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Chronic Venous Insufficiency, Varicose Veins, Lymphedema, and Arteriovenous Fistulas

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Chronic Venous Insufficiency

Chronic venous insufficiency (CVI) may be defined as symptom or signs of ambulatory venous hypertension. In developed countries, CVI affects up to half of the adult population. Furthermore, the treatment of CVI consumes up to 2% of total health spending and is a major cause of lost economic productivity. These startling data, coupled with the ineffectiveness of current treatment modalities in many of the most severely affected patients, underscore the need for more research.

Classification

Chronic venous insufficiency has proved difficult to classify for the purposes of scientific reporting. This has obfuscated attempts to directly compare the findings of different epidemiological, pathophysiological, and clinical studies. The clinical, etiological, anatomical, and pathophysiological (CEAP) classification, proposed in 1994 by the American Venous Forum, is now the most widely accepted system (Table 10.1).

Epidemiology

In industrialized countries the lifetime risks of developing varicose veins (VVs), skin changes (corona phlebectatica, lipodermatosclerosis, varicose eczema, atrophie blanche), and chronic venous ulceration (CVU) are 30% to 50%, 5% to 10%, and 1% to 2%, respectively. The bulk of advanced disease affects the elderly, with up to 5% of women over the age of 65 years having a history of CVU. However, up to 50% of affected patients, especially men, develop their ulcer before their 50th birthday. Women often relate the development of VVs to pregnancy and childbirth. The increase in female sex hormones and blood volume during the first trimester may be responsible. However, there is little evidence of an association with (multi)parity, and men and women appear to be affected almost equally by CVI. The excess of women observed in clinical practice is mainly due to their longevity and the reluctance of men to seek medical attention. There is no clear evidence that low socioeconomic class predisposes to CVI, although CVU healing and recurrence rates may be worse. Clinical experience suggests that occupations involving prolonged standing are associated with an increased prevalence and severity of CVI, poor ulcer healing, and increased recurrence rates. Data on the relationships between physical activity and CVI are conflicting, but it seems reasonable to assume that an individual with a well-developed calf muscle pump is less likely to develop CVI. Although a consistent relationship between weight and height is lacking, VVs appear to be commoner in tall men and CVU in obese women. Similarly, there is growing evidence of a hereditary predisposition to CVI. For example, patients whose parents both have VVs have a 90% chance of developing

Table 10.1. Clinical, etiological, anatomic, and pathophysiological (CEAP) classification

Clinical[1]	
Class 0	No visible or palpable signs of venous disease
Class 1	Telangiectasia[2] or reticular veins[3]
Class 2	Varicose veins[4]
Class 3	Edema
Class 4	Skin changes (lipodermatosclerosis, atrophie blanche, eczema)
Class 5	Healed ulceration
Class 6	Active ulceration
Etiological	
E_C	Congenital (may be present at birth or recognized later)
E_P	Primary (with undetermined cause)
E_S	Secondary (with known cause): postthrombotic, posttraumatic, other
Anatomical	
A_S	Superficial veins (numbered 1 to 5)[5]
A_D	Deep veins (numbered 6 to 16)[6]
A_P	Perforating veins (numbered 17 and 18)
Pathophysiological	
P_R	Reflux
P_O	Obstruction
$P_{R,O}$	Both

[1] Supplemented with (A) for asymptomatic or (S) for symptomatic, e.g., $C_{6,A}$.
[2] Intradermal venules up to 1 mm in diameter.
[3] Subdermal, nonpalpable venules up to 4 mm.
[4] Palpable subdermal veins usually larger than 4 mm.
[5] Telangiectasia/reticular veins (1); greater (long) saphenous vein above (2) below (3) knee; lesser (short) saphenous vein (4); nonsaphenous (5).
[6] Inferior vena cava (6); common (7), internal (8), external (9) iliac; pelvic (10); common (11), deep (12), superficial (13) femoral; popliteal (14); crural (15); muscular (16).

VVs, and CVU patients have a higher prevalence of inherited thrombophilia (TP). The influence of race and ethnicity is unclear, as there are few reliable data from nonwhite populations.

Normal Venous Function

Venous blood from the lower limbs returns to the right heart against gravity through the deep and superficial venous systems. The deep veins follow the named arteries and are often paired. The superficial system comprises the long saphenous vein (LSV) and short saphenous vein (SSV) and their tributaries. As there are numerous communications between the long and short saphenous systems, and between the superficial and deep systems through junctional and nonjunctional perforators, these three elements are highly interdependent, both anatomically and functionally, in health and in disease. Most of the blood draining into the superficial veins from skin and subcutaneous tissues immediately enters the deep venous system via perforators in the foot, calf, and thigh. In healthy subjects, less that 10% of the total venous return from the lower limb passes through the LSV and SSV to the saphenofemoral junction (SFJ) and saphenopopliteal junction (SPJ), respectively. Blood is forced back up the leg during leg muscle systole, and prevented from flowing back down the leg under the influence of gravity during diastole, through the actions of the muscle pumps and closure of venous valves, respectively. The act of walking sequentially compresses venous sinuses in the sole of the foot, the calf (soleus, gastrocnemius), and to a lesser extent the thigh and buttock. During relaxation these sinuses fill from the deep and superficial venous systems and valves close in the superficial and axial veins to prevent reverse flow (reflux). In both the superficial and deep systems, the density of valves is greatest in the calf and gradually diminishes in the thigh. The iliac veins and inferior vena cava are frequently devoid of valves.

When standing completely motionless, with all the leg muscles relaxed, the venous valve leaflets come to lie in a neutral midposition. As a result, the venous pressure in the dorsal foot veins comes to represent the hydrostatic pressure exerted by the unbroken column of venous blood stretching up from the foot to the right atrium (approximately 90 to 100 mm Hg in a person of average height). Contraction of the leg muscles immediately leads to the compression of deep veins and sinuses and to the movement of venous blood cranially. Retrograde blood flow is terminated by valve closure, and perforators that allow unidirectional flow from the superficial to the deep venous system only. Conventionally, this has also been ascribed to the closure of valves within the perforators. However, several studies have shown that many perforators are devoid of valves. Instead, outward flow through perforators may be

limited by external compression from contracting muscle and a pinch-cock mechanism involving the deep fascia. The importance of these mechanisms is that the very high pressures (up to 200 mm Hg) generated within the calf muscle pump are used exclusively to propel blood back up the leg against gravity, and are not transmitted to the superficial or distal deep systems. When the muscle pump relaxes, the previously expelled venous blood tends to flow caudally under gravity but is prevented from doing so by valve closure. This has the effect of dividing a single long (and heavy) column of blood into a series of shorter columns lying between closed valves. The pressure within each of these segments is low and the ambulatory venous pressure (AVP) in the dorsal foot veins falls typically to <25 mm Hg. During muscle pump diastole, blood in the superficial system flows in to the deep system along a pressure gradient.

Pathophysiology

There are three basic mechanisms that lead to raised AVP and the symptoms and signs of CVI: (1) muscle pump dysfunction, (2) valvular reflux, and (3) venous obstruction.

Aging, general debility, and a wide range of musculoskeletal or neurological lower limb pathologies can impair calf muscle pump function. The "fixed" ankle secondary to arthritis or trauma is a common example. Muscle bulk and tone are also important factors in the maintenance of perforator competence (see above). Failure of perforator competence leads to calf pump inefficiency (akin to mitral regurgitation), as well as the transmission of high pressures directly to the skin of the gaiter area.

Reflux is present in more than 90% of patients with CVI; 5% to 10% have isolated deep, 30% to 50% isolated superficial, and 50% to 60% combined. In general, superficial reflux has a better prognosis than deep reflux (especially when the latter is postphlebitic), and proximal reflux has a better prognosis than distal reflux. Valvular reflux can arise in two ways that are not mutually exclusive in any one patient:

Primary valvular incompetence (PVI): A loss of elastin and collagen in the vein wall around the valve commissures leads to dilatation, separation of the valve leaflets, and reflux. As the vein dilates, the tension in the wall increases according to the law of Laplace, which leads to further dilatation. The end result is an incompetent, elongated and tortuous varicose vein. Primary valvular incompetence may also affect the deep venous system.

Postthrombotic syndrome (PTS): Approximately 25% of CVU patients have a clear history of deep venous thrombosis (DVT), and many more have probably suffered a subclinical or undiagnosed thrombosis. Deep venous thrombosis leads to endothelial hypoxia, valvular destruction, and mural inflammation. Even though most DVTs recanalize, the end result is a thickened, valveless tube that permits gross reflux and poses an anatomical (narrowing, fibrous webs) and functional (lack of compliance) obstruction to venous outflow. Obstruction leads to the formation of collateral pathways. For example, blood may be forced out of the calf via perforators into the superficial venous system and thence up the leg with the formation of secondary VVs. Removal of such VVs increases AVP. Most patients with severe and intractable CVU have PTS.

Clinical Assessment

History

Inquiry should be made as to the duration of the present ulcer as well as the duration of ulcer disease, the number of episodes, and any precipitating factors (Table 10.2). Previous treatment history and contact allergies are recorded. Peripheral artery disease (20%), diabetes mellitus (5%), and rheumatoid arthritis (8%) often coexist. Malignancy must not be overlooked. Many patients with lower limb symptoms, and who coincidentally have VVs, have other pathology to explain their symptoms. Orthopedic, neurological, and arterial causes of leg symptoms must be excluded. Particular attention must be paid to a history of "white leg" of pregnancy, prolonged immobilization, phlebitis, and major lower limb fracture, any of which may suggest previous the PTS. A family history of venous disease, particularly early-onset, recurrent, or unusual thrombotic events, should be sought (Cornu-Thenard, 1994).

Table 10.2. Distinguishing features of arterial and venous ulcers

Clinical features	Arterial ulcer	Venous ulcer
Gender	Men > women	Women > men
Age	Usually presents >60 years	Typically develops at 40–60 years but patient may not present for medical attention until much older; multiple recurrences are the norm
Risk factors	Smoking, diabetes, hyperlipidemia and hypertension	Previous DVT, thrombophilia, varicose veins
Past medical history	Most have a clear history peripheral, coronary, and cerebrovascular disease	More than 20% have clear history of DVT, many more have a history suggestive of occult DVT, e.g., leg swelling after childbirth, hip/knee replacement or long bone fracture
Symptoms	Severe pain is present unless there is (diabetic) neuropathy, pain may be relieved by dependency	About a third have pain but it is not usually severe and may be relieved on elevation
Site	Normal and abnormal (diabetics) pressure areas (malleoli, heel, metatarsal heads, fifth metatarsal base)	Medial (70%), lateral (20%) or both malleoli and gaiter area
Edge	Regular, punched-out, indolent	Irregular, with neoepithelium (whiter than mature skin)
Base	Deep, green (sloughy) or black (necrotic) with no granulation tissue, may comprise major tendon, bone and joint	Pink and granulating but may be covered in yellow-green slough
Surrounding skin	Features of SLI	LDS, varicose eczema, atrophie blanche
Veins	Empty, guttering on elevation	Full, usually varicose
Swelling	Usually absent	Often present

Symptoms

Localized discomfort in the leg: Usually at the site of the visible VV, particularly after prolonged standing. Prominent varices may be tender, particularly in menstruating women.

Pain: Severe pain is unusual and suggests infection or arterial insufficiency.

Swelling: A feeling of swelling is common.

Venous claudication: This is unusual and due to extensive postthrombotic iliofemoral venous occlusion. There is bursting pain in the calf on walking, which is relieved only by elevating the leg. In addition, patients often complain of heaviness in the calf with ambulation.

Itching: This is common and may lead to scratching, infection, and ulceration.

Physical Examination

Varicose veins: Note the distribution of varices and any surgical scars.

Corona phlebectatica (ankle/malleolar flare): One of the earliest skin manifestations of CVI comprises dilated intra/subdermal veins at or just below the medial malleolus. Overlying skin is thin and fragile leading to a blue-bleb appearance. Trauma frequently leads to hemorrhage and ulceration.

Lipodermatosclerosis: The skin is brown (red or purple) and indurated due to hemosiderin and plasma protein deposition, leading to dermal fibrosis.

Atrophie blanche: Thin and pale skin due to the thrombotic obliteration of papillary capillaries; often at the site of previous ulceration.

Varicose eczema: Scaly dry (or weeping) skin that is often intensely pruritic and can demonstrate blanching erythema (mimicking cellulitis).

Edema: A common presentation in patients with CEAP class 3 or greater CVI. Chronic venous insufficiency may coexist with other diseases that cause edema, such as

congestive heart failure, and must be considered when evaluating CVI patients (Table 10.3).

Hemorrhage: Can be alarming, even life threatening, may be spontaneous or follow trauma. Direct pressure and elevation always arrest venous hemorrhage. As recurrent bleeding is almost inevitable, the patient should be hospitalized for definitive treatment.

Ulceration: Most CVUs can be easily differentiated from other forms of ulceration.

Arterial circulation: If pedal pulses are impalpable, measure the ankle–brachial index (ABI). An ABI of <0.8 mandates referral to a vascular surgeon. The ABI is unreliable in diabetic patients.

Investigations

Virtually all patients with CVI require further investigation, and duplex ultrasound (DU) has largely replaced all other modalities in routine clinical practice. It allows Doppler velocity information to be color coded and superimposed in real time upon a gray scale (B-mode) image. It determines the location and severity of reflux, the location of the SPJ and nonjunctional perforators, and whether the deep veins are patent. Plethysmography involves the assessment of venous function through the measurement of limb volume and nowadays is primarily a research tool. Photo (PPG) and air (APG) plethysmography are probably the most popular techniques. Ambulatory venous pressure is measured by cannulating and transducing a dorsal foot vein; it remains the research reference standard. Ascending venography determines the presence of residual thrombus, the extent of recanalization, and the distribution of collaterals. Contrast medium is injected into a dorsal foot vein and directed into the deep veins by the placement of an ankle tourniquet. The iliac system and the vena cava may not be visualized, in which case a separate injection can be made in the common femoral vein (CFV) (cavography). Descending venography involves injecting contrast medium into the CFV with the subject positioned at 60 degrees with the head up in order to assess reflux. Venography is largely reserved for patients being considered for deep venous reconstruction because it is superior to DU in determining the presence and extent of the PTS. Ovarian vein reflux and pelvic varices can be visualized by placing a catheter into the ovarian or internal iliac veins via the CFV approach. As well as this imaging being diagnostic, it also enables the ovarian vein to be embolized in women suffering from pelvic congestion syndrome. Ulcers that fail to heal, tend to bleed, or have unusual features should be biopsied at base and margin under local anesthesia.

Table 10.3. Etiological classification of lymphedema

Primary lymphedema	Congenita (onset <2 years old): sporadic
	Congenita (onset <2 years old): familial (Milroy's disease)
	Praecox (onset 2–35 years): sporadic
	Praecox (onset 2–35 years): familial (Meige's disease)
	Tarda (onset after 35 years of age)
Secondary lymphedema	Bacterial infection
	Parasitic infection (filariasis)
	Fungal infection (tinea pedis)
	Exposure to foreign-body material (silica particles)
	Primary lymphatic malignancy
	Metastatic spread to lymph nodes
	Radiotherapy to lymph nodes
	Surgical excision of lymph nodes
	Trauma (particularly degloving injuries)
	Superficial thrombophlebitis
	Deep venous thrombosis

Nonsurgical Management

The mainstay of treatment is compression with or without superficial venous surgery in the great majority of patients who have CVI due to reflux. A small minority of patients who have deep venous obstruction may benefit from surgical or endovascular reconstruction. There is considerable controversy over the role of sclerotherapy.

Dressings

No particular dressing or topical agent has been shown unequivocally to significantly

hasten CVU healing. However, they do have different physical properties, and the surgeon needs to have a basic grasp of the underlying science (and art) of wound care. Enzymatic agents (e.g., streptokinase-streptodornase) undoubtedly digest the constituents of slough. However, they are relatively ineffective against deep necrosis or hard eschar. There is evidence that they speed up healing, and may damage the wound environment. Hydrocolloid dressings come in many forms, and are generally impermeable to gases, water vapor, and bacteria. They produce a moist, acidic, low-oxygen tension wound environment that has been shown experimentally to enhance wound healing. Patients like these dressings because they are easy to use, and patients can bathe with the dressing in situ. The dressings absorb exudate (reducing the frequency of dressing changes, smell, risks of cross-infection, and costs) and may provide superior pain relief. However, in randomized controlled trials where both treatment arms have received equal and adequate compression, hydrocolloid dressings have not be shown to improve overall healing compared to any other dressing. Bead dressings (such as cadexomer iodine and dextranomer) comprise hydrophilic, polysaccharide materials that absorb large amounts of fluid and slough. The former also releases iodine in to the wound. Although they may speed up desloughing, they have not been shown to enhance healing. Paste bandages comprise a plain weave cotton fabric impregnated with zinc oxide paste, either alone or with calamine, calamine and clioquinol, coal tar, or ichthammol. These additives are designed to soothe venous eczema but are actually a common cause of contract allergy, and patch testing is recommended. Paste bandages do not retain moisture, and for this reason, and to apply compression, additional layers of bandaging are required. The Unna boot is a paste bandage containing glycerin that hardens into semirigid dressing. In trials where equal amounts of compression are applied, no form of paste bandage has been shown to improve healing over other forms of dressing. Their principal benefit is provision of inelastic compression. Alginate dressings absorb exudate and create a moist wound environment but have not been proved to speed healing. Biological dressings comprising cultured human epithelium or fibroblasts may act as a source of growth factors and act as a scaffold for the patient's own epithelial cells. But they are extremely expensive and as yet unproven.

Topical Agents

Dermatitis is common and may be endogenous (varicose or venous stasis dermatitis) or exogenous due to topically applied substances (contact dermatitis). Dermatitis is extremely morbid, associated with nonhealing, and may be irritant or allergic due to cell-mediated, delayed hypersensitivity. Early patch testing is mandatory. The use of bland paraffin preparations greatly reduces the risks of dermatitis. In patients with marked exudate, zinc oxide paste can be used to protect the surrounding skin. Acute dermatitis must be treated with removal of the offending allergen and topical steroid therapy. Topical antibiotics should be avoided.

Physical Therapy

Prolonged bed rest with leg elevation will heal virtually all CVUs. However, it is logistically impossible, and associated with decubitus complications, and as it does not address the underlying hemodynamic abnormality, recurrence is virtually inevitable. Exercise therapy aimed at improving calf muscle pump function may be of benefit and trials are under way.

Compression Therapy

Compression undoubtedly retards the development and progression of CVI. However, it is still more of an art than a science, and the quality of scientific reporting remains low. Elastic bandaging (the four-layer bandage) is favored in the United Kingdom, whereas in mainland Europe and North America inelastic bandaging (the Unna boot) is preferred. The four-layer bandage comprises orthopedic wool (to protect the bony prominences and to absorb any exudates); crepe bandage (to compress and shape the wool, and to provide a firm base for the compression bandages), elastic bandage (e.g., Elset™, Seton, applied at 50% stretch) and a self-adhesive elasticated bandage (e.g., Coban™, 3M to add to compression and fix the bandaging in place). This bandage typically exerts 40 mm Hg at the ankle and 20 mm Hg just below the knee. Once the ulcer is healed, the patient should be pre-

scribed stocking. There is no evidence that extending compression above the knee confers benefit. Compliance is a major problem.

Sclerotherapy

The role of sclerotherapy is controversial, with practitioner's views based largely on professional background and country of origin rather than on clinical comparative studies. Some sclerotherapists believe they can treat all VVs, but most accept the superiority of surgery in the presence of main stem, SFJ, or SPJ incompetence. However, the advent of foam sclerosants may revolutionize the management of such disease. The aim is to place a small volume of sclerosant in the lumen of a vein empty of blood, and then appose the walls of that vein with appropriate compression. The vein then fibroses closed without the formation of clot. Some practitioners use magnifying loupes for smaller veins, and there is increasing interest in injecting larger veins under ultrasound guidance (echosclerotherapy). The vein must be kept empty of blood both during and after the injection to prevent thrombophlebitis. Adequate compression is difficult in the perineum, upper thigh, and popliteal fossa, especially in the obese. Patients should be mobilized immediately afterward. In the U.K., most surgeons use detergents that act by directly damaging the endothelium. In mainland Europe and North America, hypertonic saline is also popular. Err on the side of caution with regard to volume and concentration until the patient's response can be assessed. The complications of injection sclerotherapy include anaphylaxis (<0.1%), allergic reactions (uncommon), ulceration (extravascular injection), arterial injection (rare and serious), pigmentation (extravasation), superficial thrombophlebitis (inadequate compression), and DVT (inadequate mobilization).

Surgical Management

There is growing evidence that saphenous surgery improves the quality of life in patients with VVs, and augments the healing and reduces the recurrence of CVU better than compression alone (Dwerryhouse et al., 1999). For optimal results, it is necessary to define the extent and severity of venous disease, usually by means of DU, prior to surgery. Surgery for CVU is different from that for uncomplicated VVs in a number of important ways. The patients are older and often have multisystem, medical comorbidity; the risks, especially DVT, are higher. Patients may require inpatient optimization of cardiorespiratory function, treatment of dermatitis, edema reduction, and desloughing of the ulcer. The effect of deep venous reflux on the efficacy of superficial venous surgery is controversial and incompletely defined. Deep reflux due to PVI may reverse once superficial reflux has been eradicated. However, most agree that patients with extensive PTS gain less benefit from surgery. Secondary VVs that are acting as collaterals must not be removed. Although postoperative compression therapy has been shown to reduce VVs and CVU recurrence, compliance is poor.

Varicose Vein Surgery

Long Saphenous Surgery

Safe and effective surgery depends on observing a few sound principles. In a patient of normal build the SFJ lies directly beneath the groin crease; in the obese it lies above. An incision made below the crease is likely to be too low. Resist the temptation to operate through an excessively small incision. Do not divide any vein until the SFJ has been unequivocally identified. Unless all tributaries are taken beyond secondary branch points, a network remains of superficial veins connecting the veins of the thigh with those of the perineum, the lower abdominal wall, and the iliac region. These cross-groin connections are a frequent cause of recurrence. Ligate the LSV deep to all tributaries flush with the CFV using nonabsorbable transfixion suture to reduce neovascularization through the stump. Directly ligate, and if large, consider stripping, any high anterolateral or posteromedial or thigh branches to reduce hematoma formation and recurrence. There is evidence to show that stripping the LSV to a hand's breadth below the knee significantly reduces recurrence by disconnecting the thigh perforators and saphenous tributaries and by removing the conduit that will allow neovascularization in the groin to reconnect with the remaining superficial venous system of the thigh and calf. Confining stripping to just below the knee, and to a downward direction, reduces

saphenous nerve injury. The theoretical advantages of invagination stripping in terms of reducing blood loss, hematoma, nerve injury, and scars have not been confirmed in trials.

Short Saphenous Surgery

Saphenopopliteal junction ligation can prove to be a challenging procedure, especially when performed for recurrent disease. Always mark the junction preoperatively with DU (some surgeon still prefer venography). The SSV can be found by following the Giacomini vein, which is a superficially placed tributary of the SSV that runs up the thigh to join the LSV. This may be large and confused with the SSV, especially if the SPJ is absent; the importance of this will be apparent on the preoperative DU. Be aware that traction on the SSV can tent up and damage the mobile and thin-walled popliteal vein. Palpation of the artery gives an indication of the depth of dissection. Beware the common peroneal nerve under medial edge of biceps femoris, which is at risk from overzealous lateral retraction as well as from a careless stitch when closing the popliteal fascia. The SSV is often closely associated with sural nerve injury and is also at risk, particular if stripping is undertaken. There are still a number of controversial issues regarding the SSV. Is it always necessary to ligate the SSV flush with the popliteal vein? Experience suggests that this counsel of perfection is hard to achieve in a significant proportion of patients without risk of collateral damage. This raises the question of what should be done with the gastrocnemius and other, often large and refluxing, muscular veins? Should the SSV be stripped or is it permissible just to remove a segment through the popliteal fossa wound? It seems likely, although there is no proof, that SSV stripping, for the same reasons as for the LSV, would reduce recurrence. However, there is concern about sural nerve injury.

Perforator Ligation

Although the advent of DU-guided subfascial endoscopic perforator surgery (SEPS) has rekindled interest in perforator ligation, there is no evidence that it alters the natural history of venous disease. Clearly, the only way to resolve this issue once and for all is to perform a randomized controlled trial of compression vs. compression and saphenous surgery vs. compression, saphenous surgery, and SEPS.

Surgery for Recurrent Veins

Recurrent LSV VVs arise because of inadequate dissection of, or neovascularization at, the SFJ in the presence of a nonstripped or incompletely stripped LSV. Standard teaching is to approach the SFJ through nonoperated tissues (usually from a lateral approach that first exposes the common femoral artery) so that the CFV can be skeletonized of branches using nonabsorbable sutures for 1 to 2 cm above and below the junction. The top of the LSV is dissected from the mass of scar tissue so that it can be stripped. However, this can be a difficult and potentially morbid operation. When the preoperative DU indicates neovascularization as opposed to an intact SFJ, the LSV can be located at the knee, a stripper passed up toward the groin, and the vein stripped without a formal redissection.

Complications

Fortunately, major complications following VV surgery are relatively rare. However, up to 20% of patients may suffer some form of minor morbidity, such as hematoma, lymphatic leak, pain, saphenous neuritis, and venous thrombosis. In the U.K., VV surgery is the commonest cause of litigation against general and vascular surgeons. This not a field for the unsupervised, inexperienced surgeon and it behooves surgeons who undertake VV surgery to carefully audit their management, techniques, and outcomes.

Deep Venous Reconstruction

These procedures have not gained widespread acceptance largely because there is little data to support their efficacy. Several different techniques have been described for suturing the edges of "floppy" valve cusps to the vein wall, rendering the valve competent. Autologous valve transplantation interposes a segment of axillary or brachial vein, containing a competent valve, into an incompetent deep vein, usually the popliteal. Procedures using synthetic, mixed, and animal valves are still experimental. An incompetent superficial femoral vein can be transected and anastomosed end to end or end

to side to a profunda femoris or long saphenous vein that has a competent valve (vein transposition). An obstructed femoral segment may be bypassed by anastomosing a transected, competent LSV to the side of the popliteal vein. Again, satisfactory long-term patency rates have been reported in small series.

Conclusions

Although the most difficult cases of leg ulceration are multifactorial in origin, CVI is the single most common underlying pathology. As such, there is hope that the prevalence of CVU may decline in the future as a result of improved thromboembolic prophylaxis and treatment. For the moment, however, CVU is a common and disabling condition that is often resistant to conservative therapy, prone to recurrence, and very expensive to manage. There needs to be a low threshold for referral to a vascular surgeon, preferably through a one-stop assessment clinic where a thorough venous and arterial duplex-based assessment can be performed. This will enable patients who might benefit from surgical intervention to be identified and treated early. It will also enable ongoing outpatient treatment to be based on an in-depth understanding of the pathophysiological mechanisms responsible in each patient. Great progress in the management of CVU has been made over the last decade because of an increased understanding of the pathophysiology and the availability of data from clinical trials that have provided a scientifically robust platform on which to base treatment algorithms. Despite all this, further research is required into the epidemiology and natural history of CVU, models of care, primary prevention, and pathogenesis.

Lymphedema

The Lymphatic System

The lymphatic system performs the following functions:

1. It removes water, electrolytes, low-molecular-weight moieties (polypeptides, cytokines, growth factors), and macromolecules (fibrinogen, albumen, globulins, coagulation and fibrinolytic factors) from the interstitial fluid (ISF) and returns them to the circulation.
2. It permits the circulation of lymphocytes and other immune cells.
3. It returns intestinal lymph (chyle), which transports cholesterol, long chain fatty acids, triglycerides, and the fat-soluble vitamins (A, D, E, and K), directly to the circulation, bypassing the liver.

Lymph from the lower limbs and abdomen drains via the cisterna chyli and thoracic duct into the left internal jugular vein at its confluence with the left subclavian vein. Lymph from the head and right arm drains via the right lymphatic duct into the right internal jugular vein. Lymphatics accompany veins everywhere except in the cortical bony skeleton and central nervous system, although the brain and retina possess cerebrospinal fluid and aqueous humor, respectively. The lymphatic system comprises lymphatic channels, lymphoid organs (lymph nodes, spleen, Peyer's patches, thymus, tonsils), and circulating elements (lymphocytes and other mononuclear immune cells).

Lymphatics originate within the ISF space from specialized endothelialized capillaries (initial lymphatics) or nonendothelialized channels such as the spaces of Disse in the liver. Initial lymphatics are unlike arteriovenous capillaries in that they are blind-ended, are much larger (50 μm) and allow the entry of molecules up to 1000 kd in size. This is because the basement membrane of these lymphatics is fenestrated, tenuous, or lacking intra- and intercellular endothelial pores. Lymphatic capillaries are anchored to interstitial matrix by filaments. In the resting state they are collapsed, but when ISF volume and pressure increases, they are held open by these filaments to facilitate increased drainage. Initial lymphatics drain into terminal (collecting) lymphatics that possess bicuspid valves and endothelial cells rich in the contractile protein actin. Larger collecting lymphatics are surrounded by smooth muscle. Valves partition the lymphatics into segments (lymphangions) that contract sequentially in order to propel lymph into the lymph trunks. Terminal lymphatics lead to lymph trunks comprising endothelium, basement membrane, and a media of smooth muscle cells that are innervated with sympathetic,

parasympathetic, and sensory nerve endings. About 10% of lymph arising from a limb is transported in deep lymphatic trunks that accompany the main neurovascular bundles. The majority of lymphatic flow, however, is conducted against the venous flow from deep to superficial in epifascial lymph trunks. Superficial trunks form lymph bundles of various sizes, are located within strips of adipose tissue, and tend to follow the course of the major superficial veins.

The distribution of fluid and protein between the vascular and ISF spaces depends on hydrostatic and oncotic pressures (Starling's forces), together with the relative impermeability of the blood capillary membrane to molecules over 70 kd. In healthy subjects there is net capillary filtration, which is removed by the lymphatic system. Small particles enter the initial lymphatics directly; larger particles are phagocytosed by macrophages and transported through the lymphatic system intracellularly. Lymph flows against a small pressure gradient due to transient increases in interstitial pressure secondary to muscular contraction and external compression, the sequential contraction and relaxation of lymphangions, and the prevention of reflux due to valves. Lymphangions respond to increased lymph flow in much the same way as the heart responds to increased venous return in that they increase their contractility and stroke volume. Transport in the main lymph ducts also depends on intrathoracic (respiration) and central venous (cardiac cycle) pressures. In the healthy limb, lymph flow is largely due to intrinsic lymphatic contractility augmented by exercise, limb movement, and external compression. However, in lymphedema, where the lymphatics are constantly distended with lymph, these external forces assume a much more important functional role.

Definition and Pathophysiology

Lymphedema may be defined as abnormal limb swelling due to the accumulation of increased amounts of high-protein ISF secondary to defective lymphatic drainage in the presence of (near) normal net capillary filtration (Szuba and Rockson, 1997). In order for edema to be clinically detectable, the ISF volume has to double. About 8 L of lymph is produced and, following resorption in lymph nodes, about 4 L enters the venous circulation. In one sense, all edema is lymphedema in that it results from an inability of the lymphatic system to clear the ISF compartment. However, in most types of edema this is because the capillary filtration rate is pathologically high and overwhelms a normal lymphatic system, resulting in the accumulation of low-protein edema fluid. By contrast, in true lymphedema, capillary filtration is normal and the edema fluid is relatively high in protein. Both mechanisms frequently coexist, as in patients with CVI.

Lymphedema can result from lymphatic aplasia, hypoplasia, dysmotility (reduced contractility with or without valvular insufficiency), obliteration by inflammatory, infective or neoplastic processes, or surgical extirpation (Table 10.4). Whatever the primary abnormality, the resultant physical or functional obstruction leads to lymphatic hypertension and distention with further secondary impairment of contractility and valvular competence. Lymphostasis and lymphotension lead to the accumulation in the ISF of fluid, proteins, growth factors and other active peptide moieties, glycosaminoglycans, and particulate matter, including bacteria. As a consequence, there is increased collagen production by fibroblasts, an accumulation of inflammatory cells (predominantly macrophages and lymphocytes), and activation of keratinocytes. The end result is protein-rich edema fluid, increased deposition of ground substance, subdermal fibrosis, and dermal thickening and proliferation. Lymphedema, unlike all other types of edema, is confined to the epifascial space. Although muscle compartments may be hypertrophied due to the increased work involved in limb movement, they are characteristically free of edema.

Two main types of lymphedema are recognized:

- Primary, in which the cause is unknown (or at least uncertain and unproved) but often presumed to be due to congenital lymphatic dysplasia
- Secondary, in which there is a clear underlying cause such as inflammation, malignancy, or surgery

Primary lymphedema is usually further subdivided on the basis of the presence of a family history, age of onset, and lymphangiographic findings (see below).

Table 10.4. Differential diagnosis of the swollen limb

Nonvascular or lymphatic	General disease states	Cardiac failure from any cause; liver failure; hypoproteinemia due to nephrotic syndrome, malabsorption, protein losing enteropathy; hyperthyroidism (myxedema); allergic disorders including angioedema and idiopathic cyclic edema; prolonged immobility and lower lib dependency
	Local disease processes	Ruptured Baker's cyst; myositis ossificans; bony or soft tissue tumors; arthritis; hemarthrosis; calf muscle hematoma; Achilles tendon rupture
	Retroperitoneal fibrosis	May lead to arterial, venous and lymphatic abnormalities
	Gigantism	Rare; all tissues are uniformly enlarged
	Drugs	Corticosteroids; estrogens; progestogens; monoamine oxidase inhibitors; phenylbutazone; methyldopa; hydralazine; nifedipine
	Trauma	Painful swelling due to reflex sympathetic dystrophy
	Obesity	Lipodystrophy, lipoidosis
Venous	Deep venous thrombosis	There may be an obvious predisposing factor such as recent surgery; the classical signs of pain and redness may be absent
	Postthrombotic syndrome	Swelling, usually of the whole leg, due to iliofemoral venous obstruction; venous skin changes, secondary varicose veins on the leg and collateral veins on the lower abdominal wall; venous claudication may be present
	Varicose veins	Simple primary varicose veins are rarely the cause of significant leg swelling
	Klippel-Trenaunay syndrome and other malformations	Rare; present at birth or develops in early childhood; comprises an abnormal lateral venous complex, capillary nevus, bony abnormalities, hypo(a)plasia of deep veins, and limb lengthening; lymphatic abnormalities often coexist
	External venous compression	Pelvic or abdominal tumor including the gravid uterus; retroperitoneal fibrosis
	Ischemia- reperfusion	Following lower limb revascularization for chronic and particularly chronic ischemia
Arterial	Arteriovenous malformation	May be associated with local or generalized swelling
	Aneurysm	Popliteal; femoral; false aneurysm following (iatrogenic) trauma

Epidemiology

Lymphedema is estimated to affect around 2% of the population and causes significant physical symptoms and complications, as well as emotional and psychological distress, which can lead to difficulties with relationships, school, and work. Many sufferers choose not to seek medical advice because of embarrassment and a belief that nothing can be done. Patients who do come forward, especially those with non–cancer-related lymphedema, often find they have limited access to appropriate expertise and treatment. Lymphedema is often misdiagnosed and mistreated by doctors, who frequently have a poor understanding of the condition, believing it to be primarily a cosmetic problem. However, early diagnosis and treatment are important because relatively simple measures can prevent the development of disabling late disease, which is often very difficult to treat.

Clinical Assessment

In most cases the diagnosis of primary or secondary lymphedema can be made, and the condition differentiated from other causes of a swollen limb, on the basis of history and examination without recourse to complex investigation. Unlike other types of edema, lymphedema characteristically involves the foot. The contour of the ankle is lost through infilling of the submalleolar depressions; a "buffalo hump" forms

on the dorsum of the foot, the toes appear square due to confinement of footwear, and the skin on the dorsum of the toes cannot be pinched due to subcutaneous fibrosis (Stemmer's sign). Lymphedema usually spreads proximally to knee level and less commonly affects the whole leg. In the early stages, lymphedema "pits," and the patient reports that the swelling is down in the morning. This represents a reversible component to the swelling, which can be controlled. Failure to do so allows fibrosis, dermal thickening, and hyperkeratosis to occur. In general, primary lymphedema progresses more slowly than secondary lymphedema. Chronic eczema, fungal infection of the skin (dermatophytosis) and nails (onychomycosis), fissuring, verrucae, and papillae (warts) are frequently seen in advanced disease. Ulceration is unusual except in the presence of chronic venous insufficiency.

Lymphangiomas are dilated dermal lymphatics that blister onto the skin surface. The fluid is usually clear but may be blood stained, and in the long term they thrombose and fibrose, forming hard nodules, raising concerns about malignancy. If they are <5 cm across, they are termed lymphangioma circumscriptum; if more widespread, lymphangioma diffusum. If they form a reticulate pattern of ridges, they are termed lymphedema ab igne. Lymphangiomas frequently weep (lymphorrhea, chylorrhea), causing skin maceration and act as a portal for infection. Protein-losing diarrhea, chylous ascites, chylothorax, chyluria, and discharge from lymphangiomas suggest lymphangiectasia (megalymphatics) and chylous reflux.

Ulceration, nonhealing bruises, and raised purple-red nodules should lead to suspicion of malignancy. Lymphangiosarcoma was originally described in postmastectomy edema (Stewart-Treves syndrome) and affects about 0.5% of patients at a mean onset of 10 years. However, lymphangiosarcoma can develop in any long-standing lymphedema but usually takes longer to manifest (20 years). It presents as single or multiple bluish/red skin and subcutaneous nodules that spread to form satellite lesions that may then become confluent. The diagnosis is usually made late, and confirmed by skin biopsy. Amputation offers the best chance of survival, but even then most patients live less than 3 years. It has been suggested that lymphedema leads to an impairment of immune surveillance and so predisposes to other malignancies, although the causal association is not as definite as it is for lymphangiosarcoma.

Primary Lymphedema

It has been proposed that all cases of primary lymphedema are due to an inherited abnormality of the lymphatic system, sometimes termed congenital lymphatic dysplasia. However, it is possible that many sporadic cases of primary lymphedema occur in the presence of a (near) normal lymphatic system and are actually examples of secondary lymphedema for which the triggering events have gone unrecognized. These might include seemingly trivial (but repeated) bacterial or fungal infections, insect bites, barefoot walking (silica), DVT, or episodes of superficial thrombophlebitis. In animal models, simple excision of lymph nodes or trunks leads to acute lymphedema that resolves within a few weeks, presumably due to collateralization. In animals, the human condition can only be mimicked by inducing extensive lymphatic obliteration and fibrosis. Even then, there may be considerable delay between the injury and the onset of edema. Primary lymphedema is much commoner in the legs than the arms. This may be due to gravity and a bipedal posture, the fact that the lymphatic system of the leg is less well developed, or the increased susceptibility of the leg to trauma or infection. Furthermore, loss of the venoarteriolar reflex (VAR), which protects lower limb capillaries from excessive hydrostatic forces in the erect posture, with age and disease (CVI, diabetes) may be important.

Primary lymphedema is often classified on the basis of apparent genetic susceptibility, age of onset, or lymphangiographic findings (Table 10.5). None of these is ideal, and the various classification systems in existence can appear confusing and conflicting as various terms and eponyms are used loosely and interchangeably. This problem has hampered research and efforts to gain a better understanding of underlying mechanisms, the effectiveness of therapy, and prognosis. Primary lymphedema, where there appears to be a genetic susceptibility or element to the disease, may be further divided into those cases that are familial (hereditary), where typically the only abnormality is lym-

Table 10.5. Lymphangiographic classification of primary lymphedema

	Congenital hyperplasia (10%)	Distal obliteration (80%)	Proximal obliteration (10%)
Age of onset	Congenital	Puberty (praecox)	Any age
Sex distribution	Male > female	Female > male	Male = female
Extent	Whole leg	Ankle, calf	Whole leg, thigh only
Laterality	Uni = bilateral	Often bilateral	Usually unilateral
Family history	Often positive	Often positive	No
Progression	Progressive	Slow	Rapid
Response to compression therapy	Variable	Good	Poor
Comments	Lymphatics are increased in number, although functionally defective; there is usually an increased number of lymph nodes; may have chylous ascites, chylothorax, and protein-losing enteropathy	Absent or reduced distal superficial lymphatics; also termed aplasia or hypoplasia	There is obstruction at the level of the aortoiliac or inguinal nodes; if associated with distal dilatation, the patient may benefit from lymphatic bypass operation; other patients have distal obliteration as well

phedema and there is a family history, and those cases that are syndromic, where the lymphedema is only one of several congenital abnormalities and is either inherited or sporadic. Syndromic lymphedema may be sporadic and chromosomal [Turner's (XO karyotype), Klinefelter's (XXY), Down (trisomy 21) syndrome], or clearly inherited and related to an identified or presumed single gene defect [lymphedema-distichiasis (autosomal dominant)], or of uncertain genetic etiology (yellow-nail and Klippel-Trenaunay-Weber syndromes). Familial (hereditary) lymphedema can be difficult to distinguish from nonfamilial lymphedema because a reliable family history may be unobtainable, the nature of the genetic predisposition is unknown, and the genetic susceptibility may translate into clinical disease only in the presence of certain environmental factors. Although the distinction may not directly affect treatment, the patients are often concerned lest they be passing on the disease to their children. Two main forms of familial (hereditary) lymphedema are recognized: Noone-Milroy (type I) and Letessier-Meige (type II). It is likely that both eponymous diseases overlap and represent more than a single disease entity and genetic abnormality. Milroy's disease is estimated to be present in 1 in 6000 live births and is probably inherited in an autosomal-dominant manner with incomplete (about 50%) penetrance. In some families, the condition may be related to abnormalities in the gene coding for a vascular endothelial growth factor (VEGF) on chromosome 5. The disease is characterized by brawny lymphedema of both legs (and sometimes the genitalia, arms, and face) that develops from birth or before puberty. The disease has been associated with a wide range of lymphatic abnormalities on lymphangiography. Meige's disease is similar to Milroy's disease except the lymphedema generally develops between puberty and middle age (50 years). It usually affects one or both legs but may involve the arms. Some, but not all, cases appear to be inherited in an autosomal-dominant manner. Lymphangiography generally shows aplasia or hypoplasia.

Lymphedema congenita (onset at or within 2 years of birth) is commoner in males, more likely to be bilateral and to involve the whole leg. Lymphedema praecox (onset from 2 to 35 years) is three times commoner in females, has a peak incidence shortly after menarche, is three times more likely to be unilateral than bilateral, and usually only extends to the knee. Lymphedema tarda develops, by definition, after the age of 35 years and is often associated with obesity, with lymph nodes being replaced by fibrofatty tissue. The cause is unknown. Lymphedema develop-

ing for the first time after 50 years should prompt a thorough search for underlying (pelvic, genitalia) malignancy. It is worth noting that, in such patients, lymphedema often commences proximally in the thigh rather than distally.

Secondary Lymphedema

This is the most common form of lymphedema. There are several well-recognized causes, including infection, inflammation, neoplasia, and trauma.

Filariasis is the commonest cause of lymphedema worldwide, affecting up to 100 million individuals. It is particularly prevalent in Africa, India, and South America, where 5% to 10% of the population may be affected. The viviparous nematode *Wucheria bancrofti*, whose only host is humans, is responsible for 90% of cases and is spread by the mosquito. The disease is associated with poor sanitation. The parasite enters lymphatics from the blood and lodges in lymph nodes, where it causes fibrosis and obstruction, due partly to direct physical damage and partly to the immune response of the host. Proximal lymphatics become grossly dilated with adult parasites. The degree of edema is often massive, in which case it is termed elephantiasis. Immature parasites (microfilariae) enter the blood at night and can be identified on a blood smear, a centrifuged specimen of urine, or in lymph itself. A complement fixation test is also available and is positive in present or past infection. Eosinophilia is usually present. Diethylcarbamazine destroys the parasites but does not reverse the lymphatic changes, although there may be some regression over time. Once the infection has been cleared, treatment is as for primary lymphedema. Public health measures to reduce mosquito breeding, protective clothing, and mosquito netting may be usefully employed to combat the condition.

Endemic elephantiasis (podoconiosis) is common in the tropics and affects more than 500,000 people in Africa. The barefoot cultivation of soil composed of alkaline volcanic rocks leads to destruction of the peripheral lymphatics by particles of silica, which can be seen in macrophages in draining lymph nodes. Plantar edema develops in childhood and rapidly spreads proximally. The condition is prevented, and its progression slowed, by the wearing of shoes.

Lymphangitis and lymphadenitis can cause lymphatic destruction that predisposes to lymphedema complicated by further acute inflammatory episodes (AIEs). Interestingly, in such patients lymphangiography has revealed abnormalities in the contralateral, unaffected limb, suggesting an underlying, possibly inherited, susceptibility. Lymphatic and lymph node destruction by tuberculosis is also a well-recognized cause of lymphedema, especially in developing countries.

Treatment (surgery, radiotherapy) for breast carcinoma is probably the commonest cause of lymphedema in developed countries but is decreasing in incidence as surgery becomes more conservative. Lymphoma may present with lymphedema, as may malignancy of the pelvic organs and external genitalia. Kaposi's sarcoma developing in the course of human immunodeficiency virus (HIV)-related illness may cause lymphatic obstruction and is a growing cause of lymphedema in certain parts of the world.

It is not unusual for patients to develop chromic localized or generalized swelling following trauma. The etiology is often multifactorial and includes disuse, venous thrombosis, and lymphatic injury or destruction. Degloving injuries and burns are particularly likely to disrupt dermal lymphatics. Tenosynovitis can also be associated with localized subcutaneous lymphedema, which can be a cause of troublesome persistent swelling following ankle and wrist sprains and repetitive strain injury.

It is important to appreciate the relationship between lymphedema and CVI. As both conditions are relatively common and often coexist in the same patient, it can be difficult to unravel which components of the patient's symptom complex are due to each pathology. There is no doubt that superficial venous thrombophlebitis (SVT) and DVT can both lead to lymphatic destruction and secondary lymphedema, especially if recurrent. Lymphedema is an important contributor to the swelling of the postphlebitic syndrome. It has also been suggested that lymphedema can predispose to DVT and possibly SVT through immobility and AIEs. Certainly, tests of venous function (duplex ultrasonography, plethysmography) are frequently abnormal in patients with lymphedema.

It is not uncommon to see patients (usually women) with lymphedema in whom a duplex ultrasound scan has revealed superficial reflux (such reflux is present subclinically in up to a third of the adult population). Although isolated superficial venous reflux rarely, if ever, leads to limb swelling, such patients are frequently misdiagnosed as having venous rather than lymphedema, and mistakenly subjected to VV surgery. Not only does such surgery invariably fail to relieve the swelling, it usually makes it worse as saphenofemoral and saphenopopliteal ligation, together with saphenous stripping, compromise still further the drainage through the subcutaneous lymph bundles (which follow the major superficial veins) and draining inguinal and popliteal lymph nodes.

Rheumatoid and psoriatic arthritis (chronic inflammation and lymph node fibrosis), contact dermatitis, snake and insect bites, and retroperitoneal fibrosis are all rare but well-documented causes of lymphedema. Pretibial myxedema is due to the obliteration of initial lymphatics by mucin. Factitious lymphedema is caused by application of a tourniquet (a "rut" and sharp cut-off is seen on examination) or "hysterical" disuse in patients with psychological problems. Generalized or localized immobility due to any cause leads to chronic limb swelling that can be misdiagnosed as lymphedema. Examples include the elderly person who spends all day (and sometimes all night) sitting in a chair (armchair legs), the hemiplegic stroke patient, and the young patient with multiple sclerosis.

Lipedema presents almost exclusively in women and comprises bilateral, usually symmetrical, enlargement of the legs and, sometimes, the lower half of the body due to the abnormal deposition of fat. It may or may not be associated with generalized obesity. There are a number of features that help to differentiate the condition from lymphedema, but lipedema may coexist with other causes of limb swelling. It has been proposed that lipedema results from, or at least is associated with, fatty obliteration of lymphatics and lymph nodes.

Investigation

It is usually possible to diagnose and manage lymphedema purely on the basis of the history and examination, especially when the swelling is mild and there are no apparent complicating features. In patients with severe, atypical, and multifactorial swelling, investigations may help confirm the diagnosis, inform management, and provide prognostic information. A full blood count, urea and electrolytes, creatinine, liver function tests, chest radiograph, and blood smear for microfilariae may be indicated. Direct lymphangiography involves the injection of contrast medium into a peripheral lymphatic vessel and subsequent radiographic visualization of the vessels and nodes. It remains the gold standard for showing structural abnormalities of larger lymphatics and nodes. However, it can be technically difficult, is unpleasant for the patient, may cause further lymphatic injury, and has largely become obsolete as a routine method of investigation. Indirect lymphangiography involves the intradermal injection of water-soluble nonionic contrast into a web space, from where it is taken up by lymphatics and then followed radiographically. It shows distal lymphatic but not normally proximal lymphatics and nodes. Isotope lymphoscintigraphy has largely replaced lymphangiography as the primary diagnostic technique in cases of clinical uncertainty. Radioactive technetium–labeled protein or colloid particles are injected into an interdigital web space and specifically taken up by lymphatics, and serial radiographs are taken with a gamma camera. The technique provides a qualitative measure of lymphatic function rather than quantitative function or anatomical detail. A single axial computed tomography (CT) slice through the mid-calf has been proposed as a useful diagnostic test for lymphedema (coarse, nonenhancing, reticular honeycomb pattern in an enlarged subcutaneous compartment), venous edema (increase volume of the muscular compartment), and lipedema (increased subcutaneous fat). Computed tomography can also be used to exclude pelvic or abdominal mass lesions. Magnetic resonance imaging (MRI) can provide clear images of lymphatic channels and lymph nodes, and can be useful in the assessment of patients with lymphatic hyperplasia. It can also distinguish venous and lymphatic causes of a swollen limb. In cases where malignancy is suspected, samples of lymph nodes may be obtained by fine-needle aspiration, needle core biopsy, or surgical excision. Skin biopsy will confirm the diagnosis of lymphangiosarcoma.

Management

Ideally, a multiprofessional team comprising physical therapists, nurses, orthotists, physicians (dermatologists, oncologists, palliative care specialists), surgeons, and social services should deliver the care. Although surgery itself has a very small role, surgeons (especially breast and vascular) are frequently asked to oversee the management of these patients. Early diagnosis and institution of management are essential because at that stage relatively simple measures can be highly effective and will prevent the development of disabling late-stage disease, which is extremely difficult to treat. There is often a latent period of several years between the precipitating event and the onset of lymphedema. The identification, education, and treatment of such at-risk patients can slow down, even prevent, the onset of disease. In patients with established lymphedema, the three goals of treatment are to relieve of pain, reduce swelling, and prevent the development of complications.

On initial presentation 50% of patients with lymphedema complain of significant pain. The pain is usually multifactorial, and its severity and underlying cause(s) vary depending on the etiology of the lymphedema. For example, following treatment for breast cancer, pain may arise from the swelling itself, radiation and surgery induced, nerve (brachial plexus and intercostobrachial nerve), bone (secondary deposits, radiation necrosis) and joint disease (arthritis, bursitis, capsulitis), and recurrent disease. The detailed treatment of such patients is beyond the scope of this chapter but involves the considered use of nonopioid and opioid analgesics, corticosteroids, tricyclic antidepressants, muscle relaxants, antiepileptics, nerve blocks, physiotherapy, adjuvant anticancer therapies (chemo-, radio-, hormonal therapy), as well as measures to reduce swelling if possible. In patients with non–cancer-related lymphedema, the best way to reduce pain is to control swelling and prevent the development of complications.

Physical therapy for lymphedema comprising bed rest, elevation, bandaging, compression garments, massage, and exercises was first described at the end of the 19th century, and through the 20th century various eponymous schools developed. Although there is little doubt that physical therapy can be highly effective in reducing swelling, its general acceptance and practice has been hampered by a lack of proper research and confusing terminology. The current preferred term is *decongestive lymphedema therapy* (DLT) and comprises two phases. The first is a short intensive period of therapist-led care, and the second is a maintenance phase where the patient uses a self-care regimen with occasional professional intervention. The intensive phase comprises skin care, manual lymphatic drainage (MLD), multilayer lymphedema bandaging (MLLB), and exercises. The length of intensive treatment depends on the disease severity, the degree of patient compliance, and the willingness and ability of the patient to take more responsibility for the maintenance phase. However, weeks rather than months should be the goal.

The patient must be carefully educated in the principles and practice of skin care. The patient should inspect the affected skin daily, with special attention paid to skin folds where maceration may occur. The limb should be washed daily, the use of bath oil (e.g., balneum) is recommended as a moisturizer, and the limb must be carefully dried afterward. A hair drier, on low heat, is more effective and hygienic, and less traumatic, than a towel. If the skin is in good condition, daily application of a bland emollient is recommended to keep the skin hydrated. If the skin is dry and flaky, then a bland ointment [e.g., 50/50 white soft paraffin/liquid paraffin (WSP/LP)] should be used twice daily, and if there is marked hyperkeratosis, then a keratolytic agent such as 5% salicylic acid can be added. Many commercially available soaps, creams, and lotions contain sensitizers, and, as patients with lymphedema are highly susceptible to contact dermatitis (eczema), are best avoided. Apart from causing intense discomfort, eczema acts as an entry point for infection. Management comprises avoidance of the allergen (patch testing may be required) and topical corticosteroids. Fungal infections are common, difficult to eradicate, and predispose to AIEs. Chronic application of antifungal creams leads to maceration, and it is better to use powders in shoes and socks. Ointment containing 3% benzoic acid helps prevent athlete's foot and can be used safely over long periods. Painting at-risk areas with an antiseptic agent such as eosin may be helpful. Lymphorrhea is uncommon but

extremely troublesome. Management comprises emollients, elevation, compression, and sometimes cautery under anesthesia.

Apart from lymphangiosarcoma, AIEs are probably the most serious complications of lymphedema and frequently lead to emergency hospital admission. About 25% of primary and 5% of secondary lymphedema patients are affected. The AIEs start rapidly, often without warning or precipitating event, with tingling, pain, and redness of the limb. Patients feel viral, and severe attacks can lead to the rapid onset of fever, rigors, headache, vomiting, and delirium. Patients who have suffered previous attacks can usually predict the onset, and many learn to carry antibiotics with them and self-medicate at the first hint of trouble. This may stave off a full-blown attack and prevent the further lymphatic injury that each AIE causes. It is rarely possible to isolate a responsible bacterium, but the majority are presumed to be streptococcal or staphylococcal in origin. The diagnosis is usually obvious but dermatitis, thrombophlebitis, and DVT are in the differential. Benzyl (intravenous) or phenoxymethyl (oral) penicillin, and flucloxacillin (or clindamycin in severe attacks), are the antibiotics of choice and should be given for 2 weeks. Rest reduces lymphatic drainage and the spread of infection, elevation reduces the edema, and heparin prophylaxis reduces the risk of DVT. Co-amoxiclav can be taken by patients who self-medicate. The use of long-term prophylactic antibiotics is not evidence-based but is probably reasonable in patients who suffer frequent attacks. However, the benefits of scrupulous compliance with physical therapy and skin care cannot be underestimated.

Several different techniques of MLD have been described and the details are beyond the scope of this chapter. However, they all aim to evacuate fluid and protein from the ISF space and stimulate lymphangion contraction. Therapists should perform MLD daily; they should also train the patient or caregiver to perform a simpler, modified form of massage termed simple lymphatic drainage (SLD). In the intensive phase, SLD supplements MLD, and once the maintenance phase is entered, SLD will carry on as daily massage.

Elastic bandages provide compression, produce a sustained high resting pressure, and compress more as limb swelling reduces. However, the sub-bandage pressure does not alter greatly in response to changes in limb circumference consequent upon muscular activity and posture. By contrast short-stretch bandages exert support through the production of a semi-rigid casing, where the resting pressure is low but changes quite markedly in response to movement and posture.

It is generally believed that nonelastic MLLB is preferable (and arguably safer) in patients with severe swelling during the intensive phase of DLT, whereas compression (hosiery, sleeves) is preferable in milder cases and during the maintenance phase. Whether the aim is to provide support or compression, the pressure exerted must be graduated (100% ankle/foot, 70% knee, 50% mid-thigh, 40% groin), and the adequacy of the arterial circulation must be assessed. As it is rarely possible to feel pulses in the lymphodematous limb, noninvasive assessment of ABI using a handheld Doppler ultrasound device is usually necessary. The details of MLLB are beyond the scope of this chapter; however, it is highly skilled and in order to be effective and safe, it needs to be applied by a specially trained therapist. It is also extremely labor intensive, needing to be changed daily. Compression garments form the mainstay of management in most clinics. The control of lymphedema requires higher pressures (30 to 40 mm Hg in the arm, 40 to 60 mm Hg in the leg) than are typically used to treat CVI. The patient should put the stocking on first thing in the morning before rising. It can be difficult to persuade patients to comply. Donning lymphedema-grade stockings is difficult, and many patients find them intolerably uncomfortable, especially in warm climates. Furthermore, although intellectually they understand the benefits, emotionally they may find wearing them presents a greater body image problem than the swelling itself.

Enthusiasm for pneumatic compression devices has waxed and waned. Unless the device being used allows the sequential inflation of multiple chambers up to 50 mm Hg, it will probably be ineffective for lymphedema. Patient benefit is maximized and complications minimized if these devices are used under the direction of a physical therapist as part of an overall package of care.

Lymph formation is directly proportional to arterial inflow, and 40% of lymph is formed

within skeletal muscle. Vigorous exercise, especially if it is anaerobic and isometric, tends to exacerbate lymphedema, and patients should be advised to avoid prolonged static activities, for example, carrying heavy shopping bags or prolonged standing. By contrast, slow rhythmic isotonic movements (e.g., swimming) and massage increase venous and lymphatic return through the production of movement between skin and underlying tissues (essential to the filling of initial lymphatics) and augmentation of the muscle pumps. Exercise also helps to maintain joint mobility. Patients who are unable to move their limbs benefit from passive exercises. When at rest, the lymphedematous limb should be positioned with the foot/hand above the level of the heart. A pillow under the mattress or blocks under the bottom of the bed encourage the swelling to go down overnight.

There are considerable, and scientifically inexplicable, differences in the use of specific drugs for venous disease and lymphedema between different countries. The benzpyrenes are a group of several thousand naturally occurring substances, of which the flavonoids have received the most attention. Enthusiasts argue that a number of clinical trials have shown benefit from these compounds, which are purported to reduce capillary permeability, improve microcirculatory perfusion, stimulate interstitial macrophage proteolysis, reduce erythrocyte and platelet aggregation, scavenge free radicals, and a exert an antiinflammatory effect. Detractors argue that the trials are small and poorly controlled, with short follow-up and soft end points, and that any benefits observed can be explained by a placebo effect. Diuretics are of no value in pure lymphedema. Their chronic use is associated with side effects including electrolyte disturbance and should be avoided.

Surgery

Surgery benefits only a small minority of patients with lymphedema. Operations fall into two categories: bypass procedures and reduction procedures. The rare patient with proximal ilioinguinal lymphatic obstruction and normal distal lymphatic channels might benefit, at least in theory, from lymphatic bypass. A number of methods have been described including the omental pedicle, the skin bridge (Gillies), anastomosing lymph nodes to veins (Neibulowitz), the ileal mucosal patch (Kinmonth), and, more recently, direct lymphovenous anastomosis. The procedures are technically demanding, not without morbidity, and there is no controlled evidence to suggest that these procedures produce an outcome superior to the best medical management alone. Limb reduction procedures are indicated when a limb is so swollen that it interferes with mobility and livelihood. These operations are not cosmetic in the sense that they do not create a normally shaped leg and are usually associated with significant scarring. Four operations have been described:

1. *Sistrunk:* A wedge of skin and subcutaneous tissue is excised and the wound closed primarily. This is most commonly employed to reduce the girth of the thigh.
2. *Homan:* Skin flaps are elevated; subcutaneous tissue is excised from beneath the flaps, which are then trimmed to size to accommodate the reduced girth of the limb and closed primarily. This is the most satisfactory operation for the calf. The main complication is skin flap necrosis. There must be at least 6 months between operations on the medial and lateral sides of the limb, and the flaps must not pass the midline. This procedure has also been used on the upper limb but is contraindicated in the presence of venous obstruction or active malignancy.
3. *Thompson:* One denuded skin flap is sutured to the deep fascia and buried beneath the second skin flap (the so-called buried dermal flap). This procedure has become less popular as pilonidal sinus formation is common, the cosmetic result is no better than that obtained with the Homan's procedure, and there is no evidence that the buried flap establishes any new lymphatic connections within the deep tissues.
4. *Charles:* This operation was initially designed for filariasis and involved excision of all the skin and subcutaneous tissues down to the deep fascia with coverage using split skin grafts. This leaves a very unsatisfactory cosmetic result, and graft failure is not uncommon. However, it does enable the surgeon to reduce greatly the girth of a massively swollen limb.

Arteriovenous Fistulas

Classification

Arteriovenous fistulas (AVFS) are broadly classified into congenital and acquired. Acquired fistulas may be traumatic, iatrogenic, or associated with malignancy, aneurysmal disease, and infection. These are not considered further. Congenital AVFs are further classified as hemangiomas or malformations. The former are characterized by endothelial hyperplasia, are not present at birth, and grow in early childhood, but in 90% of cases involute by the age of 5 to 10 years. The latter exhibit normal endothelial cell kinetics, are always preset at birth, grow and continue to grow with the child, and may enlarge dramatically at puberty or in pregnancy. Whenever vascular lesions appear and grow rapidly, it is important to exclude malignancy. Malformations may be high flow (predominantly cardiac and great vessel anomalies) or low flow (arterial, venous, lymphatic, or mixed). The processes leading to the development of the mature vascular tree are largely unknown, but presumably congenital fistulas represent a localized disorder of vessel formation. Occasionally they may be familial, and some abnormalities have been mapped to certain chromosomal loci.

Symptoms and Signs

The clinical presentations are protean and depend on the nature of the lesion, anatomical site, size, and flow.

Malformations

Although malformations are present at birth, they do not usually become symptomatic, and even go unnoticed, until later at life. They typically present at puberty or during pregnancy or following trauma to the part. There is usually an obvious swelling and discoloration, and there may be limb enlargement. Adults typically present with a lump, VVs, (ischemic) ulceration, bleeding, or an inequality in limb length. That which is visible is often the "tip of the iceberg," and the deep component may cause pain, pressure on local strictures, organ dysfunction, and internal bleeding. On examination there is discoloration and a lump. If arterial, it is typically firm, pulsates, and is associated with a thrill and a murmur and sometimes pulsatile draining veins. If primarily venous, it is soft and compressible, and reduces in size and enlarges upon elevation and dependency, respectively.

Hemangiomas

Hemangiomas present at or within a few weeks of birth. They are said to be present in 10% of Caucasian children on their first birthday, to be three times commoner in girls, to be multiple in 20%, and to affect the head and neck (60%), trunk (25%), and extremities (10%). If superficial, they are bright (strawberry nevus), and if deep dark (cavernous hemangioma), red. They are firm and rubbery and cannot be emptied of blood on compression or elevation. After an initial phase of rapid growth, they begin to involute at about 6 to 12 months of age when the red color turns to purple, gray/while flecks appear, the lesion becomes softer, and the overlying skin wrinkles. Resolution is typically completed in 50% at 5 years, 70% at 7 years, and 90% or more by 10 years. Apart from cosmetic concerns there may be ulceration and bleeding. On the face they may block vision, and depending on where they are sited may cause mass effects. Large hemangiomas involving internal organs may cause heart failure and anemia.

Diagnosis and Investigation

The diagnosis can usually be made on clinical examination. Handheld Doppler helps to confirm if there is an arterial component, and DU provides more detailed anatomical and functional information. In particular, DU permits detailed assessment of the venous system in patients with Klippel-Trenaunay syndrome where the deep venous system may be hypoplastic or even absent, having been replaced by an abnormal laterally placed venous malformation. Duplex ultrasound has largely replaced venography. Phleboliths may be seen on plain x-rays and are only usually seen in venous lesions. Magnetic resonance imaging, rather than CT, is now regarded as the definitive investigation for assessing the extent of AVF. Angiography is performed only where there is an intention to treat radiologically.

Management

Management is complex, multidisciplinary (vascular, plastic, maxillofacial, and orthopedic surgeons, interventional radiologist, cardiologist), difficult, and highly tailored to the individual patient. Many patients (and parents) simply require reassurance, and in general it pays to be as conservative as possible. Only 10% of hemangiomas fail to resolve spontaneously and many malformations remain asymptomatic. Palliation, not cure, is the principal aim, and it is important to ensure that the treatment is not worse than the disease. Venous lesions may be treated with compression bandaging and hosiery. A small minority of patients are suitable for excisional surgery. Complete excision is rarely possible, and usually the aim is to remove the most symptomatic part. Such surgery can be difficult and bloody, and recurrence is common. For these reasons, most patients are treated radiologically either by transcatheter embolization (arterial lesions) or by direct injection (venous lesions), usually under general anesthesia. This is a highly skilled and specialized branch of interventional radiology, and great care must be taken to avoid collateral damage. Extremities are particularly vulnerable. Surgical skeletonization of the arterial inflow to the lesion is now avoided, as recurrence is inevitable and such intervention prevents radiological intervention. Strong indications for intervention are hemorrhage, distal ischemia due to steal, and ulceration due to ischemia or venous hypertension.

References

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