CHAPTER 6

The lymphatic system

ANIMATIONS

The body cells are bathed in *interstitial (tissue) fluid*, which leaks constantly out of the bloodstream through the permeable walls of blood capillaries. It is therefore very similar in composition to blood plasma. Some tissue fluid returns to the capillaries at their venous end and the remainder diffuses through the more permeable walls of the lymph capillaries, forming *lymph*.

Lymph passes through vessels of increasing size and a varying number of *lymph nodes* before returning to the blood. The lymphatic system (Fig. 6.1) consists of:

- lymph
- lymph vessels
- lymph nodes
- lymph organs, e.g. spleen and thymus
- diffuse lymphoid tissue, e.g. tonsils
- bone marrow.

The first sections of this chapter explore the structures and functions of the organs listed above. In the final section, the consequences of disorders of the immune system are considered. The main effects of ageing on the lymphatic system relate to declining immunity, described in Chapter 15 (p. 384).

Functions of the lymphatic system

Tissue drainage

Every day, around 21 litres of fluid from plasma, carrying dissolved substances and some plasma protein, escape from the arterial end of the capillaries and into the tissues. Most of this fluid is returned directly to the bloodstream via the capillary at its venous end, but the excess, about 3–4 litres of fluid, is drained away by the lymphatic

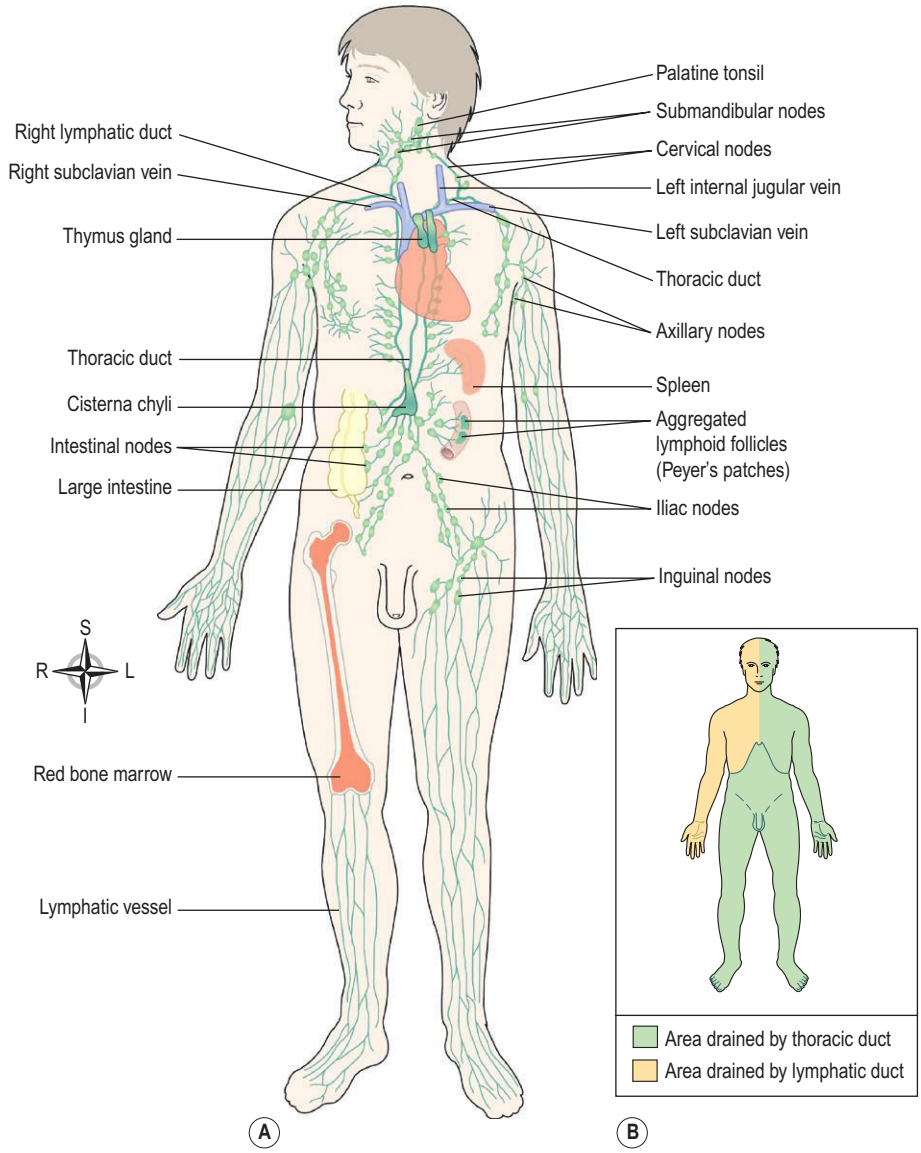

Figure 6.1 The lymphatic system. A. Major parts of the lymphatic system. **B.** Regional drainage of lymph.

vessels. Without this, the tissues would rapidly become waterlogged, and the cardiovascular system would begin to fail as the blood volume falls.

Absorption in the small intestine (Ch. 12)
Fat and fat-soluble materials, e.g. the fat-soluble vitamins, are absorbed into the central lacteals (lymphatic vessels) of the villi.

Immunity (Ch. 15)
The lymphatic organs are concerned with the production and maturation of lymphocytes, the white blood cells responsible for immunity. Bone marrow is therefore considered to be lymphatic tissue, since lymphocytes are produced there.

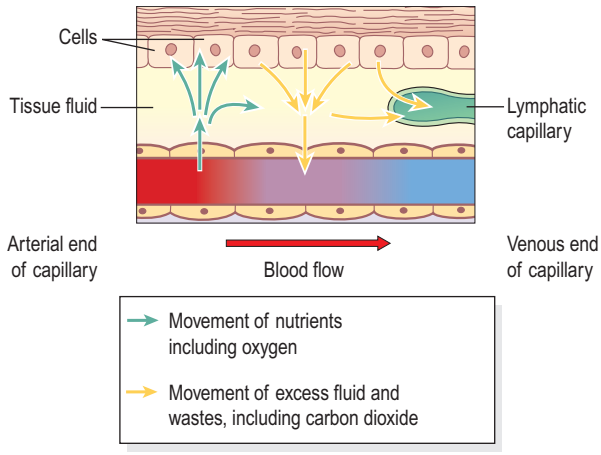

Figure 6.2 The origin of a lymph capillary.

Lymph and lymph vessels

Learning outcomes

After studying this section, you should be able to:

- describe the composition and the main functions of lymph 6.1
- identify the locations and functions of the main lymphatic vessels of the body.

Lymph

Lymph is a clear watery fluid, similar in composition to plasma, with the important exception of plasma proteins, and identical in composition to interstitial fluid. Lymph transports the plasma proteins that seep out of the capillary beds back to the bloodstream. It also carries away larger particles, e.g. bacteria and cell debris from damaged tissues, which can then be filtered out and destroyed by the lymph nodes. Lymph contains lymphocytes (defence cells, p. 380), which circulate in the lymphatic system allowing them to patrol the different regions of the body. In the lacteals of the small intestine, fats absorbed into the lymphatics give the lymph (now called *chyle*), a milky appearance.

Lymph capillaries

These originate as blind-end tubes in the interstitial spaces (Fig. 6.2). They have the same structure as blood capillaries, i.e. a single layer of endothelial cells, but their walls are more permeable to all interstitial fluid constituents, including proteins and cell debris. The tiny capillaries join up to form larger lymph vessels.

Nearly all tissues have a network of lymphatic vessels, important exceptions being the central nervous system, the cornea of the eye, the bones and the most superficial layers of the skin.

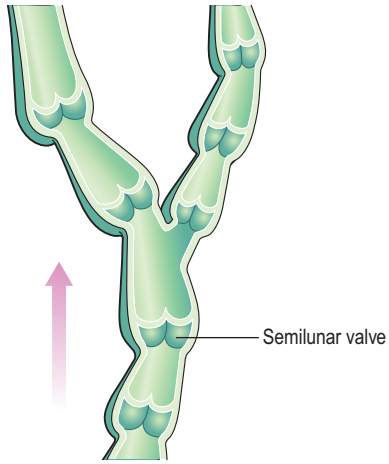

Figure 6.3 A lymph vessel cut open to show valves.

Larger lymph vessels

Lymph vessels are often found running alongside the arteries and veins serving the area. Their walls are about the same thickness as those of small veins and have the same layers of tissue, i.e. a fibrous covering, a middle layer of smooth muscle and elastic tissue and an inner lining of endothelium. Like veins, lymph vessels have numerous cup-shaped valves to ensure that lymph flows in a one-way system towards the thorax (Fig. 6.3). There is no 'pump', like the heart, involved in the onward movement of lymph, but the muscle layer in the walls of the large lymph vessels has an intrinsic ability to contract rhythmically (the lymphatic pump).

In addition, lymph vessels are compressed by activity in adjacent structures, such as contraction of muscles and the regular pulsation of large arteries. This 'milking' action on the lymph vessel wall helps to push lymph along.

Lymph vessels become larger as they join together, eventually forming two large ducts, the *thoracic duct* and *right lymphatic duct*, which empty lymph into the subclavian veins. 6.2

Thoracic duct

This duct begins at the *cisterna chyli*, which is a dilated lymph channel situated in front of the bodies of the first two lumbar vertebrae. The duct is about 40 cm long and opens into the left subclavian vein in the root of the neck. It drains lymph from both legs, the pelvic and abdominal cavities, the left half of the thorax, head and neck and the left arm (Fig. 6.1A and B).

Right lymphatic duct

This is a dilated lymph vessel about 1 cm long. It lies in the root of the neck and opens into the right subclavian vein. It drains lymph from the right half of the thorax, head and neck and the right arm (Fig. 6.1A and B).

Lymphatic organs and tissues

Learning outcomes

After studying this section, you should be able to:

- compare and contrast the structure and functions of a typical lymph node with that of the spleen
- describe the location, structure and function of the thymus gland
- describe the location, structure and function of mucosa-associated lymphatic tissue (MALT).

Lymph nodes 6.3

Lymph nodes are oval or bean-shaped organs that lie, often in groups, along the length of lymph vessels. The lymph drains through a number of nodes, usually 8–10, before returning to the venous circulation. These nodes vary considerably in size: some are as small as a pin head and the largest are about the size of an almond.

Structure

Lymph nodes (Fig. 6.4) have an outer capsule of fibrous tissue that dips down into the node substance forming partitions, or *trabeculae*. The main substance of the node consists of reticular and lymphatic tissue containing many lymphocytes and macrophages. Reticular cells produce the network of fibres that provide internal structure within the lymph node. The lymphatic tissue contains immune and defence cells, including lymphocytes and macrophages.

As many as four or five afferent lymph vessels may enter a lymph node while only one efferent vessel carries lymph away from the node. Each node has a concave surface called the hilum where an artery enters and a vein and the efferent lymph vessel leave.

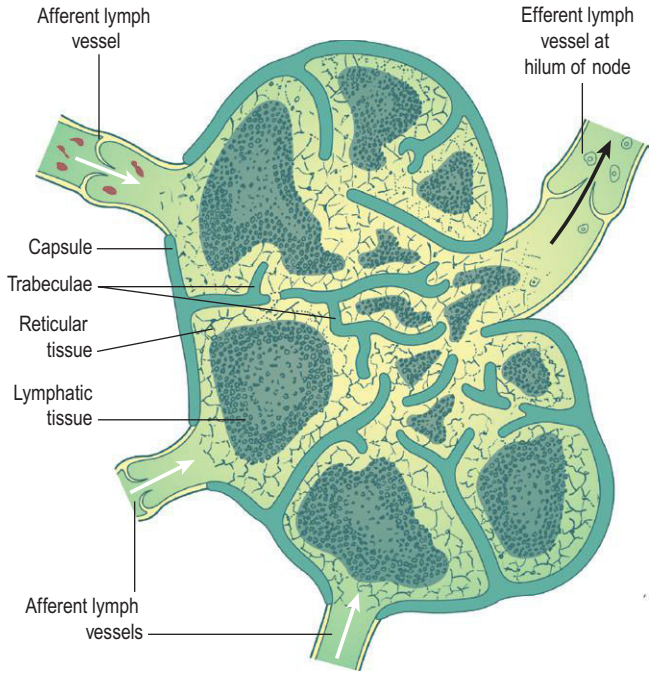

Figure 6.4 Section through a lymph node. Arrows indicate the direction of lymph flow.

The large numbers of lymph nodes situated in strategic positions throughout the body are arranged in deep and superficial groups.

Lymph from the head and neck passes through deep and superficial *cervical nodes* (Fig. 6.5).

Lymph from the upper limbs passes through nodes situated in the elbow region, then through the deep and superficial *axillary nodes*.

Lymph from organs and tissues in the thoracic cavity drains through groups of nodes situated close to the mediastinum, large airways, oesophagus and chest wall. Most of the lymph from the breast passes through the axillary nodes.

Lymph from the pelvic and abdominal cavities passes through many lymph nodes before entering the cisterna chyli. The abdominal and pelvic nodes are situated mainly in association with the blood vessels supplying the organs and close to the main arteries, i.e. the aorta and the external and internal iliac arteries.

The lymph from the lower limbs drains through deep and superficial nodes including groups of nodes behind the knee and in the groin (inguinal nodes).

Functions

Filtering and phagocytosis

Lymph is filtered by the reticular and lymphatic tissue as it passes through lymph nodes. Particulate matter may

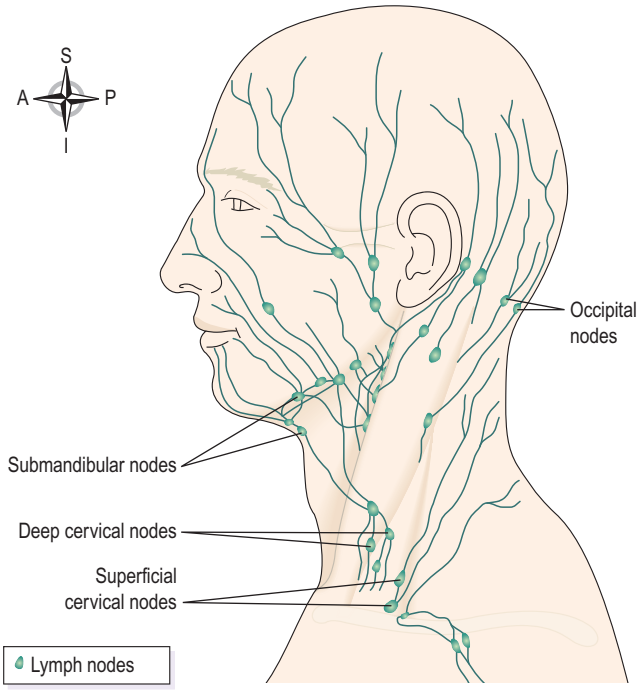

Figure 6.5 Some lymph nodes of the face and neck.

include bacteria, dead and live phagocytes containing ingested microbes, cells from malignant tumours, worn-out and damaged tissue cells and inhaled particles. Organic material is destroyed in lymph nodes by macrophages and antibodies. Some inorganic inhaled particles cannot be destroyed by phagocytosis. These remain inside the macrophages, either causing no damage or killing the cell. Material not filtered out and dealt with in one lymph node passes on to successive nodes and by the time lymph enters the blood it has usually been cleared of foreign matter and cell debris. In some cases where phagocytosis of bacteria is incomplete they may stimulate inflammation and enlargement of the node (*lymphadenopathy*).

Proliferation of lymphocytes

Activated T- and B-lymphocytes multiply in lymph nodes. Antibodies produced by sensitised B-lymphocytes enter lymph and blood draining the node.

Figure 6.6 shows a scanning electron micrograph of lymph node tissue, with reticular cells, white blood cells and macrophages.

Spleen 6.4

The spleen (Figs 6.7 and 4.13) contains reticular and lymphatic tissue and is the largest lymph organ.

The spleen lies in the left hypochondriac region of the abdominal cavity between the fundus of the stomach and the diaphragm. It is purplish in colour and varies in size in different individuals, but is usually about 12 cm long, 7 cm wide and 2.5 cm thick. It weighs about 200 g.

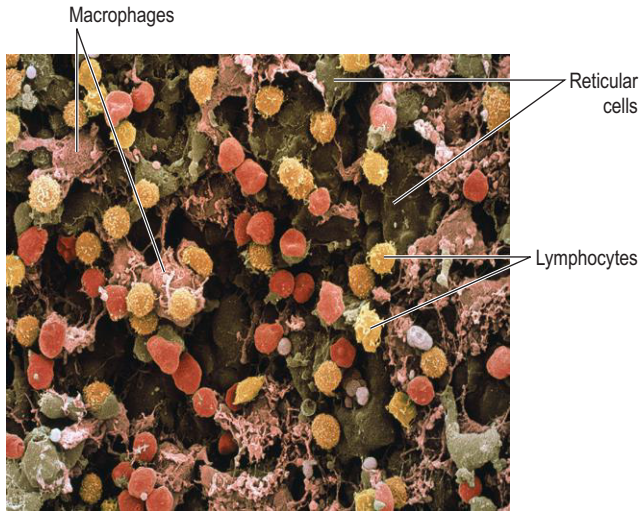

Figure 6.6 Colour scanning electron micrograph of lymph node tissue. Cell population includes reticular cells (brown), macrophages (pink) and lymphocytes (yellow).

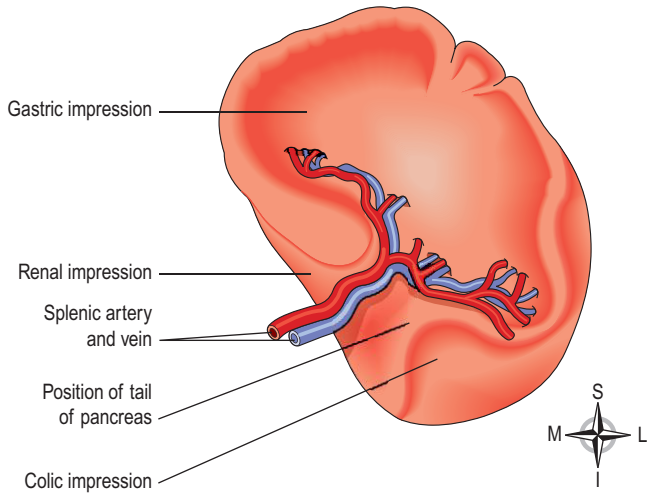

Figure 6.7 The spleen.

Organs associated with the spleen

Superiorly and posteriorly	– diaphragm
Inferiorly	– left colic flexure of the large intestine
Anteriorly	– fundus of the stomach
Medially	– pancreas and the left kidney
Laterally	– separated from the 9th, 10th and 11th ribs and the intercostal muscles by the diaphragm

Structure (Fig. 6.8)

The spleen is slightly oval in shape with the hilum on the lower medial border. The anterior surface is covered with peritoneum. It is enclosed in a fibroelastic capsule that dips into the organ, forming trabeculae. The cellular

material, consisting of lymphocytes and macrophages, is called *splenic pulp*, and lies between the trabeculae. *Red pulp* is the part suffused with blood and *white pulp* consists of areas of lymphatic tissue where there are sleeves of lymphocytes and macrophages around blood vessels.

The structures entering and leaving the spleen at the hilum are:

- splenic artery, a branch of the coeliac artery
- splenic vein, a branch of the portal vein
- lymph vessels (efferent only)
- nerves.

Blood passing through the spleen flows in sinusoids (p. 83), which have distinct pores between the endothelial cells, allowing it to come into close association with splenic pulp. This is essential for the spleen's function in removing ageing or damaged cells from the bloodstream.

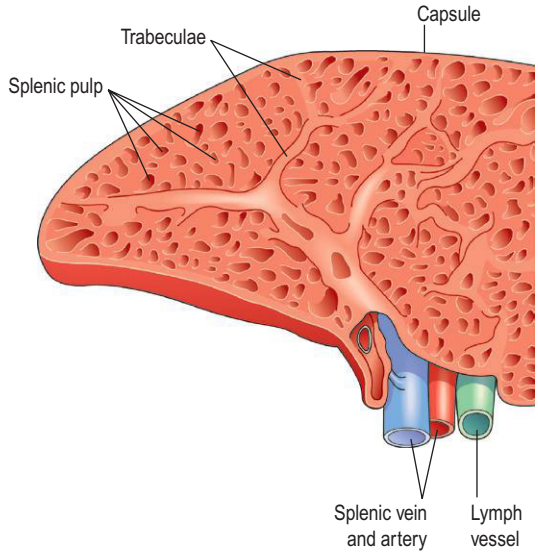

Figure 6.8 A section through the spleen.

Functions

Phagocytosis

As described previously (p. 68), old and abnormal erythrocytes are mainly destroyed in the spleen, and the breakdown products, bilirubin (Fig. 12.37) and iron, are transported to the liver via the splenic and portal veins. Other cellular material, e.g. leukocytes, platelets and bacteria, is phagocytosed in the spleen.

Unlike lymph nodes, the spleen has no afferent lymphatics entering it, so it is not exposed to diseases spread by lymph.

Storage of blood

The spleen contains up to 350 mL of blood, and in response to sympathetic stimulation can rapidly return most of this volume to the circulation, e.g. in haemorrhage.

Immune response

The spleen contains T- and B-lymphocytes, which are activated by the presence of antigens, e.g. in infection. Lymphocyte proliferation during serious infection can cause enlargement of the spleen (*splenomegaly*).

Erythropoiesis

The spleen and liver are important sites of fetal blood cell production, and the spleen can also fulfil this function in adults in times of great need.

Thymus gland 6.5

The thymus gland lies in the upper part of the mediastinum behind the sternum and extends upwards into the root of the neck (Fig. 6.9). It weighs about 10 to 15 g at birth and grows until puberty, when it begins to atrophy. Its maximum weight, at puberty, is between 30 and 40 g and by middle age it has returned to approximately its weight at birth.

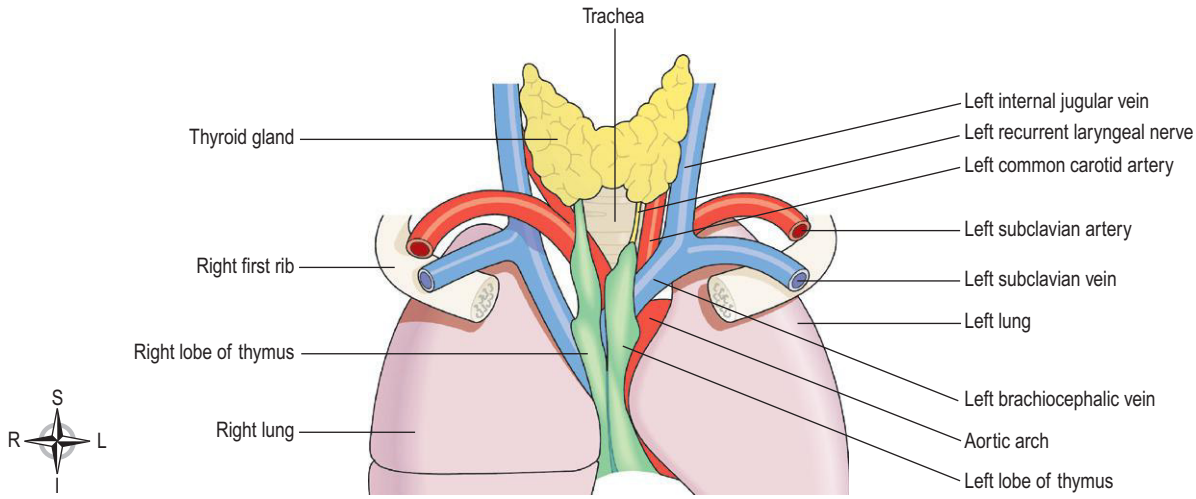

Figure 6.9 The thymus gland in the adult, and related structures.

Organs associated with the thymus

Anteriorly – sternum and upper four costal cartilages
Posteriorly – aortic arch and its branches, brachiocephalic veins, trachea
Laterally – lungs
Superiorly – structures in the root of the neck
Inferiorly – heart

Structure

The thymus consists of two lobes joined by areolar tissue. The lobes are enclosed by a fibrous capsule which dips into their substance, dividing them into lobules that consist of an irregular branching framework of epithelial cells and lymphocytes.

Function

Lymphocytes originate from stem cells in red bone marrow (p. 64). Those that enter the thymus develop into activated T-lymphocytes (p. 380).

Thymic processing produces mature T-lymphocytes that can distinguish 'self' tissue from foreign tissue, and also provides each T-lymphocyte with the ability to react to only one specific antigen from the millions it will encounter (p. 380). T-lymphocytes then leave the thymus and enter the blood. Some enter lymphoid tissues and others circulate in the bloodstream. T-lymphocyte production, although most prolific in youth, probably continues throughout life from a resident population of thymic stem cells.

The maturation of the thymus and other lymphoid tissue is stimulated by *thymosin*, a hormone secreted by the epithelial cells that form the framework of the thymus gland. Shrinking of the gland begins in adolescence and, with increasing age, the effectiveness of the T-lymphocyte response to antigens declines.

Mucosa-associated lymphoid tissue (MALT)

Throughout the body, at strategically placed locations, are collections of lymphoid tissue which, unlike the spleen and thymus, are not enclosed within a capsule. They contain B- and T-lymphocytes, which have migrated from bone marrow and the thymus, and are important in the early detection of invaders. However, as they have no afferent lymphatic vessels, they do not filter lymph, and are therefore not exposed to diseases spread by lymph. MALT is found throughout the gastrointestinal tract, in the respiratory tract and in the genitourinary tract, all systems of the body exposed to the external environment.

The main groups of MALT are the tonsils and aggregated lymphoid follicles (Peyer's patches).

Tonsils. These are located in the mouth and throat, and will therefore destroy swallowed and inhaled antigens (see also p. 245).

Aggregated lymphoid follicles (Peyer's patches). These large collections of lymphoid tissue are found in the small intestine, and intercept swallowed antigens (Fig. 12.25).

Lymph vessel pathology

Learning outcomes

After studying this section, you should be able to:

- explain the role of lymphatic vessels in the spread of infectious and malignant disease
- discuss the main causes and consequences of lymphatic obstruction.

The main involvements of lymph vessels are in relation to the spread of disease in the body, and the effects of lymphatic obstruction. Table 6.1 defines some common terms used when describing lymphatic system pathology.

Spread of disease

The materials most commonly spread via the lymph vessels from their original site to the circulating blood are fragments of tumours and infected material.

Malignant disease

Malignant tumours shed cells into the surrounding interstitial fluid, which drains into local lymphatic vessels and carries the tumour cells to the nearest set of lymph nodes. Here, if tumour cells arrive in sufficient numbers, they can establish secondary growths (metastases). From local lymph nodes, the tumour usually spreads to further lymph nodes and/or via the bloodstream to distant organs.

Infection

Infectious material may enter lymph vessels from infected tissues. If phagocytosis is not effective the infection may spread from node to node, and eventually reach the bloodstream.

Lymphangitis. This occurs in some acute bacterial infections in which the microbes in the lymph draining from the area infect and spread along the walls of lymph vessels, e.g. in acute *Streptococcus pyogenes* infection of the hand, a red line may be seen extending from the hand to the axilla. This is caused by an inflamed superficial lymph vessel and adjacent tissues. The infection may be stopped at the first lymph node or spread through the lymph drainage network to the blood.

Lymphatic obstruction

When a lymph vessel is obstructed, lymph accumulates distal to the obstruction (*lymphoedema*). The amount of resultant swelling and the size of the area affected depend on the size of the vessel involved. Lymphoedema usually leads to low-grade inflammation and fibrosis of the lymph vessel and further lymphoedema. The most common causes are tumours and following surgical removal of lymph nodes.

Tumours

A tumour may grow into, and block, a lymph vessel or node, obstructing the flow of lymph. A large tumour outside the lymphatic system may also cause sufficient pressure to stop the flow of lymph.

Surgery

In some surgical procedures lymph nodes are removed because cancer cells may have already spread to them. This aims to prevent growth of secondary tumours in local lymph nodes and further spread of the disease via the lymphatic system, e.g. axillary nodes may be removed during mastectomy (breast removal), but it can lead to obstruction of lymph drainage.

Table 6.1 Common terms used in lymphatic system pathology

Term	Definition
Lymphangitis	Inflammation of lymph vessels
Lymphadenitis	Infection of lymph nodes
Lymphadenopathy	Enlargement of lymph nodes
Splenomegaly	Enlargement of the spleen
Lymphoedema	Swelling in tissues whose lymphatic drainage has been obstructed in some way

Diseases of lymph nodes

Learning outcomes

After studying this section, you should be able to:

- describe the term lymphadenitis, listing its primary causes
- describe the effects of the two main forms of lymphoma
- explain why secondary disease of the lymph nodes is commonly found in individuals with cancer.

Lymphadenitis

Acute lymphadenitis (acute infection of lymph nodes) is usually caused by microbes transported in lymph from other areas of infection. The nodes become inflamed, enlarged and congested with blood, and chemotaxis attracts large numbers of phagocytes. If lymph node defences (phagocytes and antibody production) are overwhelmed, the infection can cause abscess formation within the node. Adjacent tissues may become involved, and infected materials transported through other nodes and into the blood.

Acute lymphadenitis is secondary to a number of conditions.

Infectious mononucleosis (glandular fever)

This is a highly contagious viral infection, usually of young adults, spread by direct contact. During the incubation period of 7–10 days, viruses multiply in the epithelial cells of the pharynx. They subsequently spread to cervical lymph nodes, then to lymphoid tissue throughout the body.

Clinical features include tonsillitis, lymphadenopathy and splenomegaly. A common complication is myalgic encephalitis (chronic fatigue syndrome, p. 185). Clinical or subclinical infection confers lifelong immunity.

Other diseases

Minor lymphadenitis accompanies many infections and indicates the mobilisation of normal protective mechanisms, e.g. proliferation of defence cells. More serious infection occurs in, e.g. measles, typhoid and cat-scratch fever, and wound or skin infections. Chronic lymphadenitis occurs following unresolved acute infections, in tuberculosis, syphilis and some low-grade infections.

Lymphomas

These are malignant tumours of lymphoid tissue and are classified as either Hodgkin's or non-Hodgkin's lymphomas.

Hodgkin's disease

In this disease there is progressive, painless enlargement of lymph nodes throughout the body, as lymphoid tissue within them proliferates. The superficial lymph nodes in the neck are often the first to be noticed. The disease is malignant and the cause is unknown. The prognosis varies considerably but the pattern of spread is predictable because the disease spreads to adjacent nodes and to other tissues in a consistent way. The effectiveness of treatment depends largely on the stage of the disease at which it begins. The disease leads to reduced immunity, because lymphocyte function is depressed, and recurrent infection is therefore common. As lymph nodes enlarge, they may compress adjacent tissues and organs. Anaemia and changes in leukocyte numbers occur if the bone marrow is involved.

Non-Hodgkin's lymphoma (NHL)

NHL is associated with immunodeficiency states and certain viral infections including HIV (p. 386). NHL includes *multiple myeloma* and *Burkitt's lymphoma* and may occur in any lymphoid tissue or in bone marrow. They are classified according to the type of cell involved and the degree of malignancy, i.e. low, intermediate or high grade. Low-grade tumours consist of well-differentiated cells and slow progress of the disease, death occurring after a period of years. High-grade lymphomas consist of poorly differentiated cells and rapid progress of the disease, death occurring in weeks or months. Some low- or intermediate-grade tumours change their status to high grade with increased rate of progress.

The expanding lymph nodes may compress adjacent tissues and organs. Immunological deficiency leads to increased incidence of infections, and if the bone marrow or spleen (or both) is involved there may be varying degrees of anaemia and leukopenia.

Disorders of the spleen

Learning outcome

After studying this section, you should be able to:

- identify the main causes of splenomegaly.

Splenomegaly

This is enlargement of the spleen, and is usually secondary to other conditions, e.g. infections, circulatory disorders, blood diseases, malignant neoplasms.

Infections

The spleen may be infected by blood-borne microbes or by local spread of infection. The red pulp becomes congested with blood and there is an accumulation of phagocytes and plasma cells. Acute infections are rare.

Chronic infections. Some chronic non-pyogenic infections cause splenomegaly, but this is usually less severe than in the case of acute infections. The most commonly occurring primary infections include:

- tuberculosis (p. 268)
- typhoid fever (p. 325)
- malaria
- infectious mononucleosis (see above).

Circulatory disorders

Splenomegaly due to congestion of blood occurs when the flow of blood through the liver is impeded by, e.g.,

fibrosis in liver cirrhosis, or portal venous congestion in right-sided heart failure.

Blood disease

Splenomegaly may be caused by blood disorders. The spleen enlarges to deal with the extra workload associated with removing damaged, worn out and abnormal blood cells in, e.g., haemolytic and macrocytic anaemia, polycythaemia and chronic myeloid leukaemia (Ch. 4).

Splenomegaly may itself cause blood disorders. When the spleen is enlarged for any reason, especially in portal hypertension, excessive and premature haemolysis of red cells or phagocytosis of normal white cells and platelets leads to marked anaemia, leukopenia and thrombocytopenia.

Tumours

Benign and primary malignant tumours of the spleen are rare but blood-spread tumour fragments from elsewhere in the body may cause metastases. Splenomegaly caused by infiltration of malignant cells is characteristic of some conditions, especially chronic leukaemia, Hodgkin's disease and non-Hodgkin's lymphoma.

Diseases of the thymus gland

Learning outcome

After studying this section, you should be able to:

- describe the principal disorders of the thymus gland.

Enlargement of the gland is associated with some autoimmune diseases, such as thyrotoxicosis and Addison's disease.

Tumours are rare, although pressure caused by enlargement of the gland may damage or interfere with the functions of adjacent structures, e.g. the trachea, oesophagus or veins in the neck.

In myasthenia gravis (p. 435), most patients have either thymic hyperplasia (the majority) or thymoma (a minority), although the role of thymic function in this disorder is not understood.

For a range of self-assessment exercises on the topics in this chapter, visit Evolve online resources: https://evolve.elsevier.com/Waugh/anatomy/