Lymphoedema

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Abstract

Lymphoedema is caused by inadequate lymphatic drainage leading to an accumulation of protein-rich fluid in the interstitium. The most important initial distinction to be made for classification of lymphoedema is between primary lymphoedema (which has a genetic cause) and secondary lymphoedema. Early diagnosis is essential as many conservative therapies are available and can prevent progression. In the Western world lymphoedema is most commonly secondary to cancer and its treatment. In endemic regions filiariasis is an important cause and a global eradication programme is underway. Recently, great progress has been made in understanding the embryology of the lymphatic system and the specific genetic causes of primary lymphoedema, leading to the hope that medical therapies may enable improvement in lymphatic function. Surgery is currently reserved for advanced disease and is performed in specialist centres, primarily to reduce the bulk of swollen tissue.

Keywords Charles; Filiariasis; Homan's; Imaging; lymphangiogram lymphoedema; lymphoedema distichiasis; lymphoscintigraphy; Milroy's; Podoconiosis

Introduction

Lymphoedema is caused by inadequacy of the lymphatic drainage system leading to an accumulation of protein-rich fluid in the interstitium. This condition can be divided into primary (genetic aetiology) and secondary lymphoedema.[1–3] Secondary lymphoedema due to infestation of the lymphatics with filarial worms is the second leading cause of chronic disability worldwide: approximately 15 million people suffer with lymphoedema and 25 million men are affected by urogenital swelling. In non-endemic regions, lymphoedema is most commonly seen following surgery and radiotherapy for cancers of the breast and urogenital tract. Lymphoedema is under-diagnosed, is difficult to treat and remains a significant cause of morbidity and mortality worldwide.[4]

Functions of the lymphatic system

The lymphatic vascular system consists of blind-ending initial lymphatic capillaries approximately 30-90 μm in diameter that are dispersed throughout the tissues and contain button-like junctions between oak leaf-shaped endothelial cells that allow fluid and cells to passively drain into the lumen. These lymphatics take up the majority of the fluid that leaves the blood capillary bed. Simple 'flaps' between the endothelial cells form the primary lymphatic valves. Lymphatic capillaries consist only of endothelial cells and flow within them is entirely passive. They drain into collecting lymphatics, which actively peristalse, and contain intra-luminal (secondary) valves to ensure unidirectional flow. In combination with compression from surrounding skeletal muscles, lymph is propelled centrally towards local draining chains of lymph nodes in which up to half the fluid is reabsorbed into the blood circulation. Lymphatics from the lower limbs drain into the cisternae chyli in the upper abdomen, and from there into the thoracic duct, which courses through the thorax and drains through a valved orifice into the central veins at the junction of the left internal jugular and subclavian veins. Lymph from the right upper limb drains at the junction of the right subclavian vein/internal jugular. The mesenteric lymphatics (lacteals) play an essential role in the absorption of long-chain fatty acids and fat-soluble substances (e.g. vitamins) and actively pump fluid from the villi. Medium chain fatty acids are absorbed directly to the blood circulation via the portal vein.[1,2]

Lymphatic vessels have a critical function in immune surveillance and the response to infection: they drain antigens and activated antigen-presenting cells into the lymph nodes from the tissues, and subsequently export immune effector cells and humoral response factors into the central blood circulation. The role in neuropathology of the recently rediscovered CNS lymphatic drainage remains to be explored. The location and function of lymphatics means that they play an important role in pathways of cancer metastases.[1]

In the limbs, lymphatic dysfunction leads to lymphoedema, a chronic incurable and debilitating condition characterized by chronic tissue oedema and impaired local immunity (recurrent cellulitis). Reflux of lymph or chyle back towards superficial draining capillaries may manifest as chylous ascites (accumulation of lymph in the abdomen), pleural effusions, pericardial effusions, chyluria, and cutaneous lymph leak.

Development of the lymphatic system

The lymphatics develop from multiple sources. Around mid gestation, a subset of venous endothelial cells in the cardinal veins commit to a lymphatic fate and migrate away from the veins to form the lymph sacs. Further sprouting of cells away from the lymph sacs produces a network of lymphatic capillaries, which later remodels to form a hierarchical draining network of initial lymphatics, pre-collecting vessels and collecting vessels. Other recently described origins of lymphatics include the yolk sac and haemogenic cells in the embryo, which make important contributions to drainage of the heart and skin.[1,2]

Collecting lymphatics develop a basement membrane and acquire pericyte coverage and intraluminal bileaflet valves. In recent years great progress has been made in understanding these processes, and several genes have been discovered, whose proteins play critical regulatory roles in lymphatic development. Examples include *SOX18*, *PROX1*, FLT4 (VEGFR3), *FOXC2*,

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CCBE1, *GJC2*, *GATA2*, *ITGA9*. This has been of great relevance in the clinic, as the genes for several lymphoedema syndromes have been described, genetic risk factors for secondary lymphoedema (e.g. following surgery) have been identified, and perhaps most importantly, molecular therapies are being developed which may one day aid in repairing a malformed or damaged lymphatic system.[3,5]

Pathogenesis

The underlying aetiology in lymphoedema is one of lymphatic dysfunction with inadequate lymph drainage. This causes swelling, inflammation and subcutaneous tissue fibrosis, initially manifesting as soft pitting oedema of the affected limb, but later as firmer and more indurated skin. The swelling and subsequent induration of the affected region cause disfigurement and in the limbs can lead to decreased mobility and function. Lymphoedema predisposes to recurrent episodes of cellulitis and lymphangitis, which can further damage the lymphatics.

Differential diagnosis of oedema

Lymphoedema must be differentiated from myriad other causes of chronic limb swelling. Systemic disorders include renal, thyroid, hepatic and cardiac dysfunction. Local disease processes include tumours, external venous compression (of any cause), aneurysms and lipodystrophy. Deep venous thrombosis and the post-thrombotic syndrome may cause acute and chronic oedema. Commonly used drugs including corticosteroids and calcium channel blockers can cause or exacerbate oedema. Factitious disease, immobility and malnutrition should be considered. Simple varicose veins are rarely the cause of significant oedema. Overgrowth syndromes are rare (and all tissues are enlarged rather than just the epifascial compartment).[6]

Classification

The most important initial distinction to be made for classification of lymphoedema is between primary lymphoedema (which has a genetic cause) and secondary lymphoedema. The clinical presentation of primary lymphoedema disorders is highly variable, with differences in clinical features, age of onset, regions affected, inheritance patterns, and genetic cause. Even within a single family affected by the same genetic mutation, penetrance of the disorder may be incomplete.[3,5]

Box 1 lists the sub-classification of primary lymphoedema incorporating the underlying genetic basis and also the common underlying causes of secondary lymphoedema.[3]

Primary and secondary lymphoedema

Primary lymphoedema diagnostic groups

1 Syndromic primary lymphoedema

2 Systemic/visceral involvement, pre- or post-natal onset

3 Lymphoedema with overgrowth, vascular, or cutaneous manifestations

4 Late-onset lymphoedema (>1 year of age)

5 Congenital onset lymphoedema (<1 year of age)

Secondary lymphoedema

In endemic regions:

Filiariasis, podoconiosis

Western world:

Malignancy and its treatment (surgery, radiotherapy)

Trauma

Lymphogranuloma venereum, tuberculosis

Box 1

Primary lymphoedema

Specific diagnoses that sub-classify primary lymphoedema include single gene disorders. These sub-classifications are contained within five diagnostic groups that are briefly outlined below.[3]

1. **Syndromic primary lymphoedema.** These patients display a number of abnormal features, only one of which is lymphoedema. Examples of such syndromes include Turner's, Noonan's and Prader Willi.
2. **Systemic/visceral involvement, pre- or post-natal onset.** Systemic (visceral) involvement includes pericardial and pleural effusions, ascites, chylous effusions, and pulmonary and intestinal lymphangiectasia. Examples include Hennekam syndrome (*CCBE1*).
3. **Lymphoedema with overgrowth, vascular, or cutaneous manifestations.** This group includes patients with Klippel-Trenaunay syndrome, characterized by limb overgrowth, an abnormal lateral venous complex, capillary naevus and hypoplasia of the deep veins. Other examples include Proteus syndrome.
4. **Late-onset lymphoedema (>1 year of age)** refers to development of swelling after the first year of life, typically in the teenage years but possibly much later. Lymphoedema distichiasis falls within this group and is caused by mutations in the gene *FOXC2*. Distichiasis refers to the presence of a double row of eyelashes, diagnostic of this condition in the presence of lymphoedema. Meige's lymphoedema (the genetic cause of which remains unknown) may also present in the teenage years, and is characterized by lower limb swelling that rarely extends above the knee and has no associated features.
5. **Congenital onset lymphoedema (<1 year of age).** This group includes patients with Milroy disease, of which approximately 70% of cases are due to mutations in *VEGFR3*. In Milroy's the lymphoedema is typically present at birth and bilateral, and is due to abnormal, non-functional lymphatics that do not absorb fluid from the tissues.

Secondary lymphoedema

Secondary lymphoedema occurs in later life and occurs after a non-genetic insult. Polymorphisms in lymphatic-related genes can place individuals at increased risk, for example in *GJC2*, for lymphoedema after breast cancer surgery.

Malignancy: In the Western world nearly all cases of secondary lymphoedema are related to malignancy or its treatment. Lymphatic dysfunction and lymphoedema are well described after treatment of a variety of cancers, including breast cancer, melanoma, gynaecologic malignancies, lymphoma, and urologic cancers.

Most cases of upper limb lymphoedema are caused by surgery and radiotherapy of the axilla in women, with breast cancer that causes damage to the lymphatics. Typical rates of lymphoedema after mastectomy have been described between 24% and 49%, with lower reported rates (4–28%) after lumpectomy. Early diagnosis and therapy after the initial appearance of oedema are very important for treatment, but the diagnosis is often delayed, particularly for Stage 1 oedema.

Filiariasis: Lymphatic filiariasis is a neglected tropical disease and a major global public health problem. The causative larvae are spread from person to person by mosquitoes in endemic regions. When an infected mosquito bites a person, the parasites are deposited in their skin and subsequently migrate to the lymphatic vessels where they develop into adult worms. Adult worms may live for 6–8 years, and during their lifetime will produce millions of larvae that circulate in the bloodstream. There are three types of worms (nematodes): (i) *Wuchereria bancrofti*, which is responsible for 90% of cases; (ii) *Brugia malayi*, which causes most of the remainder; and (iii) *Brugia timori*.[4]

Filarial infection is usually acquired during childhood and while virtually all affected have subclinical lymphatic damage, the visible lymphoedema may not develop until later in life. Clinical sequelae include lymphoedema of the limbs and genital disease (hydrocele, chylocele, and scrotal and penile oedema). Recurrent acute attacks are painful and accompanied by fever. Progressive swelling and subcutaneous fibrosis can lead to permanent disability. Up to 40% of those affected have renal manifestations, which include proteinuria and haematuria.

Other causes: the pathophysiology of podoconiosis has not been fully elucidated but appears to result from extended periods of walking barefoot on volcanic clays resulting in the uptake of irritant components of clay particles and lymphatic inflammation. This disease is prevalent in tropical Africa, Central America and northern India. Lymphogranuloma venereum is a chronic infection of the lymphatic system caused by three types of the bacterium *Chlamydia trachomatis* and is spread through sexual contact. It may present with discharge through groin lymph nodes. Lymphoedema may also be caused by local tuberculous infection.

Epidemiology

Primary lymphoedema is rare, affecting approximately 1.15/100,000 of the population less than 20 years of age in the Western world.

In endemic regions, filiariasis is a major public health problem. An estimated 120 million people in 73 countries are currently infected with filarial worms, and an estimated 1.4 billion live in areas where filiariasis is endemic – most of them in South-East Asia and Africa. Outside filarial endemic areas and in the western world the commonest cause of lymphoedema is cancer and its treatment.

Clinical evaluation

Primary lymphoedema

The clinical evaluation of patients with primary lymphoedema must include a detailed personal and family history and physical examination. The history should include the age at onset of symptoms and signs, travel, and any causes of secondary lymphoedema such as surgery, radiotherapy and trauma. A lack of family history does not exclude primary lymphoedema. A history of loose, frequent, offensive and fatty stools is suggestive of intestinal lymphangiectasia and should be asked about specifically. Patients may report recurrent episodes of cellulitis. Symptoms in the swollen limb may include a constant dull ache, 'burning' and 'bursting' sensations, general tiredness, heat sensitivity and 'pins and needles'. Increased weight of the limbs may lead to backache or other joint problems.

Clinical signs include swelling, which should also be sought in family members (who may have been unaware of mild disease). Oedema may occur in any region of the body, and the distribution reflects the genetic aetiology rather than any effect of gravity. Oedema is initially soft and non-pitting, but in advanced disease the skin becomes fibrotic. Skin changes include peau d'orange (in the breast), a pinkish-red skin discoloration, hyperkeratosis, 'mossy foot', dermatitis, eczema, ulceration and fungal infection. Cutaneous lymph vesicles (which may leak clear lymph, white chyle or blood) may occur at any site, but most commonly the thighs and genitals. Oedema of the toes produces Stemmer's sign (the inability to pinch a fold of skin on the dorsum of the toes). Distichiasis is an additional row of typically smaller eyelashes, and in the presence of lymphoedema is diagnostic of lymphoedema distichiasis (*FOXC2*). Milroy's disease is characterized by oedema of the leg and foot (a 'buffalo hump') and small upturned toenails (Figure 1).

Arteriovenous, venous or capillary malformations, or any discrepancies in limb length should be recorded. Hypotrichosis-lymphoedema-telangiectasia (caused by mutations in *SOX18*) is characterized by sparse body hair and telangiectasia. Cellulitis, lymphangitis and malnutrition should be noted.

Secondary lymphoedema

Swelling typically occurs in the limbs distal to the site of radiotherapy or surgery. A radiotherapy planning tattoo may be present. There may be signs related to the underlying disease that has been treated (e.g. scars).

Rarely, a cutaneous malignancy, for example, lymphoedema-associated angiosarcoma (Stewart-Treves syndrome) may be suspected and biopsied. It occurs in approximately 0.03% of patients surviving 10 or more years after radical mastectomy, but any chronic lymphoedema is a risk factor for the development of malignancy. Angiosarcomas are a subtype of soft-tissue sarcoma

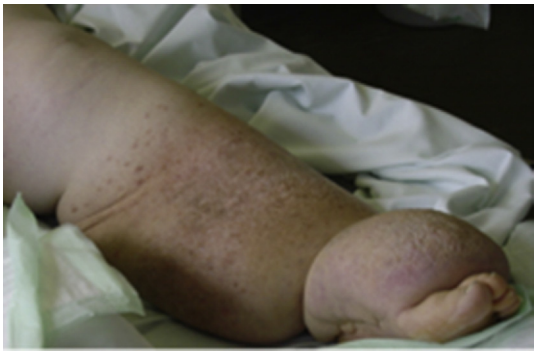

Figure 1 Lymphoedema of the lower limb.

and are aggressive, malignant endothelial-cell tumours of blood vascular or lymphatic origin.

Staging

Staging of lymphoedema is based on clinical findings alone, and is performed according to International Society of Lymphology criteria (Table 1). In relevant cases it is also important to describe the degree of disability caused by the swelling.[6]

Investigation of lymphoedema (and its differentials)

Basic investigations

An ECG, chest radiograph, echocardiogram and serum B natriuretic peptide level may aid in assessment of cardiac function. Renal, hepatic (serum albumin) and thyroid function should be checked. Urinalysis in the presence of filiariasis may demonstrate proteinuria and haematuria (due to renal involvement). Milky white urine suggests chyluria due to chyle reflux from mesenteric lymphatics. Filarial serology may be positive with previous or present filarial infection, and a full blood count may show an eosinophilia. Parasites may be seen on a blood smear (ideally taken at night). Duplex ultrasound is useful for excluding venous oedema, although primary lymphoedema is associated with venous reflux.

Imaging lymphoedema

Lymphoscintigraphy: Radionuclide lymphoscintigraphy is currently the standard investigation to evaluate lymphatic function, and can differentiate between venous (rapid tracer clearance) and lymphatic (delayed tracer clearance) dysfunction as the cause of oedema. A technetium-labelled colloid is injected into the web spaces of the toes or fingers. Subsequent drainage of the colloid from the injection site, and the time it takes for it to reach the knee, groin, or axilla (depending on the injection site) are recorded using a gamma camera. Lymphoscintigraphy provides low-resolution images of the course of major lymphatics and lymph nodes as well as semi-quantitative data on presence and speed of radiotracer transport. Delayed or absent radiotracer transport suggests lymphatic abnormalities.

Lymphography: Radio-opaque contrast lymphography involves direct cannulation of a lymphatic vessel (using a microscope, under general anaesthetic), typically on the dorsum of the foot. Oil-based iodinated contrast is then injected and either spiral CT or serial plain radiographs are obtained through the leg, pelvis, abdomen and groin to delineate the lymphatics (Figures 2 and 3). This allows imaging of specific lymphatics draining from an affected region, and provides information on lymphatic anatomy. Typical abnormal anatomy that can be demonstrated with this technique includes megalymphatics and lymphatic hypoplasia. This technique is typically reserved for more complex cases where there is diagnostic uncertainty. MR lymphography is an evolving technique that may in time replace lymphography as it does not require direct injection of contrast and avoids the use of ionizing radiation.[7]

Clinical staging of lymphoedema

Stage	Description
0	Sub-clinical condition where swelling is not evident despite impaired lymph transport as demonstrated by imaging of lymphatic function. The 'normal' legs of patients with unilateral swelling often show abnormal lymphatic drainage when investigated
1	Oedema is minimal, and resolves with leg elevation. The interstitial fluid has a relatively high protein content, and oedema may show pitting
2	Swelling does not resolve with leg elevation. Oedema may become non-pitting as tissue fibrosis ensues
3	Oedema is non-pitting, and the skin displays trophic changes such as acanthosis, fat deposits and warty overgrowths. Also described as elephantiasis

Table 1

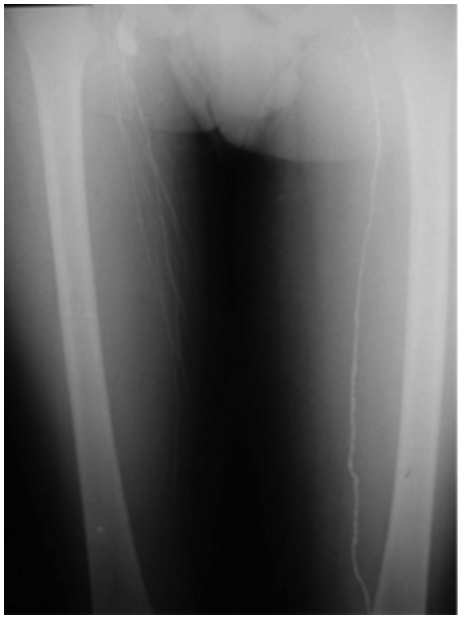

Figure 2 Plain radiograph lymphangiography. Right: normal, left: hypoplastic.

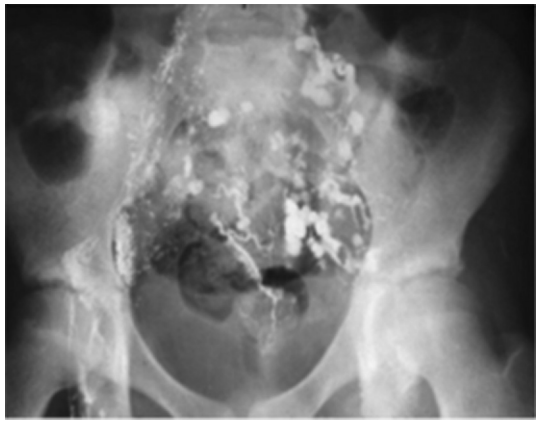

Figure 3 Pelvic megalymphatics.

Indo-cyanine green: Indo-cyanine green lymphography is performed by subcutaneous injection of fluorescent dye, which is then visualized with a near infra-red camera. This allows visualization of lymphatic pumping and reflux in real-time.

Standard computed tomography and magnetic resonance imaging: Both CT and MRI have a role in excluding proximal obstruction in lymphoedema, and in assessing the severity of causative malignant disease in secondary lymphoedema. Dilated lymph vessels may occasionally be identified by MRI. Unfortunately neither of these common investigations can differentiate lymphoedema from oedema of another cause, and so some direct assessment of lymphatic structure and function is required. Rarely, axial imaging is required to exclude gigantism (when all tissues will be enlarged).

Further tests

Biopsy of lymph nodes should be avoided in longstanding lymphoedema as this may exacerbate the swelling but if required in suspected malignancy then fine needle aspirate may be performed. Skin biopsy is only indicated in cases of suspected skin malignancy or differential diagnosis of warty lesions. For suspected primary lymphoedema, genetic testing should be directed towards possible causes after clinical classification as described in Box 1, and in a multidisciplinary team including a clinical geneticist.

Lymphoedema prevention

The Global Programme to Eliminate Lymphatic Filiariasis

In 2000 the World Health Organization launched a Global Programme to Eliminate Lymphatic Filiariasis (GPELF). Its goal is to eliminate lymphatic filiariasis as a public-health problem by 2020, and its strategy is based on two key components, firstly interruption of transmission through annual mass drug administration to the entire at-risk population in endemic areas, and second alleviation of suffering through morbidity management and disability prevention. This programme is based on treatment with albendazole, and either ivermectin or diethylcarbamazine, which will clear microfilariae from the bloodstream. Most adult worms will also be killed (which may provoke an inflammatory reaction in the lymphatics that temporarily worsens lymph drainage).[4]

Management of lymphoedema

The management of lymphoedema is multidisciplinary and may require input from various teams at different stages of the disease, including a lymphatic specialist, psychologist, physiotherapist, clinical geneticist and in some cases a surgeon specializing in lymphatic disorders.[8–12]

Conservative therapies

All patients will require a clear explanation of the cause of their disease, and access to support groups. Non-operative (conservative) therapies aim to alleviate symptoms and prevent progression of swelling. These do not correct the underlying problem, and treatment must be maintained lifelong.[10]

A recent systematic review of randomized controlled trials found substantial clinical and methodological heterogeneity but concluded that most active treatments result in a reduction in limb volume, but there is no evidence of superiority of one treatment over another.

Conservative therapy is based on complex decongestive therapy (CDT), which is also known as decongestive lymphatic therapy (DLT). Treatment consists of manual lymphatic drainage (MLD), compression garments, exercises and skin care. These therapies are the same regardless of the underlying aetiology and are thought to act by opening up collateral lymphatic pathways. Compression can be achieved with multilayer bandaging, garments and intermittent pneumatic compression. The efficacy of treatment in reducing swelling is significantly reduced in the advanced stages of lymphoedema. A scrotal support may be required if the genitals are grossly swollen.

Two randomized controlled trials showed intermittent pneumatic compression (IPC) had benefits over CDT or self massage but three other randomized controlled trials failed to show superiority of IPC compared to lymphatic massage, skin care or an elastic sleeve. Intermittent pneumatic compression devices may play a role in those who are immobile, for example, the elderly or those who are bedbound by their disease and in whom spontaneous exercise/isotonic physical exercise is not fully possible.

Long-term follow-up is generally lacking in randomized trials, but most protocols include long-term use of minimal-stretch elastic garments to attempt to maintain the reduction in oedema achieved by physical therapy. Contraindications include arterial insufficiency, a painful post-phlebitic limb and swelling due to malignant infiltration. It has been suggested that the highest compression level tolerated by the patient (typically 20–60 mmHg) is likely to be the most effective.

Meticulous skin care is essential to prevent cellulitis and lymphangitis. Particular attention should be paid to breaches in the skin, often found in or around the toes, which allow bacteria to penetrate and may be difficult for the patient to identify. Patients will require specially made footwear, particularly as constrictive orthotics will irritate the skin and produce an entry lesion.

A calorie-restricted diet in combination with a supervised exercise programme may help to reduce the contribution of body fat to swelling in some patients. In one study carried out in women with post-mastectomy lymphoedema, weight loss was shown to reduce volume in the lymphoedematous arm more than the healthy arm.

Medical therapy

Co-existent symptomatic pericardial and pleural effusions may require drainage, and medium-chain-triglyceride diets are of benefit in managing intestinal lymphangiectasia and chylous reflux/leak disorders.

Diuretics may provide a short-term benefit in reducing swelling in some cases, but their long-term use should be avoided. They may have a role in some selected cases with ascites/hydrothorax.

Episodes of cellulitis and sepsis can be life threatening, and may further damage remaining lymphatics. Antibiotics are required for acute attacks of cellulitis, and should be directed towards cultured organisms with advice from a microbiologist. If

attacks are recurrent then prophylactic broad-spectrum antibiotics may be prescribed. Prophylactic antifungal therapy is recommended to prevent athlete's foot, preferring dry powders over creams.

Surgical therapy

The various operations available can be grouped into physiological procedures aiming to improve the lymphatic drainage, and reduction surgery that aims to remove the lymphoedematous tissue.[9,11,12]

Reduction surgery: Excisional operations and the major debulking procedures (Charles' and Homan's reductions) are reserved for severe lymphoedema, and can alleviate symptoms and improve mobility by removing excess weight. These procedures generally involve removal of a large volume of fibrosclerotic connective tissue, excess adipose tissue, and excess skin. Liposuction is ideally performed at an earlier stage in the disease, prior to the development of fibrosis.

Liposuction – Lymphoedema leads to excess amounts of adipose tissue in the affected limb. Suction-assisted lipectomy (liposuction) can be performed to consistently and effectively restore near normal limb volume and contour. Removal of adipose tissue – the 'solid component' of the swollen limb – can improve tissue tonicity, range of motion and quality of life. Liposuction may also reduce the incidence of cellulitis, although some authors have reported a return of the preoperative incidence of cellulitis during follow-up. It has most commonly been utilized in the upper limbs following treatment for breast cancer, but can also be performed in the lower limbs; good results have been reported at 10 years follow-up.[8–10]

Liposuction is considered a safe and minimally invasive procedure, and the most commonly reported complications are skin staining and temporary paraesthesia. As with other reduction procedures, lymphatic drainage (as assessed by lymphoscintigraphy) is not improved and ongoing use of compression garments is required.

Charles' reduction – The 'Charles' debulking procedure is reserved for patients who have poor-quality skin (fibrotic, vesicles, etc) and involves excision of all superficial tissues in the leg, down to the deep fascia, from just above the ankle to just below the knee (Figure 4). The periosteum over the tibia is left intact. Muscle and periosteum is then covered with split thickness skin grafts typically taken from the abdomen or thigh. The outcome is not cosmetic but a considerable reduction in the volume and weight of the leg is achieved. This can allow the patient to wear non-specialist clothing and dramatically increase mobility.

Homan's reduction – In Homan's procedure (Figure 5), large skin flaps are elevated from the subcutaneous fat. The underlying oedematous subcutaneous tissue and redundant skin are subsequently excised and the skin flaps are sutured together.

Sistrunk's procedure – involves the excision of a large wedge or ellipse of skin and subcutaneous tissue, which is then closed with skin sutures.

Scrotal reduction – A large central wedge is excised from the scrotum, and the spermatic cord and testicles are preserved. Skin flaps are then resutured (Figure 6). There is evidence to suggest that this cohort of patients demonstrate the greatest improvement in quality of life following reduction surgery.

Complications associated with reduction surgery include haematoma formation, infection/sepsis, delayed wound healing, poor skin graft survival, deep vein thrombosis, scarring/poor cosmesis, nerve damage and reduced limb function. Skin flaps may necrose. It is essential not to fashion these flaps too thinly in order to preserve their blood supply. The risk of recurrence of lymphoedema is lower following a Charles' reduction compared with Homan's/Sistrunk's, because all epifascial tissues are removed. A Charles procedure, however, carries the risk of poor skin graft survival.

Physiological operations:

Lymphovenous shunt – These microsurgical techniques involve anastomosing lymphatics to small veins, lymph nodes to veins, or lymphatics to lymphatics (to bridge gaps) in an attempt

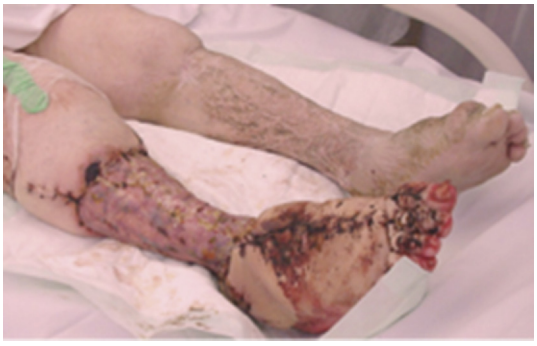

Figure 4 Charles' reduction. The left leg shows the final result and the right leg the immediate post-operative appearance. Wedge excisions have been performed on the feet and toes.

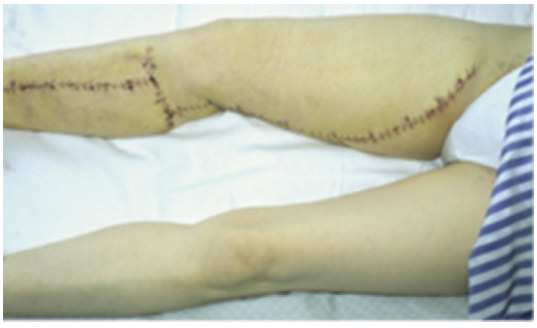

Figure 5 Homan's reduction of the thigh and leg.

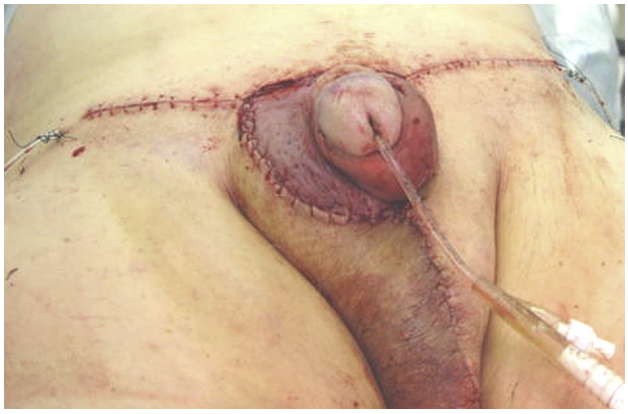

Figure 6 Scrotal reduction.

to increase lymph drainage from oedematous regions. Successful short-term reductions in limb volume have been reported but reproducible long-term quantitative follow-up of these techniques is lacking.[13,14]

Mesenteric bridge – This procedure may be of benefit in a highly selected group of patients with relatively normal lower limb lymphatic drainage up to the groin but then an interruption in the lymph node chain at the groin. A section of small bowel mesentery is raised (with an accompanying short section of bowel) and the submucosal mesenteric lymphatic plexus is attached to groin lymph nodes.

Lymph node autotransplantation – Microanastomosis into the axilla of patients who have had axillary lymph node dissection for cancer has recently been shown to improve lymphatic drainage in some patients.[15]

Treatment of lymphatic vesicles – Lymph and chyle reflux disorders produce patient-specific symptoms depending on the pattern of reflux, for example leakage of vesicles around the scrotum or thigh. Selected cases may benefit from ligation of lymphatics, local diathermy, or image-guided sclerotherapy. ◆

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