6 The lymphatic system

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All body tissues are bathed in tissue fluid, consisting of the diffusible constituents of blood and waste materials from cells. Some tissue fluid returns to the capillaries at their venous end and the remainder diffuses through the more permeable walls of the lymph capillaries and becomes 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.

Functions of the lymphatic system include the following.

- *Tissue drainage.* Every day, around 21 litres of plasma fluid, 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 3–4 litres of fluid are drained away by the lymphatic vessels. Without this, the tissues would rapidly become waterlogged, and the cardiovascular system would begin to fail as the blood volume falls.

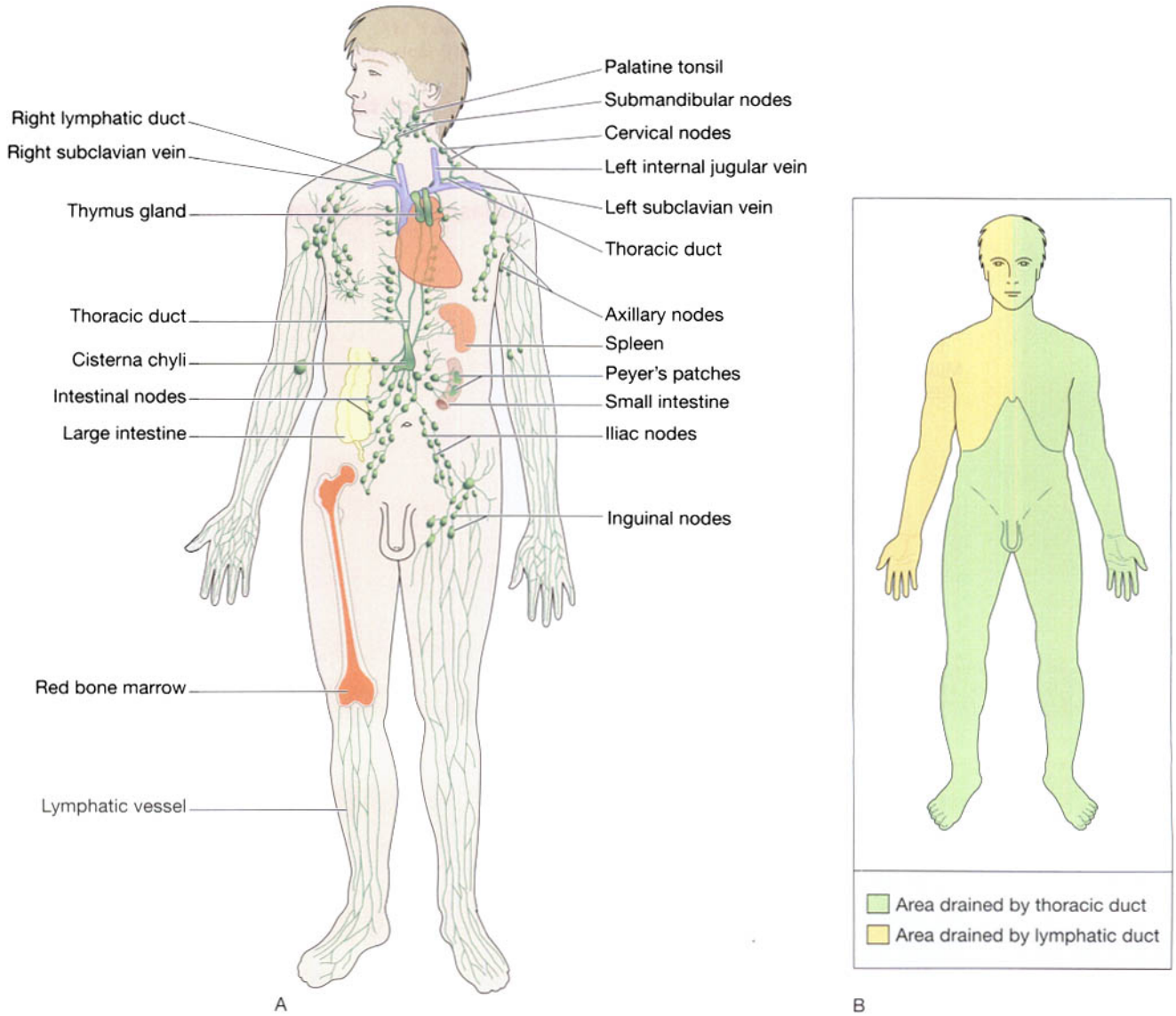


Figure 6.1 A. The lymphatic system. B. Lymph drainage. Green area drained by the thoracic duct; gold area drained by the right lymphatic duct.

- *Absorption in the small intestine.* Fat and fat-soluble materials, e.g. the fat-soluble vitamins, are absorbed into the central lacteals (lymphatic vessels) of the villi.
- *Immunity.* The lymphatic organs are concerned with the production and maturation of lymphocytes, the white blood cells that are primarily responsible for provision of immunity. Bone marrow is therefore considered to be lymphatic tissue, since lymphocytes are produced there.

LYMPH

Learning outcome

After studying this section, you should be able to:

- describe the composition and the main functions of 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, 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 VESSELS

Learning outcome

After studying this section, you should be able to:

- identify the locations and functions of the main lymphatic vessels of the body.

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.

All tissues of the body have a network of lymphatic vessels, with the exception of the central nervous system, the bones and the most superficial layers of the skin.

Larger lymph vessels

The walls of lymph vessels 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. Lymph vessels have numerous cup-shaped valves which ensure that lymph flows in one way only, i.e. towards the thorax (Fig. 6.3). There is no 'pump', like the heart, involved in the onward movement of lymph but the muscle tissue in the walls of the large lymph vessels has an intrinsic ability to contract rhythmically (the lymphatic pump).

In addition, any structure that periodically compresses the lymphatic vessels can assist in the movement of lymph along the vessels, commonly including the contraction of adjacent muscles and the pulsation of large arteries.

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

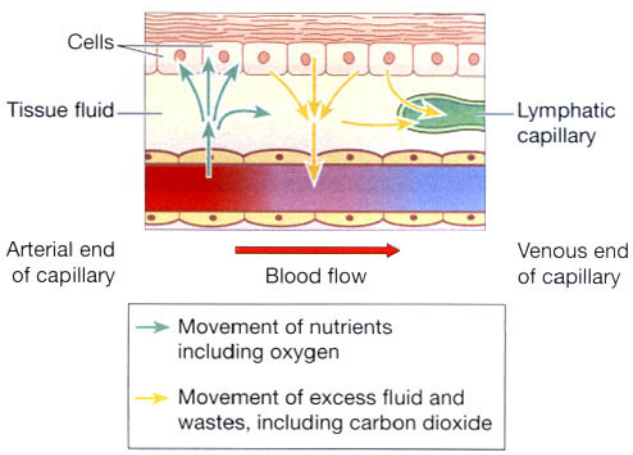


Figure 6.2 The origin of a lymph capillary.

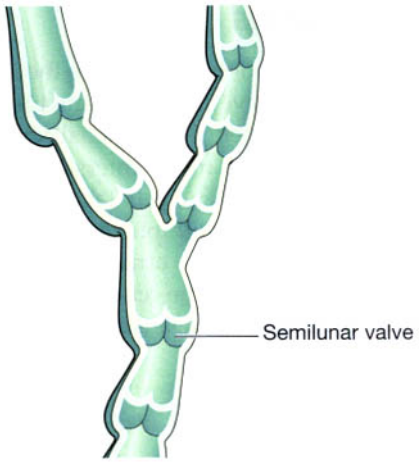


Figure 6.3 A lymph vessel cut open to show valves.

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).

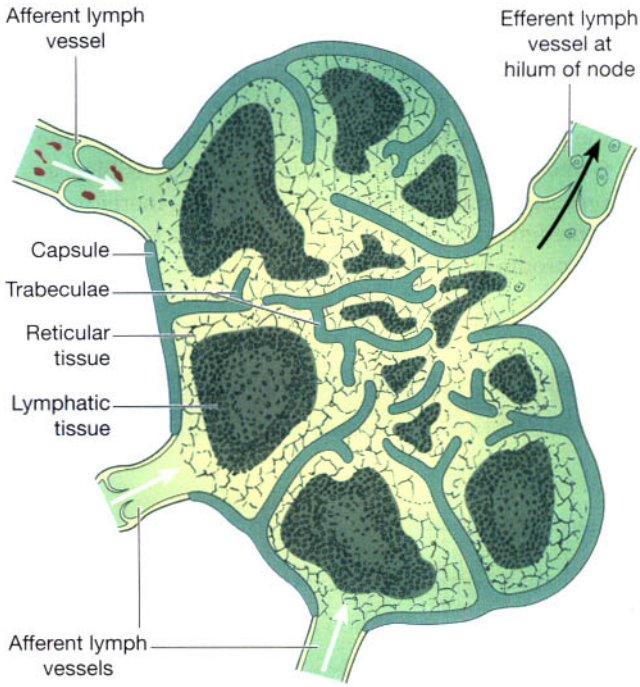


Figure 6.4 Section of a lymph node. Arrows indicate the direction of lymph flow.

Lymph nodes

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 to 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 of lymph nodes

Lymph nodes (Fig. 6.4) have an outer capsule of fibrous tissue which 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.

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.

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).

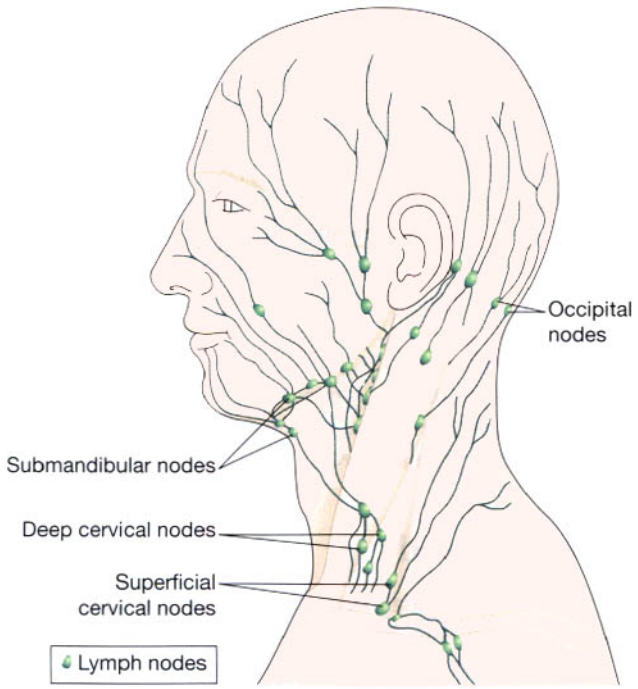


Figure 6.5 Some lymph nodes of the face and neck.

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 that are 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 of lymph nodes

Filtering and phagocytosis

Lymph is filtered by the reticular and lymphoid tissue as it passes through lymph nodes. Particulate matter may include microbes, 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

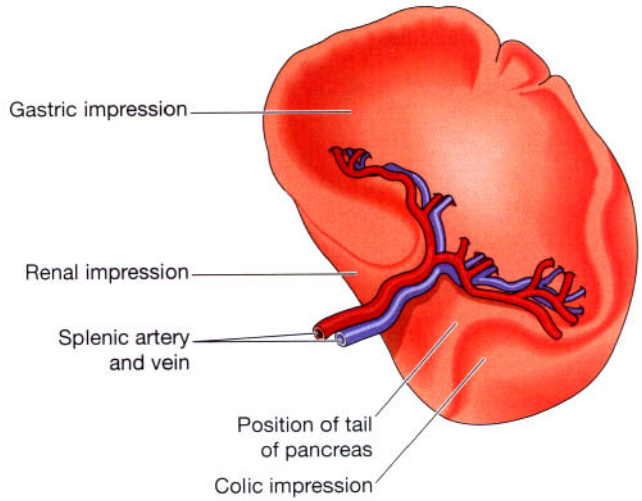


Figure 6.6 The spleen.

remain inside the macrophages, either causing no damage or killing the cell. Material not filtered off 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 microbes 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.

Spleen

The spleen (Fig. 6.6) is formed by 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.

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

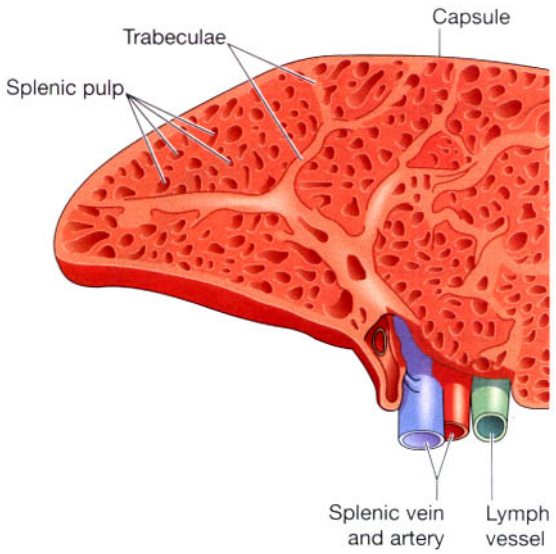


Figure 6.7 A section of the spleen.

Structure (Fig. 6.7)

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 it 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 sinuses which have distinct pores between the endothelial cells, allowing it to come into close association with splenic pulp.

Functions

Phagocytosis

As described previously (p. 64), old and abnormal erythrocytes are destroyed in the spleen and the breakdown products, bilirubin and iron, are passed to the liver via the splenic and portal veins. Other cellular material, e.g. leukocytes, platelets and microbes, are 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 a large part 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

The thymus gland lies in the upper part of the mediastinum behind the sternum and extends upwards into the root of the neck (Fig. 6.8). It weighs about 10 to 15 g at birth and grows until the individual reaches 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.

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 pluripotent stem cells in red bone marrow. Those that enter the thymus develop into activated T-lymphocytes (p. 379).

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

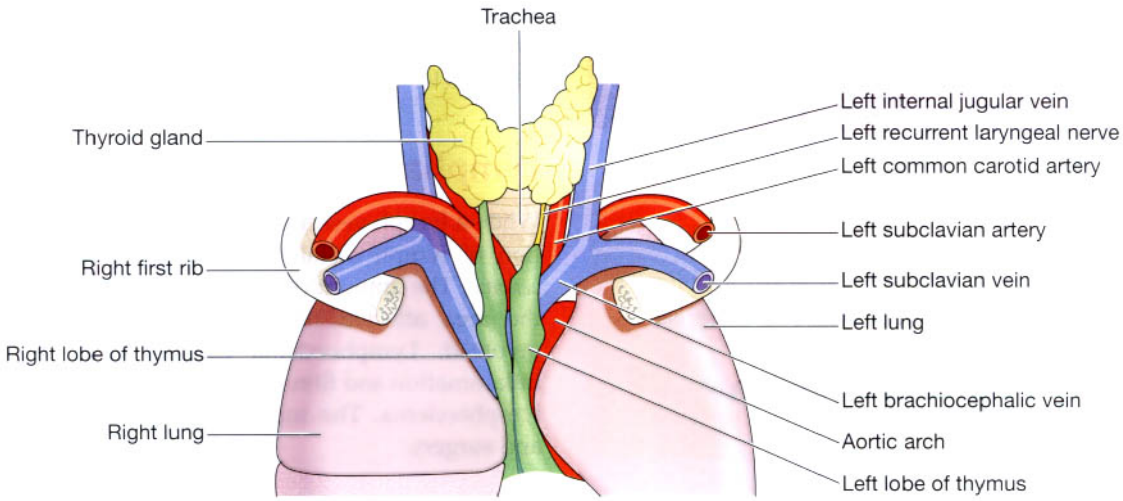


Figure 6.8 The thymus gland in the adult, and related structures.

encounter (p. 374). 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, continues probably 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. Involution 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 in 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 Peyer's patches.

Tonsils. These are located in the mouth and throat, and will therefore destroy swallowed and inhaled antigens (see also p. 243).

Peyer's patches. These large collections of lymphoid tissue are found in the small intestine, and intercept swallowed antigens.

PATHOLOGY ASSOCIATED WITH LYMPH VESSELS

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
- the effects of lymphatic obstruction.

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.

Fragments of tumours

Tumour cells may enter a lymph capillary draining a tumour, or a larger vessel when a tumour has eroded its wall. Cells from a malignant tumour, if not phagocytosed, settle and multiply in the first lymph node they encounter. Later, there may be further spread to other lymph nodes, to the blood and to other parts of the body via the blood. In this sequence of events, each new metastatic tumour becomes a source of malignant cells that may spread by the same routes.

Infected material

Infected material may enter lymph vessels either at their origin in the interstitial spaces, or through the walls of larger vessels invaded by microbes when infection spreads locally. If phagocytosis is not effective the infection may spread from node to node, and eventually reach the bloodstream.

Lymphangitis (infection of lymph vessel walls). This occurs in some acute pyogenic 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 there is an accumulation of lymph distal to the obstruction, called *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 surgery.

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 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 is done 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.

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 on the body
- explain why secondary disease of the lymph nodes in 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 may cause abscess formation within the node. Adjacent tissues may become involved, and infected materials may be 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 to 10 days, viruses multiply in the epithelial cells of the pharynx. They subsequently spread to cervical 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. 184). Clinical or subclinical infection confers life-long immunity.

Other diseases

Minor lymphadenitis accompanies many infections and indicates the mobilisation of normal protective resources. More serious infection occurs in:

- measles
- anthrax
- typhoid fever
- wound and skin infections
- cat-scratch fever.

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 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 rate of progress 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 lymphomas

These tumours, e.g. *multiple myeloma* and *Burkitt's lymphoma*, may occur in any lymphoid tissue and 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 and/or spleen is involved there may be varying degrees of anaemia and leukopenia.

Malignant neoplastic metastases

Metastatic tumours develop in lymph nodes in any part of the body. Lymph from a tumour may contain cancer cells that are filtered off by the lymph nodes. If not phagocytosed they multiply, forming metastatic tumours. Nodes nearest the primary tumour are affected first but there may be further spread through the sequence of nodes, eventually reaching the bloodstream.

DISORDERS OF THE SPLEEN

Learning outcome

After studying this section, you should be able to:

- identify the main causes of splenomegaly.

Splenomegaly (enlargement of the spleen)

Enlargement of the spleen 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
- typhoid fever
- malaria
- brucellosis (undulant fever)
- infectious mononucleosis.

Circulatory disorders

Splenomegaly due to congestion of blood occurs when the flow of blood through the liver is impeded by, e.g., fibrosis in cirrhosis of liver, portal venous congestion in right-sided heart failure.

Blood diseases

Splenomegaly may be caused by blood diseases. 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.

Splenomegaly may cause blood disease. 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 metastatic tumours. Splenomegaly caused by infiltration of malignant cells is characteristic of some conditions, especially chronic leukaemia, Hodgkin's disease and non-Hodgkin 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. Autoimmune conditions are those in which the immune system treats normal body cells or secretions as antigens and destroys them (p. 385).

Tumours are rare and seldom metastasise. 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, an autoimmune disease in which there is skeletal muscle weakness (p. 385), most patients have either thymic hyperplasia (majority) or thymoma (minority).

7 The nervous system

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The nervous system detects and responds to changes inside and outside the body. Together with the endocrine system it controls important aspects of body function and maintains homeostasis. Nervous system stimulation provides an immediate response while endocrine activity is, in the main, slower and more prolonged (Ch. 8).

The nervous system consists of the brain, the spinal cord and peripheral nerves. Organisation of nervous tissue within the body enables rapid communication between different parts of the body.

Response to changes in the internal environment maintains homeostasis and regulates involuntary functions, e.g. blood pressure and digestive activity. Response to changes in the external environment maintains posture and other voluntary activities.

For descriptive purposes the parts of the nervous system are grouped as follows:

- *the central nervous system* (CNS), consisting of the brain and the spinal cord
- *the peripheral nervous system* (PNS) consisting of all the nerves outside the brain and spinal cord.

The PNS comprises paired cranial and sacral nerves – some of these are sensory (afferent), some are motor (efferent) and some mixed. It is useful to consider two functional parts within the PNS:

- the sensory division
- the motor division (Fig. 7.1).

In turn the motor division is involved in activities that are:

- *voluntary* – the somatic nervous system (movement of voluntary muscles)
- *involuntary* – the autonomic nervous system (functioning of smooth and cardiac muscle and glands). The autonomic nervous system has two parts: *sympathetic* and *parasympathetic*.

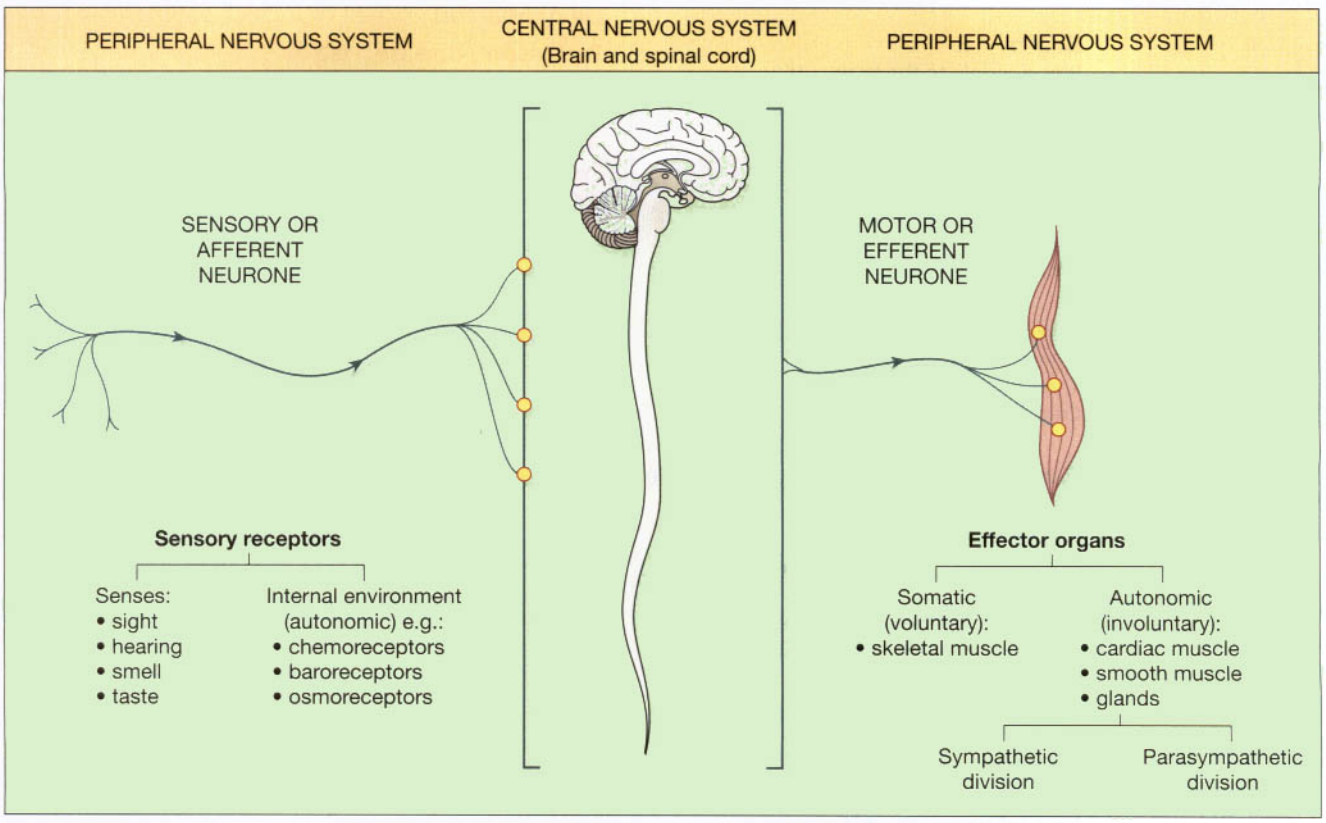


Figure 7.1 Functional components of the nervous system.

NEURONES

Learning outcomes

After studying this section you should be able to:

- describe the structure of a myelinated neurone
- compare and contrast the transmission of impulses in myelinated and unmyelinated neurones
- state the functions of sensory and motor nerves
- describe the events that occur following release of a neurotransmitter at a synapse
- identify the common neurotransmitters in the peripheral nervous system.

The nervous system consists of a vast number of cells called *neurones* (Fig. 7.2), supported by a special type of connective tissue, *neuroglia*. Each neurone consists of a *cell body* and its processes, one *axon* and many *dendrites*. Neurones are commonly referred to simply as nerve cells. Bundles of axons bound together are called *nerves*. Neurones cannot divide and for survival they need a continuous supply of oxygen and glucose. Unlike many other cells, neurones can synthesise chemical energy (ATP) only from glucose. The effects of damage to neurones are described on page 175.

The physiological 'units' of the nervous system are *nerve impulses*, or *action potentials*, which are akin to tiny electrical charges. However, unlike ordinary electrical wires, the neurones are actively involved in conducting nerve impulses. In effect the strength of the impulse is maintained throughout the length of the neurone.

Some neurones initiate nerve impulses while others act as 'relay stations' where impulses are passed on and sometimes redirected.

Properties of neurones

Neurones have the characteristics of *irritability* and *conductivity*.

Irritability is the ability to initiate nerve impulses in response to stimuli from:

- outside the body, e.g. touch, light waves
- inside the body, e.g. a change in the concentration of carbon dioxide in the blood alters respiration; a thought may result in voluntary movement.

In the body this stimulation may be described as partly electrical and partly chemical—electrical in that motor

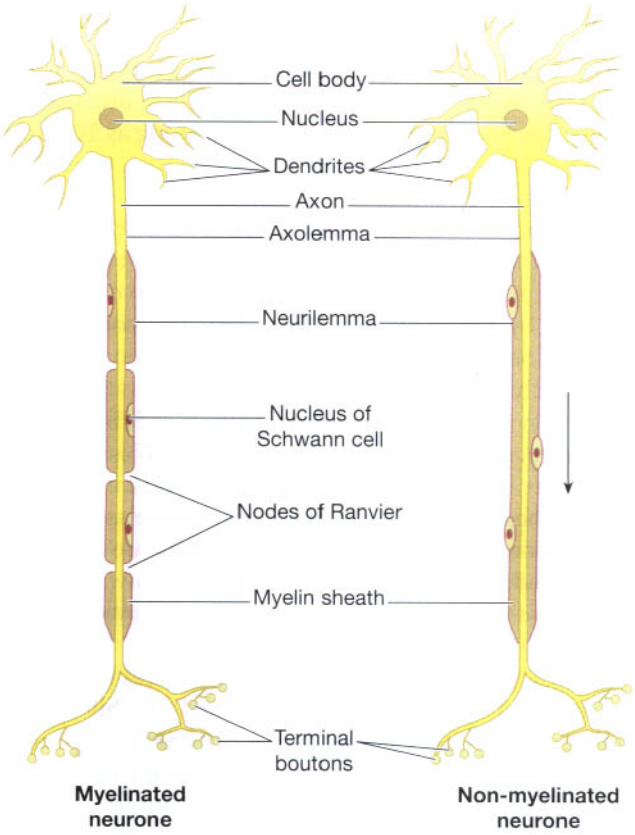


Figure 7.2 The structure of neurones. (Arrow indicates direction of impulse conduction.)

neurones and sensory nerve endings initiate nerve impulses, and chemical in the transmission of impulses between one neurone and the next or between a neurone and an effector organ.

Conductivity means the ability to transmit an impulse.

Cell bodies

Nerve cells vary considerably in size and shape but they are all too small to be seen by the naked eye. Cell bodies form the *grey matter* of the nervous system and are found at the periphery of the brain and in the centre of the spinal cord. Groups of cell bodies are called *nuclei* in the central nervous system and *ganglia* in the peripheral nervous system.

Axons and dendrites

Axons and dendrites are extensions of cell bodies and form the *white matter* of the nervous system. Axons are found deep in the brain and in groups, called *tracts*, at the periphery of the spinal cord. They are referred to as *nerves* or *nerve fibres* outside the brain and spinal cord.

Axons

Each nerve cell has only one axon, carrying nerve impulses away from the cell body. They are usually longer than the dendrites, sometimes as long as 100 cm.

Structure of an axon

The membrane of the axon is called *axolemma* and it encloses the cytoplasmic extension of the cell body.

Large axons and those of peripheral nerves are surrounded by a *myelin sheath* (Fig. 7.3A). This consists of a series of *Schwann cells* arranged along the length of the axon. Each one is wrapped around the axon so that it is covered by a number of concentric layers of Schwann cell plasma membrane. Between the layers of plasma membrane there is a small amount of fatty substance called *myelin*. The outermost layer of Schwann cell plasma membrane is sometimes called *neurilemma*. There are tiny areas of exposed axolemma between adjacent Schwann cells, called *nodes of Ranvier*, which assist the rapid transmission of nerve impulses.

Postganglionic fibres and some small fibres in the central nervous system are *non-myelinated*. In this type a number of axons are embedded in Schwann cell plasma membranes (Fig. 7.3B). The adjacent Schwann cells are in close association and there is no exposed axolemma. The speed of transmission of nerve impulses is significantly slower in non-myelinated fibres.

Dendrites

The dendrites are the many short processes that receive and carry incoming impulses towards cell bodies. They have the same structure as axons but they are usually shorter and branching. In motor neurones they form part of synapses (Fig. 7.8A) and in sensory neurones they form the sensory receptors that respond to stimuli.

The nerve impulse (action potential)

An impulse is initiated by stimulation of sensory nerve endings or by the passage of an impulse from another nerve. Transmission of the impulse, or action potential, is due to movement of ions across the nerve cell membrane. In the resting state the nerve cell membrane is *polarised* due to differences in the concentrations of ions across the plasma membrane. This means that there is a different electrical charge on each side of the membrane that is called the *resting membrane potential*. At rest the charge on the outside is positive and inside it is negative. The principal ions involved are:

- sodium (Na^+) the main extracellular cation
- potassium (K^+) the main intracellular cation.

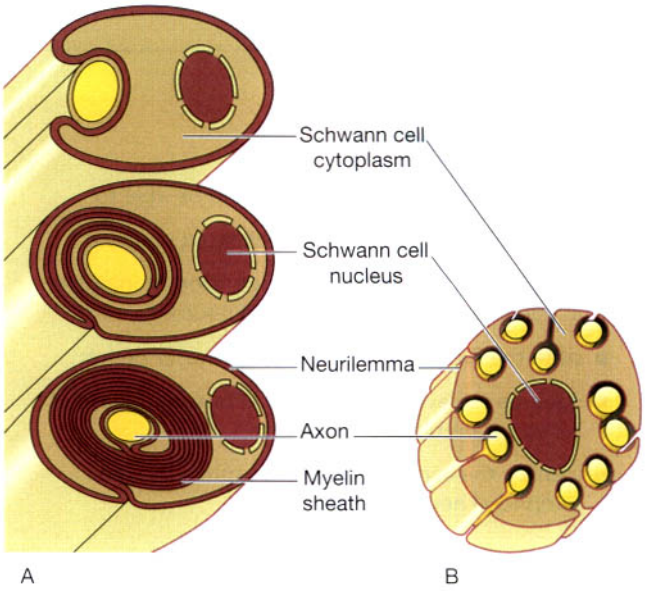


Figure 7.3 Nerve fibres: A. Myelinated. B. Non-myelinated.

In the *resting state* there is a continual tendency for these ions to diffuse along their concentration gradients, i.e. K^+ outwards and Na^+ into cells. When stimulated, the permeability of the nerve cell membrane to these ions changes. Initially Na^+ floods into the neurone from the ECF causing *depolarisation*, creating a *nerve impulse* or *action potential*. Depolarisation is very rapid, enabling the conduction of a nerve impulse along the entire length of a neurone in a few milliseconds (ms). It passes from the point of stimulation in one direction only, i.e. away from the point of stimulation towards the area of resting potential. The one-way direction of transmission is ensured because following depolarisation it takes time for *repolarisation* to occur.

During this process K^+ floods out of the neurone and the movement of these ions returns the membrane potential to its resting state. This is called the *refractory period* during which restimulation is not possible. As the neurone returns to its original resting state, the action of the *sodium pump* expels Na^+ from the cell in exchange for K^+ (p. 34).

In myelinated neurones, the insulating properties of the myelin sheath prevent the movement of ions. Therefore electrical changes across the membrane can only occur at the gaps in the myelin sheath, i.e. at the nodes of Ranvier. When an impulse occurs at one node, depolarisation passes along the myelin sheath to the next node so that the flow of current appears to 'leap' from one node to the next. This is called *saltatory conduction* (Fig. 7.4).

The speed of conduction depends on the diameter of the neurone: the larger the diameter, the faster the conduction. Myelinated fibres conduct impulses faster

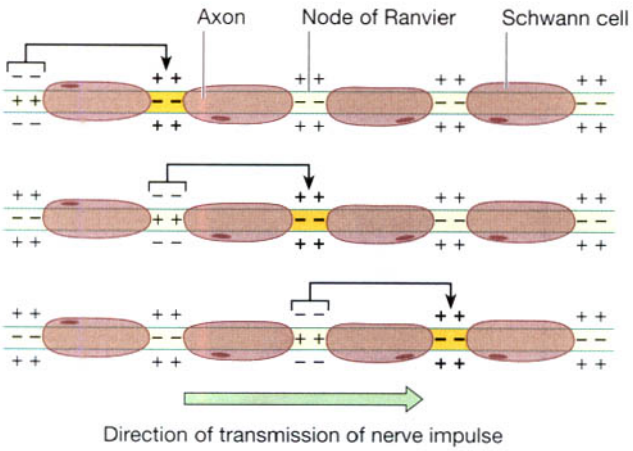


Figure 7.4 Saltatory conduction of an impulse in a myelinated nerve fibre.

than unmyelinated fibres because saltatory conduction is faster than the complete conduction, or *simple propagation* (Fig. 7.5). The fastest fibres can conduct impulses to, e.g., skeletal muscles at a rate of 130 metres per second while the slowest impulses travel at 0.5 metres per second.

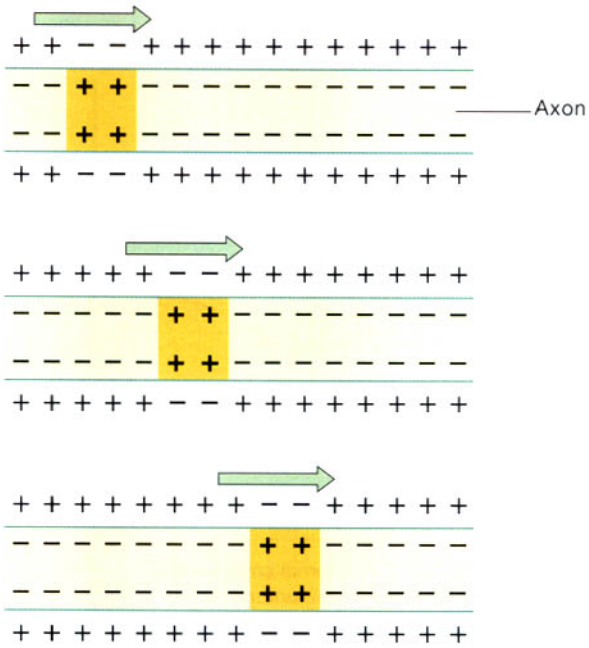


Figure 7.5 Simple propagation of an impulse in a non-myelinated nerve fibre. (Arrows indicate the direction of impulse transmission.)

Types of nerves (Fig. 7.6)

Sensory or afferent nerves

When action potentials are generated by sensory receptors on the dendrites of these neurones, they are transmitted to the spinal cord by the sensory nerve fibres. The impulses may then pass to the brain or to connector neurones of reflex arcs in the spinal cord (p. 159).

Sensory receptors

Specialised endings of sensory neurones respond to different stimuli (changes) inside and outside the body.

Somatic, cutaneous or *common senses.* These originate in the skin. They are: pain, touch, heat and cold. Sensory nerve endings in the skin are fine branching filaments without myelin sheaths (Fig. 7.7). When stimulated, an impulse is generated and transmitted by the sensory nerves to the brain where the sensation is perceived.

Proprioceptor senses. These originate in muscles and joints and contribute to the maintenance of balance and posture.

Special senses. These are sight, hearing, smell, touch and taste (Ch. 8).

Autonomic afferent nerves. These originate in internal organs, glands and tissues, e.g. baroreceptors, chemoreceptors, and are associated with reflex regulation of involuntary activity and visceral pain.

Motor or efferent nerves

Motor nerves originate in the brain, spinal cord and autonomic ganglia. They transmit impulses to the effector organs: muscles and glands. There are two types:

- *somatic nerves*—involved in voluntary and reflex skeletal muscle contraction
- *autonomic nerves* (sympathetic and parasympathetic)—involved in cardiac and smooth muscle contraction and glandular secretion.

Mixed nerves

In the spinal cord, sensory and motor nerves are arranged in separate groups, or *tracts*. Outside the spinal cord, when sensory and motor nerves are enclosed within the same sheath of connective tissue they are called *mixed nerves*.

The synapse and neurotransmitters

There is always more than one neurone involved in the transmission of a nerve impulse from its origin to its destination, whether it is sensory or motor. There is no physical contact between these neurones. The point at which the nerve impulse passes from one to another is the *synapse* (Fig. 7.8). At its free end the axon of the

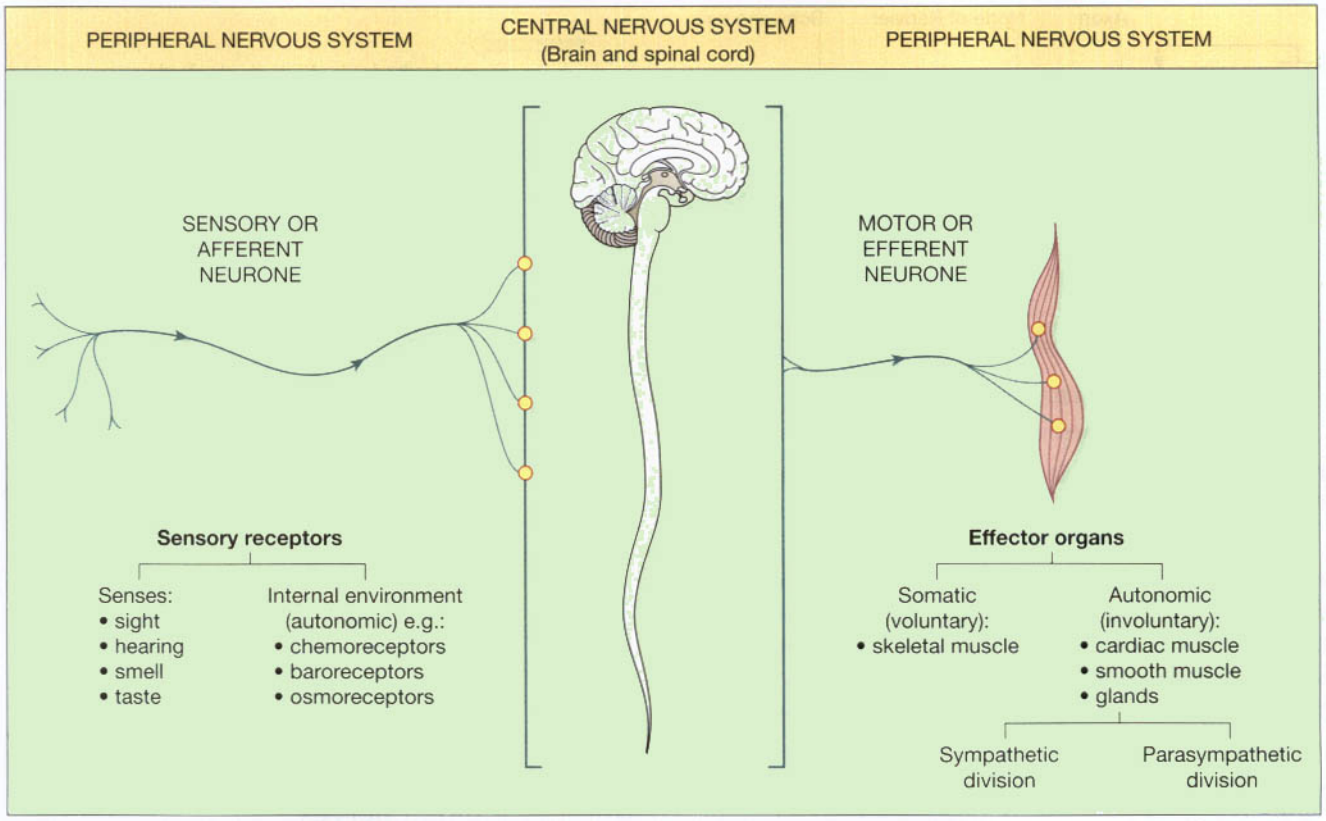


Figure 7.6 Functional components of the nervous system.

presynaptic neurone breaks up into minute branches which terminate in small swellings called *synaptic knobs*, or terminal boutons. These are in close proximity to the dendrites and the cell body of the *postsynaptic neurone*. The space between them is the *synaptic cleft*. In the ends of synaptic knobs there are spherical *synaptic vesicles*, containing a chemical, the *neurotransmitter*, which is released into synaptic clefts. Neurotransmitters are synthesised by nerve cells, actively transported along the axons and stored in the synaptic vesicles. They are released by exocytosis in response to the action potential and diffuse across the synaptic cleft. They act on specific receptor sites on the postsynaptic membranes. Their action is short lived as immediately they have stimulated the postsynaptic neurone or effector organ, such as a muscle fibre, they are either inactivated by enzymes or taken back into the synaptic knob. A knowledge of the action of different neurotransmitters is important because some drugs neutralise or prolong their effect. Usually neurotransmitters have an excitatory effect at the synapse but they are sometimes inhibitory.

The neurotransmitters in the brain and spinal cord and their modes of action are not yet fully understood. It is believed however that *noradrenaline, gamma aminobutyric acid (GABA)* and *acetylcholine* act as neurotransmitters. Other substances, such as dopamine, serotonin (5-hydroxytryptamine), enkephalins, endorphins and substance P, have similar functions. Figure 7.9 summarises the neurotransmitters known to function in the peripheral nervous system. Somatic nerves carry impulses directly

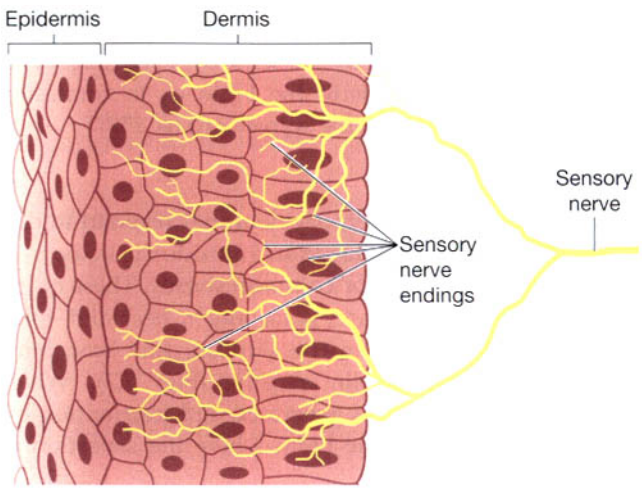


Figure 7.7 Sensory nerve endings in the skin.



Figure 7.8 Diagram of a synapse.

to the synapses at skeletal muscles: the neuromuscular junctions. In autonomic nerves, impulses travel along two nerves (preganglionic and postganglionic) and across two synapses to the effector organs in both the sympathetic and the parasympathetic divisions.

The neuromuscular junction

The axons of *motor neurones*, conveying impulses to skeletal muscle to produce contraction, divide into fine filaments terminating in minute pads called *motor end-plates* (Fig. 7.10). At the point where the nerve reaches the muscle, the myelin sheath is absent and the fine filament passes to a sensitive area on the surface of the muscle fibre. Each muscle fibre is stimulated through a single motor end-plate, and one motor nerve has many motor end-plates. The motor end-plate and the sensitive area of muscle fibre through which it is stimulated is analogous to the synapse between neurones and is known as the neuromuscular junction. The nerve impulse is passed across the gap between the motor end-plate and the muscle fibre by the neurotransmitter, *acetylcholine*. The group of muscle fibres and the motor end-plates of the nerve fibre that supplies them constitute a *motor unit*. Nerve impulses cause serial contraction of motor units in a muscle and each unit contracts to its full capacity. The *strength* of the contraction depends on the *number* of motor units in action at a particular time.

The endings of *autonomic nerves* supplying smooth muscle and glands branch near their effector structure and release a neurotransmitter which stimulates or depresses the activity of the structure (Figs 7.9, 7.43 and 7.44).

CENTRAL NERVOUS SYSTEM

Learning outcomes

After studying this section you should be able to:

- outline the functions of 4 types of neuroglial cells
- describe the structure of the meninges
- describe the flow of cerebrospinal fluid in the brain
- list the functions of cerebrospinal fluid.

The central nervous system consists of the brain and the spinal cord.

Neuroglia

The neurones of the central nervous system are supported by four types of non-excitable *glial cells* that make up a quarter to a half of the volume of brain tissue. Unlike nerve cells these continue to replicate throughout life. They are *astrocytes, oligodendrocytes, microglia* and *ependymal cells*.

Astrocytes

These cells form the main supporting tissue of the central nervous system. They are star-shaped with fine branching processes and they lie in a mucopolysaccharide ground substance. At the free ends of some of the processes there are small swellings called *foot processes*. Astrocytes are found in large numbers adjacent to blood vessels with their foot processes forming a sleeve round them. This means that the blood is separated from the neurones by the capillary wall and a layer of astrocyte foot processes which together constitute the *blood–brain*

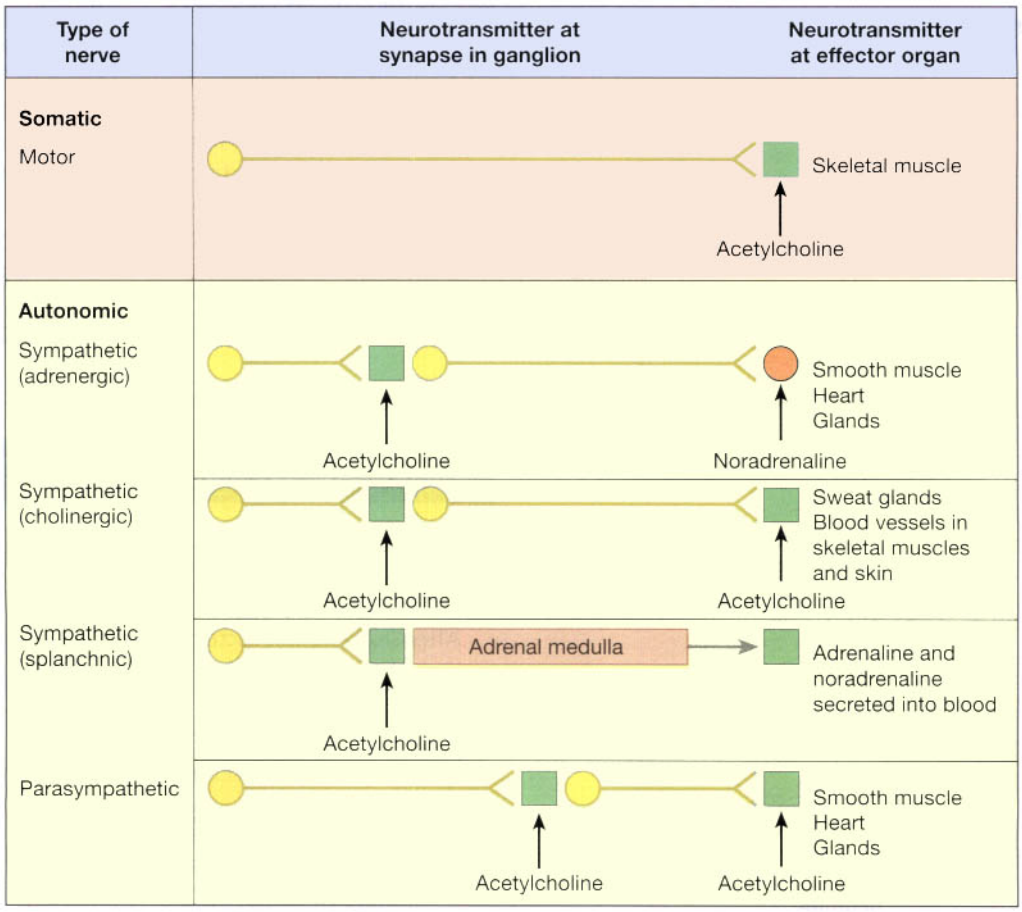


Figure 7.9 Neurotransmitters at synapses in the peripheral nervous system.

barrier (Fig. 7.11). Their functions are analogous to those of fibroblasts elsewhere in the body.

The blood–brain barrier is a selective barrier that protects the brain from potentially toxic substances and chemical variations in the blood, e.g. after a meal. Oxygen, carbon dioxide, alcohol, barbiturates, glucose and lipophilic substances quickly cross the barrier into the brain. Some large molecules, drugs, inorganic ions and amino acids pass slowly from the blood to the brain.

Oligodendrocytes

These cells are smaller than astrocytes and are found:

- in clusters round nerve cell bodies, the grey matter where they are thought to have a supportive function
- adjacent to, and along the length of, myelinated nerve fibres.

The oligodendrocytes form and maintain myelin, having the same functions as Schwann cells in peripheral nerves.

Microglia

These cells are derived from monocytes that migrate from the blood into the nervous system before birth. They are found mainly in the area of blood vessels. They enlarge and become phagocytic in areas of inflammation and cell destruction.

Ependymal cells

These cells form the epithelial lining of the ventricles of the brain and the central canal of the spinal cord.

Membranes covering the brain and spinal cord (the meninges)

The brain and spinal cord are completely surrounded by three membranes, the *meninges*, lying between the skull and the brain and between the vertebrae and the spinal cord (Fig. 7.12). Named from outside inwards they are:

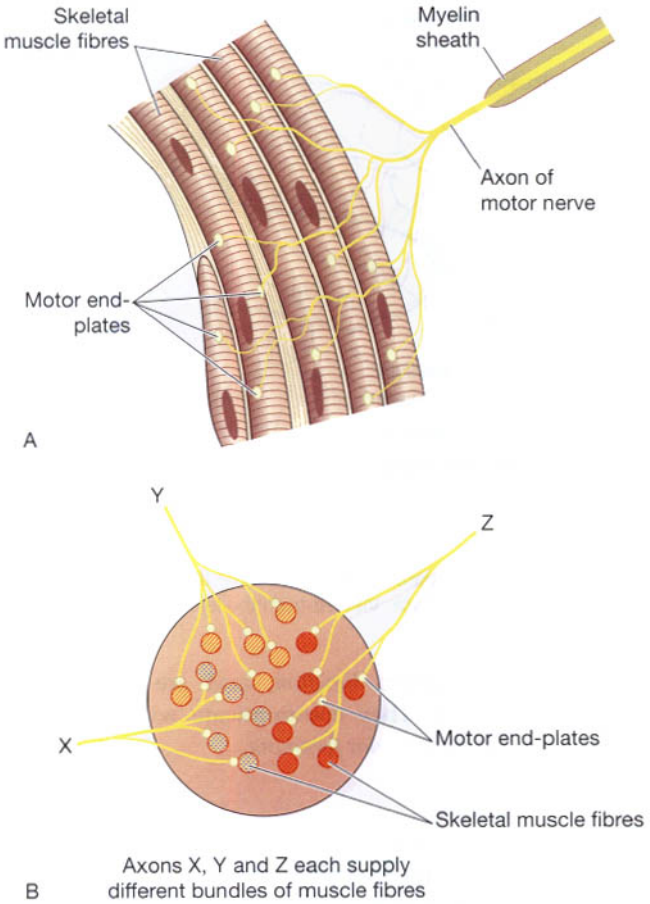


Figure 7.10 Motor unit: A. Longitudinal section. B. Cross-section.

- dura mater
- arachnoid mater
- pia mater.

The dura and arachnoid maters are separated by a potential space, the *subdural space*. The arachnoid and pia maters are separated by the *subarachnoid space*, containing *cerebrospinal fluid*.

Dura mater

The cerebral dura mater consists of two layers of dense fibrous tissue. The outer layer takes the place of the periosteum on the inner surface of the skull bones and the inner layer provides a protective covering for the brain. There is only a potential space between the two layers except where the inner layer sweeps inwards between the cerebral hemispheres to form the *falx cerebri*; between the cerebellar hemispheres to form the *falx cerebelli*; and between the cerebrum and cerebellum to form the *tentorium cerebelli* (Fig. 7.12).

Venous blood from the brain drains into venous sinuses between the layers of dura mater. The *superior sagittal sinus* is formed by the falx cerebri, and the tentorium cerebelli forms the *straight* and *transverse sinuses* (see Figs 5.37 and 5.38, p. 101).

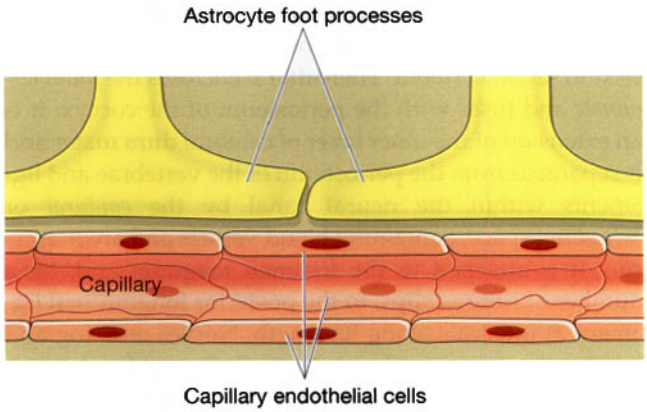
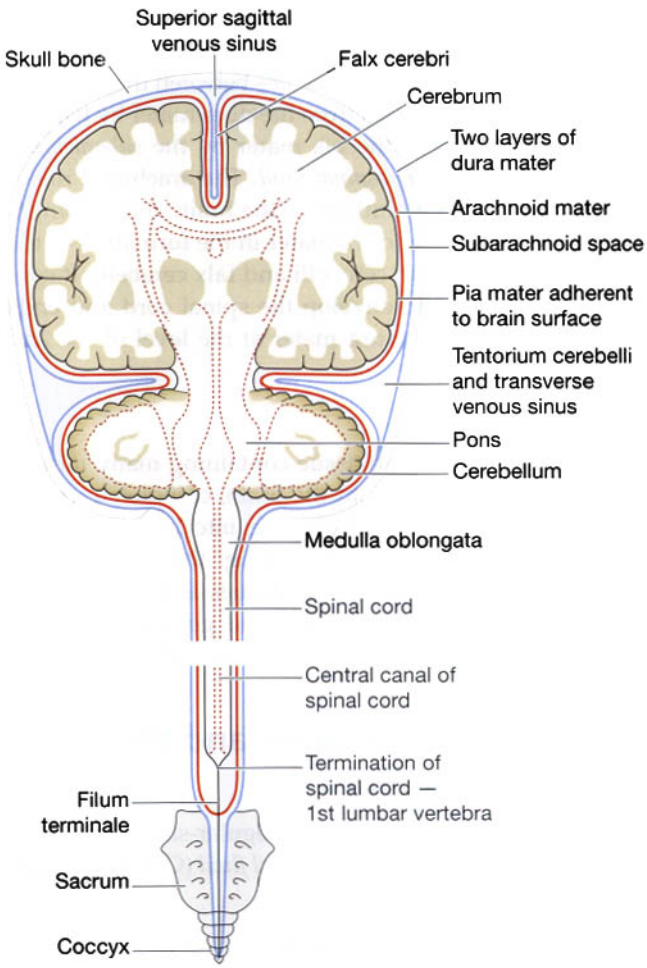


Figure 7.11 Blood–brain barrier.



Spinal dura mater forms a loose sheath round the spinal cord, extending from the foramen magnum to the second sacral vertebra. Thereafter it encloses the *filum terminale* and fuses with the periosteum of the coccyx. It is an extension of the inner layer of cerebral dura mater and is separated from the periosteum of the vertebrae and ligaments within the neural canal by the *epidural* or *extradural* space, containing blood vessels and areolar tissue. It is attached to the foramen magnum and, by a number of fibrous slips, to the posterior longitudinal ligament at intervals along its length. Nerves entering and leaving the spinal cord pass through the epidural space. These attachments stabilise the spinal cord in the neural canal. Dyes, used for diagnostic purposes, and local anaesthetics or analgesics to relieve pain, may be injected into the epidural space.

Arachnoid mater

This delicate serous membrane lies between the dura and pia maters. It is separated from the dura mater by the *subdural space*, and from the pia mater by the *subarachnoid space*, containing *cerebrospinal fluid*. The arachnoid mater passes over the convolutions of the brain and accompanies the inner layer of dura mater in the formation of the falx cerebri, tentorium cerebelli and falx cerebelli. It continues downwards to envelop the spinal cord and ends by merging with the dura mater at the level of the 2nd sacral vertebra.

Pia mater

This is a fine connective tissue containing many minute blood vessels. It adheres to the brain, completely covering the convolutions and dipping into each fissure. It continues downwards surrounding the spinal cord. Beyond the end of the cord it continues as the *filum terminale*, pierces the arachnoid tube and goes on, with the dura mater, to fuse with the periosteum of the coccyx.

Ventricles of the brain and the cerebrospinal fluid

Within the brain there are four irregular-shaped cavities, or *ventricles*, containing *cerebrospinal fluid* (CSF) (Fig. 7.13). They are:

- right and left lateral ventricles
- third ventricle
- fourth ventricle.

The lateral ventricles

These cavities lie within the cerebral hemispheres, one on each side of the median plane just below the *corpus callosum*. They are separated from each other by a thin

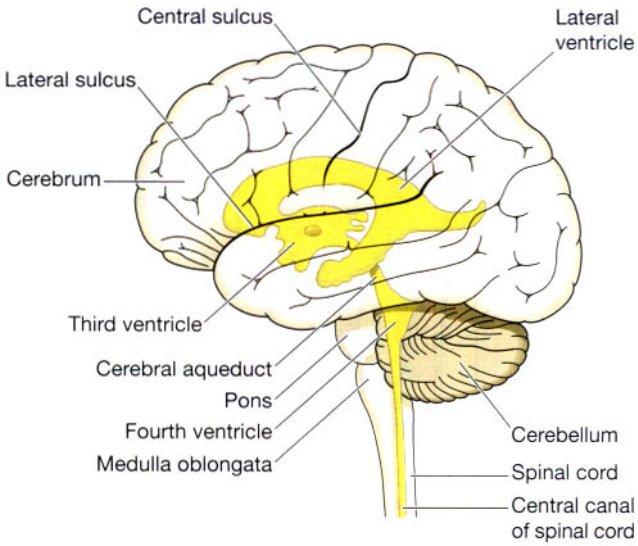


Figure 7.13 The positions of the ventricles of the brain (in yellow) superimposed on its surface. Viewed from the left side.

membrane, the *septum lucidum*, and are lined with ciliated epithelium. They communicate with the third ventricle by *interventricular foramina*.

The third ventricle

The third ventricle is a cavity situated below the lateral ventricles between the two parts of the *thalamus*. It communicates with the fourth ventricle by a canal, the *cerebral aqueduct* or *aqueduct of the midbrain*.

The fourth ventricle

The fourth ventricle is a diamond-shaped cavity situated below and behind the third ventricle, between the *cerebellum* and *pons*. It is continuous below with the *central canal* of the spinal cord and communicates with the subarachnoid space by foramina in its roof. Cerebrospinal fluid enters the subarachnoid space through these openings and through the open distal end of the central canal of the spinal cord.

Cerebrospinal fluid (CSF) (Fig. 7.14)

Cerebrospinal fluid is secreted into each ventricle of the brain by *choroid plexuses*. These are vascular areas where there is a proliferation of blood vessels surrounded by ependymal cells in the lining of ventricle walls. CSF passes back into the blood through tiny diverticula of arachnoid mater, called *arachnoid villi* (arachnoid granulations), that project into the venous sinuses. The movement of CSF from the subarachnoid space to venous sinuses depends upon the difference in pressure on each side of the walls of the arachnoid villi, which act as one-way valves. When

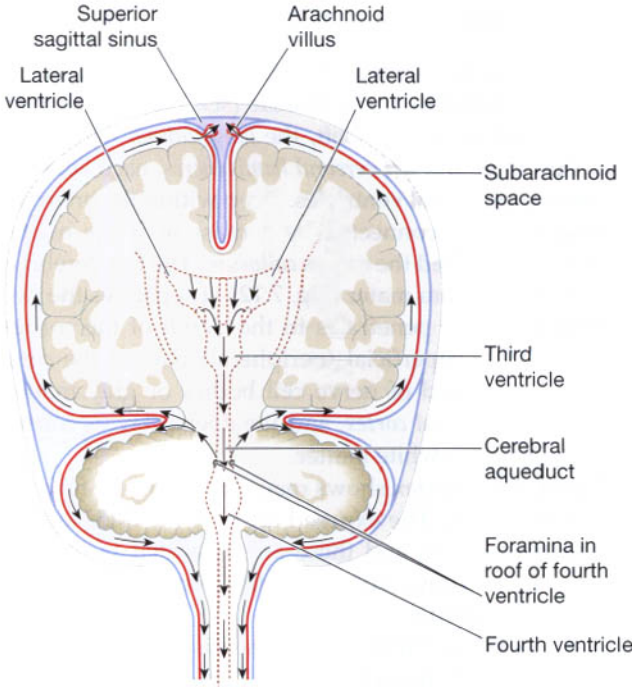


Figure 7.14 Arrows showing the flow of cerebrospinal fluid.

CSF pressure is higher than venous pressure CSF passes into the blood and when the venous pressure is higher the arachnoid villi collapse, preventing the passage of blood constituents into the CSF. There may also be some reabsorption of CSF by cells in the walls of the ventricles.

From the roof of the fourth ventricle CSF flows through foramina into the subarachnoid space and completely surrounds the brain and spinal cord. There is no intrinsic system of CSF circulation but its movement is aided by pulsating blood vessels, respiration and changes of posture.

CSF is secreted continuously at a rate of about 0.5 ml per minute, i.e. 720 ml per day. The amount around the brain and spinal cord remains fairly constant at about 120 ml, which means that absorption keeps pace with secretion. CSF pressure may be measured using a vertical tube attached to a lumbar puncture needle. It remains fairly constant at about 10 cmH_2O when the individual is lying on his side and about 30 cmH_2O when sitting up. If the brain is enlarged by, e.g. haemorrhage or tumour, some compensation is made by a reduction in the amount of CSF. When the volume of brain tissue is reduced, such as in degeneration or atrophy, the volume of CSF is increased. CSF is a clear, slightly alkaline fluid with a specific gravity of 1.005, consisting of:

- water
- mineral salts
- glucose
- plasma proteins: small amounts of albumin and globulin
- creatinine, urea } small amounts
- a few leukocytes.

Functions of cerebrospinal fluid

- It supports and protects the brain and spinal cord.
- It maintains a uniform pressure around these delicate structures.
- It acts as a cushion and shock absorber between the brain and the cranial bones.
- It keeps the brain and spinal cord moist and there may be interchange of substances between CSF and nerve cells, such as nutrients and waste products.

BRAIN

Learning outcomes

After studying this section you should be able to:

- describe the blood supply to the brain
- name the lobes and sulci of the brain
- outline the functions of the cerebrum
- identify the main sensory and motor areas of the cerebrum
- describe the position and functions of the midbrain, pons, medulla oblongata and reticular activating system
- outline the position and functions of the basal nuclei, thalamus and hypothalamus
- describe the structure and functions of the cerebellum.

The brain constitutes about one-fiftieth of the body weight and lies within the cranial cavity. The parts are (Fig. 7.15):

- cerebrum
- midbrain, pons, medulla oblongata } the brain stem
- cerebellum.

Blood supply to the brain

The circulus arteriosus and its contributing arteries (see Fig. 5.34, p. 100) play a vital role in maintaining a constant supply of oxygen and glucose to the brain even when a contributing artery is narrowed or the head is moved. The brain receives about 15% of the cardiac output, approximately 750 ml of blood per minute. Autoregulation keeps blood flow to the brain constant by adjusting the diameter of the arterioles across a wide range of arterial blood pressure (about 65–140 mmHg) with changes occurring only outside these limits.

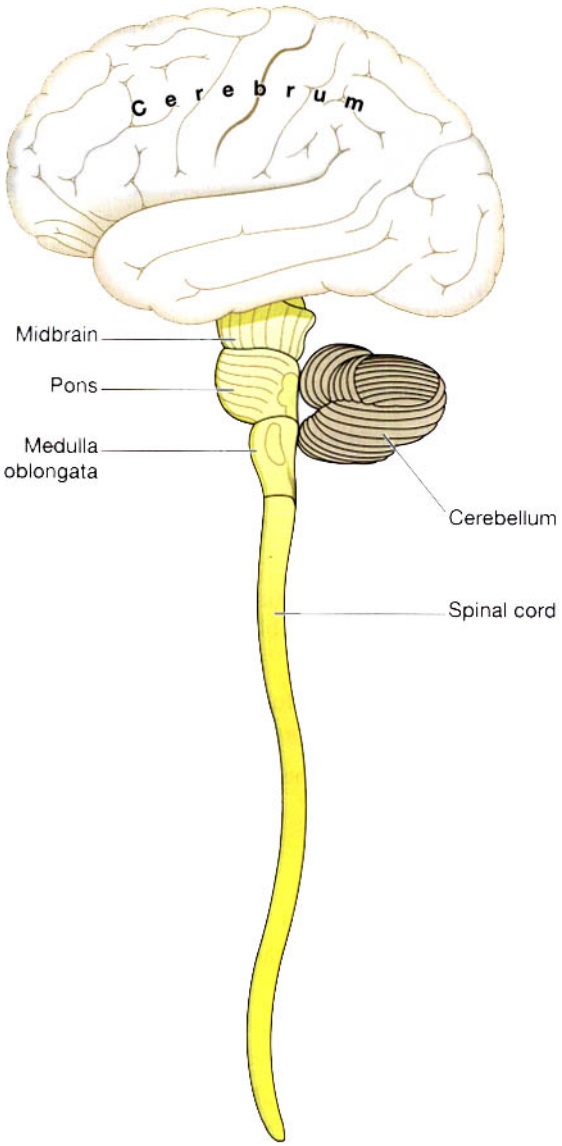


Figure 7.15 The parts of the central nervous system.

Cerebrum

This is the largest part of the brain and it occupies the anterior and middle cranial fossae (see Fig. 16.8, p. 393). It is divided by a deep cleft, the *longitudinal cerebral fissure*, into *right* and *left cerebral hemispheres*, each containing one of the lateral ventricles. Deep within the brain the hemispheres are connected by a mass of white matter (nerve fibres) called the *corpus callosum*. The falx cerebri is formed by the dura mater (Fig. 7.12). It separates the two hemispheres and penetrates to the depth of the corpus callosum. The superficial (peripheral) part of the cerebrum is composed of nerve cell bodies or grey matter, forming the *cerebral cortex*, and the deeper layers consist of nerve fibres or white matter.

The cerebral cortex shows many infoldings or furrows of varying depth. The exposed areas of the folds are the *gyri* or *convolutions* and these are separated by *sulci* or *fissures*. These convolutions greatly increase the surface area of the cerebrum.

For descriptive purposes each hemisphere of the cerebrum is divided into *lobes* which take the names of the bones of the cranium under which they lie:

- frontal
- parietal
- temporal
- occipital.

The boundaries of the lobes are marked by deep sulci (fissures). These are the *central, lateral* and *parieto-occipital sulci* (Fig. 7.16).

Interior of the cerebrum (Fig. 7.17)

The surface of the cerebral cortex is composed of grey matter (nerve cell bodies). Within the cerebrum the lobes are connected by masses of nerve fibres, or tracts, which make up the white matter of the brain. The afferent and

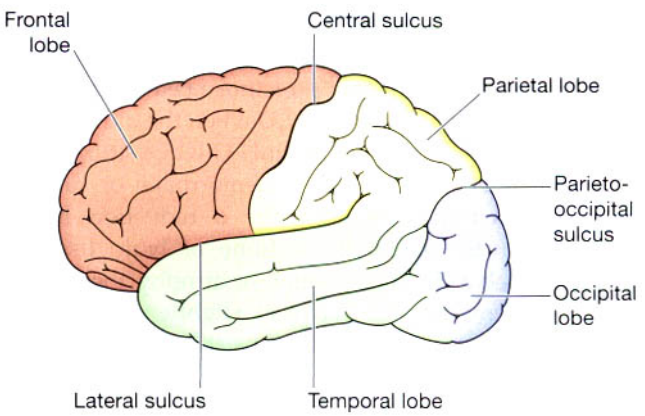
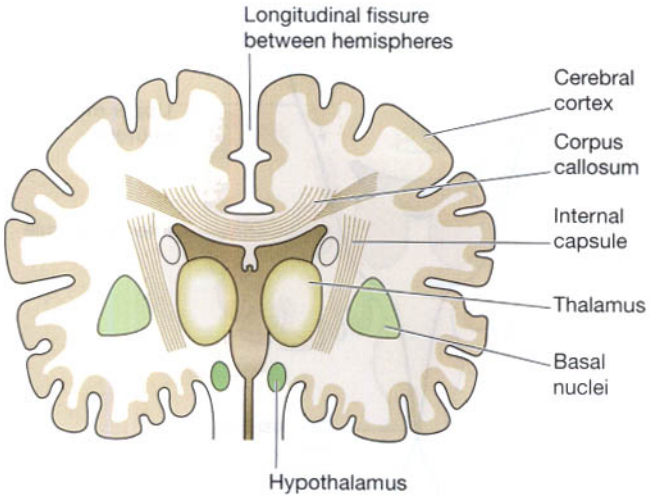
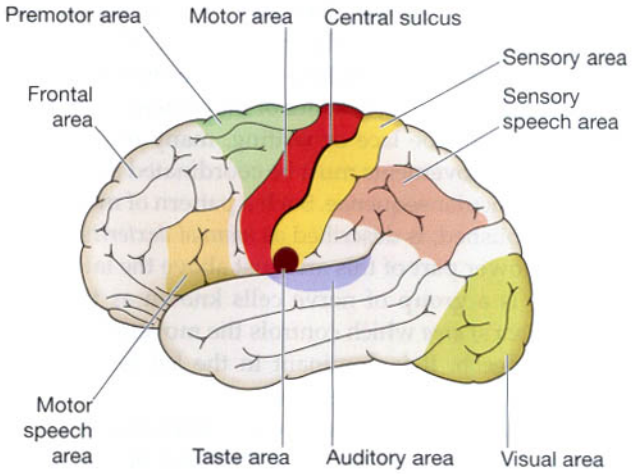


Figure 7.16 The lobes and sulci of the cerebrum.





efferent fibres linking the different parts of the brain and spinal cord are as follows.

- *Association (arcuate) fibres* connect different parts of a cerebral hemisphere by extending from one gyrus to another, some of which are adjacent and some distant.
- *Commissural fibres* connect corresponding areas of the two cerebral hemispheres; the largest and most important commissure is the corpus callosum.
- *Projection fibres* connect the cerebral cortex with grey matter of lower parts of the brain and with the spinal cord, e.g. the internal capsule.

The *internal capsule* is an important area consisting of projection fibres. It lies deep within the brain between the basal nuclei (ganglia) and the thalamus. Many nerve impulses passing to and from the cerebral cortex are carried by fibres that form the internal capsule. Motor fibres within the internal capsule form the *pyramidal tracts* (corticospinal tracts) that cross over (decussate) at the medulla oblongata.

Functions of the cerebrum

There are three main varieties of activity associated with the cerebral cortex:

- mental activities involved in memory, intelligence, sense of responsibility, thinking, reasoning, moral sense and learning are attributed to the *higher centres*
- sensory perception, including the perception of pain, temperature, touch, sight, hearing, taste and smell
- initiation and control of skeletal (voluntary) muscle contraction.

Functional areas of the cerebrum (Fig. 7.18)

The main areas of the cerebrum associated with sensory perception and voluntary motor activity are known but it is unlikely that any area is associated exclusively with only one function. Except where specially mentioned, the different areas are active in both hemispheres.

Motor areas of the cerebrum

The precentral (motor) area. This lies in the frontal lobe immediately anterior to the *central sulcus*. The cell bodies are pyramid shaped (Betz's cells) and they initiate the contraction of skeletal muscles. A nerve fibre from a Betz's cell passes downwards through the internal capsule to the medulla oblongata where it crosses to the opposite side then descends in the spinal cord. At the appropriate level in the spinal cord the nerve impulse crosses a synapse to stimulate a second neurone which terminates at the motor end-plate of a muscle fibre. This means that the motor area of the *right hemisphere* of the cerebrum controls voluntary muscle movement on the left side of the body and vice versa. The neurone with its cell body in the cerebrum is the *upper motor neurone* and the other, with its cell body in the spinal cord, is the *lower motor neurone* (Fig. 7.19). Damage to either of these neurones may result in paralysis.

In the motor area of the cerebrum the body is represented upside down, i.e. the cells nearest the vertex control the feet and those in the lowest part control the head, neck, face and fingers (Fig. 7.20A). The sizes of the areas of cortex representing different parts of the body are proportional to the *complexity of movement* of the body part, not to its size. Figure 7.20A shows that, in comparison with the trunk, the hand, foot, tongue and lips are represented by large cortical areas.

The premotor area. This lies in the frontal lobe immediately anterior to the motor area. The cells are thought to exert a controlling influence over the motor area, ensuring an orderly series of movements. For example, in tying a shoe lace or writing, many muscles contract but the movements must be coordinated and carried out in a particular sequence. Such a pattern of movement, when established, is described as *manual dexterity*.

In the lower part of this area just above the lateral sulcus there is a group of nerve cells known as the *motor speech (Broca's) area* which controls the movements necessary for speech. It is dominant in the *left hemisphere* in *right-handed people* and vice versa.

The frontal area. This extends anteriorly from the premotor area to include the remainder of the frontal lobe. It is a large area and is more highly developed in humans than in other animals. It is thought that communications between this and the other regions in the cerebrum are responsible for the behaviour, character and emotional state of the individual. No particular behaviour, character or intellectual trait has, so far, been attributed to the activity of any one group of cells.

Sensory areas of the cerebrum

The postcentral (sensory) area. This is the area behind the central sulcus. Here sensations of pain, temperature, pressure and touch, knowledge of muscular movement and the position of joints are perceived. The sensory area of the *right hemisphere* receives impulses from the *left side of the body* and vice versa. The size of the areas representing different parts of the body (Fig. 7.20B) is proportional to the *extent of sensory innervation*, e.g. the large area for the face is consistent with the extensive sensory nerve supply by the three branches of the trigeminal nerves (5th cranial nerves).

The parietal area. This lies behind the postcentral area and includes the greater part of the parietal lobe of the cerebrum. Its functions are believed to be associated with obtaining and retaining accurate knowledge of objects. It has been suggested that objects can be recognised by touch alone because of the knowledge from past experience (memory) retained in this area.

The sensory speech area. This is situated in the lower part of the parietal lobe and extends into the temporal lobe. It is here that the spoken word is perceived. There is a dominant area in the *left hemisphere* in *right-handed* people and vice versa.

The auditory (hearing) area. This lies immediately below the lateral sulcus within the temporal lobe. The cells receive and interpret impulses transmitted from the inner ear by the cochlear (auditory) part of the vestibulocochlear nerves (8th cranial nerves).

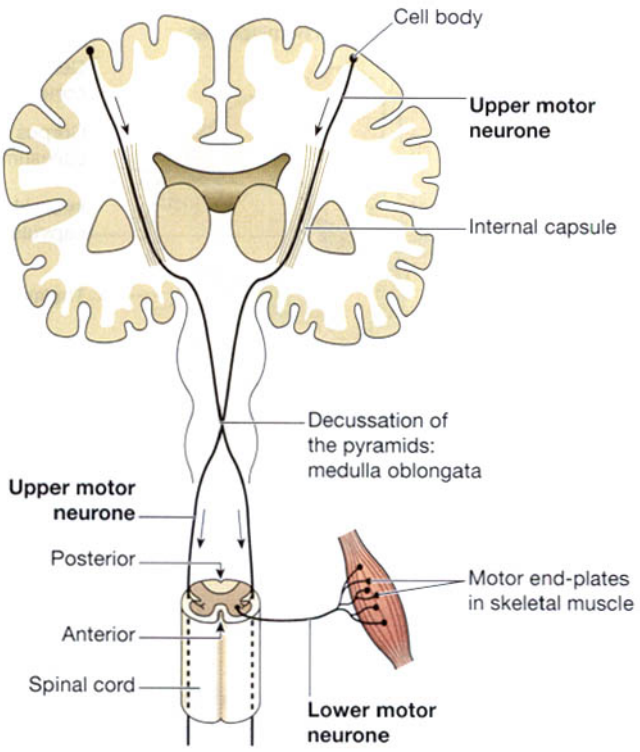


Figure 7.19 The motor nerve pathways: upper and lower motor neurones.

The olfactory (smell) area. This lies deep within the temporal lobe where impulses from the nose via the olfactory nerves (1st cranial nerves) are received and interpreted.

The taste area. This is thought to lie just above the lateral sulcus in the deep layers of the sensory area. This is the area where impulses from special nerve endings in taste buds in the tongue and in the lining of the cheeks, palate and pharynx are perceived as taste.

The visual area. This lies behind the parieto-occipital sulcus and includes the greater part of the occipital lobe. The optic nerves (2nd cranial nerves) pass from the eye to this area which receives and interprets the impulses as visual impressions.

Other areas of the cerebrum

Deep within the cerebral hemispheres there are groups of cell bodies called *nuclei* (previously called ganglia) which act as relay stations where impulses are passed from one neurone to the next in a chain (Fig. 7.17). Important masses of grey matter include:

- basal nuclei
- thalamus
- hypothalamus.

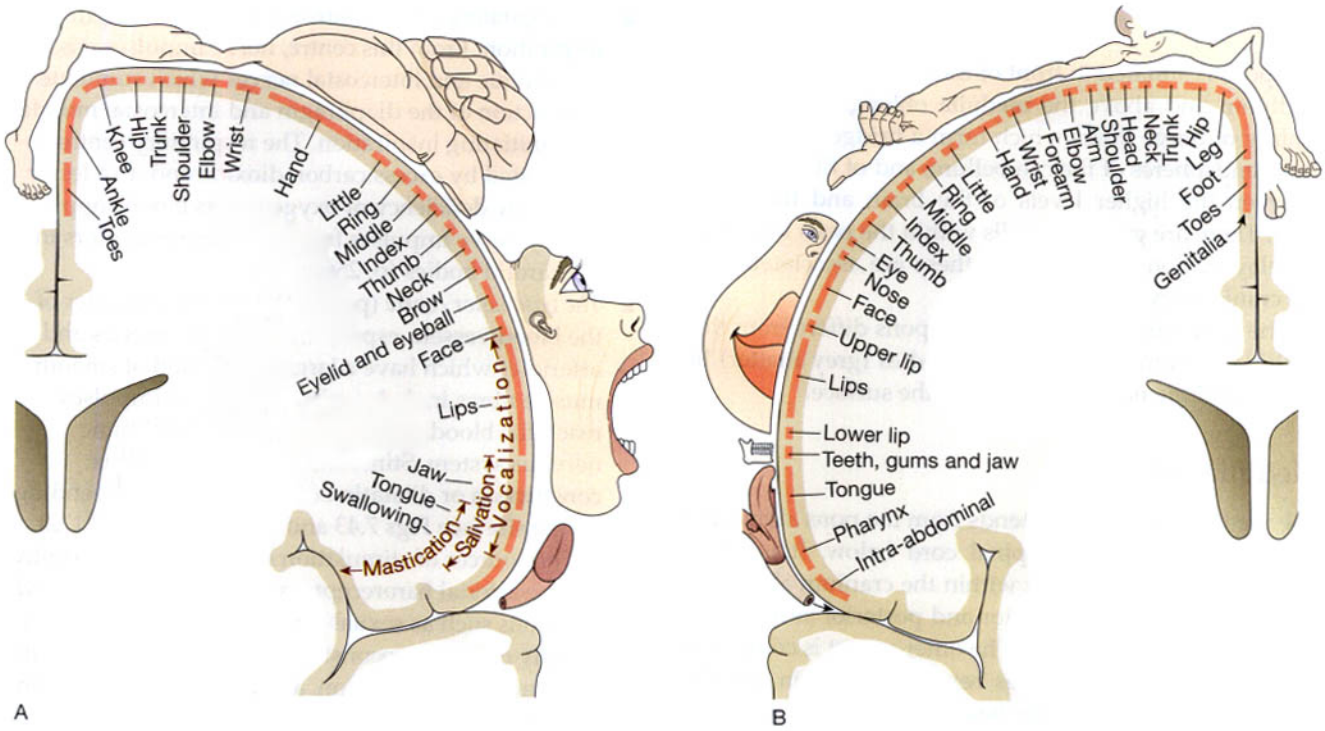


Figure 7.20 A. The *motor homunculus* showing how the body is represented in the motor area of the cerebrum. B. The *sensory homunculus* showing how the body is represented in the sensory area of the cerebrum. (Both A and B are from Penfield W, Rasmussen T 1950 The cerebral cortex of man. Macmillan, New York. © 1950 Macmillan Publishing Co., renewed 1978 Theodore Rasmussen.)

Basal nuclei. These are areas of grey matter, lying deep within the cerebral hemispheres, with connections to the cerebral cortex and thalamus. The basal nuclei form part of the extrapyramidal tracts and are thought to be involved in initiating muscle tone in slow and coordinated activities. If control is inadequate or absent, movements are jerky, clumsy and uncoordinated.

Thalamus. The thalamus consists of two masses of nerve cells and fibres situated within the cerebral hemispheres just below the corpus callosum, one on each side of the third ventricle. Sensory input from the skin, viscera and special sense organs is transmitted to the thalamus before redistribution to the cerebrum.

Hypothalamus. The hypothalamus is composed of a number of groups of nerve cells. It is situated below and in front of the thalamus, immediately above the *pituitary gland*. The hypothalamus is linked to the posterior lobe of the pituitary gland by nerve fibres and to the anterior lobe by a complex system of blood vessels. Through these connections, the hypothalamus controls the output of hormones from both lobes of the gland (see p. 215).

Other functions with which the hypothalamus is concerned include control of:

- the autonomic nervous system (p. 170)
- appetite and satiety
- thirst and water balance
- body temperature (p. 365)
- emotional reactions, e.g. pleasure, fear, rage
- sexual behaviour including mating and child rearing
- biological clocks or circadian rhythms, e.g. sleeping and waking cycles, body temperature and secretion of some hormones.

Brain stem

Midbrain

The midbrain is the area of the brain situated around the cerebral aqueduct between the cerebrum above and the *pons* below. It consists of groups of cell bodies and nerve fibres (tracts) which connect the cerebrum with lower parts of the brain and with the spinal cord. The cell bodies act as relay stations for the ascending and descending nerve fibres.

Pons

The pons is situated in front of the cerebellum, below the midbrain and above the medulla oblongata. It consists mainly of nerve fibres which form a bridge between the two hemispheres of the cerebellum, and of fibres passing between the higher levels of the brain and the spinal cord. There are groups of cells within the pons which act as relay stations and some of these are associated with the cranial nerves.

The anatomical structure of the pons differs from that of the cerebrum in that the cell bodies (grey matter) lie deeply and the nerve fibres are on the surface.

Medulla oblongata

The medulla oblongata extends from the pons above and is continuous with the spinal cord below. It is about 2.5 cm long and it lies just within the cranium above the foramen magnum. Its anterior and posterior surfaces are marked by central fissures. The outer aspect is composed of *white matter* which passes between the brain and the spinal cord, and *grey matter* lies centrally. Some cells constitute relay stations for sensory nerves passing from the spinal cord to the cerebrum.

The vital centres, consisting of groups of cells associated with autonomic reflex activity, lie in its deeper structure. These are the:

- cardiac centre
- respiratory centre
- vasomotor centre
- reflex centres of vomiting, coughing, sneezing and swallowing.

The medulla oblongata has several special features:

- *Decussation (crossing) of the pyramids*. In the medulla *motor nerves* descending from the motor area in the cerebrum to the spinal cord in the pyramidal (corticospinal) tracts cross from one side to the other. This means that the left hemisphere of the cerebrum controls the right half of the body, and vice versa. These tracts are the main pathway for impulses to skeletal (voluntary) muscles.
- *Sensory decussation*. Some of the *sensory nerves* ascending to the cerebrum from the spinal cord cross from one side to the other in the medulla. Others decussate at lower levels, i.e. in the spinal cord.
- *The cardiovascular centre* controls the rate and force of cardiac contraction (p. 87). Sympathetic and parasympathetic nerve fibres originating in the medulla pass to the heart. Sympathetic stimulation increases the rate and force of the heartbeat and parasympathetic stimulation has the opposite effect.
- *The respiratory centre* controls the rate and depth of respiration. From this centre, nerve impulses pass to the phrenic and intercostal nerves which stimulate contraction of the diaphragm and intercostal muscles, thus initiating inspiration. The respiratory centre is stimulated by excess carbon dioxide and, to a lesser extent, by deficiency of oxygen in its blood supply and by nerve impulses from the chemoreceptors in the carotid bodies (p. 256).
- *The vasomotor centre* (p. 80) controls the diameter of the blood vessels, especially the small arteries and arterioles which have a large proportion of smooth muscle fibres in their walls. Vasomotor impulses reach the blood vessels through the autonomic nervous system. Stimulation may cause either constriction or dilatation of blood vessels depending on the site (see Figs 7.43 and 7.44, pp. 171 and 172).

  The sources of stimulation of the vasomotor centre are the arterial baroreceptors, body temperature and emotions such as sexual excitement and anger. Pain usually causes vasoconstriction although severe pain may cause vasodilatation, a fall in blood pressure and fainting.
- *Reflex centres*. When irritating substances are present in the stomach or respiratory tract, nerve impulses pass to the medulla oblongata, stimulating the reflex centres which initiate the reflex actions of vomiting, coughing and sneezing to expel the irritant.

Reticular formation

The reticular formation is a collection of neurones in the core of the brain stem, surrounded by neural pathways which conduct ascending and descending nerve impulses between the brain and the spinal cord. It has a vast number of synaptic links with other parts of the brain and is therefore constantly receiving 'information' being transmitted in ascending and descending tracts.

Functions

The reticular formation is involved in:

- coordination of skeletal muscle activity associated with voluntary motor movement and the maintenance of balance
- coordination of activity controlled by the autonomic nervous system, e.g. cardiovascular, respiratory and gastrointestinal activity
- selective awareness that functions through the *reticular activating system* (RAS) which selectively blocks or passes sensory information to the cerebral cortex, e.g. the slight sound made by a sick child moving in bed may arouse his mother but the noise of regularly passing trains may be suppressed.

Cerebellum

The cerebellum (Fig. 7.21) is situated behind the pons and immediately below the posterior portion of the cerebrum occupying the posterior cranial fossa. It is ovoid in shape and has two hemispheres, separated by a narrow median strip called the *vermis*. Grey matter forms the surface of the cerebellum, and the white matter lies deeply.

Functions

The cerebellum is concerned with the coordination of voluntary muscular movement, posture and balance. Cerebellar activities are not under voluntary control. The cerebellum controls and coordinates the movements of various groups of muscles ensuring smooth, even, precise actions. It coordinates activities associated with the *maintenance of the balance and equilibrium* of the body. The sensory input for these functions is derived from the muscles and joints, the eyes and the ears. *Proprioceptor impulses* from the muscles and joints indicate their position in relation to the body as a whole and those impulses from the eyes and the semicircular canals in the ears provide information about the position of the head in space. Impulses from the cerebellum influence the contraction of skeletal muscle so that balance and posture are maintained.

Damage to the cerebellum results in clumsy uncoordinated muscular movement, staggering gait and inability to carry out smooth, steady, precise movements.

SPINAL CORD

Learning outcomes

After studying this section you should be able to:

- describe the gross structure of the spinal cord
- state the functions of the sensory (afferent) nerve tracts in the spinal cord
- state the functions of the motor (efferent) nerve tracts in the spinal cord
- explain the events of a simple reflex arc.

The spinal cord is the elongated, almost cylindrical part of the central nervous system, which is suspended in the vertebral canal surrounded by the meninges and cerebrospinal fluid (Fig. 7.22). It is continuous above with the medulla oblongata and extends from the *upper border of the atlas* to the lower border of the *1st lumbar vertebra* (Fig. 7.23). It is approximately 45 cm long in an adult Caucasian male, and is about the thickness of the little finger. When a specimen of cerebrospinal fluid is required it is taken from a point below the end of the cord, i.e. below the level of the 2nd lumbar vertebra. This procedure is called *lumbar puncture*.

Except for the cranial nerves, the spinal cord is the nervous tissue link between the brain and the rest of the body (Fig. 7.24). Nerves conveying impulses from the

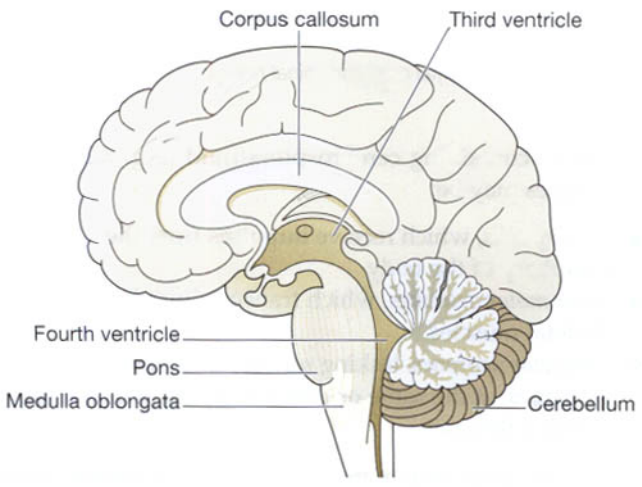


Figure 7.21 The cerebellum and associated structures.

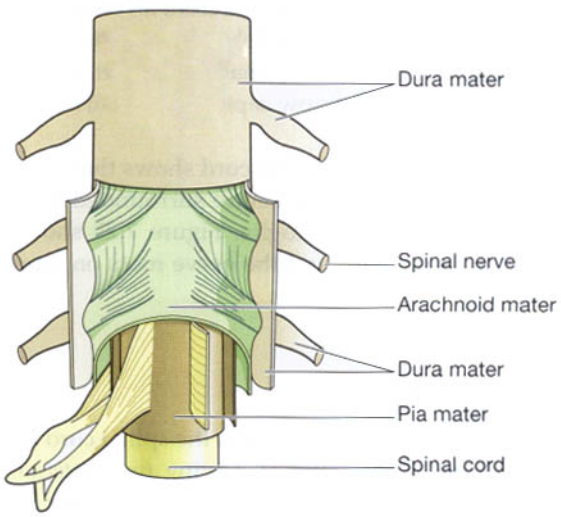


Figure 7.22 The meninges covering the spinal cord. Each cut away to show the underlying layers.

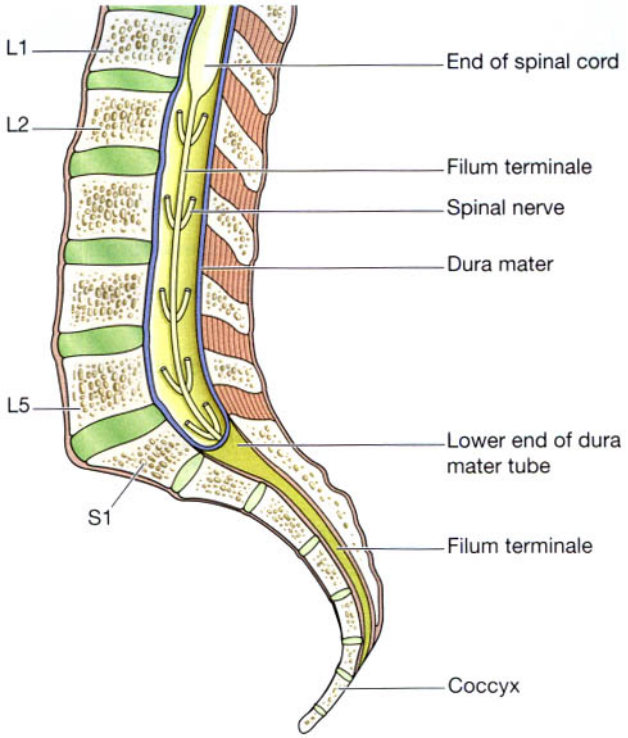


Figure 7.23 Section of the distal end of the vertebral canal.

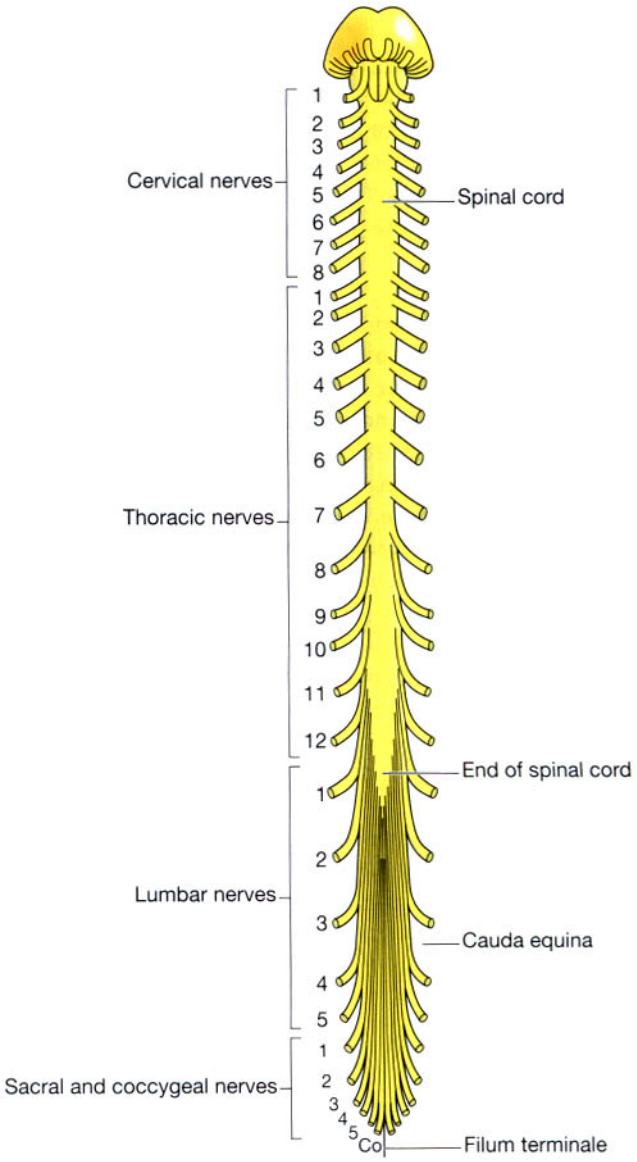


Figure 7.24 The spinal cord and spinal nerves.

brain to the various organs and tissues descend through the spinal cord. At the appropriate level they leave the cord and pass to the structure they supply. Similarly, sensory nerves from organs and tissues enter and pass upwards in the spinal cord to the brain.

Some activities of the spinal cord are independent of the brain, i.e. *spinal reflexes*. To facilitate these there are extensive neurone connections between sensory and motor neurones at the same or different levels in the cord.

The spinal cord is incompletely divided into two equal parts, anteriorly by a short, shallow *median fissure* and posteriorly by a deep narrow septum, the *posterior median septum*.

A cross-section of the spinal cord shows that it is composed of grey matter in the centre surrounded by white matter supported by neuroglia. Figure 7.25 shows the parts of the spinal cord and the nerve roots on one side. The other side is the same.

Grey matter

The arrangement of grey matter in the spinal cord resembles the shape of the letter H, having *two posterior, two anterior* and *two lateral columns*. The area of grey matter lying transversely is the *transverse commissure* and it is pierced by the central canal, an extension from the fourth ventricle, containing cerebrospinal fluid (Fig. 7.25). The cell bodies may be:

- *sensory cells*, which receive impulses from the periphery of the body
- *lower motor neurones*, which transmit impulses to the skeletal muscles
- *connector neurones*, linking sensory and motor neurones, at the same or different levels, which form spinal reflex arcs.

At each point where nerve impulses are passed from one neurone to another there is a synaptic cleft and a neurotransmitter (Fig. 7.8).

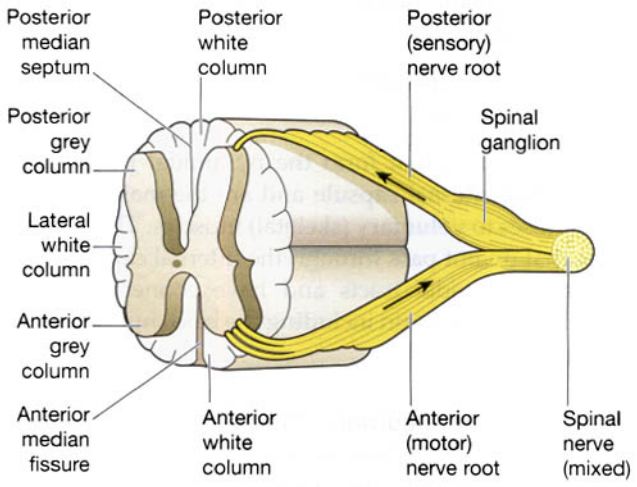


Figure 7.25 A section of the spinal cord showing nerve roots on one side.

Posterior columns of grey matter

These are composed of cell bodies which are stimulated by *sensory impulses* from the periphery of the body. The nerve fibres of these cells contribute to the formation of the white matter of the cord and transmit the sensory impulses upwards to the brain.

Anterior columns of grey matter

These are composed of the *cell bodies of the lower motor neurones* which are stimulated by the axons of the upper motor neurones or by the *cell bodies of connector neurones* linking the anterior and posterior columns to form reflex arcs.

The posterior root (spinal) ganglia are composed of cell bodies which lie just outside the spinal cord on the pathway of the sensory nerves. All sensory nerve fibres pass through these ganglia. The only function of the cells is to promote the onward movement of nerve impulses.

White matter

The white matter of the spinal cord is arranged in three *columns* or *tracts*; anterior, posterior and lateral. These tracts are formed by *sensory nerve fibres* ascending to the brain, *motor nerve fibres* descending from the brain and fibres of *connector neurones*.

Tracts are often named according to their points of origin and destination, e.g. spinothalamic, corticospinal.

Sensory nerve tracts (afferent or ascending) in the spinal cord

There are two main sources of sensation transmitted to the brain via the spinal cord.

1. *The skin*. Sensory receptors (nerve endings) in the skin, called *cutaneous receptors*, are stimulated by pain, heat, cold and touch, including pressure. Nerve impulses generated are conducted by three neurones to the sensory area in the *opposite hemisphere of the cerebrum* where the sensation and its location are perceived (Fig. 7.26). Crossing to the other side, or *decussation*, occurs either at the level of entry into the cord or in the medulla.
2. *The tendons, muscles and joints*. Sensory receptors are nerve endings in these structures, called *proprioceptors*, and they are stimulated by stretch. Together with impulses from the eyes and the ears they are associated with the maintenance of balance and posture and with perception of the position of the body in space. These nerve impulses have two destinations:

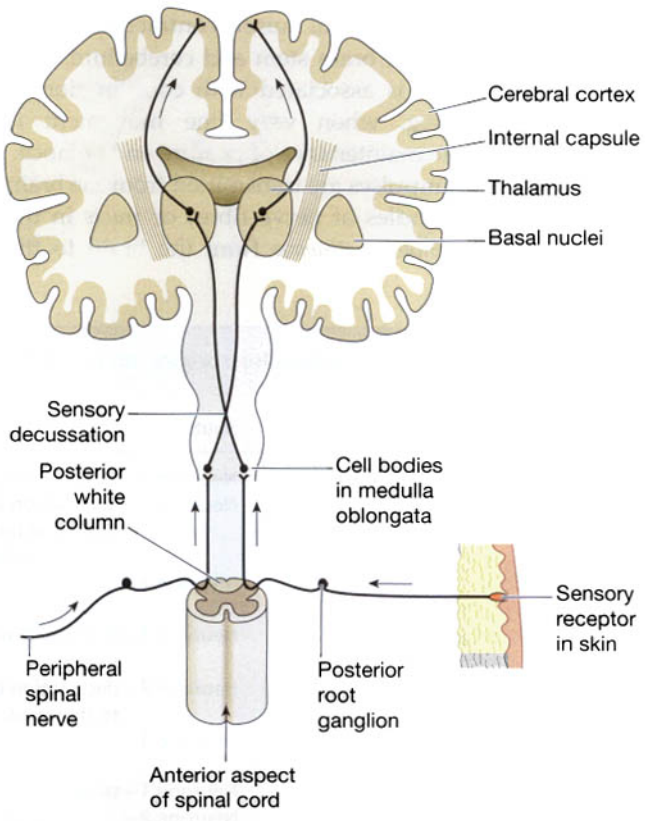


Figure 7.26 One of the sensory nerve pathways from the skin to the cerebrum.

- by a three-neurone system the impulses reach the sensory area of the *opposite hemisphere of the cerebrum*
- by a two-neurone system the nerve impulses reach the *cerebellar hemisphere on the same side*.

Table 7.1 provides further information about the origins, routes of transmission and the destinations of sensory nerve impulses.

Motor nerve tracts (efferent or descending) in the spinal cord

Neurones which transmit nerve impulses away from the brain are motor (efferent or descending) neurones. Motor neurone stimulation results in:

- contraction of skeletal (striated, voluntary) muscle
- contraction of smooth (involuntary) muscle, cardiac muscle and the secretion by glands controlled by nerves of the *autonomic nervous system* (p. 170).

Voluntary muscle movement

The contraction of the muscles which move the joints is, in the main, under conscious (voluntary) control, which means that the stimulus to contract originates at the level of consciousness in the cerebrum. However, some nerve impulses which affect skeletal muscle contraction are initiated in the midbrain, brain stem and cerebellum. This involuntary activity is associated with coordination of muscle activity, e.g. when very fine movement is required and in the maintenance of posture and balance.

Efferent nerve impulses are transmitted from the brain to the body via bundles of nerve fibres or *tracts* in the spinal cord. The *motor pathways* from the brain to the muscles are made up of two *neurones* (Fig. 7.19). These tracts are either:

- pyramidal (corticospinal)
- extrapyramidal.

The motor fibres that form the pyramidal tracts travel through the internal capsule and are the main pathway for impulses to voluntary (skeletal) muscles. Those motor fibres that do not pass through the internal capsule form the extrapyramidal tracts and have connections with many parts of the brain including the basal nuclei and the thalamus.

The upper motor neurone. This has its cell body (Betz's cell) in the *precentral sulcus area* of the cerebrum. The axons pass through the internal capsule, pons and medulla. In the spinal cord they form the *lateral corticospinal tracts* of white matter and the fibres terminate in close association with the cell bodies of the *lower motor neurones* in the anterior columns of grey matter. The axons of these upper motor neurones make up the pyramidal tracts and decussate in the medulla oblongata, forming the pyramids.

The lower motor neurone. This has its cell body in the *anterior horn of grey matter* in the spinal cord. Its axon emerges from the spinal cord by the *anterior root*, joins with the incoming sensory fibres and forms the *mixed spinal nerve* which passes through the *intervertebral foramen*. Near its termination in muscle the axon branches into a variable number of tiny fibres which form *motor end-plates*, each of which is in close association with a sensitive area on the wall of a muscle fibre. The motor

Table 7.1 Sensory nerve impulses: origins, routes, destinations

Receptor	Route	Destination
Pain, touch, temperature	Neurone 1 – to spinal cord by posterior root Neurone 2 – decussation on entering spinal cord then in anterolateral spinothalamic tract to thalamus Neurone 3 –	to parietal lobe of cerebrum
Touch, proprioceptors	Neurone 1 – to medulla in posterior spinothalamic tract Neurone 2 – decussation in medulla, transmission to thalamus Neurone 3 –	to parietal lobe of cerebrum
Proprioceptors	Neurone 1 – to spinal cord Neurone 2 –	no decussation, to cerebellum in posterior spinocerebellar tract

Table 7.2 Extrapyramidal upper motor neurones: origins and tracts

Origin	Name of tract	Site in spinal cord	Functions
Midbrain and pons	Rubrospinal tract decussates in brain stem	Lateral column	Control of skilled muscle movement
Reticular formation	Reticulospinal tract does not decussate	Lateral column	Coordination of muscle movement
Midbrain and pons	Tectospinal tract decussates in midbrain	Anterior column	Maintenance of posture and balance
Midbrain and pons	Vestibulospinal tract, some fibres decussate in the cord	Anterior column	

end-plates of each nerve and the muscle fibres they supply form a *motor unit* (Fig. 7.10). The neurotransmitter that conveys the nerve impulse across the synapse to stimulate the muscle fibre is *acetylcholine*. Motor units contract as a whole and the strength of contraction of a muscle depends on the number of motor units in action at a time.

The lower motor neurone has been described as the *final common pathway* for the transmission of nerve impulses to skeletal muscles. The cell body of this neurone is influenced by a number of upper motor neurones originating from various sites in the brain and by some neurones which begin and end in the spinal cord. Some of these neurones stimulate the cell bodies of the lower motor neurone while others have an inhibiting effect. The outcome of these influences is smooth, coordinated muscle movement, some of which is voluntary and some involuntary.

Involuntary muscle movement

Upper motor neurones. These have their cell bodies in the brain at a level *below* the cerebrum, i.e. in the midbrain, brain stem, cerebellum or spinal cord. They influence muscle activity in relation to the maintenance of posture and balance, the coordination of muscle movement and the control of muscle tone.

Table 7.2 shows details of the area of origin of these neurones and the tracts which their axons form before reaching the cell of the lower motor neurone in the spinal cord.

Spinal reflexes. These consist of three elements:

- sensory neurones
- connector neurones in the spinal cord
- lower motor neurones.

In the simplest *reflex arc* there is only one of each (Fig. 7.27). A *reflex action* is an immediate motor response to a sensory stimulus. Many connector and motor neurones may be stimulated by afferent impulses from a small area of skin, e.g. the pain impulses initiated by touching a very hot surface with the finger are transmitted to the spinal cord by sensory nerves. These stimulate many connector and lower motor neurones in the cord which results in the contraction of many skeletal muscles of the

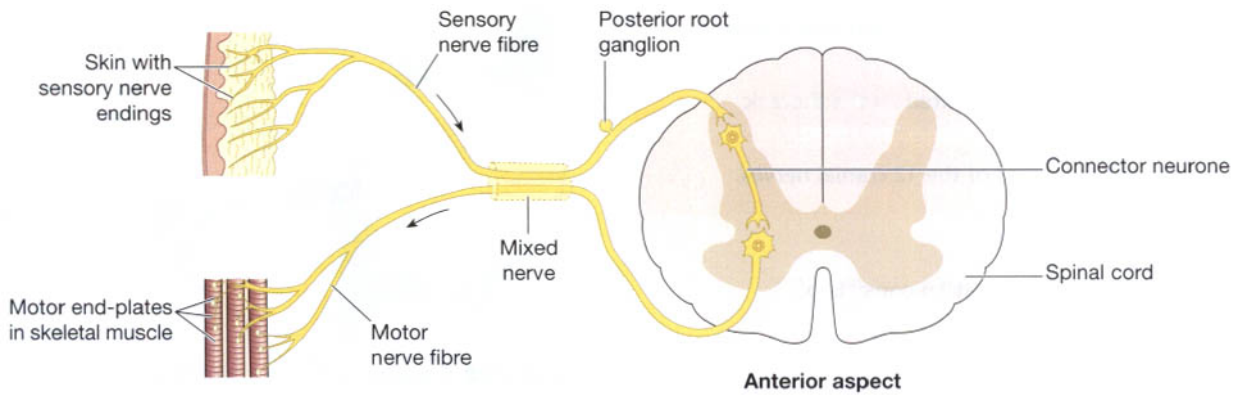


Figure 7.27 A simple reflex arc involving one side only.

hand, arm and shoulder, and the removal of the finger. Reflex action takes place very quickly, in fact, the motor response may have occurred simultaneously with the perception of the pain in the cerebrum. Reflexes of this type are invariably protective but they can on occasion be inhibited. For example, if it is a precious plate that is very hot when lifted every effort will be made to overcome the pain to prevent dropping it!

Stretch reflexes. Only two neurones are involved. The cell body of the lower motor neurone is stimulated by the sensory neurone. There is no connector neurone involved. The *knee jerk* is one example, but this type of reflex can be demonstrated at any point where a stretched tendon crosses a joint. By tapping the tendon just below the knee when it is bent, the sensory nerve endings in the tendon and in the thigh muscles are stretched. This initiates a nerve impulse which passes into the spinal cord to the cell body of the lower motor neurone in the anterior column of grey matter on the same side. As a result the thigh muscles suddenly contract and the foot kicks forward. This is used as a test of the integrity of the reflex arc. This type of reflex has a protective function—it prevents excessive joint movement that may damage tendons, ligaments and muscles.

Autonomic reflexes. See page 172.

PERIPHERAL NERVOUS SYSTEM

Learning outcomes

After studying this section you should be able to:

- state the origins of the paired spinal nerves
- outline the function of a nerve plexus
- list the spinal nerves entering each plexus and the main nerves emerging from it
- describe the areas innervated by the thoracic nerves
- outline the functions of the 12 cranial nerves.

This part of the nervous system consists of:

- 31 pairs of spinal nerves
- 12 pairs of cranial nerves
- the autonomic part of the nervous system.

Most of the nerves of the peripheral nervous system are composed of *sensory nerve fibres* conveying afferent impulses from sensory end organs to the brain, and *motor nerve fibres* conveying efferent impulses from the brain through the spinal cord to the effector organs, e.g. skeletal muscles, smooth muscle and glands.

Each nerve consists of numerous nerve fibres collected into bundles. Each bundle has several coverings of protective connective tissue (Fig. 7.28).

- *Endoneurium* is a delicate tissue, surrounding each individual fibre, which is continuous with the septa that pass inwards from the perineurium.
- *Perineurium* is a smooth connective tissue, surrounding each *bundle* of fibres.
- *Epineurium* is the fibrous tissue which surrounds and encloses a number of bundles of nerve fibres. Most large nerves are covered by epineurium.

Spinal nerves

There are *31 pairs of spinal nerves* that leave the vertebral canal by passing through the intervertebral foramina formed by adjacent vertebrae. They are named and grouped according to the vertebrae with which they are associated (Fig. 7.24):

- 8 cervical
- 12 thoracic
- 5 lumbar
- 5 sacral
- 1 coccygeal.

Although there are only seven cervical vertebrae, there are eight nerves because the first pair leave the vertebral

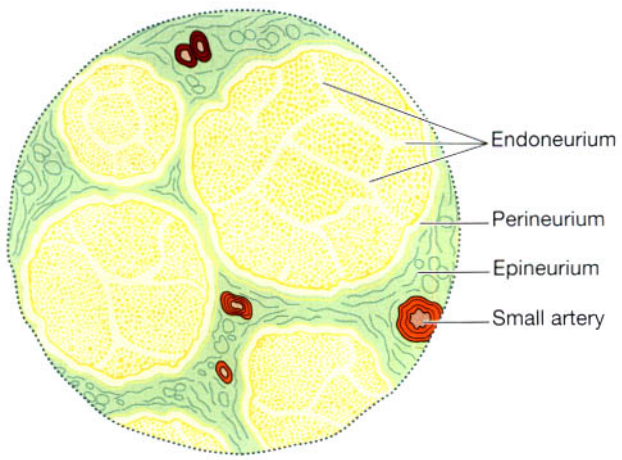


Figure 7.28 Transverse section of a peripheral nerve showing the protective coverings.

canal between the occipital bone and the atlas and the eighth pair leave below the last cervical vertebra. Thereafter the nerves are given the name and number of the vertebra immediately *above*.

The lumbar, sacral and coccygeal nerves leave the *spinal cord* near its termination at the level of the first lumbar vertebra, and extend downwards inside the vertebral canal in the subarachnoid space, forming a sheaf of nerves which resembles a horse's tail, the *cauda equina*. These nerves leave the vertebral canal at the appropriate lumbar, sacral or coccygeal level, depending on their destination.

The spinal nerves arise from both sides of the spinal cord and emerge through the intervertebral foramina. Each nerve is formed by the union of a *motor and a sensory nerve root* and is, therefore, a *mixed nerve*. Each spinal nerve has a contribution from the sympathetic part of the autonomic nervous system in the form of a *preganglionic fibre* (see Fig. 7.43, p. 171).

For details of the bones and muscles mentioned in the following section see Chapters 16 to 18. Bones and joints are supplied by adjacent nerves.

Nerve roots (Fig. 7.29)

The anterior nerve root consists of *motor nerve fibres* which are the axons of the nerve cells in the anterior column of grey matter in the spinal cord and, in the thoracic and lumbar regions, *sympathetic nerve fibres* which are the axons of cells in the lateral columns of grey matter.

The posterior nerve root consists of *sensory nerve fibres*. Just outside the spinal cord there is a *spinal ganglion* (posterior root ganglion), consisting of a little cluster of cell bodies. Sensory nerve fibres pass through these ganglia before entering the spinal cord. The area of skin supplied by each nerve is called a *dermatome* (Figs 7.34 and 7.38).

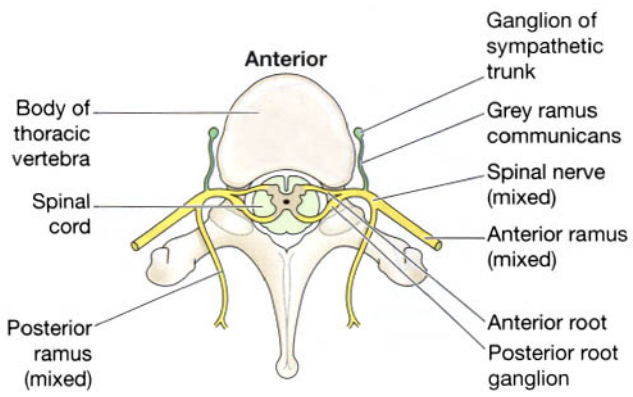


Figure 7.29 The relationship between sympathetic and mixed spinal nerves. Sympathetic part in green.

For a very short distance after leaving the spinal cord the nerve roots have a covering of *dura* and *arachnoid maters*. These terminate before the two roots join to form the mixed spinal nerve. The nerve roots have no covering of pia mater.

Immediately after emerging from the intervertebral foramen each spinal nerve divides into a ramus communicans, a posterior ramus and an anterior ramus.

The rami communicans are part of preganglionic sympathetic neurones of the autonomic nervous system (p. 170).

The posterior rami pass backwards and divide into medial and lateral branches to supply skin and muscles of relatively small areas of the posterior aspect of the head, neck and trunk.

The anterior rami supply the anterior and lateral aspects of the neck, trunk and the upper and lower limbs.

In the cervical, lumbar and sacral regions the anterior rami unite near their origins to form large masses of nerves, or *plexuses*, where nerve fibres are regrouped and rearranged before proceeding to supply skin, bones, muscles and joints of a particular area (Fig. 7.30). This

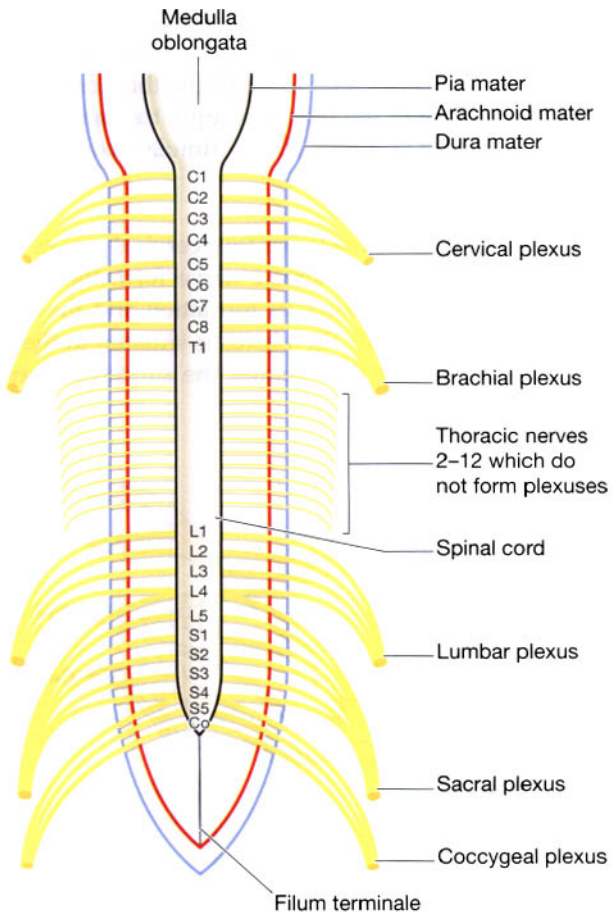


Figure 7.30 The meninges covering the spinal cord, spinal nerves and the plexuses they form.

means that these structures have a nerve supply from more than one spinal nerve and therefore damage to one spinal nerve does not cause loss of function of a region.

In the thoracic region the anterior rami do not form plexuses.

There are five large plexuses of mixed nerves formed on each side of the vertebral column. They are the:

- cervical plexuses
- brachial plexuses
- lumbar plexuses
- sacral plexuses
- coccygeal plexuses.

Cervical plexus (Fig. 7.31)

This is formed by the anterior rami of the first four cervical nerves. It lies opposite the 1st, 2nd, 3rd and 4th cervical vertebrae under the protection of the sterno-cleidomastoid muscle.

The superficial branches supply the structures at the back and side of the head and the skin of the front of the neck to the level of the sternum.

The deep branches supply muscles of the neck, e.g. the sternocleidomastoid and the trapezius.

The phrenic nerve originates from cervical roots 3, 4 and 5 and passes downwards through the thoracic cavity in front of the root of the lung to supply the muscle of the diaphragm with impulses which stimulate contraction.

Brachial plexus

The anterior rami of the lower four cervical nerves and a large part of the first thoracic nerve form the brachial plexus. Figure 7.32 shows its formation and the nerves which emerge from it. The plexus is situated in the neck and shoulder above and behind the subclavian vessels and in the axilla.

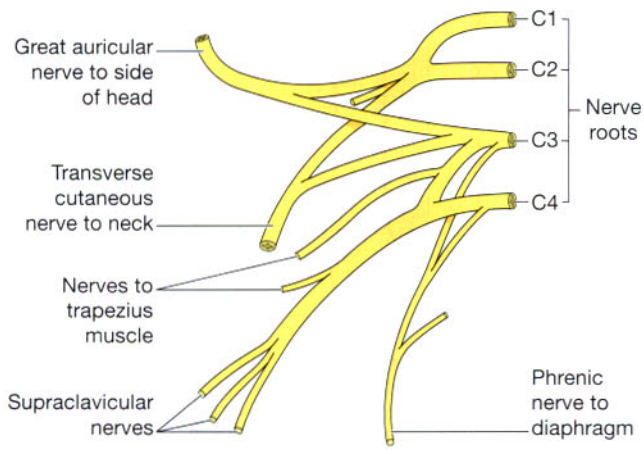


Figure 7.31 The cervical plexus.

The branches of the brachial plexus supply the skin and muscles of the upper limbs and some of the chest muscles. Five large nerves and a number of smaller ones emerge from this plexus, each with a contribution from more than one nerve root, containing sensory, motor and autonomic fibres:

- axillary (circumflex) nerve: C5, 6
- radial nerve: C5, 6, 7, 8, T1
- musculocutaneous nerve: C5, 6, 7
- median nerve: C5, 6, 7, 8, T1
- ulnar nerve: C7, 8, T1
- medial cutaneous nerve: C8, T1.

The axillary (circumflex) nerve winds round the humerus at the level of the surgical neck. It then breaks up into minute branches to supply the deltoid muscle, shoulder joint and overlying skin.

The radial nerve is the largest branch of the brachial plexus. It supplies the triceps muscle behind the humerus, crosses in front of the elbow joint then winds round to the back of the forearm to supply extensors of the wrist and finger joints. It continues into the back of the hand to supply the skin of the thumb, the first two fingers and the lateral half of the third finger.

The musculocutaneous nerve passes downwards to the lateral aspect of the forearm. It supplies the muscles of the upper arm and the skin of the forearm.

The median nerve passes down the midline of the arm in close association with the brachial artery. It passes in front of the elbow joint then down to supply the muscles

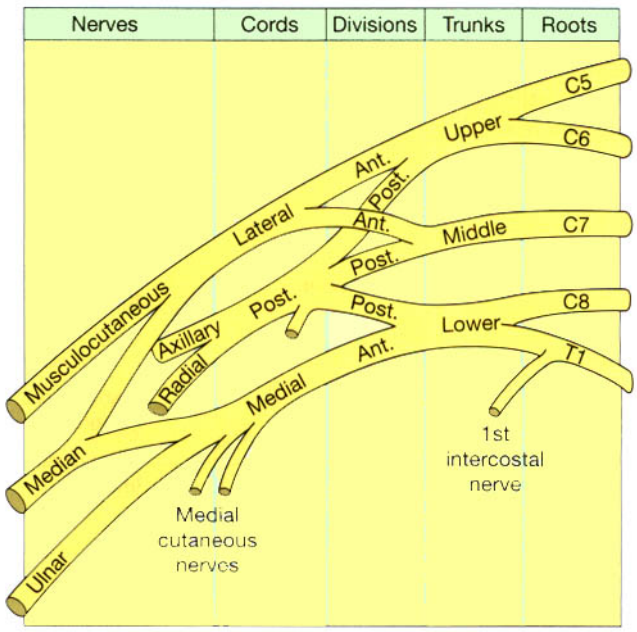


Figure 7.32 The brachial plexus.

of the front of the forearm. It continues into the hand where it supplies small muscles and the skin of the front of the thumb, the first two fingers and the lateral half of the third finger. It gives off no branches above the elbow.

The ulnar nerve descends through the upper arm lying medial to the brachial artery. It passes behind the medial epicondyle of the humerus to supply the muscles on the ulnar aspect of the forearm. It continues downwards to supply the muscles in the palm of the hand and the skin of the whole of the little finger and the medial half of the third finger. It gives off no branches above the elbow.

The main nerves of the arm are presented in Figure 7.33. The distribution and origins of the cutaneous sensory nerves of the arm are shown in Figure 7.34, i.e. the dermatomes.

Lumbar plexus (Figs 7.35, 7.37 and 7.38)

The lumbar plexus is formed by the anterior rami of the first three and part of the fourth lumbar nerves. The plexus is situated in front of the transverse processes of the lumbar vertebrae and behind the psoas muscle. The main branches, and their nerve roots are:

- iliohypogastric nerve: L1
- ilioinguinal nerve: L1
- genitofemoral: L1, 2
- lateral cutaneous nerve of thigh: L2, 3
- femoral nerve: L2, 3, 4
- obturator nerve: L2, 3, 4
- lumbosacral trunk: L4, (5).

The iliohypogastric, ilioinguinal and *genitofemoral nerves* supply muscles and the skin in the area of the lower abdomen, upper and medial aspects of the thigh and the inguinal region.

The lateral cutaneous nerve of the thigh supplies the skin of the lateral aspect of the thigh including part of the anterior and posterior surfaces.

The femoral nerve is one of the larger branches. It passes behind the inguinal ligament to enter the thigh in close association with the femoral artery. It divides into cutaneous and muscular branches to supply the skin and the muscles of the front of the thigh. One branch, the *saphenous nerve*, supplies the medial aspect of the leg, ankle and foot.

The obturator nerve supplies the adductor muscles of the thigh and skin of the medial aspect of the thigh. It ends just above the level of the knee joint.

The lumbosacral trunk descends into the pelvis and makes a contribution to the sacral plexus.

Sacral plexus (Figs 7.36, 7.37 and 7.38)

The sacral plexus is formed by the anterior rami of the lumbosacral trunk and the first, second and third sacral

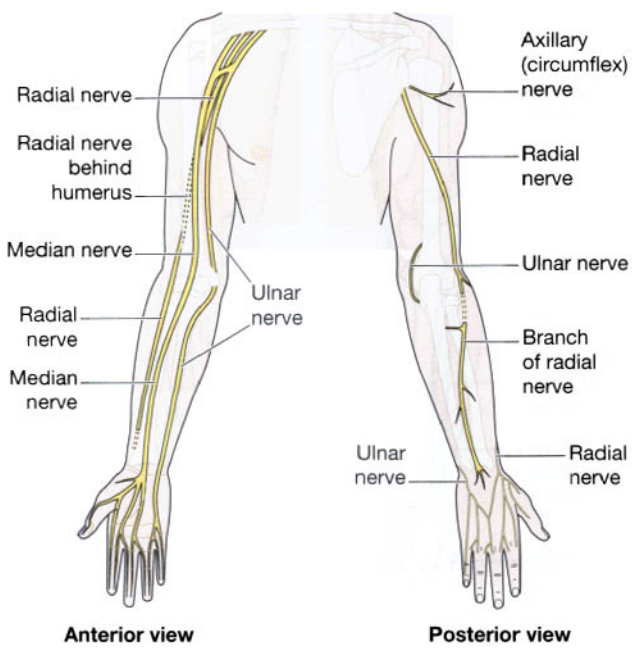


Figure 7.33 The main nerves of the arm.

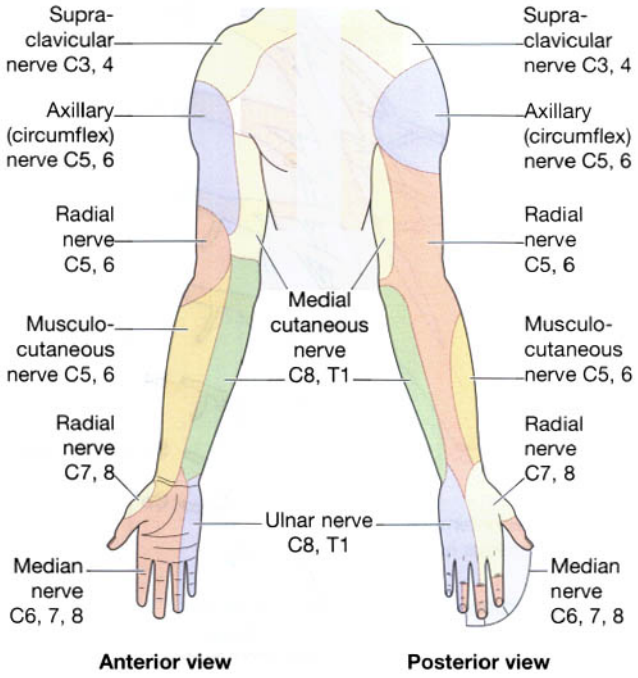


Figure 7.34 The distribution and origins of the cutaneous nerves of the arm.

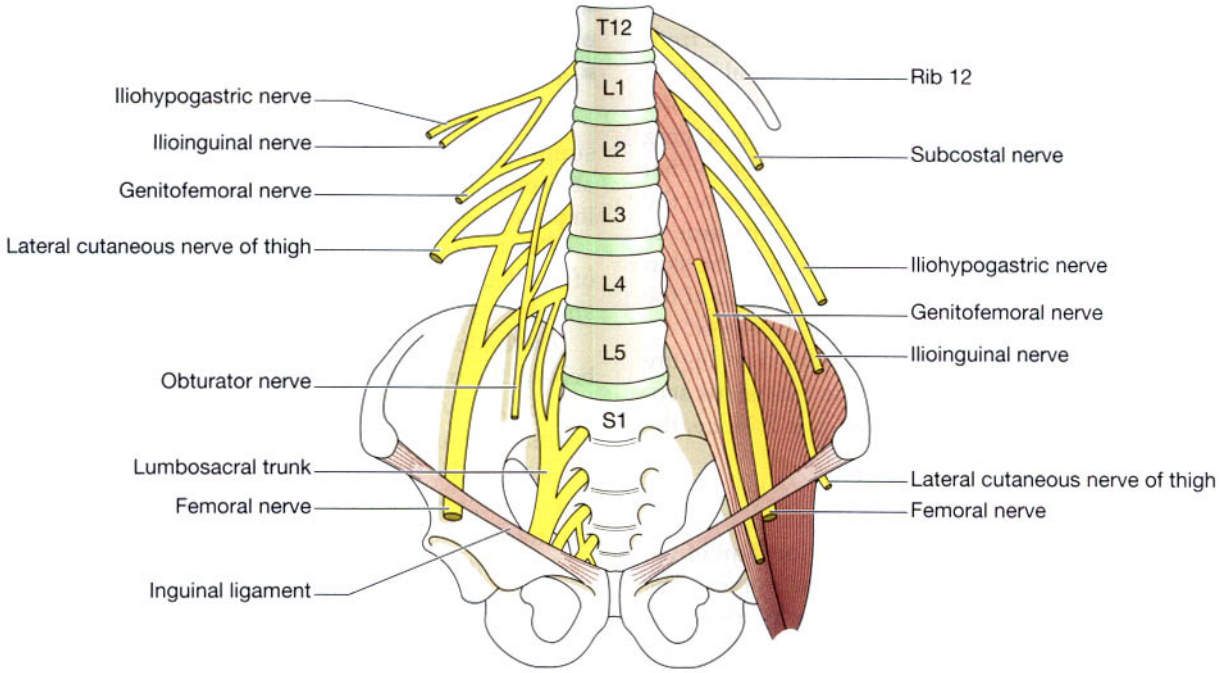


Figure 7.35 The lumbar plexus.

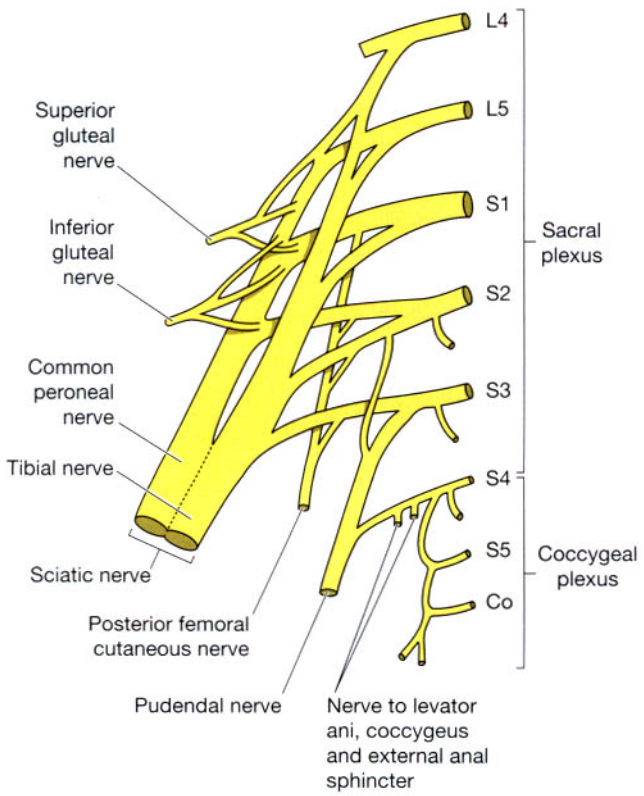


Figure 7.36 Sacral and coccygeal plexuses.

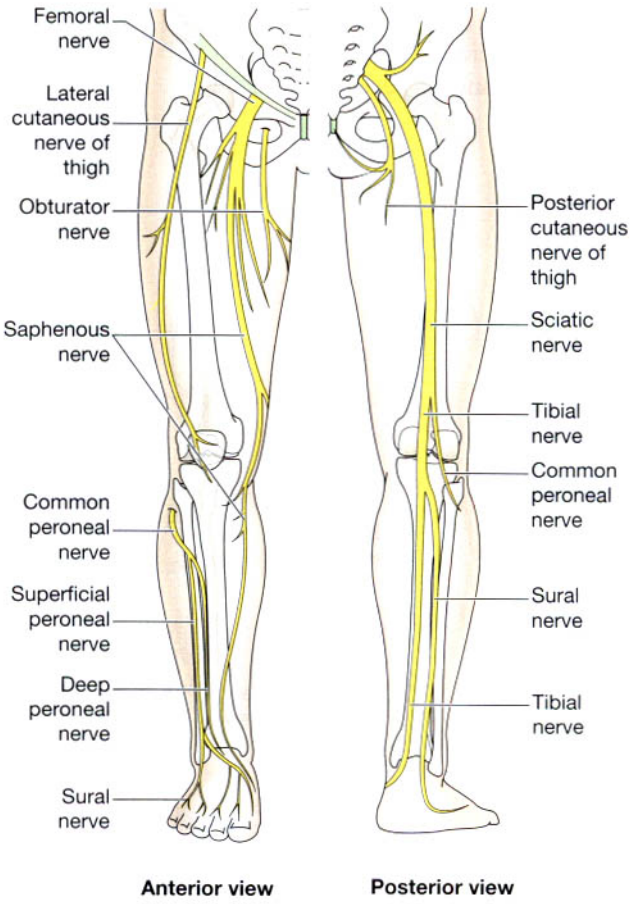


Figure 7.37 The main nerves of the leg.

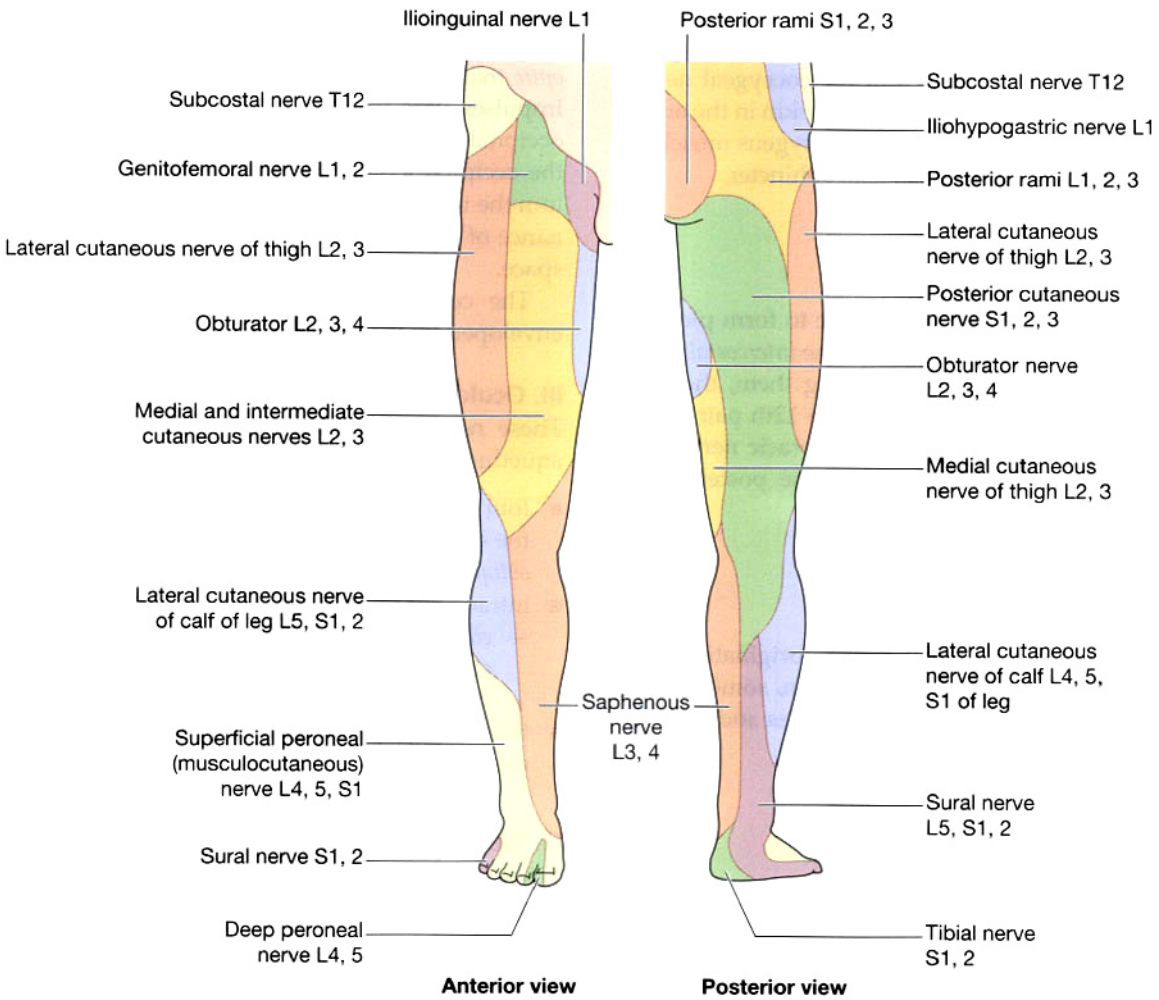


Figure 7.38 Distribution and origins of the cutaneous nerves of the leg.

nerves. The lumbosacral trunk is formed by the fifth and part of the fourth lumbar nerves. It lies in the posterior wall of the pelvic cavity.

The sacral plexus divides into a number of branches, supplying the muscles and skin of the pelvic floor, muscles around the hip joint and the pelvic organs. In addition to these it provides the *sciatic nerve* which contains fibres from L4, 5, S1, 2, 3.

The sciatic nerve is the largest nerve in the body. It is about 2 cm wide at its origin. It passes through the greater sciatic foramen into the buttock then descends through the posterior aspect of the thigh supplying the hamstring muscles. At the level of the middle of the femur it divides to form the *tibial* and the *common peroneal nerves*.

The tibial nerve descends through the popliteal fossa to the posterior aspect of the leg where it supplies muscles and skin. It passes under the medial malleolus to supply muscles and skin of the sole of the foot and toes. One of the main branches is the *sural nerve* which supplies the tissues in the area of the heel, the lateral aspect of the ankle and a part of the dorsum of the foot.

The common peroneal nerve descends obliquely along the lateral aspect of the popliteal fossa, winds round the neck of the fibula into the front of the leg where it divides into the *deep peroneal* (anterior tibial) and the *superficial peroneal* (musculocutaneous) nerves. These nerves supply the skin and muscles of the anterior aspect of the leg and the dorsum of the foot and toes.

The pudendal nerve (S2, 3, 4). The perineal branch supplies the external anal sphincter, the external urethral sphincter and adjacent skin. Figures 7.37 and 7.38 show the main nerves of the leg, the dermatomes and the origins of the main nerves.

Coccygeal plexus (Fig. 7.36)
The coccygeal plexus is a very small plexus formed by part of the fourth and fifth sacral and the coccygeal nerves. The nerves from this plexus supply the skin in the area of the coccyx and the levators ani and coccygeus muscles of the pelvic floor and the external anal sphincter.

Thoracic nerves

The thoracic nerves *do not* intermingle to form plexuses. There are 12 pairs and the first 11 are the *intercostal nerves*. They pass between the ribs supplying them, the intercostal muscles and overlying skin. The 12th pair are the *subcostal nerves*. The 7th to the 12th thoracic nerves also supply the muscles and the skin of the posterior and anterior abdominal walls (Fig. 7.39).

Cranial nerves (Fig. 7.40)

There are 12 pairs of cranial nerves originating from nuclei in the inferior surface of the brain, some sensory, some motor and some mixed. Their names and numbers are:

I.	Olfactory: sensory
II.	Optic: sensory
III.	Oculomotor: motor
IV.	Trochlear: motor
V.	Trigeminal: mixed
VI.	Abducent: motor
VII.	Facial: mixed
VIII.	Vestibulocochlear (auditory): sensory
IX.	Glossopharyngeal: mixed
X.	Vagus: mixed
XI.	Accessory: motor
XII.	Hypoglossal: motor.

I. Olfactory nerves (sensory)
These are the nerves of the *sense of smell*. Their nerve endings and fibres originate in the upper part of the mucous membrane of the nasal cavity, pass upwards through the cribriform plate of the ethmoid bone and then go to the *olfactory bulb* (see Fig. 8.23, p. 206). The nerves then proceed backwards as the olfactory tract, to the area for the perception of smell in the temporal lobe of the cerebrum.

II. Optic nerves (sensory)
These are the nerves of the *sense of sight*. The fibres originate in the retinae of the eyes and they combine to form the optic nerves (see Fig. 8.13, p. 200). They are directed backwards and medially through the posterior part of the orbital cavity. They then pass through the *optic foramina* of the sphenoid bone into the cranial cavity and join at the *optic chiasma*. The nerves proceed backwards as the *optic tracts* to the *lateral geniculate bodies* of the thalamus. Impulses pass from these to the centre for sight in the occipital lobes of the cerebrum and to the cerebellum. In the occipital lobe sight is perceived, and in the cerebellum the impulses from the eyes contribute to the maintenance of balance, posture and orientation of the head in space.

The central retinal artery and vein enter the eye enveloped by the fibres of the optic nerve.

III. Oculomotor nerves (motor)
These nerves arise from nerve cells near the cerebral aqueduct. They supply:

- four extraocular muscles, which move the eyeball, i.e. the *superior, medial* and *inferior recti* and the *inferior oblique muscle*
- intraocular muscles:
  - *ciliary muscles* which alter the shape of the lens, changing its refractive power
  - *circular muscles of the iris* which constrict the pupil
- the *levator palpebrae* muscle which raises the upper eyelid.

IV. Trochlear nerves (motor)
These nerves arise from nerve cells near the cerebral aqueduct. They supply the *superior oblique muscles* of the eyes.

V. Trigeminal nerves (mixed)
These nerves contain motor and sensory fibres and are among the largest of the cranial nerves. They are the chief sensory nerves for the face and head (including the oral and nasal cavities and teeth), receiving impulses of pain, temperature and touch. The motor fibres stimulate the muscles of mastication.

There are three main branches of the trigeminal nerves. The dermatomes supplied by the sensory fibres on the right side are shown in Figure 7.41.

The ophthalmic nerves are sensory only and supply the lacrimal glands, conjunctiva of the eyes, forehead, eyelids, anterior aspect of the scalp and mucous membrane of the nose.

The maxillary nerves are sensory only and supply the cheeks, upper gums, upper teeth and lower eyelids.

The mandibular nerves contain both sensory and motor fibres. These are the largest of the three divisions and they supply the teeth and gums of the lower jaw, pinnae of the ears, lower lip and tongue. The motor fibres supply the muscles of mastication.

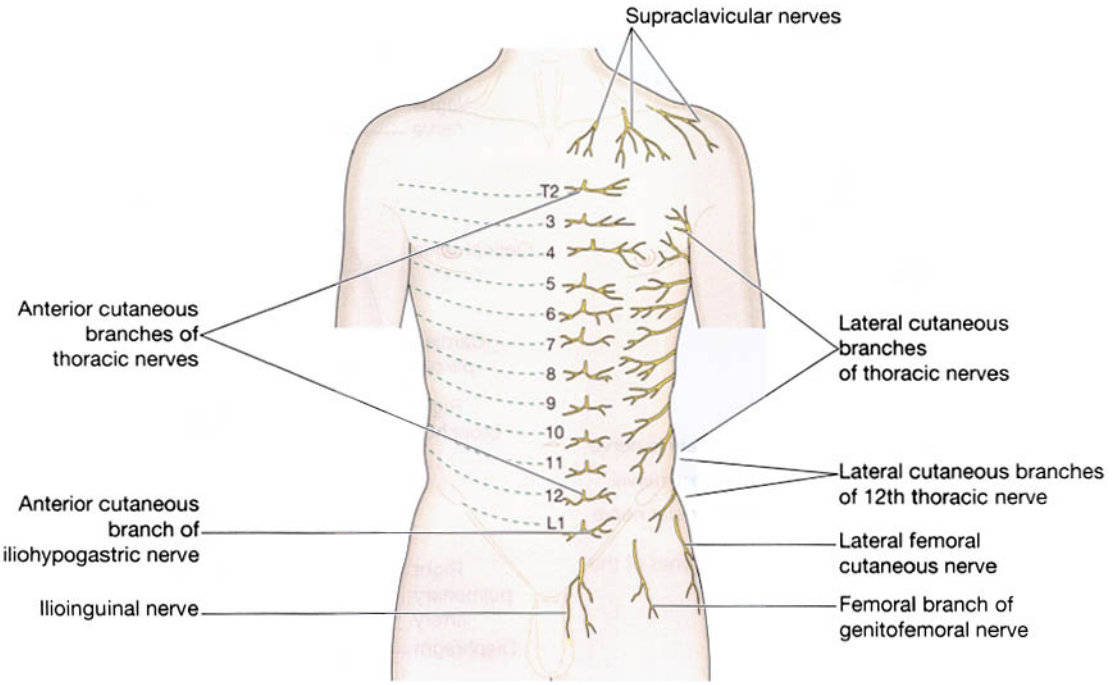


Figure 7.39 Segmental distribution of the thoracic cutaneous nerves.

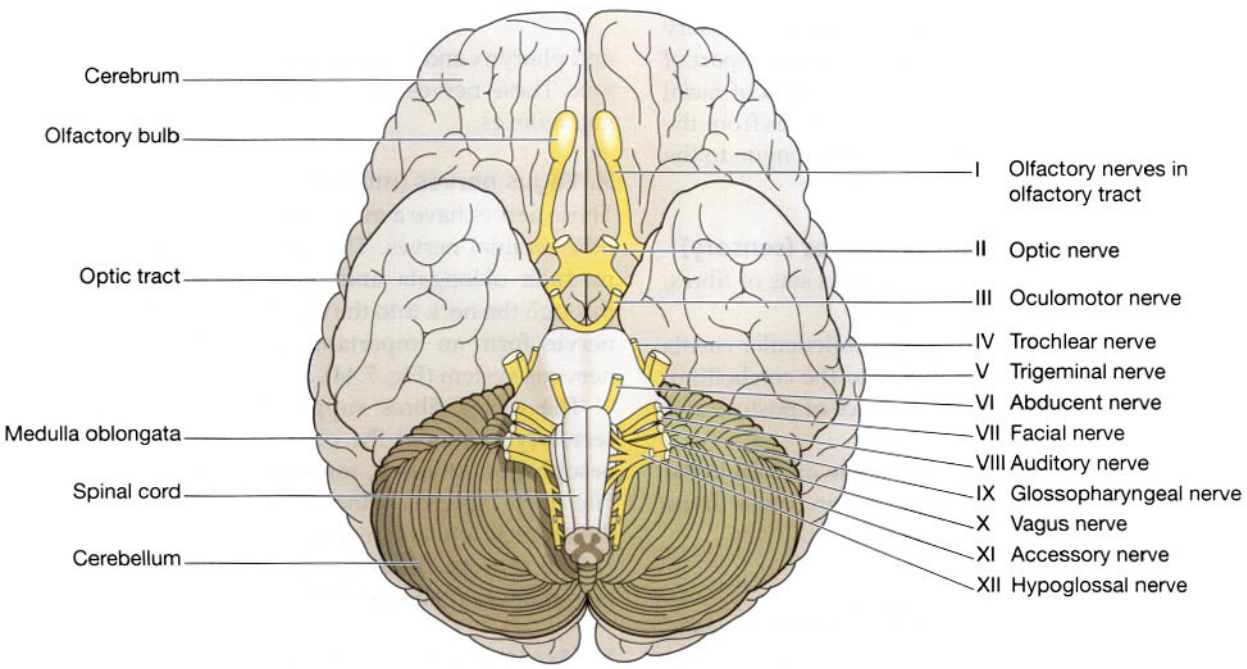


Figure 7.40 The inferior surface of the brain showing the cranial nerves.

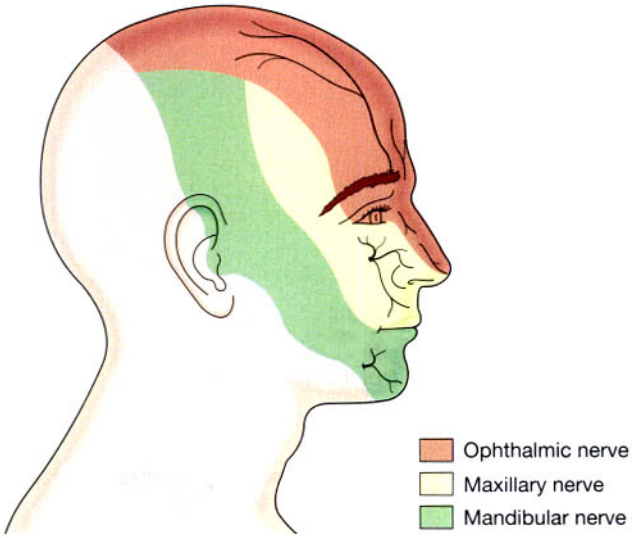


Figure 7.41 The cutaneous distribution of the main branches of the right trigeminal nerve.

VI. Abducent nerves (motor)

These nerves arise from a group of nerve cells lying under the floor of the fourth ventricle. They supply the *lateral rectus muscles* of the eyeballs.

VII. Facial nerves (mixed)

These nerves are composed of both motor and sensory nerve fibres, arising from nerve cells in the lower part of the pons. The motor fibres supply the muscles of facial expression. The sensory fibres convey impulses from the taste buds in the anterior two-thirds of the tongue to the taste perception area in the cerebral cortex.

VIII. Vestibulocochlear (auditory) nerves (sensory)

These nerves are composed of two distinct sets of fibres, vestibular nerves and cochlear nerves.

The vestibular nerves arise from the semicircular canals of the inner ear and convey impulses to the cerebellum. They are associated with the maintenance of posture and balance.

The cochlear nerves originate in the organ of Corti in the inner ear and convey impulses to the hearing areas in the cerebral cortex where sound is perceived.

IX. Glossopharyngeal nerves (mixed)

These nerves arise from nuclei in the medulla oblongata. The motor fibres stimulate the muscles of the tongue and pharynx and the secretory cells of the parotid (salivary) glands.

The sensory fibres convey impulses to the cerebral cortex from the posterior third of the tongue, the tonsils and pharynx and from taste buds in the tongue and pharynx. These nerves are essential for the swallowing and gag reflexes.

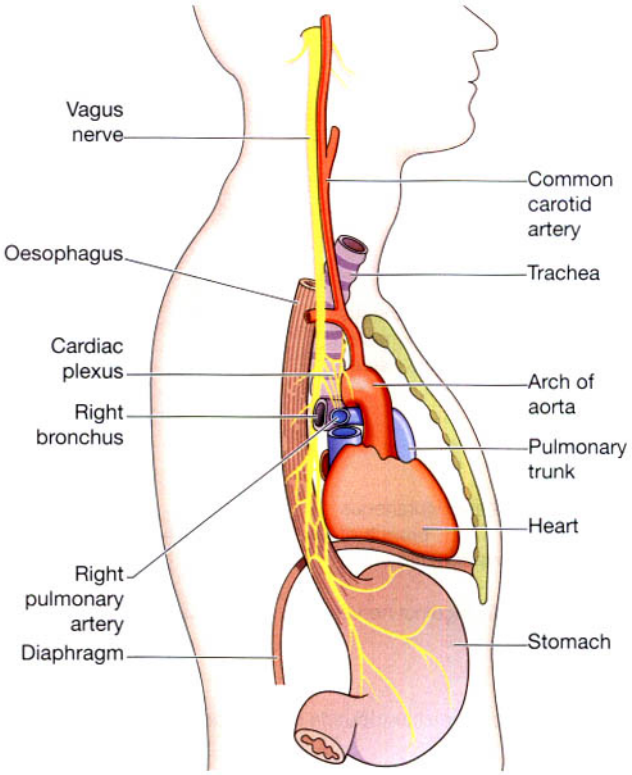


Figure 7.42 The position of the vagus nerve in the thorax viewed from the right side.

X. Vagus nerves (mixed) (Fig. 7.42)

These nerves have a more extensive distribution than any other cranial nerves. They arise from nerve cells in the medulla oblongata and other nuclei, and pass down through the neck into the thorax and the abdomen. These nerves form an important part of the parasympathetic nervous system (Fig. 7.44).

The motor fibres supply the smooth muscles and secretory glands of the pharynx, larynx, trachea, heart, oesophagus, stomach, intestines, pancreas, gall bladder, bile ducts, spleen, kidneys, ureter and blood vessels in the thoracic and abdominal cavities.

The sensory fibres convey impulses from the lining membranes of the same structures to the brain.

XI. Accessory nerves (motor)

These nerves arise from cell bodies in the medulla oblongata and in the spinal cord. The fibres supply the *sternocleidomastoid* and *trapezius muscles*. Branches join the vagus nerves and supply the *pharyngeal* and *laryngeal muscles*.

XII. Hypoglossal nerves (motor)

These nerves arise from cells in the medulla oblongata. They supply the muscles of the tongue and muscles surrounding the hyoid bone and contribute to swallowing and speech.

A summary of the cranial nerves is given in Table 7.3.

Table 7.3 Summary of the cranial nerves

Name and no.	Central connection	Peripheral connection	Function
I. Olfactory (sensory)	Smell area in temporal lobe of cerebrum through olfactory bulb	Mucous membrane in roof of nose	Sense of smell
II. Optic (sensory)	Sight area in occipital lobe of cerebrum Cerebellum	Retina of the eye	Sense of sight Balance
III. Oculomotor (motor)	Nerve cells near floor of aqueduct of midbrain	Superior, inferior and medial rectus muscles of the eye Ciliary muscles of the eye Circular muscle fibres of the iris	Moving the eyeball Focusing Regulating the size of the pupil
IV. Trochlear (motor)	Nerve cells near floor of aqueduct of midbrain	Superior oblique muscles of the eye	Movement of the eyeball
V. Trigeminal (mixed)	Motor fibres from the pons Sensory fibres from the trigeminal ganglion	Muscles of mastication Sensory to gums, cheek, lower jaw, iris, cornea	Chewing Sensation from the face
VI. Abducent (motor)	Floor of fourth ventricle	Lateral rectus muscle of the eye	Movement of the eye
VII. Facial (mixed)	Pons	Sensory fibres to the tongue Motor fibres to the muscles of the face	Sense of taste Movements of facial expression
VIII. Vestibulocochlear (sensory) (a) Vestibular (b) Cochlear	 Cerebellum Hearing area of cerebrum	 Semicircular canals in the inner ear Organ of Corti in cochlea	 Maintenance of balance Sense of hearing
IX. Glossopharyngeal (mixed)	Medulla oblongata	Parotid gland Back of tongue and pharynx	Secretion of saliva Sense of taste Movement of pharynx
X. Vagus (mixed)	Medulla oblongata	Pharynx, larynx; organs, glands ducts, blood vessels in the thorax and abdomen	Movement and secretion
XI. Accessory (motor)	Medulla oblongata	Sternocleidomastoid, trapezius, laryngeal and pharyngeal muscles	Movement of the head, shoulders, pharynx and larynx
XII. Hypoglossal (motor)	Medulla oblongata	Tongue	Movement of tongue

AUTONOMIC NERVOUS SYSTEM

Learning outcomes

After studying this section you should be able to:

- identify the two divisions of the autonomic nervous system
- compare and contrast the structures and neurotransmitters of the two divisions
- compare and contrast the effects of stimulation of the two divisions on body systems
- explain how referred pain occurs.

The autonomic or involuntary part of the nervous system (Fig. 7.6) controls the functions of the body carried out 'automatically', i.e. initiated in the brain below the level of the cerebrum. Although stimulation does not occur voluntarily the individual may be conscious of its effects, e.g. an increase in the heart rate.

The effects of autonomic control are rapid and essential for homeostasis.

The effector organs are:

- smooth muscle
- cardiac muscle
- glands (Fig. 7.6).

Effects of autonomic stimulation include:

- changes in rate and force of the heartbeat
- stimulation or depression of secretion of glands
- vasoconstriction or vasodilatation
- bronchoconstriction or bronchodilation
- changes in size of the pupils of the eyes.

The *efferent (motor) nerves* of the autonomic nervous system arise from nerve cells in the brain and emerge at various levels between the midbrain and the sacral region of the spinal cord. Many of them travel within the same nerve sheath as the peripheral nerves of the central nervous system to reach the organs which they innervate.

The autonomic nervous system is divided into two divisions:

- *sympathetic* (thoracolumbar outflow)
- *parasympathetic* (craniosacral outflow).

The two divisions have both structural and functional differences. They normally work in an opposing manner, enabling or restoring balance of involuntary functions, maintaining homeostasis. Sympathetic activity tends to predominate in stressful situations and parasympathetic activity during rest.

Each division has two efferent neurones in its peripheral pathways between the central nervous system and effector organs. These are:

- the preganglionic neurone
- the postganglionic neurone.

The cell body of the preganglionic neurone is in the brain or spinal cord. Its axon terminals synapse with the cell body of the postganglionic neurone in an *autonomic ganglion* outside the central nervous system. The postganglionic neurone conducts impulses to the effector organ (Fig. 7.9).

Sympathetic nervous system

Neurones convey impulses from their origin in the hypothalamus, reticular formation and medulla oblongata to effector organs and tissues (Fig. 7.43). The first neurone has its cell body in the brain and its fibre extends into the spinal cord.

The preganglionic neurone. This has its cell body in the *lateral column of grey matter* in the spinal cord between the levels of the 1st thoracic and 2nd or 3rd lumbar vertebrae. The nerve fibre of this cell leaves the cord by the anterior root and terminates in one of the ganglia either in the *lateral chain of sympathetic ganglia* or passes through it to one of the *prevertebral ganglia*. Acetylcholine is the neurotransmitter.

The postganglionic neurone. This has its cell body in a ganglion and terminates in the organ or tissue supplied. Noradrenaline is usually the neurotransmitter.

Sympathetic ganglia

The lateral chains of sympathetic ganglia. These are chains of ganglia which extend from the upper cervical level to the sacrum, one chain lying on each side of the bodies of the vertebrae. The ganglia are attached to each other by nerve fibres. Preganglionic neurones that emerge from the cord may synapse with the cell body of the postganglionic neurone at the same level or they may pass up or down the chain through one or more ganglia before synapsing. For example, the nerve which dilates the pupil of the eye leaves the cord at the level of the 1st thoracic vertebra and passes up the chain to the superior cervical ganglion before it synapses with the cell body of the postsynaptic neurone. The postganglionic neurones then pass to the eyes. The major exception is that there is no parasympathetic supply to the sweat glands, the skin

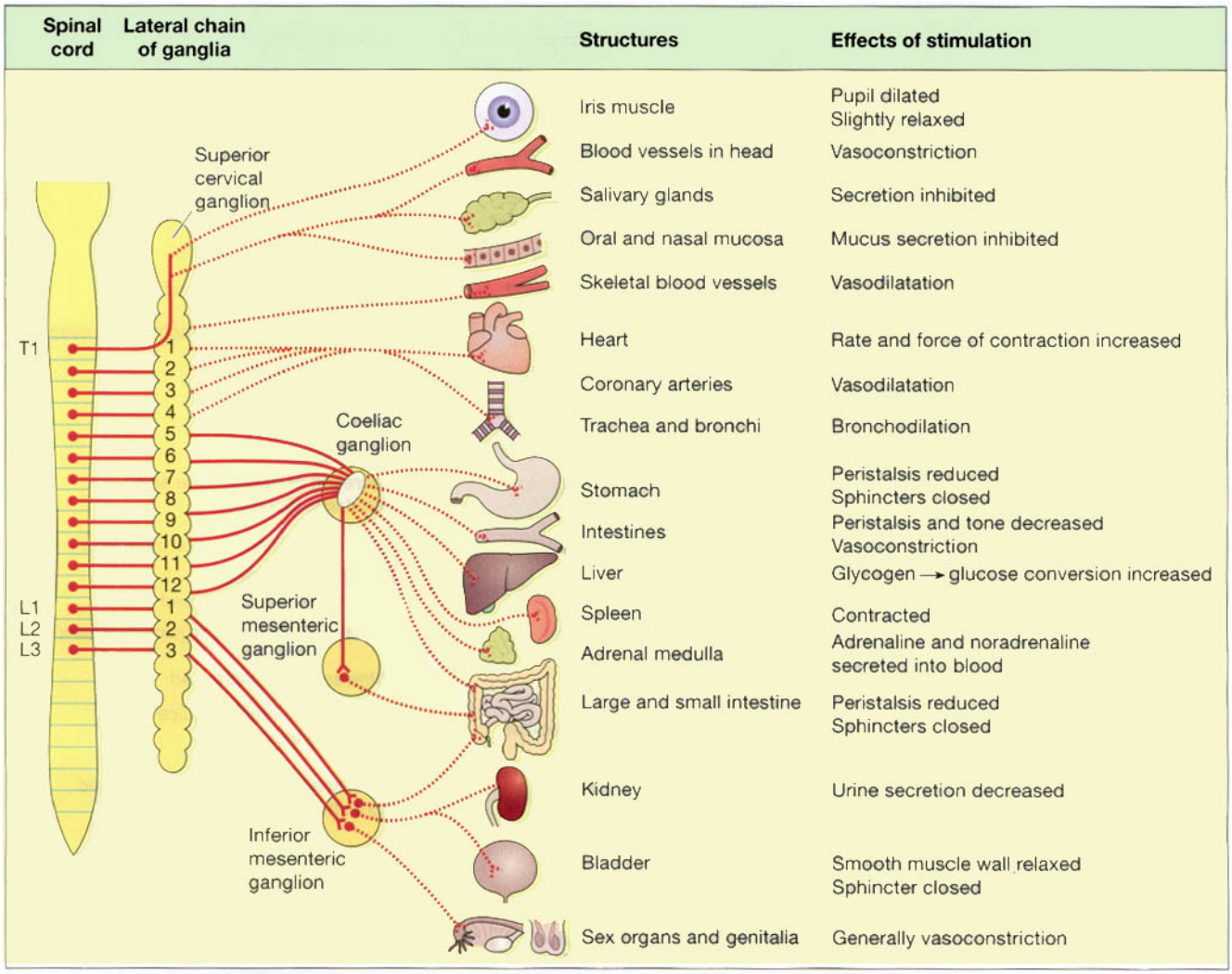


Figure 7.43 The sympathetic outflow, the main structures supplied and the effects of stimulation. Solid red lines – preganglionic fibres; broken lines – postganglionic fibres. There is a right and left lateral chain of ganglia.

and blood vessels of skeletal muscles. These structures are supplied by only sympathetic fibres, some of which have acetylcholine and some adrenaline and noradrenaline as their neurotransmitter. They have, therefore, the effects of both sympathetic and parasympathetic nerve supply (Fig. 7.43).

Prevertebral ganglia. There are three prevertebral ganglia situated in the abdominal cavity close to the origins of arteries of the same names:

- coeliac ganglion
- superior mesenteric ganglion
- inferior mesenteric ganglion.

The ganglia consist of nerve cell bodies rather diffusely distributed among a network of nerve fibres which form plexuses. Preganglionic sympathetic fibres pass through the lateral chain to reach these ganglia.

Parasympathetic nervous system

Two neurones (preganglionic and postganglionic) are involved in the transmission of impulses from their source to the effector organ (Fig. 7.44). The neurotransmitter at both synapses is acetylcholine.

The preganglionic neurone. This has its cell body either in the brain or in the spinal cord. Those originating in the brain are the *cranial nerves* III, VII, IX and X, arising from nuclei in the midbrain and brain stem, and their nerve fibres terminate outside the brain. The cell bodies of the *sacral outflow* are in the lateral columns of grey

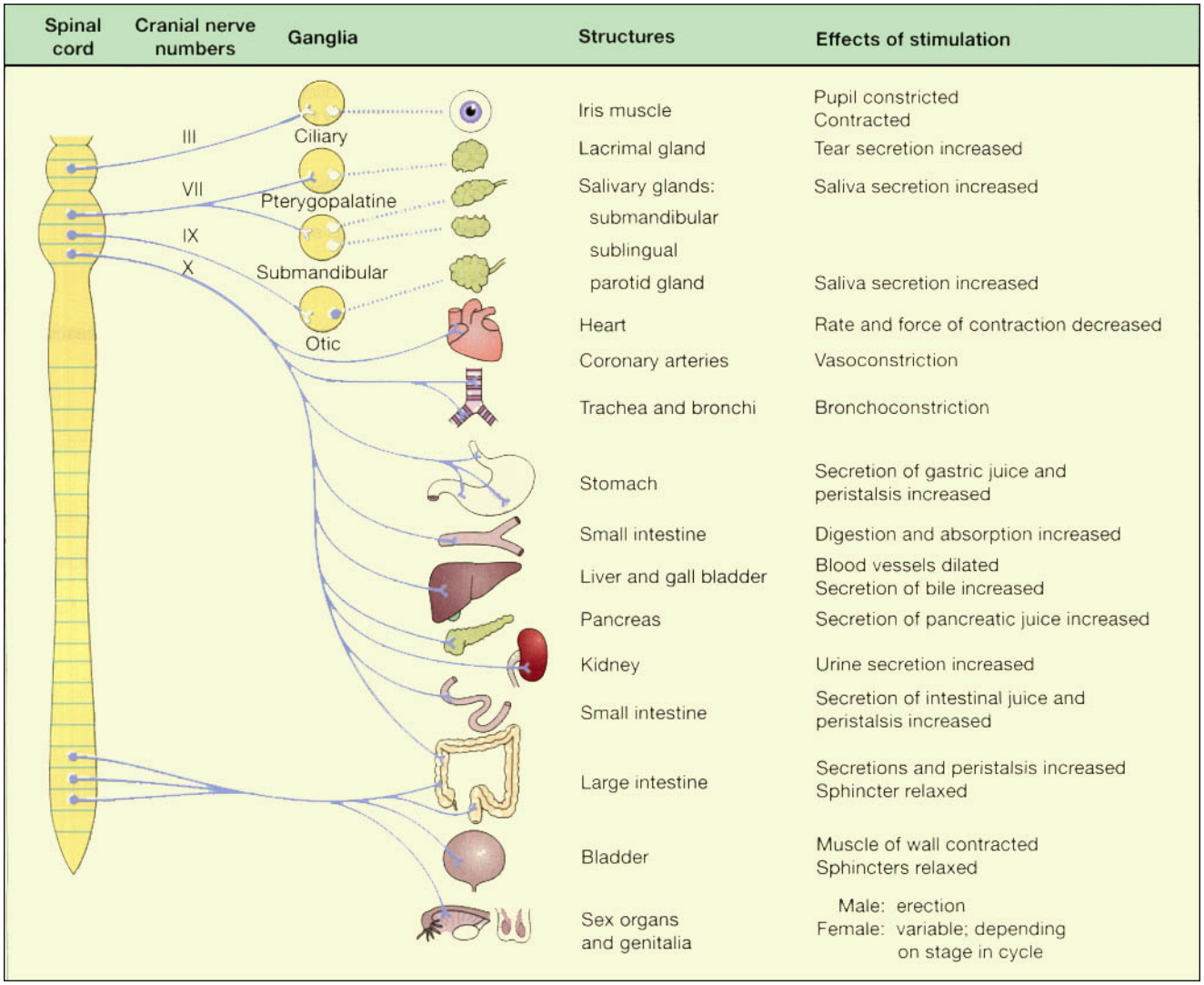


Figure 7.44 The parasympathetic outflow, the main structures supplied and the effects of stimulation. Solid blue lines – preganglionic fibres; broken lines – postganglionic fibres. Where there are no broken lines, the postganglionic neurone is in the wall of the structure.

matter at the distal end of the spinal cord. Their fibres leave the cord in sacral segments 2, 3 and 4 and synapse with postganglionic neurones in the walls of pelvic organs.

The postganglionic neurone. This has its cell body either in a ganglion or in the wall of the organ supplied.

Functions of the autonomic nervous system

The autonomic nervous system is involved in a complex of reflex activities which, like the reflexes described previously, depend on sensory input to the brain or spinal cord, and on motor output. In this case the reflex action is rapid contraction, or inhibition of contraction, of involuntary (smooth and cardiac) muscle or glandular secretion. These reflexes are coordinated subconsciously in the brain, i.e. below the level of the cerebrum. Some sensory input does reach consciousness and may result in temporary inhibition of the reflex action, e.g. reflex micturition can be inhibited temporarily.

The majority of the organs of the body are supplied by both sympathetic and parasympathetic nerves which have opposite effects that are finely balanced to ensure the optimum functioning of the organ.

Sympathetic stimulation prepares the body to deal with exciting and stressful situations, e.g. strengthening its

defences in danger and in extremes of environmental temperature. The adrenal glands are stimulated to secrete the hormones adrenaline and noradrenaline into the bloodstream. These hormones potentiate and sustain the effects of sympathetic stimulation. It is sometimes said that sympathetic stimulation mobilises the body for 'fight or flight'.

Parasympathetic stimulation has a tendency to slow down body processes except digestion and absorption of food and the functions of the genitourinary systems. Its general effect is that of a 'peace maker' allowing restoration processes to occur quietly and peacefully.

Normally the two systems function together maintaining a regular heartbeat, normal temperature and an internal environment compatible with the immediate external surroundings.

Effects of autonomic stimulation

Cardiovascular system

Sympathetic stimulation

- Exerts an accelerating effect upon the sinoatrial node in the heart, increasing the rate and force of the heartbeat.
- Causes dilatation of the coronary arteries, increasing the blood supply to cardiac muscle.
- Causes dilatation of the blood vessels supplying skeletal muscle, increasing the supply of oxygen and nutritional materials and the removal of metabolic waste products, thus increasing the capacity of the muscle to work.
- Raises peripheral resistance and blood pressure by constricting the small arteries and arterioles in the skin. In this way an increased blood supply is available for highly active tissue, such as skeletal muscle, heart, brain.
- Constricts the blood vessels in the secretory glands of the digestive system, reducing the flow of digestive juices. This raises the volume of blood available for circulation in dilated blood vessels.
- Blood coagulation occurs more quickly because of vasoconstriction.

Parasympathetic stimulation

- Decreases the rate and force of the heartbeat.
- Causes constriction of the coronary arteries reducing the blood supply to cardiac muscle.

The parasympathetic nervous system exerts little or no effect on blood vessels except the coronary arteries.

Respiratory system

Sympathetic stimulation

This causes dilatation of the airways, especially the bronchioles, allowing a greater amount of air to enter the lungs at each inspiration and increases the respiratory rate. In conjunction with the increased heart rate, the oxygen intake and carbon dioxide output of the body are increased.

Parasympathetic stimulation

Produces constriction of the bronchi.

Digestive and urinary systems

Sympathetic stimulation

- *The liver* converts an increased amount of glycogen to glucose, making more carbohydrate immediately available to provide energy.
- *The adrenal (suprarenal) glands* are stimulated to secrete adrenaline and noradrenaline which potentiate and sustain the effects of sympathetic stimulation.
- *The stomach* and *small intestine*. Smooth muscle contraction and secretion of digestive juices are inhibited, delaying digestion, onward movement and absorption of food and the tone of sphincter muscles is increased.
- *Urethral* and *anal sphincters*. The muscle tone of the sphincters is increased, inhibiting micturition and defecation.
- *The bladder wall* relaxes.
- *The metabolic rate* is greatly increased.

Parasympathetic stimulation

- *The stomach* and *small intestine*. The rate of digestion and absorption of food is increased.
- *The pancreas*. There is an increase in the secretion of pancreatic juice and the hormone insulin.
- *Urethral* and *anal sphincters*. Relaxation of the internal urethral sphincter is accompanied by contraction of the muscle of the bladder wall and micturition occurs. Similar relaxation of the internal anal sphincter is accompanied by contraction of the muscle of the rectum and defecation occurs. In both cases there is voluntary relaxation of the external sphincters.

Eye

Sympathetic stimulation

This causes contraction of the radiating muscle fibres of the iris, *dilating* the pupil. Retraction of the levator

palpebral muscles occurs, opening the eyes wide and giving the appearance of alertness and excitement. The ciliary muscle that adjusts the thickness of the lens is slightly relaxed.

Parasympathetic stimulation

This causes contraction of the circular muscle fibres of the iris, constricting the pupil. The eyelids tend to close, giving the appearance of sleepiness.

Skin

Sympathetic stimulation

- Causes increased secretion of sweat, leading to increased heat loss from the body.
- Produces contraction of the arrectores pilorum (the muscles in the hair follicles of the skin), giving the appearance of 'goose flesh'.
- Causes constriction of the blood vessels preventing heat loss.

There is no parasympathetic nerve supply to the skin. Some sympathetic fibres are adrenergic, causing vasoconstriction, and some are cholinergic, causing vasodilatation (Fig. 7.9).

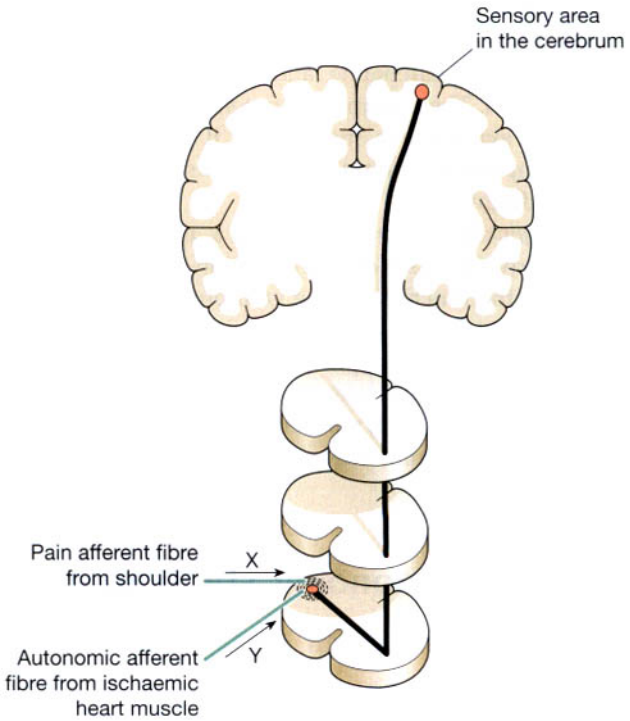


Figure 7.45 Referred pain. Pain perceived to originate from the tissues supplied by the damaged nerve. Y stimulates X and pain is perceived in the shoulder.

Afferent impulses from viscera

Sensory fibres from the viscera travel with autonomic fibres and are sometimes called *autonomic afferents*. The impulses they transmit are associated with:

- visceral reflexes, usually at an unconscious level, e.g. cough, blood pressure
- sensation of, e.g., hunger, thirst, nausea, sexual sensation, rectal and bladder distension
- visceral pain.

Visceral pain

Normally the viscera are insensitive to cutting, burning and crushing. However, a sensation of dull, poorly located pain is experienced when:

- visceral nerves are stretched
- a large number of fibres are stimulated
- there is ischaemia and local accumulation of metabolites
- the sensitivity of nerve endings to painful stimuli is increased, e.g. during inflammation.

If the cause of the pain, e.g. inflammation, affects the parietal layer of a serous membrane (pleura, peritoneum) the pain is acute and easily located over the site of inflammation. This is because the peripheral spinal (somatic) nerves supplying the superficial tissues also supply the parietal layer of serous membrane. They transmit the impulses to the cerebral cortex where *somatic pain* is perceived and accurately located. Appendicitis is an example of this type of pain. Initially it is dull and vaguely located around the midline of the abdomen. As the condition progresses the parietal peritoneum becomes involved and acute pain is clearly located in the right iliac fossa, i.e. over the appendix.

Referred pain (Fig. 7.45)

In some cases of visceral disease pain may be perceived to occur in superficial tissues remote from the viscus, i.e. referred pain. This occurs when sensory fibres from the viscus enter the same segment of the spinal cord as somatic nerves, i.e. those from the superficial tissues. It is believed that the sensory nerve from the viscus stimulates the closely associated nerve in the spinal cord and it transmits the impulses to the sensory area in the cerebral cortex where the pain is perceived as originating in the area supplied by the somatic nerve. Examples of referred pain are given in Table 7.4.

Table 7.4 Referred pain

Tissue of origin of pain	Site of referred pain
Heart	Left shoulder
Liver, Biliary tract	Right shoulder
Kidney, Ureter	Loin and groin
Uterus	Low back
Male genitalia	Low abdomen
Prolapsed intervertebral disc	Leg

RESPONSE OF NERVOUS TISSUE TO INJURY

Learning outcome

After studying this section you should be able to:

- outline the response of nervous tissue to injury.

Neurone damage

Damage to the nerve cells or their processes can lead to rapid necrosis with sudden acute functional failure, or to slow atrophy with gradually increasing dysfunction. These changes are associated with:

- hypoxia and anoxia
- nutritional deficiencies
- poisons, e.g. organic lead
- trauma
- infections
- ageing
- hypoglycaemia.

Neurone regeneration (Fig. 7.46)

Neurones of the brain, spinal cord and ganglia reach maturity a few weeks after birth and are not replaced when they are damaged or die.

The axons of *peripheral nerves* may regenerate if the cell body remains intact. Distal to the damage the axon and myelin sheath disintegrate and are removed by macrophages, but the Schwann cells survive and proliferate within the neurilemma. The live proximal part of the

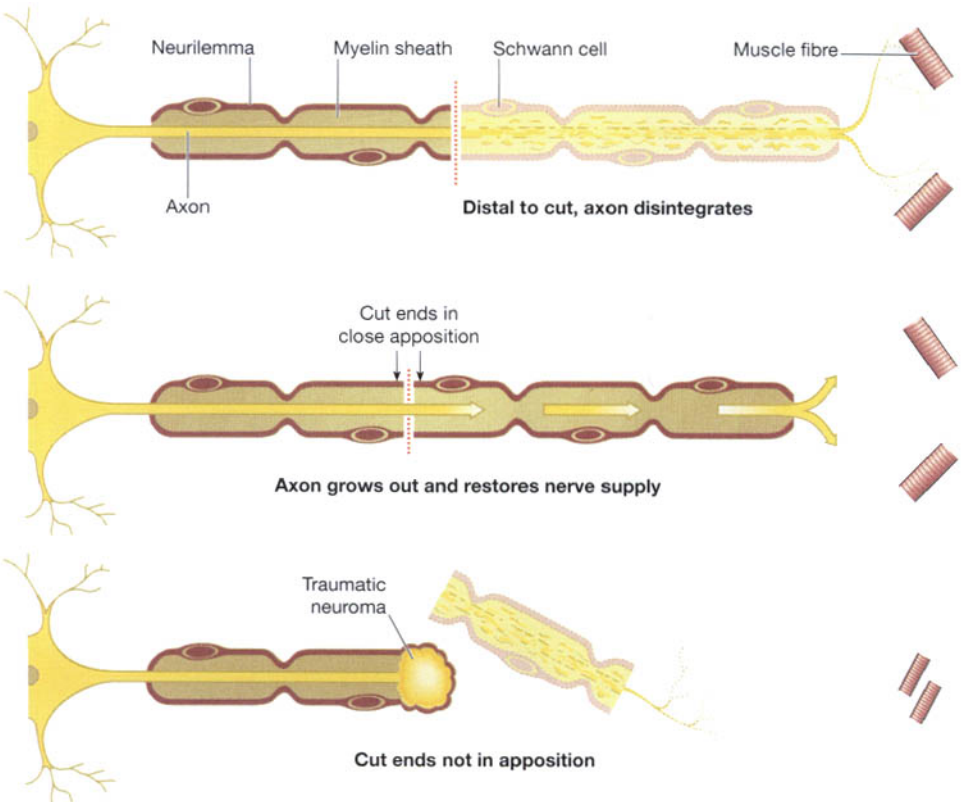


Figure 7.46 Regrowth of peripheral nerves following injury.

axon grows along the original track (about 3 mm per day), provided the two parts of neurilemma are correctly positioned and in close apposition. Restoration of function depends on the re-establishment of satisfactory connections with the end organ. When the neurilemma is out of position or destroyed the sprouting axons and Schwann cells form a tumour-like cluster (*traumatic neuroma*) producing severe pain, e.g. following some fractures and amputation of limbs.

Neuroglia damage

Astrocytes

When severely damaged, astrocytes undergo necrosis and disintegrate. In less severe and chronic conditions there is proliferation of astrocyte processes and later cell atrophy (*gliosis*). This process occurs in many diseases and is analogous to fibrosis in other tissues.

Oligodendrocytes

These cells form and maintain myelin, having the same functions as Schwann cells in peripheral nerves. They increase in number around degenerating neurones and are destroyed in demyelinating diseases such as *multiple sclerosis* (p. 184).

Microglia

Microglia are derived from monocytes that migrate from the blood into the nervous system before birth, and are found mainly around blood vessels. Where there is inflammation and cell destruction the microglia increase in size and become phagocytic.

Effects of poisons on the central nervous system

Many chemical substances encountered either as drugs or in the environment may damage the nervous system. Neurone metabolism may be disturbed directly or result from damage to other organs, e.g. liver, kidneys. The outcome depends on the toxicity of the substance, the dose and the duration of exposure, ranging from short-term neurological disturbance to encephalopathy which may cause coma and death.

DISORDERS OF THE BRAIN

Learning outcomes

After studying this section you should be able to:

- list three causes of raised intracranial pressure (ICP)
- relate the effects of raised ICP to the functions of the brain and changes in vital signs
- outline how the brain is damaged during different types of head injury
- describe four complications of head injury
- explain the effects of cerebral hypoxia and stroke
- outline the causes and effects of dementia
- relate the pathology of Parkinson's disease to its effects on body function.

Increased intracranial pressure

This is a very serious complication of many conditions. The cranium forms a rigid cavity enclosing:

- the brain
- cerebral blood vessels and blood
- cerebrospinal fluid (CSF).

An increase in volume of any one of these will lead to raised intracranial pressure. Sometimes its effects are more serious than the condition causing it, e.g. by disrupting the blood supply or distorting the shape of the brain especially if the intracranial pressure (ICP) rises rapidly. A slow rise in ICP allows time for compensatory adjustment to be made, i.e. a slight reduction in the volume of circulating blood and of CSF. The slower the rise in ICP, the more effective the compensation. Rising ICP is accompanied by bradycardia and hypertension. As it reaches its limit a further small increase in pressure is followed by a sudden and usually serious reduction in the cerebral blood flow. The result is hypoxia and a rise in carbon dioxide levels, causing arteriolar dilatation which further increases the ICP. This leads to progressive loss of functioning neurones, which exacerbates bradycardia and hypertension. Further cerebral hypoxia causes *vasomotor paralysis* and death.

The causes of increased ICP are described on the following pages and include:

- cerebral oedema
- hydrocephalus, the accumulation of excess CSF
- expanding lesions inside the skull, also known as space-occupying lesions
  –haemorrhage, haematoma (traumatic or spontaneous)
  –tumours (primary or secondary).

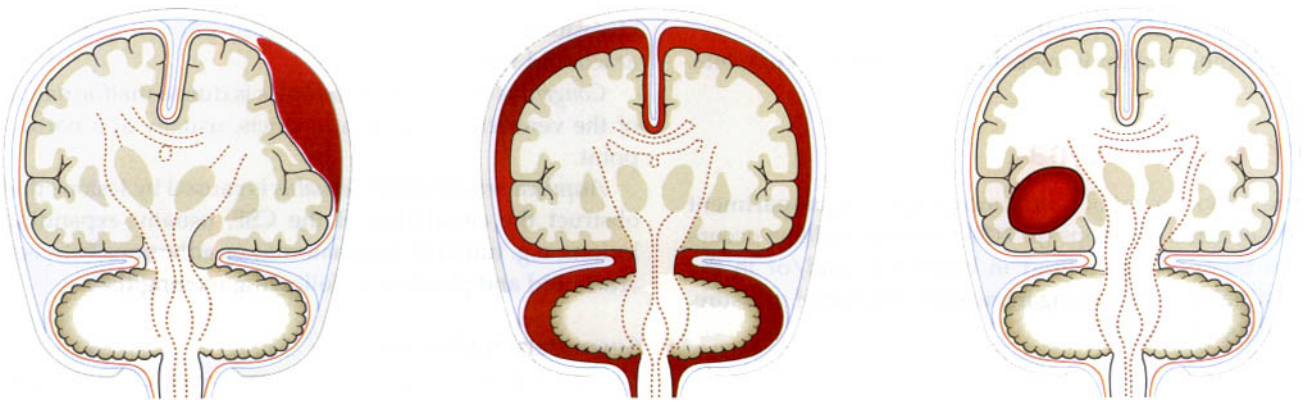
Expanding lesions may occur in the brain or in the meninges and they may damage the brain in various ways (Fig. 7.47).

Effects of increased ICP

Displacement of the brain

Lesions causing displacement are usually one-sided but may affect both sides. Such lesions may cause:

- *herniation* (displacement of part of the brain from its usual compartment) of the cerebral hemisphere between the corpus callosum and the free border of the falx cerebri on the same side



A Subdural haematoma B Subarachnoid haemorrhage C Tumour or intracerebral haemorrhage

Figure 7.47 Effects of different types of expanding lesions inside the skull: A. Subdural haematoma. B. Subarachnoid haemorrhage. C. Tumour or intracerebral haemorrhage.

- herniation of the midbrain between the pons and the free border of the tentorium cerebelli on the same side
- compression of the subarachnoid space and flattening of the cerebral convolutions
- distortion of the shape of the ventricles and their ducts
- herniation of the cerebellum through the foramen magnum
- protrusion of the medulla oblongata through the foramen magnum (*'coning'*).

Obstruction of the flow of cerebrospinal fluid

The ventricles or their ducts may be pushed out of position or a duct obstructed. The effects depend on the position of the lesion, e.g. compression of the aqueduct of the midbrain causes dilatation of the lateral ventricles and the third ventricle, further increasing the ICP.

Vascular damage

There may be stretching or compression of blood vessels, causing:

- haemorrhage when stretched blood vessels rupture
- ischaemia and infarction due to compression of blood vessels
- papilloedema (oedema round the optic disc) due to compression of the retinal vein in the optic nerve sheath where it crosses the subarachnoid space.

Neural damage

The vital centres in the medulla oblongata may be damaged when the increased ICP causes 'coning'. Stretching may damage cranial nerves, especially the oculomotor (III) and the abducent (VI), causing disturbances of eye movement and accommodation.

Bone changes

Prolonged increase of ICP causes bony changes, e.g.:

- erosion, especially of the sphenoid
- stretching and thinning before ossification is complete.

Cerebral oedema

There is movement of fluid from its normal compartment when oedema develops (p. 118). Cerebral oedema occurs when there is excess fluid in brain cells and/or in the interstitial spaces, causing increased intracranial pressure. It is associated with:

- traumatic injury
- haemorrhage
- infections, abscesses
- hypoxia
- local ischaemia, infarcts
- tumours
- inflammation of the brain or meninges
- hypoglycaemia.

Cytotoxic oedema

The neurones and neuroglial cells contain excess water due to disturbances of their osmotic pressure caused by retention of excess electrolytes. The permeability of the capillary walls is normal.

Vaosgenic oedema

Excess fluid collects in the interstitial spaces, especially round nerve fibres. The permeability of the capillary walls is increased and plasma proteins pass out of the capillaries, increasing the osmotic pressure in the interstitial spaces which causes oedema.

Hydrocephalus

In this condition the volume of CSF is abnormally high and is usually accompanied by increased ICP. An obstruction to CSF flow (Fig. 7.14) is the most common cause. It is described as *communicating* when there is free flow of CSF from the ventricular system to the subarachnoid space and *non-communicating* when there is not, i.e. there is obstruction in the system of ventricles, foramina or ducts.

Enlargement of the head occurs in children when ossification of the cranial bones is incomplete but, in spite of this, the ventricles dilate and cause stretching and thinning of the brain. After ossification is complete, hydrocephalus leads to a marked increase in ICP and destruction of neural tissue.

Primary hydrocephalus

This is usually caused by obstruction to the flow of CSF and may be communicating or non-communicating. Occasionally it is caused by malabsorption of CSF by the arachnoid villi.

Congenital primary hydrocephalus is due to malformation of the ventricles, foramina or ducts, usually at a narrow point.

Acquired primary hydrocephalus is caused by lesions that obstruct the circulation of the CSF, usually expanding lesions, e.g. tumours, haematomas or adhesions between arachnoid and pia maters, following meningitis.

Secondary hydrocephalus

Compensatory increases in the amount of CSF and ventricle capacity occur when there is atrophy of brain tissue, e.g. in dementia and following cerebral infarcts. There may not be a rise in ICP.

Head injuries

The brain may be injured by a blow to the head or movement of the brain during sudden acceleration or deceleration of the head. The damage to the brain may be serious even when there is no outward sign of injury.

Blow to the head

At the site of injury there may be:

- a scalp wound, with haemorrhage between scalp and skull bones
- damage to the underlying meninges and/or brain with local haemorrhage inside the skull
- depressed fracture of the skull, causing local damage to the underlying meninges and brain tissue
- temporal bone fracture, making an opening between the middle ear and the meninges
- fracture involving the air sinuses of the sphenoid, ethmoid or frontal bones, making an opening between the nose and the meninges.

Acceleration–deceleration injuries

Because the brain floats relatively freely in 'a cushion' of CSF, sudden acceleration or deceleration has an inertia effect, i.e. there is delay between the movement of the head and the corresponding movement of the brain. During this period the brain may be compressed and damaged at the site of impact. In '*contre coup*' injuries, brain damage is more severe on the side opposite to the site of impact. Other injuries include:

- nerve cell damage, usually to the frontal and parietal lobes, due to movement of the brain over the rough surface of bones of the base of the skull
- nerve fibre damage due to stretching, especially following rotational movement
- haemorrhage due to rupture of blood vessels in the subarachnoid space *on the side opposite* the impact or more diffuse small haemorrhages, following rotational movement.

Complications of head injury

If the individual survives the immediate effects, complications may develop hours or days later. Sometimes they are the first indication of serious damage caused by a seemingly trivial injury. Their effects may be to increase ICP, damage brain tissue or provide a route of entry for microbes.

Traumatic intracranial haemorrhage

Haemorrhage may occur causing secondary brain damage at the site of injury, on the opposite side of the brain or diffusely throughout the brain. If bleeding continues, the expanding haematoma damages the brain and increases the ICP.

Extradural haemorrhage

This may follow a direct blow that may or may not cause a fracture. The individual may recover quickly and indications of increased ICP only appear several hours later as the haematoma grows and the outer layer of dura mater (periosteum) is stripped off the bone. The haematoma grows rapidly when arterial blood vessels are damaged. In children there is rarely a fracture because the skull bones are still soft and the joints have not fused. The haematoma usually remains localised.

Acute subdural haemorrhage

This is due to haemorrhage from small veins in the dura mater or from larger veins between the layers of dura mater before they enter the venous sinuses. The blood may spread in the subdural space over one or both hemispheres (Fig. 7.47B). There may be concurrent subarachnoid haemorrhage, especially when there are extensive brain contusions and lacerations.

Chronic subdural haemorrhage

This may occur weeks or months after minor injuries and sometimes there is no history of injury. It occurs most commonly in people in whom there is some cerebral atrophy, e.g. the elderly and alcoholics. Evidence of increased ICP may be delayed when brain volume is reduced. The haematoma formed gradually increases in size due to repeated small haemorrhages and causes mild chronic inflammation and accumulation of inflammatory exudate. In time it is isolated by a wall of fibrous tissue.

Intracerebral haemorrhage and cerebral oedema

These occur following contusions, lacerations and shearing injuries associated with acceleration and deceleration, especially rotational movements.

Cerebral oedema is a common complication of contusions of the brain, leading to increased ICP, hypoxia and further brain damage.

Meningitis

Inflammation of the meninges may occur following a compound fracture of the skull that is accompanied by leakage of CSF and blood from the site, providing a route

of entry for microbes. The escape of CSF and blood may be through:

- skin, in compound fractures of the skull
- middle ear, in fractures of the temporal bone (CSF otorrhoea)
- nose, in fractures of sphenoid, ethmoid or frontal bones when the air sinuses are involved (CSF rhinorrhoea).

Post-traumatic epilepsy

This is usually characterised by seizures (fits) and may develop in the first week or several months after injury. Early development is most common after severe injuries, although in children the injury itself may have appeared trivial. After depressed fractures or large haematomas epilepsy tends to develop later.

Persistent vegetative state

In this condition there is severe brain damage that results in unconsciousness but the vital centres that control homeostasis remain intact, e.g. breathing, blood pressure.

Circulatory disturbances affecting the brain

A number of abnormalities of the circulation, not associated with head injuries, commonly affect the brain.

Cerebral hypoxia

Hypoxia may be due to:

- disturbances in the autoregulation of blood supply to the brain
- conditions affecting cerebral blood vessels.

When the mean blood pressure falls below about 60 mmHg there is failure of the autoregulating mechanisms that control the blood flow to the brain by adjusting the diameter of the arterioles. The consequent rapid decrease in the cerebral blood supply leads to hypoxia and lack of glucose. If severe hypoxia is sustained for more than a few minutes there is irreversible brain damage. The neurones are affected first, then the neuroglial cells and later the meninges and blood vessels. Conditions in which autoregulation breaks down include:

- cardiorespiratory arrest
- sudden severe hypotension
- carbon monoxide poisoning
- hypercapnia (excess blood carbon dioxide)
- drug overdosage with, e.g., narcotics, hypnotics, analgesics.

Conditions affecting cerebral blood vessels that may lead to hypoxia include:

- occlusion of a cerebral artery by, e.g., atheroma, thrombosis, rapidly expanding lesion, embolism
- arterial stenosis that occurs in arteritis, e.g. polyarteritis nodosa, syphilis, diabetes, degenerative changes in the elderly.

If the individual survives the initial episode of ischaemia, infarction, necrosis and loss of function of the affected area of brain occurs.

Stroke (cerebrovascular disease)

This condition is a common cause of death and disability, especially in the elderly. Predisposing factors include:

- hypertension
- atheroma
- cigarette smoking
- diabetes mellitus.

It occurs when a vascular disease suddenly interrupts flow of blood to the brain causing hypoxia. The effects include paralysis of a limb or one side of the body and disturbances of speech and vision. The nature and extent of cerebral impairment depends on the size and location of the affected blood vessels. The main causes are cerebral infarction (approx 85%) and spontaneous intracranial haemorrhage (15%).

Cerebral infarction

This is caused by atheroma complicated by thrombosis (p. 113) or blockage of an artery by an embolus from, e.g., infective endocarditis. When complete recovery occurs within 24 hours, the event is called a *transient ischaemic attack* (TIA). Recurrence or *completed stroke* associated with permanent damage may follow.

Spontaneous intracranial haemorrhage

The haemorrhage may be into the subarachnoid space or intracerebral (Fig. 7.48). It is commonly associated with an aneurysm or hypertension. In each case the escaped blood may cause arterial spasm, leading to ischaemia, infarction, fibrosis (gliosis) and hypoxic brain damage. A severe haemorrhage may be instantly fatal while repeated small haemorrhages have a cumulative effect in extending brain damage (multi-infarct dementia).

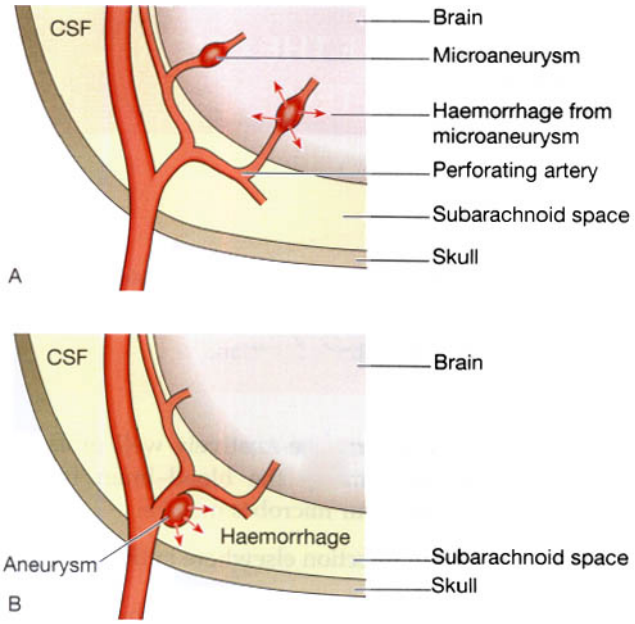


Figure 7.48 Types of haemorrhage causing stroke: A. Intracerebral. B. Subarachnoid.

Intracerebral haemorrhage

Prolonged hypertension leads to the formation of multiple microaneurysms in the walls of very small arteries in the brain. Rupture of one or more of these, due to continuing rise in blood pressure, is usually the cause of intracerebral haemorrhage. The most common sites are branches of the middle cerebral artery in the region of the internal capsule and the basal nuclei (ganglia).

Severe haemorrhage. This causes compression and destruction of tissue, a sudden increase in ICP and distortion and herniation of the brain. Death follows when the vital centres in the medulla oblongata are damaged by haemorrhage or if there is coning due to increased ICP.

Less severe haemorrhage. This causes paralysis and loss of sensation of varying severity, affecting the side of the body opposite the haemorrhage. If the bleeding stops and does not recur an *apoplectic cyst* develops, i.e. the haematoma is walled off by gliosis, the blood clot is gradually absorbed and the cavity filled with tissue exudate. When the ICP returns to normal some functions may be restored, e.g. speech and movement of limbs.

Subarachnoid haemorrhage

This is mostly due to rupture of a berry aneurysm on one of the major cerebral arteries or bleeding from a congenitally malformed blood vessel. The blood may remain localised but usually spreads in the subarachnoid space round the brain and spinal cord, causing a general increase in ICP without distortion of the brain (Fig. 7.47B). The irritant effect of the blood may cause arterial spasm, leading to ischaemia, infarction, gliosis and the effects of localised brain damage. It occurs most commonly in middle life, but occasionally in young people due to rapture of a malformed blood vessel. This condition is often fatal or results in permanent disability.

Dementia

Dementia is caused by progressive, irreversible degeneration and atrophy of the cerebral cortex and results in mental deterioration, usually over several years. There is gradual impairment of memory (especially short term), intellect and reasoning. Emotional lability and personality change may also occur.

Alzheimer's disease

This condition was previously called pre-senile dementia and is the commonest form of dementia. It is of unknown aetiology although genetic factors may be involved. Females are affected twice as often as males and it usually affects those over 60 years, the incidence increasing with age. There is progressive atrophy of the cerebral cortex accompanied by deteriorating mental functioning. Death usually occurs between 2 and 8 years after onset.

Huntington's disease (chorea)

This usually manifests itself between the ages of 30 and 50 years. It is caused by a genetic abnormality associated with deficient production of the neurotransmitter gamma aminobutyric acid (GABA). By the time of onset, the individual may have passed the genetic abnormality on to the next generation. Extrapyramidal changes cause *chorea*, rapid uncoordinated jerking movements of the limbs and involuntary twitching of the facial muscles. As the disease progresses, cortical atrophy causes personality changes and dementia.

Secondary dementias

Dementia may occur in association with other diseases:

- cerebrovascular disease – *multi-infarct dementia* is the cumulative result of several small cerebral infarcts leading to the gradually increasing impairment of mental function
- infections, e.g. encephalitis, neurosyphilis, human immunodeficiency virus (HIV), Creutzfeldt–Jakob disease



Figure 7.49 Shuffling gait of Parkinson's disease.

- cerebral trauma
- chronic abuse of alcohol and some drugs
- vitamin B deficiency
- effects of metabolic disorders, e.g. hypothyroidism, uraemia, liver failure.

Parkinson's disease

In this disease there is gradual degeneration of dopamine-releasing neurones in the extrapyramidal system. This leads to lack of control and coordination of muscle movement resulting in:

- fixed muscle tone causing expressionless facial features, rigidity of voluntary muscles causing the slow and characteristic stiff shuffling gait and stooping posture
- muscle tremor of extremities, e.g. 'pill rolling' movement of the fingers.

The cause is usually unknown but some cases are associated with repeated trauma as in, e.g., 'punch drunk' boxers; tumours, causing midbrain compression; drugs, e.g. phenothiazines; heavy metal poisoning. There is progressive physical disability but the intellect is not impaired (Fig. 7.49).

INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Learning outcome

After studying this section you should be able to:

- describe common infections of the nervous system and their effects on body function.

The brain and spinal cord are relatively well protected from microbial infection by the blood–brain barrier. When infection does occur microbes may be:

- blood-borne from infection elsewhere in the body, e.g. lung abscess
- introduced through a skull fracture (p. 179)
- spread through the skull bones from, e.g., middle ear infection, mastoiditis, skull bone infection
- introduced during a surgical procedure, e.g. lumbar puncture.

The microbes usually involved are bacteria and viruses, occasionally protozoa and fungi. The infection may originate in the meninges (*meningitis*) or in the brain (*encephalitis*), then spread from one site to the other.

Pyogenic infection

Pyogenic meningitis

Meningitis is most commonly transmitted through contact with an infected individual. Pyogenic (bacterial) infection of the meninges is usually preceded by a mild respiratory tract infection during which a few bacteria enter the bloodstream. They are carried to the meninges where they may remain localised in the extradural or subdural space. If an abscess forms it may rupture into the subarachnoid space and spread to the brain, causing encephalitis and further abscess formation. Infection of the arachnoid mater tends to spread diffusely in the subarachnoid space round the brain and spinal cord.

The onset is usually sudden with severe headache, neck stiffness, photophobia and fever. This may be accompanied by a petechial rash in some cases. Mortality and morbidity rates are considerable.

Pyogenic encephalitis

This may involve single or multiple sites, usually with abscess formation. The microbes are either bloodborne or spread from adjacent meningeal infection. The effects include the following.

- Inflammatory oedema and abscess formation lead to increased ICP, hypoxia and further brain damage.
- When meningitis follows encephalitis, healing takes place with the formation of fibrous adhesions which may interfere with CSF circulation and cause hydrocephalus, or compress blood vessels, causing hypoxia.
- Following encephalitis and brain abscess, healing is associated with gliosis and, as destroyed nerve cells are not replaced, loss of function depends on the site and extent of brain damage.

Viral infections

Viral infections of the nervous system are relatively rare even when caused by *neurotropic viruses*, i.e. those with an affinity for the nervous system. Viruses may cause meningitis, encephalitis or lesions of the neurones of spinal cord and peripheral nerves. Most viruses are bloodborne although a few travel along peripheral nerves, e.g. rabies virus and possibly polioviruses. They enter the body via:

- alimentary tract, e.g. poliomyelitis
- respiratory tract, e.g. shingles
- skin abrasions, e.g. rabies.

The effects of viral infections vary according to the site and the amount of tissue destroyed. Viruses are believed to damage nerve cells by:

- 'taking over' their metabolism
- stimulating an immune reaction which may explain why signs of some infections do not appear until there is a high antibody titre, 1 to 2 weeks after infection.

Viral meningitis

This is sometimes called 'aseptic' meningitis because cultures for bacteria are sterile. It is usually a relatively mild infection followed by complete recovery.

Viral encephalitis

Viral encephalitis may affect a wide variety of sites and, as nerve cells are not replaced, loss of function reflects the extent of damage. In severe infection neurones and neuroglia may be affected, followed by necrosis and gliosis. Early senility may develop or, if vital centres in the medulla oblongata are involved, death may ensue. In mild cases recovery is usually complete with little loss of function.

Herpes simplex encephalitis. This is an acute, often fatal, condition causing necrosis of areas of the cerebrum, usually the temporal lobes. If the patient survives the initial acute phase there may be residual dysfunction, e.g. behavioural disturbance and loss of memory.

Herpes zoster neuritis (shingles)

Herpes zoster viruses cause chickenpox (varicella) mainly in children and shingles (zoster) in adults. Susceptible children may contract chickenpox from a patient with shingles but not the reverse. Adults infected with the viruses may show no immediate signs of disease. The viruses may remain dormant in posterior root ganglia of the spinal nerves then become active years later, causing shingles. Reactivation may be either spontaneous or associated with the following factors:

- local trauma involving the dermatome, i.e. the area supplied by the affected peripheral nerve
- exposure of the dermatome to irradiation, e.g. sun, X-rays
- depression of the immunological system, e.g. by drugs, old age, AIDS.

The posterior root ganglion becomes acutely inflamed. From there the *viruses* pass along the sensory nerve to the surface tissues supplied, e.g. skin, cornea. The tissues become inflamed and vesicles, containing serous fluid and viruses, develop along the course of the nerve. This is accompanied by persistent pain and hypersensitivity to touch (*hyperaesthesia*). Recovery is usually slow and there may be some loss of sensation, depending on the severity of the disease. The infection is usually unilateral and the most common sites are:

- nerves supplying the trunk, sometimes two or three adjacent dermatomes (Fig. 7.39)
- the ophthalmic division of the trigeminal nerve (Fig. 7.41), causing *trigeminal neuralgia*, and, if vesicles form on the cornea, there may be ulceration, scarring and residual interference with vision.

Poliomyelitis

This disease is usually caused by *polioviruses* and, occasionally, by other *enteroviruses*. The infection is spread by food contaminated by infected faecal matter and the initial virus multiplication occurs in the alimentary tract. The viruses are then bloodborne to the nervous system and invade anterior horn cells in the spinal cord. Usually there is a mild febrile illness with no indication of nerve

damage. In mild cases there is complete recovery but there is permanent disability in many others. Paralytic disease is believed to be precipitated by muscular exercise during the early febrile stage. Irreversible damage to lower motor neurones causes muscle paralysis which, in the limbs, may lead to deformity because of the unopposed tonal contraction of antagonistic muscles. Death may occur owing to respiratory paralysis. Vaccination programmes have now almost eradicated this disease in developed countries.

Rabies

All warm-blooded animals are susceptible to the rabies virus, which is endemic in many countries but not in Britain. The main reservoirs of virus are wild animals, some of which may be carriers. These may infect domestic pets which then become the main source of human infection. The viruses multiply in the salivary glands and are present in large numbers in saliva. They enter the body through skin abrasions and are believed to travel to the brain along the nerves. The incubation period varies from about 2 weeks to several months, possibly reflecting the distance viruses travel between the site of entry and the brain. Extensive damage to the basal nuclei, midbrain, medulla oblongata and the posterior root ganglia of the peripheral nerves causes meningeal irritation, extreme hyperaesthesia, muscle spasm and convulsions. *Hydrophobia* and overflow of saliva from the mouth are due to painful spasm of the throat muscles that inhibits swallowing. In the advanced stages muscle spasm may alternate with flaccid paralysis and death is usually due to respiratory muscle spasm or paralysis.

Not all people exposed to the virus contract rabies, but in those who do, the mortality rate is high.

Human immunodeficiency virus (HIV)

The brain is often affected in individuals with AIDS (p. 385) resulting in, e.g.:

- opportunistic infection
- dementia.

Creutzfeldt–Jakob disease

This infective condition may be caused by a 'slow' virus, the nature and transmission of which is poorly understood. It is thought to be via a heat-resistant transmissible particle known as a *prion protein*. It is a rapidly progressive form of dementia for which there is no known treatment so the condition is always fatal.

Myalgic encephalitis (ME)

This condition is also known as post-viral syndrome or chronic fatigue syndrome. It affects mostly teenagers and young adults and the aetiology is unknown. Sometimes the condition follows a viral illness. The effects include malaise, severe fatigue, poor concentration and myalgia. Recovery is usually spontaneous but sometimes results in chronic disability.

DEMYELINATING DISEASES

Learning outcome

After studying this section you should be able to:

- explain how the signs and symptoms of demyelinating disease are related to pathological changes in the nervous system.

These diseases are caused either by injury to axons or by disorders of cells that secrete myelin, i.e. oligodendrocytes and Schwann cells.

Multiple (disseminated) sclerosis (MS)

In this disease there are areas of demyelinated white matter, called *plaques*, irregularly distributed throughout the brain and spinal cord. Grey matter in the brain and spinal cord may also be affected because of the arrangement of satellite oligodendrocytes round cell bodies. In the early stages there may be little damage to axons. It usually develops between the ages of 20 and 40 years and there is an increased incidence of MS among siblings, especially twins, and parents of patients. It is not known whether this is due to genetic or environmental factors or a combination of both. The actual cause(s) of MS are not known but several factors have been suggested, more than one of which may be involved.

Environment before adolescence is suggested because the disease is most prevalent in people who spend their preadolescent years in temperate climates, and people who move to other climates after that age retain their susceptibility to MS. People moving into a temperate area during adolescence or later life appear not to be susceptible.

Genetically abnormal myelin is present in many patients and may be antigenic, causing the development of autoimmunity.

Viral infection by slow-growing viruses that attack myelin has been suggested but so far no virus has been identified.

Effects of multiple sclerosis

Neuronal damage leads to a variety of dysfunctions, depending on the sites and sizes of demyelinated plaques. Plaques damage white matter leading to upper motor neurone dysfunction causing:

- weakness of skeletal muscles and sometimes paralysis
- lack of coordination and movement
- disturbed sensation, e.g. burning or pins and needles
- incontinence of urine
- visual disturbances especially blurring and double vision. The optic nerves are commonly affected early in the disease.

The disease pattern is usually one of relapses and remissions of widely varying duration. Each relapse causes further loss of nervous tissue and progressive dysfunction. In some cases there may be chronic progression without remission, or acute disease rapidly leading to death.

Acute disseminating encephalomyelitis

This is a rare but serious condition that may occur:

- during or very soon after a virus infection, e.g. measles, chickenpox, mumps, respiratory infection
- following primary immunisation against viral diseases, mainly in older children and adults.

The cause of the acute diffuse demyelination is not known. It has been suggested that autoimmunity to myelin is triggered either by viruses during a viral infection, such as measles or rubella, or by viruses present in vaccines. The effects vary considerably, according to the distribution and degree of demyelination. The early febrile state may progress to paralysis and coma. Most patients survive the initial phase and recover with no residual dysfunction but some have severe impairment of a wide variety of neurological functions.

PHENYLKETONURIA

Learning outcome

After studying this section you should be able to:

- describe the causes and effects of phenylketonuria.

This is a genetic disorder in which the gene needed for synthesising the enzyme *phenylalanine hydroxylase* is absent. This enzyme normally converts phenylalanine to tyrosine in the liver (see Figs 2.8 and 3.4, pp. 24 and 32). Phenylalanine is the intermediate metabolite that accumulates in the liver cells and overflows into the blood (Fig. 7.50). In high quantities it is toxic to the nervous system and if untreated this condition results in brain damage and mental retardation within a few months. Tyrosine is a constituent of the skin pigment melanin and depigmentation occurs: affected children are fair skinned and blonde. The incidence of this disease is now low in developed countries because it is detected by screening all newborn infants and providing early treatment.

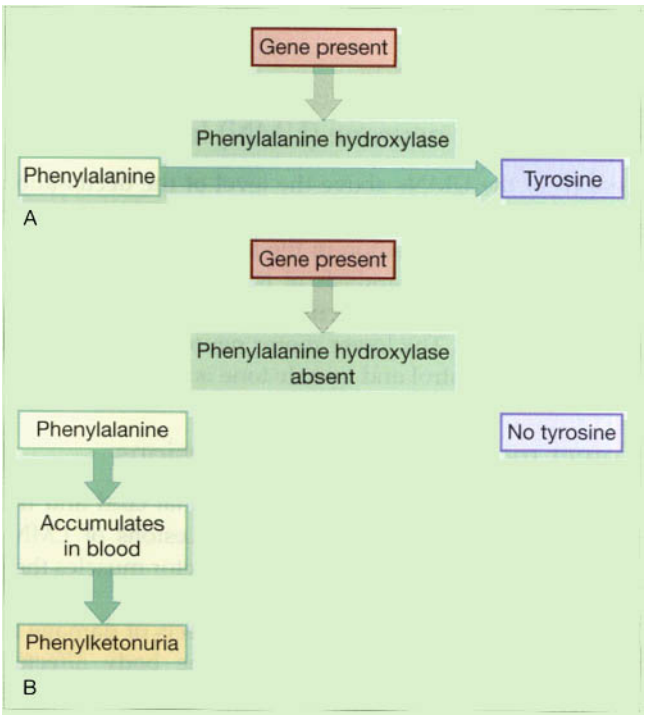


Figure 7.50 Phenylketonuria: A. Phenylalanine present. B. Phenylalanine absent.

DISEASES OF THE SPINAL CORD

Learning outcome

After studying this section you should be able to:

- explain how disorders of the spinal cord cause abnormal body function.

Because space in the neural canal and intervertebral foramina is limited, any condition which distorts their shape or reduces the space may damage the spinal cord or peripheral nerve roots, or cause ischaemia by compressing blood vessels. Such conditions include:

- fracture and/or dislocation of vertebrae
- tumours of the meninges or vertebrae
- prolapsed intervertebral disc.

The effects of disease or injury depend on the severity of the damage, the type and position of the neurones involved, i.e. motor, sensory, proprioceptor, autonomic, connector neurones in reflex arcs in the spinal cord or in peripheral nerves.

Motor neurones

Upper motor neurone (UMN) lesions

Lesions of the UMNs above the level of the decussation of the pyramids affect the opposite side of the body, e.g. haemorrhage or infarction in the internal capsule of one hemisphere causes paralysis of the opposite side of the body. Lesions below the decussation level affect the same side of the body. The lower motor neurones are released from cortical control and muscle tone is increased.

Lower motor neurone (LMN) lesions

The cell bodies of LMNs are in the spinal cord and the axons are part of peripheral nerves. Lesions of LMNs lead to weakness or paralysis of the effector muscles they supply.

Table 7.5 gives a summary of the effects of damage to the motor neurones. The parts of the body affected depend on which neurones have been damaged and their site in the brain, spinal cord or peripheral nerve.

Motor neurone disease

This is a chronic progressive degeneration of motor neurones, occurring mainly in men between 60 and 70 years of age. The cause is not known. Motor neurones in the cerebral cortex, brain stem and anterior horns of the spinal cord are destroyed and replaced by gliosis. Early effects are usually weakness and twitching of the small muscles of the hand, and muscles of the arm and shoulder girdle. The legs are affected later. Death is usually due to the involvement of the respiratory centre in the medulla oblongata.

Table 7.5 Summary of effects of damage to motor neurones

Upper motor neurone	Lower motor neurone
Muscle weakness and spastic paralysis	Muscle weakness and flaccid paralysis
Exaggerated tendon reflexes	Absence of tendon reflexes
Muscle twitching	Muscle wasting Contracture of muscles Impaired circulation

Sensory neurones

The sensory functions lost as a result of disease or injury depend on which neurones have been damaged and their position in the brain or spinal cord, or the peripheral nerve involved. In the brain, neurones connecting the thalamus and the cerebrum pass through the internal capsule. Damage in this area by, e.g., haemorrhage, usually from a berry aneurysm, may lead to loss of sensation but does not affect cerebellar function unless upper motor neurones have also been damaged. Spinal cord damage leads to loss of sensation and cerebellar function. Peripheral nerve damage leads to loss of reflex activity, loss of sensation and of cerebellar function.

Mixed motor and sensory conditions

Subacute combined degeneration of the spinal cord

This condition most commonly occurs as a complication of pernicious anaemia. Vitamin B_{12} is associated with the formation and maintenance of myelin by Schwann cells and oligodendrocytes. Although degeneration of the spinal cord may be apparent before the anaemia it is arrested by treatment with vitamin B_{12}. This type of degeneration may

occasionally complicate chronic conditions, such as diabetes mellitus, leukaemia and carcinoma.

The degeneration of nerve fibre myelin occurs in the posterior and lateral columns of white matter in the spinal cord, especially in the upper thoracic and lower cervical regions. Less frequently the changes occur in the posterior root ganglia and peripheral nerves. Demyelination of proprioceptor fibres (sensory) leads to ataxia and involvement of upper motor neurones leads to increased muscle tone and spastic paralysis.

Compression of the spinal cord and nerve roots

The causes include:

- prolapsed intervertebral disc
- syringomyelia
- tumours: metastatic, meningeal or nerve sheath
- fractures with displacement of bone fragments.

Prolapsed intervertebral disc (Fig. 7.51)

This is the most common cause of compression of the spinal cord and/or nerve roots. The bodies of the vertebrae are separated by the intervertebral discs, each consisting of an outer rim of cartilage, the *annulus fibrosus*, and a central core of soft gelatinous material, the *nucleus pulposus*.

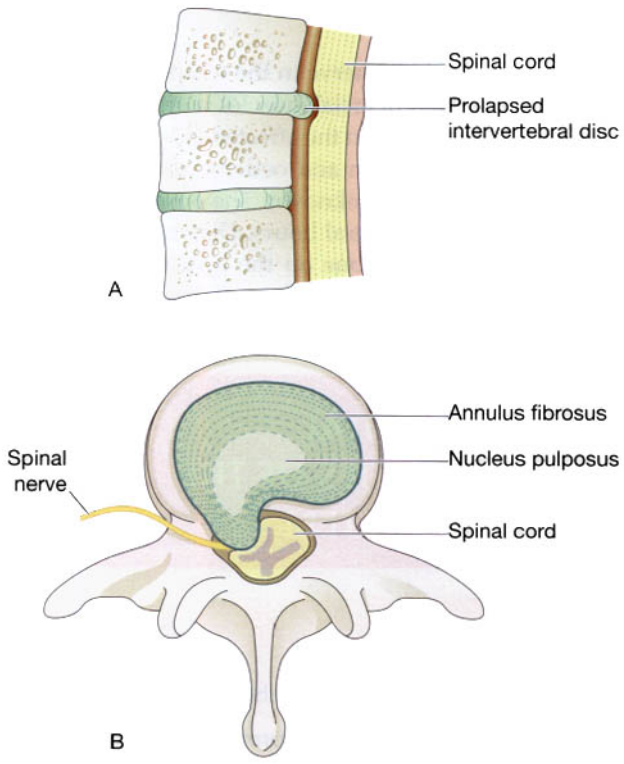


Figure 7.51 Prolapsed intervertebral disc. A. Viewed from the side. B. Viewed from above.

Prolapse of a disc is herniation of the nucleus pulposus, causing the annulus fibrosus and the posterior longitudinal ligament to protrude into the neural canal. It is most common in the lumbar region usually below the level of the spinal cord, i.e. below L2, so the injury is to nerve roots only. If it occurs in the cervical region, the cord may also be compressed. Herniation may occur suddenly, typically in young adults during strenuous exercise or exertion, or progressively in older people when bone disease or degeneration of the disc leads to rupture during minimal exercise. The hernia may be:

- one-sided, causing pressure damage to a nerve root
- midline, compressing the spinal cord, the anterior spinal artery and possibly bilateral nerve roots.

The outcome depends upon the size of the hernia and the length of time the pressure is applied. Small herniations cause local pain due to pressure on the nerve endings in the posterior longitudinal ligament.

Large herniations may cause:

- unilateral or bilateral paralysis
- acute or chronic pain perceived to originate from the area supplied by the compressed sensory nerve, e.g. in the leg or foot
- compression of the anterior spinal artery, causing ischaemia and possibly necrosis of the spinal cord
- local muscle spasm due to pressure on motor nerves.

Syringomyelia

This dilatation (syrinx) of the central canal of the spinal cord occurs most commonly in the cervical region and is associated with congenital abnormality of the distal end of the fourth ventricle. As the central canal dilates, pressure causes progressive damage to sensory and motor neurones. Early effects include dissociated anaesthesia, i.e. insensibility to heat and pain, due to compression of the sensory fibres that cross the cord immediately they enter. In the long term there is destruction of motor and sensory tracts, leading to spastic paralysis and loss of sensation and reflexes.

Tumours and displaced fragments of fractured vertebrae

These may affect the spinal cord and nerve roots at any level. The pressure damage initially causes pain and later, if the pressure is not relieved, there may be loss of sensation and paralysis. The areas affected depend on the site of pressure.

DISEASES OF PERIPHERAL NERVES

Learning outcomes

After studying this section you should be able to:

- compare and contrast the causes and effects of parenchymal and interstitial neuropathies
- describe the effects of Guillain–Barré syndrome and Bell's palsy.

Neuropathies

This is a group of diseases of peripheral nerves not associated with inflammation. They are classified as:

- parenchymal (polyneuropathy): several neurones are affected
- interstitial (mononeuropathy): a single neurone is usually affected.

Parenchymal neuropathy

Polyneuropathy or damage to a number of neurones and their myelin sheaths occurs in metabolic or toxic disorders, e.g.:

- nutritional deficiencies, e.g. folic acid, vitamins B_1, B_2, B_6, B_{12}
- metabolic disorders, e.g. diabetes mellitus
- chronic diseases, e.g. renal failure, hepatic failure, carcinoma
- toxic reactions to, e.g., lead, arsenic, mercury, carbon tetrachloride, aniline dyes and some drugs, such as phenytoin, chloroquine
- infections, e.g. influenza, measles, typhoid fever, diphtheria, leprosy.

The long neurones are usually affected first, e.g. those supplying the feet and legs. The outcome depends upon the cause of the neuropathy and the extent of the damage.

Interstitial neuropathy

Usually only one neurone is damaged (*mononeuropathy*) and the most common cause is ischaemia due to pressure. Example include:

- pressure applied to cranial nerves in cranial bone foramina due to distortion of the brain by increased ICP
- compression of a nerve in a confined space caused by surrounding inflammation and oedema, e.g. the median nerve in the carpal tunnel (see p. 427)
- external pressure on a nerve, e.g. an unconscious person lying with an arm hanging over the side of a bed or trolley
- compression of the axillary (circumflex) nerve by ill-fitting crutches
- trapping a nerve between the broken ends of a bone
- ischaemia due to thrombosis of blood vessels supplying a nerve.

The resultant dysfunction depends on the site and extent of the injury.

Neuritis

Acute idiopathic inflammatory polyneuropathy (Guillain–Barré syndrome)

This is a sudden, acute, progressive, bilateral ascending paralysis, beginning in the lower limbs and spreading to the arms, trunk and cranial nerves. It usually occurs 1 to 3 weeks after an upper respiratory tract infection. There is widespread inflammation accompanied by some demyelination of spinal, peripheral and cranial nerves and the spinal ganglia. Paralysis may affect all the limbs and the respiratory muscles. Patients who survive the acute phase usually recover completely in weeks or months.

Bell's palsy

Compression of a facial nerve in the temporal bone foramen causes paralysis of facial muscles with drooping and loss of facial expression on the affected side. The immediate cause is inflammation and oedema of the nerve but the underlying cause is unknown. The onset may be sudden or develop over several hours. Distortion of the features is due to muscle tone on the unaffected side, the affected side being expressionless. Recovery is usually complete within a few months.

DEVELOPMENTAL ABNORMALITIES OF THE NERVOUS SYSTEM

Learning outcomes

After studying this section you should be able to:

- describe developmental abnormalities of the nervous system
- relate their effects to abnormal body function.

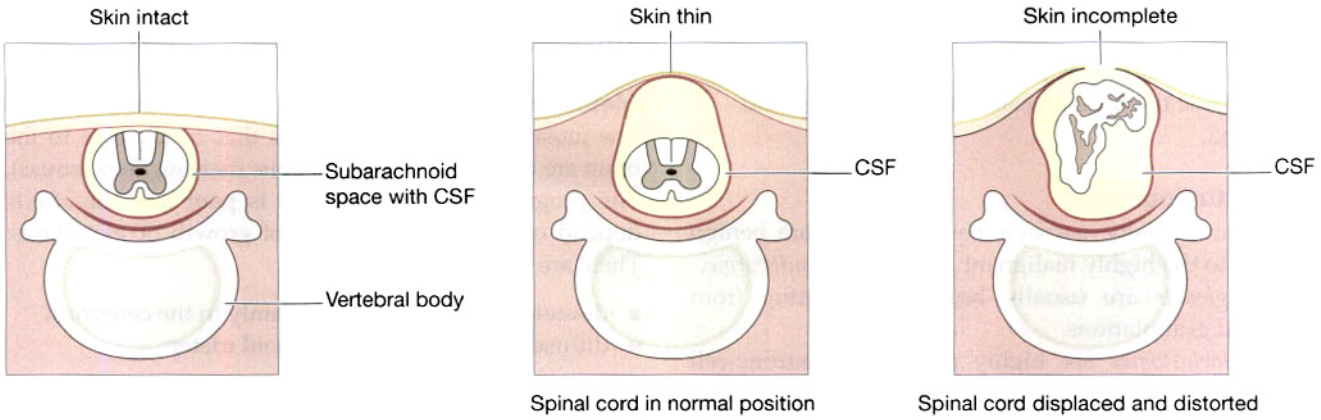


Figure 7.52 Spina bifida.

Spina bifida

This is a congenital malformation of the neural canal and spinal cord (Fig. 7.52). The neural arches of the vertebrae are absent and the dura mater is abnormal, most commonly in the lumbosacral region. The causes are not known, although the condition is associated with dietary deficiency of folic acid at the time of conception. They may be of genetic origin or due to environmental factors, e.g. irradiation, or maternal infection (rubella) at a critical stage in development of the fetal vertebrae and spinal cord. The effects depend on the extent of the abnormality.

Occult spina bifida

The skin over the defect is intact and excessive growth of hair over the site may be the only sign of abnormality. This is sometimes associated with minor nerve defects that commonly affect the bladder.

Meningocele

The skin over the defect is very thin and there is dilatation of the subarachnoid space posteriorly. The spinal cord is correctly positioned.

Meningomyelocele

The subarachnoid space is dilated posteriorly, the spinal cord is displaced backwards and may be adherent to the posterior wall of the arachnoid dilatation. The skin is often deficient with leakage of CSF, and the meninges may become infected. Serious nerve defects result in paraplegia and lack of sphincter control causing incontinence of urine and faeces. There may also be mental retardation.

Hydrocephalus (see p. 178).

TUMOURS OF THE NERVOUS SYSTEM

Learning outcome

After studying this section you should be able to:

- outline the effects of tumours of the nervous system.

Most tumours of the nervous system are of neuroglial origin. Neurones are rarely involved because they do not normally multiply. Metastases of nervous tissue tumours are rare. Because of this, the rate of growth of a tumour is more important than the likelihood of spread outside the nervous system. In this context, 'benign' means slow-growing and 'malignant' rapid-growing. Signs of raised ICP appear after the limits of compensation have been reached.

Within the confined space of the skull, haemorrhage in a tumour exacerbates the increased ICP caused by the tumour.

Slow-growing tumours

These allow time for adjustment to compensate for increasing intracranial pressure, so the tumour may be quite large before its effects are evident. Compensation involves gradual reduction in the volume of cerebrospinal fluid and circulating blood.

Rapidly growing tumours

These do not allow time for adjustment to compensate for the rapidly increasing ICP, so the effects quickly become apparent (Fig. 7.47C). Complications include:

- neurological impairment, depending on tumour site and size
- effects of increased ICP (p. 177)
- necrosis of the tumour, causing haemorrhage and oedema.

Specific tumours

Gliomas are usually astrocytomas, ranging from benign tumours to the highly malignant *glioblastoma multiforme*.

Meningiomas are usually benign, originating from arachnoid granulations.

Medulloblastomas are highly malignant neurone-cell tumours, occurring mainly in the cerebellum in children. They are believed to originate from primitive cells prior to differentiation into neurones and neuroglia.

Metastases in the brain

The most common primary sites that metastasise to the brain are the breast, lungs and bone marrow (leukaemias). The prognosis of this condition is poor and the effects depend on the site(s) and rate of growth of metastases. There are two forms:

- discrete multiple tumours, mainly in the cerebrum
- diffuse tumours in the arachnoid mater.

8

The special senses

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The special senses of hearing, sight, smell and taste all have specialised sensory receptors (nerve endings) outside the brain. These are found in the ears, eyes, nose and mouth. The ear is also involved in the maintenance of balance. In the brain the incoming nerve impulses undergo complex processes of integration and coordination that result in perception of sensory information and a variety of responses inside and outside the body.

HEARING AND THE EAR

Learning outcomes

After studying this section you should be able to:

- describe the structure of the outer, middle and inner parts of the ear
- explain the physiology of hearing.

The ear is the organ of hearing. It is supplied by the 8th *cranial nerve*, i.e. the *cochlear part* of the *vestibulocochlear* nerve which is stimulated by vibrations caused by sound waves.

With the exception of the auricle (pinna), the structures that form the ear are encased within the petrous portion of the temporal bone.

Structure

The ear is divided into three distinct parts (Figs 8.1 and 8.6):

- outer ear
- middle ear (tympanic cavity)
- inner ear.

Outer ear

The outer ear consists of the auricle (pinna) and the external acoustic meatus.

The auricle (pinna)

The auricle is the expanded portion projecting from the side of the head. It is composed of *fibroelastic cartilage* covered with skin. It is deeply grooved and ridged and the most prominent outer ridge is the *helix*.

The lobule (earlobe) is the soft pliable part at the lower extremity, composed of fibrous and adipose tissue richly supplied with blood.

External acoustic meatus (auditory canal)

This is a slightly 'S'-shaped tube about 2.5 cm long extending from the auricle to the *tympanic membrane* (eardrum). The lateral third is cartilaginous and the remainder is a canal in the temporal bone. The meatus is lined with skin containing hairs continuous with that of the auricle. There are numerous *sebaceous* and *ceruminous glands* in the skin of the lateral third. Ceruminous glands

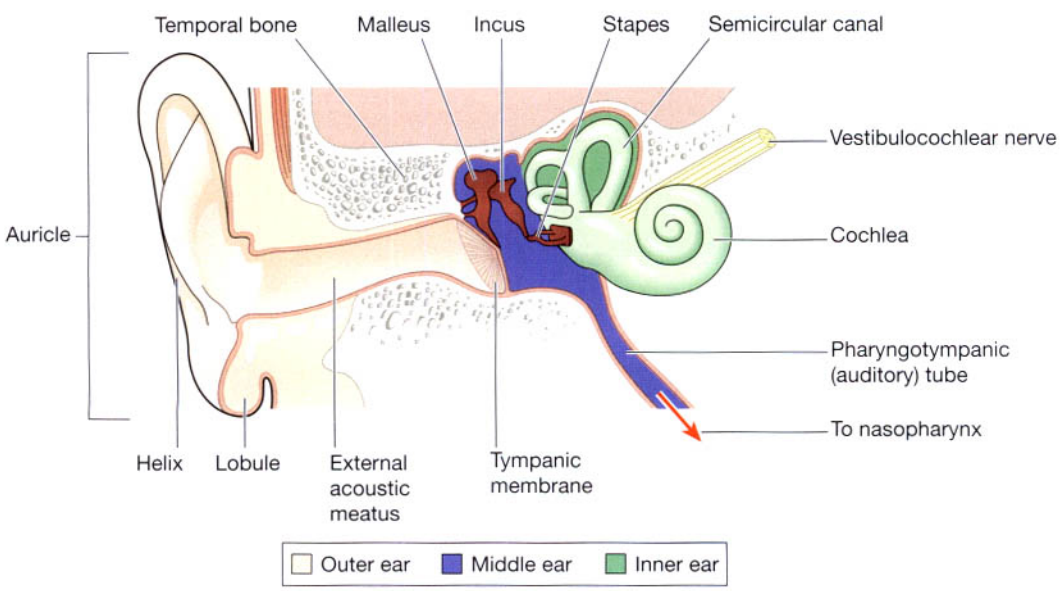


Figure 8.1 The parts of the ear.

are modified sweat glands that secrete *cerumen* (wax), a sticky material containing lysozyme and immunoglobulins. Foreign materials, e.g. dust, insects and microbes, are prevented from reaching the tympanic membrane by wax, hairs and the curvature of the meatus. Movements of the temporomandibular joint during chewing and speaking 'massage' the cartilaginous meatus, moving the wax towards the exterior.

The tympanic membrane (eardrum) (Fig. 8.2) completely separates the external acoustic meatus from the middle ear. It is oval-shaped with the slightly broader edge upwards and is formed by three types of tissue: the outer covering of *hairless skin*, the middle layer of *fibrous tissue* and the inner lining of *mucous membrane* continuous with that of the middle ear.

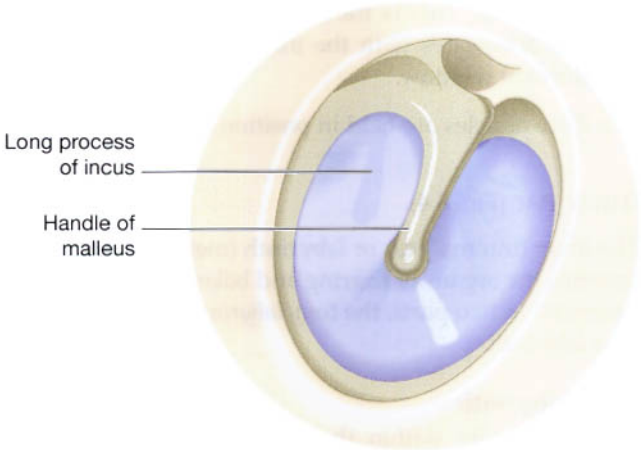


Figure 8.2 The tympanic membrane viewed through an auriscope showing the shadows cast by the malleus and the incus.

Middle ear (tympanic cavity)

This is an irregular-shaped air-filled cavity within the petrous portion of the temporal bone. The cavity, its contents and the air sacs which open out of it are lined with either simple squamous or cuboidal epithelium.

The lateral wall of the middle ear is formed by the tympanic membrane.

The roof and floor are formed by the temporal bone.

The posterior wall is formed by the temporal bone with openings leading to the *mastoid antrum* through which air passes to the air cells within the mastoid process.

The medial wall is a thin layer of temporal bone in which there are two openings:

- oval window
- round window (see Fig. 8.6).

The oval window is occluded by part of a small bone called the *stapes* and the round window, by a fine sheet of *fibrous tissue*.

Air reaches the cavity through the *pharyngotympanic (auditory or Eustachian)* tube which extends from the nasopharynx. It is about 4 cm long and is lined with ciliated epithelium. The presence of air at atmospheric pressure on both sides of the tympanic membrane is maintained by the pharyngotympanic tube and enables the membrane to vibrate when sound waves strike it. The pharyngotympanic tube is normally closed but when there is unequal pressure across the tympanic membrane, e.g. at high altitude, it is opened by swallowing or yawning and the ears 'pop', equalising the pressure again.

Auditory ossicles (Fig. 8.3)

These are three very small bones that extend across the middle ear from the tympanic membrane to the oval window (Fig. 8.1). They form a series of movable joints with each other and with the medial wall of the cavity at the oval window. They are named according to their shapes.

The malleus. This is the lateral hammer-shaped bone. The handle is in contact with the tympanic membrane and the head forms a movable joint with the incus.

The incus. This is the middle anvil-shaped bone. Its body articulates with the malleus, the long process with the stapes, and it is stabilised by the short process, fixed by fibrous tissue to the posterior wall of the tympanic cavity.

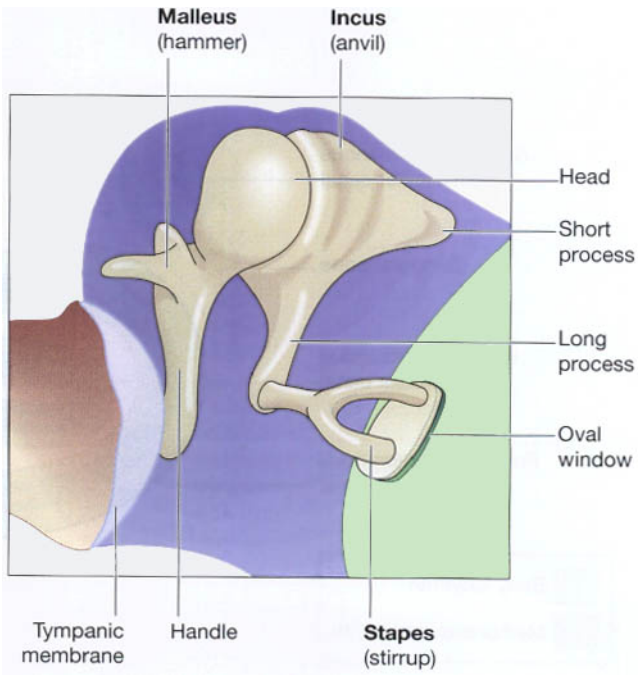


Figure 8.3 The auditory ossicles.

The stapes. This is the medial stirrup-shaped bone. Its head articulates with the incus and its footplate fits into the oval window.

The three ossicles are held in position by fine ligaments.

Inner ear (Fig. 8.4)

The inner (internal) ear or labyrinth (meaning 'maze') ear contains the organs of hearing and balance. It is generally described in two parts, the *bony labyrinth* and the *membranous labyrinth.*

Bony labyrinth

This is a cavity within the temporal bone lined with periosteum. It is larger than, and encloses, the membranous labyrinth of the same shape which fits into it, like a tube within a tube. Between the bony and membranous labyrinth there is a layer of watery fluid called *perilymph* and within the membranous labyrinth there is a similarly watery fluid, *endolymph.*

The bony labyrinth consists of:

- 1 vestibule
- 1 cochlea
- 3 semicircular canals.

The vestibule. This is the expanded part nearest the middle ear. It contains the oval and round windows in its lateral wall.

The cochlea. This resembles a snail's shell. It has a broad base where it is continuous with the vestibule and a narrow apex, and it spirals round a central bony column.

The semicircular canals. These are three tubes arranged so that one is situated in each of the three planes of space. They are continuous with the vestibule.

Membranous labyrinth

This contains endolymph and lies within its bony counterpart. It comprises:

- the vestibule, which contains the *utricle* and *saccule*
- the cochlea
- three semicircular canals.

The cochlea

A cross-section of the cochlea (Fig. 8.5) contains three compartments:

- the scala vestibuli
- the scala media, or *cochlear duct*
- the scala tympani.

In cross-section the bony cochlea has two compartments containing perilymph: the scala vestibuli, which originates at the oval window, and the scala tympani, which ends at the round window. The two compartments are continuous with each other and Figure 8.6 shows the relationship between these structures. The cochlear duct

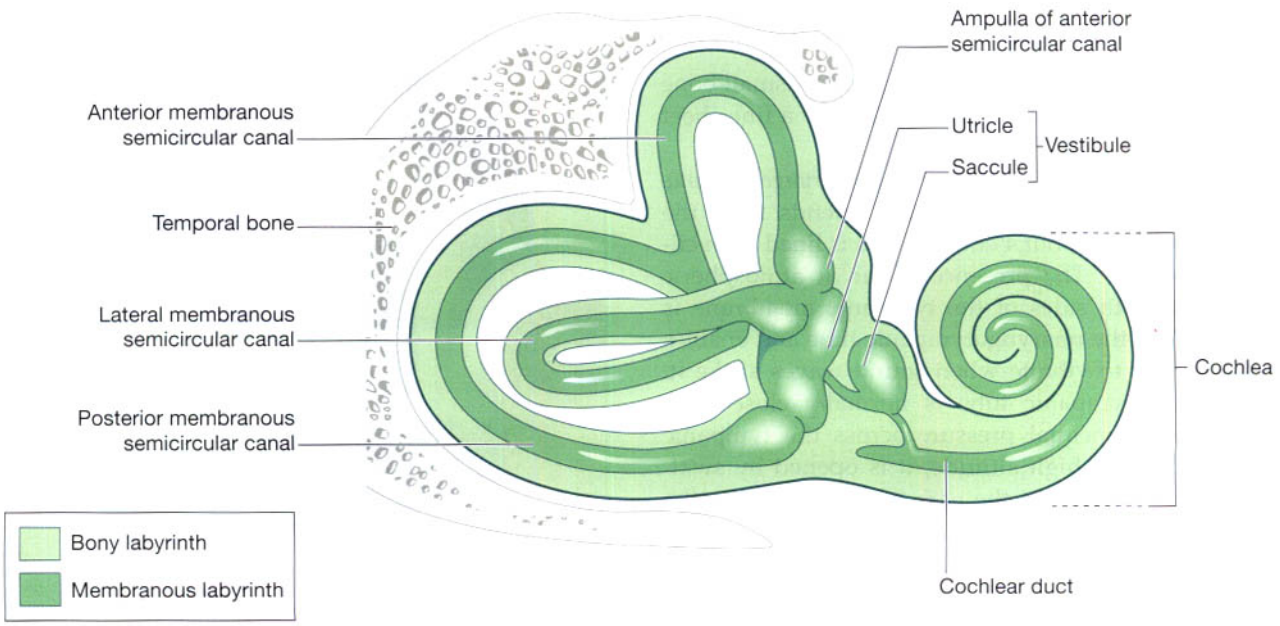


Figure 8.4 The inner ear. The membranous labyrinth within the bony labyrinth.

is part of the membranous labyrinth and is triangular in shape. On the *basilar membrane*, or base of the triangle, there are *supporting cells* and specialised *cochlear hair cells* containing auditory receptors. These cells form the *spiral organ* (of Corti), the sensory organ that responds to vibration by initiating nerve impulses that are then perceived as hearing by the brain. The *auditory receptors* are dendrites of efferent nerves that combine forming the cochlear (auditory) part of the vestibulocochlear nerve (8th cranial nerve), which passes through a foramen in the temporal bone to reach the hearing area in the temporal lobe of the cerebrum (see Fig. 7.18, p. 151).

Physiology of hearing

Every sound produces *sound waves* or vibrations in the air, which travel at about 332 metres (1088 feet) per second. The auricle, because of its shape, concentrates the waves and directs them along the auditory meatus causing the tympanic membrane to vibrate. Tympanic membrane vibrations are transmitted and amplified through the middle ear by movement of the ossicles (Fig. 8.6). At their medial end the footplate of the stapes rocks to and fro in the oval window, setting up fluid waves in the perilymph of the scala vestibuli. Some of the force of these waves is transmitted along the length of the scala vestibuli and scala tympani, but most of the pressure is transmitted into the cochlear duct. This causes a corresponding wave motion in the endolymph, resulting in vibration of the basilar membrane and stimulation of the auditory receptors in the hair cells of the spiral organ. The nerve impulses generated pass to the brain in the cochlear (auditory) portion of the *vestibulocochlear nerve* (8th cranial nerve). The fluid wave is finally expended into the middle ear by vibration of the membrane of the round window. The vestibulocochlear nerve transmits the impulses to the hearing area in the cerebrum where sound is perceived and to various nuclei in the pons and the midbrain.

Sound waves have properties of *pitch* and *volume*, or intensity (Fig. 8.7). Pitch is determined by the frequency of the sound waves and is measured in hertz (Hz). The volume depends on the amplitude of the sound waves and is measured in decibels (dB). Very loud noise is damaging to the ear, particularly when prolonged because it damages the sensitive hair cells of the spiral organ.

Because of the structure of the inner ear, sounds of different frequencies stimulate the basilar membrane at different places along its length allowing discrimination of pitch. Additionally, the greater the amplitude of the wave created in the endolymph, the greater the stimulation of the auditory receptors in the hair cells in the spiral organ, enabling perception of volume.

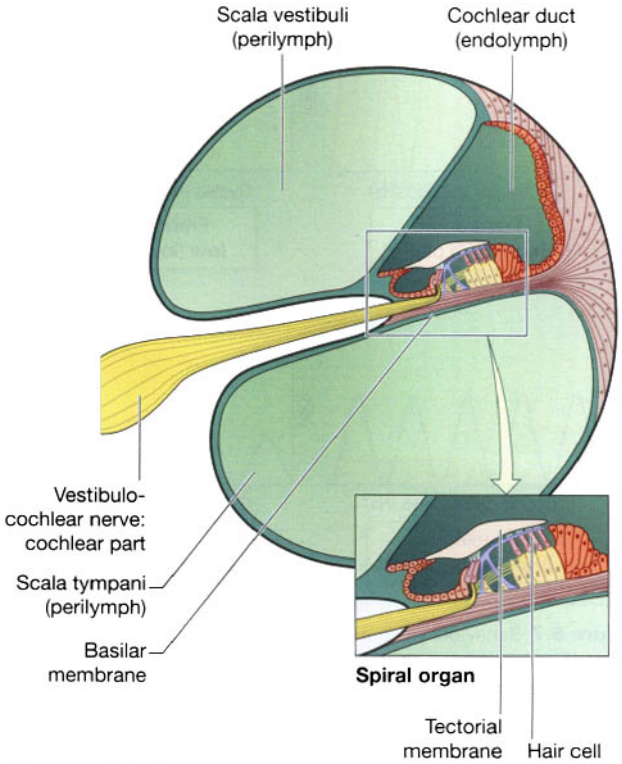


Figure 8.5 A cross-section of the cochlea showing the spiral organ (of Corti).

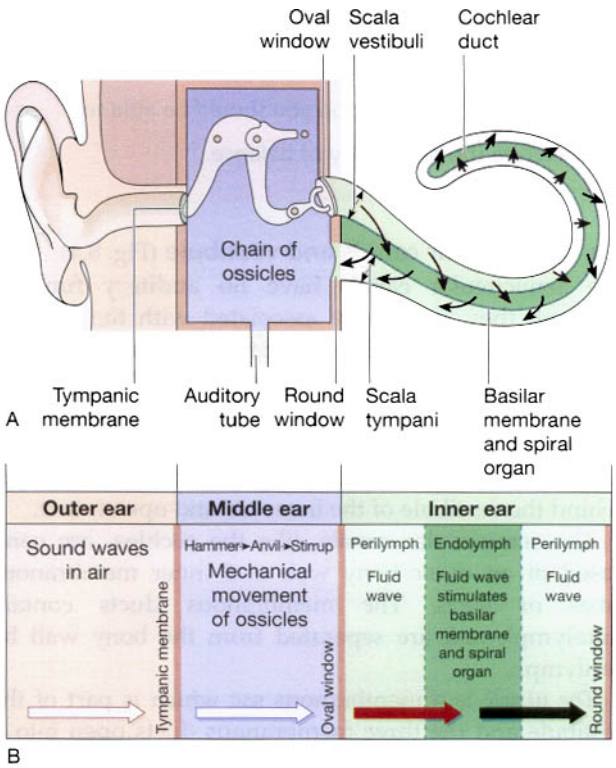


Figure 8.6 Passage of sound waves: A. The ear with cochlea uncoiled. B. Summary of transmission.

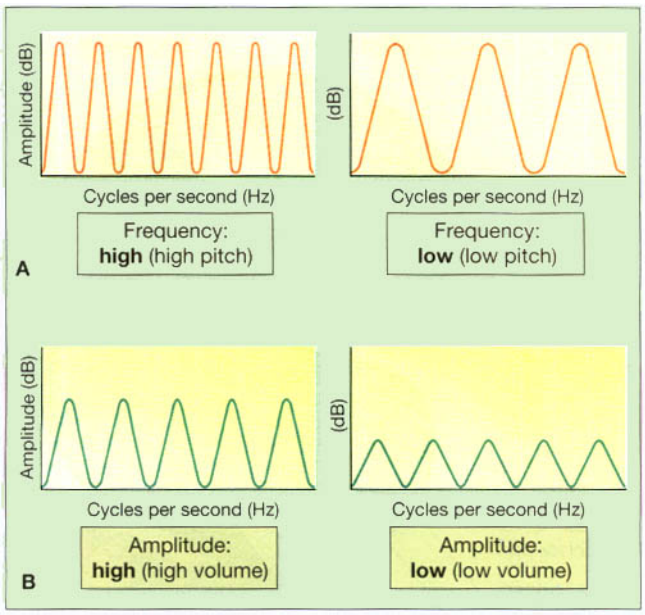


Figure 8.7 Behaviour of sound waves. A. Difference in frequency but of the same amplitude. B. Difference in amplitude but of the same frequency.

BALANCE AND THE EAR

Learning outcome

After studying this section you should be able to:

- describe the physiology of balance.

The semicircular canals and vestibule (Fig. 8.4)

The semicircular canals have no auditory function although they are closely associated with the cochlea. They provide information about the position of the head in space, contributing to maintenance of posture and balance.

There are three semicircular canals, one lying in each of the three planes of space. They are situated above and behind the vestibule of the inner ear and open into it.

The semicircular canals, like the cochlea, are composed of an outer bony wall and inner membranous tubes or *ducts*. The membranous ducts contain endolymph and are separated from the bony wall by perilymph.

The utricle is a membranous sac which is part of the vestibule and the three membranous ducts open into it at their dilated ends, the *ampullae*. The *saccule* is a part of the vestibule and communicates with the utricle and the cochlea.

In the walls of the utricle, saccule and ampullae there are fine specialised epithelial cells with minute projections, called *hair cells*. Amongst the hair cells there are sensory nerve endings which combine forming the *vestibular part* of the vestibulocochlear nerve.

Physiology of balance

The semicircular canals and the vestibule (utricle and saccule) are concerned with balance. Any change of position of the head causes movement in the perilymph and endolymph, which bends the hair cells and stimulates the sensory nerve endings in the utricle, saccule and ampullae. The resultant nerve impulses are transmitted by the vestibular nerve which joins the cochlear nerve to form the vestibulocochlear nerve. The vestibular branch passes first to the *vestibular nucleus*, then to the *cerebellum*.

The cerebellum also receives nerve impulses from the eyes and proprioceptors (sensory receptors) in the skeletal muscles and joints. Impulses from these three sources are coordinated and efferent nerve impulses pass to the cerebrum and to skeletal muscles. This results in awareness of body position, maintenance of upright posture and fixing of the eyes on the same point, independently of head movements.

SIGHT AND THE EYE

Learning outcomes

After studying this section you should be able to:

- describe the gross structure of the eye
- describe the route taken by a nerve impulse from the retina to the cerebrum
- describe how light entering the eye is focused on the retina
- state the functions of the extraocular muscles of the eye
- describe the functions of the accessory organs of the eye.

The eye is the organ of the sense of sight situated in the orbital cavity and it is supplied by the *optic nerve* (2nd cranial nerve).

It is almost spherical in shape and is about 2.5 cm in diameter. The space between the eye and the orbital

cavity is occupied by adipose tissue. The bony walls of the orbit and the fat help to protect the eye from injury.

Structurally the two eyes are separate but, unlike the ear, some of their activities are coordinated so that they function as a pair. It is possible to see with only one eye but three-dimensional vision is impaired when only one eye is used, especially in relation to the judgement of distance.

Structure (Fig. 8.8)

There are three layers of tissue in the walls of the eye. They are:

- the outer fibrous layer: sclera and cornea
- the middle vascular layer or *uveal tract*: choroid, ciliary body and iris
- the inner nervous tissue layer: retina.

Structures inside the eyeball are the lens, aqueous fluid (humour) and vitreous body (humour).

Sclera and cornea

The sclera, or white of the eye, forms the outermost layer of tissue of the posterior and lateral aspects of the eyeball and is continuous anteriorly with the transparent *cornea*. It consists of a firm fibrous membrane that maintains the shape of the eye and gives attachment to the *extraocular* or *extrinsic muscles* of the eye (p. 203).

Anteriorly the sclera continues as a clear transparent epithelial membrane, the *cornea*. Light rays pass through the cornea to reach the retina. The cornea is convex anteriorly and is involved in *refracting* or bending light rays to focus them on the retina.

Choroid (Figs 8.8 and 8.9)

The choroid lines the posterior five-sixths of the inner surface of the sclera. It is very rich in blood vessels and is deep chocolate brown in colour. Light enters the eye through the pupil, stimulates the nerve endings in the retina and is then absorbed by the choroid.

Ciliary body

The ciliary body is the anterior continuation of the choroid consisting of *ciliary muscle* (smooth muscle fibres) and secretory epithelial cells. It gives attachment to the *suspensory ligament* which, at its other end, is attached to the capsule enclosing the lens. Contraction and relaxation of the ciliary muscle changes the thickness of the lens which *bends*, or *refracts* light rays entering the eye to focus them on the retina. The epithelial cells secrete *aqueous fluid* into the anterior segment of the eye, i.e. the space between the lens and the cornea (anterior and posterior chambers). The ciliary body is supplied by parasympathetic branches of the oculomotor nerve (3rd cranial nerve). Stimulation causes contraction of the smooth muscle and accommodation of the eye (p. 202).

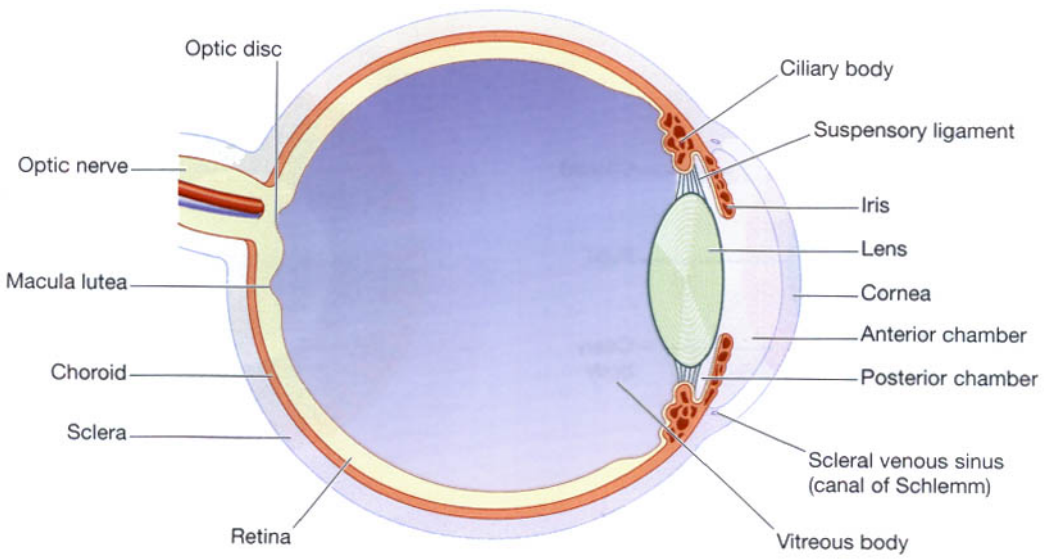


Figure 8.8 Section of the eye.

Iris

The iris is the visible coloured part of the eye and extends anteriorly from the ciliary body, lying behind the cornea in front of the lens. It divides the anterior segment of the eye into *anterior* and *posterior chambers* which contain *aqueous fluid* secreted by the ciliary body. It is a circular body composed of pigment cells and two layers of smooth muscle fibres, one circular and the other radiating (Fig. 8.9). In the centre there is an aperture called the *pupil*.

The iris is supplied by parasympathetic and sympathetic nerves. Parasympathetic stimulation constricts the pupil and sympathetic stimulation dilates it (see Figs 7.43 and 7.44, pp. 171 and 172).

The colour of the iris is genetically determined and depends on the number of pigment cells present. Albinos have no pigment cells and people with blue eyes have fewer than those with brown eyes.

Lens (Fig. 8.10)

The lens is a *highly elastic* circular biconvex body, lying immediately behind the pupil. It consists of fibres enclosed within a capsule and it is suspended from the ciliary body by the *suspensory ligament*. Its thickness is controlled by the ciliary muscle through the suspensory ligament. The lens bends (refracts) light rays reflected by objects in front of the eye. It is the only structure in the eye that can vary its refractory power, achieved by changing its thickness. When the ciliary muscle contracts, it moves forward, releasing its pull on the lens, increasing its thickness. The nearer is the object being viewed the thicker the lens becomes to allow focusing.

Retina

The retina is the innermost layer of the wall of the eye (Fig. 8.8). It is an extremely delicate structure and is especially adapted for stimulation by light rays. It is composed of several layers of nerve cell bodies and their axons, lying on a pigmented layer of epithelial cells which attach it to the choroid. The layer highly sensitive to light is the layer of sensory receptor cells: rods and cones.

The retina lines about three-quarters of the eyeball and is thickest at the back and thins out anteriorly to end just behind the ciliary body. Near the centre of the posterior part is the *macula lutea*, or yellow spot (Figs 8.11 and 8.12). In the centre of the area there is a little depression called the *fovea centralis*, consisting of only cone-shaped cells. Towards the anterior part of the retina there are fewer cone- than rod-shaped cells (Fig. 8.11).

The rods and cones contain photosensitive pigments that convert light rays into nerve impulses and this is explained on page 202.

About 0.5 cm to the nasal side of the macula lutea all the nerve fibres of the retina converge to form the *optic*

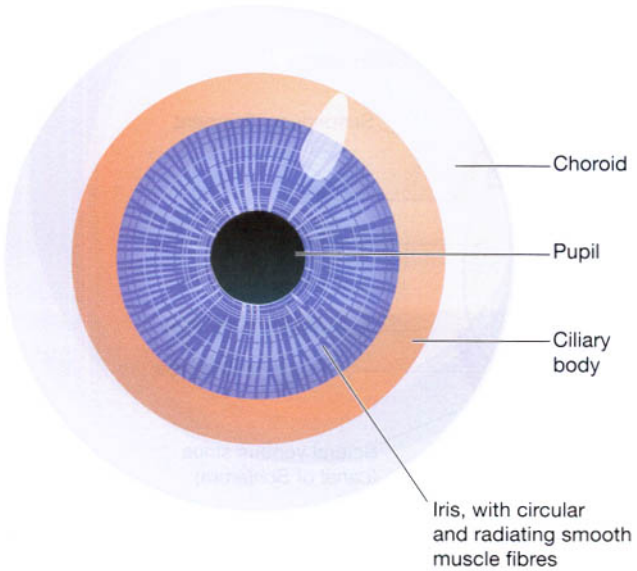


Figure 8.9 The choroid, ciliary body and iris. Viewed from the front.

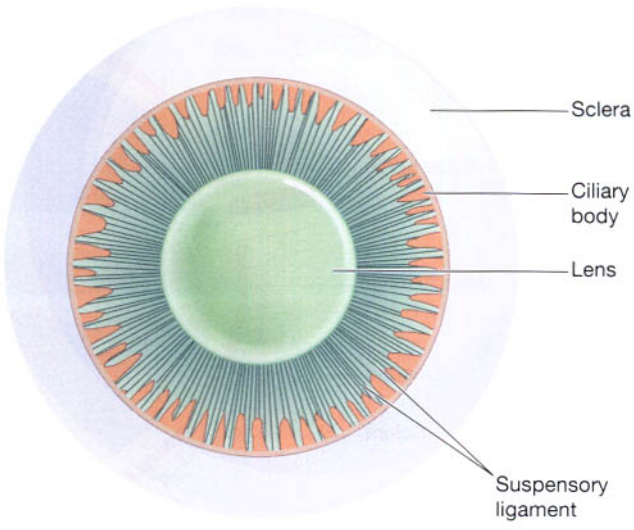


Figure 8.10 The lens and suspensory ligament viewed from the front. The iris has been removed.

nerve. The small area of retina where the optic nerve leaves the eye is the *optic disc* or *blind spot*. It has no light-sensitive cells.

Blood supply to the eye

The eye is supplied with arterial blood by the *ciliary arteries* and the *central retinal artery*. These are branches of the ophthalmic artery, one of the branches of the internal carotid artery.

Venous drainage is by a number of veins, including the *central retinal vein*, which eventually empty into a deep venous sinus.

The central retinal artery and vein are encased in the optic nerve, entering the eye at the optic disc.

Interior of the eye

The anterior segment of the eye, i.e. the space between the cornea and the lens, is incompletely divided into *anterior* and *posterior chambers* by the iris (Fig. 8.8). Both chambers contain a clear *aqueous fluid (humour)* secreted into the posterior chamber by ciliary glands. It circulates in front of the lens, through the pupil into the anterior chamber and returns to the venous circulation through the *scleral venous sinus* (canal of Schlemm) in the angle between the iris and cornea (Fig. 8.8). There is continuous production and drainage but the intraocular pressure remains fairly constant between 1.3 and 2.6 kPa (10 to 20 mmHg). An increase in this pressure causes *glaucoma* (p. 210). Aqueous fluid supplies nutrients and removes waste from the transparent structures in the front of the eye that have no blood supply, i.e. the cornea, lens and lens capsule.

Behind the lens and filling the posterior segment (cavity) of the eyeball is the *vitreous body (humour)*. This is a soft, colourless, transparent, jelly-like substance composed of 99% water, some salts and mucoprotein. It maintains sufficient intraocular pressure to support the retina against the choroid and prevent the walls of the eyeball from collapsing.

The eye keeps its shape because of the intraocular pressure exerted by the vitreous body and the aqueous fluid. It remains fairly constant throughout life.

Optic nerves (second cranial nerves) (Fig. 8.13)

The fibres of the optic nerve originate in the retina of the eye. All the fibres converge to form the optic nerve about 0.5 cm to the nasal side of the macula lutea. The nerve pierces the choroid and sclera to pass backwards and medially through the orbital cavity. It then passes through the optic foramen of the sphenoid bone, backwards and medially to meet the nerve from the other eye at the *optic chiasma*.

Optic chiasma

This is situated immediately in front of and above the pituitary gland which is in the hypophyseal fossa of the sphenoid bone (see Fig. 9.2, p. 215). In the optic chiasma the nerve fibres of the optic nerve from the nasal side of each retina cross over to the opposite side. The fibres from the temporal side do not cross but continue backwards on the same side. This crossing over provides both cerebral hemispheres with sensory input from each eye.

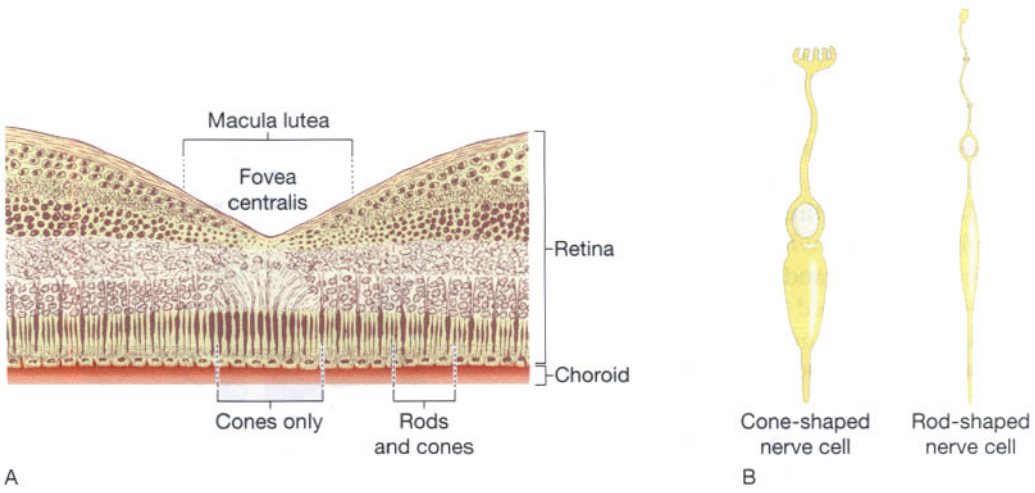


Figure 8.11 The retina: A. Magnified section. B. Light-sensitive nerve cells: rods and cones.

Optic tracts

These are the pathways of the optic nerves, posterior to the optic chiasma. Each tract consists of the nasal fibres from the retina of one eye and the temporal fibres from the retina of the other. The optic tracts pass backwards through the cerebrum to synapse with nerve cells of the *lateral geniculate bodies* of the thalamus. From there the nerve fibres proceed backwards and medially as the *optic radiations* to terminate in the *visual area* of the cerebral cortex in the occipital lobes of the cerebrum. Other neurones originating in the lateral geniculate bodies convey impulses from the eyes to the *cerebellum* where, together with impulses from the semicircular canals of the ears and from the skeletal muscles and joints, they contribute to the maintenance of posture and balance.

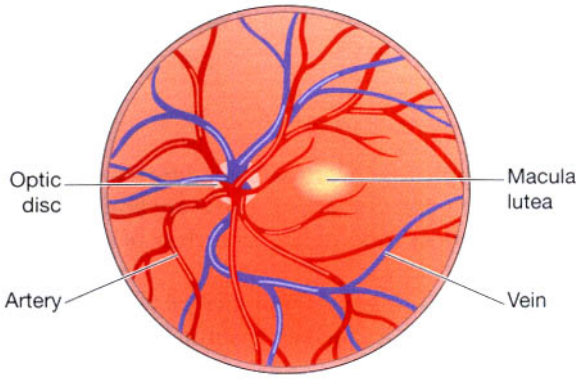


Figure 8.12 The retina as seen through the pupil with an ophthalmoscope.

Physiology of sight

Light waves travel at a speed of 186 000 miles (300 000 kilometres) per second. Light is reflected into the eyes by objects within the field of vision. White light is a combination of all the colours of the visual spectrum (rainbow), i.e. red, orange, yellow, green, blue, indigo and violet. This is demonstrated by passing white light through a glass prism which *refracts* or bends the rays of the different colours to a greater or lesser extent, depending on their wavelengths (Fig. 8.14). Red light has the longest wavelength and violet the shortest.

This range of colour is the *spectrum of visible light*. In a rainbow, white light from the sun is broken up by raindrops which act as prisms and reflectors.

The electromagnetic spectrum

The electromagnetic spectrum is broad but only a small part is visible to the human eye (Fig. 8.15). Beyond the long end there are infrared waves (heat), microwaves and radio waves. Beyond the short end there are ultraviolet (UV), X-rays and gamma rays. UV light is not normally visible because it is absorbed by a yellow pigment in the lens. Following removal of the lens (cataract extraction), UV light is visible and it has been suggested that long-term exposure may damage the retina.

A specific colour is perceived when only one wavelength is *reflected* by the object and all the others are *absorbed*, e.g. an object appears red when only the red wavelength is reflected. Objects appear white when all wavelengths are reflected, and black when they are all absorbed.

In order to achieve clear vision, light reflected from objects within the visual field is focused on to the retina of each eye. The processes involved in producing a clear image are *refraction of the light rays*, changing the *size of the pupils* and *accommodation of the eyes*.

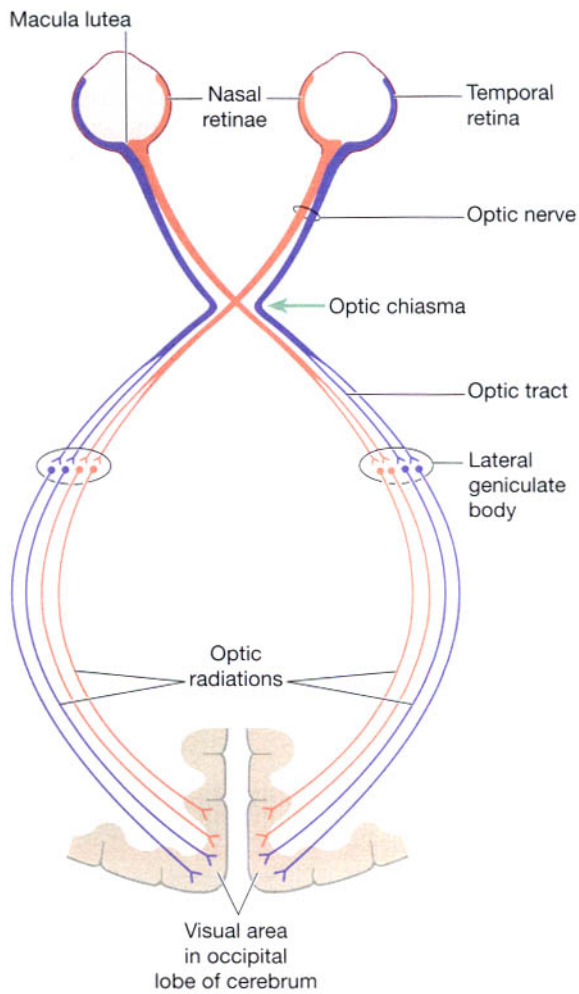


Figure 8.13 The optic nerves and their pathways.

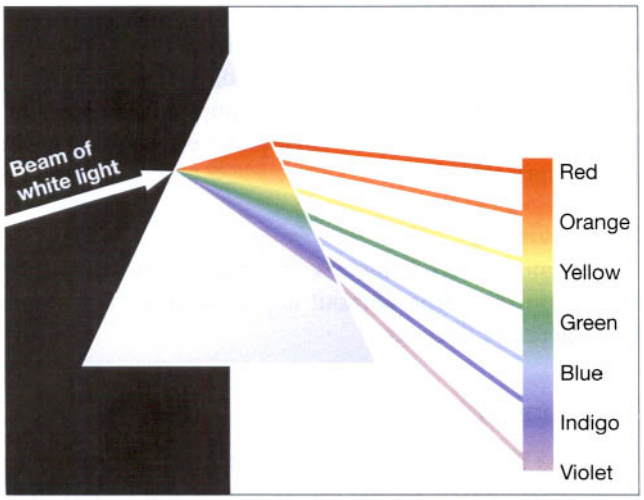


Figure 8.14 Refraction: white light broken into the colours of the visible spectrum when passed through a prism.

Although these may be considered as separate processes, effective vision is dependent upon their coordination.

Refraction of the light rays

When light rays pass from a medium of one density to a medium of a different density they are refracted or bent; for example in the eye the biconvex lens bends and focuses light rays (Fig. 8.16). This principle is used to focus light on the retina. Before reaching the retina light rays pass successively through the conjunctiva, cornea, aqueous fluid, lens and vitreous body. They are all more dense than air and, with the exception of the lens, they have a constant refractory power, similar to that of water.

Abnormal refraction within the eye is corrected using biconvex or biconcave lenses, which are shown on page 212.

Lens

The lens is a biconvex elastic transparent body suspended behind the iris from the ciliary body by the suspensory ligament. It is the only structure in the eye that changes its refractive power. Light rays entering the eye need to be bent (refracted) to focus them on the retina. Light from distant objects needs least refraction and, as the object comes closer, the amount of refraction needed is increased. To increase the refractive power the ciliary muscle contracts, releasing its pull on the suspensory ligament and the anterior surface of the lens bulges forward, increasing its convexity. This focuses light rays from near objects on the retina. When the ciliary muscle relaxes it slips backwards, increasing its pull on the suspensory ligament, making the lens thinner (Fig. 8.17). This focuses light rays from distant objects on the retina.

Size of the pupils

Pupil size influences accommodation by controlling the amount of light entering the eye. In a bright light the pupils are constricted. In a dim light they are dilated.

If the pupils were dilated in a bright light, too much light would enter the eye and damage the sensitive retina. In a dim light, if the pupils were constricted, insufficient light would enter the eye to activate the photosensitive pigments in the rods and cones which stimulate the nerve endings in the retina.

The iris consists of one layer of circular and one of radiating smooth muscle fibres. Contraction of the circular fibres constricts the pupil, and contraction of the radiating fibres dilates it. The size of the pupil is controlled by the autonomic nervous system. Sympathetic stimulation dilates the pupils and parasympathetic stimulation causes constriction.

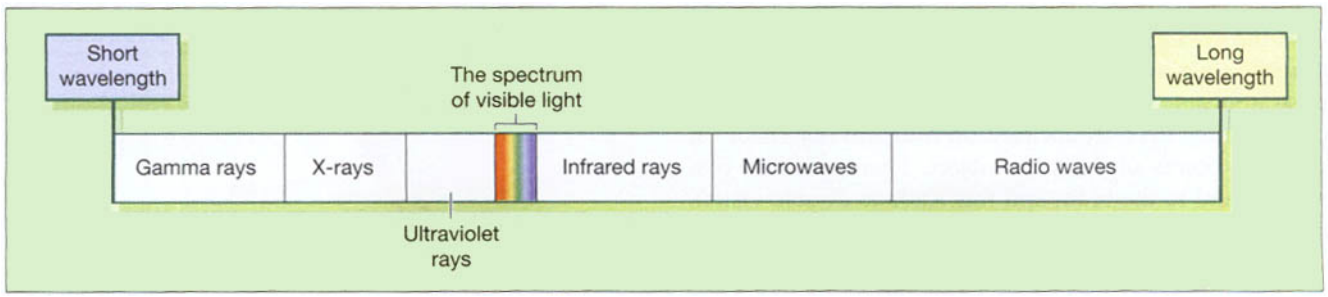


Figure 8.15 The electromagnetic spectrum.

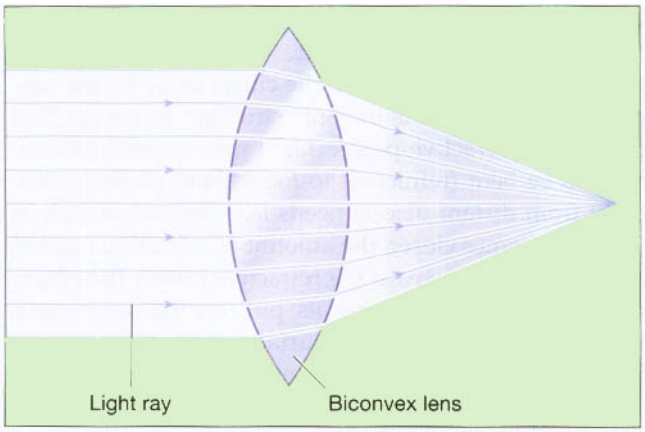


Figure 8.16 Refraction of light rays passing through a biconvex lens.

Accommodation of the eyes to light

(Figs 8.17 and 8.18)

Close vision

In order to focus on near objects, i.e. within about 6 metres, the eye must make the following adjustments:

- constriction of the pupils
- convergence of the eyeballs
- changing the power of the lens.

Constriction of the pupils. This assists accommodation by reducing the width of the beam of light entering the eye so that it passes through the central curved part of the lens.

Convergence (movement) of the eyeballs. Light rays from nearby objects enter the two eyes at different angles and for clear vision they must stimulate *corresponding areas* of the two retinae. Extraocular muscles move the eyes and to obtain a clear image they rotate the eyes so that they *converge* on the object viewed. This coordinated muscle activity is under autonomic control. When there is voluntary movement of the eyes both eyes move and convergence is maintained. The nearer an object is to the eyes the greater the eye rotation needed to achieve convergence, e.g. an individual focusing near the tip of his nose appears to be 'cross-eyed'. If convergence is not complete the eyes are focused on different objects or on different points of the same object. There are then two images sent to the brain and this leads to double vision, *diplopia*. After a period of time during which convergence is not possible the brain tends to ignore the impulses received from the divergent eye (see squint, p. 211).

Changing the power of the lens. Changes in the thickness of the lens are made to focus light on the retina. The amount of adjustment depends on the distance of the object from the eyes, i.e. the lens is thicker for near vision and at its thinnest when focusing on objects at more than 6 metres' distance (Fig. 8.17). Looking at near objects 'tires' the eyes more quickly, owing to the continuous use of the ciliary muscle.

Distant vision

Objects more than 6 metres away from the eyes are focused on the retina without adjustment of the lens or convergence of the eyes.

Functions of the retina

The retina is the *photosensitive* part of the eye. The light-sensitive nerve cells are the *rods* and *cones* and their distribution in the retina is shown in Figure 8.11A. Light rays cause chemical changes in photosensitive pigments in these cells and they generate nerve impulses which are conducted to the occipital lobes of the cerebrum via the optic nerves.

The rods are more sensitive than the cones. They are stimulated by low-intensity or dim light, e.g. by the dim light in the interior of a darkened room.

The cones are sensitive to bright light and colour. The different wavelengths of visible light stimulate photosensitive pigments in the cones, resulting in the perception of different colours. In bright light the light rays are focused on the macula lutea.

The rods are more numerous towards the periphery of the retina. *Visual purple (rhodopsin)* is a photosensitive pigment present only in the rods. It is bleached (degraded)

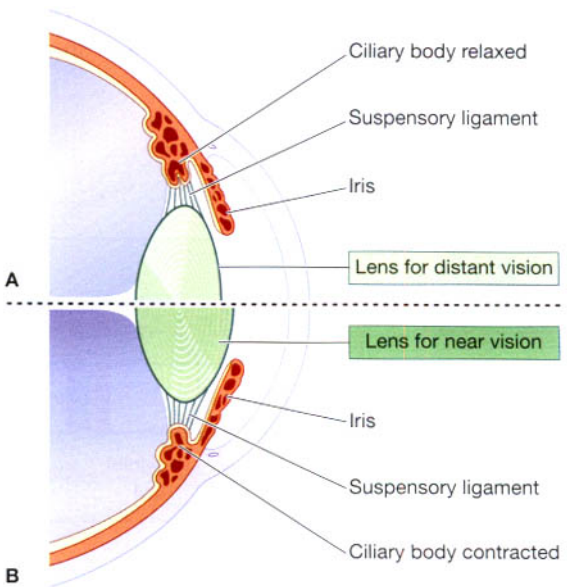


Figure 8.17 The shape of the lens: A. Distant vision. B. Near vision.

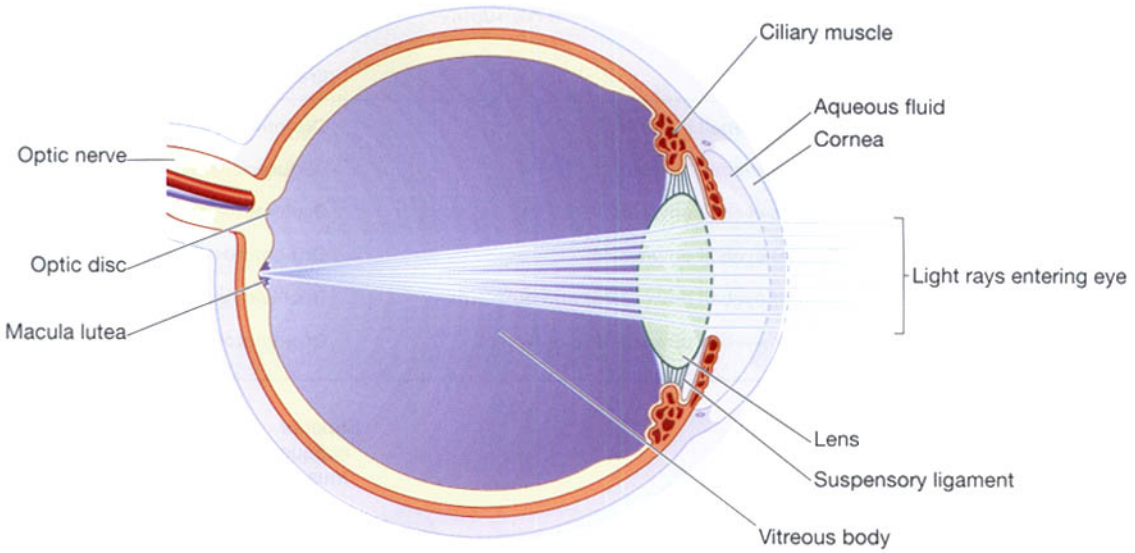


Figure 8.18 Section of the eye showing the focusing of light rays on the retina.

by bright light and is quickly regenerated when an adequate supply of vitamin A is available (p. 274).

Dark adaptation. When exposed to bright light, the rhodopsin within the sensitive rods is completely degraded. This is not significant until the individual moves into a darkened area where the light intensity is insufficient to stimulate the cones, and temporary visual impairment results whilst the rhodopsin is being regenerated within the rods, 'dark adaptation'. When regeneration of rhodopsin occurs, normal sight returns.

It is easier to see a dim star in the sky at night if the head is turned slightly away from it because light of low intensity is then focused on an area of the retina where there is a greater concentration of rods. If looked at directly the light intensity of a dim star is not sufficient to stimulate the less sensitive cones in the area of the macula lutea. In dim evening light different colours cannot be distinguished because the light intensity is insufficient to stimulate colour-sensitive pigments in cones.

Breakdown and regeneration of the visual pigments in cones is similar to that of rods.

Binocular vision (Fig. 8.19)

Binocular or stereoscopic vision has certain advantages. Each eye 'sees' a scene slightly differently. There is an overlap in the middle but the left eye sees more on the left than can be seen by the other eye and vice versa. The images from the two eyes are fused in the cerebrum so that only one image is perceived.

Binocular vision provides a much more accurate assessment of one object relative to another, e.g. its distance, depth, height and width. People with monocular vision may find it difficult, for example, to judge the speed and distance of an approaching vehicle.

Extraocular muscles of the eye

The eyeballs are moved by six *extrinsic muscles*, attached at one end to the eyeball and at the other to the walls of the orbital cavity. There are four *straight* (rectus) muscles and two *oblique* muscles (Fig. 8.20). They are:

- medial rectus
- lateral rectus
- superior rectus
- inferior rectus
- superior oblique
- inferior oblique.

Movement of the eyes to look in a particular direction is under voluntary control, but coordination of movement, needed for convergence and accommodation to near or distant vision, is under autonomic (involuntary) control. Movements of the eyes made by the action of these muscles are shown in Table 8.1.

Nerve supply to the muscles of the eye

Nerves shown in Table 8.1 supply the extrinsic muscles. The *oculomotor nerves* supply the *intrinsic muscles* of the iris and ciliary body.

Table 8.1 Extrinsic muscles of the eye: their actions and cranial nerve supply

Name	Action	Cranial nerve supply
Medial rectus	Rotates eyeball inwards	Oculomotor nerve (3rd cranial nerve)
Lateral rectus	Rotates eyeball outwards	Abducent nerve (6th cranial nerve)
Superior rectus	Rotates eyeball upwards	Oculomotor nerve (3rd cranial nerve)
Inferior rectus	Rotates eyeball downwards	Oculomotor nerve (3rd cranial nerve)
Superior oblique	Rotates eyeball downwards and outwards	Trochlear nerve (4th cranial nerve)
Inferior oblique	Rotates eyeball upwards and outwards	Oculomotor nerve (3rd cranial nerve)

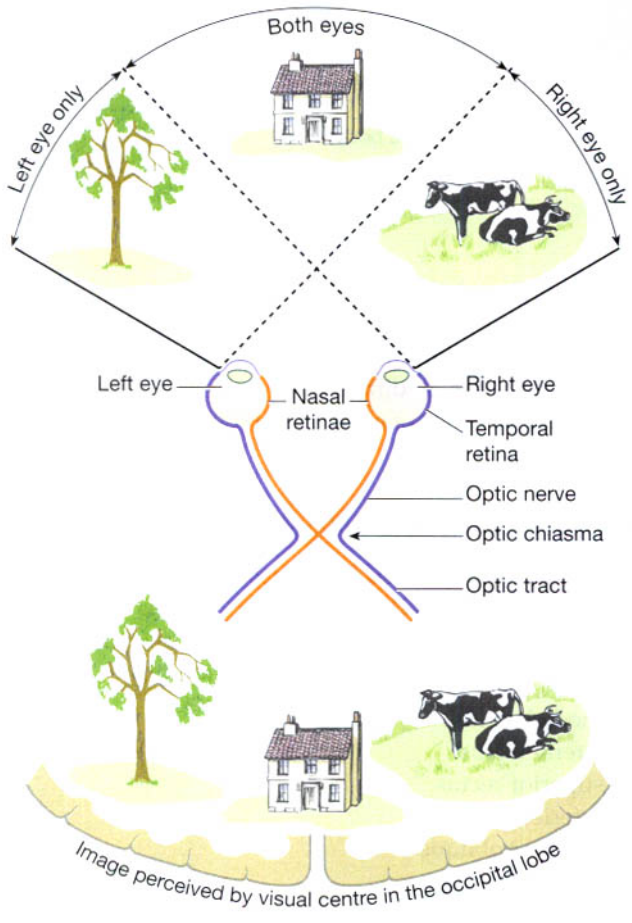


Figure 8.19 Parts of the visual field – monocular and binocular.

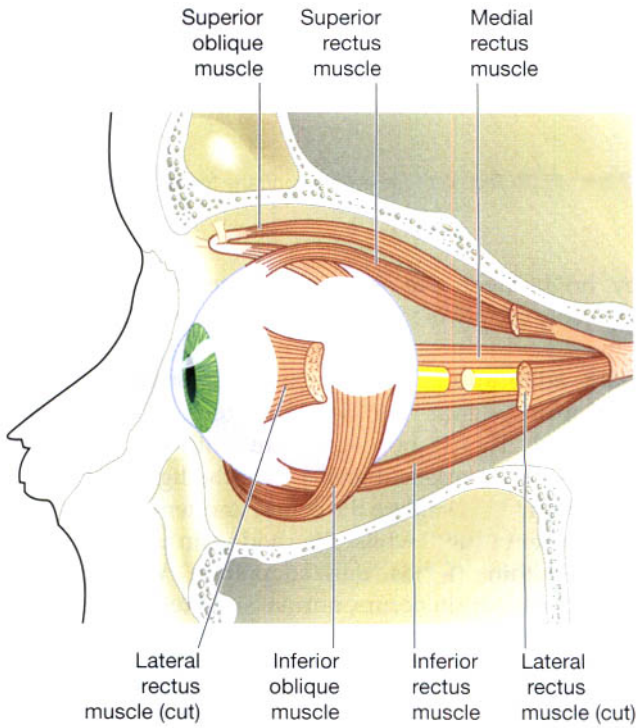


Figure 8.20 The extrinsic muscles of the eye.

Accessory organs of the eye

The eye is a delicate organ which is protected by several structures (Fig. 8.21):

- eyebrows
- eyelids and eyelashes
- lacrimal apparatus.

Eyebrows

These are two arched ridges of the supraorbital margins of the frontal bone. Numerous hairs (eyebrows) project obliquely from the surface of the skin. They protect the anterior aspect of the eyeball from sweat, dust and other foreign bodies.

Eyelids (palpebrae)

The eyelids are two movable folds of tissue situated above and below the front of each eye. On their free edges there are short curved hairs, the *eyelashes*. The layers of tissue which form the eyelids are:

- a thin covering of skin
- a thin sheet of loose (areolar) tissue
- two muscles – the *orbicularis oculi* and *levator palpebrae superioris*
- a thin sheet of dense connective tissue, the *tarsal plate*, larger in the upper than in the lower eyelid, which supports the other structures
- a lining of *conjunctiva*.

Conjunctiva

This is a fine transparent membrane which lines the eyelids and the front of the eyeball (Fig. 8.21). Where it lines the eyelids it consists of highly vascular columnar epithelium. Corneal conjunctiva consists of less-vascular stratified epithelium. When the eyelids are closed the conjunctiva becomes a closed sac. It protects the delicate cornea and the front of the eye. When eyedrops are administered they are placed in the lower conjunctival sac. The medial and lateral angles of the eye where the upper and lower lids come together are called respectively the *medial canthus* and the *lateral canthus*.

Eyelid margins

Along the edges of the lids there are numerous *sebaceous glands*, some with ducts opening into the hair follicles of the *eyelashes* and some on to the eyelid margins between the hairs. *Tarsal glands* (meibomian glands) are modified sebaceous glands embedded in the tarsal plates with ducts that open on to the inside of the free margins of the eyelids. They secrete an oily material, spread over the conjunctiva by blinking, which delays evaporation of tears.

Functions

The *eyelids* and *eyelashes* protect the eye from injury.

- Reflex closure of the lids occurs when the conjunctiva or eyelashes are touched, when an object comes close to the eye or when a bright light shines into the eye – this is called the *conjunctival* or *corneal reflex*.
- Blinking at about 3- to 7-second intervals spreads tears and oily secretions over the cornea, preventing drying.

When the *orbicularis oculi* contracts, the eyes close. When the *levator palpebrae* contract the eyelids open (see Fig. 18.1, p. 430).

Lacrimal apparatus (Fig. 8.22)

For each eye this consists of:

- 1 lacrimal gland and its ducts
- 2 lacrimal canaliculi
- 1 lacrimal sac
- 1 nasolacrimal duct.

The lacrimal glands are exocrine glands situated in recesses in the frontal bones on the lateral aspect of each eye just behind the supraorbital margin. Each gland is

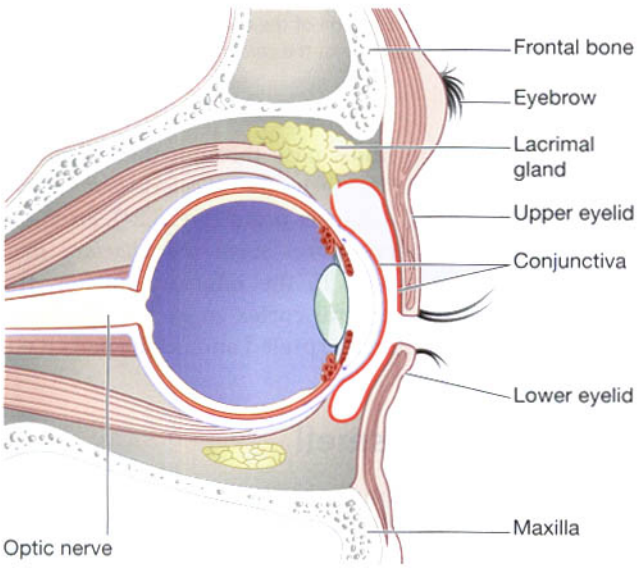


Figure 8.21 Section of the eye and its accessory structures.

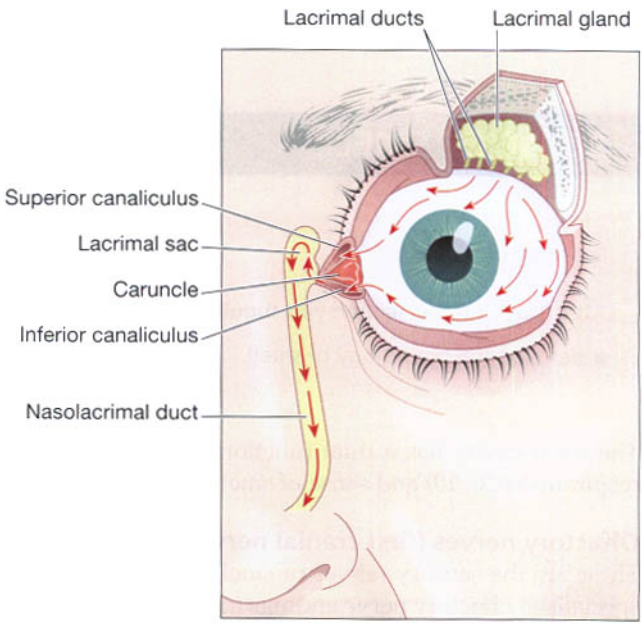


Figure 8.22 The lacrimal apparatus. Arrows show the direction of the flow of tears.

approximately the size and shape of an almond, and is composed of secretory epithelial cells. The glands secrete *tears* composed of water, mineral salts, antibodies, and *lysozyme*, a bactericidal enzyme.

The tears leave the lacrimal gland by several small ducts and pass over the front of the eye under the lids towards the medial canthus where they drain into the *two lacrimal canaliculi*; the opening of each is called the *punctum*. The two canaliculi lie one above the other, separated by a small red body, the *caruncle*. The tears then drain into the *lacrimal sac* which is the upper expanded end of the *nasolacrimal duct*. This is a membranous canal approximately 2 cm long, extending from the lower part of the lacrimal sac to the nasal cavity, opening at the level of the inferior concha. Normally the rate of secretion of tears keeps pace with the rate of drainage. When a foreign body or other irritant enters the eye the secretion of tears is greatly increased and the conjunctival blood vessels dilate. Secretion of tears is also increased in emotional states, e.g. crying.

Functions

The fluid that fills the conjunctival sac consists of tears and the oily secretion of tarsal glands and is spread over the cornea by blinking. The functions of this mixture of fluids include:

- washing away irritating materials, e.g. dust, grit
- the bacteriocidal enzyme lysozyme prevents microbial infection
- its oiliness delays evaporation and prevents drying of the conjunctiva
- nourishment of the cornea.

SENSE OF SMELL

Learning outcome

After studying this section you should be able to:

- describe the physiology of smell.

The nasal cavity has a dual function: a passageway for respiration (Ch. 10) and sense of smell.

Olfactory nerves (first cranial nerves)

These are the sensory nerves of smell. They originate as specialised olfactory nerve endings (*chemoreceptors*) in the mucous membrane of the roof of the nasal cavity above the superior nasal conchae (Fig. 8.23). On each side of the

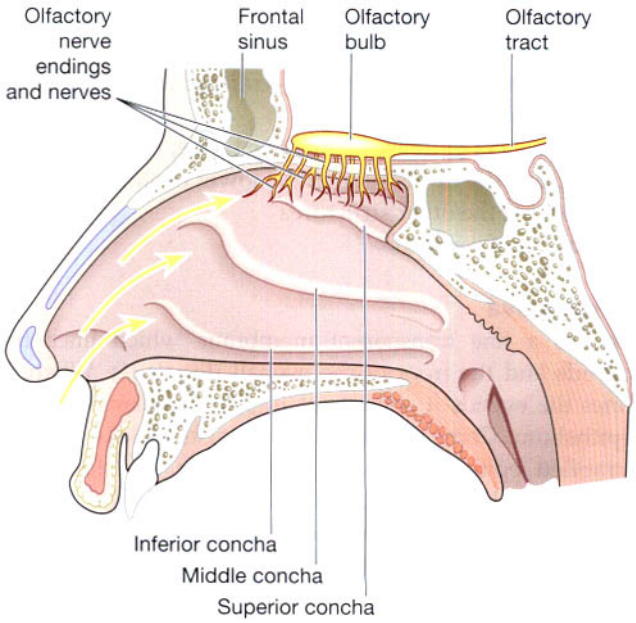


Figure 8.23 The olfactory structures.

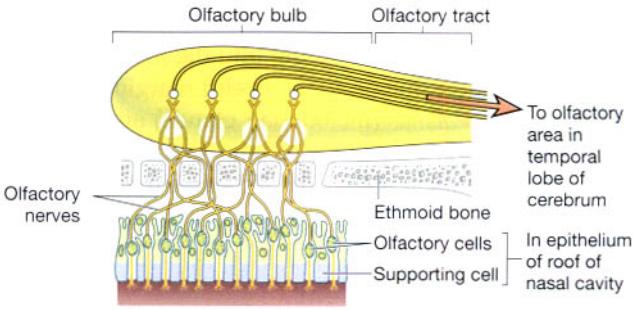


Figure 8.24 An enlarged section of the olfactory apparatus in the nose and on the inferior surface of the cerebrum.

nasal septum nerve fibres pass through the cribriform plate of the ethmoid bone to the *olfactory bulb* where interconnections and synapses occur (Fig. 8.24). From the bulb, bundles of nerve fibres form the *olfactory tract* which passes backwards to the olfactory area in the *temporal lobe* of the cerebral cortex in each hemisphere where the impulses are interpreted and odour perceived.

Physiology of smell

The sense of smell in human beings is generally less acute than in other animals. Many animals are known to secrete odorous chemicals called *pheromones* that play an important part in chemical communication in, for example, territorial behaviour, mating and the bonding

of mothers and their newborn offspring. The role of pheromones in human communication is unknown.

All odorous materials give off volatile molecules, which are carried into the nose with the inhaled air and stimulate the olfactory chemoreceptors when dissolved in mucus.

The air entering the nose is warmed and convection currents carry eddies of inspired air to the roof of the nasal cavity. 'Sniffing' concentrates volatile molecules in the roof of the nose. This increases the number of olfactory receptors stimulated and thus the perception of the smell. The sense of smell may affect the appetite. If the odours are pleasant the appetite may improve and vice versa. When accompanied by the sight of food, an appetising smell increases salivation and stimulates the digestive system (Ch. 12). The sense of smell may create long-lasting memories, especially to distinctive odours, e.g. hospital smells, favourite or least-liked foods.

Inflammation of the nasal mucosa prevents odorous substances from reaching the olfactory area of the nose, causing loss of the sense of smell (*anosmia*). The usual cause is the common cold.

Adaptation. When an individual is continuously exposed to an odour, perception of the odour decreases and ceases within a few minutes. This loss of perception only affects that specific odour and adaptation probably occurs both in the cerebrum and in the sensory receptors in the nasal cavity.

SENSE OF TASTE

Learning outcome

After studying this section you should be able to:

- describe the physiology of taste.

Taste buds contain sensory receptors (chemoreceptors) that are found in the papillae of the tongue and widely distributed in the epithelia of the tongue, soft palate, pharynx and epiglottis. They consist of small sensory nerve endings of the glossopharyngeal, facial and vagus nerves (cranial nerves VII, IX and X). Some of the cells have hair-like microvilli on their free border, projecting towards tiny pores in the epithelium (Fig. 8.25). The sensory receptors are stimulated by chemicals that enter the pores dissolved in saliva. Nerve impulses are generated and conducted along the glossopharyngeal, facial and vagus nerves before synapsing in the medulla and thalamus. Their final destination is the *taste area* in the parietal lobe of the cerebral cortex where taste is perceived (see Fig. 7.18, p. 151).

Physiology of taste

Four fundamental sensations of taste have been described—sweet, sour, bitter and salt. This is probably an oversimplification because perception varies widely and many 'tastes' cannot be easily classified. However, some tastes consistently stimulate taste buds in specific parts of the tongue (see Fig. 12.12, p. 290):

- sweet and salty, mainly at the tip
- sour, at the sides
- bitter, at the back.

The sense of taste triggers salivation and the secretion of gastric juice (Ch. 12). It also has a protective function, e.g. when foul-tasting food is eaten then reflex gagging or vomiting may be induced.

The sense of taste is impaired when the mouth is dry because substances can be 'tasted' only if they are in solution.

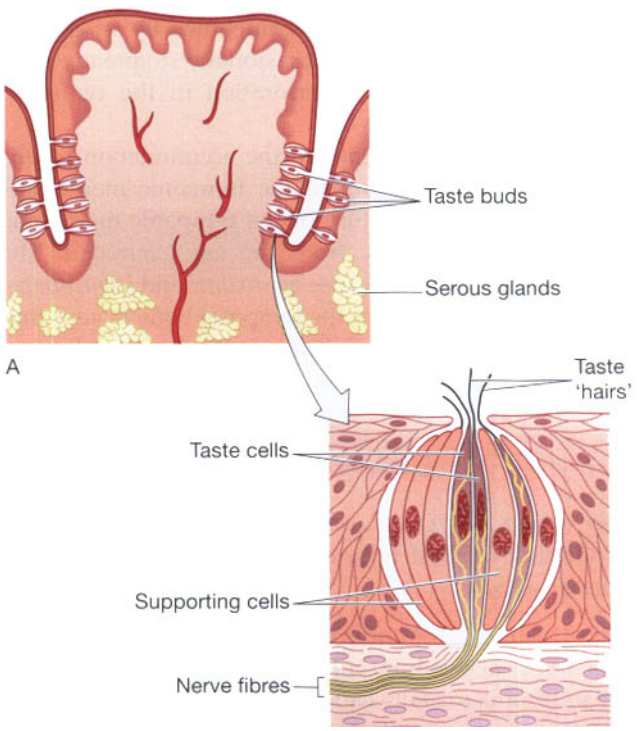


Figure 8.25 Structure of taste buds: A. A section of a papilla. B. A taste bud – greatly magnified.

DISEASES OF THE EAR

Learning outcomes

After studying this section you should be able to:

- describe the causes and effects of diseases of the ear
- compare and contrast the features of conductive and sensorineural deafness.

External otitis

Infection by *Staphylococcus aureus* is the usual cause of localised inflammation (boils) in the external auditory meatus. When more generalised, the inflammation may be caused by bacteria or fungi or by an allergic reaction to, e.g., dandruff, soaps, hair sprays, hair dyes.

Acute otitis media

This is inflammation of the middle ear cavity usually caused by upward spread of microbes from an upper respiratory tract infection via the auditory tube. It is very common in children and is accompanied by severe earache on the affected side. Occasionally it spreads from the outer ear through a perforation in the tympanic membrane.

Microbial infection leads to the accumulation of pus and the outward bulging of the tympanic membrane. Sometimes there is rupture of the tympanic membrane and purulent discharge from the ear (*otorrhoea*). The spread of infection may cause *mastoiditis* and *labyrinthitis*. As the petrous portion of the temporal bone is very thin the infection may spread through the bone and cause meningitis and brain abscess.

Serous otitis media

Also known as '*glue ear*', or secretory otitis media, this is a collection of fluid (*effusion*) in the middle ear cavity. Causes include:

- obstruction of the auditory tube by, for example, pharyngeal swelling, enlarged adenoids or tumour
- barotrauma (usually caused by descent in an aeroplane when suffering from a cold)
- untreated acute otitis media.

In adults the individual suffers from deafness and (usually painless) blockage of the ear, whereas young children show delay in speech development and behavioural disorders owing to deafness. Air already present in the middle ear is absorbed and a negative pressure develops. At first there is retraction of the tympanic membrane, then fluid is drawn into the low-pressure cavity from surrounding blood vessels. Conductive hearing loss occurs and there may or may not be secondary infection. This is a common cause of hearing impairment in children.

Chronic otitis media

In this condition there is permanent perforation of the tympanic membrane following acute otitis media (especially when recurrent, persistent or untreated) and mechanical or blast injuries. During the healing process stratified epithelium from the outer ear sometimes grows into the middle ear, forming a *cholesteatoma*. This is a collection of desquamated epithelial cells and purulent material. Continued development of cholesteatoma may lead to:

- destruction of the ossicles and conduction deafness
- erosion of the roof of the middle ear and meningitis
- spread of infection to the inner ear that may cause labyrinthitis.

Otosclerosis

This is a common cause of progressive conductive hearing loss in young adults that may affect one ear but is more commonly bilateral. It is usually hereditary, more common in females than males and often worsens during pregnancy. Abnormal bone develops around the footplate of the stapes fusing it to the oval window, reducing the ability to transmit sound waves across the tympanic cavity.

Presbycusis

This form of hearing impairment commonly accompanies the ageing process. Degenerative changes in the sensory cells of the spiral organ (of Corti) result in sensorineural (perceptive) deafness. Perception of high-frequency sound is impaired first and later low-frequency sound may also be affected. The individual develops difficulty in discrimination, e.g. following a conversation, especially in the presence of background noise.

Ménière's disease

In this condition there is accumulation of endolymph causing distension and increased pressure within the

membranous labyrinth with destruction of the sensory cells in the ampulla and cochlea. It is usually unilateral at first but both ears may be affected later. The cause is not known. Ménière's disease is associated with recurrent episodes of incapacitating dizziness (vertigo), nausea and vomiting, lasting for several hours. Periods of remission vary from days to months. During and between attacks there may be continuous ringing in the affected ear (tinnitus). Loss of hearing is experienced during episodes, and permanent hearing impairment may gradually develop over a period of years as the spiral organ (of Corti) is destroyed.

Labyrinthitis

This may be caused by development of a fistula from a cholesteatoma (see above) or rarely by spread of infection from the middle ear. In some cases the spiral organ is destroyed, causing sudden total nerve deafness in the affected ear.

Motion sickness

Repetitive motion causes excessive stimulation of the semicircular canals and vestibular apparatus and results in nausea and vomiting in some people.

Deafness

Hearing impairment can be classified in two main categories: *conductive* and *sensorineural*. Common causes are shown in Box 8.1. Hearing impairment can also be *mixed* when there is a combination of conductive and sensorineural deafness in one ear.

Box 8.1 Common causes of deafness

Conductive	Sensorineural
Wax or foreign body	Presbycusis
Acute otitis media	Noise pollution
Serous otitis media	Congenital
Chronic otitis media	Ménière's disease
Barotrauma	Ototoxic drugs, e.g. aminoglycosides, diuretics, chemotherapy
Otosclerosis	
External otitis	Infections, e.g. mumps, herpes zoster, meningitis, syphilis
Injury of the tympanic membrane	

Conductive deafness

This is due to impaired transmission of sound waves from the outside to the oval window, i.e. an abnormality of the outer or middle ear.

Sensorineural (perceptive) deafness

This is the result of disease of the cochlea, the cochlear branch of the vestibular nerve or the hearing area of the brain. The individual usually perceives noise but cannot discriminate between sounds, i.e. hears but cannot understand.

Risk factors for *congenital deafness* include:

- family history of hereditary deafness
- viruses, e.g. maternal rubella during the first 3 months of pregnancy
- acute hypoxia at birth.

DISEASES OF THE EYE

Learning outcome

After studying this section you should be able to:

- describe the pathological changes and effects of diseases of the eye.

Inflammation

Stye (hordeolum)

This is an acute and painful bacterial infection of sebaceous or tarsal glands of the eyelid margin. A 'crop' of styes may occur due to localised spread to adjacent glands. Infection of tarsal glands may block their ducts, leading to cyst formation (*chalazion*) which may damage the cornea. The most common infecting organism is *Staphylococcus aureus*.

Blepharitis

This is chronic inflammation of the eyelid margins, which is usually caused by microbes or allergy, e.g. staphylococcal infection or seborrhoea (excessive sebaceous gland secretion). If ulceration occurs, healing by fibrosis may distort the eyelid margins, preventing complete closure of the eye. This may lead to drying of the eye, conjunctivitis and possibly corneal ulceration.

Conjunctivitis

Inflammation of the conjunctiva may be caused by irritants, such as smoke, dust, wind, cold or dry air, microbes or antigens. Corneal ulceration (see below) is a rare complication.

Microbial infection. In adults this is usually caused by strains of staphylococci, streptococci, pneumococci and haemophilus.

Neonatal conjunctivitis. This occurs within 28 days of birth and is commonly caused by *Neisseria gonorrhoea*, *Chlamydia trachomatis* or herpes simplex virus. It is usually acquired when microbes contaminate the baby's eyes during delivery. Infection may cause corneal ulceration (see below).

Allergic conjunctivitis. This may be a complication of hay fever or be caused by a wide variety of airborne antigens, e.g. dust, pollen, fungus spores, animal dander, cosmetics, hair sprays, soaps. The condition sometimes becomes chronic.

Trachoma. This is a chronic inflammatory condition caused by *Chlamydia trachomatis* in which fibrous tissue forms in the conjunctiva and cornea, leading to eyelid deformity, and is a common cause of blindness in tropical countries. The microbes are spread by flies, communal use of contaminated washing water, cross-infection between mother and child, contaminated towels and clothing.

Corneal ulcer

This is local necrosis of corneal tissue, usually associated with corneal infection (*keratitis*) following trauma (e.g. abrasion), or infection spread from the conjunctiva or eyelids. Common infecting microbes include staphylococci, pneumococci and herpes simplex viruses. Acute pain, injection (redness of the cornea), photophobia and lacrimation interfere with sight during the acute phase. In severe cases extensive ulceration or perforation and healing by fibrosis can cause opacity of the cornea and irreversible loss of sight.

Inflammation of the uveal tract (iris, ciliary body, choroid)

Anterior uveitis (iritis, iridocyclitis). Iridocyclitis (inflammation of iris and ciliary body) is the more common and it may be acute or chronic. The infection may have spread from the outer eye but in most cases the cause is unknown. There is usually moderate to severe pain, redness, blurring of vision, lacrimation and photophobia. In severe cases adhesions form between the iris and lens capsule, preventing the circulation of aqueous fluid in the posterior and anterior chambers. This may cause the lens to bulge and occlude the scleral venous sinus (canal of Schlemm), raising intraocular pressure causing *chronic closed-angle glaucoma* (see below). Acute infection usually resolves in several days or weeks while the chronic form may last for months or years.

Posterior uveitis (choroiditis, chorioretinitis). This affects the posterior segment of the eye and chorioretinitis is the more common condition. It may be caused by spread of infection from the anterior segment (front) of the eye or be secondary to a wide variety of systemic conditions, including rheumatoid arthritis, Reiter's syndrome, inflammatory bowel disease and brucellosis. Complications of uveitis include retinal detachment due to accumulation of inflammatory exudate, secondary glaucoma, cataract.

Glaucoma

This is a group of conditions in which there is increased intraocular pressure due to impaired drainage of aqueous fluid through the scleral venous sinus (canal of Schlemm) in the angle between the iris and cornea in the anterior chamber. Persistently raised intraocular pressure may damage the optic nerve by:

- mechanical compression of the axons
- compression of the blood supply causing ischaemia of the axons.

Damage to the optic nerve impairs vision and the extent varies from some visual impairment to complete blindness.

Primary glaucomas

Chronic open-angle glaucoma. There is a gradual painless rise in intraocular pressure with progressive loss of vision. Peripheral vision is lost first but may not be noticed until only central (*tunnel*) vision remains. As the condition progresses, atrophy of the optic disc occurs leading to irreversible blindness. It is commonly bilateral and occurs mostly in people over 40 years of age. The cause is not known but there is a familial tendency.

Acute closed-angle glaucoma. This is most common in people over 40 years of age and usually affects one eye. During life the lens gradually increases in size, pushing the iris forward. In dim light when the pupil dilates the lax iris bulges still further forward, and may come into contact with the cornea blocking the scleral venous sinus (canal of Schlemm) suddenly raising the intraocular pressure. Sudden severe pain, photophobia, lacrimation and loss of vision accompany an acute attack. It may resolve spontaneously if the iris responds to bright light, constricting the pupil and releasing the pressure on the scleral venous

sinus. After repeated attacks spontaneous recovery may be incomplete and vision is progressively impaired.

Chronic closed-angle glaucoma. The intraocular pressure rises gradually without symptoms. Peripheral vision deteriorates first followed by atrophy of the optic disc and blindness.

Congenital glaucoma. This abnormal development of the anterior chamber is often familial or due to maternal infection with rubella in early pregnancy.

Secondary glaucoma

The most common primary disorder is anterior uveitis with the formation of adhesions (see above). Other predisposing primary conditions include intraocular tumours, enlarged cataracts, central retinal vein occlusion, intraocular haemorrhage, trauma to the eye.

Strabismus (squint, cross-eye)

This is the inability of the eyes to move together so that the same image falls on the corresponding parts of the retina in both eyes. The result is that two images are sent to the brain, one from each eye, instead of one integrated image. It is caused by extraocular muscle weakness or defective nerve supply to the muscle, i.e. defective cranial nerves III, IV or VI. In most cases the image falling on the squinting eye is suppressed by the brain, otherwise there is double vision (diplopia).

Cataract

This is opacity of the lens which may be age-related or congenital, bilateral or unilateral.

In *age-related cataract* there is gradual development of lens opacity that usually develops during older age as the result of exposure to a variety of predisposing factors including: UV light, X-rays, cigarette smoke, diabetes mellitus, ocular trauma, uveitis, systemic drug therapy, e.g. corticosteroids, chlorpromazine.

Congenital cataract may be due to genetic abnormality, e.g. Down's syndrome, or maternal infection in early pregnancy, e.g. rubella. Early treatment is required to prevent permanent blindness.

The extent of visual impairment depends on the location and extent of the opacity.

Retinopathies

Vascular retinopathies

Occlusion of the central retinal artery or vein causes sudden painless unilateral loss of vision. *Arterial occlusion* is usually due to embolism from, e.g. atheromatous plaques, endocarditis, retinal artery sclerosis. *Venous occlusion* is usually associated with arteriosclerosis in the elderly or with venous thrombosis elsewhere in the body. The retinal veins become distended and retinal haemorrhages occur. Predisposing factors include glaucoma, diabetes mellitus, hypertension, increased blood viscosity.

Diabetic retinopathy

This occurs in Type I and Type II diabetes mellitus (p. 234) and changes in retinal blood vessels are associated more with the duration of diabetes than with its severity. Capillary microaneurysms develop and later there may be proliferation of blood vessels. Haemorrhages, fibrosis and secondary retinal detachment may occur, leading to retinal degeneration and loss of vision.

Retinopathy of prematurity

Previously known as retrolental fibroplasia this condition affects premature babies. Known risk factors include: birth before 32 weeks' gestation, birth weight less than 1500 g, requirement for oxygen therapy, apnoea and sepsis. There is abnormal development of retinal blood vessels and formation of fibrovascular tissue in the vitreous body causing varying degrees of interference with light transmission. In severe cases there may also be haemorrhage in the vitreous body, retinal detachment and blindness.

Retinal detachment

This painless condition occurs when a tear or hole in the retina allows fluid to accumulate between the layers of retinal cells or between the retina and choroid. It is usually localised at first but as fluid collects the detachment spreads. There are spots before the eyes, flashing lights due to abnormal stimulation of sensory cells, and progressive loss of vision, sometimes described as a 'shadow' or 'curtain'. In many cases the cause is unknown but it may be associated with trauma to the eye or head, tumours, haemorrhage, cataract surgery when the pressure in the eye is reduced or diabetic retinopathy.

Retinitis pigmentosa

This is an hereditary disease in which there is degeneration of the retina, mainly affecting the rods. Defective vision in dim light usually becomes apparent in early childhood, leading to tunnel vision and eventually, blindness.

Keratomalacia

In this condition there is corneal ulceration, usually with secondary infection. The lacrimal glands and conjunctiva may be involved. It is caused by chronic vitamin A and protein deficiency in the diet. There may be softening or even perforation of the cornea. Night blindness (defective adaptation to dim light) is usually an early sign of deficiency of vitamin A which is required for the regeneration of rhodopsin (visual purple) after it has been exposed to light.

Tumours

Choroidal malignant melanoma

This is the most common ocular malignancy and it occurs between 40 and 70 years of age. Vision is not normally affected until the tumour causes retinal detachment or secondary glaucoma, usually when well advanced. The tumour spreads locally in the choroid, and bloodborne metastases develop mainly in the liver.

Retinoblastoma

This is a malignant tumour derived from embryonic retinal cells. A small number of cases are familial. It is usually evident before the age of 4 years and may be bilateral. The condition presents with a squint and enlargement of the eye. As the tumour grows visual impairment develops and the pupil looks pale. It spreads locally to the vitreous body and may grow along the optic nerve, invading the brain.

Disorders of the lacrimal apparatus

Acute dacryoadenitis

This is inflammation of the lacrimal gland, usually unilateral. It may be due to spread of infection from the eyelids or surrounding structures, or be associated with measles, mumps or influenza. This rare infection usually resolves but occasionally an abscess forms.

Dacryocystitis

This inflammation of the lacrimal sac is usually associated with partial or complete obstruction of the lacrimal duct. In infants there may be congenital stenosis of the duct. In adults the blockage may be due to nasal trauma, deviated nasal septum, nasal polyp or acute inflammatory nasal congestion.

REFRACTIVE ERRORS OF THE EYE

Learning outcome

After studying this section you should be able to:

- describe the corrective lenses used to treat refractive errors of the eye.

In the *emetropic* or normal eye, light from near and distant objects is focused on the retina (Fig. 8.26A).

In *hypermetropia*, or farsightedness, a near image is focused behind the retina because the eyeball is too short (Fig. 8.26B). A *biconvex lens* corrects this (Fig. 8.26C). Distant objects are focused normally.

In *myopia*, or nearsightedness, the eyeball is too long and distant objects are focused in front of the retina (Fig. 8.26D). Correction is achieved using a *biconcave lens* (Fig. 8.26E). Near objects are seen in focus as the eye can accommodate normally.

Astigmatism results in blurred vision when there is abnormal curvature of part of the cornea or lens that prevents focusing on the retina. Correction requires cylindrical lenses.

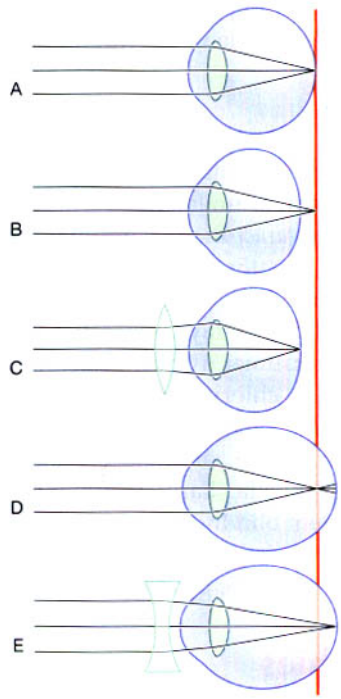


Figure 8.26 Common refractive errors of the eye and corrective lenses. A. Normal eye. B and C. Farsightedness. D and E. Nearsightedness.

9 The endocrine system

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The endocrine system consists of glands widely separated from each other with no direct anatomical links (Fig. 9.1). Endocrine glands consist of groups of secretory cells surrounded by an extensive network of capillaries which facilitates diffusion of *hormones* (chemical messengers) from the secretory cells into the bloodstream. They are commonly referred to as the *ductless glands* because the hormones are secreted and diffuse directly into the bloodstream.

A hormone is formed in one organ or gland and carried in the blood to another organ (*target organ* or *tissue*), probably quite distant, where it influences cellular activity, especially growth and metabolism. Most hormones are synthesised from amino acids (amines, polypeptides and proteins; see p. 23) or are cholesterol-based lipids (steroids).

Homeostasis of the internal environment is maintained partly by the autonomic nervous system and partly by the endocrine system. The autonomic nervous system is concerned with rapid changes, while hormones of the endocrine system are mainly involved in slower and more precise adjustments.

The endocrine system consists of a number of distinct glands and some tissues in other organs. Although the hypothalamus is classified as a part of the brain and not as an endocrine gland it controls the pituitary gland and has an indirect effect on many others. The endocrine glands are:

- 1 pituitary gland
- 1 thyroid gland
- 4 parathyroid glands
- 2 adrenal (suprarenal) glands
- the pancreatic islets (islets of Langerhans)
- 1 pineal gland or body
- 1 thymus gland
- 2 ovaries in the female
- 2 testes in the male.

The ovaries and the testes secrete hormones associated with the reproductive system after puberty. Their functions are described in Chapter 19.

When a hormone arrives at its target cell, it binds to a specific area, the *receptor*, where it acts as a switch influencing chemical or metabolic reactions inside the cell. The receptors for water-soluble hormones are situated on the cell membrane and those for lipid-soluble hormones are inside the cell. Examples are shown in Box 9.1.

The level of a hormone in the blood is variable and self-regulating within its normal range. A hormone is released in response to a specific stimulus and usually its action reverses or negates the stimulus through a *negative feedback mechanism* (see p. 6). This may be controlled either indirectly through the release of hormones by the hypothalamus and the anterior pituitary gland, e.g. steroid and thyroid hormones, or directly by blood levels of the stimulus, e.g. insulin and glucagon.

Box 9.1 Examples of lipid-soluble and water-soluble hormones

Lipid-soluble hormones	Water-soluble hormones
Steroids e.g. glucocorticoids, mineralocorticoids	Adrenaline, noradrenaline
Thyroid hormones	Insulin
	Glucagon

The effect of a *positive feedback mechanism* is amplification of the stimulus and increasing release of the hormone until a particular process is complete and the stimulus ceases, e.g. release of oxytocin during labour (pp. 7 and 218).

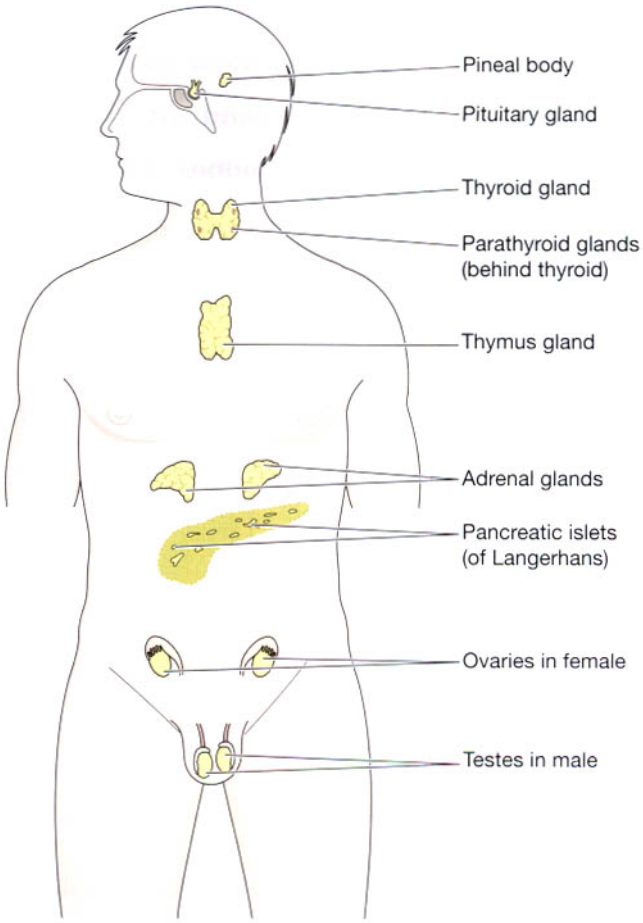


Figure 9.1 Positions of the endocrine glands.

PITUITARY GLAND AND HYPOTHALAMUS

Learning outcomes

After studying this section you should be able to:

- describe the structure of the hypothalamus and the pituitary gland
- explain the influence of the hypothalamus on the lobes of the pituitary gland
- outline the actions of the hormones secreted by the anterior and posterior lobes of the pituitary gland.

The pituitary gland (hypophysis) and the hypothalamus act as a unit, regulating the activity of most of the other endocrine glands. The pituitary gland lies in the hypophyseal fossa of the sphenoid bone below the hypothalamus, to which it is attached by a *stalk* (Fig. 9.2). It is the size of a pea, weighs about 500 mg and consists of three distinct parts that originate from different types of cells. The *anterior pituitary* (adenohypophysis) is an upgrowth of glandular epithelium from the pharynx and the *posterior pituitary* (neurohypophysis) is a downgrowth of nervous tissue from the brain. There is a network of nerve fibres between the hypothalamus and the posterior pituitary. Between these lobes there is a thin strip of tissue called the *intermediate lobe* and its function in humans is not known.

Blood supply

Arterial blood. This is supplied by branches from the internal carotid artery. The anterior lobe is supplied indirectly by blood that has already passed through a capillary bed in the hypothalamus but the posterior lobe is supplied directly.

Venous blood. This comes from both lobes, containing hormones, and leaves the gland in short veins that enter the venous sinuses between the layers of dura mater.

The influence of the hypothalamus on the pituitary gland

The influence of the hypothalamus on the release of hormones is different in the anterior and posterior lobes of the pituitary gland.

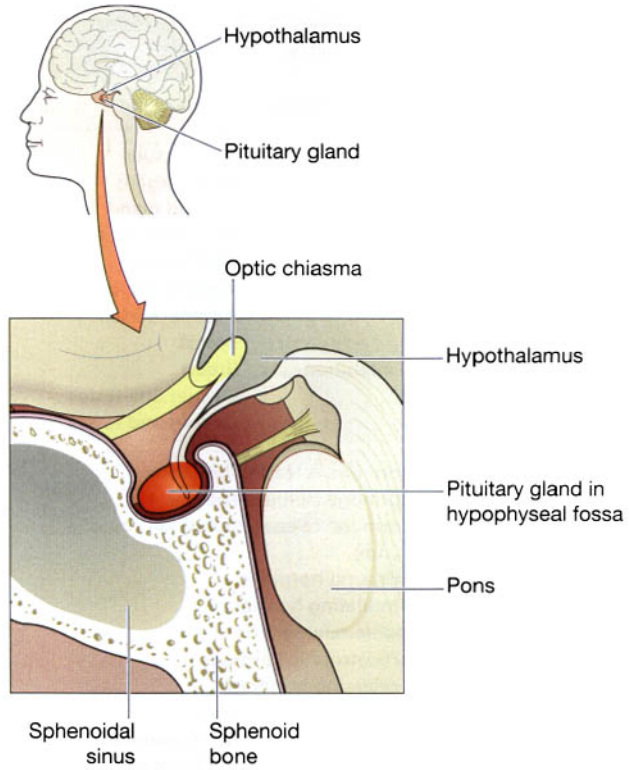


Figure 9.2 The position of the pituitary gland and its associated structures.

The anterior pituitary. This is supplied indirectly with arterial blood that has already passed through a capillary bed in the hypothalamus (Fig. 9.3A). This network of blood vessels forms part of the *pituitary portal system*, which transports blood from the hypothalamus to the anterior pituitary where it enters thin-walled vascular sinusoids and is in very close contact with the secretory cells. As well as providing oxygen and nutrients, this blood transports *releasing* and *inhibiting hormones* secreted by the *hypothalamus*. These hormones influence secretion and release of other hormones formed in the anterior pituitary. The releasing and inhibiting hormones that stimulate and inhibit secretion of specific anterior pituitary hormones are shown in Table 9.1.

The posterior pituitary. This is formed from nervous tissue and consists of nerve cells surrounded by supporting cells called *pituicytes*. These neurones have their cell bodies in the supraoptic and paraventricular nuclei of the hypothalamus and their axons form a bundle known as the *hypothalamohypophyseal tract* (Fig. 9.3A). Posterior pituitary hormones are synthesised in the nerve cell bodies, transported along the axons and then stored in vesicles within the axon terminals (Fig. 9.3B). Their release by exocytosis is triggered by nerve impulses from the hypothalamus.

Table 9.1 Hormones of the hypothalamus, anterior pituitary and their target tissues

Hypothalamus	Anterior pituitary	Target gland or tissue
GHRH	GH	Most tissues Many organs
GHRIH	GH inhibition TSH inhibition	Thyroid gland Pancreatic islets Most tissues
TRH	TSH	Thyroid gland
CRH	ACTH	Adrenal cortex
PRH	PRL	Breast
PIH	PRL inhibition	Breast
LHRH or GnRH	FSH LH	Ovaries and testes Ovaries and testes

GHRH = growth hormone releasing hormone
GH = growth hormone (somatotrophin)
GHRIH = growth hormone release inhibiting hormone (somatostatin)
TRH = thyroid releasing hormone
TSH = thyroid stimulating hormone
CRH = corticotrophin releasing hormone
ACTH = adrenocorticotrophic hormone
PRH = prolactin releasing hormone
PRL = prolactin (lactogenic hormone)
PIH = prolactin inhibiting hormone (dopamine)
LHRH = luteinising hormone releasing hormone
GnRH = gonadotrophin releasing hormone
FSH = follicle stimulating hormone
LH = luteinising hormone

Anterior pituitary

Some of the hormones secreted by the anterior lobe (adenohypophysis) stimulate or inhibit secretion by other endocrine glands (target glands) while others have a direct effect on target tissues. Table 9.1 summarises the main relationships between the hormones of the hypothalamus, the anterior pituitary and target glands or tissues.

The release of an anterior pituitary hormone follows stimulation of the gland by a specific *releasing hormone* produced by the hypothalamus and conveyed to the gland through the pituitary portal system of blood vessels. The whole system is controlled by a *negative feedback mechanism*. That is, when there is a low level of a hormone in the blood supplying the hypothalamus it produces the appropriate releasing hormone which stimulates release of a *trophic hormone* by the anterior pituitary. This in turn stimulates the target gland to produce and release its hormone. As a result the blood level of that hormone rises and inhibits the secretion of releasing factor by the hypothalamus (Fig. 9.4).

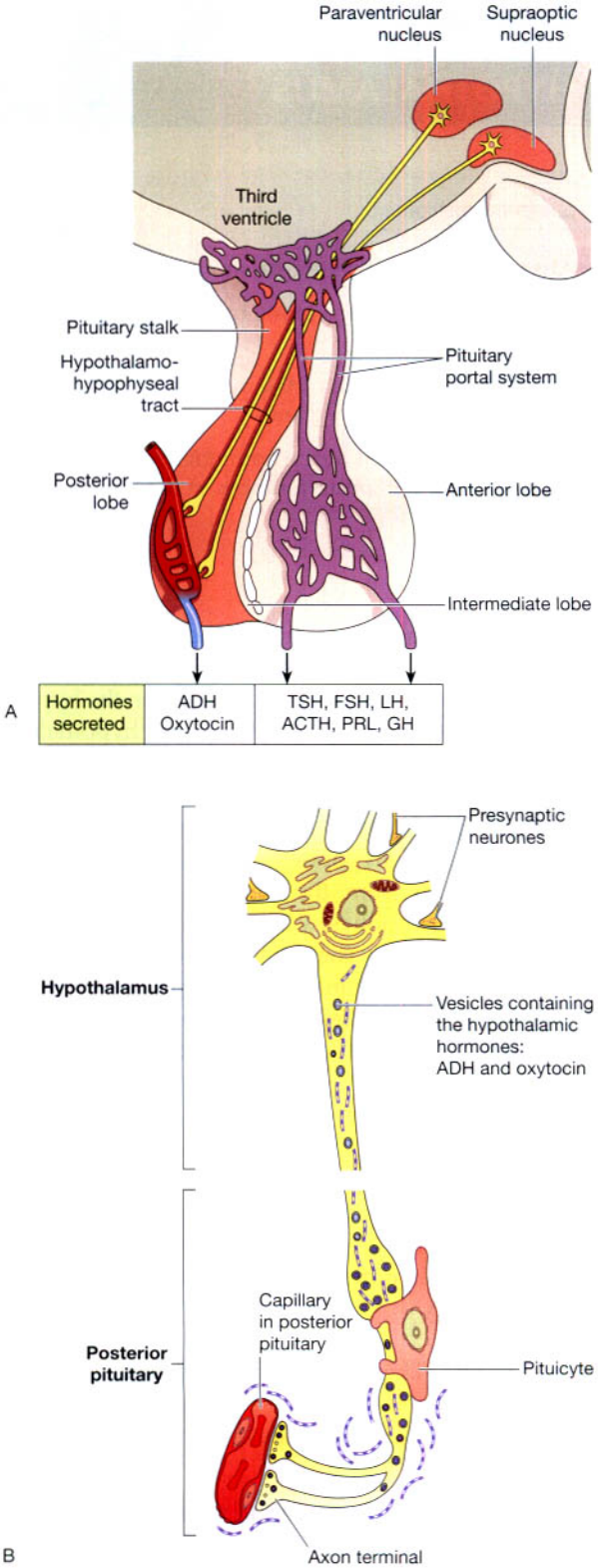


Figure 9.3 The pituitary gland: A. The lobes of the pituitary gland and their relationship with the hypothalamus. B. Synthesis and storage of antidiuretic hormone and oxytocin.

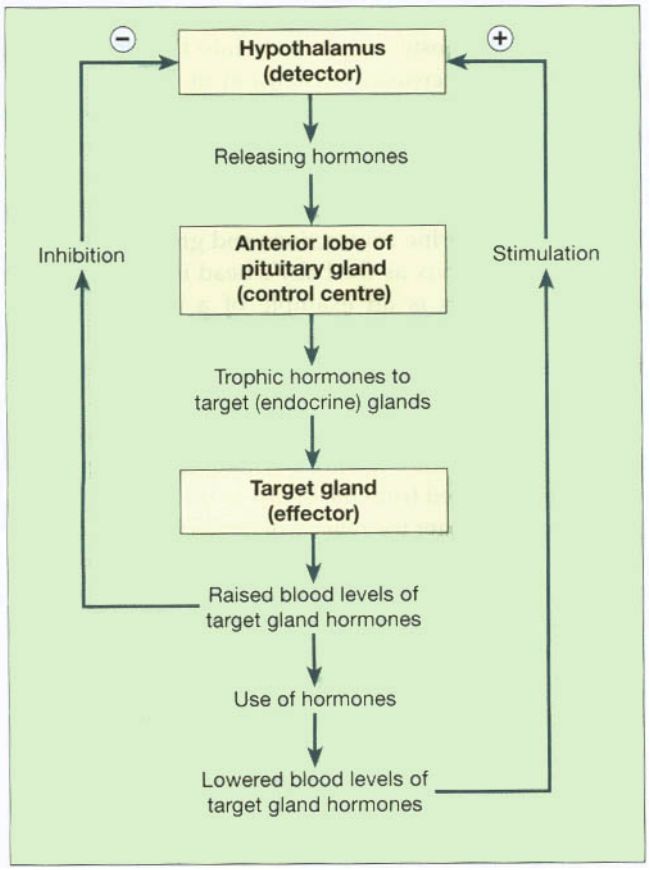


Figure 9.4 Negative feedback regulation of secretion of hormones by the anterior lobe of the pituitary gland.

Growth hormone (GH)

This is the most abundant hormone synthesised by the anterior pituitary. It stimulates growth and division of most body cells but especially those in the bones and skeletal muscles. It also regulates aspects of metabolism in many organs, e.g. liver, intestines and pancreas; stimulates protein synthesis; promotes breakdown of fats; and increases blood glucose levels (see Ch. 12).

Its release is stimulated by *growth hormone releasing hormone* (GHRH) and suppressed by *growth hormone release inhibiting hormone* (GHRIH) both of which are secreted by the hypothalamus. Secretion of GH is greater at night during sleep although hypoglycaemia, exercise and anxiety also stimulate release. The daily amount secreted peaks in adolescence and then declines with age. Inhibition of GH secretion occurs by a negative feedback mechanism when the blood level rises and also when GHRIH (*somatostatin*) is released by the hypothalamus. GHRIH also suppresses secretion of TSH and gastrointestinal secretions, e.g. gastric juice, gastrin and cholecystokinin (see Ch. 12).

Thyroid stimulating hormone (TSH)

This hormone is synthesised by the anterior pituitary and its release is stimulated by TRH from the hypothalamus. It stimulates growth and activity of the thyroid gland, which secretes the hormones *thyroxine* (T_4) and *triiodothyronine* (T_3). Release is lowest in the early evening and highest during the night. Secretion is regulated by a negative feedback mechanism (Fig. 9.4). When the blood level of thyroid hormones is high, secretion of TSH is reduced, and vice versa.

Adrenocorticotrophic hormone (corticotrophin, ACTH)

Corticotrophin releasing hormone (CRH) from the hypothalamus promotes the synthesis and release of ACTH by the anterior pituitary. This increases the concentration of cholesterol and steroids within the adrenal context and the output of steroid hormones, especially *cortisol*.

ACTH levels are highest at about 8 a.m. and fall to their lowest about midnight, although high levels sometimes occur at midday and 6 p.m. This circadian rhythm is maintained throughout life. It is associated with the sleep pattern and adjustment to changes takes several days, following, e.g., shift work changes, travel to a different time zone (jet lag).

Secretion is also regulated by a negative feedback mechanism, being suppressed when the blood level of ACTH rises (Fig. 9.4). Other factors that stimulate secretion include hypoglycaemia, exercise and other stressors, e.g. emotional states and fever.

Prolactin

This hormone stimulates *lactation* (milk production) and has a direct effect on the breasts immediately after parturition (childbirth). The blood level of prolactin is stimulated by prolactin releasing hormone (PRH) released from the hypothalamus and it is lowered by prolactin inhibiting hormone (PIH, *dopamine*) and by an increased blood level of prolactin. After birth, suckling stimulates prolactin secretion and lactation. The resultant high blood level is a factor in reducing the incidence of conception during lactation.

Prolactin together with oestrogens, corticosteroids, insulin and thyroxine is involved in initiating and maintaining lactation. Prolactin secretion is related to sleep, i.e. it is raised during any period of sleep, night or day. Emotional stress increases production.

Gonadotrophins

After puberty two gonadotrophins (sex hormones) are secreted by the anterior pituitary in response to *luteinising hormone releasing hormone* (LHRH), also known as

gonadotrophin releasing hormone (GnRH). In both males and females these are:

- follicle stimulating hormone (FSH)
- luteinising hormone (LH).

In both sexes. FSH stimulates production of gametes (ova or spermatozoa).

In females. LH and FSH are involved in secretion of the hormones *oestrogen* and *progesterone* during the menstrual cycle (see Figs 19.8 and 19.9, pp. 444 and 445). As the levels of oestrogen and progesterone rise secretion of LH and FSH is suppressed.

In males. LH, also called interstitial cell stimulating hormone (ICSH) stimulates the interstitial cells of the testes to secrete the hormone *testosterone* (see Ch. 19).

Table 9.2 summarises the hormonal secretions of the anterior pituitary.

Posterior pituitary

The structure of the posterior pituitary gland and its relationship with the hypothalamus is explained on page 215. *Oxytocin* and *antidiuretic hormone* (ADH or vasopressin) are the hormones synthesised in the hypothalamus and then released from the axon terminals within the posterior pituitary gland (Fig. 9.3B). These hormones act directly on non-endocrine tissue and their release by exocytosis is stimulated by nerve impulses from the hypothalamus.

Oxytocin

Oxytocin stimulates two target tissues during and after parturition (childbirth): uterine smooth muscle and the muscle cells of the lactating breast.

During parturition increasing amounts of oxytocin are released by the posterior pituitary into the bloodstream in response to increasing distension of sensory stretch receptors in the uterine cervix by the baby's head. Sensory impulses are generated and travel to the control centre in the hypothalamus, stimulating the posterior pituitary to release more oxytocin. In turn this stimulates more forceful uterine contractions and greater stretching of the uterine cervix as the baby's head is forced further downwards. This is an example of a *positive feedback mechanism* which stops soon after the baby is delivered when distension of the uterine cervix is greatly reduced (Fig. 9.5).

The process of milk ejection also involves a positive feedback mechanism. Suckling generates sensory impulses that are transmitted from the breast to the hypothalamus. The impulses trigger the release of oxytocin from the posterior pituitary and oxytocin stimulates contraction of the myoepithelial cells around the glandular cells and ducts of the lactating breast to contract, ejecting milk. Suckling also inhibits the release of *prolactin inhibiting hormone* (PIH), prolonging prolactin secretion and lactation. The role of this hormone in males and non-lactating females remains unclear.

Antidiuretic hormone (ADH) or vasopressin

The main effect of antidiuretic hormone is to reduce urine output (diuresis is the production of a large volume of urine). ADH increases the permeability to water of the distal convoluted and collecting tubules of the nephrons of the kidneys (Ch. 13). As a result the reabsorption of water from the glomerular filtrate is increased. The amount of ADH secreted is influenced by the osmotic pressure of the blood circulating to the *osmoreceptors* in the hypothalamus.

As the osmotic pressure rises, the secretion of ADH increases as in, for example, dehydration and following

Table 9.2 Summary of the hormones secreted by the anterior pituitary gland and their functions

Hormone	Function
Growth hormone (GH)	Regulates metabolism, promotes tissue growth especially of bones and muscles
Thyroid stimulating hormone (TSH)	Stimulates growth and activity of thyroid gland and secretion of T_3 and T_4
Adrenocorticotrophic hormone (ACTH)	Stimulates the adrenal cortex to secrete glucocorticoids
Prolactin (PRL)	Stimulates milk production in the breasts
Follicle stimulating hormone (FSH)	Stimulates production of sperm in the testes, stimulates secretion of oestrogen by the ovaries, maturation of ovarian follicles, ovulation
Luteinising hormone (LH)	Stimulates secretion of testosterone by the testes, stimulates secretion of progesterone by the corpus luteum

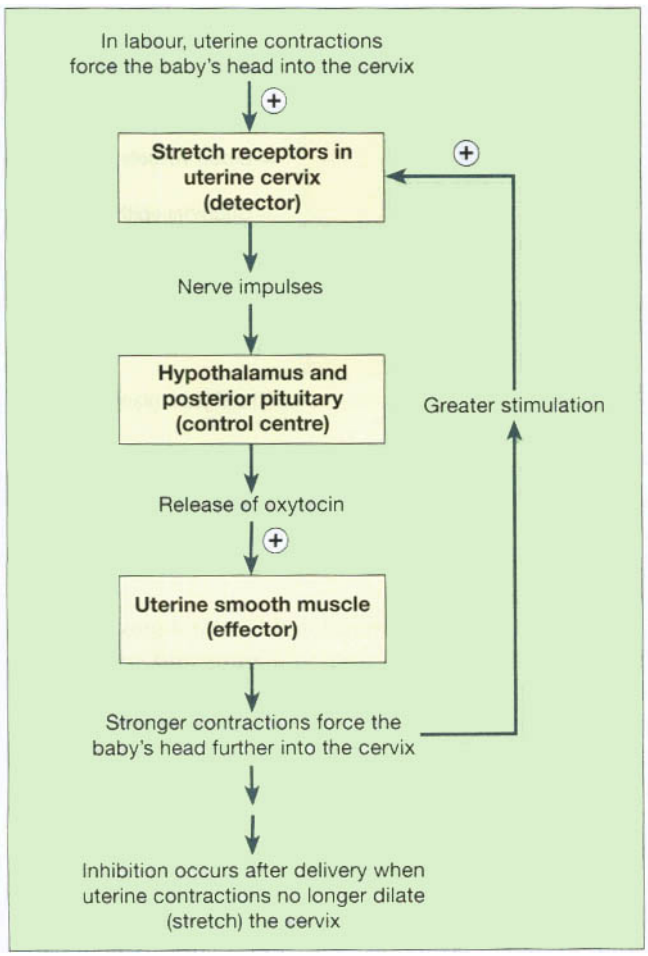


Figure 9.5 Regulation of secretion of oxytocin through a positive feedback mechanism.

haemorrhage. More water is therefore reabsorbed and the urine output is reduced. This means that the body retains more water and the rise in osmotic pressure is reversed. Conversely, when the osmotic pressure of the blood is low, for example after a large fluid intake, secretion of ADH is reduced, less water is reabsorbed and more urine is produced (Fig. 9.11).

At high concentrations, for example after severe blood loss, ADH causes smooth muscle contraction, especially vasoconstriction in the blood vessels of the skin and abdominal organs. This has a *pressor effect*, raising systemic blood pressure; the alternative name of this hormone, vasopressin, reflects this effect.

THYROID GLAND (Fig. 9.6)

Learning outcomes

After studying this section you should be able to:

- describe the position of the thyroid gland and its related structures
- describe the microscopic structure of the thyroid gland
- outline the actions of the thyroid hormones
- explain how blood levels of the thyroid hormones T_3 and T_4 are regulated.

The thyroid gland is situated in the neck in front of the larynx and trachea at the level of the 5th, 6th and 7th cervical and 1st thoracic vertebrae. It is a highly vascular gland that weighs about 25 g and is surrounded by a fibrous capsule. It resembles a butterfly in shape, consisting of *two lobes*, one on either side of the thyroid

Table 9.3 Common effects of abnormal secretion of thyroid hormones

Hyperthyroidism: increased T_3 and T_4 secretion	Hypothyroidism: decreased T_3 and T_4 secretion
Increased basal metabolic rate	Decreased basal metabolic rate
Anxiety, physical restlessness, mental excitability	Depression, psychosis, mental slowness, lethargy
Hair loss	Dry skin, brittle hair
Tachycardia, palpitations, atrial fibrillation	Bradycardia
Warm sweaty skin, heat intolerance	Dry cold skin, prone to hypothermia
Diarrhoea	Constipation
Weight loss, good appetite	Weight gain, anorexia
Exophthalmos in Graves' disease	

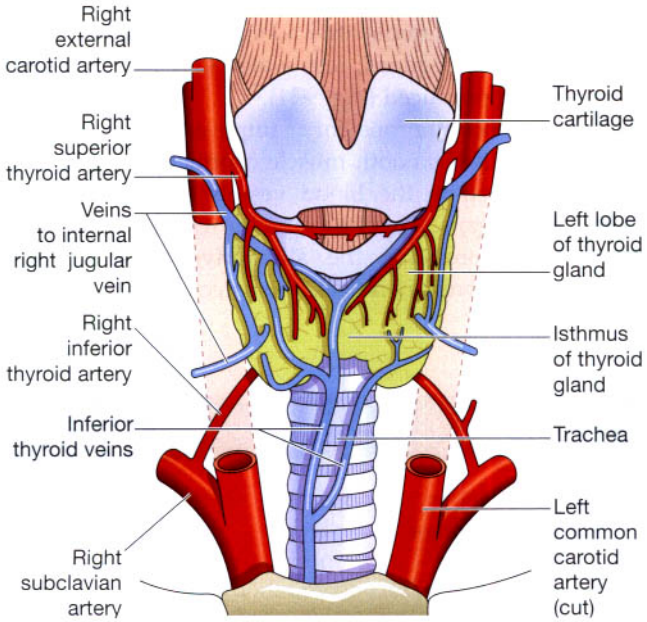


Figure 9.6 The position of the thyroid gland and its associated structures.

cartilage and upper cartilaginous rings of the trachea. The lobes are joined by a narrow *isthmus*, lying in front of the trachea.

The lobes are roughly cone-shaped, about 5 cm long and 3 cm wide.

The *arterial blood supply* to the gland is through the superior and inferior thyroid arteries. The superior thyroid artery is a branch of the external carotid artery and the inferior thyroid artery is a branch of the subclavian artery.

The *venous return* is by the thyroid veins which drain into the internal jugular veins.

Two parathyroid glands lie against the posterior surface of each lobe and are sometimes embedded in thyroid tissue. The recurrent laryngeal nerve passes upwards close to the lobes of the gland and on the right side it lies near the inferior thyroid artery (Fig. 9.9).

The gland is composed of cuboidal epithelium that forms spherical follicles. These secrete and store *colloid*, a thick sticky protein material (Fig. 9.7). Between the follicles there are other cells found singly or in small groups: *parafollicular cells*, also called C-cells, which secrete the hormone *calcitonin*.

Thyroxine and triiodothyronine

Iodine is essential for the formation of the thyroid gland hormones, thyroxine (T_4) and triiodothyronine (T_3). The body's main sources of iodine are seafood, vegetables grown in iodine-rich soil and iodinated table salt in the diet. The thyroid gland selectively takes up iodine from the blood, a process called *iodine trapping*.

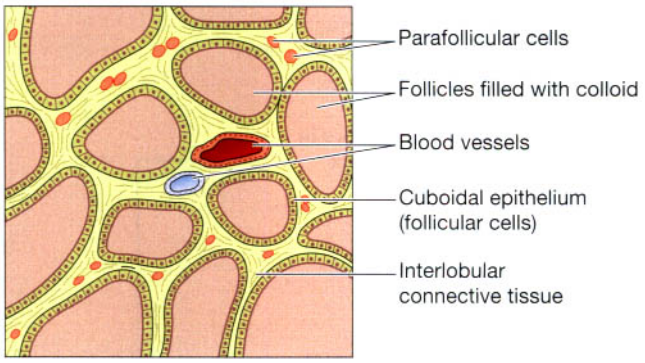


Figure 9.7 The microscopic structure of the thyroid gland.

The thyroid hormones are synthesised as large precursor molecules called *thyroglobulin*, the major constituent of colloid. The release of T_3 and T_4 into the blood is regulated by *thyroid stimulating hormone* (TSH) from the anterior pituitary.

Secretion of TSH is stimulated by the *thyroid releasing hormone* (TRH) from the hypothalamus and secretion of TRH is stimulated by exercise, stress, malnutrition, low plasma glucose and sleep. The level of secretion of TSH depends on the plasma levels of T_3 and T_4 because these hormones affect the sensitivity of the anterior pituitary to TRH. Increased levels of T_3 and T_4 decrease TSH secretion and vice versa (Fig. 9.8). When the supply of iodine is deficient, excess TSH is secreted and there is proliferation of thyroid gland cells and enlargement of the gland (see Goitre, p. 230). Secretion of T_3 and T_4 begins about the third month of fetal life and is increased at puberty and in women during the reproductive years, especially during pregnancy. Otherwise, it remains fairly constant throughout life.

Thyroid hormones enter the target cells and regulate the expression of genes in the nucleus, i.e. they increase or decrease the synthesis of some proteins including enzymes. They combine with specific receptor sites and enhance the effects of other hormones, e.g. adrenaline and noradrenaline.

T_3 and T_4 affect most cells of the body by:

- increasing the basal metabolic rate and heat production
- regulating metabolism of carbohydrates, proteins and fats.

T_3 and T_4 are essential for normal growth and development, especially of the skeleton and nervous system. Most other organs and systems are also influenced by thyroid hormones – physiological effects of T_3 and T_4 on the heart, skeletal muscles, skin, digestive and reproductive systems are more evident when there is underactivity or overactivity of the thyroid gland. These changes are listed in Table 9.3.

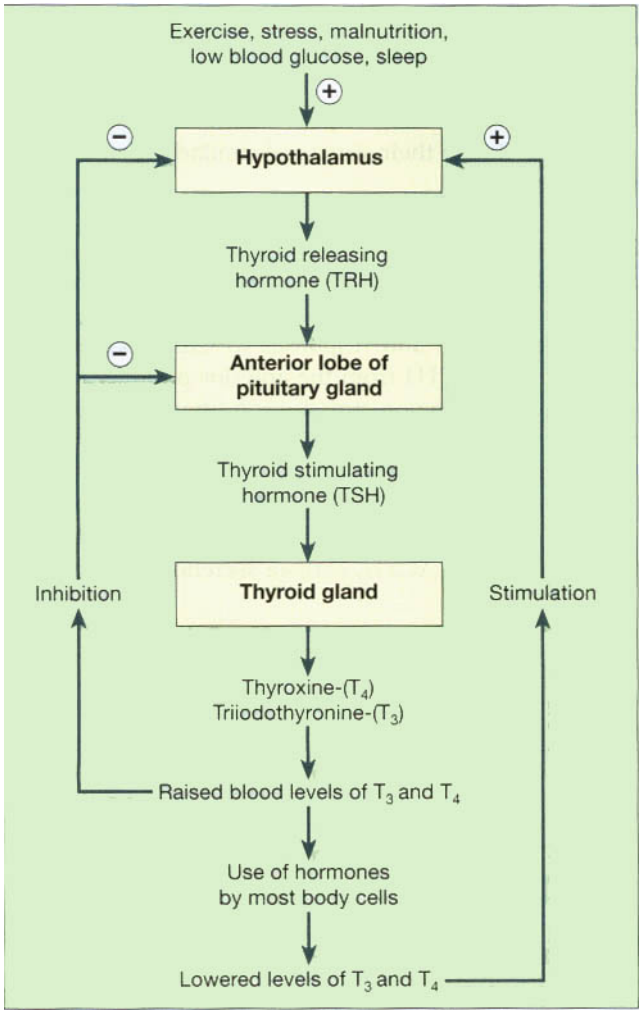


Figure 9.8 Regulation of the secretion of thyroxine (T_4) and triiodothyronine (T_3).

Calcitonin

This hormone is secreted by the parafollicular or C-cells in the thyroid gland. It acts on bone and the kidneys to reduce the blood calcium (Ca^{2+}) level when it is raised. It reduces the reabsorption of calcium from bones and inhibits reabsorption of calcium by the renal tubules. Its effect is opposite to that of parathyroid hormone (PTH, parathormone), the hormone secreted by the parathyroid glands. Release of calcitonin is stimulated by an increase in the blood calcium level.

This hormone is important during childhood when bones undergo considerable changes in size and shape.

PARATHYROID GLANDS

Learning outcomes

After studying this section you should be able to:

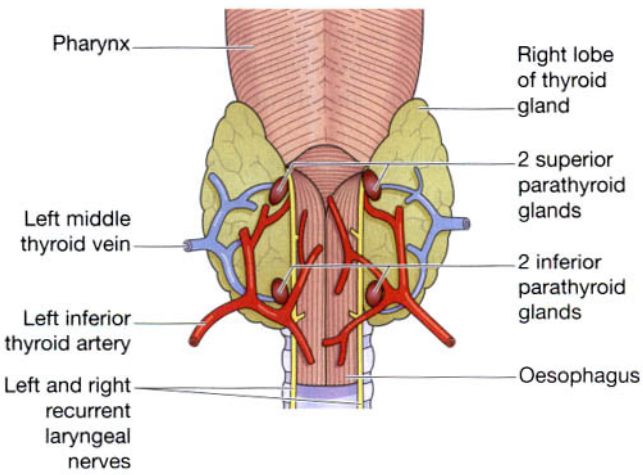
- describe the position and gross structure of the parathyroid glands
- outline the functions of parathyroid hormone and calcitonin
- explain how blood levels of parathyroid hormone and calcitonin are regulated.

There are four small parathyroid glands, two embedded in the posterior surface of each lobe of the thyroid gland (Fig. 9.9). They are surrounded by fine connective tissue capsules. The cells forming the glands are spherical in shape and are arranged in columns with channels containing blood between them.

Function

The parathyroid glands secrete *parathyroid hormone* (PTH, parathormone). Secretion is regulated by the blood level of calcium. When this falls, secretion of PTH is increased and vice versa.

The main function of PTH is to increase the blood calcium level when it is low. This is achieved by indirectly increasing the amount of calcium absorbed from the small



intestine and reabsorbed from the renal tubules. If these sources provide inadequate supplies then PTH stimulates osteoclasts (bone-destroying cells) and resorption of calcium from bones.

Parathormone and calcitonin from the thyroid gland act in a complementary manner to maintain blood calcium levels within the normal range. This is needed for:

- muscle contraction
- blood clotting
- nerve impulse transmission.

ADRENAL (SUPRARENAL) GLANDS

Learning outcomes

After studying this section you should be able to:

- describe the structure of the adrenal glands
- describe the actions of each of the three groups of adrenocorticoid hormones
- explain how blood levels of glucocorticoids are regulated
- describe the actions of adrenaline and noradrenaline
- outline how the adrenal glands respond to stress.

There are two adrenal glands, one situated on the upper pole of each kidney enclosed within the renal fascia (see Fig. 13.2, p. 340). They are about 4 cm long and 3 cm thick.

The *arterial blood supply* to the glands is by branches from the abdominal aorta and renal arteries.

The *venous return* is by suprarenal veins. The right gland drains into the inferior vena cava and the left into the left renal vein.

The glands are composed of two parts which have different structures and functions. The outer part is the *cortex* and the inner part the *medulla*. The adrenal cortex is essential to life but the medulla is not.

Adrenal cortex

The adrenal cortex produces three groups of steroid hormones from cholesterol. They are collectively called *adrenocorticocoids* (corticosteroids, corticoids). They are:

- glucocorticoids
- mineralocorticoids
- sex hormones (androgens).

The hormones in each group have different characteristic actions but due to their structural similarity their actions may overlap.

Glucocorticoids

Cortisol (hydrocortisone), *corticosterone* and *cortisone* are the main glucocorticoids. They are essential for life, regulating metabolism and responses to stress. Secretion is stimulated by ACTH from the anterior pituitary and by stress (Fig. 9.10). In non-stressful conditions secretion has marked circadian variations. The highest level of hormones occurs between 4 a.m. and 8 a.m. and the lowest, between midnight and 3 a.m. When the sleeping and waking pattern is changed it takes several days for adjustment of the ACTH/cortisol secretion to take place (see p. 217).

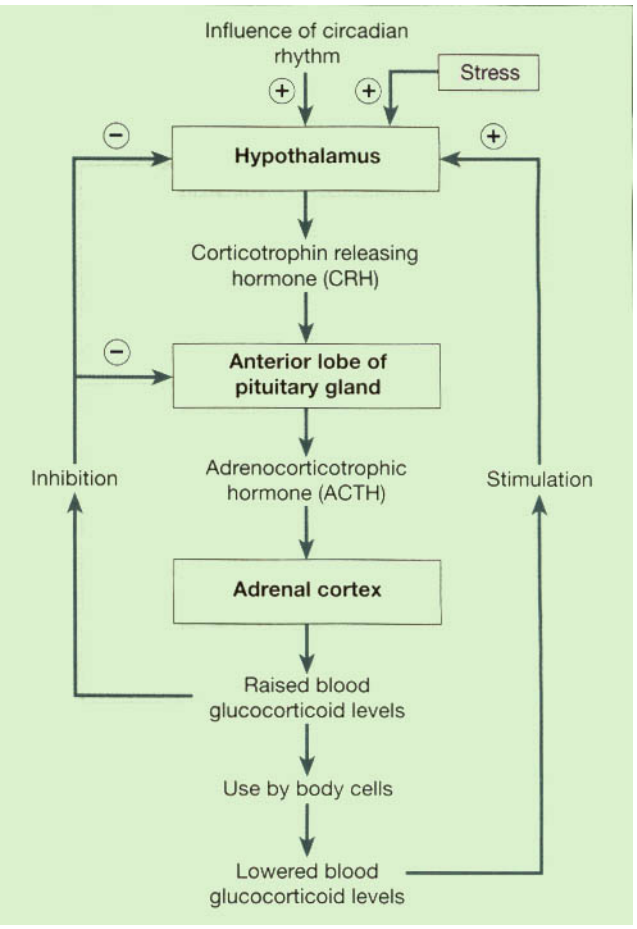


Figure 9.10 Regulation of glucocorticoid secretion.

Glucocorticoids have widespread effects and these include:

- *gluconeogenesis* (formation of new sugar from, for example, protein) and hyperglycaemia (raised blood glucose level)
- *lipolysis* (breakdown of triglycerides into fatty acids and glycerol for energy production)
- stimulating breakdown of protein, releasing amino acids, which can be used for synthesis of other proteins, e.g. enzymes, or for energy (ATP) production (p. 316)
- promoting absorption of sodium and water from renal tubules (a weak mineralocorticoid effect).

In pathological and pharmacological quantities glucocorticoids:

- have an anti-inflammatory action
- suppress the immune response
- suppress the response of tissues to injury
- delay wound healing.

Mineralocorticoids (aldosterone)

Aldosterone is the main mineralocorticoid. Its functions are associated with the maintenance of water and electrolyte balance in the body. It stimulates the reabsorption of sodium (Na^+) by the renal tubules and excretion of potassium (K^+) in the urine. Sodium reabsorption is also accompanied by retention of water and therefore aldosterone is involved in the regulation of blood volume and blood pressure too.

The blood potassium level regulates the amount of aldosterone produced by the adrenal cortex. When the blood potassium level rises, more aldosterone is secreted (Fig. 9.11). Low blood potassium has the opposite effect. *Angiotensin* (see below) also stimulates the release of aldosterone.

Renin–angiotensin–aldosterone system. When renal blood flow is reduced or blood sodium levels fall the enzyme *renin* is secreted by kidney cells. Renin converts the plasma protein *angiotensinogen*, produced by the liver, to *angiotensin 1*. Angiotensin converting enzyme (ACE), formed in small quantities in the lungs, proximal kidney tubules and other tissues converts angiotensin 1 to *angiotensin 2*, which stimulates secretion of aldosterone (Fig. 9.11). It also causes vasoconstriction and increases blood pressure.

Sex hormones

Sex hormones secreted by the adrenal cortex are mainly *androgens* (male sex hormones) and the amounts produced are insignificant compared with those secreted by the testes and ovaries in late puberty and adulthood. Their role is unclear but it is thought that they contribute to the onset of puberty (see Ch. 19). An elevated level in females causes masculinisation. Control of secretion is poorly understood.

Adrenal medulla

The medulla is completely surrounded by the cortex. It develops from nervous tissue in the embryo and is part of the sympathetic division of the autonomic nervous system. It is stimulated by its extensive sympathetic nerve supply to produce the hormones *adrenaline* and *noradrenaline*.

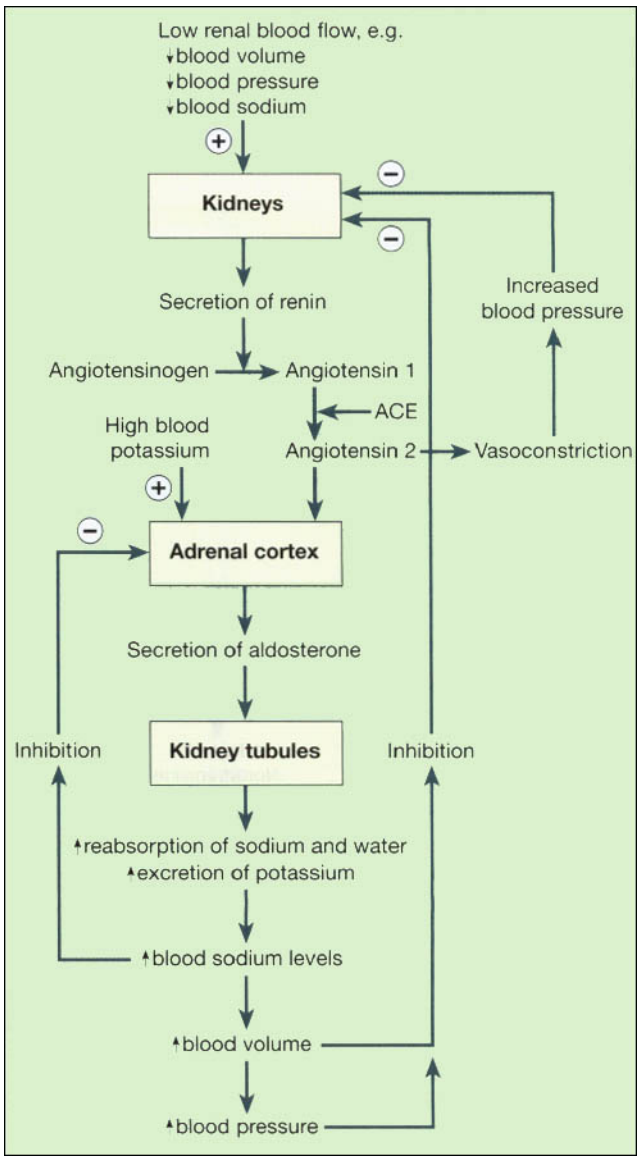


Figure 9.11 Regulation of aldosterone secretion.

Adrenaline and noradrenaline

Noradrenaline is the postganglionic neurotransmitter of the sympathetic division of the autonomic nervous system (see Fig. 7.9, p. 146). Adrenaline and some noradrenaline are released into the blood from the adrenal medulla during stimulation of the sympathetic nervous system (see Fig. 7.43, p. 171). They are structurally very similar and this explains their similar effects. Together they potentiate the fight or flight response after initial sympathetic stimulation by:

- increasing heart rate
- increasing blood pressure
- diverting blood to essential organs including the heart, brain and skeletal muscles by dilating their blood vessels and constricting those of less essential organs, such as the skin
- increasing metabolic rate
- dilating the pupils.

Adrenaline has a greater effect on the heart and metabolic processes whereas noradrenaline has more influence on blood vessels.

Response to stress

When the body is under stress homeostasis is disturbed. To restore it and, in some cases, to maintain life there are immediate and, if necessary, longer-term responses. Stressors include exercise, fasting, fright, temperature changes, infection, disease and emotional disturbances/situations.

The *immediate response* is sometimes described as preparing for 'fight or flight'. This is mediated by the sympathetic part of the autonomic nervous system and the principal effects are shown in Figure 9.12.

In the *longer term*, ACTH from the anterior pituitary stimulates the release of glucocorticoids and mineralocorticoids from the adrenal cortex and a more prolonged response to stress occurs.

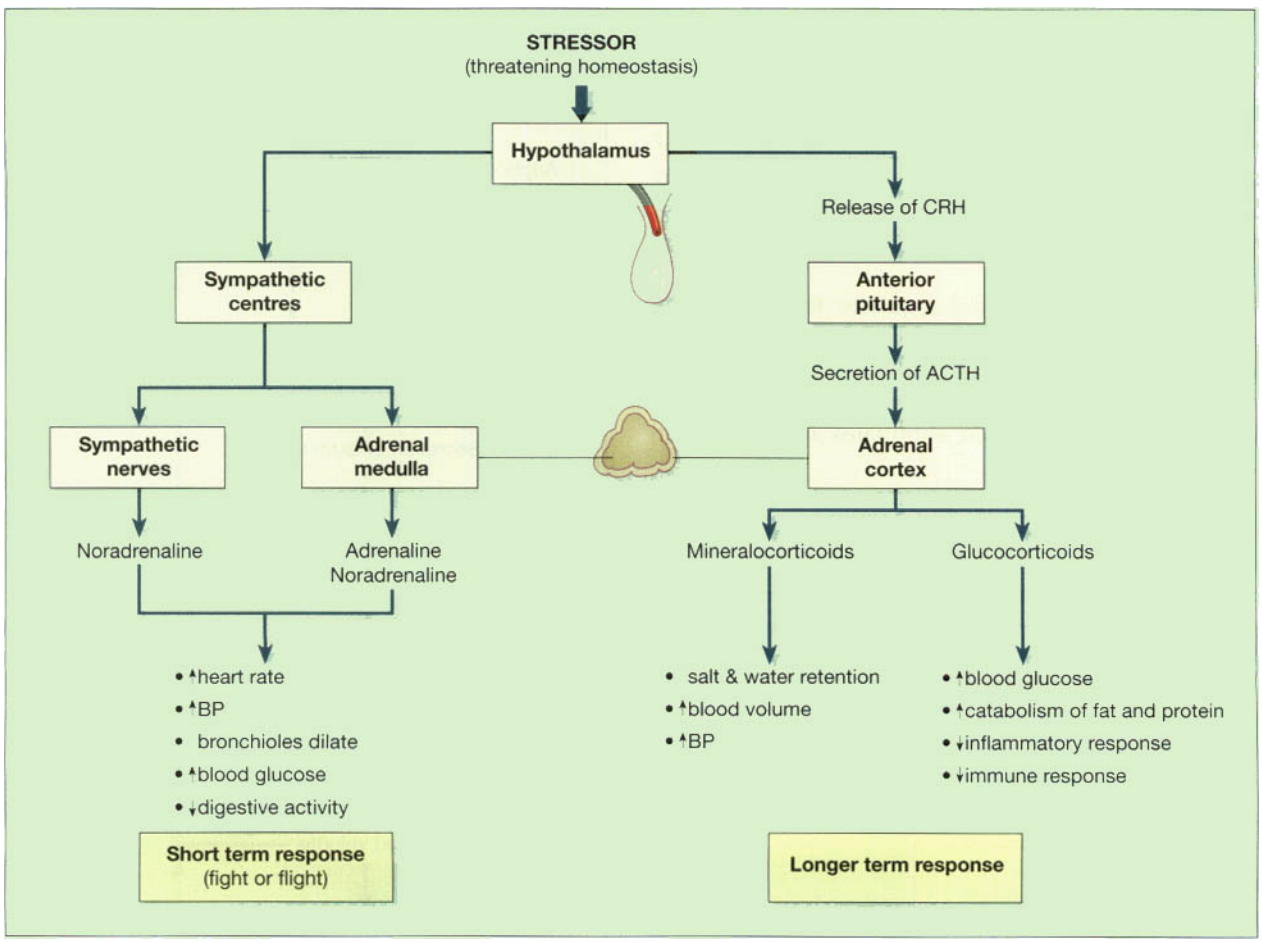


Figure 9.12 Responses to stressors that threaten homeostasis. CRH = corticotrophin releasing hormone. ACTH = adrenocorticotrophic hormone.

PANCREATIC ISLETS

Learning outcomes

After studying this section you should be able to:

- list the hormones secreted by the endocrine pancreas
- describe the actions of insulin and glucagon
- explain how blood glucose levels are regulated.

The cells which make up the pancreatic islets (islets of Langerhans) are found in clusters irregularly distributed throughout the substance of the pancreas. Unlike the exocrine pancreas, which produces pancreatic juice, there are no ducts leading from the clusters of islet cells. Pancreatic hormones are secreted directly into the bloodstream and circulate throughout the body.

There are three main types of cells in the pancreatic islets:

- α (alpha) cells that secrete *glucagon*
- β (beta) cells that secrete *insulin*
- δ (delta) cells that secrete *somatostatin* (GHRIH, p. 217).

The normal blood glucose level is between 2.5 and 5.3 mmol/litre (45 to 95 mg/100 ml). Blood glucose levels are controlled mainly by the opposing actions of insulin and glucagon:

- glucagon increases blood glucose levels
- insulin reduces blood glucose levels.

Insulin

The main function of insulin is to lower blood levels of absorbed nutrients when they rise above normal. When these nutrients, especially glucose, are in excess of immediate needs insulin promotes storage by:

- acting on cell membranes and stimulating uptake and use of glucose by muscle and connective tissue cells
- increasing conversion of glucose to glycogen (glycogenesis), especially in the liver and skeletal muscles
- accelerating uptake of amino acids by cells, and the synthesis of protein
- promoting synthesis of fatty acids and storage of fat in adipose tissue (lipogenesis)
- decreasing glycogenolysis
- preventing the breakdown of protein and fat, and *gluconeogenesis* (formation of new sugar from, e.g. protein).

Secretion of insulin is stimulated by increased blood glucose and amino acid levels, and gastrointestinal hormones, e.g. gastrin, secretin and cholecystokinin. Secretion is decreased by sympathetic stimulation, glucagon, adrenaline, cortisol and somatostatin (GHRIH) secreted by cells of the pancreatic islets.

Insulin is a polypeptide consisting of about 50 amino acids. Amounts are expressed in international units (IU).

Glucagon

The effects of glucagon increase blood glucose levels by stimulating, e.g.:

- conversion of glycogen to glucose in the liver and skeletal muscles (glycogenolysis)
- gluconeogenesis.

Secretion of glucagon is stimulated by a low blood glucose level and exercise and decreased by somatostatin and insulin.

Somatostatin (GHRIH)

The effect of this hormone, also produced by the hypothalamus, is to inhibit the secretion of both insulin and glucagon.

PINEAL GLAND OR BODY

Learning outcomes

After studying this section you should be able to:

- state the position of the pineal gland
- outline the actions of melatonin.

The pineal gland is a small body attached to the roof of the third ventricle and is connected to it by a short stalk containing nerves, many of which terminate in the hypothalamus. The pineal gland is about 10 mm long, is reddish brown in colour and is surrounded by a capsule.

Melatonin

This is the hormone secreted by the pineal gland. Secretion is influenced by the amount of light entering the eye stimulating the optic pathways and levels fluctuate during each 24-hour period, being highest at night and lowest around midday. Although its functions are not fully understood, it is believed to be associated with:

- coordination of the circadian and diurnal rhythms of many tissues, possibly by influencing the hypothalamus
- inhibition of growth and development of the sex organs before puberty, possibly by preventing synthesis or release of gonadotrophins.

The gland tends to atrophy after puberty and may become calcified in later life.

THYMUS GLAND

Learning outcomes

After studying this section you should be able to:

- state the position of the thymus gland
- outline the actions of thymosin.

The location and structure of the thymus gland are described on page 134.

Thymosin

This is the hormone secreted by the thymus gland and is required for the development of T-lymphocytes for cell-mediated immunity (Ch. 15).

LOCAL HORMONES

Learning outcome

After studying this section you should be able to:

- name substances that act as local hormones.

A number of body tissues not normally described as endocrine glands secrete substances that act locally. Some of these are described below.

Histamine

This hormone is synthesised by mast cells in the tissues and basophils in blood. It is released as part of the inflammatory process, increasing capillary permeability and dilatation. It also causes contraction of smooth muscle of the bronchi and alimentary tract and stimulates the secretion of gastric juice.

Serotonin (5-hydroxytryptamine, 5-HT)

This is present in platelets, in the brain and in the intestinal wall. It causes intestinal secretion and contraction of smooth muscle and its role in haemostasis (blood clotting) is outlined in Chapter 4.

Prostaglandins (PGs)

These are lipid substances that act as local hormones and have wide-ranging physiological effects in:

- the inflammatory response
- potentiating pain
- fever
- regulating blood pressure
- blood clotting
- uterine contractions during labour.

Other chemically similar compounds include *leukotrienes* and *thromboxanes*. They are active substances found in only small amounts, as they are rapidly degraded.

Erythropoietin

This hormone is synthesised by the kidneys and increases erythropoiesis (the rate of red blood cell formation, see Fig. 4.4, p. 63).

Gastrointestinal hormones

Several local hormones, including gastrin, secretin and cholecystokinin (CCK), influence the secretion of digestive juices and their functions are explained in Chapter 12.

DISORDERS OF THE ANTERIOR PITUITARY

Learning outcomes

After studying this section you should be able to:

- list the causes of diseases in this section
- relate the features of the diseases in this section to abnormal growth and development.

Endocrine disorders are commonly caused by *tumours* or *autoimmune diseases* and their effects are usually the result of:

- hypersecretion (overproduction) of hormones
- hyposecretion (underproduction) of hormones.

The abnormalities described in this section are those in which there is a general effect but no specific target gland. Abnormal secretion of *stimulating hormones* are included with the disorders of their target glands.

Hypersecretion of anterior pituitary hormones

Gigantism and acromegaly

The most common cause is prolonged hypersecretion of growth hormone (GH), usually by a hormone-secreting pituitary tumour. The conditions are only occasionally due to excess growth hormone releasing hormone (GHRH) secreted by the hypothalamus. As the tumour increases in size compression of nearby structures may lead to:

- hyposecretion of other pituitary hormones of both the anterior and posterior lobes
- hyposecretion of hormone-releasing factors by the hypothalamus
- damage to the optic nerves, causing visual disturbances.

Effects of excess GH

These include:

- excessive growth of bones
- enlargement of internal organs
- growth of excess connective tissue
- enlargement of the heart and a rise in blood pressure
- reduced glucose tolerance and a predisposition to diabetes mellitus.

Gigantism. This occurs when there is excess GH while epiphyseal cartilages of long bones are still growing, i.e. during childhood before ossification of bones is complete. It is evident mainly in the bones of the limbs and affected individuals may grow to heights of 2.1 to 2.4 m, although body proportions remain normal (Fig. 9.13).

Acromegaly (meaning 'large extremities'). This occurs when there is excess GH after ossification is complete. The bones become abnormally thick due to ossification of periosteum and there is thickening of the soft tissues. These changes are most noticeable as coarse facial features, an enlarged tongue and excessively large hands and feet (Fig. 9.14).

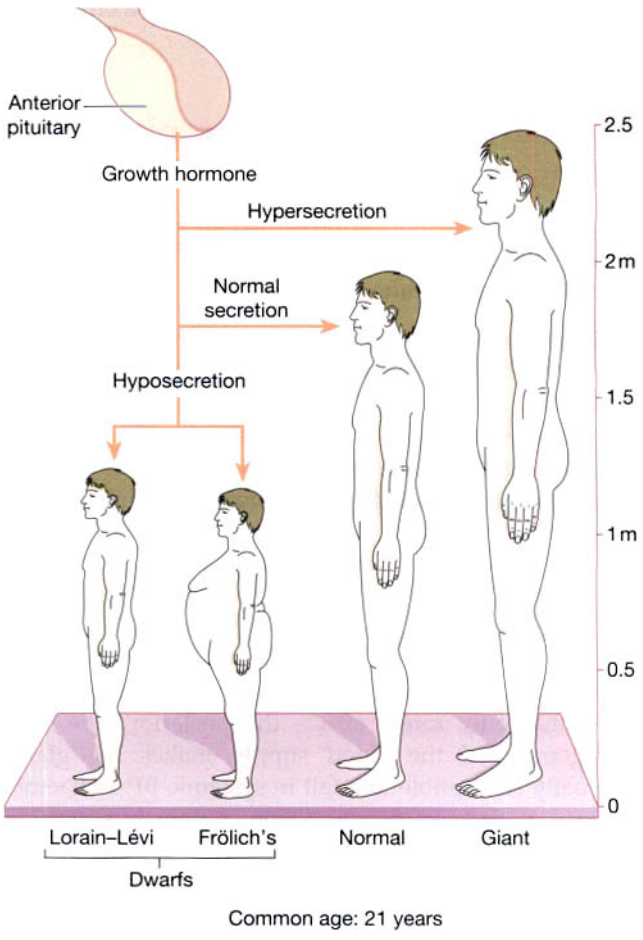


Figure 9.13 Effects of normal and abnormal growth hormone secretion.

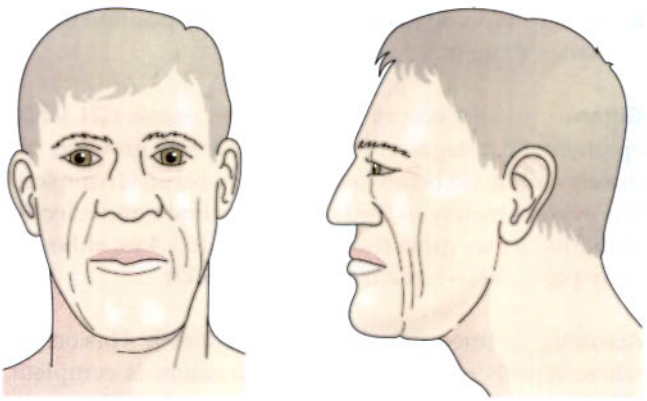


Figure 9.14 Facial features in acromegaly.

Hyperprolactinaemia

This is caused by a hormone-secreting tumour. It causes galactorrhoea, amenorrhoea and sterility in women and impotence in men.

Hyposecretion of anterior pituitary hormones

The number of hormones and the extent of hyposecretion varies. *Panhypopituitarism* is absence of all hormones. Causes of hyposecretion include:

- tumours of the hypothalamus or pituitary
- trauma, usually caused by fractured base of skull or surgery
- pressure caused by a tumour adjacent to the pituitary gland, e.g. glioma, meningioma
- infection, e.g. meningitis, encephalitis, syphilis
- ischaemic necrosis
- ionising radiation or cytotoxic drugs.

Ischaemic necrosis

Simmond's disease is hypofunction of the anterior pituitary gland that only rarely affects the posterior lobe. The arrangement of the blood supply makes the gland unusually susceptible to a fall in systemic BP. Ischaemic necrosis of the gland may follow severe hypotensive shock causing deficient stimulation of target glands and hypofunction of all or some of the thyroid, adrenal cortex and gonads. The outcome depends on the extent of pituitary necrosis and hormone deficiency. In severe cases, glucocorticoid deficiency may be life threatening or fatal. When this condition is associated with severe haemorrhage during or after childbirth it is known as *Sheehan's syndrome* and in this situation the other effects are preceded by failure of lactation.

Pituitary dwarfism (Lorain–Lévi syndrome)

This is caused by severe deficiency of GH, and possibly of other hormones, in childhood. The individual is of small stature but is well proportioned and mental development is not affected. Puberty is delayed and there may be episodes of hypoglycaemia. The condition may be due to genetic abnormality or a tumour.

Fröhlich's syndrome

In this condition there is panhypopituitarism but the main features are associated with deficiency of GH, FSH and LH. In children the effects are diminished growth, lack of sexual development, obesity with female distribution of fat and retarded mental development. In a similar condition in adults, obesity and sterility are the main features. It may be the result of a tumour of the anterior pituitary and/or the hypothalamus but in most cases the cause is unknown.

DISORDERS OF THE POSTERIOR PITUITARY

Learning outcomes

After studying this section you should be able to:

- list the causes of diabetes insipidus
- relate the features of diabetes insipidus to abnormal secretion of antidiuretic hormone.

Diabetes insipidus

This is a relatively rare condition usually caused by hyposecretion of ADH due to damage to the hypothalamus by, e.g., trauma, tumour, encephalitis. Occasionally it occurs when the renal tubules do not respond to ADH. Water reabsorption by the renal tubules is deficient, leading to excretion of excessive amounts of dilute urine, often more than 10 litres daily, causing dehydration, extreme thirst and polydipsia. Water balance is disturbed unless fluid intake is greatly increased to compensate for excess losses.

DISORDERS OF THE THYROID GLAND

Learning outcome

After studying this section you should be able to:

- compare and contrast the effects of hyperthyroidism and hypothyroidism, relating them to the actions of T_3 and T_4.

These fall into three main categories:

- abnormal secretion of thyroid hormones (T_3 and T_4)
  - hyperthyroidism
  - hypothyroidism
- *goitre* – enlargements of the thyroid gland
- *tumours*.

Abnormal thyroid function may arise not only from thyroid disease but also from disorders of the pituitary or hypothalamus; in addition, insufficient dietary iodine causes deficiency in thyroid hormone production. The main effects are caused by an abnormally high or low basal metabolic rate.

Abnormal secretion of thyroid hormones

Hyperthyroidism

This syndrome, also known as *thyrotoxicosis*, arises as the body tissues are exposed to excessive levels of T_3 and T_4. The main effects are due to increased basal metabolic rate (Table 9.3).

In the elderly, cardiac failure is another common consequence as the ageing heart works harder to deliver more blood and nutrients to the hyperactive body cells. The main causes are:

- Graves' disease
- toxic nodular goitre
- toxic adenoma (a benign tumour, p. 231).

Graves' disease (Fig. 9.15)

Sometimes called *exophthalmic goitre*, this accounts for 90% of cases of thyrotoxicosis. More women are affected than men and this disorder usually occurs between the ages of 30 and 50 years. There is diffuse swelling (hyperplasia) of the gland with secretion of excess T_3 and T_4. In addition to the effects of hyperthyroidism, there may also be exophthalmos. This is an 'organ-specific' autoimmune condition where autoantibodies that mimic the action of TSH are produced and stimulate high levels of T_3 and T_4 secretion.



Figure 9.15 Features of Graves' disease.

Exophthalmos (protrusion of the eyeballs). This is due to the deposition of excess fat and fibrous tissue behind the eyes; it is often present in Graves' disease. It may be caused by autoimmunity different from that associated with hyperplasia of the gland. Effective treatment of thyrotoxicosis does not reduce the exophthalmos. In severe cases the eyelids may not completely cover the eyes during blinking and sleep, leading to drying of the conjunctiva and predisposing to infection. It does not occur in other forms of thyrotoxicosis.

Toxic nodular goitre

In this condition one or two nodules of a gland that is already affected by goitre (see Simple goitre, p. 230) become active and secrete excess T_3 and T_4 causing the effects of hyperthyroidism (Table 9.3). It is more common in women than men and after middle age. As this condition affects an older age group than Graves' disease, arrhythmias and cardiac failure are more common. Exophthalmos does not occur in this type of hyperthyroidism.

Hypothyroidism

This occurs when there is insufficient T_3 and T_4 secretion causing:

- cretinism in children
- myxoedema in adults.

Cretinism

This condition is *endemic* in areas remote from the sea where the soil and diet are severely deficient in iodine and there is therefore insufficient iodine for synthesis of T_3 and T_4. In *sporadic* cases there is congenital absence of the thyroid gland. In both situations retarded physical growth and mental development become evident within a few weeks or months of birth. Unless treatment begins early in life the individual remains severely mentally retarded, has disproportionately short limbs, a large protruding tongue, coarse dry skin, poor abdominal muscle tone and an umbilical hernia (Fig. 9.16).

Myxoedema

This condition is prevalent in the elderly and is five times more common in females than males. Deficiency of T_3 and T_4 in adults results in an abnormally low metabolic rate and other effects shown in Table 9.3. There may be accumulation of polysaccharide substances in the subcutaneous tissues especially of the face (Fig. 9.17). The commonest causes are:

- autoimmune thyroiditis
- severe iodine deficiency (see goitre)
- iatrogenic, e.g. antithyroid drugs, surgical removal of thyroid tissue, ionising radiation.

Autoimmune thyroiditis

The most common cause of acquired hypothyroidism is *Hashimoto's disease*. It is more common in women than men. Similar conditions that are less common include *primary myxoedema* and *focal thyroiditis* and like Graves' disease it is also an organ-specific autoimmune condition. Autoantibodies that react with thyroglobulin and thyroid gland cells develop and prevent synthesis and release of thyroid hormones causing hypothyroidism.



Figure 9.16 Features of cretinism.

Simple goitre

This is enlargement of the thyroid gland without signs of hyperthyroidism. Secretion of T_3 and T_4 is reduced and the low levels stimulate secretion of TSH resulting in hyperplasia of the thyroid gland (Fig. 9.18). Sometimes the extra thyroid tissue is able to maintain normal hormone levels but if not, hypothyroidism develops. Causes are:

- persistent iodine deficiency
- genetic abnormality
- iatrogenic, e.g. antithyroid drugs, surgical removal of excess thyroid tissue.



Figure 9.17 Facial features of myxoedema.

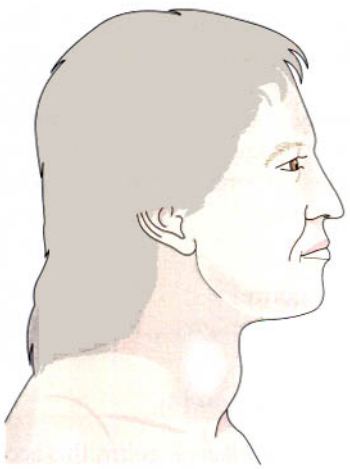


Figure 9.18 Enlarged thyroid gland in simple goitre.

The enlarged gland may cause pressure damage to adjacent tissues, especially if it lies in an abnormally low position, i.e. behind the sternum. The structures most commonly affected are the oesophagus, causing dysphagia; the trachea, causing dyspnoea; and the recurrent laryngeal nerve, causing hoarseness of voice.

Tumours of the thyroid gland

Benign tumours

Single adenomas are fairly common and may become cystic. Sometimes the adenoma secretes hormones and thyrotoxicosis may develop. The tumours have a tendency to become malignant especially in the elderly.

Malignant tumours

These are rare and are usually well differentiated but are sometimes anaplastic.

DISORDERS OF THE PARATHYROID GLANDS

Learning outcome

After studying this section you should be able to:

- explain how the diseases in this section are related to abnormal secretion of parathyroid hormone.

Hyperparathyroidism

Excess secretion of parathyroid hormone (PTH), usually by benign tumours of a gland, causes reabsorption of calcium from bones, raising the blood calcium level (hypercalcaemia). The effects may be:

- formation of renal calculi complicated by pyelonephritis and renal failure
- polyuria and polydipsia
- anorexia
- muscle weakness
- general fatigue
- calcification of soft tissue.



Figure 9.19 Characteristic positions adopted during tetanic spasms.

Hypoparathyroidism

Parathyroid hormone (PTH) deficiency causes hypocalcaemia, i.e. an abnormally low level of calcium in the blood. This reduces absorption of calcium from the small intestine and reabsorption from bones and glomerular filtrate. Low blood calcium causes:

- *tetany* (Fig. 9.19)
- psychiatric disturbances
- paraesthesia
- grand mal epilepsy
- development of cataract (opacity of the lens) and brittle nails.

The causes of hypoparathyroidism include:

- damage to or removal of the glands during thyroidectomy
- ionising radiation, usually from radioactive iodine used to treat hyperthyroidism
- development of autoantibodies to PTH and parathyroid cells
- congenital abnormality of the glands.

Tetany

This is caused by hypocalcaemia. There are very strong painful spasms of skeletal muscles, causing characteristic bending inwards of the hands, forearms and feet (Fig. 9.19). In children there may be laryngeal spasm and convulsions. Hypocalcaemia is associated with:

- hypoparathyroidism
- deficiency of vitamin D or dietary deficiency of calcium

- chronic renal failure when there is excretion of excess calcium in the urine
- alkalosis; metabolic due to persistent vomiting, ingestion of excess alkali to alleviate gastric disturbances or respiratory due to hyperventilation.

DISORDERS OF THE ADRENAL CORTEX

Learning outcomes

After studying this section you should be able to:

- relate the features of Cushing's syndrome to the actions of adrenocorticoids
- relate the features of Addison's disease to the actions of adrenocorticoids.

Hypersecretion of glucocorticoids (Cushing's syndrome)

Cortisol is the main glucocorticoid hormone secreted by the adrenal cortex. Causes of hypersecretion include:

- hormone-secreting adrenal tumours, benign or malignant
- hypersecretion of adrenocorticotrophic hormone (ACTH) by the anterior pituitary
- abnormal secretion of ACTH by a non-pituitary tumour, e.g. bronchial carcinoma, pancreatic tumour, carcinoid tumours
- prolonged therapeutic use of ACTH or glucocorticoids, e.g. prednisolone, in high doses.

Hypersecretion of cortisol has a wide variety of effects but they may not all be present (Fig. 9.20). They include:

- painful adiposity of the face (*moon face*), neck and abdomen
- excess protein catabolism, causing thinning of subcutaneous tissue and muscle wasting, especially of the limbs

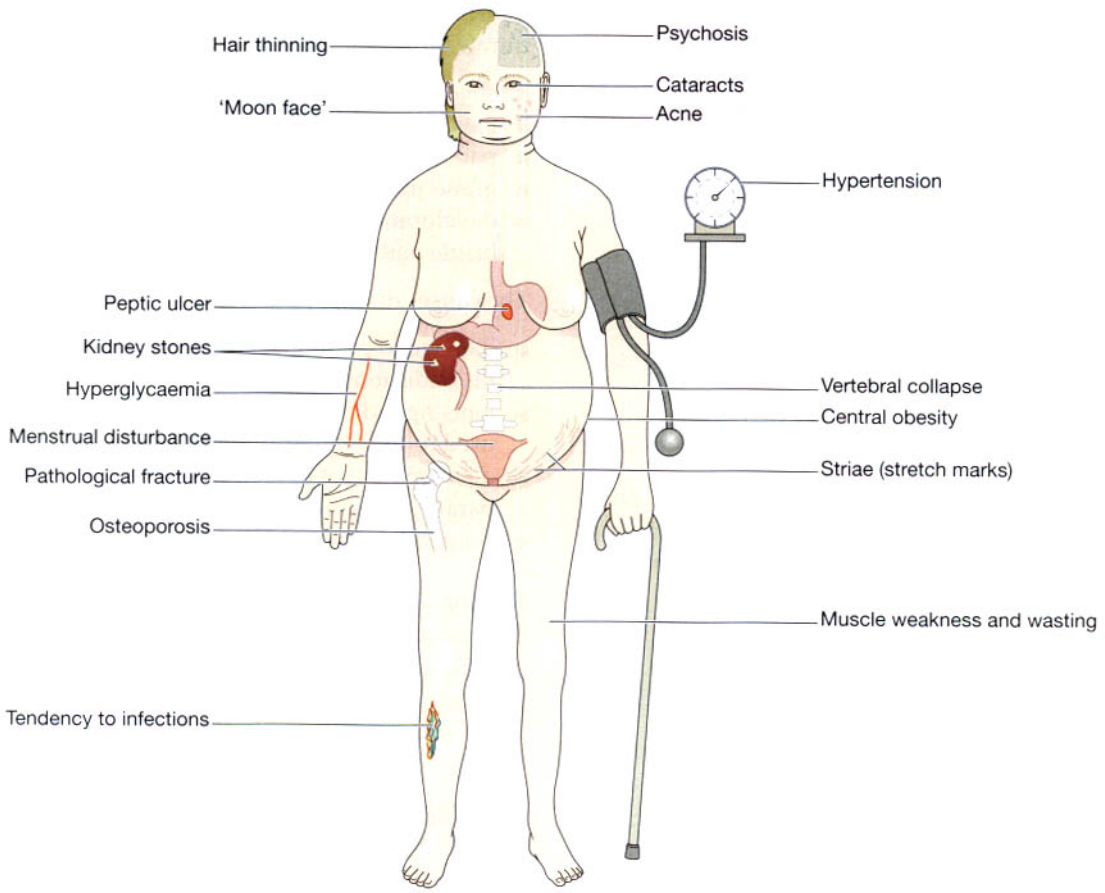


Figure 9.20 The systemic features of Cushing's syndrome.

- diminished protein synthesis
- suppression of growth hormone, causing arrest of growth in children
- osteoporosis and kyphosis if vertebral bodies are involved
- pathological fractures
- excessive gluconeogenesis with hyperglycaemia and glycosuria
- atrophy of lymphoid tissue and depressed immune response
- susceptibility to infection due to reduced febrile response, depressed immune response and phagocytosis, impaired migration of phagocytes
- insomnia, excitability, euphoria, psychosis, depression
- hypertension
- menstrual disturbances
- formation of renal calculi
- peptic ulceration.

Hyposecretion of glucocorticoids

Inadequate secretion of cortisol causes diminished gluconeogenesis, low blood glucose, muscle weakness and pallor. It may be primary, i.e. due to adrenal cortex disease, or secondary due to deficiency of ACTH from the anterior pituitary. In primary deficiency there is also hyposecretion of aldosterone (see below) but in secondary deficiency, aldosterone secretion is not usually affected.

Hypersecretion of mineralocorticoids

Excess aldosterone affects kidney function, causing:

- excessive reabsorption of sodium chloride and water, causing increased blood volume and hypertension
- excessive excretion of potassium, causing *hypokalaemia*, which leads to cardiac arrhythmia, alkalosis, syncope and muscle weakness.

Primary aldosteronism (Conn's syndrome)

This is due to an excessive secretion of mineralocorticoids, independent of the renin–angiotensin–aldosterone system. It is usually caused by a tumour affecting only one adrenal gland.

Secondary aldosteronism

This is caused by overstimulation of normal glands by the excessively high blood levels of renin and angiotensin that result from low renal perfusion or low blood sodium.

Hyposecretion of mineralocorticoids

Hypoaldosteronism results in failure of the kidneys to regulate sodium, potassium and water excretion, leading to:

- blood sodium deficiency (hyponatraemia) and potassium excess (hyperkalaemia)
- dehydration, low blood volume and low blood pressure, especially if arteriolar constriction is defective due to deficiency of noradrenaline.

There is usually hyposecretion of other cortical hormones, as in Addison's disease.

Chronic adrenal cortex insufficiency (Addison's disease)

This is due to hyposecretion of glucocorticoid and mineralocorticoid hormones. The most common causes are development of autoantibodies to cortical cells, metastatic tumours and infections. Autoimmune disease of some other glands is associated with Addison's disease, e.g. thyrotoxicosis and hypoparathyroidism. The most important effects are:

- muscle weakness and wasting
- gastrointestinal disturbances, e.g. vomiting, diarrhoea, anorexia
- increased pigmentation of the skin, especially of exposed areas, due to excess ACTH and the related melanin-stimulating hormone secreted by the anterior pituitary
- listlessness and tiredness
- hypoglycaemia
- mental confusion
- menstrual disturbances and loss of body hair in women
- electrolyte imbalance, including hyponatraemia, low blood chloride levels and hyperkalaemia
- chronic dehydration, low blood volume and hypotension.

The adrenal glands have a considerable reserve of tissue and Addison's disease is not usually severely debilitating unless more than 90% of cortical tissue is destroyed.

Acute adrenal cortical insufficiency (Addisonian crisis)

This is characterised by sudden severe nausea, vomiting, diarrhoea, hypotension, electrolyte imbalance and, in severe cases, circulatory collapse. It is precipitated when an individual with chronic adrenal cortex insufficiency is subjected to stress, e.g. an acute infection.

DISORDERS OF THE ADRENAL MEDULLA

Learning outcome

After studying this section you should be able to:

- explain how the features of the diseases in this section are related to excessive secretion of adrenaline and noradrenaline.

Tumours

Hormone-secreting tumours are the main abnormality. The effects of excess adrenaline and noradrenaline include:

- hypertension, often associated with arteriosclerosis and cerebral haemorrhage
- hyperglycaemia and glycosuria
- excessive sweating and alternate flushing and blanching
- raised metabolic rate
- nervousness
- headache.

Phaeochromocytoma

This is a *benign tumour*, occurring in one or both glands. The secretion of hormones may be at a steady high level or in intermittent bursts.

Neuroblastoma

This is a *malignant tumour*, occurring in infants and children under 15 years of age. Tumours that develop early tend to be highly malignant but in this condition there may be spontaneous regression.

DISORDERS OF THE PANCREATIC ISLETS

Learning outcomes

After studying this section you should be able to:

- compare and contrast the onset and features of types I and II diabetes mellitus
- state the common causes of secondary diabetes
- relate the signs and symptoms of diabetes mellitus to deficient secretion of insulin
- explain how the causes and effects of the following conditions occur: diabetic ketoacidosis and hypoglycaemic coma
- describe the long term complications of diabetes mellitus

Diabetes mellitus

This is due to deficiency or absence of insulin or rarely to impairment of insulin activity (insulin resistance) causing varying degrees of disruption of carbohydrate and fat metabolism.

Type I, insulin-dependent diabetes mellitus (IDDM)

This occurs mainly in children and young adults and the onset is usually sudden. The deficiency or absence of insulin is due to the destruction of β-islet cells. The causes are unknown but there is a familial tendency, suggesting genetic involvement. In many cases an autoimmune reaction has occurred in which autoantibodies to β-islet cells are present. Antibodies to viruses are present in some cases and these may destroy the β-islet cells directly or by an autoimmune mechanism.

Type II, non-insulin-dependent diabetes mellitus (NIDDM)

This is the most common form of diabetes, accounting for about 90% of cases. Most patients are obese and it tends to develop in women over 75 years and men over 65 years. The cause is unknown. Insulin secretion may be below or above normal. Deficiency of glucose inside body cells may occur when there is hyperglycaemia and a high insulin level. This may be due to changes in cell membranes which block the insulin-assisted movement of glucose into cells (insulin resistance).

Secondary diabetes

This may develop as a complication of:

- acute and chronic pancreatitis
- some drugs, e.g. corticosteroids, phenytoin, thiazide diuretics
- secondary to other hormonal disturbances involving hypersecretion of e.g. growth hormone, thyroid hormones, cortisol, adrenaline
- pregnancy (gestational diabetes).

Gestational diabetes

This develops during pregnancy and usually disappears after delivery; however, diabetes often recurs in later life. Raised blood glucose levels during pregnancy predispose to the birth of excessively large babies and also to stillbirths and deaths shortly after birth.

Effects of diabetes mellitus

Raised blood glucose level

After the intake of a carbohydrate meal the blood glucose level remains high because:

- glucose uptake and use by body cells is defective
- conversion of glucose to glycogen in the liver and muscles is diminished
- there is gluconeogenesis from protein in response to deficiency of intracellular glucose.

Glycosuria and polyuria

The concentration of glucose in the glomerular filtrate is the same as in the blood and, although diabetes raises the renal threshold for glucose, it is not all reabsorbed by the tubules (p. 344). The remaining glucose in the filtrate raises the osmotic pressure, water reabsorption is reduced and the volume of urine produced is increased. This causes electrolyte imbalance and excretion of urine of high specific gravity. Polyuria leads to hypovolaemia, extreme thirst and polydipsia.

Weight loss

In diabetes, cells fail to metabolise glucose in the normal manner, resulting in weight loss due to:

- gluconeogenesis from amino acids and body protein, causing tissue wasting, tissue breakdown and further increase in blood glucose
- catabolism of body fat, releasing some of its energy and excess production of ketoacids.

Ketoacidosis

This is due to the accumulation of the intermediate metabolite, acetyl coenzyme A, which cannot enter the citric acid cycle without oxaloacetic acid (see Fig. 12.48, p. 318). In diabetes the amount of available oxaloacetic acid is reduced because glucose metabolism is reduced. As a result excess acetyl coenzyme A is converted to ketones, which are acidic. When these accumulate in the blood, the pH drops, causing ketoacidosis. Ketones are excreted in the urine (ketonuria) and by the lungs. The consequences are:

- hyperventilation and the excretion of excess bicarbonate
- acidification of urine and high filtrate osmotic pressure which leads to excessive loss of water (polyuria), ammonia, sodium and potassium
- coma due to a combination of low blood pH (acidosis), high plasma osmotic pressure and electrolyte imbalance.

Acute complications of diabetes mellitus

Diabetic ketoacidosis (diabetic coma, hyperglycaemic coma)

This mainly affects insulin-dependent diabetics. Ketoacidosis develops owing to increased insulin requirement or increased resistance to insulin due to some added stress, such as pregnancy, microbial infection, infarction, cerebrovascular accident. The inadequate supply of insulin may also be due to failure by the patient to administer the prescribed dose or inadequate adjustment of the prescribed dose to meet the patient's increased needs. In some cases severe and dangerous ketoacidosis may occur without loss of consciousness.

The factors that predispose to the development of hyperglycaemic coma in either type of diabetes include:

- hypovolaemia with severe dehydration due to persistent polyuria
- high blood osmotic pressure due to excess blood glucose, leading to electrolyte imbalance
- acidosis due to accumulation of ketoacids.

Hypoglycaemic coma

This occurs in insulin-dependent diabetics when the insulin administered is in excess of that needed to balance the food intake and expenditure of energy. Because neurones are more dependent on glucose for their energy needs than are other cells, glucose deprivation causes disturbed neural function, leading to coma and, if prolonged, irreversible damage. Hypoglycaemia may be the result of:

- accidental overdose of insulin
- delay in eating after insulin administration
- gastrointestinal disturbances in which carbohydrate absorption is diminished, e.g., vomiting, diarrhoea
- increased metabolic rate in, e.g. unexpected exercise, acute febrile illness
- an insulin-secreting tumour, especially if it produces irregular bursts of secretion.

Common signs and symptoms of hypoglycaemia include drowsiness, confusion, speech difficulty, sweating, trembling and anxiety.

Long-term complications of diabetes mellitus

Cardiovascular disturbances

Changes in blood vessels occur even when the disease is well controlled by insulin and/or diet.

Diabetic macroangiopathy

The most common lesions are atheroma and calcification of the tunica media of the large muscular arteries. In insulin-dependent diabetics these changes may occur at a relatively early age. The most common sequelae are serious and often fatal: peripheral vascular disease, myocardial infarction, cerebral ischaemia and infarction.

Diabetic microangiopathy

There is thickening of the epithelial basement membrane of arterioles, capillaries and sometimes of venules. These changes may lead to:

- peripheral vascular disease, progressing to gangrene
- retinopathy, in which microaneurysms and small haemorrhages cause numerous small necrotic points in the retina, leading to loss of sight
- glomerulosclerosis, leading to nephrotic syndrome and renal failure
- peripheral neuropathy, especially when myelination is defective.

Infection

Diabetics are highly susceptible to infection, especially by bacteria and fungi, possibly because phagocyte activity is depressed by insufficient intracellular glucose. Infection may cause:

- complications in areas affected by *peripheral neuropathy* and changes in blood vessels, e.g. in the feet when sensation and blood supply are impaired
- boils and carbuncles
- vaginal candidiasis (thrush)
- pyelonephritis.

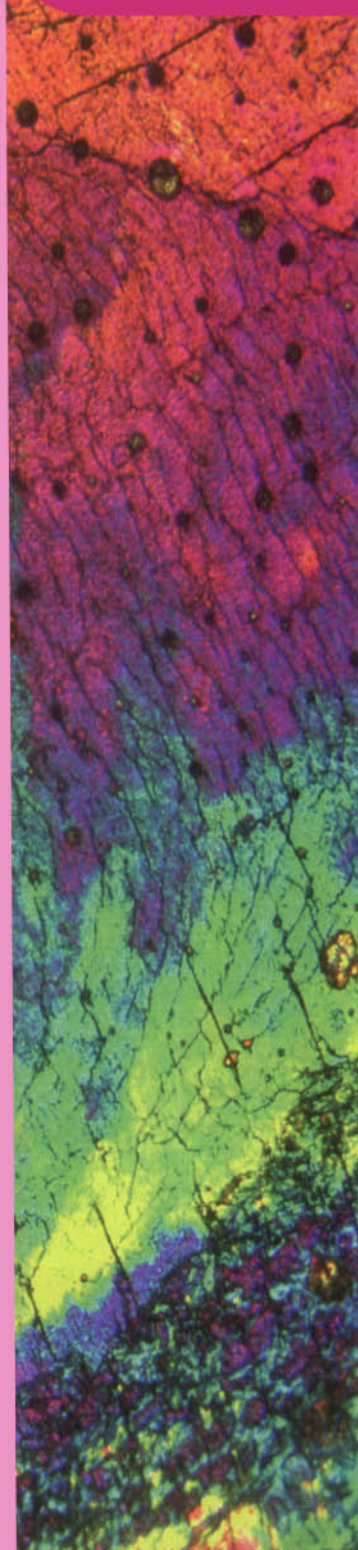
Renal failure

This is due to changes affecting the walls of small blood vessels and infection, and is a common cause of death in diabetics (see Diabetic kidney, p. 352).

3

Intake of raw materials and elimination of waste

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The respiratory system

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The cells of the body need energy for their chemical activity that maintains homeostasis. Most of this energy is derived from chemical reactions which can only take place in the presence of oxygen (O_2). The main waste product of these reactions is carbon dioxide (CO_2). The respiratory system provides the route by which the supply of oxygen present in the atmospheric air gains entry to the body and it provides the route of excretion of carbon dioxide.

The condition of the atmospheric air entering the body varies considerably according to the external environment, e.g. it may be dry, cold and contain dust particles or it may be moist and hot. As the air breathed in moves through the air passages to reach the lungs, it is warmed or cooled to body temperature, moistened to become saturated with water vapour and 'cleaned' as particles of dust stick to the mucus which coats the lining membrane. Blood provides the transport system for these gases between the lungs and the cells of the body. Exchange of gases between the blood and the lungs is called *external respiration* and that between the blood and the cells *internal respiration*. The organs of the respiratory system are:

- nose
- pharynx
- larynx
- trachea
- two bronchi (one bronchus to each lung)
- bronchioles and smaller air passages
- two lungs and their coverings, the pleura
- muscles of respiration – the intercostal muscles and the diaphragm.

A general view of the organs of the respiratory system is given in Figure 10.1.

NOSE AND NASAL CAVITY

Learning outcomes

After studying this section, you should be able to:

- describe the location of the nasal cavities
- relate the structure of the nasal cavities to their function in respiration
- outline the physiology of smell.

Position and structure

The nasal cavity is the first of the respiratory organs and consists of a large irregular cavity divided into two equal passages by a *septum*. The posterior bony part of the septum is formed by the perpendicular plate of the ethmoid bone and the vomer. Anteriorly it consists of hyaline cartilage (Fig. 10.2).

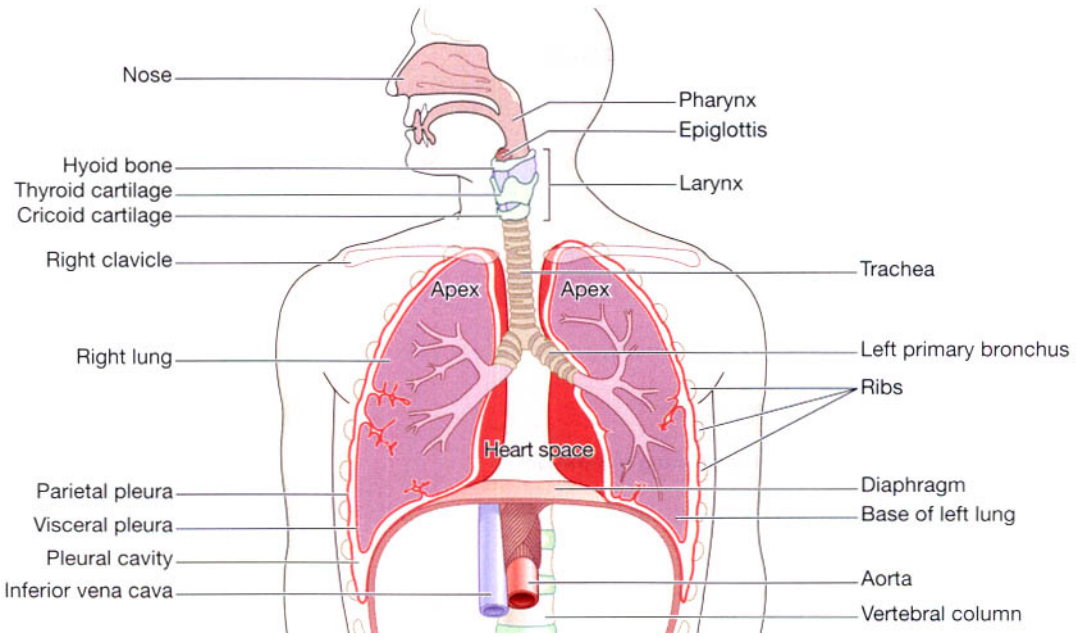


Figure 10.1 The organs of respiration.

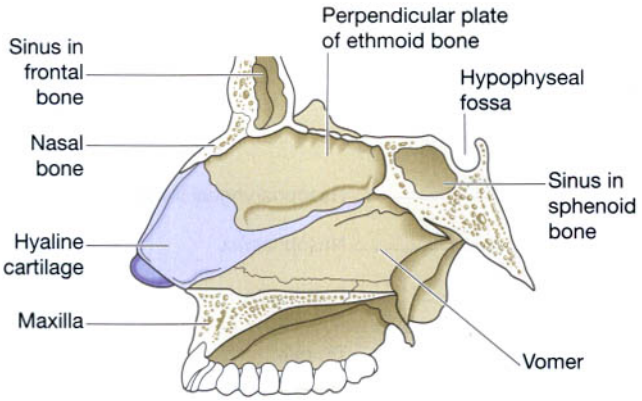


Figure 10.2 Structures forming the nasal septum.

The roof is formed by the cribriform plate of the ethmoid bone, and the sphenoid bone, frontal bone and nasal bones.

The floor is formed by the roof of the mouth and consists of the hard palate in front and the soft palate behind. The hard palate is composed of the maxilla and palatine bones and the soft palate consists of involuntary muscle.

The medial wall is formed by the *septum*.

The lateral walls are formed by the maxilla, the ethmoid bone and the inferior conchae (Fig. 10.3).

The posterior wall is formed by the posterior wall of the pharynx.

Lining of the nose

The nose is lined with very vascular *ciliated columnar epithelium* (ciliated mucous membrane) which contains mucus-secreting goblet cells (p. 43). At the anterior nares this blends with the skin and posteriorly it extends into the nasal part of the pharynx.

Openings into the nasal cavity

The anterior nares, or nostrils, are the openings from the exterior into the nasal cavity. Hairs are present in this area.

The posterior nares are the openings from the nasal cavity into the pharynx.

The paranasal sinuses are cavities in the bones of the face and the cranium which contain air. There are tiny openings between the paranasal sinuses and the nasal cavity. They are lined with mucous membrane, continuous with that of the nasal cavity. The main sinuses are:

- maxillary sinuses in the lateral walls
- frontal and sphenoidal sinuses in the roof (Fig. 10.3)
- ethmoidal sinuses in the upper part of the lateral walls (Fig. 10.3).

The sinuses function in speech and also serve to lighten the skull. *The nasolacrimal ducts* extend from the lateral walls of the nose to the conjunctival sacs of the eye (p. 205). They drain tears from the eyes.

Respiratory function of the nose

The nose is the first of the respiratory passages through which the inspired air passes. The function of the nose is to begin the process by which the air is *warmed, moistened and 'filtered'*.

The projecting *conchae* (Figs 10.3 and 10.4) increase the surface area and cause turbulence, spreading inspired air

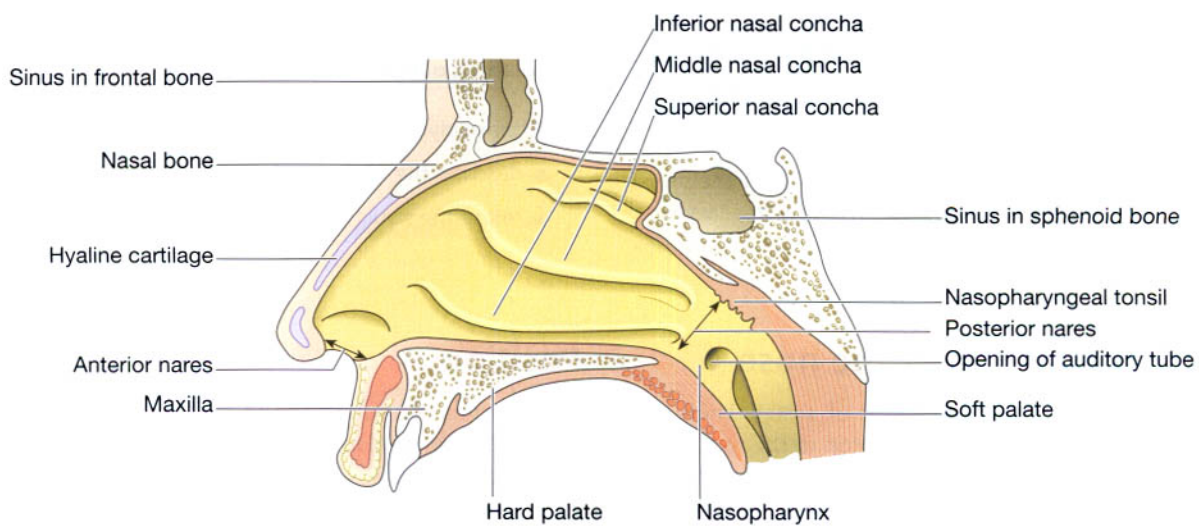


Figure 10.3 Lateral wall of right nasal cavity.

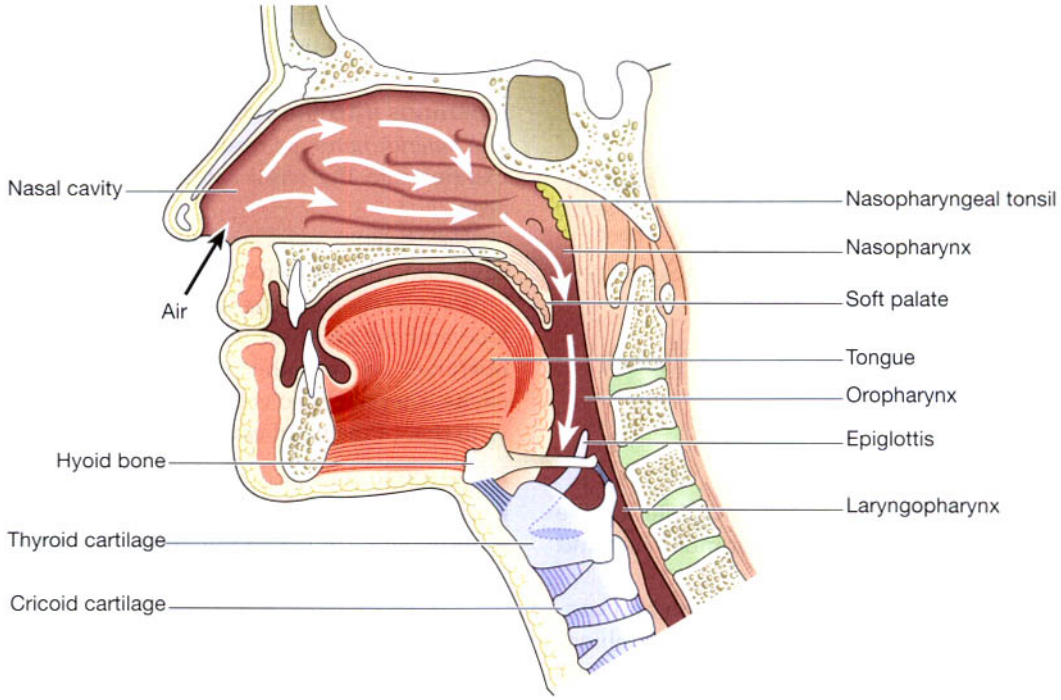


Figure 10.4 The pathway of air from the nose to the larynx.

over the whole nasal surface. The large surface area maximises warming, humidification and filtering.

Warming. This is due to the immense vascularity of the mucosa. This explains the large blood loss when a nosebleed (epistaxis) occurs.

Filtering and cleaning of air. This occurs as hairs at the anterior nares trap larger particles. Smaller particles such as dust and microbes settle and adhere to the mucus. Mucus protects the underlying epithelium from irritation and prevents drying. Synchronous beating of the cilia wafts the mucus towards the throat where it is swallowed or expectorated.

Humidification. This occurs as air travels over the moist mucosa and becomes saturated with water vapour. Irritation of the nasal mucosa results in *sneezing*, a reflex action that forcibly expels an irritant.

Olfactory function of the nose

The nose is the organ of the sense of smell. There are nerve endings that detect smell, located in the roof of the nose in the area of the cribriform plate of the ethmoid bones and the superior conchae. These nerve endings are stimulated by chemical substances given off by odorous materials. The resultant nerve impulses are conveyed by the *olfactory nerves* to the brain where the sensation of smell is perceived (p. 206).

PHARYNX

Learning outcomes

After studying this section, you should be able to:

- describe the location of the pharynx
- relate the structure of the pharynx to its function.

Position

The pharynx is a tube 12 to 14 cm long that extends from the base of the skull to the level of the 6th cervical vertebra. It lies behind the nose, mouth and larynx and is wider at its upper end.

Structures associated with the pharynx

Superiorly – the inferior surface of the base of the skull
Inferiorly – it is continuous with the oesophagus
Anteriorly – the wall is incomplete because of the openings into the nose, mouth and larynx
Posteriorly – areolar tissue, involuntary muscle and the bodies of the first six cervical vertebrae

For descriptive purposes the pharynx is divided into three parts: *nasopharynx, oropharynx* and *laryngopharynx*.

The nasopharynx. The nasal part of the pharynx lies behind the nose above the level of the soft palate. On its lateral walls are the two openings of the *auditory tubes*, one leading to each middle ear. On the posterior wall there are the *pharyngeal tonsils* (adenoids), consisting of lymphoid tissue. They are most prominent in children up to approximately 7 years of age. Thereafter they gradually atrophy.

The oropharynx. The oral part of the pharynx lies behind the mouth, extending from below the level of the soft palate to the level of the upper part of the body of the 3rd cervical vertebra. The lateral walls of the pharynx blend with the soft palate to form two folds on each side. Between each pair of folds there is a collection of lymphoid tissue called the *palatine tonsil*.

During swallowing, the nasal and oral parts are separated by the soft palate and the *uvula*.

The laryngopharynx. The laryngeal part of the pharynx extends from the oropharynx above and continues as the oesophagus below, i.e. from the level of the 3rd to the 6th cervical vertebrae.

Structure

The pharynx is composed of three layers of tissue:

1. *Mucous membrane lining.* The mucosa varies slightly in the different parts. In the nasopharynx it is continuous with the lining of the nose and consists of ciliated columnar epithelium; in the oropharynx and laryngopharynx it is formed by tougher stratified squamous epithelium which is continuous with the lining of the mouth and oesophagus.
2. *Fibrous tissue.* This forms the intermediate layer. It is thicker in the nasopharynx, where there is little muscle, and becomes thinner towards the lower end, where the muscle layer is thicker.
3. *Muscle tissue.* This consists of several involuntary *constrictor muscles* that play an important part in the mechanism of swallowing (deglutition) which, in the pharynx, is not under voluntary control. The upper end of the oesophagus is closed by the lower constrictor muscle, except during swallowing.

Blood and nerve supply

Blood is supplied to the pharynx by several branches of the facial artery. The venous return is into the facial and internal jugular veins.

The nerve supply is from the pharyngeal plexus, formed by parasympathetic and sympathetic nerves. Parasympathetic supply is by the *vagus* and *glossopharyngeal* nerves. Sympathetic supply is by nerves from the *superior cervical ganglia* (p. 170).

Functions

Passageway for air and food. The pharynx is an organ involved in both the respiratory and the digestive systems: air passes through the nasal and oral parts, and food through the oral and laryngeal parts.

Warming and humidifying. By the same methods as in the nose, the air is further warmed and moistened as it passes through the pharynx.

Taste. There are olfactory nerve endings of the sense of taste in the epithelium of the oral and pharyngeal parts.

Hearing. The auditory tube, extending from the nasal part to each middle ear, allows air to enter the middle ear. Satisfactory hearing depends on the presence of air at atmospheric pressure on each side of the *tympanic membrane* (ear drum) (p. 193).

Protection. The lymphatic tissue of the pharyngeal and laryngeal tonsils produces antibodies in response to antigens, e.g. microbes (Ch. 15). The tonsils are larger in children and tend to atrophy in adults.

Speech. The pharynx functions in speech; by acting as a resonating chamber for the sound ascending from the larynx, it helps (together with the sinuses) to give the voice its individual characteristics.

LARYNX

Learning outcomes

After studying this section, you should be able to:

- describe the structure and function of the larynx
- outline the physiology of speech generation.

Position

The larynx or 'voice box' extends from the root of the tongue and the hyoid bone to the trachea. It lies in front of the laryngopharynx at the level of the 3rd, 4th, 5th and 6th cervical vertebrae. Until puberty there is little difference in the size of the larynx between the sexes. Thereafter it grows larger in the male, which explains the prominence of the 'Adam's apple' and the generally deeper voice.

Structures associated with the larynx

Superiorly – the hyoid bone and the root of the tongue
Inferiorly – it is continuous with the trachea
Anteriorly – the muscles attached to the hyoid bone and the muscles of the neck
Posteriorly – the laryngopharynx and 3rd to 6th cervical vertebrae
Laterally – the lobes of the thyroid gland

Structure

Cartilages

The larynx is composed of several irregularly shaped cartilages attached to each other by ligaments and membranes. The main cartilages are:

- 1 thyroid cartilage
- 1 cricoid cartilage
- 2 arytenoid cartilages

} hyaline cartilage

- 1 epiglottis – elastic fibrocartilage.

The thyroid cartilage (Figs 10.6 and 10.7). This is the most prominent and consists of two flat pieces of hyaline cartilage, or *laminae*, fused anteriorly, forming the *laryngeal prominence* (Adam's apple). Immediately above the laryngeal prominence the laminae are separated, forming a V-shaped notch known as the *thyroid notch*. The thyroid cartilage is incomplete posteriorly and the posterior border of each lamina is extended to form two processes called the *superior* and *inferior cornu*.

The upper part of the thyroid cartilage is lined with stratified squamous epithelium like the larynx, and the lower part with ciliated columnar epithelium like the trachea. There are many muscles attached to its outer surface.

The cricoid cartilage (Fig. 10.5). This lies below the thyroid cartilage and is also composed of hyaline cartilage. It is shaped like a signet ring, completely encircling the larynx with the narrow part anteriorly and the broad part posteriorly. The broad posterior part articulates with the arytenoid cartilages above and with the inferior cornu of the thyroid cartilage below. It is lined with ciliated columnar epithelium and there are muscles and ligaments attached to its outer surface (Fig. 10.7). The lower border of the cricoid cartilage marks the end of the upper respiratory tract.

The arytenoid cartilages. These are two roughly pyramid-shaped hyaline cartilages situated on top of the broad part of the cricoid cartilage forming part of the posterior wall of the larynx. They give attachment to the vocal cords and to muscles and are lined with ciliated columnar epithelium.

The epiglottis. This is a leaf-shaped fibroelastic cartilage attached to the inner surface of the anterior wall of the thyroid cartilage immediately below the thyroid notch. It rises obliquely upwards behind the tongue and the body of the hyoid bone. It is covered with stratified squamous epithelium. If the larynx is likened to a box then the epiglottis acts as the lid; it closes off the larynx during swallowing, protecting the lungs from accidental inhalation of foreign objects.

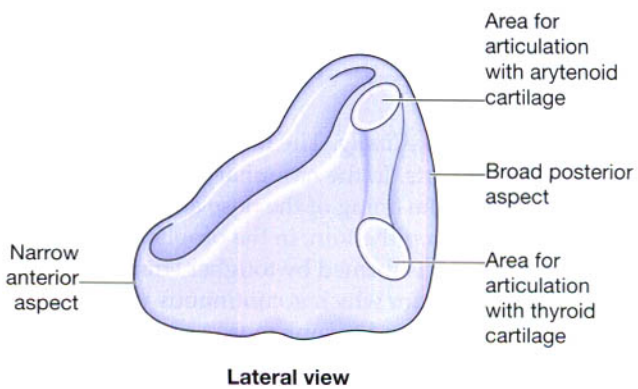


Figure 10.5 Cricoid cartilage.

Ligaments and membranes

There are several ligaments that attach the cartilages to each other and to the hyoid bone (Figs 10.6, 10.7 and 10.8).

Blood and nerve supply

Blood is supplied to the larynx by the superior and inferior laryngeal arteries and drained by the thyroid veins, which join the internal jugular vein.

The parasympathetic nerve supply is from the superior laryngeal and recurrent laryngeal nerves, which are branches of the vagus nerves, and the sympathetic nerves are from the superior cervical ganglia, one on each side. These provide the motor nerve supply to the muscles of the larynx and sensory fibres to the lining membrane.

Interior of the larynx

The *vocal cords* are two pale folds of mucous membrane with cord-like free edges which extend from the inner wall of the thyroid prominence anteriorly to the arytenoid cartilages posteriorly (Fig. 10.8).

When the muscles controlling the vocal cords are relaxed, the vocal cords open and the passageway for air coming up through the larynx is clear; the vocal cords are said to be *abducted* (Fig. 10.9A). The pitch of the sound produced by vibrating the vocal cords in this position is low. When the muscles controlling the vocal cords contract, the vocal cords are stretched out tightly across the larynx (Fig. 10.9B)—they are said to be *adducted*. When the vocal cords are stretched to this extent, and are vibrated by air passing through from the lungs, the sound produced is high pitched. The pitch of the voice is therefore determined by the tension applied to the vocal cords by the appropriate sets of muscles. When not in use, the vocal cords are adducted.

Functions

Production of sound. Sound has the properties of *pitch, volume* and *resonance*.

- Pitch of the voice depends upon the *length* and *tightness* of the cords. At puberty, the male vocal cords begin to grow longer, hence the lower pitch of the adult male voice.
- Volume of the voice depends upon the *force* with which the cords vibrate. The greater the force of expired air the more the cords vibrate and the louder the sound emitted.
- Resonance, or tone, is dependent upon the shape of the mouth, the position of the tongue and the lips, the facial muscles and the air in the paranasal sinuses.

Speech. This occurs during expiration when the sounds produced by the vocal cords are manipulated by the tongue, cheeks and lips.

Protection of the lower respiratory tract. During swallowing (deglutition) the larynx moves upwards, occluding the opening into it from the pharynx and the

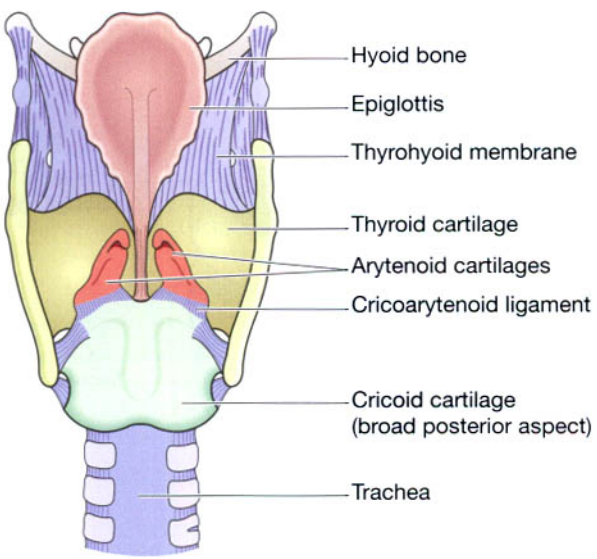


Figure 10.6 Larynx – viewed from behind.

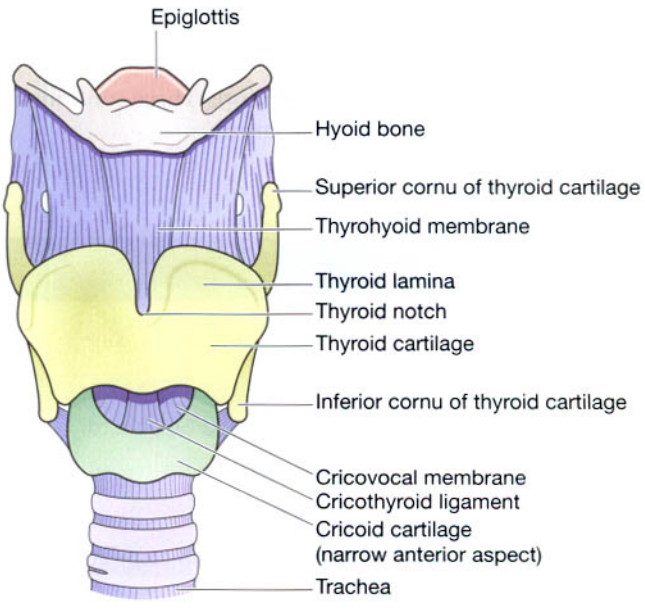


Figure 10.7 Larynx – viewed from the front.

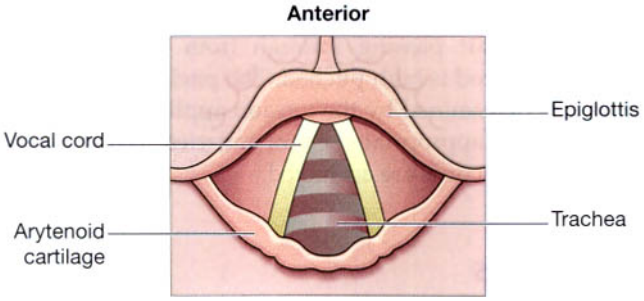


Figure 10.8 Interior of the larynx viewed from above.

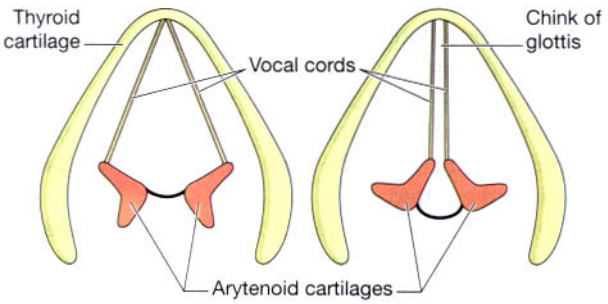


Figure 10.9 The extreme positions of the vocal cords.

hinged epiglottis closes over the larynx. This ensures that food passes into the oesophagus and not into the lower respiratory passages (p. 295).

Passageway for air. This is between the pharynx and trachea.

Humidifying, filtering and warming. These continue as inspired air travels through the larynx.

TRACHEA

Learning outcomes

After studying this section, you should be able to:

- describe the location of the trachea
- outline the structure of the trachea
- explain the functions of the trachea in respiration.

Position

The trachea or windpipe is a continuation of the larynx and extends downwards to about the level of the 5th thoracic vertebra where it divides (bifurcates) at the *carina* into the right and left bronchi, one bronchus going to each lung. It is approximately 10 to 11 cm long and lies mainly in the median plane in front of the oesophagus (Fig. 10.10).

Structures associated with the trachea (Fig. 10.11)

Superiorly	–	the larynx
Inferiorly	–	the right and left bronchi
Anteriorly	–	upper part: the isthmus of the thyroid gland lower part: the arch of the aorta and the sternum
Posteriorly	–	the oesophagus separates the trachea from the vertebral column
Laterally	–	the lungs and the lobes of the thyroid gland.

Structure

The trachea is composed of from 16 to 20 incomplete (C-shaped) rings of hyaline cartilages lying one above the other. The cartilages are incomplete posteriorly. Connective tissue and involuntary muscle join the cartilages and form the posterior wall where they are incomplete. The soft tissue posterior wall is in contact with the oesophagus (Fig. 10.10).

There are three layers of tissue which 'clothe' the cartilages of the trachea.

The outer layer. This consists of fibrous and elastic tissue and encloses the cartilages.

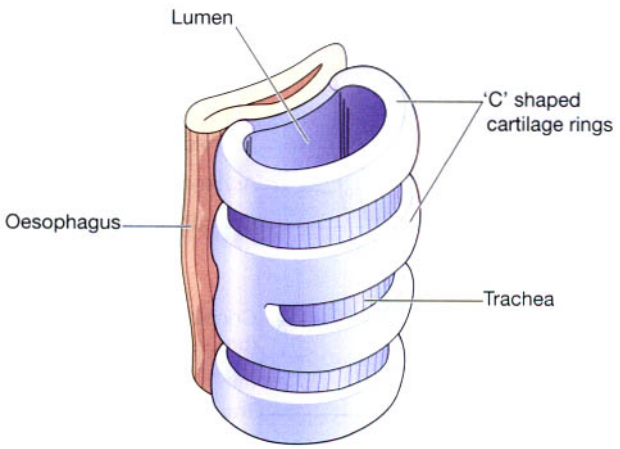


Figure 10.10 The relationship of the trachea to the oesophagus.

The middle layer. This consists of cartilages and bands of smooth muscle that wind round the trachea in a helical arrangement. There is some areolar tissue, containing blood and lymph vessels and autonomic nerves.

The inner lining. This consists of ciliated columnar epithelium, containing mucus-secreting goblet cells.

Blood and nerve supply, lymph drainage

The arterial blood supply. This is mainly by the inferior thyroid and bronchial arteries and the *venous return* is by the inferior thyroid veins into the brachiocephalic veins.

The *nerve supply.* This is by parasympathetic and sympathetic fibres. Parasympathetic supply is by the recurrent laryngeal nerves and other branches of the vagi. Sympathetic supply is by nerves from the sympathetic ganglia.

Lymph. Lymph from the respiratory passages passes through lymph nodes situated round the trachea and in the *carina*, the area where it divides into two bronchi.

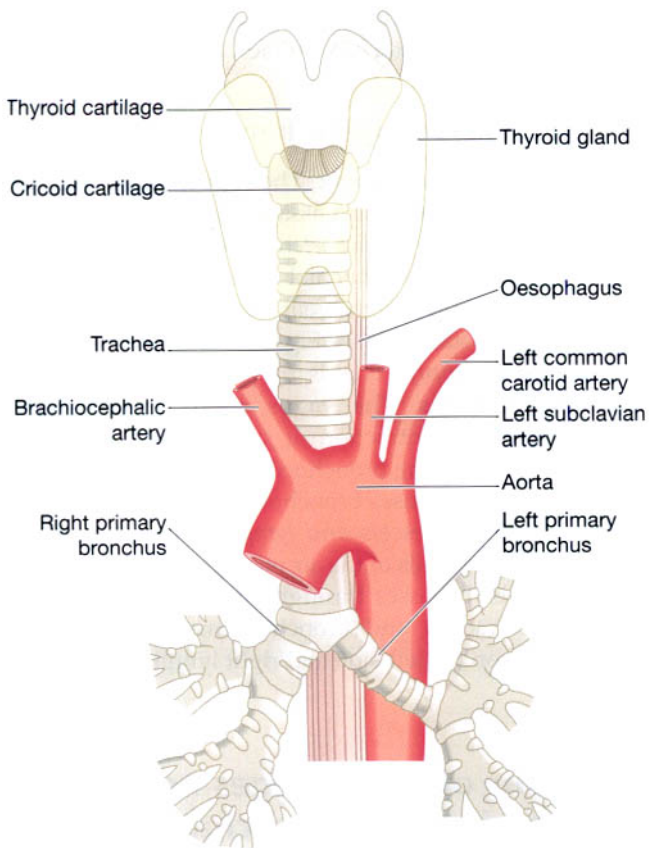


Figure 10.11 The trachea and some of its associated structures.

Functions

Support and patency. The arrangement of cartilage and elastic tissue prevents kinking and obstruction of the airway as the head and neck move. The absence of cartilage posteriorly allows the trachea to dilate and constrict in response to nerve stimulation, and for indentation as the oesophagus distends during swallowing. The cartilages prevent collapse of the tube when the internal pressure is less than intrathoracic pressure, i.e. at the end of forced expiration.

Mucociliary escalator. This is the synchronous and regular beating of the cilia of the mucous membrane lining that wafts mucus with adherent particles upwards towards the larynx where it is swallowed or expectorated (Fig. 10.12).

Cough reflex. Nerve endings in the larynx, trachea and bronchi are sensitive to irritation that generates nerve impulses which are conducted by the vagus nerves to the respiratory centre in the brain stem (p. 256). The reflex motor response is deep inspiration followed by closure of the glottis. The abdominal and respiratory muscles then contract and suddenly the air is released under pressure expelling mucus and/or foreign material from the mouth.

Warming, humidifying and filtering of air. These continue as in the nose, although air is normally saturated and at body temperature when it reaches the trachea.

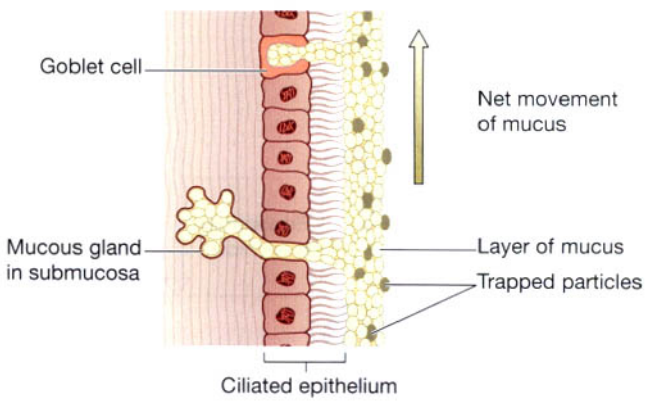


Figure 10.12 Microscopic view of ciliated mucous membrane.

BRONCHI AND SMALLER AIR PASSAGES

Learning outcomes

After studying this section, you should be able to:

- name the air passage of the bronchial tree in descending order of size
- describe the structure and changing functions of the different levels of airway.

The two primary bronchi are formed when the trachea divides, i.e. about the level of the 5th thoracic vertebra (Fig. 10.13).

The right bronchus. This is wider, shorter and more vertical than the left bronchus and is therefore the more likely of the two to become obstructed by an inhaled foreign body. It is approximately 2.5 cm long. After entering the right lung at the hilum it divides into three branches, one to each lobe. Each branch then subdivides into numerous smaller branches.

The left bronchus. This is about 5 cm long and is narrower than the right. After entering the lung at the hilum it divides into two branches, one to each lobe. Each branch then subdivides into progressively smaller tubes within the lung substance.

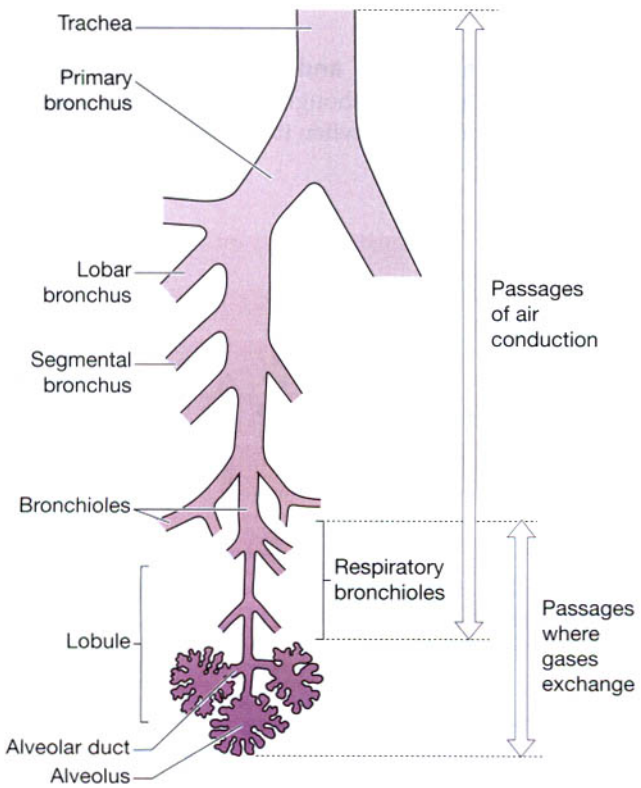


Figure 10.13 Lower respiratory tract.

Bronchi and bronchioles

Structure

The bronchi are composed of the same tissues as the trachea. They are lined with ciliated columnar epithelium. The bronchi progressively subdivide into *bronchioles* (Fig. 10.13), *terminal bronchioles, respiratory bronchioles, alveolar ducts* and finally, *alveoli*. Towards the distal end of the bronchi the cartilages become irregular in shape and are absent at bronchiolar level. In the absence of cartilage the smooth muscle in the walls of the bronchioles becomes thicker and is responsive to autonomic nerve stimulation and irritation. Ciliated columnar mucous membrane changes gradually to non-ciliated cuboidal-shaped cells in the distal bronchioles.

Blood and nerve supply, lymph drainage

The arterial blood supply. The supply to the walls of the bronchi and smaller air passages is through branches of the *right and left bronchial arteries* and the *venous return* is mainly through the bronchial veins. On the right side they empty into the azygos vein and on the left into the superior intercostal vein (see Figs 5.42 and 5.43, p. 103)

The nerve supply. This is by parasympathetic and sympathetic nerves. The vagus nerves (parasympathetic) stimulate contraction of smooth muscle in the bronchial tree, causing bronchoconstriction, and sympathetic stimulation causes bronchodilatation (Ch. 7).

The lymphatic vessels and lymph nodes. Lymph is drained from the walls of the air passages in a network of lymph vessels. It passes through lymph nodes situated around the trachea and bronchial tree then into the thoracic duct on the left side and right lymphatic duct on the other.

Functions of air passages not involved in gaseous exchange

Control of air entry. The diameter of the respiratory passages may be altered by contraction or relaxation of

the involuntary muscles in their walls, thus regulating the volume of air entering the lungs. These changes are controlled by the autonomic nerve supply: parasympathetic stimulation causes constriction and sympathetic stimulation causes dilatation (p. 173).

The following functions continue as in the upper airways:

- warming and humidifying
- support and patency
- removal of particulate matter
- cough reflex.

Respiratory bronchioles and alveoli

Structure

Lobules are the blind ends of the respiratory tract distal to the terminal bronchioles, consisting of: *respiratory bronchioles, alveolar ducts* and *alveoli* (tiny air sacs) (Fig. 10.13). It is in these structures that the process of gas exchange occurs. The walls gradually become thinner until muscle and connective tissue fade out leaving a single layer of simple squamous epithelial cells in the alveolar ducts and alveoli. These distal respiratory passages are supported by a loose network of elastic connective tissue in which macrophages, fibroblasts, nerves and blood and lymph vessels are embedded. The alveoli are surrounded by a network of capillaries. The exchange of gases during respiration takes place across two membranes, the alveolar and capillary membranes.

Interspersed between the squamous cells are other cells that secrete *surfactant*, a phospholipid fluid which prevents the alveoli from drying out. In addition, surfactant reduces surface tension and prevents alveolar walls collapsing during expiration. Secretion of surfactant into the distal air passages and alveoli begins about the 35th week of fetal life. Its presence in newborn babies facilitates expansion of the lungs and the establishment of respiration. It may not be present in sufficient amounts in the immature lungs of premature babies, causing difficulty in establishing respiration.

Functions of respiratory bronchioles and alveoli

External respiration. (See p. 255.)

Defence against microbes. At this level, ciliated epithelium, goblet cells and mucus are no longer present. Defence relies on protective cells present within the lung tissue. These include lymphocytes and plasma cells, which produce antibodies in the presence of antigens, and macrophages and polymorphonuclear lymphocytes, which are phagocytic. These cells are most active in the distal air passages where ciliated epithelium has been replaced by flattened cells.

Warming and humidifying. These continue as in the upper airways. Inhalation of dry or inadequately humidified air over a period of time causes irritation of the mucosa and facilitates the establishment of pathogenic microbes.

LUNGS

Learning outcomes

After studying this section, you should be able to:

- describe the location and gross anatomy of the lungs
- identify the functions of the pleura
- describe the pulmonary blood supply.

Position and associated structures

(Fig. 10.14)

There are two lungs, one lying on each side of the midline in the thoracic cavity. They are cone-shaped and are described as having an *apex*, a *base, costal surface* and *medial surface*.

The apex. This is rounded and rises into the root of the neck, about 25 mm (1 inch) above the level of the middle third of the clavicle. The structures associated with it are the first rib and the blood vessels and nerves in the root of the neck.

The base. This is concave and semilunar in shape and is closely associated with the thoracic surface of the diaphragm.

The costal surface. This surface is convex and is closely associated with the costal cartilages, the ribs and the intercostal muscles.

The medial surface. This surface is concave and has a roughly triangular-shaped area, called the *hilum*, at the level of the 5th, 6th and 7th thoracic vertebrae. Structures which form the *root of the lung* enter and leave at the hilum. These include the primary bronchus, the

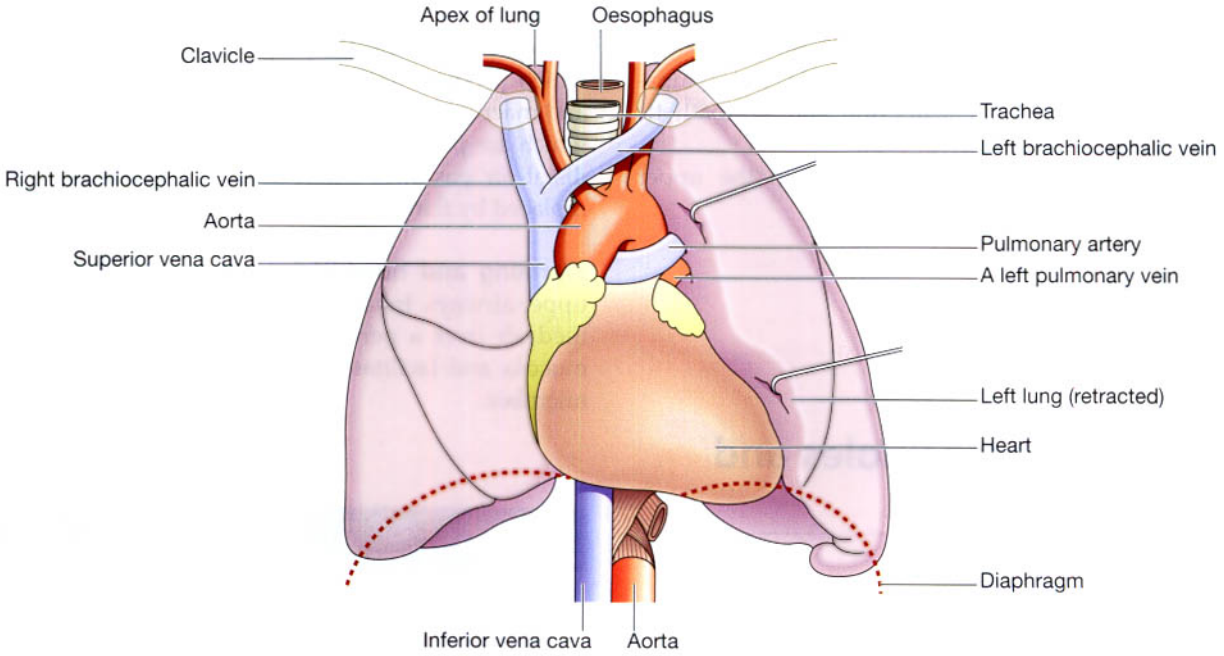


Figure 10.14 Organs associated with the lungs.

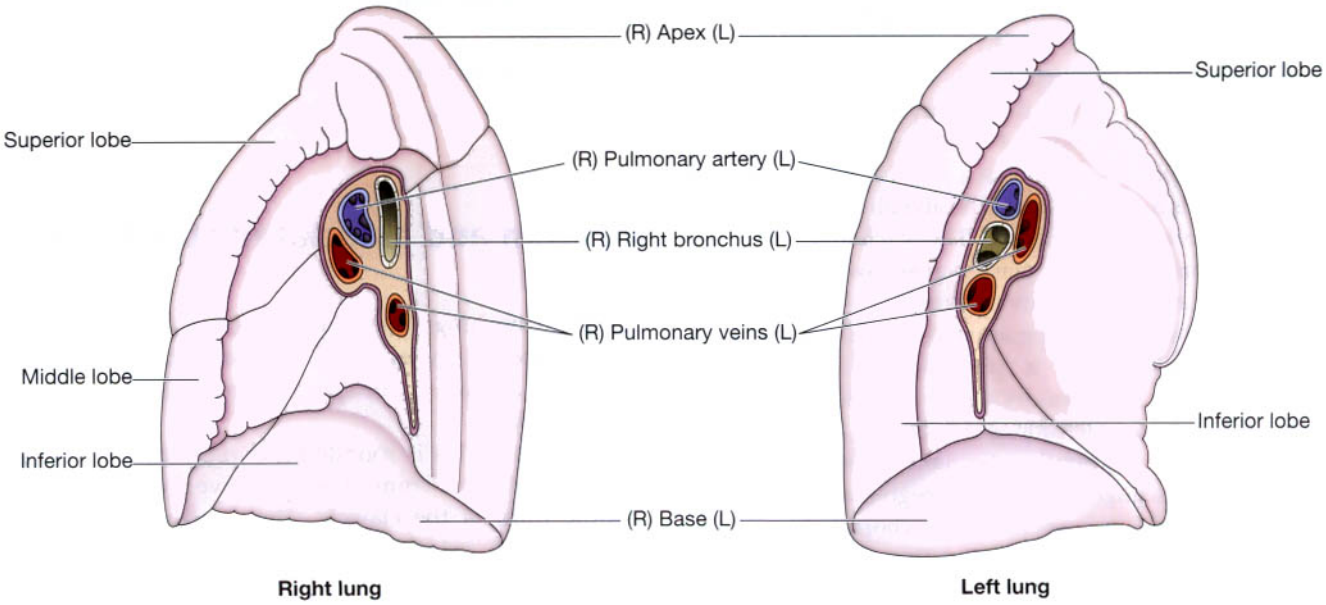


Figure 10.15 The lobes of the lungs and vessels/airways of each hilum – medial views.

pulmonary artery supplying the lung and the two pulmonary veins draining it, the bronchial artery and veins, and the lymphatic and nerve supply (Fig. 10.15).

The area between the lungs is the *mediastinum*. It is occupied by the heart, great vessels, trachea, right and left bronchi, oesophagus, lymph nodes, lymph vessels and nerves.

Organisation of the lungs

The *right lung* is divided into three distinct lobes: superior, middle and inferior.

The *left lung* is smaller as the heart is situated left of the midline. It is divided into only two lobes: superior and inferior.

Pleura and pleural cavity

The pleura consists of a closed sac of serous membrane (one for each lung) which contains a small amount of serous fluid. The lung is invaginated into this sac so that it forms two layers: one adheres to the lung and the other to the wall of the thoracic cavity (Figs 10.1 and 10.16).

The visceral pleura. This is adherent to the lung, covering each lobe and passing into the fissures which separate them.

The parietal pleura. This is adherent to the inside of the chest wall and the thoracic surface of the diaphragm. It remains detached from the adjacent structures in the mediastinum and is continuous with the visceral pleura round the edges of the hilum.

The *pleural cavity.* This is only a potential space. In health, the two layers of pleura are separated by only a thin film of serous fluid which allows them to glide over each other, preventing friction between them during breathing. The serous fluid is secreted by the epithelial cells of the membrane.

The two layers of pleura, with serous fluid between them, behave in the same way as two pieces of glass separated by a thin film of water. They glide over each other easily but can be pulled apart only with difficulty, because of the surface tension between the membranes and the fluid. If either layer of pleura is punctured, the underlying lung collapses due to its inherent property of elastic recoil.

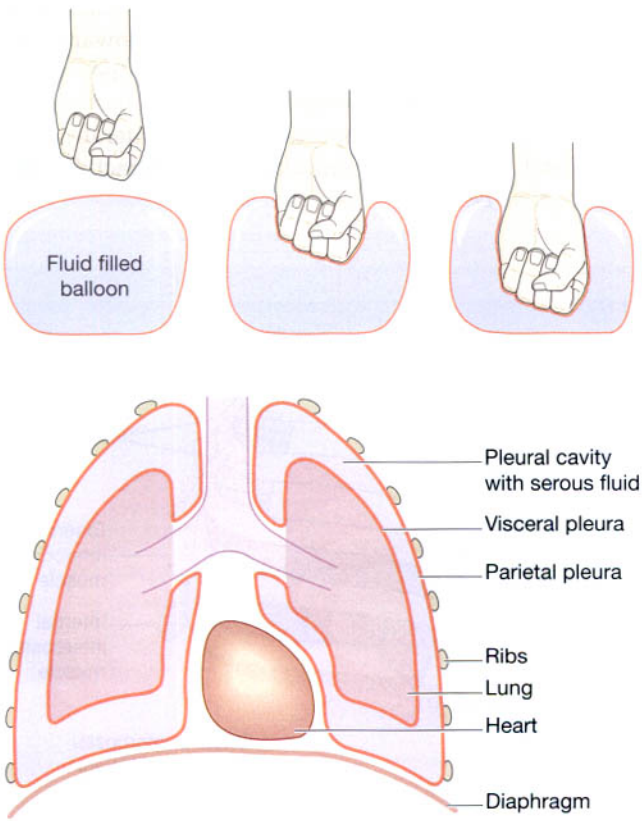


Figure 10.16 The relationship of the pleura to the lungs.

Interior of the lungs

The lungs are composed of the bronchi and smaller air passages, alveoli, connective tissue, blood vessels, lymph vessels and nerves. The left lung is divided into two lobes and the right, into three (Fig. 10.15). Each lobe is made up of a large number of lobules.

Pulmonary blood supply (Fig. 10.17)

The *pulmonary artery* divides into two, one branch conveying *deoxygenated blood* to each lung. Within the lungs each pulmonary artery divides into many branches which eventually end in a dense capillary network around the walls of the alveoli (Fig. 10.18). The walls of the alveoli and those of the capillaries each consist of only one layer of flattened epithelial cells. The exchange of gases between air in the alveoli and blood in the capillaries takes place across these two very fine membranes. The pulmonary capillaries join up, eventually

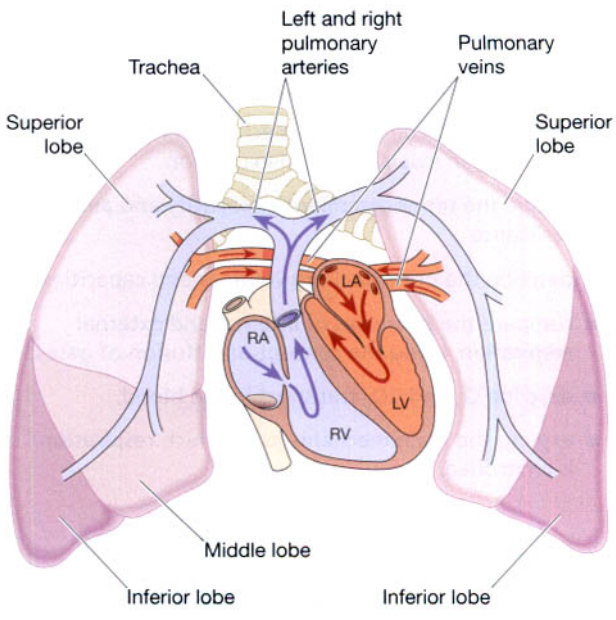


Figure 10.17 The flow of blood between heart and lungs.

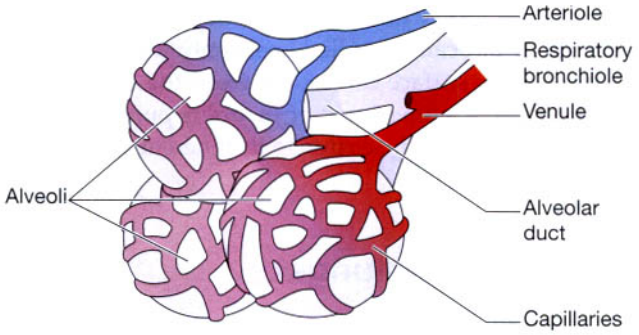


Figure 10.18 The capillary network surrounding the alveoli.

becoming *two pulmonary veins* in each lung. They leave the lungs at the hilum and convey *oxygenated blood* to the left atrium of the heart. The innumerable blood capillaries and blood vessels in the lungs are supported by connective tissue.

The blood supply to the respiratory passages, lymphatic drainage and nerve supply has already been described (p. 248).

RESPIRATION

Learning outcomes

After studying this section, you should be able to:

- describe the actions of the main muscles of respiration during ventilation
- compare and contrast the mechanical events occurring in inspiration and expiration
- define the terms compliance, elasticity and airflow resistance
- describe the principal lung volumes and capacities
- compare the processes of internal and external respiration, using the concept of diffusion of gases
- describe O_2 and CO_2 transport in the blood
- explain the main mechanisms by which respiration is controlled.

Inflation and deflation of the lungs occurring with each breath ensures that regular exchange of gases takes place between the alveoli and the external air.

Muscles of respiration

The expansion of the chest during inspiration occurs as a result of muscular activity, partly voluntary and partly involuntary. The main muscles of respiration in normal quiet breathing are the *intercostal muscles* and the *diaphragm*. During difficult or deep breathing they are assisted by the muscles of the neck, shoulders and abdomen.

Intercostal muscles

There are 11 pairs of intercostal muscles that occupy the spaces between the 12 pairs of ribs. They are arranged in two layers, the external and internal intercostal muscles (Fig. 10.19).

The external intercostal muscle fibres. These extend in a downwards and forwards direction from the lower border of the rib above to the upper border of the rib below.

The internal intercostal muscle fibres. These extend in a downwards and backwards direction from the lower border of the rib above to the upper border of the rib below, crossing the external intercostal muscle fibres at right angles.

The first rib is fixed. Therefore, when the intercostal muscles contract they pull all the other ribs towards the first rib. Because of the shape of the ribs they move outwards when pulled upwards. In this way the thoracic cavity is enlarged anteroposteriorly and laterally. The intercostal muscles are stimulated to contract by the *intercostal nerves*.

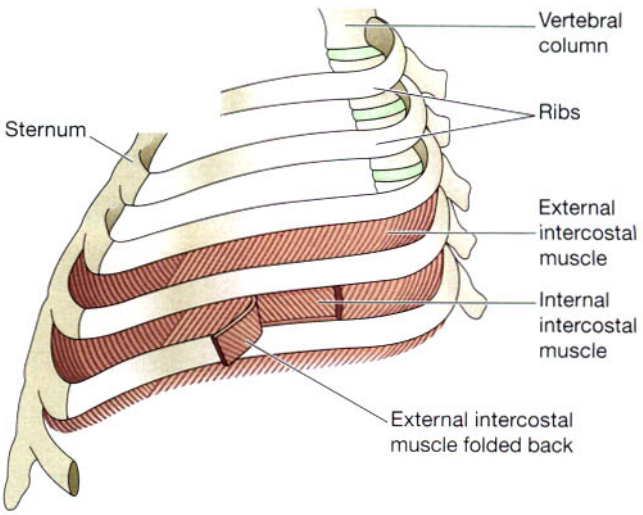


Figure 10.19 The intercostal muscles and the bones of the thorax.

Diaphragm

The diaphragm is a dome-shaped structure separating the thoracic and abdominal cavities. It forms the floor of the thoracic cavity and the roof of the abdominal cavity and consists of a central tendon from which muscle fibres radiate to be attached to the lower ribs and sternum and to the vertebral column by two crura. When the muscle of the diaphragm is relaxed, the central tendon is at the level of the 8th thoracic vertebra (Fig. 10.20). When it contracts, its muscle fibres shorten and the central tendon is pulled downwards to the level of the 9th thoracic vertebra, enlarging the thoracic cavity in length. This decreases pressure in the thoracic cavity and increases it in the abdominal and pelvic cavities. The diaphragm is supplied by the *phrenic nerves*.

The intercostal muscles and the diaphragm contract *simultaneously* ensuring the enlargement of the thoracic cavity in all directions, that is from back to front, side to side and top to bottom (Fig. 10.21).

Cycle of respiration

This occurs 12 to 15 times per minute and consists of three phases:

- inspiration
- expiration
- pause.

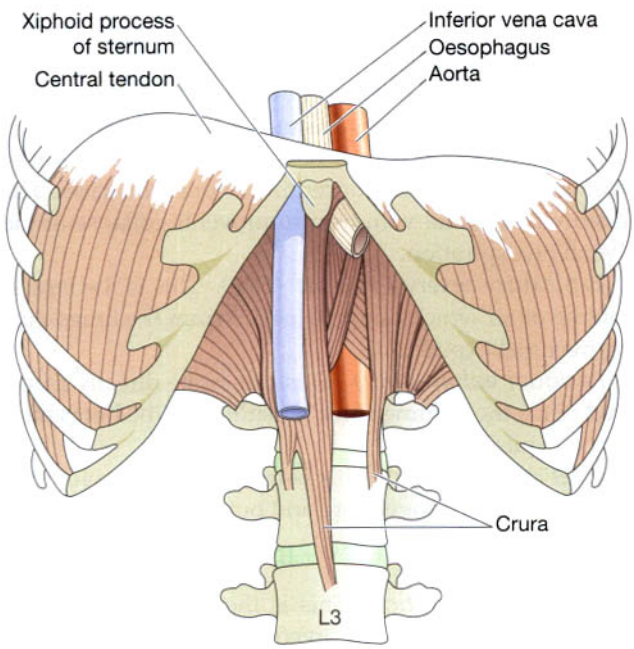


Figure 10.20 The diaphragm.

As described previously, the visceral pleura is adherent to the lungs and the parietal pleura to the inner wall of the thorax and to the diaphragm. Between them there is a thin film of serous fluid (p. 251).

Inspiration

When the capacity of the thoracic cavity is increased by simultaneous contraction of the intercostal muscles and the diaphragm, the parietal pleura moves with the walls of the thorax and the diaphragm. This reduces the pressure in the pleural cavity to a level considerably lower than atmospheric pressure. The visceral pleura follows the parietal pleura pulling the lung with it. This stretches the lungs and the pressure within the alveoli and in the air passages falls, drawing air into the lungs in an attempt to equalise the atmospheric and alveolar air pressures.

The process of inspiration is *active*, as it requires expenditure of energy for muscle contraction. The negative pressure created in the thoracic cavity aids venous return to the heart and is known as the *respiratory pump*.

Expiration

Relaxation of the intercostal muscles and the diaphragm results in downward and inward movement of the rib cage (Fig. 10.21) and elastic recoil of the lungs. As this occurs, pressure inside the lungs exceeds that in the atmosphere and therefore air is expelled from the respiratory tract. The lungs still contain some air and are prevented from complete collapse by the intact pleura. This process is *passive* as it does not require the expenditure of energy.

After expiration, there is a *pause* before the next cycle begins.

Physiological variables affecting respiration

Elasticity. Elasticity is the term used to describe the ability of the lung to return to its normal shape after each breath. Loss of elasticity of the connective tissue in the lungs necessitates forced expiration and increased effort on inspiration.

Compliance. This is a measure of the distensibility of the lungs, i.e. the effort required to inflate the alveoli. When compliance is low the effort needed to inflate the lungs is greater than normal, e.g. in some diseases where elasticity is reduced or when insufficient surfactant is present. It should be noted that compliance and elasticity are opposing forces.

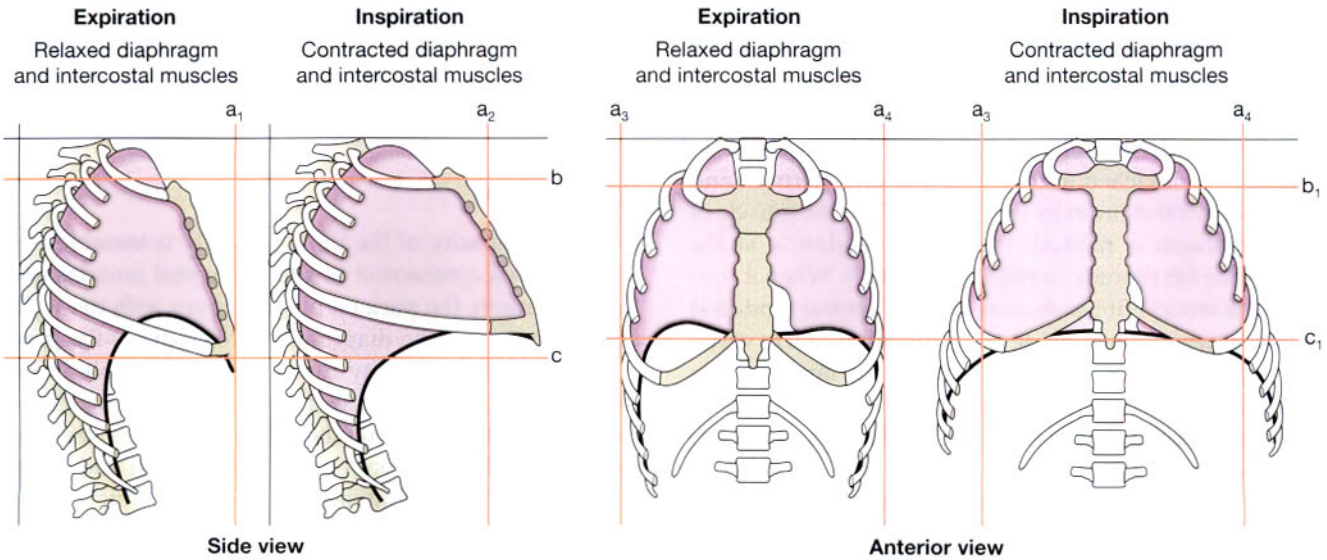


Figure 10.21 The changes in capacity of the thoracic cavity and the lungs during breathing.

Airflow resistance. When this is increased, e.g. in bronchoconstriction, more respiratory effort is required to inflate the lungs.

Lung volumes and capacities (Fig. 10.22)

In normal quiet breathing there are about 15 complete respiratory cycles per minute. The lungs and the air passages are never empty and, as the exchange of gases takes place only across the walls of the alveolar ducts and alveoli, the remaining capacity of the respiratory passages is called the *anatomical dead space* (about 150 ml).

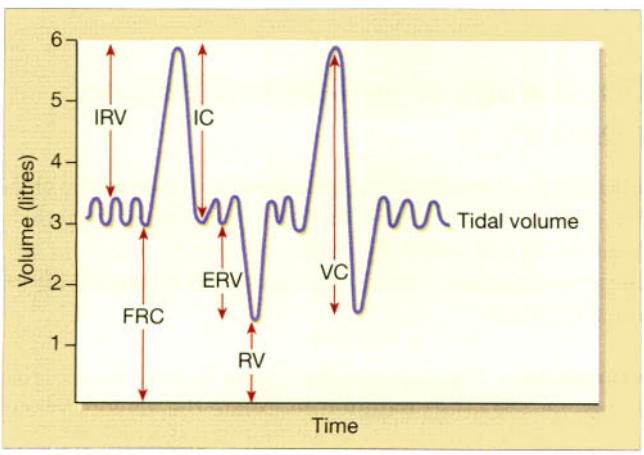


Figure 10.22 Lung volumes and capacities: IRV = inspiratory reserve volume; IC = inspiratory capacity; FRC = functional residual capacity; ERV = expiratory reserve volume; RV = residual volume; VC = vital capacity.

Tidal volume (TV). This is the amount of air which passes into and out of the lungs during each cycle of quiet breathing (about 500 ml).

Inspiratory reserve volume (IRV). This is the extra volume of air that can be inhaled into the lungs during maximal inspiration.

Inspiratory capacity (IC). This is the amount of air that can be inspired with maximum effort. It consists of the tidal volume (500 ml) plus the inspiratory reserve volume.

Functional residual capacity (FRC). This is the amount of air remaining in the air passages and alveoli at the end of quiet expiration. Tidal air mixes with this air, causing relatively small changes in the composition of alveolar air. As blood flows continuously through the pulmonary capillaries this means that the interchange of gases is not interrupted between breaths, preventing marked changes in the concentration of blood gases. The functional residual volume also prevents collapse of the alveoli on expiration.

Expiratory reserve volume (ERV). This is the largest volume of air which can be expelled from the lungs during maximal expiration.

Residual volume (RV). This cannot be directly measured but is the volume of air remaining in the lungs after forced expiration.

Vital capacity (VC). This is the maximum volume of air which can be moved into and out of the lungs:

VC = Tidal volume + IRV + ERV

Alveolar ventilation. This is the volume of air that moves into and out of the alveoli per minute. It is equal to the tidal volume minus the anatomical dead space, multiplied by the respiratory rate:

Alveolar ventilation = (TV – anatomical dead space) × respiratory rate
= (500 – 150) ml × 15 per minute
= 5.25 litres per minute

Lung function tests are carried out to determine respiratory function and are based on the parameters outlined above. Results of these tests can help in diagnosis and monitoring of respiratory disorders.

Composition of air

Atmospheric pressure at sea level is 101.3 kilopascals (kPa)* or 760 mmHg. With the increase in height above sea level, atmospheric pressure is progressively reduced and at 5500 m, about two-thirds the height of Mount Everest (8850 m), it is about half that at sea level. Under water, pressure increases by approximately 1 atmosphere per 10 m below sea level.

Air is a mixture of gases: nitrogen, oxygen, carbon dioxide, water vapour and small quantities of inert gases. The percentage of each is listed in Table 10.1. Each gas in the mixture exerts a part of the total pressure proportional to its concentration, i.e. the *partial pressure* (Table 10.2). This is denoted as, e.g. PO_2, PCO_2.

Alveolar air

The composition of alveolar air remains fairly constant and is different from atmospheric air. It is saturated with water vapour and contains more carbon dioxide, and less oxygen. Saturation with water vapour provides 6.3 kPa (47 mmHg) thus reducing the partial pressure of all the other gases present. Gaseous exchange between the alveoli and the bloodstream (*external respiration*) is a continuous process, as the alveoli are never empty, so it is independent of the respiratory cycle. During each inspiration only some of the alveolar gases are exchanged.

Table 10.1 The composition of inspired and expired air

	Inspired air %	Expired air %
Oxygen	21	16
Carbon dioxide	0.04	4
Nitrogen and rare gases	78	78
Water vapour	Variable	Saturated

*1 mmHg = 133.3 Pa = 0.133 kPa
1 kPa = 7.5 mmHg

Expired air

This is a mixture of alveolar air and atmospheric air in the dead space. Its composition is shown in Table 10.1.

Diffusion of gases

Exchange of gases occurs when a difference in partial pressure exists across semipermeable membranes. Gases move by diffusion from the higher concentration to the lower until equilibrium is established (p. 26). Atmospheric nitrogen is not used by the body so its partial pressure remains unchanged and is the same in inspired and expired air, alveolar air and in the blood.

External respiration

This is exchange of gases by diffusion between the alveoli and the blood. Each alveolar wall is one cell thick and is surrounded by a network of tiny capillaries (the walls of which are also only one cell thick). The total area for gas exchange in the lungs is 70 to 80 square metres. Venous blood arriving at the lungs has travelled from all the active tissues of the body, and contains high levels of CO_2 and low levels of O_2. Carbon dioxide diffuses from venous blood down its concentration gradient into the alveoli until equilibrium with alveolar air is reached. By the same process, oxygen diffuses from the alveoli into the blood. The slow flow of blood through the capillaries increases the time available for diffusion to occur. When blood leaves the alveolar capillaries, the oxygen and carbon dioxide concentrations are in equilibrium with those of alveolar air (Fig. 10.23).

Internal respiration

This is exchange of gases by diffusion between blood in the capillaries and the body cells. Gaseous exchange does

Table 10.2 Partial pressures of gases

Gas	Alveolar air kPa	Alveolar air mmHg	Deoxygenated blood kPa	Deoxygenated blood mmHg	Oxygenated blood kPa	Oxygenated blood mmHg
Oxygen	13.3	100	5.3	40	13.3	100
Carbon dioxide	5.3	40	5.8	44	5.3	40
Nitrogen and other inert gases	76.4	573	76.4	573	76.4	573
Water vapour	6.3	47				
	101.3	760				

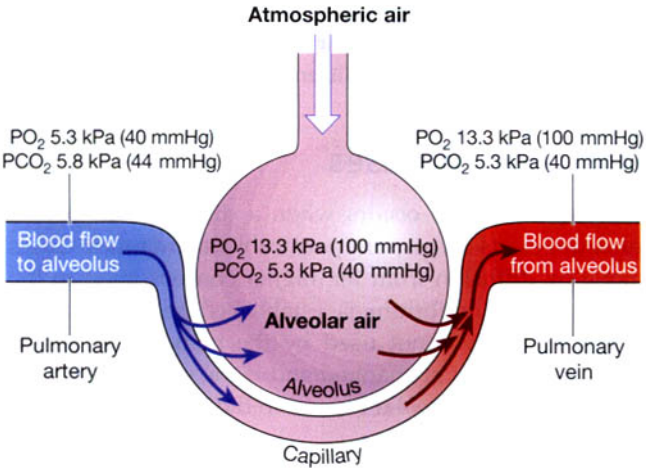


Figure 10.23 External respiration: exchange of gases between alveolar air and capillary blood.

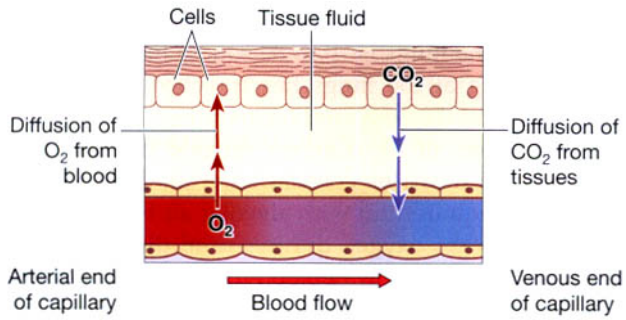


Figure 10.24 Internal respiration: exchange of gases between capillary blood and tissue cells.

not occur across the walls of the arteries carrying blood from the heart to the tissues, because their walls are too thick. PO_2 of blood arriving at the capillary bed is therefore the same as blood leaving the lungs. Blood arriving at the tissues has been cleansed of its CO_2 and saturated with O_2 during its passage through the lungs, and therefore has a higher PO_2 and a lower PCO_2 than the tissues. This creates concentration gradients between the blood and the tissues, and gaseous exchange therefore occurs (Fig. 10.24). O_2 diffuses from the bloodstream through the capillary wall into the tissues. CO_2 diffuses from the cells into the extracellular fluid then into the bloodstream towards the venous end of the capillary.

Transport of gases in the bloodstream

Transport of blood oxygen and carbon dioxide is essential for internal respiration to occur.

Oxygen

Oxygen is carried in the blood:

- in chemical combination with haemoglobin as *oxyhaemoglobin* (98.5% of blood O_2)
- in solution in plasma water (1.5% of blood O_2).

Oxyhaemoglobin is an unstable compound that under certain conditions readily dissociates releasing oxygen. Factors that increase dissociation include raised carbon dioxide content of tissue fluid, raised temperature and 2,3-diphosphoglycerate (2,3-DPG is a substance present in red blood cells). In active tissues there is increased production of carbon dioxide and heat which leads to increased release of oxygen. In this way oxygen is available to tissues in greatest need. When oxygen leaves the erythrocyte, the deoxygenated haemoglobin turns purplish in colour.

Carbon dioxide

Carbon dioxide is one of the waste products of metabolism. It is excreted by the lungs and is transported by three mechanisms:

- most of it is in the form of bicarbonate ions (HCO_3^-) in the plasma (70% of blood CO_2)
- some is dissolved in the plasma (7% of blood CO_2)
- some is carried in erythrocytes, loosely combined with haemoglobin as *carbaminohaemoglobin* (23% of blood CO_2).

Control of respiration

Control of respiration is normally involuntary. Voluntary control is exerted during activities such as speaking and singing but is overridden if blood CO_2 rises (hypercapnia).

The respiratory centre

This is formed by groups of nerve cells that control the rate and depth of respiration (Fig. 10.25). They are situated in the brain stem, in the *medulla oblongata* and the *pons*. The interrelationship between these groups of cells is complex. In the medulla there are *inspiratory neurones* and *expiratory neurones*. Neurones in the *pneumotaxic* and *apneustic centres*, situated in the pons, influence the inspiratory and expiratory neurones of the medulla.

Motor impulses leaving the respiratory centre pass in the *phrenic* and *intercostal nerves* to the diaphragm and intercostal muscles respectively.

Chemoreceptors

These are receptors that respond to changes in the partial pressures of oxygen and carbon dioxide in the blood and cerebrospinal fluid. They are located centrally and peripherally.

Central chemoreceptors. These are on the surface of the medulla oblongata and are bathed in cerebrospinal fluid. When the arterial PCO_2 rises (hypercapnia), even slightly, the central chemoreceptors respond by stimulating the respiratory centre, increasing ventilation of the lungs and reducing arterial PCO_2. The sensitivity of the central chemoreceptors to raised arterial PCO_2 is the most important factor in maintaining homeostasis of blood gases in health. A small reduction in PO_2 (hypoxaemia) has the same, but less pronounced effect, but a substantial reduction has a depressing effect.

Peripheral chemoreceptors. These are situated in the arch of the aorta and in the carotid bodies (Fig. 10.25). They are more sensitive to small rises in arterial PCO_2 than to similarly low arterial PO_2 levels. Nerve impulses, generated in the peripheral chemoreceptors, are conveyed by the *glossopharyngeal* and *vagus nerves* to the medulla and stimulate the respiratory centre. The rate and depth of breathing are then increased. An increase in blood acidity (decreased pH or raised $[H^+]$) stimulates the peripheral chemoreceptors, resulting in increased ventilation, increased CO_2 excretion and increased blood pH.

Other factors that influence respiration

Breathing may be modified by the higher centres in the brain by:

- speech, singing
- emotional displays, e.g. crying, laughing, fear
- drugs, e.g. sedatives, alcohol
- sleep.

Temperature influences breathing. In fever respiration is increased due to increased metabolic rate while in hypothermia it is depressed, as is metabolism. Temporary changes in respiration occur in swallowing, sneezing and coughing.

The *Hering–Breuer reflex* prevents overinflation of the lungs. Stretch receptors situated in the thoracic wall generate nerve inhibitory impulses when the lungs have inflated. They travel via the vagus nerves to the respiratory centre.

Normally, quiet breathing is adequate to maintain arterial PO_2 and PCO_2 levels; however, on strenous exercise, both the rate and depth of breathing increase, increasing oxygen uptake and carbon dioxide excretion in order to meet increased needs and so maintain homeostasis. When intense respiratory effort is required, the *accessory muscles of respiration* are used. The most important is the *sternocleidomastoid* (Fig. 18.1). Contraction of these muscles in addition to the diaphragm and intercostal muscles ensures the maximum increase in the capacity of the thoracic cavity.

Effective control of respiration enables the body to maintain homeostasis of blood gases over a wide range of physiological, environmental and pathological conditions.

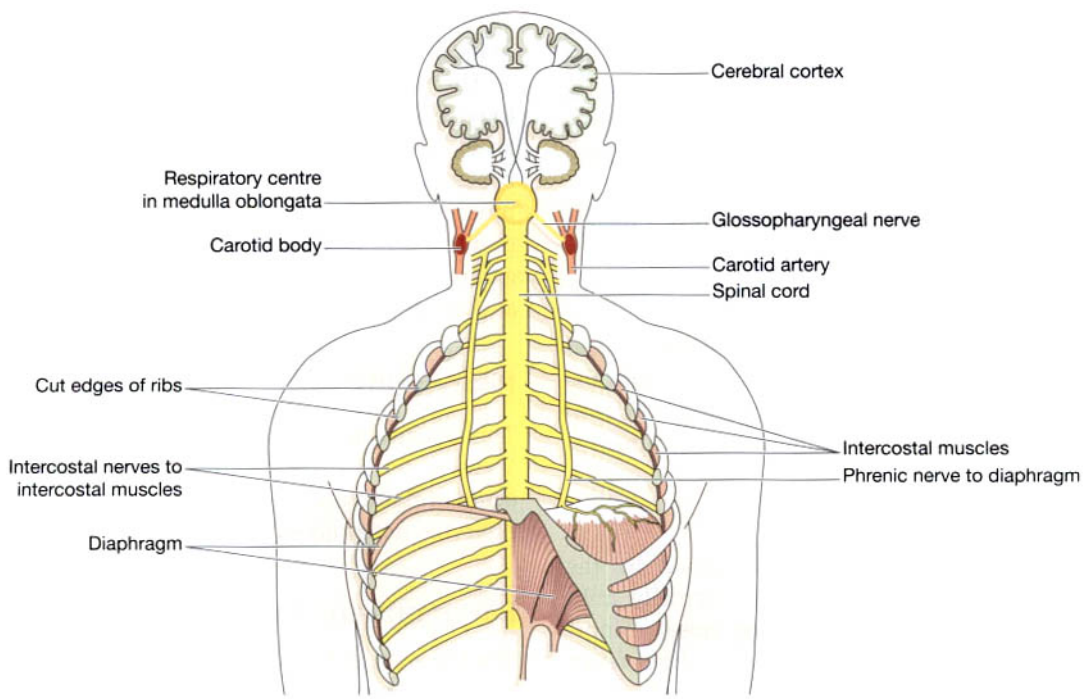


Figure 10.25 Some of the nerves involved in control of respiration.

DISORDERS OF THE UPPER RESPIRATORY TRACT

Learning outcomes

After studying this section, you should be able to:

- describe the main inflammatory and infectious disorders of the upper respiratory tract
- outline the main tumours of the upper respiratory tract.

Infectious and inflammatory disorders

Inflammation of the upper respiratory tract can be caused by inhaling irritants, but is commonly due to infection. Such infections are usually caused by viruses that lower the resistance of the respiratory tract to other infections. This allows bacteria dormant in the tract to invade the tissues. Such infections are a threat to life only if:

- they spread to the lungs or other organs
- inflammatory swelling and exudate block the airway.

Microbes are usually spread by droplet infection, in dust or by contaminated equipment and dressings. If not completely resolved, acute infection may become chronic.

Viruses enter host cells and replicate inside them, where they are protected both from the body's own defences and from many drug treatments. Interferons secreted by lymphocytes provide some degree of protection against viruses by limiting their ability to replicate (p. 374).

Viral infections cause acute inflammation of mucous membrane, leading to tissue congestion and profuse exudate of watery fluid. Secondary infection by bacteria usually results in purulent discharge.

Viral infections commonly cause severe illness and sometimes death in infants, young children and the elderly. In adults influenza is an incapacitating condition but is rarely fatal unless infection spreads to the lungs.

Common cold and influenza

The common cold (coryza) is usually caused by the rhinoviruses and is a highly infectious, normally mild illness characterised mainly by a runny nose (rhinorrhoea), sneezing, sore throat and sometimes slight fever. Normally a cold runs its course over a few days. Influenza is caused by a different group of viruses and produces far more severe symptoms than a cold, including very high temperatures and muscle pains; complete recovery can take weeks and secondary bacterial infections are more common than with a simple cold.

Sinusitis

This is usually caused by spread of microbes from the nose and pharynx to the mucous membrane lining the paranasal sinuses in maxillary, sphenoidal, ethmoidal and frontal bones. The primary viral infection is usually followed by bacterial infection, e.g. *Streptococcus pyogenes, Streptococcus pneumoniae, Staphylococcus aureus*. The congested mucosa may block the openings between the nose and the sinuses, preventing drainage of mucopurulent discharge. If there are repeated attacks or if recovery is not complete, the infection may become chronic.

Tonsillitis

Viruses and *Streptococcus pyogenes* are common causes of inflammation of the palatine tonsils, palatine arches and walls of the pharynx. Severe infection may lead to suppuration and abscess formation (*quinsy*). Occasionally the infection spreads into the neck causing cellulitis. Following acute tonsillitis, swelling subsides and the tonsil returns to normal but repeated infection may lead to chronic inflammation, fibrosis and permanent enlargement. Endotoxins from tonsillitis caused by *Streptococcus pyogenes* are associated with the development of rheumatic fever and glomerulonephritis.

The nasopharyngeal tonsils lie on the upper wall of the nasopharynx (Fig. 10.3) and, when inflamed, are better known as the *adenoids*. Temporary enlargement is a protective reaction to infection of nasal and pharyngeal mucosa, and the tissue returns to normal after the infection has subsided, but repeated infections can leave them enlarged and fibrotic. This can cause airway obstruction and can be a problem especially in children.

Pharyngitis

This usually accompanies common colds and tonsillitis. Viruses, with superimposed bacterial infection, cause acute inflammation of the mucous membrane of the pharynx, nose and sinuses.

Laryngitis and tracheitis

The larynx and trachea are subject to the same viral and bacterial infections as the nose and pharynx. The infection may become chronic, expecially in tobacco smokers and

people who live or work in a polluted atmosphere. Acute inflammation may follow damage caused by an endotracheal tube, especially if it is used for long periods or has an inflated cuff.

Laryngotracheobronchitis (*croup* in children) is a rare but serious complication of upper respiratory tract infections. The airway is obstructed by marked swelling around the larynx and epiglottis, accompanied by wheeze and breathlessness (dyspnoea).

Diphtheria

This is an infection of the pharynx, caused by *Corynebacterium diphtheriae*, that may extend to the nasopharynx and trachea. A thick fibrous membrane forms over the area and may obstruct the airway. Powerful exotoxins may severely damage cardiac and skeletal muscle, the liver, kidneys and adrenal glands. Where immunisation is widespread diphtheria is comparatively rare.

Hay fever (allergic rhinitis)

In this condition, *atopic* ('immediate') hypersensitivity develops to foreign proteins (antigens), e.g. pollen, mites in pillow feathers, animal dander. The acute non-microbial inflammation of nasal mucosa and conjunctiva causes *rhinorrhoea* (excessive watery exudate from the nose), redness of the eyes and excessive secretion of tears. The first time the antigen is encountered and absorbed, IgE antibodies are produced by B-lymphocytes which adhere to the surface of mast cells and basophils in the mucosa. Subsequent contact with the same antigen causes an immediate antigen/antibody reaction, stimulating the release of histamine and related substances from the granules of mast cells and basophils. These substances cause vasodilatation, increased permeability of capillary walls, hypersecretion by glands and swelling of tissues (see Fig. 15.1, p. 375). Atopic hypersensitivity tends to run in families, but no genetic factor has yet been identified. Other forms of atopic hypersensitivity include:

- childhood onset asthma (see below)
- eczema in infants and young children
- food allergies.

Tumours

Benign (haemangiomata)

These occur in the nasal septum. They consist of abnormal proliferations of blood vessels interspersed with collagen fibres of irregular size and arrangement. The blood vessels tend to rupture and cause persistent bleeding (epistaxis).

Malignant

Carcinoma of the nose, sinuses, nasopharynx and larynx is relatively rare.

DISEASES OF THE BRONCHI

Learning outcomes

After studying this section, you should be able to:

- compare the causes and pathology of chronic and acute bronchitis
- discuss the causes and disordered physiology of asthma
- explain the main physiological abnormality in bronchiectasis.

Acute bronchitis

This is usually a secondary bacterial infection of the bronchi. It is usually preceded by a common cold or influenza and it may also complicate measles and whooping cough in children. The viruses depress normal defence mechanisms, allowing bacteria already present in the respiratory tract to multiply, e.g. *Streptococcus pneumoniae, Haemophilus influenzae, Streptococcus pyogenes, Staphylococcus aureus*. Downward spread of infection may lead to bronchiolitis, and bronchopneumonia may develop, especially in children and in debilitated, often elderly, adults.

Chronic bronchitis

Chronic bronchitis is defined clinically when an individual has had a cough with sputum for 3 months in 2 successive years. It is a progressive inflammatory disease resulting from prolonged irritation of the bronchial epithelium. One or more of the following predisposing factors are usually present:

- acute bronchitis commonly caused by *Haemophilus influenzae* or *Streptococcus pneumoniae*
- cigarette smoking
- atmospheric pollutants, e.g. motor vehicle exhaust fumes, industrial chemicals, sulphur dioxide, urban fog
- previous episodes of acute bronchitis.

It develops mostly in middle-aged men who are chronic heavy smokers and may have a familial predisposition.

The changes occurring in the mucous membrane of the bronchi include:

- thickening
- increase in the number and size of mucous glands
- oedema
- reduction in the number of ciliated cells
- narrowing of bronchioles due to fibrosis following repeated inflammatory episodes.

Reduced ciliary activity causes stagnation in the bronchi of the excessive amount of mucus secreted. If the mucus and bronchial lining are colonised by bacteria, pus is formed. Stagnant mucus may partially or completely obstruct small bronchioles. The severe difficulty in breathing (*dyspnoea*) with active expiratory effort raises the air pressure in the alveoli and may rupture the alveolar walls, causing *emphysema* (p. 261). Damp cold conditions tend to exacerbate the disease, and spread of infected mucus to the alveoli may cause pneumonia. As the disease progresses inflamed tissue of the bronchi is progressively replaced by fibrous tissue. Ventilation of the lungs is severely impaired, causing breathlessness, leading to hypoxia, pulmonary hypertension and right-sided heart failure. As respiratory failure develops, arterial blood PO_2 is reduced (*hypoxaemia*) and is accompanied by a rise in arterial blood PCO_2 (*hypercapnia*). When the condition becomes more severe, the respiratory centre in the medulla responds to hypoxaemia rather than to hypercapnia.

Asthma

Asthma is an inflammatory disease of the airways in which the mucous membrane and muscle layers of the bronchi become thickened and the mucous glands enlarge, reducing airflow in the lower respiratory tract. During an asthmatic attack spasmodic contraction of bronchial muscle (*bronchospasm*) constricts the airway and there is excessive secretion of thick sticky mucus which further reduces the airway. Inspiration is normal but only partial expiration is achieved, so the lungs become hyperinflated and there is severe dyspnoea and wheezing. The duration of attacks usually varies from a few minutes to hours, and very occasionally, days (*status asthmaticus*). In severe acute attacks the bronchi may be obstructed by mucus plugs, leading to acute respiratory failure, hypoxia and possibly death.

Non-specific factors that may precipitate asthma attacks include:

- cold air
- cigarette smoking
- air pollution
- upper respiratory tract infection
- emotional stress
- strenuous exercise.

There are two types of asthma which, generally, give rise to identical symptoms and are treated in the same way. Important differences include typical age of onset and the contribution of an element of allergy.

Childhood onset (extrinsic, allergic, atopic) asthma

This type occurs in children and young adults who have atopic (Type 1) hypersensitivity to foreign protein, e.g. pollen, dust containing mites from carpets, feather pillows, animal dander, fungi. A history of infantile eczema or food allergies is common and there are often close family members with a history of allergy.

The same disease process occurs as in hay fever. Antigens (allergens) are inhaled and absorbed by the bronchial mucosa. This stimulates the production of IgE antibodies that bind to the surface of mast cells and basophils round the bronchial blood vessels. When the allergen is encountered again, the antigen/antibody reaction results in the release of histamine and other related substances that stimulate mucus secretion and muscle contraction. Attacks tend to become less frequent and less severe with age.

Adult onset (intrinsic) asthma

This type occurs later in adult life and there is no history of childhood allergic reactions. It is associated with chronic inflammation of the upper respiratory tract, e.g. chronic bronchitis, nasal polyps. Antigens are rarely identified but drug hypersensitivity may develop later, especially to aspirin and penicillin. Attacks tend to increase in severity and there may be irreversible damage to the lungs. Eventually, impaired lung ventilation leads to hypoxia, pulmonary hypertension and right-sided heart failure.

Most asthmatics, whatever the aetiology, can usually have their disease well controlled with inhaled anti-inflammatory and bronchodilator agents, and live a normal life.

Bronchiectasis

This is permanent abnormal dilatation of bronchi and bronchioles. It is associated with chronic bacterial infection and in some cases there is a history of childhood bronchiolitis and bronchopneumonia, cystic fibrosis, or bronchial tumour. The bronchi become obstructed by

mucus, pus and inflammatory exudate and the alveoli *distal* to the blockage collapse as trapped air is absorbed. Interstitial elastic tissue degenerates and is replaced by fibrous adhesions that attach the bronchi to the parietal pleura. The pressure of inspired air in these damaged bronchi leads to dilatation *proximal* to the blockage. The persistent severe coughing to remove copious purulent sputum causes intermittent increases in pressure in the blocked bronchi, leading to further dilatation.

The lower lobe of the lung is usually affected. Suppuration is common. If a blood vessel is eroded, haemoptysis may occur or pyaemia, leading to abscess formation elsewhere in the body, commonly the brain. Progressive fibrosis of the lung leads to hypoxia, pulmonary hypertension and right-sided heart failure.

DISORDERS OF THE LUNGS

Learning outcomes

After studying this section, you should be able to:

- discuss the pathologies of the main forms of emphysema
- describe the causes and effects of lung infection, including pneumonia, abscess and tuberculosis
- describe the main pneumoconioses
- outline the main causes and consequences of chemically-induced lung disease
- describe the main causes and consequences of lung cancer
- discuss the causes and effects of collapse of all or part of a lung

Emphysema (Fig. 10.26)

Pulmonary emphysema

In this form of the disease there is irreversible distension of the respiratory bronchioles, alveolar ducts and alveoli reducing the surface area for the exchange of gases. There are two main types and both are usually present.

Panacinar emphysema

The walls between *adjacent alveoli* break down, the *alveolar ducts* dilate and there is loss of interstitial elastic tissue. The lungs become distended and their capacity is increased. Because the volume of air in each breath remains unchanged it constitutes a smaller proportion of the total volume of air in the distended alveoli, reducing the partial pressure of oxygen. The consequence of this is to reduce the concentration gradient of O_2 across the alveolar membrane, therefore decreasing diffusion of O_2 into the blood. The merging of alveoli reduces the surface area for diffusion of gases. Homeostasis of arterial blood O_2 and CO_2 levels is maintained at rest by hyperventilation. As the disease progresses the combined effect of these changes may lead to hypoxia, pulmonary hypertension and eventually right-sided heart failure. Predisposing factors include:

- cigarette smoking, believed to promote the release of proteolytic enzymes from mast cells and basophils in the lungs
- acute inflammation of bronchi and lungs
- increased pressure caused by coughing which stretches the already damaged structures
- congenital deficiency of an antiproteolytic enzyme, α_1-antitrypsin, which causes deficiency of supporting elastic tissue in the lungs.

Centrilobular emphysema

In this form there is irreversible dilatation of the *respiratory bronchioles* in the centre of lobules. When inspired air reaches the dilated area the pressure falls, leading to a reduction in alveolar air pressure, reduced ventilation efficiency and reduced partial pressure of oxygen. As the disease progresses the resultant hypoxia leads to pulmonary hypertension and right-sided heart failure. Predisposing conditions, exacerbated by persistent severe coughing, include recurrent bronchiolitis, pneumoconiosis, chronic bronchitis and cigarette smoking.

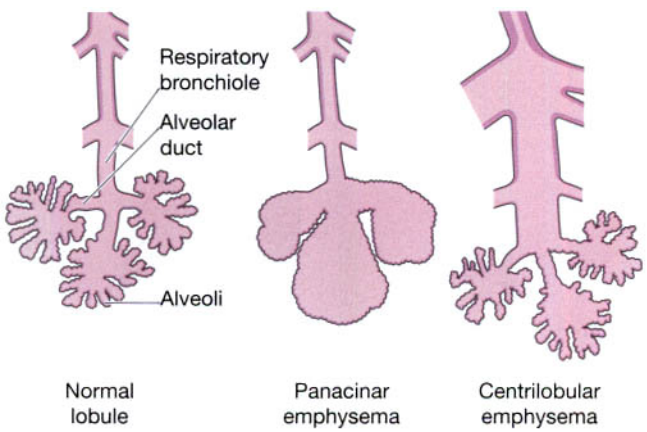


Figure 10.26 Emphysema.

Interstitial emphysema

Interstitial emphysema means the presence of air in the thoracic interstitial tissues, and this may happen in one of the following ways:

- from the outside by injury, e.g. fractured rib, stab wound
- from the inside when an alveolus ruptures through the pleura, e.g. during an asthmatic attack, in bronchiolitis, coughing as in whooping cough.

The air in the tissues usually tracks upwards to the soft tissues of the neck where it is gradually absorbed, causing no damage. A large quantity in the mediastinum may limit heart movement.

Pneumonia (Fig. 10.27)

This occurs when protective processes fail to prevent inhaled or blood-borne microbes reaching and *colonising* the lungs. The following are some predisposing factors.

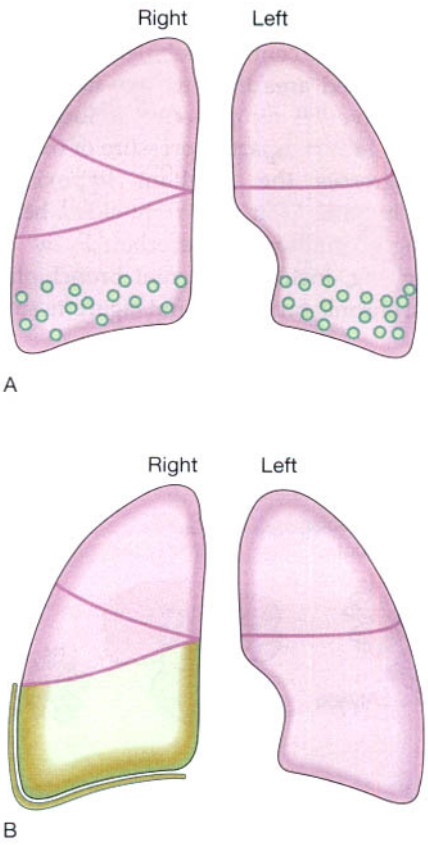


Figure 10.27 Distribution of infected tissue in: A. Bronchopneumonia. B. Lobar pneumonia.

Impaired coughing. The effectiveness of coughing as an aid to the removal of infected mucus may be reduced when the individual is unconscious or by damage to:

- sensory nerve endings in the walls of the respiratory passages
- the cough reflex centre in the medulla oblongata
- nerves to the respiratory passages, lungs and muscles of respiration
- the diaphragm and intercostal muscles.

Voluntary inhibition may occur if coughing causes pain, e.g. following abdominal surgery.

Damage to the epithelial lining of the tract. Ciliary action may be impaired or the epithelium destroyed by, e.g., tobacco smoking, inhaling noxious gases, infection.

Defective alveolar phagocytosis. Depressed macrophage activity may be caused by tobacco smoking, alcohol, anoxia, oxygen toxicity.

Pulmonary oedema and congestion. Bronchopneumonia frequently occurs in patients with hypostatic pulmonary oedema and congestive heart failure. The relationship is not clear.

General lowering of resistance to infection. Factors involved include:

- leukopenia
- chronic diseases
- impaired immune response caused by, e.g., ionising radiation, corticosteroid drugs
- unusually virulent infections
- hypothermia.

Lobar pneumonia

This is infection of one or more lobes by *Streptococcus pneumoniae*, mainly Types 1, 2 and 3. The infection leads to production of watery inflammatory exudate in the alveoli. This accumulates and fills the lobule then overflows into adjacent lobules, spreading the microbes. It is of sudden onset and pleuritic pain accompanies inflammation of the visceral pleura. If not treated by antibacterial drugs the disease goes through a series of stages followed by resolution and reinflation of the lobes in 2 to 3 weeks.

Complications of lobar pneumonia

Incomplete resolution. If the fibrous exudate, formed as the infection subsides, is not completely cleared it may become permanently solid, tough, leathery and airless, reducing the surface area for gaseous exchange.

Pleural effusion and empyema. When infection spreads to the pleura, inflammatory exudate accumulates (*effusion*) in the pleural cavity and pus is formed (*empyema*). Healing may lead to formation of fibrous adhesions which prevent normal expansion of the lung.

Spread of infection. This may be to local tissues or cause:

- pericarditis
- acute endocarditis
- meningitis
- acute otitis media
- arthritis.

Lung abscess. This may develop but only rarely when antimicrobial drugs are available.

Cardiac complications. These include endocarditis or toxic myocarditis that may lead to heart failure, especially in elderly people.

Bronchopneumonia

Infection is spread from the bronchi to terminal bronchioles and alveoli. As these become inflamed, fibrous exudate accumulates and there is an influx of leukocytes. Small foci of consolidation develop. There is frequently incomplete resolution with fibrosis. Bronchiectasis is a common complication leading to further acute attacks, lung fibrosis and progressive destruction of lung substance. Bronchopneumonia occurs most commonly in infancy and old age, and death is fairly common, especially when the condition complicates debilitating diseases. Predisposing factors include:

- debility due to, e.g., cancer, uraemia, cerebral haemorrhage, congestive heart failure, malnutrition, hypothermia
- chronic bronchitis
- bronchiectasis
- cystic fibrosis
- general anaesthetics which depress respiratory and ciliary activity
- acute viral infections
- inhalation of gastric contents in, e.g., unconsciousness, very deep sleep, following excessive alcohol consumption, drug overdose
- inhalation of infected material from the paranasal sinuses or upper respiratory tract.

Microbes causing bronchopneumonia

Staphylococcus aureus. Infection is usually preceded by influenza, measles, whooping cough or chronic lung disease. Incomplete resolution may cause abscess formation, with rupture into the pleural cavity, empyema and possibly pneumothorax. Pleural adhesions may form during healing and limit lung expansion.

Friedländer's bacillus (*Klebsiella pneumoniae*). This commensal is sometimes present in the upper respiratory tract, especially where there is advanced dental caries. It commonly causes pneumonia in men over 50 years and is often associated with diabetes mellitus and alcoholism.

Legionella pneumonophila. These microbes are widely distributed in water tanks, shower heads and air conditioning systems, and are therefore commonly found in institutions such as hospitals and hotels. They may cause a severe form of pneumonia (*Legionnaires' disease*), complicated by gastrointestinal disturbances, headache, mental confusion and renal failure.

Streptococcus pyogenes. Infection is usually preceded by influenza or measles. In very severe cases death may occur within a few days.

Pseudomonas pyocyanea. This organism causes a type of pneumonia acquired by cross-infection in hospitals, especially in patients with mechanically assisted ventilation or tracheostomy. It is resistant to many antibacterial agents and multiplies at room temperature in, e.g., water, soap solution, eye drops, ointments, weak antiseptics.

***Streptococcus pneumoniae* (pneumococcus).** This is a commensal in the respiratory tract which may cause lobar pneumonia or bronchopneumonia, usually preceded by virus infection. It affects mainly debilitated bed-ridden patients when there is stagnation of mucus in the respiratory passages.

Other organisms. Some viruses, protozoa and fungi may cause pneumonia in people whose general resistance is lowered or whose immune systems are depressed by, e.g., drugs.

Lung abscess

Local suppuration and necrosis within the lung substance is most commonly caused by: *Streptococcus viridans, Streptococcus pyogenes, Streptococcus pneumoniae, Staphylococcus aureus.*

Sources of infection

Inhalation. Infected matter from the paranasal sinuses, gums and the upper respiratory passages may be inhaled. An important predisposing factor is inhalation

of regurgitated gastric contents that may occur during coma, emergency anaesthesia, very deep sleep, following alcohol consumption, drug overdose or sniffing volatile gases from, e.g., glue (*aspiration pneumonia*). The hydrochloric acid and food particles cause severe irritation of the upper respiratory tract, allowing bacteria already present to invade the tissues and spread to the lungs.

Pneumonia. Lung abscess may complicate pneumonia, especially when the latter is caused by *Staphylococcus aureus, Streptococcus pneumoniae* or Friedländer's bacillus.

Septic embolism. Thrombophlebitis and right-sided endocarditis are the main sources of septic emboli that cause lung abscess.

Traumatic penetration of the lung. Pathogenic microbes may enter the lung when both skin and lung are penetrated, e.g. in compound fracture of rib, stab wound, gunshot wound, during surgery.

Local spread of infection. Microbes may spread from the pleural cavity, oesophagus, spine or a subphrenic abscess. Recovery from lung abscess may be complete or lead to complications, e.g.:

- chronic suppuration
- septic emboli may spread to other parts of the body, e.g. the brain, causing cerebral abscess or meningitis
- subpleural abscesses may spread and cause empyema and possibly bronchopleural fistula formation
- erosion of a pulmonary blood vessel, leading to haemorrhage.

Tuberculosis

This infection is caused by one of two forms of mycobacteria.

Mycobacterium tuberculosis. Humans are the main host. The microbes cause pulmonary tuberculosis and are spread either by droplet infection from an individual with active tuberculosis, or in dust contaminated by infected sputum.

Mycobacterium bovis. Animals are the main host. The microbes are usually spread to humans by untreated milk from infected cows, causing infection of the alimentary tract. In Britain the incidence has been greatly reduced by the elimination of bovine tuberculosis and the pasteurisation of milk. It is still a significant infection in many countries.

Phases of pulmonary tuberculosis

Primary tuberculosis

When microbes are inhaled they colonise a lung bronchiole, usually towards the apex of the lung. There may be no evidence of clinical disease during the initial stage of non-specific inflammation. Later, cell-mediated T-lymphocytes respond to the microbes (antigens) and the individual becomes *sensitised*. Macrophages surround the microbes at the site of infection, forming *Ghon foci* (tubercles). Some macrophages containing live microbes are spread in lymph and infect hilar lymph nodes. *Primary complexes* are formed, consisting of Ghon foci plus infected hilar lymph nodes. Necrosis (caseation) may reduce the core of foci to a cheese-like substance consisting of dead macrophages, dead lung tissue and live and dead microbes. Primary tuberculosis is usually asymptomatic. There are various outcomes.

- The disease may be permanently arrested, the foci becoming fibrosed and calcified.
- Microbes may survive in the foci and become the source of *postprimary infection* months or years later.
- The disease may spread:
  - throughout the lung, forming multiple small foci; to the respiratory passages, causing bronchopneumonia or bronchiectasis; to the pleura causing pleurisy, with or without effusion
  - to other parts of the body via lymph and blood leading to wide spread of the infection and the development of numerous small foci throughout the body (*miliary tuberculosis*).

Weight loss and malaise develop insidiously, and night sweats are common.

Secondary (postprimary) tuberculosis

This phase occurs only in people *previously sensitised* by a primary lesion, usually situated in the apex of one or both lungs. It may be caused by a new infection or by reactivation of infection by microbes surviving in Ghon foci. As sensitisation has already occurred, T-lymphocytes stimulate an immediate immune reaction, followed by phagocytosis. The subsequent course of the disease is variable, e.g.:

- it may be arrested, healing occurring with fibrosis and calcification of the foci
- foci, containing live microbes, may be walled off by fibrous tissue, becoming a potential source of future infection
- live microbes in foci may break out through the fibrous walls and cause further infection
- pleurisy with or without effusion or empyema may develop

- haemoptysis (expectoration of blood-stained sputum) may occur if a small blood vessel is eroded and bleeds into the respiratory tract
- caseous material containing live microbes may be expectorated, leaving cavities in the lung, and become a source of infection of:
  - the other lung, bronchi, trachea and larynx
  - the alimentary tract when microbes are swallowed
- microbes may spread in blood and lymph, leading to widespread infection and the development of numerous small foci throughout the body (miliary tuberculosis).

Bovine tuberculosis follows the same course but primary complexes develop in the intestines.

Pneumoconioses (occupational lung diseases)

This group of lung diseases is caused by inhaling organic or inorganic atmospheric pollutants. To cause pneumoconiosis, particles must be so small that they are carried in inspired air to the level of the respiratory bronchioles and alveoli where they can only be cleared by phagocytosis. Larger particles are trapped by mucus higher up the tract and expelled by ciliary action and coughing. Other contributory factors include:

- high concentration of pollutants in the air
- long exposure to pollutants
- reduced numbers of macrophages and ineffectual phagocytosis
- cigarette smoking.

Coal workers' pneumoconiosis

This is caused by inhaling dust from soft bituminous coal. It occurs in two forms.

Simple pneumoconiosis

The particles of coal dust lodge mainly in the upper two-thirds of the lungs and are ingested by macrophages inside the alveoli. Some macrophages remain in the alveoli and some move out into the surrounding tissues and adhere to the outside of the alveolar walls, respiratory bronchioles, blood vessels and to the visceral pleura. Macrophages are unable to digest inorganic particles and when they die they are surrounded by fibrous tissue. Fibrosis is progressive during exposure to coal dust but tends to stop when exposure stops. Early in the disease there may be few clinical signs unless emphysema develops or there is concurrent chronic bronchitis.

Pneumoconiosis with progressive massive fibrosis

This develops in a small number of cases, sometimes after the worker is no longer exposed to coal dust. Masses of fibrous tissue develop and progressively encroach on the blood vessels and bronchioles. Large parts of the lung are destroyed and emphysema is extensive, leading to pulmonary oedema, pulmonary hypertension and right-sided cardiac failure. The reasons for the severity of the disease are not clear. One factor may be hypersensitivity to antigens released by the large number of dead macrophages. About 40% of the patients have tuberculosis.

Silicosis

This may be caused by long-term exposure to dust containing silicon compounds. High-risk industries are:

- quarrying granite, slate, sandstone
- mining hard coal, gold, tin, copper
- stone masonry and sand blasting
- glass and pottery work.

When silica particles are inhaled they accumulate in the alveoli. The particles are ingested by macrophages, some of which remain in the alveoli and some move out into the connective tissues around respiratory bronchioles and blood vessels and close to the pleura. Progressive fibrosis is stimulated which eventually obliterates the blood vessels and respiratory bronchioles. Fibrous adhesions form between the two layers of pleura, and eventually fix the lung to the chest wall. The relationship between the presence of silicon and the production of excess fibrous tissue is not clear. It may be that:

- inflammation is caused by silicic acid which gradually forms when silicon compounds dissolve
- there is an immune reaction in which silicon is the antigen
- fibrosis is stimulated by enzymes released when macrophages containing silicon die.

Silicosis appears to predispose to the development of tuberculosis which rapidly progresses to tubercular bronchopneumonia and possibly to miliary tuberculosis. Gradual destruction of lung tissue leads to pulmonary hypertension and right-sided heart failure.

Asbestos-related diseases

Disease caused by inhaling asbestos fibres usually develop after 10 to 20 years' exposure but sometimes after only 2 years. Asbestos miners and workers involved in making and using some products containing asbestos

are at risk. The types associated with disease are crocidolite (blue asbestos), chrysotile (white asbestos) and amosite (brown asbestos).

Asbestosis

This occurs when asbestos fibres are inhaled in dust. In spite of their large size the particles penetrate to the level of respiratory bronchioles and alveoli. Macrophages accumulate in the alveoli and the shorter fibres are ingested. The larger fibres form *asbestos bodies*, consisting of fibres surrounded by macrophages, protein material and iron deposits. Their presence in sputum indicates exposure to asbestos but not necessarily that there is asbestosis. The macrophages that have engulfed fibres move out of the alveoli and accumulate round respiratory bronchioles and blood vessels, stimulating the formation of fibrous tissue. There is progressive destruction of lung tissue, with the development of dyspnoea, chronic hypoxia, pulmonary hypertension and right-sided cardiac failure. The link between inhaled asbestos and fibrosis is not clear. It may be that asbestos stimulates the macrophages to secrete enzymes that promote fibrosis or that it stimulates an immune reaction causing fibrosis.

Pleural mesothelioma

The majority of cases of this malignant tumour of the pleura are linked with previous exposure to asbestos dust, e.g. asbestos workers and people living near asbestos mines and factories. Mesothelioma may develop after widely varying duration of exposure to asbestos, from 3 months to 60 years, and is usually associated with crocidolite fibres (blue asbestos). The latent period between exposure and the appearance of symptoms may range from 10 to 40 years. The tumour involves both layers of pleura and as it grows it obliterates the pleural cavity, compressing the lung. Lymph and blood-spread metastases are commonly found in the hilar and mesenteric lymph nodes, the other lung, liver, thyroid and adrenal glands, bone, skeletal muscle and brain.

Byssinosis

This is caused by the inhalation of fibres of cotton, flax and hemp over a period of years. The fibres cause bronchial irritation and possibly the release of histamine-like substances. At first, breathless attacks similar to asthma occur only when the individual is at work. Later, they become more persistent and chronic bronchitis and emphysema may develop, leading to chronic hypoxia, pulmonary hypertension and right-sided heart failure.

Table 10.3 Conditions caused by inhaled contaminants

Disease	Contaminant
Farmer's lung	Mouldy hay
Bagassosis	Mouldy sugar waste
Bird handler's lung	Moulds in bird droppings
Malt worker's lung	Mouldy barley

Extrinsic allergic alveolitis

This group of conditions is caused by inhaling materials contaminated by moulds and fungi, e.g. those in Table 10.3. The contaminants act as antigens causing antigen/antibody reactions in the walls of the alveoli. There is excess fluid exudate and the accumulation of platelets, lymphocytes and plasma cells. The alveolar walls become thick and there is progressive fibrosis, leading to pulmonary hypertension and right-sided heart failure.

Chemically induced lung diseases

Paraquat (1,1-dimethyl-4,4 bipyridylium chloride)

Within hours of ingestion of this weedkiller it is blood-borne to the lungs and begins to cause irreversible damage. The alveolar membrane becomes swollen, pulmonary oedema develops and alveolar epithelium is destroyed. The kidneys are also damaged and death may be due to combined respiratory and renal failure or cardiac failure.

Cytotoxic drugs (busulphan, bleomycin, methotrexate)

These and other drugs used in cancer treatment may cause inflammation that heals by fibrosis of interstitial tissue in the lungs and is followed by alveolar fibrosis.

Oxygen toxicity

The lungs may be damaged by a high concentration of oxygen administered for several days, e.g. in intensive care units, to premature babies in incubators. The mechanisms involved are unknown but effects include:

- progressive decrease in lung compliance
- pulmonary oedema
- fibrosis of lung tissue
- breakdown of capillary walls.

In severe cases pneumonia may develop followed by pulmonary hypertension and right-sided heart failure.

Retinopathy of prematurity. This affects premature babies requiring high-concentration oxygen therapy. The oxygen may stimulate immature retinal blood vessels to constrict causing fibrosis, retinal detachment and blindness (p. 211).

Bronchial carcinoma

Primary bronchial carcinoma is a common form of malignancy. The tumour usually develops in a main bronchus, forming a large friable mass that projects into the lumen sometimes causing obstruction. Mucus then collects and predisposes to development of infection. As the tumour grows it may erode a blood vessel, causing haemoptysis.

The cause is not known but there is a strong positive association with cigarette smoking and the inhalation of other people's smoke (passive smoking).

Spread of bronchial cancer

This does not follow any particular pattern or sequence. The modes of spread are infiltration of local tissues and the transport of tumour fragments in blood and lymph. If blood or lymph vessels are eroded, fragments may spread while the tumour is quite small. A metastatic tumour may, therefore, cause symptoms before the primary in the lung has been detected.

Local spread. This may be within the lung, to the other lung or to mediastinal structures, e.g. blood vessels, nerves, oesophagus.

Lymphatic spread. Tumour fragments spread along lymph vessels to successive lymph nodes in which they may cause metastatic tumours. Fragments may enter lymph draining from a tumour or gain access to a larger vessel when its walls have been eroded by a growing tumour. Early symptoms may be due to pressure caused by enlarged lymph nodes in the thorax.

Blood spread. Tumour cells usually enter the blood when a blood vessel is eroded by local spread of the tumour. The most common sites of bloodborne metastases are the liver, brain, adrenal glands, bones and kidneys.

Lung collapse (Fig. 10.28)

The clinical effects of collapse of all or part of a lung depend on how much of the lung is affected. Fairly large sections of a single lung can be out of action without obvious symptoms. The term *atelectasis* is often used to described lung collapse. There are four main causes of this condition:

- obstruction of an airway (absorption collapse)
- impaired surfactant function
- pressure collapse
- alveolar hypoventilation.

Obstruction of an airway (absorption collapse)

The amount of lung affected depends on the size of the obstructed air passage. Distal to the obstruction air is trapped and absorbed, the lung collapses and secretions

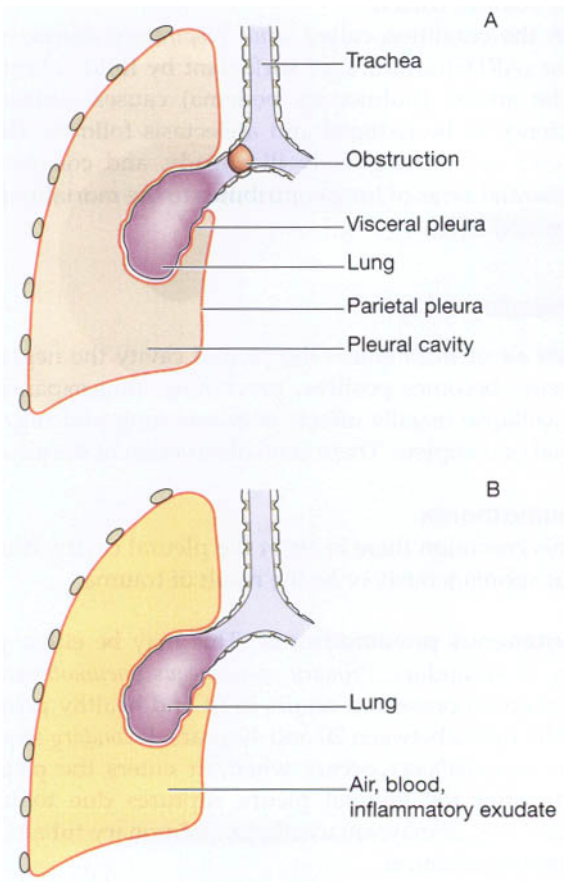


Figure 10.28 Collapse of a lung: A. Absorption collapse. B. Pressure collapse.

collect. These may become infected, causing abscess formation. Short-term obstruction is usually followed by reinflation of the lung without lasting ill-effects. Prolonged obstruction leads to progressive fibrosis and permanent collapse. Sudden obstruction may be due to inhalation of a foreign body or a mucus plug formed during an asthmatic attack or in chronic bronchitis. Gradual obstruction may be due to a bronchial tumour or pressure on a bronchus by, e.g., enlarged mediastinal lymph nodes, aortic aneurysm.

Impaired surfactant function

Premature babies, born before the 34th week, are unable to expand their lungs by their own respiratory effort because their lungs are too immature to produce surfactant (p. 249). Surfactant coats the inner surface of each alveolus and reduces surface tension, allowing alveolar expansion during inspiration. These babies need to be mechanically ventilated until their lungs begin to produce surfactant. This problem is called *respiratory disease of the newborn* (RDN).

In the condition called *adult respiratory distress syndrome* (ARDS), dilution of surfactant by fluid collecting in the alveoli (pulmonary oedema) causes surfactant efficiency to be reduced and atelectasis follows. These patients are often gravely ill already, and collapse of substantial areas of lung contributes to the mortality rate of around 50%.

Pressure collapse

When air or fluid enters the pleural cavity the negative pressure becomes positive, preventing lung expansion. The collapse usually affects only one lung and may be partial or complete. There is no obstruction of the airway.

Pneumothorax

In this condition there is air in the pleural cavity. It may occur spontaneously or be the result of trauma.

Spontaneous pneumothorax. This may be either primary or secondary. *Primary spontaneous pneumothorax* is of unknown cause and occurs in fit and healthy people, usually males between 20 and 40 years. *Secondary spontaneous pneumothorax* occurs when air enters the pleural cavity after the visceral pleura ruptures due to lung disease, e.g. emphysema, asthma, pulmonary tuberculosis, bronchial cancer.

Traumatic pneumothorax. This is due to a penetrating injury, e.g. compound fracture of rib, stab or gunshot wound, surgery.

Tension pneumothorax. This occurs as a complication when a flap or one-way valve develops between the lungs and the pleural cavity. Air enters the pleural cavity during inspiration but cannot escape on expiration and steadily accumulates. This causes shift of the mediastinum and compression of the other lung resulting in severe respiratory distress and is often fatal.

Haemothorax

This is blood in the pleural cavity. It may be caused by:

- penetrating chest injury involving blood vessels
- ruptured aortic aneurysm
- erosion of a blood vessel by a malignant tumour.

Pleural effusion

This is excess fluid in the pleural cavity and may be caused by:

- increased hydrostatic pressure, e.g. heart failure, increased blood volume
- increased capillary permeability due to local inflammation, e.g. pneumonia, pulmonary tuberculosis, bronchial cancer, mesothelioma
- decreased plasma osmotic pressure, e.g. nephrotic syndrome (p. 352), cirrhosis of the liver (p. 335)
- impaired lymphatic drainage, e.g. malignant tumour involving the pleura.

Fibrous adhesions which limit reinflation may form between the layers of pleura, following haemothorax and pleural effusion.

Alveolar hypoventilation

In the normal individual breathing quietly at rest there will always be some atelectatic lobules within the lungs due to the low tidal volume. These lobules will re-expand without difficulty at the next deep inspiration. Another common cause of hypoventilation atelectasis occurs postoperatively, particularly after chest and upper abdominal surgery, when pain restricts thoracic expansion. Postoperative atelectasis predisposes to chest infections, because mucus collects in the underventilated airways and is not expectorated.