Chronic lower limb oedema

Physiology

Oedema develops when the capillary filtration rate exceeds the lymphatic drainage rate for a sufficient period of time. Interstitial fluid volume must double before it is clinically detectable.1

Capillary filtration

Fluid exchange across capillary walls is a passive process governed by the Starling principle:

Filtration rate is proportional to the hydraulic drive across the capillary minus the osmotic suction.

Hydraulic drive is the capillary filtration pressure minus the interstitial pressure.

Osmotic suction is the plasma colloid osmotic pressure minus the interstitial colloid osmotic pressure.

In all tissues, for most of the time the balance of pressures favours filtration of fluid across the capillary membrane into the interstitial fluid.

Lymph drainage

Contrary to popular belief, little fluid is reabsorbed by the capillary and most of it is returned to the circulation via the lymphatic.

Lymph drainage begins in thin-walled, superficial initial lymphatics with wide (14 nm) oblique intercellular junctions that function as flap valves. They freely allow passage of fluid and protein into the lymphatic but prevent back flow. The initial lymphatics unite to form collecting vessels which feed into afferent lymph trunks alongside major vascular bundles. These have muscular contractile walls and semilunar valves to direct lymph flow centrally. Approximately eight litres of fluid a day pass through the afferent lymphatics. The afferent lymphatics drain into lymph nodes, where approximately four litres of fluid are absorbed daily by the nodal microcirculation, the remainder passing on to the thoracic duct via efferent lymphatics. The duct empties into the left subclavian vein at its junction with the jugular vein.

The safety margin

Three buffering mechanisms provide a 15 mmHg margin to protect against oedema formation:

1 Rise in interstitial pressure. When filtration rate increases, the interstitial pressure of normally hydrated tissue rises markedly for only a small rise in interstitial volume. This reduces filtration pressure. The mechanism is overwhelmed in the subcutis at pressures above 2 mmHg when compliance increases sharply.

2 Fall in interstitial colloid osmotic pressure. An increase in filtration rate lowers the interstitial protein concentration and therefore increases absorptive osmotic suction.

3 Increased lymph flow. Lymph flow increases when interstitial volume and pressure increase, but the maximum rise is equivalent to a 5 mmHg safety factor.

Pathophysiology

Oedema forms due to either an increase in capillary filtration or a reduction in lymph drainage, or a combination of the two. The causes of oedema formation are listed in Table 1.

Diagnosis

When faced with a patient with lower limb oedema, certain clinical features provide clues to the underlying pathophysiology. Important points to elicit in the history include:

- Full medical history, taking into consideration both conditions that increase capillary filtration and those that impair lymphatic drainage (Table 1). Venous disease is particularly important, for example, varicose veins, deep vein thrombosis (DVT) and right heart failure.
Drug history: for example, 50% of patients on calcium-channel blockers develop peripheral oedema, and long-term diuretics contribute to idiopathic or periodic oedema in women.

Mobility and posture are important for both venous and lymphatic drainage. Is the patient sitting with legs dependent all day and perhaps most of the night?

Family history: primary lymphoedema is often familial.

Does the oedema disperse readily overnight? If it does not, this suggests a lymph problem. Oedema due to increased filtration will subside on elevation of legs.

Recurrent cellulitis indicates impaired lymph drainage, but swelling (lymphoedema) may be minimal between attacks.

There should be a general examination of the patient for features of heart failure, venous disease and malignancy. Bilateral oedema suggests systemic factors (e.g. heart failure) whereas unilateral oedema indicates a cause within that body quadrant or lower limb. Unilateral chronic oedema should always prompt examination for underlying malignancy, including search for inguinal lymphadenopathy and abdominal masses.

Pitting is not a diagnostic sign. Filtration oedema comprises only water and it pits readily. Lymphoedema contains protein and water and produces a brawny swelling with characteristic skin changes (elephantiasis). However, lymphoedema always pits to some extent except in the advanced fibrotic form.

Skin changes can be associated with several conditions which cause lower limb swelling:
- lymphoedema
- venous hypertension
- lipodermatosclerosis
- cellulitis, especially recurrent
- skin disease (e.g. psoriasis, eczema)
- pretibial myxoedema.

The skin changes associated with lymphoedema and venous hypertension are listed in Table 2.

### Investigations

Full blood count, renal and liver (especially albumin) function tests are useful blood tests. Further imaging, such as lymphoscintigraphy or MRI, depends on clinical suspicion.

### Suspected venous oedema

When there is suspected venous oedema, the following investigations should be performed:
- d dimers
- compression ultrasonography
- contrast venography for presence of thrombus
- venous duplex ultrasound to assess for superficial or deep system incompetence
- computed tomography (CT) of the abdomen/pelvis if there is concern about obstructive pelvic pathology.

### Suspected lymphoedema

Lymphoscintigraphy (isotope lymphography) is the best method of investigation of suspected lymphoedema. It involves injection of radiolabelled colloid or protein into the first webspace of each foot and monitoring progress towards draining lymph nodes with a gamma camera. Tracer appearance outside main lymph routes, especially the skin (dermal

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical signs</th>
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<tbody>
<tr>
<td>Lymphoedema</td>
<td>Skin thickening (inability to pinch a fold of skin at the base of the second toe)</td>
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<tr>
<td></td>
<td>Enhanced skin creases</td>
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<td></td>
<td>Warty texture to skin (hyperkeratosis)</td>
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<td></td>
<td>Papillomatosis</td>
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<td></td>
<td>These changes are called elephantiasis</td>
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<tr>
<td>Venous hypertension</td>
<td>Skin pigmentation (haemosiderin deposition)</td>
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<tr>
<td></td>
<td>Varicose eczema</td>
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<tr>
<td></td>
<td>Atrophic blanche</td>
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<td></td>
<td>Oedema</td>
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<td>Venous ulceration</td>
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<td></td>
<td>Lipodermatosclerosis</td>
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Table 1. Causes of oedema formation.

<table>
<thead>
<tr>
<th>Increased filtration</th>
<th>Reduced lymph drainage</th>
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<tbody>
<tr>
<td>Increased capillary pressure:</td>
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<tr>
<td>- increased venous pressure eg right ventricular failure, DVT, obstructing malignancy, overtransfusion</td>
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<td>- increased blood flow eg A-V fistula, inflammation</td>
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<td>Reduced plasma proteins:</td>
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<tr>
<td>- increased loss eg nephrotic syndrome, protein-losing enteropathy</td>
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<td>- reduced synthesis eg cirrhosis, advanced cancer</td>
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<tr>
<td>- malabsorption, malnutrition</td>
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<tr>
<td>Increased capillary permeability:</td>
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<td>- inflammation eg infection, dermatitis</td>
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<td>Primary lymphatic insufficiency:</td>
<td></td>
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<td>- Milroy’s, onset at or soon after birth and familial</td>
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<tr>
<td>- Meige’s, occurs after puberty, commoner in women, often familial</td>
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<tr>
<td>- Sporadic</td>
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<tr>
<td>Secondary lymphatic insufficiency:</td>
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<td>- surgery eg lymph node dissection, radiotherapy for cancer</td>
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<tr>
<td>- infection eg filariasis (commonest cause of lymphoedema worldwide), recurrent cellulitis, erysipelas</td>
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<td>- accidental trauma</td>
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<td>Dysfunctional lymphatics:</td>
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<tr>
<td>- dependency syndrome (armchair legs)</td>
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<tr>
<td>- loss of mobility</td>
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</table>

DVT = deep vein thrombosis.
back flow), indicates lymph reflux usually due to proximal obstruction. Poor transit from the injection site suggests hypoplasia of the peripheral lymphatic system.

Direct contrast X-ray lymphography (lymphangiography)

Lymph vessels are first identified with a vital dye. A contrast medium (eg lipiodol) is then injected directly into a peripheral lymphatic vessel, usually the dorsum of the foot. In a normal limb, the lymphangiogram will show opacification of 5–15 collecting vessels as they converge on to the lowermost inguinal lymph nodes.

Computed tomography and magnetic resonance imaging

CT and magnetic resonance imaging (MRI) show a characteristic honeycomb pattern in the subcutaneous compartment not seen in other oedemas. MRI is the superior method as it detects water. Skin thickening is not a diagnostic characteristic of lymphoedema. The muscle compartment deep to the fascia, which is unchanged in lymphoedema, is enlarged in post-thrombotic syndrome.

Treatment

Once systemic causes have been excluded or treated, attention should be directed towards improving venous and lymph drainage (Table 3).

Venous drainage

Compression hosiery aids venous drainage. Arterial circulation should be assessed by foot pulse palpation or ankle brachial pressure index measurement prior to compression. Varicose eczema is treated with topical steroid and emollient.

Surgical options for varicose veins include injection sclerotherapy and surgery. Surgery is directed at the underlying abnormality (ie saphenofemoral or saphenopopliteal incompetence)4. If deep veins are competent in the presence of refluxing superficial veins, superficial venous surgery is potentially curative. It is important to ensure superficial veins are not acting as collaterals for deep veins blocked by thrombus4.

There are no uniformly agreed guidelines as to which patients should receive treatment but those with signs of venous hypertension (eg skin changes and oedema) receive priority due to risk of ulceration.

Post-thrombotic syndrome (pain, swelling, dermatitis, ulceration) develops as a result of high venous pressure due to thrombotic damage to valves. It complicates 50–75% of DVTs and has a strong association with ipsilateral recurrent thrombosis. The risk is halved by the use of graded compression stockings after DVT.

Lymph drainage

Physical treatment to reduce swelling. Treatment is aimed at controlling lymph formation and improving lymph drainage through existing lymphatic vessels and collateral routes by applying normal physiological processes which stimulate lymph flow.

Table 3. Physical treatments for lymphoedema.

<table>
<thead>
<tr>
<th>Process</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Exercise</td>
<td>Dynamic muscle contraction encourages drainage, both passive (movement of lymph along tissue planes and non-contractile lymph vessels) and active (increased contractility of collecting lymph vessels)</td>
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<tr>
<td>Compression (hosiery)</td>
<td>Opposes capillary filtration. Acts as a counterforce to muscle contractions (so generating greater interstitial pressure changes and lymph flow)</td>
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<tr>
<td>Manual lymphatic drainage</td>
<td>Form of massage that stimulates lymph flow in more proximal, normally draining lymphatics to siphon lymph from congested areas (particularly trunk) and direct it to normally draining lymph basins</td>
</tr>
<tr>
<td>Multilayer bandaging</td>
<td>An intensive treatment in combination with exercise to reduce large, misshappen lower limbs and permit better control from subsequent maintenance treatment with hosiery*</td>
</tr>
<tr>
<td>Pneumatic compression</td>
<td>Softens and reduces limb volume, but can forcibly displace fluid into trunk and genitalia. Hosiery must always be worn afterwards</td>
</tr>
<tr>
<td>Elevation</td>
<td>Does not stimulate lymph drainage but lowers venous pressure and therefore filtration, allowing lymph drainage to catch up</td>
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*Care should be exercised in patients with cardiac failure.

Prevention of acute inflammatory episodes (cellulitis or lymphangitis) is crucial because they can cause severe constitutional upset and deterioration in swelling. Care of skin, good hygiene, control of disease such as tinea pedis, and careful antiseptic dressings after minor wounds are all important. Prompt treatment of infection is of prime importance; patients should be taught to recognise signs of infection, and be given their own supply of antibiotics so they can start treatment without delay. Prophylactic antibiotics (eg phenoxymethylpenicillin 500 mg daily) are indicated for recurrent infection for an indefinite period.

Surgery is of value only in a few patients in whom the size and weight of the limb inhibit its use and interfere with mobility after physical treatment. The aim is to debulk excessive tissue or bypass local lymphatic defects.

References

2 Mortimer PS. Disorders of lymphatic ves-
SELF-ASSESSMENT QUESTIONNAIRE

Dermatology

Ten self-assessment questions (SAQs) based on the published articles will appear at the end of each CME specialty featured in Clinical Medicine. The questions have been validated for the purpose of CME by independent experts. Two (2) CME credits will be awarded to those achieving 80% correct answers. This opportunity is open only to RCP Fellows and Collegiate Members in the UK who are registered for CME*.

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Guidelines on completing the answer sheet

Your completed answer sheet will be scanned to enable a quick and accurate analysis of results. To aid this process, please keep the following in mind:

1. Please print your GMC Number firmly and neatly.
2. Only write in allocated areas on the form.
3. Only use pens with black or dark blue ink.
4. For optimum accuracy, ensure printed numbers avoid contact with box edges.
5. Please shade circles like this: ●
Not like this: ○
6. Please mark any mistakes made like this: ✗
7. Please do not mark any of the black squares on the corners of each page.
8. Please fill in your full name and address on the back of the answer sheet in the space provided; this will be used to mail the form back to you after marking.

Q1 Dermatomyositis:

a) has a bimodal age distribution
b) when associated with calcification has a worse prognosis
c) is associated with malignancy in 80% of patients over the age of 40 years
d) photosensitivity is a recognised feature of the skin rash
e) is undiagnosable in the presence of normal skin and muscle biopsies

Q2 In systemic sclerosis:

a) prognosis is related to the degree of internal organ involvement
b) digital ulceration is a recognised feature
c) vasodilators are able to produce symptomatic benefit
d) spontaneous resolution of the skin lesions is recognised to occur
e) the anticentromere antibody is negative in the limited form