Lymphatics & Lymph nodes

ACUTE LYMPHANGITIS
INVESTIGATION
LYMPHOEDEMA
FILARIASIS
LYMPHANGIOMA
LYMPH NODES
LYMPHOMAS

Acute Lymphangitis

Acute lymphangitis occurs when infection, commonly by *Streptococcus pyogenes,* spreads beyond a point of infection to the group of lymph nodes draining that area, where an abscess may form. Occasionally, the infection bypasses one group to affect another at a higher level. For example, if the point of infection is in the foot, an abscess may form in the external iliac group of nodes rather than the superficial (lower) and deep inguinal groups and, because the point of infection may have healed and been forgotten, by the time the mass appears it may be mistaken for an appendix abscess.

Acute lymphangitis is seen as red blushes and streaks in the skin, corresponding to the inflamed lyrnphatics (Fig. 13.1).

Treatment consists of bed rest, with the affected limb comfortably elevated, and giving cloxacillin, which usually causes rapid resolution. *Only* when there are definite signs Of pus should an incision be made.

Postlymphatic oedema. Permanent lymphatic obstruction can follow in the wake of acute lymphangitis, leading to persistent oedema.

Fig. 13.1 Acute lyrnphangitis of the arm. Red streaks extend from the infection on the forearm up to the enlarged and tender axillary lymph nodes. Toxaemia is often severe and is greater the more the infection has extended proximally.

Chronic lymphangitis may follow repeated attacks of acute lymphangitis (see acquired (secondary) lymphoedema, below).

Investigations

Lymphangiography is used to diagnose lymphoedema and to demonstrate the nature of lymphatic abnormality. The procedure is also used to detect malignant disease in the iliac and para-aortic lymph nodes, but is being replaced by computed tomography (CT) and high-resolution ultrasonography as these techniques become more generally available.

Technique. Pedal iymphangiogram. Blue dye is injected subcutaneously between the toes to outline the lymphatic vessels. A small indsion is made on the dorsum $_0$f each foot and a 30G needle is passed into a vessel. Using an infusion pump, oils' contrast medium (ultrafluid lipiodolj is injected slowly and subsequently lodges in the sinuses of the pelvic and abdominal lymph nodes.

Small metastatic deposits in the nodes cause filling defects due to obliteration of the lymph node sinuses (Fig. 13.2) and large metastatic deposits produce larger filling defects and generalised enlargement- of the affected lymph nodes (Fig. 13.3). Malignant lymphoma produces generalised enlargement of the affected nodes with a 'foamy' or 'reticular' pattern of opacification (Fig. 13.4).
Lymphangiography occasionally demonstrates small metastases in para-aortic and iliac lymph nodes which appear normal on CT (Fig. 13.5) but, in gcnera], CT is more accurate.

FIg. 13.2 Lymphangiogram showing filling defect in an inguinal node Caused by metastatic melanoma,
FIg. 13.3 Lymphangiogram showing enlarged para-aortic nodes due to metastases from a testicular teratoma.
Fig. 13.4 Lymphsng,ogrsm show;no oeneralized enlargement of the left iliac lymph nodes (arrowed) due t. Hodgkin's lymphoms.
FIg. 13.5 Lymphangiogram showing small filling defect in a right external iliac

node (arrowed) due to metastatic carcinoma of the ovary. The CT scan was normal.

Isotope lymphangiography
Use of radiolabelled colloid is replacing lymphangiography for a functional assessment of the lymphatic system. The technique involves injecting radiolabelled colloid into the dorsum of the foot and screening the leg with a gamma camera. Clearance can then be assessed and used as a function of lymphatic efficiency.

Lymphoedema

Lymphoedema is caused by the accumulation of fluid in the extracellular, extravascular fluid compartment, and in the limbs it accumulates mainly in the sub-cutaneous tissues. *The physical sign of pitting* on pressure over the lower part of the tibia is present in *early* lymphoedema just as it is in oedema due to back pressure (venous oedema), or as a result of factors associated with right ventricular failure and also the several causes of low plasma proteins. With the passing of time, lymphoedema characteristically becomes *non pitting oederna,* the subcutaneous thickening with fibrous tissue being worsened by recurring low-grade lymphangitis and cellulitis. Lymphoedema can be congenital or acquired.

Congenital lymphoedema
The clinical classification of congenital lymphoedema (Milroy's disease) depends on the age of onset; *lymphoedema con genita* being present at birth, *lymphoedema praecox* presenting at puberty, and *lymphoedema tarda'* in adult life, but the condition is now commonly classified according to the findings at lymphangiography;
  Hypoplasia and aplasia are the commonest congenital abnormalities which result in lymphoedema.
The number of lymph vessels and nodes draining the affected limb is reduced, usually in the thigh where one or two vessels opacify instead of the usual five or more (Fig. 13.6). Hypoplasia sometimes affects the para-aortic and pelvic lymph vessels and nodes, but this is less common (Fig. 13.7). Lymphatic hypoplasia can be an incidental finding in patients being examined by pedal lymphangiography to stage malignant disease, and is probably much more common than actual clinical lymphoedema.

Fig. 13.6 Congenital lymphoedema of right leg due to lymphatic hypoplasia.

FIg. 13.7 Bipedal lymphangiogram showing aplasia of the right iliac nodes and vessels its a patient with lymphoedema of the right leg. The vessels below the inguinal ligament were normal.

Hypoplasia can be confidently diagnosed if a lymphatic vessel is cannulated and these abnormalities demonstrated, but it is sometimes impossible to find a lymphatic vessel in the subcutaneous tissues of the affected limb, and these patients are usually diagnosed as suffering from 'lymphatic aplasia'.

Retrograde obliteration. In patients with longstanding lymphoedema of presumed congenital origin, lvmphangiography may show that the main vessels are obstructed in the lower part of the limb, and this phenomenon is attributed to 'retrograde obliteration'

or 'die-back' of overloaded lymph vessels. This process probably contributes to the gradual increase in swelling which is such a common feature of lymphoedema.

Varicose lymphatics are a rare cause of congenital lymphoedema. The lymph vessels are dilated and tortuous and the condition is often associated with congenital arteriovenous fistulas.

Acquired lyrnphoederna (secondary lymphoederna)

This form of Ivmphoedema is usually due to obstruction and in such cases lvmphangiography shows obstruction to the main lymphatic vessels with 'dermal back flow' into the subcutaneous lymph vessels (Figs 13.8 and 13.9). The causes of obstructive lvmphoedema are:

• Trauma, e.g. removal of axillary lymphatics in radical mastectomy;
• Repeated acute infection, as in those who go about barefoot;
• Chronic *bacterial* infection, e.g. tuberculosis, fungus infection, and also chronic infection of the cervix, even uterus; also *parasitic* infestation, e.g. filariasis;
• Advanced malignant disease.

Fig. 13.8 Obstructive lymphoedema of the left arm secondary to radical mastectomy plus radiotherapy.
Fig 13 9 Obstructive iymphoedema of the right leg following radiothera,ay and a Wertheim's hysterectomy for carcinoma of the cervix

Again, prolonged lymphatic obstruction usually results in 'die-back' of the affected vessels, so that the site of the obstruction moves distally and this may account for the progressive nature of obstructive lymphoedema. The process is accelerated by soft-tissue infection and lymphangitis. In some patients with mild congenital lymphatic hypoplasia, lymphoedema is precipitated as a result of lymphangitis.

Differential diagnosis of lymphoedema. *Bilateral* oedema of the legs always requires an examination to exclude cardiac, renal and metabolic (hypoproteinaemia) causes. *Unilateral* lymphoedema may be confused with that caused by deep vein thrombosis, compression or stricture, particularly of the common iliac vein on the left side (Fig. 13.10) (Cockett). Operations to mohiise the aortic bifurcation, if causing compression, or to perform direct venous disobliteration or venoplasty are stilt under trial.

Fig. 13.10 Lymphoedema of the left leg due to compression of the left common iliac vein.

Treatment of lymphoedema
Palliative. For all attacks of inflammation, prolonged bedrest, elevation, and the appropriate antibiotic are important. Even in between attacks, the patient should sleep with the foot of the bed raised and may require the use of efficient elastic stocking pressure, e.g. Sigvaris®. Intermittent diuresis, induced by modern diuretic drugs, is also helpful. An intermittent limb compression pump can also be applied when available.

Surgery is reserved for those with severe disability. One of many surgical procedures is the removal of all the abnormal subcutaneous tissues and the covering of the exposed deeper tissues with a split skin graft (flaying operation). Another method is to bury the dermal part of the excess skin like a swiss-wIt cake along the whole length of the leg, so that the subdermal lymphatics may orientate themselves lengthwise and thereby assist drainage (Fig. 13.11). Other operations seeking to divert the lymph flow through the deep fascia by removing strips of it (Kondoleon's operation) or across the obstructed zone by a skin pedicle bridge, have failed, though a bridge of mesentry and iieum, bereft of mucosa, is being tried (Kinmonth) in early cases; otherwise it is difficult to reduce the great mass of subcutaneous tissue.

Fig. 13.11 Swiss roll operabon ~uned dwrnts, see text) *(N. Thompson).*

Venous lymphatic anastomoses (microsurgery). The treatment br anastomosis of dilated lymphatics to veins has proved partially successful. In those patients where lymphoedema follows either block dissection or radiotherapy to nodes, some improvement has been seen (O'Brien). The operation is not always predictable.

Chylous reflux
When lymphangtography reveals a backflow of milky chyle from the osterria chyli, with dilated lymphatics, resulting in cutaneous chylous vesicles and fistulas on the limbs, ligation and excision of the Iymphatics on the posterior abdominal wall may cure the reflux. though Iymphoedema persists.

Filariasis

Filariasis is a disease widely spread through tropical and subtropical countries.[1] It is due to a nematode worm, *Filaria sanguinis hominis,* which is transmitted by a mosquito **(Culex** *fatigans).* Once in the human body, the female worm finds its way to the lymphatics and lymph nodes (especially the inguinal group). It attains sexual maturity in 6—18 months and produces vast numbers of microfllariae, so that there may be 50 million in the blood at one time. These can be discovered microscopically in a *nocturnal* blood smear. Obstruction of the lymph vessels ensues and this is manifested in varicosities of the lymphatic vessels producing chylous ascites and hydroceles and, sometimes, chyluria and chylous flstulas on the scrotum and groins; and solid oedema (elephantiasis) (Fig. 13.12) often affecting the legs, scrotum and arms, though it may occur anywhere. The oedema does not seem to be obstructive in origin, as lymphangiography in these patients shows that the main vessels in the lower limbs are patent and that the para-aortic vessels are dilated (Fig. 13.13). The dilatation itself may be responsible for lymphoedema and chylous reflux by rendering the lymphatic valves incompetent (as with varicose veins) and allowing reflux from the main paraaortic vessels into the smaller vessels draining the subcutaneous and retroperitoneal tissues.

   Treatment. The best method of treatment known at present is diethylcarbamazine-citrate (Banocide~), which appears to sterilize or kill the adult female worm. Suramin may be used for persistent cases, but its use is restricted due to its nephrotoxicity. Prevention by antimosquito measures is, of course, vitally important. Elephantiasis may require surgery (see below).

Fig. 13.12 Lymphoedema (elephantiasis) due to fiariasis *(R.S. Naik).*
Fig. 13.13 Reflux from dilated nonobstructed para-aortic vessels into the left kidney in a patient with chyluria due to filariasis.

Lymphangioma

Capillary lymphangioma. Localised congenital anomalies may be composed of capillary-like lesions in the skin. They are brownish papules or wartlike ex crescences. On examination with a lens, small vesicles can be seen, which are lymphatic naevi.

Cavernous lymphangioma is often associated with the preceding variety, and Consists of masses of lymphatic cysts, particularly in the neck or axilla, the condition being termed a *cystic hygrorna* (Chapter 36). A similar lymphangiectatic condition may affect the lips (macrocheiia) or the tongue (macroglosia) producing sometimes gross soft-tissue enlargement.

Lymph Nodes

Acute inflammation
Lymph nodes draining an area where there is acute infection will also become inflamed (see above).

Chronic inflammation
This is either simple (pyogertic) or specific.

Chronic simple lymphadenitis is due to persistence of infection, such as occurs in recurrent tonsillitis or pediculosis capitis, and the cause should be treated.

Chronic specific lymphadenitis. **Tuberculous lymphadenitis** is common in children and young adults, particularly those who have been in contact with open human tuberculosis or who drink infected milk. It also occurs in the aged. The cervical lymph nodes are most often seen to be enlarged, but the remnants of disease may be observed in the mediastinal and mesenteric lymph nodes as speckled calcification on routine radio-graphs. Axi]lary lymph nodes may be involved by spread from the mediastinum.

Tubercle bacilli most commonly reach a lymph node by lymphatics, when tubercles first form in the cortex. Microscopically, endothelial cells and lymphocytes are in evidence. Giant cells are seen with many nuclei arranged round the periphery like a horseshoe.

The stages of infection show most clearly in the neck. From the tonsillar portal of entry the infection spreads by the lymphatics to the nearest lymph node. If the disease spreads, several lymph nodes are involved. They coalesce and break down to form caseous tubercu]ous pus, which may perforate the deep fascia and present as a fluctuant swelling on the surface (collar-stud abscess) (Fig. 13.14). This skin

gradually becomes indurated, breaks down, and forms a sinus which if ignored will remain unhealed for years. From each of these stages resolution may take place with calcification (if caseation has occurred), and with much scarring (if sinuses have formed).

The following treatment is required for tulerculous lymphadenitis.

• Attention to nutrition and general health.

• Tuberculous material is aspirated for culture and drug sensitivity tests. A specimen must be obtained before the antituberculous drugs are started.

• Antituberculotas drugs are given immediately after the aspiration (see Chapter 7).

• When the patient's condition begins to improve, breaking-down tuberculous lymph nodes must be removed, because the drugs will not reach the organisms in the avascular caseous material.

FIg. 13.14 A summary of the natural history ol tuberculous lymphadenitis.

Syphilitic adenitis. 'Shotty' lymph nodes in the groin associated with a genital chancre are characteristic. Those in the submandibular region draining a chancre of the lip are softer. During the secondary stage, a generalised enlargement of lymph nodes occurs. Especially noticeable are those above the internal epicondyles and along the posterior border of the sternomastoid.

Other infections.

Glandular fever (syn. infective mononudeosis) is an acute viral infection. After an Incubation period of 5—14 days. enlarged, elastic and slightly tender lymph nodes appear. associated with an irregular fever and often a sore throat, a rash, and splenic enlargement. The blood examination is diagnostic, revealing an absolute and relative lymphocytosis. and an unusual concentration of sheep-cell agglutinins (the heterophile antibody of the Paul— Bunnell reaction). The condition may be mistaken for acute leukaemia or lymphoma. Treatment is symptomatic, and recovery is the rule, although it may be some months before the lymph nodes return to normal. The patient is isolated in the early stages.

Toxoplasmosis. Toxoplasma gondii. a small, intracellular protozoan is liable to be transmitted from mammals to humans who eat raw or underdone meat which has not been previously frozen. The most tragic manifestation is neonatal jaundice and encephalomyelitis followed by hydrocephalus or microcephaly, blindness and intracerebra] calcification. Occasionally, the disease manifests itself in children and adults with enlarged lymph nodes and fever. A complement fixation test is necessary for diagnosis.

Cat-scratch fever is due to a virus of the lymphogranuloma— psittacosis group. Localised inflammation occurs at the site of the lesion, associated with fever,

malaise, and anorexia. This subsides in a few days, but from two to several weeks later the regional lymph nodes become enlarged. Suppuration often occurs, but the pus is sterile, and after evacuation the abscess subsides. Diagnosis is usually suggested by unilateral involvement of lymph nodes and the history of cat scratches. it is conflnned by a skin test with antigen prepared from human lymph node pus. This distinguishes the condition from chronic pyogenic or tuberculous adenitis with which it is often confused. Broad-spectrum antibiotics help only in reducing the fever.

GeneraUsed lymphadenopathy (in homosexualS) can be due to infection with HIV (AiDS, Chapter 7) and is now recorded in heterosexuals.

Lymphoma

Progressive diseases arise from lymphoreticular system: lymphomas, leukaemia, myeloma and polycythaemia rubra vera. The lymphomas arise from stem cell (B, T or histiocyte). They may start as slowly growing, well-differentiated lesions and then become rapidly growing and more primitive as time goes on ('drift back'). Lymphomas are subdivided into Hodgkin's & non-Hodgkin's lymphomas. Hodgkin's lymphoma has particular pleomorphic characteristics whereas non-Hodgkin's lymphoma features nodular (follicular) or diffuse lymphocytic, undifferentiated and histiocytic varieties.

Hodgkin's lymphoma:

Hodgkin's lymphoma is the commonest type of lymphoma and can occur wherever there is lymphoid tissue.

Pathology:

On macroscopic section the involved nodes are pink-grey in colour and of rubbery consistency. Except in the more anaplastic forms, the nodes are discrete with no periadenitis. The spleen, when involved, does not at first have the same homogeneous appearance as the lymph nodes, but as the disease advances the infiltration becomes more diffuse. Bone deposits occur in the vertebral column and pelvis. Rarely, Hodgkin's lymphoma may be confined to a single organ such as the stomach.

Histological **appearance** may vary with the stage of the disease but a striking feature is the cellular pleomorphism (Figs 13.15, 13.16 and 13.17).

Clinical features (Fig. 13.18 and Table 13.1). The disease is more common in males, and usually it affects young adults (age group 25-40 years).

The most common presentation is painless progressive lymph node enlargement in the cervical or supraclavicular region, which may or may not be associated with generalised symptoms such as malaise, fever, weight loss or pruritus. Pressure effects such as superior vena-caval obstruction from enlarged mediastinal lymph nodes may follow or even be the presenting feature. Bone pain, particularly in the back, may indicate vertebral collapse secondary to bony metastases. *A* recognised but unexplained symptom is pain in the sites of disease induced by drinking alcohol.

Fig. 13.15 Lymphocytic predominance (best prognosis).

Fig. **13.16** Section of whole lymph node showing nodular sclerosis (fair prognosis).

Fig. 13.17 Mixed cellularity. The normal nodal architecture is replaced by a cellular infiltration with lymphocytes, reticulum cells (histiocytes), eosinophils and fibrous tissue, and the characteristic Reed-Steinberg cells will be seen — a giant cell containing two large mirror-image nuclei which may overlap (like pennies on a plate). This type also carries a fair prognosis, but when there is lymphocyte depletion and a preponderance of reticulum cells Oristiocytes) the prognosis is poor.

Fig. 13.18 The position of Hodgkin's lymphoma when the patient was seen first, In 14 per cent of cases more than one region was involved

Table **13.1** The four stages of Hodgkin's lymphoma
Stage I   Confined to one lymph node site
Stage II   In more than one site either all above or all below
        the diaphragm
Stage Ill   Nodes involved above and below diaphragm
Stage IV   Spread beyond lymphatic node system. e.g. liver
        and bone

For subgroups A and B see text.

On examination, the involved nodes tend to be discrete, nontender and rubbery in consistency, as opposed to tuberculosis where the nodes are matted together. In late or lymphocyte depleted cases, however, the nodes may become matted. Splenomegaly and hepatomegaly is a variable accompaniment (see below). As the disease advances irregular elevations of the temperature may occur. (The periodic Pel-Ebstein fever, originally described as a feature of Hodgkin's disease, is a

mistake. This Pel-Ebstein fever was due to brucellosis.) With dissemination bony metastases, anaemia and pancytopenia may develop. There may also be skin deposits in advanced cases. Jaundice due to excessive haemolysis of red cells or diffuse liver involvement is also seen.

The course of the disease is very variable: death may follow in weeks but long-term survivals are not uncommon and with modern methods of treatment the disease may be cured.

The clinical staging of Hodgkin's lymphoma (Table 13.1). The clinical staging of Hodgkin's lymphoma is necessary to determine accurately the extent of the disease, the subsequent treatment and the prognosis. *Accurate staging may prevent unnecessary, unpleasant and dangerous treatments, e.g. cytotoxic drugs.*

The disease is subdivided into four stages (Table 13.1). Each stage is further subdivided into groups A or B according to the absence or presence of associated gerteralised symptoms such as weight loss, fever, pruritus, anaemia and bone pain.

Special investigations leading to dinical staging. The following procedures are currently in use.

• *Node excision biopsy* to establish the diagnosis and accurate histological grading. Biopsy can be achieved with a spring-loaded Trucut needle under imaging control. The specimen is large enough for histological study including the use of immune markers to categorise the disease accurately.

• *Chest radiography* to demonstrate enlarged mediastinal nodes and tomography where indicated.

• *Intravenous urography* may show distortion or compression of the renal calyces by retroperitoneal nodes.

• *Lower limb lymphangiography* will demonstrate both pelvic and retroperitoneal nodes. Unfortunately this investigation is associated with both false positive and false negative results, and is now rarely used.

• *Ultrasonography.*

• *Computed tomography.*

• *Laparotomy/splenectOmylliVer and node biopsy* are used less frequently to stage Hodgkin's lymphoma, because radiotherapy alone is used only for stage I disease and the accuracy of imaging for staging has improved.

The relationship between histological grade, clinical stage and survival. There are two clinical varieties of Hodgkin's lymphoma, a localized, predominantly nonaggressive form, and an aggressive, progressive and fatal variety. Between these two extremes there are intermediate or changing types of disease.

Histologically inactive disease is lymphocyte predominant, clinically stage I and potentially curable. Progressive disease is characterized histologically by diffuse

fibrosis, lymphocyte depletion and domination by histiocytes (reticulum cells). Clinically, it is seen in stage TuB and IV and is associated with systemic symptoms. Changing disease is characterised by mixed cellularity or nodular sclerosis in stage II or III disease. Nodular sclerosis in stage I disease, however, may be associated with a good prognosis.

Treatment policy for Hodgkin's lymphoma. There are two forms of treatment available according to the accurate staging of the disease, namely radiotherapy and combination chemotherapy. Both treatments are associated with bone marrow depression and toxic side effects and must be carefully planned and controlled with regular blood counts. Radiotherapy is the treatment of choice in stage I, whereas combination chemotherapy is used for the other stages.

Prognosis. This will vary according to the stage and histology, but the results are improving, with a better than 80 per cent cure in the good prognostic groups (see above).