend to occur on the medial ankle, in the area of lipodermatosclerosis. They may be single or multiple, and are typically tender, shallow, and have a red base that may be exudative. The borders are irregular and not undermined, but if left unattended, the ulcers may extend to cover the entire circumference (Figure 3).

AETIOLOGY OF CVI

New guidelines for the classification and grading of CVI were published in 1996, based on Clinical, aEtiological, Anatomical, and Pathophysiological data (the CEAP system). This system attempts to provide an organised categorisation of the key elements of the venous abnormalities, and to clarify the interrelationships among the clinical manifestations.

Table 1 provides a general classification of CVI, based on its aetiology. The development of the signs and symptoms of CVI of the lower extremity is most commonly the result of deep venous valvular reflux (80-90% of cases). Deep venous reflux occurs in most instances as a result of previous deep venous thrombosis with subsequent recanalisation, vein.
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Figure 3 Extensive venous ulceration, associated with severe CVI

inflammation, and valve scarring and destruction. Primary valvular incompetence unrelated to the sequel of DVT can also produce significant deep venous reflux and its complications. In this form, venous valves may be elongated, redundant, or lacking the structural integrity necessary to maintain valve function. The complications of CVI can also occur as a result of abnormalities in the superficial venous system alone. This is relatively uncommon and accounts for 10-20% of cases; it is generally secondary to long or short saphenous vein valve incompetence. Symptoms in these circumstances are often improved with ablation or stripping of the superficial vein. The consequences of deep venous incompetence (post phlebitic syndrome) are generally more devastating and difficult to manage.

Chronic venous obstruction occurs when veins fail to recanalise after DVT. This accounts for approximately 10% of cases of CVI. Proximal (iliac or femoral) vein thrombosis producing chronic obstruction can be managed surgically with venous bypass. Diffuse thrombosis involving several areas of the lower extremity can be very difficult to treat satisfactorily if significant symptoms occur. As many as 85% of patients with acute iliofemoral thrombosis develop venous ulceration within 10 years of the event.

PATHOPHYSIOLOGY OF CVI

Whatever the cause of venous insufficiency, the end result is venous hypertension. The normal pressure in the superficial leg veins during exercise is maintained between 20 and 30 mmHg by the action of the calf-muscle pump and competent venous valves, but progressively increases to 60 to 90 mmHg in the presence of valvular incompetence or venous obstruction. The deleterious effect of venous hypertension in CVI is aggravated by loss of the normal reflex constriction of the precapillary arterioles during standing, which helps to protect the capillary bed from surges in hydrostatic pressure. In these patients, exaggerated pressures are transmitted directly to the capillary network of the skin.

Sustained hypertension at the capillary level is associated with many morphological changes including elongation and dilatation of the capillary bed, increased surface area of the endothelium, increased type IV collagen in the basement membrane, and the formation of a pericapillary fibrin cuff. These abnormal capillaries are more permeable to large molecules, including fibrinogen, and it is hypothesised that leaked fibrinogen is converted to fibrin in the pericapillary space. Other studies have shown that the fibrinolytic activity of blood and tissues in patients with lipodermatosclerosis, results in a decreased clearance of fibrin. Although the functional significance of pericapillary fibrin is unclear, studies in patients with lipodermatosclerosis have documented diminished cutaneous oxygenation, which improves with the administration of oxygen, suggesting that a diffusion barrier, rather than deficient transport, is responsible for low oxygen tissue pressure.

Other changes in the microcirculation include fragmentation and obliteration of the cutaneous lymphatic network and decreased lymphatic flow. These changes appear to be correlated with the severity of the venous hypertension, and may contribute to the local oedema and inflammation associated with CVI.

Rheological disorders have also been associated with venous hypertension. Low shear stresses are associated with erythrocyte aggregation, and the lowest shear stresses are found in association with the highest venous pressures. Erythrocyte aggregation reduces oxygen transport capacity, slows arteriolar circulation, and enlarges the capillary spaces. Leucocytes also aggregate in capillary beds with low shear stresses and may activate, releasing proteolytic enzymes, resulting in increased capillary permeability and local inflammatory changes.

EPIDEMIOLOGY AND NATURAL HISTORY

The prevalence of oedema, trophic skin changes, or ulceration has been observed in 2% of the population. A number of cross-sectional studies have estimated the prevalence of active venous ulcers in the community to be between 0.06% and 1%. These studies have confirmed that
leg ulcers are slightly more common in women, particularly in the older age groups, and there is a marked increase with advancing age. Venous ulcers are chronic and recurrent; up to 50% of ulcers may be present for seven to nine months, between 8% and 34% may be present for more than five years, and between 67% and 75% of patients have recurrent ulcers. Table 2 lists the risk factors known to be associated with CVI.

The association of deep venous thrombosis with chronic leg oedema, pigmentation, and ulceration is well established as the 'postphlebitic syndrome'. Several prospective studies have examined the relationship between DVT and the development of CVI. These studies report the occurrence of oedema in about two thirds of patients, skin pigmentation in one third, and venous ulceration in about 4%. Trophic skin changes tend to occur between two and four years after the diagnosis of DVT, with no further changes between five and twelve years. The risk of trophic skin changes appears to be greatest with proximal thrombosis, as compared with distal thrombosis, and deep, or deep and superficial thrombosis, as compared with superficial thrombosis alone.

Despite its well-recognised association, the attributable risk of DVT for CVI cannot be calculated owing to lack of suitable controlled, prospective studies. There is some evidence suggesting that conditions other than DVT may produce CVI. In some studies fewer than one third of patients have a history compatible with DVT or phlebitis, and in others, no more than 50% of patients with CVI have post-thrombotic changes noted on venography. In addition, up to 40% of patients with DVT will develop signs of CVI in the opposite, uninvolved limb. Other conditions that may be important in the development of CVI include previous leg injury or surgery, primary valve or venous wall degeneration, congenital absence of valves, and arteriovenous shunts.

**INVESTIGATION OF CVI**

Investigation serves to confirm the diagnosis of CVI, to ascertain its aetiology (reflux or obstruction), and to localise the anatomical site and level of disease.

There are a number of functional and imaging techniques available to investigate this condition. Photoplethysmography and air plethysmography involve the use of light and air to estimate the blood flow and volume changes in the veins of the lower extremities. These tests can provide haemodynamic measurements that approximate to those made by direct venous pressure measurement. Nevertheless, Duplex ultrasonography is regarded as the method of choice because it is accurate, reproducible, and non-invasive. Duplex ultrasound consists of realtime B-mode imaging of the deep and superficial veins combined with directional pulsed Doppler assessment of blood flow. In B-mode imaging, a real-time scanner rapidly and automatically sweeps the ultrasound beam over the area to be imaged and constructs an image from the returned signals and allows for detection of movement in the structures imaged. In contrast the directional pulsed Doppler transducers detect relative motion between the source of the signal and the reflector of the signal.

In peripheral vascular studies, the sources of the reflected signals are red blood cells moving in the vessels, and flow analysis can be performed by listening to the audible signal or by recording the spectral analysis of the signal. A computer analysis of the spectral display can determine flow velocity, direction, and characteristics of flow (laminar or turbulent). Combining real-time, B-mode ultrasound with directional pulsed Doppler can provide complementary information regarding anatomical structures and blood flow patterns.

A number of studies have demonstrated the accuracy of B-mode ultrasound or duplex scanning in the diagnosis of DVT. As compared with venography, sensitivity ranges from 86% to 96%, and specificity from 80% to 100%, with most errors occurring in the calf veins. In the diagnosis of DVT there is an absence of spontaneous venous flow, and absent phasicity of flow with respiration (92% sensitivity and 92% specificity). B-mode ultrasound also has the advantage of visualising other anatomical structures in the leg that can produce pain or swelling and mimic venous disease, such as ruptured Baker's cyst, soft tissue haematoma, popliteal aneurysm, and soft tissue masses.

In the diagnosis of venous reflux, duplex scanning has been shown to be superior to descending venography in correlating with the degree of venous reflux as measured by foot volumetry and with the clinical severity of disease as determined by clinical examination. Duplex scanning is 84% sensitive and 88% specific in the diagnosis of deep venous insufficiency as compared with direct venous pressure measurements and venous filling times.

It is important to assess patients for arterial disease when evaluating patients with leg ulcers. A useful screening test is the ankle to brachial blood pressure ratio (the ankle/brachial index or ABI) as measured by Doppler ultrasound. An ABI of 0.9 or higher is normal; in patients with intermittent claudication related to arterial insufficiency the ABI is usually 0.5 to 0.9; and in patients with critical ischaemia associated with rest pain the ABI is usually less than 0.5. Concomitant arterial disease is common in patients with venous ulcers. In one study of 600 patients with leg ulcers, 11% had no palpable ankle or foot pulses, 21% had an ABI of less than 0.9, and 10% had an ABI of less than 0.7. Arterial insufficiency was more likely in older patients, and in those with a history of ischaemic heart disease or cerebrovascular disease, or if the ulcer was on the foot rather than the ankle or leg. Diagnosing arterial insufficiency will allow essential revascularisation to be carried out and will avoid complications due to inappropriate compression therapy.

**TREATMENT OF CVI**

The aims of treatment in patients with CVI include: reduction of oedema, elimination of lipodermatosclerosis, and healing of ulcers. Treatment options include mechanical therapy (eg compression), drug treatment, and surgery.

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**Table 2 Risk factors associated with CVI**

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<th>Risk Factor</th>
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<tr>
<td>Gender (female)</td>
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<tr>
<td>Age (old)</td>
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<tr>
<td>Family history</td>
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<tr>
<td>History of DVT</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
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<tr>
<td>Obesity</td>
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<tr>
<td>Occupation (involving long hours of standing)</td>
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<tr>
<td>Cigarette smoking</td>
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<tr>
<td>Varicose veins</td>
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</table>
Clinical Focus: Venous Disease

Over recent years, manufacturers have come up with more cosmetically acceptable hosiery, and a number of innovations have been developed to improve compression stockings compliance, which is a major problem, often related to cosmesis, poor fitting, or reduced patient mobility. Among these innovations are stockings with zippered backs; and leggings with a gradient (class III and IV). Despite the proven effectiveness of compression stockings in improving venous ambulatory pressures in patients with CVI, other animal and clinical studies have demonstrated that compression also improves the cutaneous microcirculation, as well as lymphatic flow. Compression therapy has also been shown to enhance fibrinolysis, and it may be an important mechanism in reducing fibrosis and promoting ulcer healing.

Cohort studies have suggested that ulcer healing rate, rate of recurrence, and time to first recurrence are significantly improved in patients compliant with compression therapy. To be effective, compression stockings must be capable of exerting 20-30 mmHg of pressure at the ankle and less at the knee. For most patients, knee-high stockings are sufficient; thigh-high stockings are less desirable due to impediment of venous flow at the popliteal space with knee bending. Table 4 shows the compression stocking pressure gradients used in chronic venous and lymphatic disorders and their indications for use. In CVI, at least a class II compression is required, although severe CVI will require an increased pressure gradient (class III and IV). Despite the proven effectiveness of compression stockings, compliance is a major problem, often related to cosmesis, poor fitting, or reduced patient mobility. Over recent years, manufacturers have come up with more cosmetically acceptable hosiery, and a number of innovations have been introduced to accommodate patients with reduced strength and mobility; including stockings with zippered backs; and leggings with a series of interlocking bands fastened with Velcro.

In patients with massive oedema or obesity, standard compression stockings may be ineffective. An alternative approach is the use of intermittent pneumatic compression (IPC) pumps. These devices consist of plastic air chambers that encircle the lower leg; periodically the air chamber fills to a preset pressure, compressing the leg, and then deflates. IPC pumps may consist of a single chamber or multiple chambers that inflate sequentially from the foot to the knee. IPC pumps have been shown to be effective in the prevention of postoperative DVT, and superior to compression stockings in the healing of venous ulcers. They are contraindicated in arterial insufficiency and uncompensated congestive cardiac failure.

The use of medicated compression bandages in the treatment of CVI was first described in 1854 by Unna. Contemporary ‘Unna boots’ are roll bandages impregnated with a uniformly-spread paste of zinc oxide, calamine lotion, glycerine, and gelatin. Used in a three- or four-layered compression bandage, they can be effective in healing venous ulcers, but have the disadvantage of pressure variability that depends on the person who applies them. Over recent years, results with this type of compression have been improved by the specific training of nursing staff in this technique, both in hospital and in the community. A recent randomised controlled trial of four-layered bandaging showed that this technique carried out in community-based leg ulcer clinics is more cost-effective than traditional home-based district nurse treatment.

**MECHANICAL THERAPY**

Simple elevation of the legs above heart level for 30 minutes three or four times per day is effective in reducing oedema and improving the cutaneous microcirculation in patients with CVI. In more advanced disease, leg elevation alone will not be sufficient, and compression stockings will be required. It is not clear how compression stockings produce their beneficial effects. Many, but not all, studies of graduated compression stockings demonstrate diminished venous reflux, increased blood flow velocity in the deep veins, and improved venous ambulatory pressures in patients with CVI. Other animal and clinical studies have demonstrated that compression also improves the cutaneous microcirculation, as well as lymphatic flow. Compression therapy has also been shown to enhance fibrinolysis, and it may be an important mechanism in reducing fibrosis and promoting ulcer healing.

**DRUG TREATMENT IN CVI**

Diuretics may occasionally have a role in the treatment of CVI, but their use should be restricted to a short period of time in patients with severe oedema. In the treatment of ulcers, the use of topical antibiotics, in the absence of clinical infection, does not appear to be useful and may be harmful owing to the increased susceptibility of contact dermatitis patients with CVI and emergence of resistant organisms. Routine administration of systemic antibiotics has not been shown to improve ulcer healing rate, and should be reserved for ulcers that are obviously infected, or are complicated by cellulitis.

Topical antiseptics, including hydrogen peroxide, povidone-iodine, acetic acid, and sodium hypochlorite, have all been shown to have cellular toxicities that exceed their bactericidal activities, and all except hydrogen peroxide have been found to impair wound epithelialisation, and are not recommended.

Silver sulphadiazine has been used to promote wound healing in burns, but has not been found to confer much benefit in the healing of venous ulcers, compared with standard occlusive or nonadherent dressings, and has a tendency to cause local skin reactions.

Enzyme debriding agents, krill enzymes, platelet-derived growth factor, epidermal growth factor, and fibroblast growth factor have all been used with some effect in the treatment of venous ulcers, but compelling evidence for their routine use, in randomised controlled studies, is lacking.

Other drugs with potential usefulness either enhance fibrinolysis or improve venomotor tone and capillary flow. For most patients, knee-high stockings are sufficient; thigh-high stockings are less desirable due to impediment of venous flow at the popliteal space with knee bending. Table 4 shows the compression stocking pressure gradients used in chronic venous and lymphatic disorders and their indications for use. In CVI, at least a class II compression is required, although severe CVI will require an increased pressure gradient (class III and IV). Despite the proven effectiveness of compression stockings, compliance is a major problem, often related to cosmesis, poor fitting, or reduced patient mobility. Over recent years, manufacturers have come up with more cosmetically acceptable hosiery, and a number of innovations have been introduced to accommodate patients with reduced strength and mobility; including stockings with zippered backs; and leggings with a series of interlocking bands fastened with Velcro.

<table>
<thead>
<tr>
<th>COMPRESSION CLASS</th>
<th>PRESSURE GRADIENT</th>
<th>INDICATIONS FOR USE</th>
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<tbody>
<tr>
<td>I</td>
<td>20-30 mmHg</td>
<td>mild venous insufficiency without oedema, mild varicose veins, varicosis during pregnancy</td>
</tr>
<tr>
<td>II</td>
<td>30-40 mmHg</td>
<td>marked varicose veins including pregnancy moderate oedema, thrombophlebitis minor venous ulceration, mild CVI post-sclerotherapy, post-varicose vein surgery</td>
</tr>
<tr>
<td>III</td>
<td>40-50 mmHg</td>
<td>severe CVI, post-thrombotic syndrome severe oedema, venous ulceration, lymphoedema</td>
</tr>
<tr>
<td>IV</td>
<td>50-60 mmHg</td>
<td>very severe CVI, severe lymphoedema</td>
</tr>
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*Table 4 Compression stocking pressure gradient and indications for use.*
integrity. Stanazole, an anabolic steroid, stimulates blood fibrinolysis and has been compared with placebo in the healing of lipodermatosclerosis. Although the healing rate was twice that of the placebo, the results did not reach statistical significance. Oxpentifylline (Trental), a cytokine antagonist with profibrinolytic activity, has been found effective in ulcer healing in one small study. However, adverse effects from the drug may include oedema, depression, vomiting, dyspepsia and diarrhoea.

Horse-chestnut seed extract stimulates the release of prostaglandins from the F series which mediate veno­statin and integrity. Stanazole, an anabolic steroid, stimulates blood fibrinolysis and has been compared with placebo in the healing of lipodermatosclerosis. Although the healing rate was twice that of the placebo, the results did not reach statistical significance. Oxpentifylline (Trental), a cytokine antagonist with profibrinolytic activity, has been found effective in ulcer healing in one small study. However, adverse effects from the drug may include oedema, depression, vomiting, dyspepsia and diarrhoea.

Hydroxyethylrutosides are a mixture of semisynthetic flavinoids that act on the microvascular endothelium to reduce permeability. In placebo-controlled trials they have been shown to reduce leg volume and circumference, and afford a greater relief from pain, night cramps and restless legs. In the treatment of venous ulcers, however, results have been equivocal.

Recently a randomised, placebo-controlled, double-blind trial has demonstrated that enteric-coated aspirin, 300mg daily, reduces ulcer size and accelerates ulcer healing compared with placebo.

SURGERY IN CVI

Surgical management is most often reserved for severe or medically refractory CVI. Venous stripping, perforator ligation, and valvular reconstruction are the major surgical techniques used in CVI treatment. Surgery is thought to produce beneficial effects by reducing venous reflux from the deep to the superficial veins and thereby modifying the effects of venous hypertension on cutaneous tissues. In patients with isolated superficial venous insufficiency, stripping of the incompetent superficial varicose veins may be curative. In contrast, patients with valvular incompetence due to deep vein obstruction may not benefit from this procedure. For these patients, ligation of the perforating or communicating veins from knee to ankle, described by Cockett and Dodd in Britain and Linton in the USA, was a popular surgical procedure in the 1940s and 1950s but fell out of favour by the mid 1980s because of poor cosmesis, problems with wound healing, and a high recurrence rate (50% at five years). The technique has been reinvented in recent years in the form of a minimally invasive laparoscopic procedure: subfascial endoscopic perforator ligation, which has much less morbidity compared with Cockett and Linton procedures. Over 50% of patients with venous ulcers will benefit from superficial venous surgery. Valvular reconstruction and venous valve transplantation from the upper extremities to the lower extremities are surgical options available currently under investigation for patients with deep venous disease.

Split thickness skin grafting can be successful in covering venous ulcers, and may be performed at the same time as the perforator ligation or follow as a separate procedure. Wide excision of the ulcer bed and surrounding tissues, followed by free flap transfer to close the defect has been shown to be cost effective compared with local wound care.

SUMMARY

Chronic venous insufficiency is a common problem in the primary care setting and is associated with significant morbidity and healthcare costs. Patients may be relatively asymptomatic with only minor cosmetic concerns, or may be plagued with leg aching, heaviness, and cramping associated with oedema, chronic eczema, pigmentation, fibrosis, and ulceration. The single most helpful confirmatory test is Duplex ultrasound. In those with leg ulcers, determination of the ABI by Doppler ultrasound can assess the presence and severity of arterial insufficiency. Leg elevation and compression is the mainstay of treatment, although compliance is a major problem. In recalcitrant cases intermittent pneumatic compression may be helpful. There is no clear advantage among the various ulcer dressings, although patients may prefer hydrocolloid occlusive dressings because of their convenience. Antibiotics, used systemically, should be reserved for patients with heavily infected ulcers and cellulitis. topical antibiotics and antiseptics are not recommended. A number of drug treatments are available but few offer any clear advantages. Recombinant growth factors and Hydroxyethylrutosides show promise but are as yet unproven. Aspirin has a beneficial effect on ulcer healing. A large proportion of patients will benefit from superficial venous surgery.

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A full list of references relating to the text is available on request from Mr P Wilson, Department of Surgery, Royal Lancaster Infirmary.