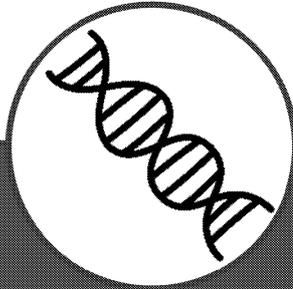


Note – this is a draft copy of the textbook and not the final version.



F170 Fundamentals of Human Biology

Topic 1: Human cells and tissues

1.1. Understanding and observing life

1.1.1. Cells

Life is abundant on Earth; we find it in almost every location across the globe, in locations such as at the bottom of the deep ocean by hydrothermal vents, where temperatures are high and oxygen concentrations are low. Yet even in these habitats, life persists, and the cell.

What is a cell?

The **cell** is the fundamental unit of life. All living organisms are composed of cells. Cells carry out essential biological processes required to enable life, such as ATP production, growth, and reproduction.

Many organisms consist only of a single cell. Known as unicellular organisms, they include bacteria and some algae. Other organisms, including humans, are multicellular – made up of many cells working together in coordinated systems to enable the survival of the organism.

Structure and function of eukaryotic cell components

Eukaryotic cells contain many specialised structures, each with a distinct form adapted to its function. These subcellular structures, known as **organelles**, work together to support the survival of the organism.

Most eukaryotic cells contain a core set of components:

- cell membrane
- cytoplasm
- nucleus

The quantity of these and other organelles present within the cell is affected by the organism's environment and its developmental stage.

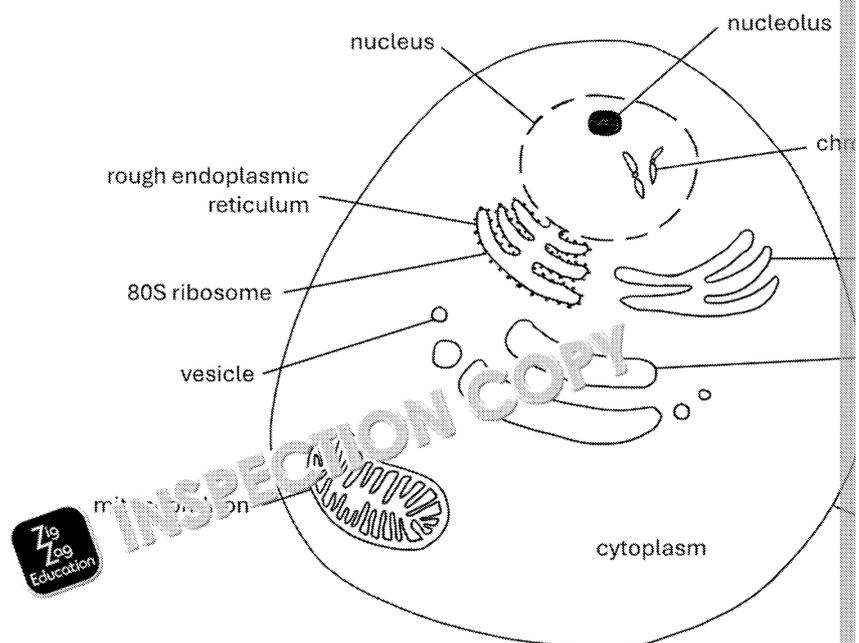


Figure F1.1. A diagram of a generalised animal cell and its organelles.

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Cell surface membrane

The cell surface membrane, also known as the plasma membrane, encloses the cell, separating the intracellular environment and the external surroundings. It is composed of a phospholipid bilayer with proteins, cholesterol, and carbohydrates. It is selectively permeable; the membrane-embedded components regulate the entry and exit of substances and assist their transport through the membrane. Glycoproteins and glycolipids enable cell-to-cell communication and responses to environmental signals. The cell surface membrane can change shape, and this enables processes including **endocytosis**, **exocytosis**, and cell signalling.

Cytoplasm

The cytoplasm is a jelly-like substance made primarily of water with dissolved salts and other molecules. It is the site of many metabolic reactions, and intracellular communications are transmitted through the cytoplasm. Membrane-bound organelles are suspended within the cytoplasm, and are interlinked through it.

Nucleus

Most eukaryotic cells have a nucleus. The nucleus contains the genetic material of the cell and controls cellular activities using enzymes and other factors. It is surrounded by the nuclear membrane perforated by nuclear pores. This separates and protects the DNA from the cytoplasm. The pores allow the selective exchange of molecules, including mRNA, nucleotides and proteins in.

Nucleolus

The nucleolus is a dense, spherical region within the nucleus, which produces ribosomes. Ribosomes are synthesised and combined with proteins to create ribosomes.

Mitochondria

Mitochondria (singular: mitochondrion) are the site of aerobic respiration, responsible for the production of adenosine triphosphate (ATP) – the energy currency of the cell. Through a series of enzyme-controlled reactions, mitochondria release energy stored in the bonds of molecules, such as carbohydrates, lipids and proteins, to produce ATP. ATP is then used for energy-dependent cellular processes, including active transport, protein synthesis, and muscle contraction.

The enzymes and cofactors required for these reactions are either present within the interior fluid, known as the **matrix**, or are bound to the inner mitochondrial membrane. The inner membrane is highly folded into **cris**tae (singular: crista), greatly increasing surface area and the rate of ATP production.

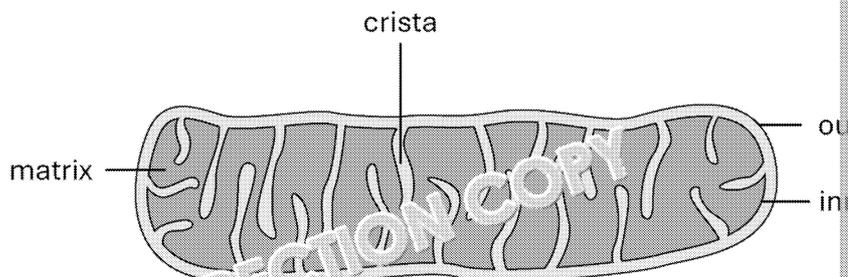


Figure F1.2. A 2D diagram of the internal structure of a mitochondrion.

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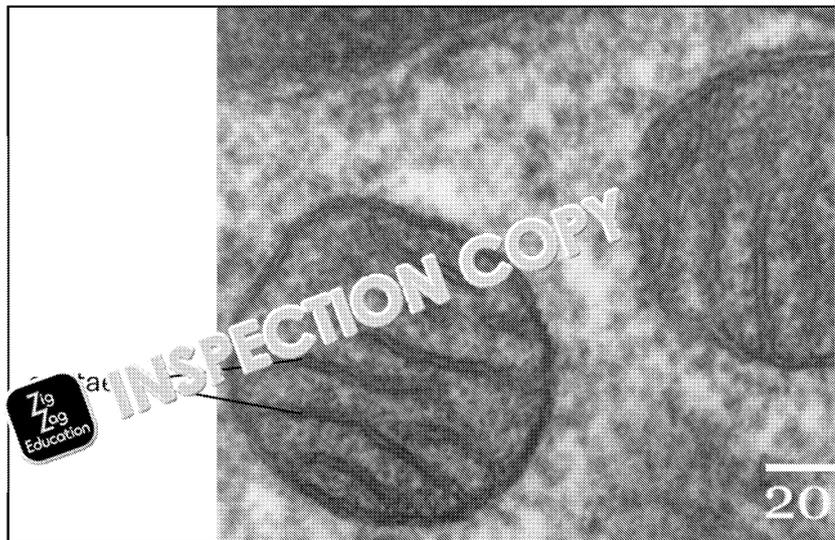


Figure F1.3. A transmission electron photomicrograph of mitochondria, showing the cristae.

Mitochondria have their own mitochondrial DNA (mtDNA), which contains 37 genes for rRNA and tRNA. They also have specific ribosomes (called mitoribosomes), so they can synthesize proteins, replicate independently, and regulate aspects of their internal environment. The endosymbiont theory (see page 20) which suggests that mitochondria were once free-living prokaryotes that were maternally inherited and is implicated in some inherited metabolic diseases (see page 20).

Ribosomes

Ribosomes are composed of proteins and ribosomal RNA (rRNA) and are not membrane-bound organelles. Each ribosome contains a small subunit that binds the mRNA strand, and a large subunit that reads the mRNA triplet code with the corresponding amino acid and joins them together to form a polypeptide chain.

Ribosomes are manufactured in the nucleolus then transported to the cytoplasm where they can be free in the cytoplasm and synthesize proteins for internal use, or bound to the membrane of the endoplasmic reticulum to produce proteins for secretion or insertion into membranes.

Smooth and rough endoplasmic reticulum (SER/RER)

The endoplasmic reticulum (ER) is a network of single-membraned structures that form the inner envelope. It exists in two forms:

- rough ER (RER) – studded with ribosomes that synthesise proteins destined for **secretion** by exocytosis or membrane insertion
- smooth ER (SER) – lacks ribosomes; it manufactures carbohydrates and lipids

The RER packages newly synthesised proteins into transport vesicles which move to the Golgi apparatus.

The quantity of each form of ER varies depending on the role of the cell. For instance, cells which **secrete** proteins such as antibodies, hormones or digestive enzymes (e.g. plasma cells, pancreatic cells) have extensive RER, but cells involved in **lipid** metabolism (e.g. liver cells) have prominent SER.

rough
endoplasmic
reticulum
(RER)

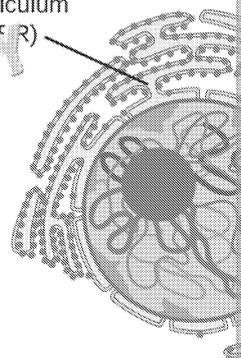


Figure F1.4. A diagram showing the structure of the rough endoplasmic reticulum.

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Golgi body/apparatus

The Golgi body, or Golgi apparatus, is another single-membrane-bound organelle, structurally similar to the SER. It consists of a stack of flattened, membrane-bound sacs called **cisternae** (singular: cisterna), where proteins, carbohydrates and lipids are modified, sorted, and packaged for delivery.

Modifications to molecules arriving at the Golgi apparatus include:

- **glycosylation**, where carbohydrate groups are attached to proteins (to form glycoproteins) or lipids (making glycolipids)
- the addition of functional groups (such as PO_4^{2-} ions onto carbohydrates)
- the activation of enzymes by combining them with cofactors

Once modified, molecules are enclosed within vesicles that bud off from the Golgi apparatus.

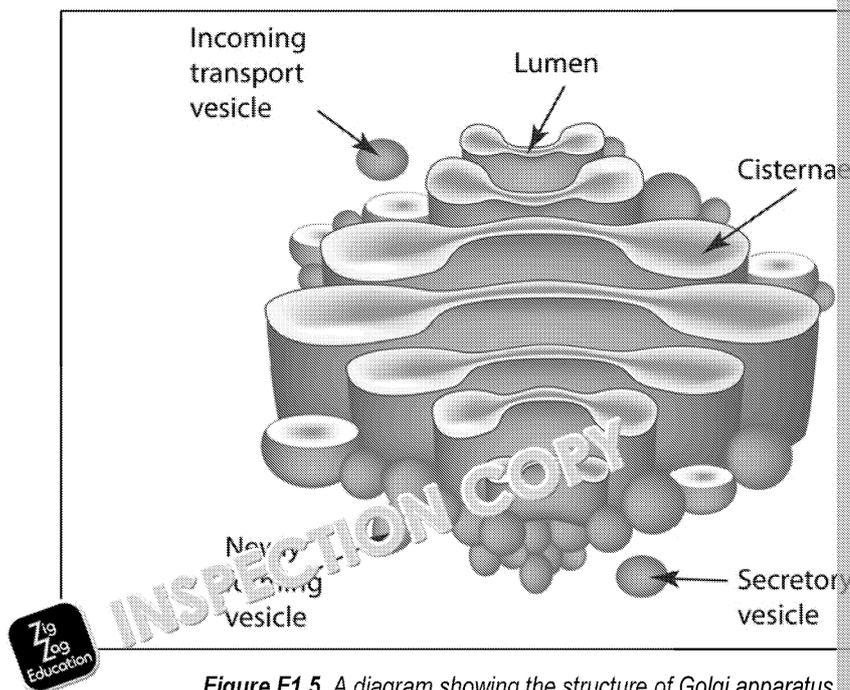


Figure F1.5. A diagram showing the structure of Golgi apparatus.

Vesicles and lysosomes

Vesicles and lysosomes are single-membrane-bound structures, formed by pinching off from the endoplasmic reticulum or Golgi apparatus. This traps the contents inside the vesicle membrane.

Transport vesicles move substances between organelles, for instance from the ER to the Golgi apparatus.

Secretory vesicles transport contents to the cell surface membrane for secretion out of the cell by exocytosis, e.g. antibodies, hormones, digestive enzymes and skin oils. The secretory vesicle fuses with the surface membrane and unwraps, releasing its contents outside the cell.

Lysosomes, derived from the Golgi apparatus, remain in the cell and carry **hydrolytic enzymes** to break down cellular debris, such as worn organelles, and **pathogens** and their **toxins** through phagocytosis. They are involved in **apoptosis** (programmed cell death) under specific conditions, leading to the destruction of the cell.

hydrolytic enzymes – substances by adding water and include proteases

pathogen – a bacterium which can cause disease

toxin – a poison released that causes harm to the infected individual

apoptosis – programmed the total destruction of a coordinated process.

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Cilia and flagella

Cilia

Cilia (singular: cilium) are hair-like **projections** of the cell surface, composed of **microtubules** enclosed by the plasma membrane. Cilia can be motile, beating rhythmically from side to side to move substances across a surface, or non-motile (stationary) and function as sensory organelles or signalling hubs.

In humans, cells with motile cilia are found on the lining of the trachea and along the **oviduct**. In the trachea, the cilia move mucus to the back of the throat, keeping the lungs clear of pathogens and debris. In the oviduct, cilia move the egg cell towards the uterus. This ensures that if the egg cell is fertilised, the embryo reaches the uterus. If it remains unfertilised, it passes out of the body.

Non-motile cilia are found within the nose, inner ear, and retina of the eye, and perform sensory functions. They are also located within the kidney, where they help to filter blood.

Cilia contain microtubules that provide structure. Nine pairs of fused microtubules are positioned around the outer part of the cilia in a wheel-like arrangement. In motile cilia, there are a further two unfused microtubules in the centre: the 9+2 arrangement. As the parallel pairs of microtubules move over each other, driven by motor proteins and using ATP, the motile cilia move.

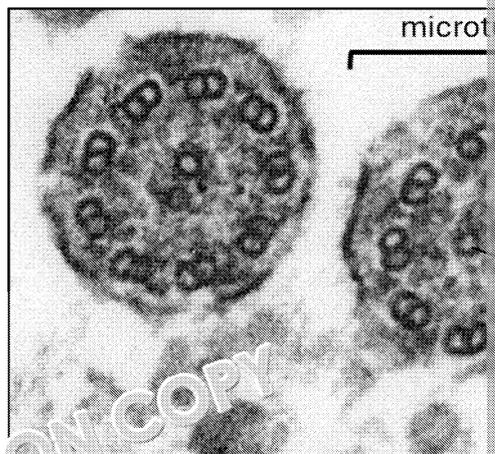


Figure F1.6. A transmission electron micrograph showing the 9+2 arrangement of microtubules in a cilium.

Flagella

Flagella (singular: flagellum) are longer tail-like projections, anchored to the cell. In humans, sperm cells are the only cells with a flagellum. Powered by ATP, they generate movement that propels the cell forward. As with motile cilia, they also have the 9+2 microtubule arrangement.

Microvilli

Microvilli are short, finger-like cell surface membrane extensions containing actin filaments. Intestinal epithelial cells have microvilli that vastly increase the surface area, which greatly increases absorption of nutrients and water from the gut.

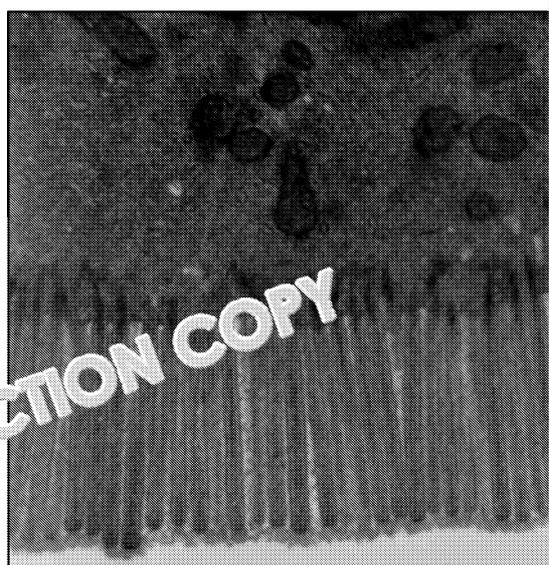


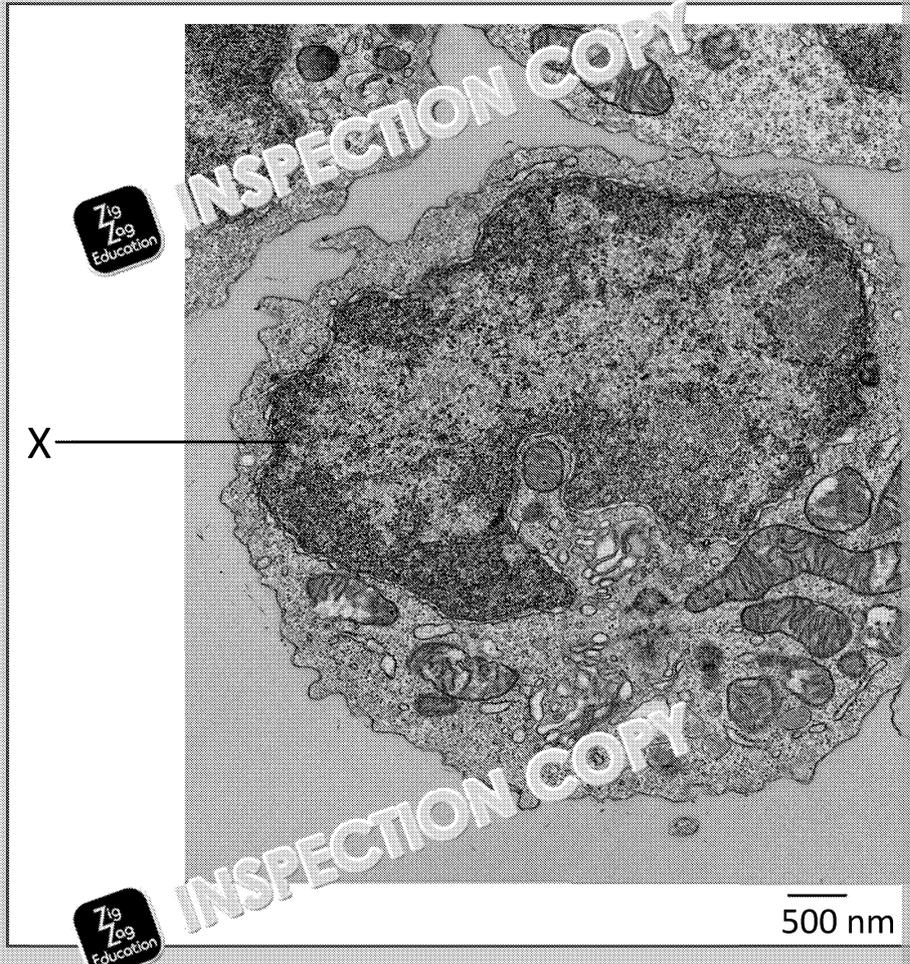
Figure F1.7. A transmission electron micrograph showing microvilli on the surface of an intestinal epithelial cell.

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Apply your knowledge

1. Describe the function of the nucleolus and state its location within the cell.
2. Identify parts X and Y on the electron micrograph of a B lymphocyte, and explain your choices for your choices.



3. Explain the structural and functional differences between the rough endoplasmic reticulum and smooth endoplasmic reticulum (SER).
4. Compare and contrast the functions of cilia, flagella and microvilli, and state an example of each.

Adult stem cells

What are stem cells?

Stem cells are undifferentiated cells that have not adopted any specific function, such as generating movement, and therefore can develop into a range of specialised cell types. Due to their ability to divide indefinitely via mitosis, stem cells play a vital role in growth, tissue development and repair throughout an organism's life.

Stem cells are classified based on their ability to differentiate:

- Totipotent – can form all cell types, so capable of forming a whole organism. Found in the first 16 embryonic cells.
- Pluripotent – can form almost all specialised cells from all tissue types but cannot form extra-embryonic stem cells. Found as embryonic stem cells.
- Multipotent – can form specialised cells within a specific tissue type only; for instance, in adult bone marrow can differentiate into all specialised blood cells but cannot form other tissues such as muscle or nerve. Found in adult stem cells.

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Adult stem cells

Adult stem cells are multipotent and are found within all tissue types, such as muscle. They are responsible for repairing tissue by replacing damaged cells, and enable adaptation during growth.

Haematopoietic stem cells

Haematopoietic stem cells are found within adult bone marrow and can differentiate into:

- erythrocytes (red blood cells)
- leucocytes (white blood cells)
- thrombocytes (platelets)

This process is continuous throughout life. Mature erythrocytes lack a nucleus and have a lifespan of about 120 days, while some leucocytes may function for only a few days.

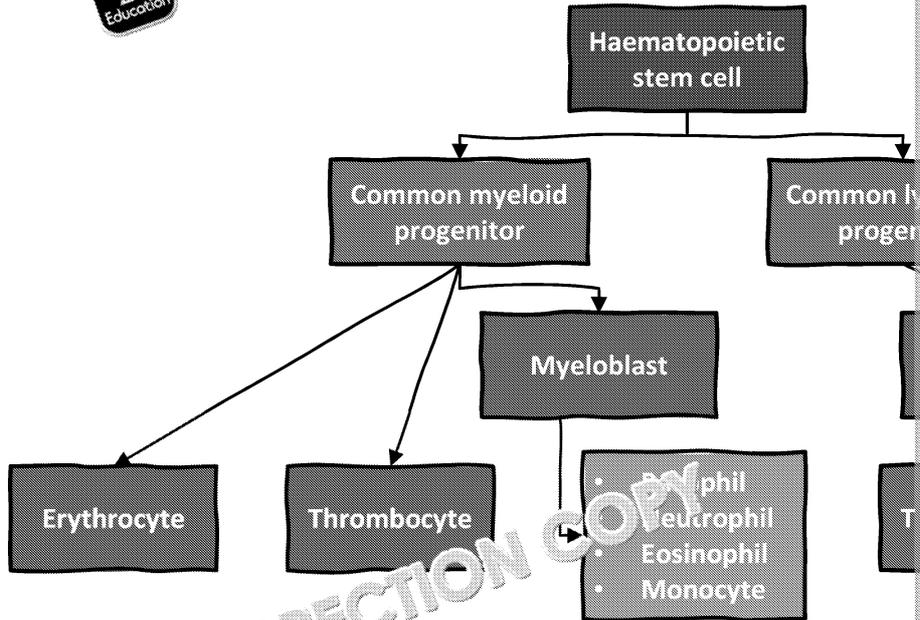


Figure F1.8 Haematopoietic stem cell differentiation pathway showing how erythrocytes, thrombocytes and all leucocytes are produced from a common stem cell.

Other tissue-specific stem cells

Skin stem cells are found in the basal layer of the epidermis. They are responsible for producing skin cells, but do not produce hair follicle cells, which are made from different stem cells. Skin is replenished approximately every 28 days.

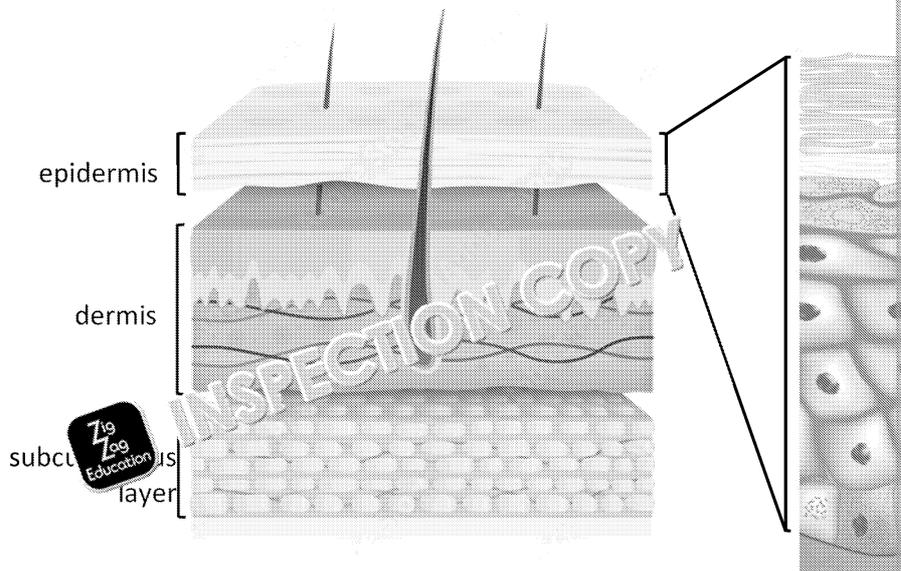


Figure F1.9. Skin stem cells are located at the bottom of the epidermis in the basal layer.

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Specific muscle stem cells known as satellite cells are present within muscle fibres. They are activated by growth factors or mechanical stress (such as strength training) and are responsible for the formation of new muscle fibres.

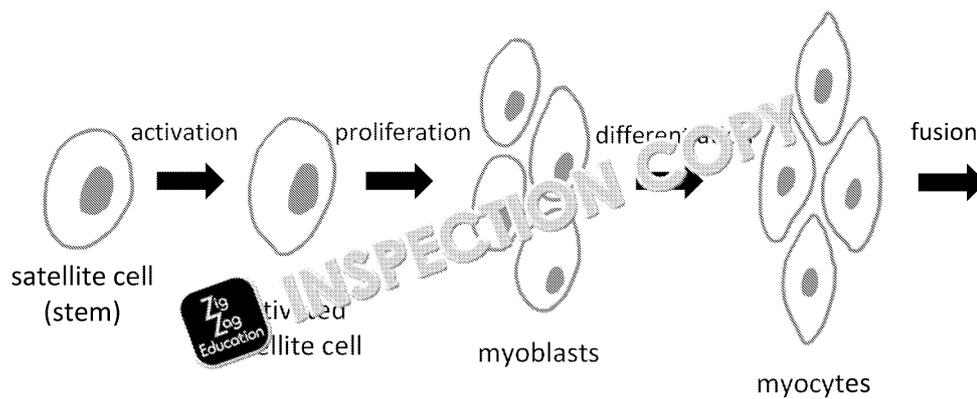


Figure F1.10. Muscle satellite cells mature into myofibres when activated.

Stem cell differentiation

Stem cells can remain inactive for extended periods – a state known as quiescence. They can also proliferate slowly, such as bone and brain, and also applies to haematopoietic stem cells. Quiescence helps protect the genome by limiting exposure to mutation-inducing factors.

In contrast, some stem cells divide frequently to replenish tissues with high turnover rates, such as the skin and gut lining. After division by **mitosis** (see section 1.1.5), stem cells may remain undifferentiated and continue through **interphase**, enter quiescence phase G_0 , or differentiate into specialised cells.

mitosis – generates two daughter cells
interphase – the cell carries out its normal functions, by replicating its DNA

Differentiation involves activating genes that code for proteins essential for specific functions (e.g. haemoglobin in erythrocytes), while silencing other genes not required for that cell type. Silenced genes are tightly wound around histone proteins forming a compact structure that prevents transcription. This restricts mRNA synthesis of unnecessary proteins.

Whether a stem cell remains undifferentiated or becomes specialised is influenced by the surrounding microenvironment. These include hormones and growth factors from neighbouring cells, and those which trigger tissue maturation during puberty, or create specific leucocytes during infection. Environmental triggers such as mechanical stimuli (e.g. repeated muscle stretching) or nutrient availability can also promote or inhibit differentiation.

It is essential that the body tightly regulates the proliferation of stem cells and their differentiated cells. Delayed differentiation can lead to impaired tissue repair and ageing. Excessive proliferation can lead to tumour development, with potential progression to cancer and **metastasis** causing secondary tumours.

Uses for stem cells

The **umbilical cord** provides a rich source of multipotent stem cells that can be harvested without invasive medical procedures. Both umbilical and adult multipotent stem cells can be artificially reprogrammed into pluripotent stem cells *in vitro*, which makes them more useful in medicine and research. Once in this state, they can be expanded to produce large quantities, induced into dormancy for storage until needed.

Pluripotent stem cells support lab-based research into complex diseases (e.g. Huntington's disease) and are used to create cultured tissues for testing drug efficacy. If harvested from a patient's own tissues, pluripotent stem cells can be used to make patient-specific tissues that can be transplanted back into the patient's body because the tissue will not be rejected as foreign (non-self).

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However, using stem cells to treat disease or damage is still, for the large part, possible. This is complex medicine which involves detailed understanding of how cells specialise, and how molecules interact to enable cell signalling. Therefore, the use of stem cells for medicinal purposes is still in its infancy. Current experimental uses include leukaemia, minimising nerve damage caused by multiple sclerosis, repairing damaged heart tissue, and growing skin tissue for regrafting onto burn victims.

Recall questions



1. Outline the similarities between multipotent, pluripotent and totipotent stem cells.
2. Describe the role that stem cells have in tissue repair and regeneration.
3. Outline the factors that influence the differentiation of stem cells.
4. Discuss whether using embryonic stem cells should be encouraged or discouraged, for or against.

Structure and function of highly specialised cells

Highly specialised cells have structural adaptations that enable efficient function. The human body contains approximately 30 trillion cells, and each cell works together with other cells to form a cohesive, living system.

Sperm cells

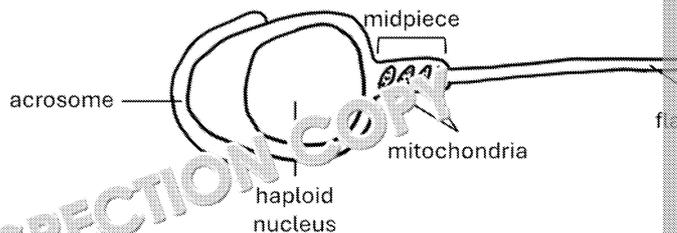


Figure F1.11. A diagram of a sperm cell showing specialised features.

The sperm cell is the male **gamete**, responsible for delivering genetic material to the female egg cell (ovum) during fertilisation, starting the formation of a new human life. As a gamete, it is **haploid**, meaning it carries half the usual number of chromosomes found in a typical body cell. Its structural specialisations are tightly linked to its function:

- a long flagellum which acts as a whip-like tail, propelling it through the fluid environment of the reproductive tract
- many mitochondria, concentrated in the midpiece to supply ATP, powering the cell
- the acrosome, a cap-like structure at the tip of the head, contains digestive enzymes that can break down the ovum's outer layers, facilitating entry during fertilisation

Ova

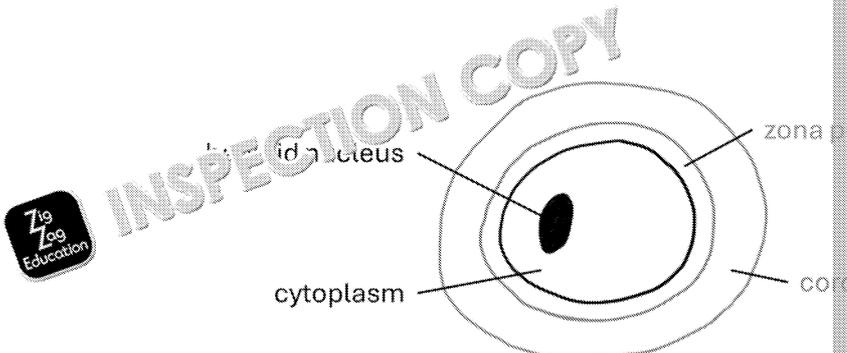


Figure F1.12. A diagram of an ovum, showing specialised features.

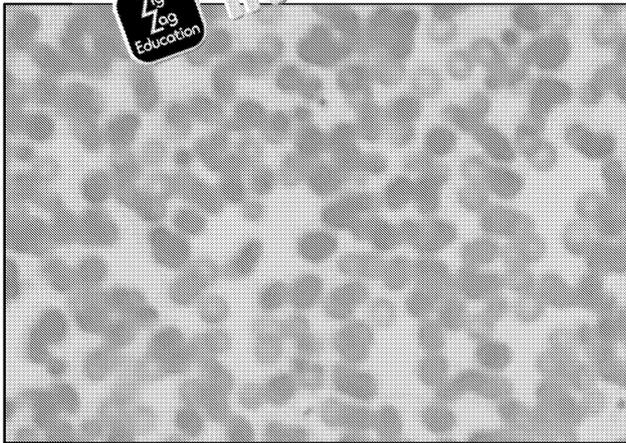
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The egg cell, or ovum (plural: ova), is the female gamete, also haploid, and carries genetic material to be fused with that of the sperm cell. Its adaptations support early-stage embryonic development and cellular protection:

- A nutrient-rich cytoplasm contains lipids to sustain the developing **embryo** prior to implantation.
- The zona pellucida, a jelly-like layer surrounding the cell membrane, offers structural protection from mechanical damage, and is involved in fertilisation.
- An outer coating of follicle cells called the corona radiata, derived from the ovaries, and provides additional protection during fertilisation.

Erythrocytes



biconcave shape

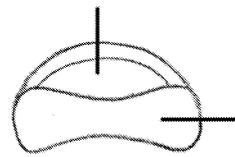


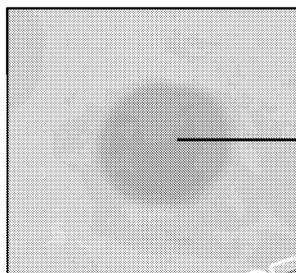
Figure F1.13. A light photomicrograph showing human red blood cells at $\times 100$ magnification showing a transverse section through a red blood cell to reveal its biconcave shape.

Erythrocytes, red blood cells, transport oxygen throughout the body. Mature erythrocytes have several key adaptations:

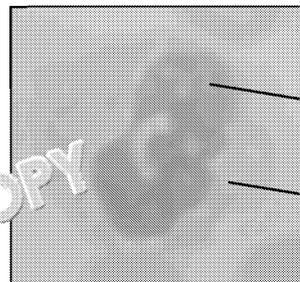
- no nucleus or other organelles, maximising space for haemoglobin
- haemoglobin in its **conjugated protein**, which reversibly binds oxygen
- a biconcave disc shape, which increases the surface-area-to-volume ratio, improving the rate of oxygen diffusion into and out of the cell

Their lack of organelles also limits energy usage and prevents them from completing their relatively short lifespan (approximately 120 days).

Leucocytes



nucleus



neutrophil

Figure F1.14. Light photomicrographs of a plasma cell (B lymphocyte) and a neutrophil at $\times 100$ magnification showing the differences in their specialised features as viewed when stained using methylene blue.

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Leucocytes, or white blood cells, are immune cells with diverse specialisations that protect the body from pathogens.

Neutrophils

Neutrophils are the most common type of leucocyte in circulation. They have a biconcave shape that enables them to squeeze between cells to reach sites of infection. Granulated with digestive enzymes used to destroy pathogens via phagocytosis.

Lymphocytes

Lymphocytes are produced either in the **Bone marrow** (B lymphocytes) or the **thymus gland** (T lymphocytes) and are divided into subtypes with a specialised immune function:

T lymphocytes	T helper cells	Produce interleukins , a cell-signalling molecule, which stimulates antibody production. Activate the other T cell types. Stimulate macrophages to destroy the pathogen by releasing enzymes.
	T killer cells	Produce a chemical called perforin , which makes holes in the target cell membrane, causing the cell to rupture and die.
	T memory cells	Provide immunological memory: upon reinfection, they stimulate T killer cells which swiftly destroy the pathogen.
	T regulator cells	Oversee the immune system: <ul style="list-style-type: none"> Prevents over-reaction and destruction of self-cells. Suppresses processes that are initiated to destroy self-cells.
B lymphocytes	Plasma cells	Rapidly manufacture large quantities of antibodies to fight an infection. <ul style="list-style-type: none"> Have a large nucleus and lots of rough endoplasmic reticulum.
	B effector cells	Divide to create clones of plasma cells.
	B memory cells	Provide immunological memory for antibody production. Upon reinfection they provide a rapid and amplified antibody response.

Table F1.1 Functions of the subtypes of B lymphocytes and T lymphocytes

Eosinophils

Eosinophils fight parasitic infections by producing toxic granules which can kill these organisms. When viewed using a light microscope, these granules can be seen in the cytoplasm, surrounding a **bilobed** nucleus. If over-stimulated, they can cause allergic reactions and inflammation, which can lead to tissue damage.

Monocytes

Monocytes are precursors for tissue-specific macrophages. They circulate in the blood where they differentiate into localised immune cells, such as Kupffer cells in the liver and microglia in the nervous system. These macrophages are specialised to clear damaged cells and debris from their respective tissues.

Sensory, relay and motor neurons

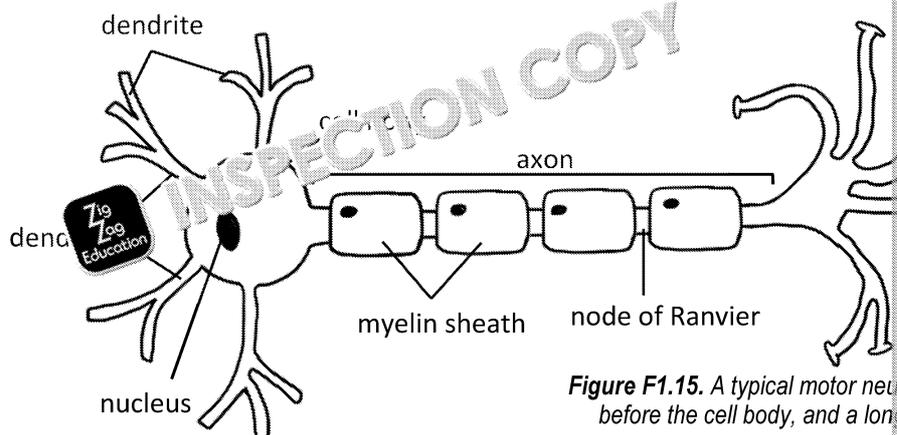


Figure F1.15. A typical motor neuron with a short axon before the cell body, and a long axon after the cell body.

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Neurons are highly specialised cells responsible for conducting electrical impulses through the nervous system. These signals allow the brain to receive information from receptors and send commands to effectors. These rapid responses to internal and external environmental changes. Due to their complex structure, neurons do not undergo mitosis, which is why nerve damage is often permanent.

Neurons have the following specialised features:

- Dendrons and dendrites – extend towards the cell body and branch into dendrites in sensory neurons or receptors. Multiple dendrites per neuron allow multiple pathways to the cell body.
- Axon – a long, thin extension that conducts electrical impulses away from the cell body towards neurons or effectors.
- Axon terminals – located at the end of the axon, these branch out to form synapses with multiple target cells.
- Myelin sheath – present on many but not all neurons, it is a fatty insulating layer that surrounds the axon. It insulates the axon and prevents current leakage, supporting faster impulse conduction.
- Nodes of Ranvier – gaps between each myelin segment, which allow impulses to jump between segments in a process called saltatory conduction, greatly increasing conduction speed by up to 100 times.

There are three types of neuron:

- Sensory neurons – transmit signals from sensory receptors to a relay neuron in the CNS. The cell body is located centrally and the dendron and axon are of roughly equal length.
- Relay neurons – found in the central nervous system, they connect sensory neurons to motor neurons, enabling signal processing and integration. They typically have a central cell body with short dendrons receiving incoming signals, and a short axon transmitting impulses onwards.
- Motor neurons – carry signals from the CNS to effectors, such as muscles or glands. They typically have long dendrons connecting to other neurons, a cell body positioned near the base of the long axon that extends to the effector.

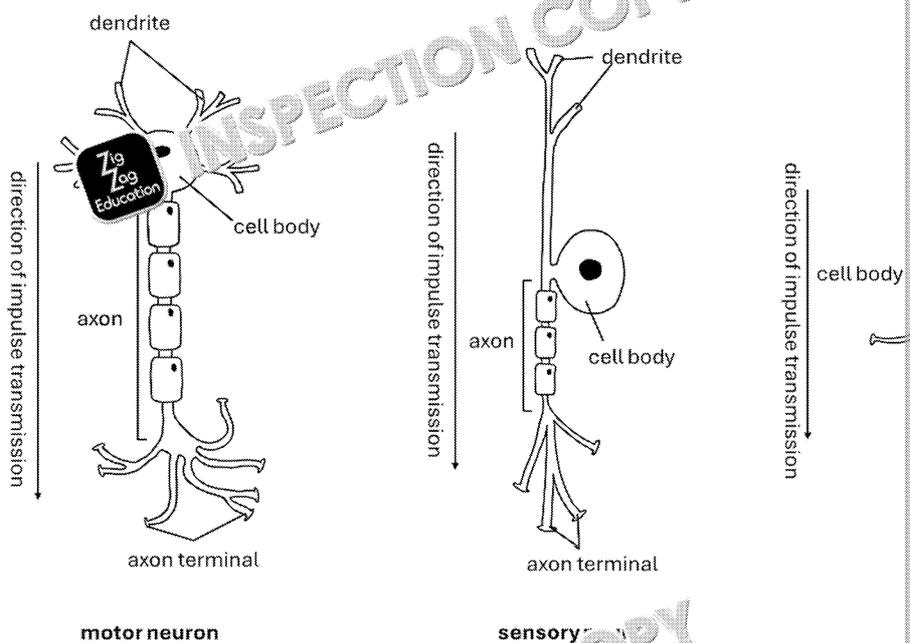


Figure F1.16. Diagram showing the structure of motor, sensory and relay neurons and the direction of impulse transmission.

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Hepatocytes

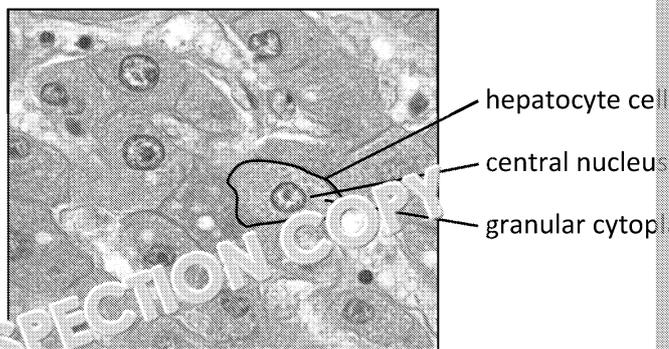


Figure F1.17. Light photomicrograph showing hepatocytes, each with a distinct nucleus.

Hepatocytes are specialised epithelial cells that make up approximately 80 % of the liver's mass. These cells are essential in metabolic processing, including the **catabolism** of toxic substances such as alcohol and drugs into non-toxic substances.

Key structural features include:

- granular cytoplasm, indicative of high metabolic activity
- many mitochondria, supplying the ATP required for the energy-intensive biochemical reactions
- central nucleus, enabling regulation of complex metabolic functions
- extensive rough and smooth endoplasmic reticulum, producing enzymes and proteins for protein synthesis
- many lysosomes, supporting waste disposal and cellular recycling

Renal tubule epithelial cells

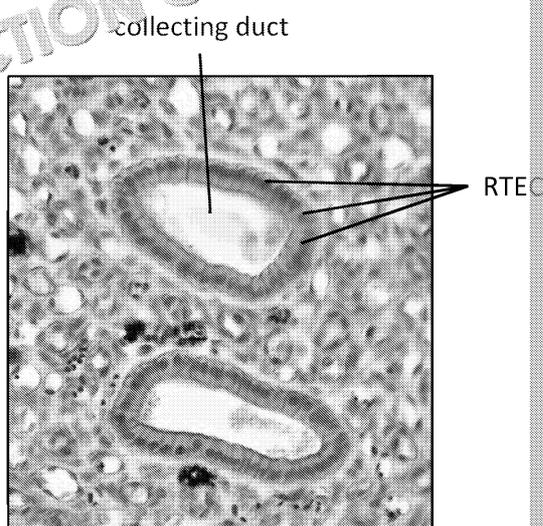


Figure F1.18. Light photomicrograph showing a cross section through the kidney collecting ducts. The renal tubule epithelial cells can be identified with large, darkly staining nuclei.

Renal tubule epithelial cells line the kidney nephrons, Bowman's capsule and are involved in the filtration of blood, excretion of metabolic waste and regulation of water and electrolyte balance. The morphology (size, shape and structure) varies depending on the location. These cells contain many mitochondria that produce ATP used for active transport and filtration. They also have granular cytoplasm to support high levels of protein synthesis and metabolic activity.



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Photoreceptor cells

The retina at the back of the eye detects visible light and transmits electrical impulse nerve. Photoreceptor cells – rods and cones – respond to light differently: rods are sensitive to low light levels whereas cones are sensitive to specific wavelengths of light. This means that rods are optimised for low-light conditions and are found in greatest concentrations around the periphery of the retina while cones enable colour vision in bright light and are densely clustered in the fovea.

Cone photoreceptor cells

There are three types of cones in the human eye giving us trichromatic vision. They are sensitive to red (long), green (medium) or blue (short) wavelengths of light. Cone cells have a complex structure with three segments that link to a neuron in the optic nerve. These are:

- Outer segment – has a flattened disc-like shape with many membrane layers containing light-sensitive photopigments. This arrangement forms a vast surface area.
- Inner segment – contains many mitochondria, the cell nucleus and endoplasmic reticulum for protein production and synthesis.
- Lower segment – links with a neuron in the optic nerve via a synapse.

Rod photoreceptor cells

Rod cells have a similar layout to cone cells but differ structurally with a rod-shaped outer segment that is slightly longer and thinner than cone cells.

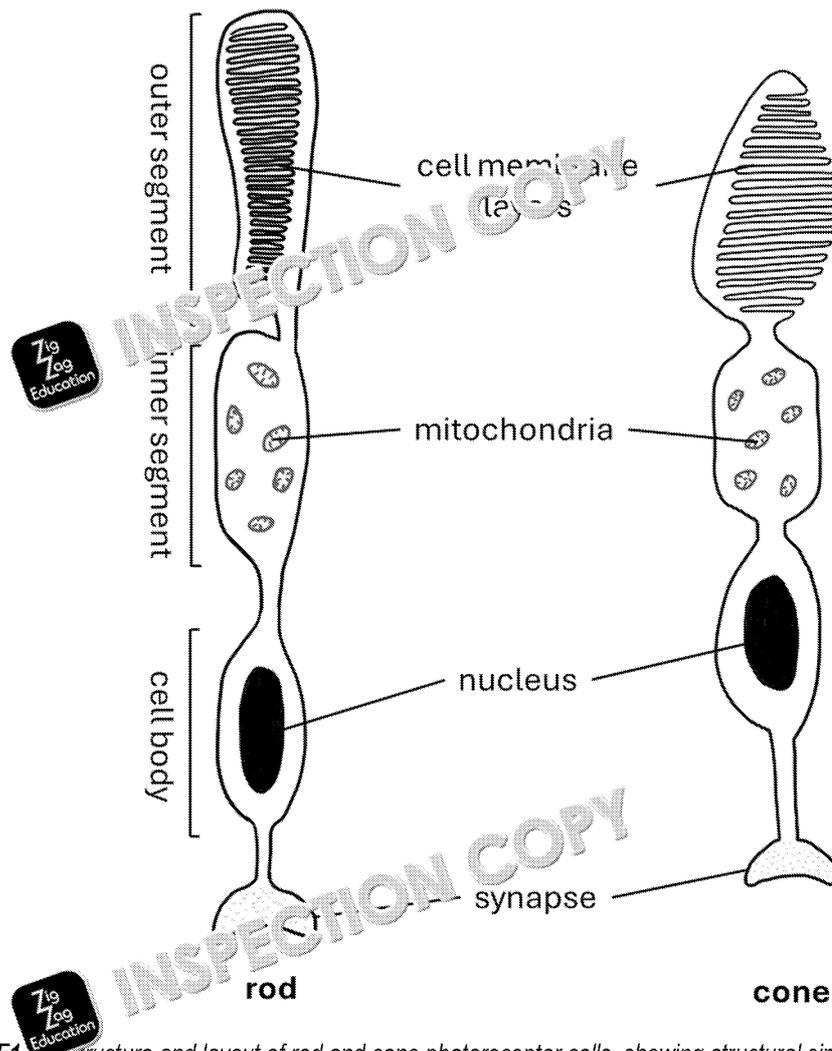


Figure F1.1. Structure and layout of rod and cone photoreceptor cells, showing structural similarities.

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Tracheal and oviduct ciliated epithelial cells

Tracheal columnar epithelium contains two main cell types: goblet cells, which release mucus that traps pathogens and dirt particles, and ciliated cells that have motile cilia which beat rhythmically to move this mucus up the trachea to the throat for expulsion or digestion. This provides some protection to the lungs against infection and contamination.

Oviduct epithelium also features ciliated cells that transport the ovum from the ovary to the uterus. They facilitate the movement of sperm cells toward the egg cell for potential fertilisation, and they ensure that they move appropriately through the system, either for implantation or expulsion if fertilisation does not occur.



Figure F1.20

Alveoli squamous epithelial cells

Squamous epithelial tissue lining the alveoli (singular: alveolus) of the lungs consists of extremely thin, flat cells, arranged in a single layer. This minimal thickness facilitates rapid gaseous exchange between the air in the alveoli and blood in the surrounding capillaries. Their flattened shape and close proximity to the capillary walls minimise diffusion distance, allowing efficient transfer of oxygen into the blood and carbon dioxide out of the blood.

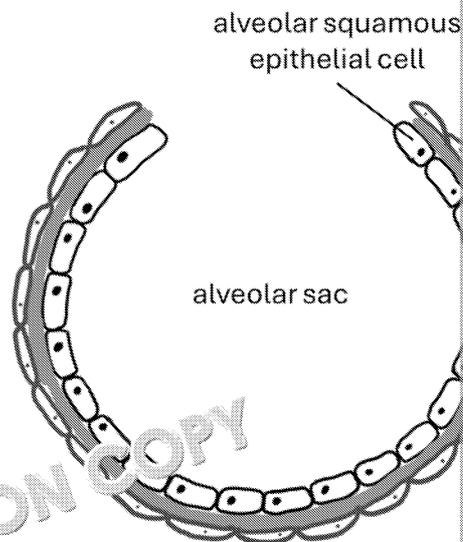


Figure F1.21. Squamous epithelial cells show their flattened shape and close proximity to the capillary walls.

Muscle

There are three distinct types of muscle cells, each specialised for different forms of movement:

- Skeletal/striated – provides voluntary, conscious movement of limbs.
- Smooth – provides involuntary movement, such as through the digestive tract, the pupils in the eyes, and the erector pili muscles which raise or lower the hairs on our body.
- Cardiac – provides involuntary, regular, and rhythmic contraction of the heart.

All muscle cell types contain actin and myosin proteins which slide over each other and shorten cell length to contract muscle and cause movement. They all contain large quantities of mitochondria, to provide sufficient ATP to facilitate this movement.



Figure F1.22. Structural overview of cardiac, skeletal, and smooth muscles.

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Skeletal muscle cells

Skeletal muscle fibres are formed by the fusion of immature muscle cells (myoblasts), which mature to create large, **multinucleated** cylindrical fibres with several nuclei and shared cytoplasm (see 'Other tissue-specific stem cells', page 8).

Nuclei are positioned just inside the cell surface membrane, preventing the obstruction of contractile fibres. The nucleus is a cell organelle to allow rapid synthesis of muscle proteins for efficient muscle maintenance.

Muscle fibres contain actin and myosin proteins that are regularly arranged in **sarcomeres**, the striated appearance of skeletal muscle fibre is individually innervated and can contract. This enables the strength of contraction to be controlled and varied.

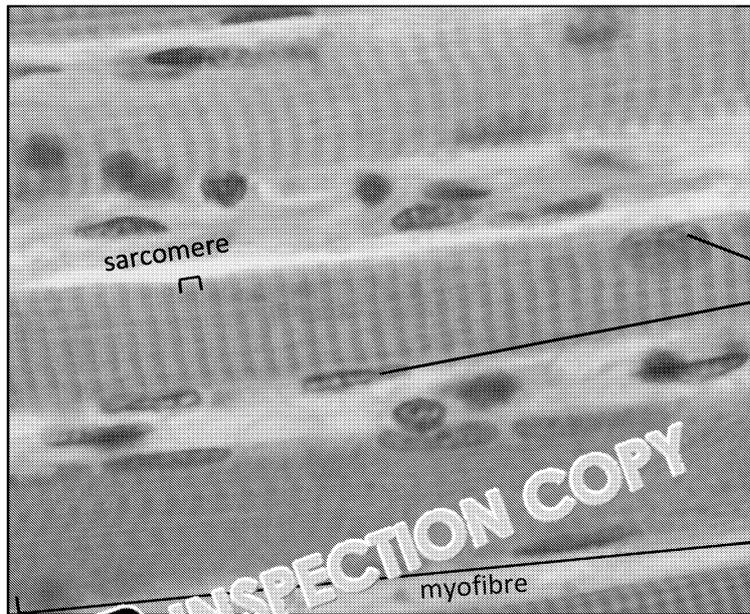


Figure F1.23. The striated appearance of skeletal muscle, as seen using a light microscope.

Cardiac muscle cells

Cardiac muscle is found in the heart and is striated like skeletal muscle because of the presence of sarcomeres. Cells remain separate, so are **uninucleate**, but the Y-shaped cells are interconnected via **intercalated discs** – specialised junctions enabling rapid signal transmission between cells. Their coordinated response to a single stimulus ensures synchronous contractions, which is vital for effective blood circulation.

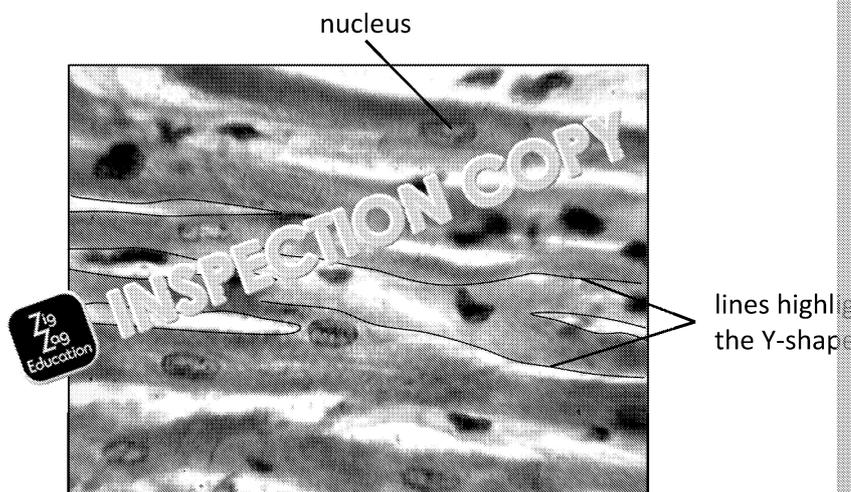


Figure F1.24. A light micrograph of cardiac muscle, showing the Y-shaped cells and the dark lines highlighting the Y-shape.

multinucleated
sarcomeres
actin and myosin
enable

multinucleated
per myofibre

uninucleated
intercalated discs
junctions
cells
transmission

lines highlighting
the Y-shape

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Smooth muscle cells

Smooth muscle fibres control involuntary movement and regulatory functions as blood pressure and **sphincter** control. Cells are spindle-shaped, with a wide section and narrow, tapered ends and centrally located nuclei. They lack sarco so appear non-striated (not striped) under the microscope. Instead, the contractile proteins – actin and myosin – are dispersed throughout the cytoplasm. This allows contractile intensity to vary and long-duration contractions to be maintained with minimal energy, such as when controlling sphincters.

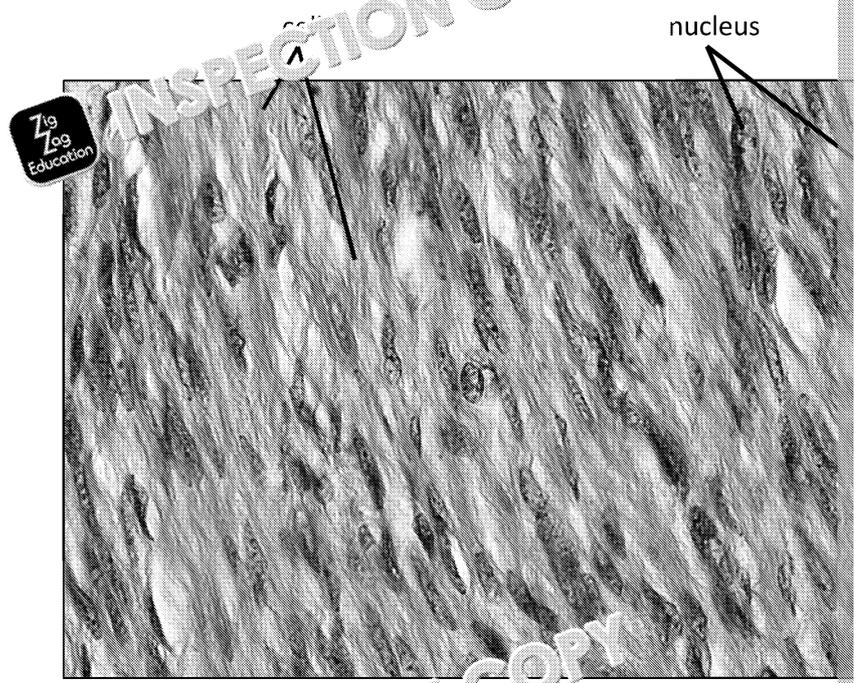


Figure F1.25. A light micrograph of smooth muscle, at $\times 400$ magnification.

Gastric pit epithelium

Gastric pits are invaginations in the stomach lining formed by columnar epithelium. They contain underlying gastric glands that secrete hydrochloric acid, enzymes and mucosal secretions for the maintenance of the stomach environment.

The epithelia increase the surface area for secretion and absorption. They have rough endoplasmic reticulum and vesicles that support the synthesis and export of enzymes and mucins. The stomach lining forms a protective barrier against self-digestion by enzymes and acids.

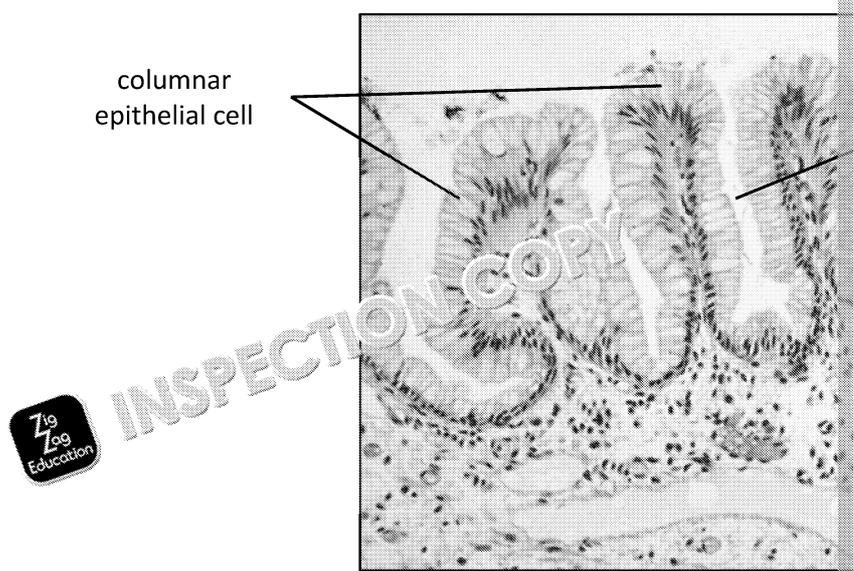


Figure F1.26. A low power light micrograph showing columnar epithelial cells lining a gastric pit.

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Recall questions

1. Describe the adaptations of erythrocytes and explain how their ability to transport oxygen.
2. Explain why sperm and ova are haploid but all other specialised cells are diploid.
3. Compare the adaptations of the tracheal ciliated epithelial cells and describe how these adaptations support their function.

Comparing eukaryotic and prokaryotic cells

Prokaryotic cells lack a nucleus. DNA is located in a central region called the nucleoid. Plasmids are small, circular DNA molecules of lengths called plasmids. Plasmids contain only a few genes that can be replicated independently of the chromosomal DNA.

There are no membrane-bound organelles in prokaryotic organisms, so although parts of the cell are specialised for specialised functions, these occur in unsegmented regions. Protein synthesis is carried out by ribosomes that are smaller and less dense (70S) than eukaryotic cells (80S).

Most prokaryotes have a cell wall containing peptidoglycan and may have short hair-like pili that extend out from the cell surface. These are used to attach the cell to surfaces. Some prokaryotes use flagella to move through their environment.

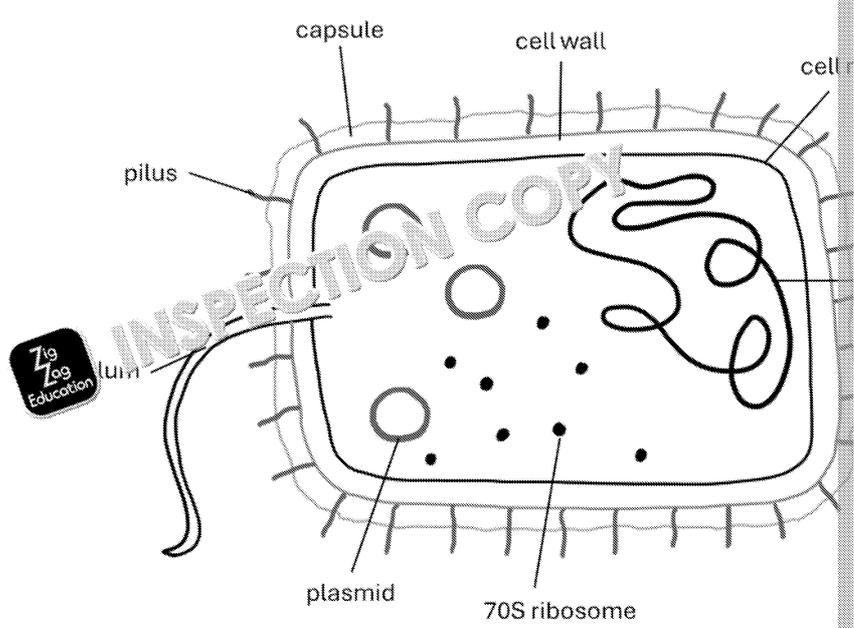


Figure F1.27. Diagram of a generalised prokaryotic bacterial cell. See page 2 for diagram of a generalised eukaryotic animal cell.

Differences in ribosomes

Prokaryotes and eukaryotes have different ribosomes: 70S or 80S. This value describes the sedimentation coefficient of the ribosome following ultracentrifugation, which reflects differences in their size and shape. There are also differences in protein content.

	Prokaryotic ribosome	Eukaryotic ribosome
Size	70S	80S
Location	Free in cytoplasm	Free in cytoplasm or attached to endoplasmic reticulum
Protein content	Less protein content	More protein content

Table F1.2. Summary of prokaryotic and eukaryotic ribosome features.

Mitochondria and chloroplasts have 70S ribosomes.

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Endosymbiotic theory

Endosymbiotic theory proposes that about 1.5 billion years ago mitochondria were free-living prokaryotes. At some point shortly after this, these bacteria were engulfed by another ancestral cell but were not digested and a **symbiotic** relationship developed, benefiting both organisms. Over time, the engulfed bacteria transferred much of their DNA to the host cell and lost their ability to reproduce independently, evolving into mitochondria.

The recognition that mitochondria have their own DNA (mtDNA) and produce their own ribosomes, which are of a similar size and density to prokaryotic ribosomes, provides evidence to support the theory. Other features suggest they were once independent organisms.



Further your knowledge

A similar explanation has been proposed for chloroplasts in plant cells, which contain their own DNA. They are thought to have originated from cyanobacteria through the same symbiotic process.

Apply your knowledge

- Describe the main structural differences between eukaryotic cells and prokaryotic cells.
- Describe and explain the evidence to support endosymbiotic theory. Suggest why this theory is widely accepted.



Practice questions: Cells

- The diagram shows a cone photoreceptor, a highly specialised cell within the retina.
 - Label the three missing organelles (A, B and C on the diagram) in the photoreceptor cell. (3)



The top organelle is heavily folded. Explain why this is important in a cone photoreceptor. (2)

A _____

The cone photoreceptor is one of millions within the nervous system relaying information from the eye to the brain.

B _____

- Describe the pathway through which electrical signals pass, starting with the trigger of photons and ending with the central nervous system. (3)

C _____



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1.1.2. Observing cells and organelles

Cells are usually too small to observe with the naked eye and require a microscope to

The light microscope

There are several key parts to a light microscope:

Objective lenses

usually a rotating set of three lenses with magnifications of $\times 4$, $\times 10$ and $\times 40$.

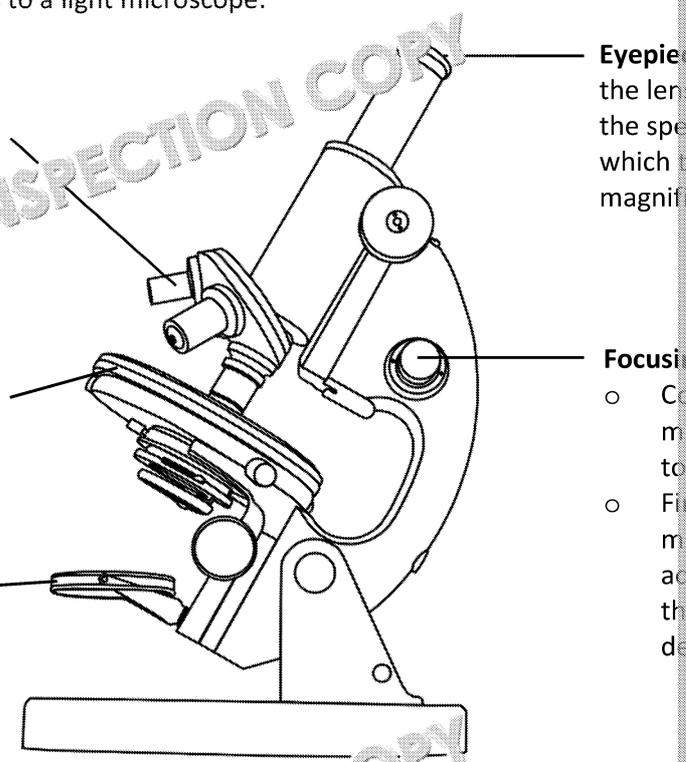


Stage

the platform where the glass slide holding the specimen is placed and secured with clips.

Light/mirror

illuminates the specimen from below, allowing light to pass through the specimen and lenses to reach the eye.



Eyepiece
the lens
the spec
which ty
magnifi

Focusing
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Figure 1.1.2.1 The key parts of a light microscope.



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Using a light microscope

When using a light microscope, it is important to avoid contact between the lens and slide to prevent damage to the specimen or lens, and to adjust the brightness so it is safe to view.

To observe a specimen using a light microscope:

1. Place slide on stage and secure with clips.
2. Set objective lens to lowest magnification.
3. Raise stage to its highest point close to the lens.
4. Turn on light source or direct light onto the mirror and check brightness through eyepiece.
5. Use the coarse focus wheel, followed by the fine focus wheel, to bring the specimen into focus.
6. Adjust objective lens to medium then high magnification and refocus using wheels at each magnification.

Advantages and limitations of the light microscope

The light microscope is a familiar piece of equipment when studying biology at school. There are many advantages to using a light microscope, but they do have limitations as described below.

Advantages	Disadvantages
<ul style="list-style-type: none"> • Inexpensive and easy to use. • Quick specimen preparation. • Enables viewing in natural colour with the option to use stains to improve contrast. • Portable and suitable for classroom use. • Can observe living specimens in real time. 	<ul style="list-style-type: none"> • Limited resolution (~200 nm). • Small organelles are not visible. • Only thin specimens can be viewed due to shallow depth of view. • Thick specimens must be treated to be viewed effectively. • Provides only 2D visualisation.

Table F1.3. Advantages and disadvantages of the light microscope.

Apply your knowledge

1. List four success factors that, if achieved, will ensure that a clear, sharp image is produced using the light microscope.
2. When viewing an image on a smartphone, zooming in will initially show more detail but the image becoming pixilated. Use the terms 'magnification' and 'resolution' to explain this.

Preparing temporary slides

Many specimens can be viewed using a light microscope, although slide preparation is required for each sample. Some samples are dry, some are wet or in suspension, and some require special treatment.

Slides prepared in school or college are temporary slides: they are made and used in a single session and then disposed of afterwards. In contrast, permanent slides are professionally prepared and can last for many years.

Preparing temporary slides

Dry biological specimens include thin plant leaves, human hair, and animal fur. If the specimen is thin and flat, such as a hair, then it can be viewed directly. However, non-flat specimens are placed on a glass slide and secured with a coverslip to gently flatten and stabilise the specimen. This ensures the image is clear and steady, and protects the sample and the microscope lenses.

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Figure F1.29. A human head louse (*Pediculus humanus capitis*) attached to a human hair at $\times 3.5$ magnification.

Preparing wet slides

Wet samples, or those that require hydration to stop them from drying out quickly in a microscope, need preparing directly on the slide using this standard procedure:

1. Place specimen flat and open on the glass slide.
2. Add 1–2 drops of water using a pipette to hydrate the sample.
3. Use tweezers to carefully flatten the sample into the water puddle.
4. Hold a coverslip at a 45° angle with one edge touching the slide.
5. Lower the coverslip onto the specimen to prevent air bubbles between the glass and specimen.

Staining specimens

For some samples, stains can be added to a sample either instead of, or as well as, water. Stains improve contrast between organelles, which improves differentiation between different cell types. Stains are also used to identify bacterial cells and to identify cells in a blood sample. Common human tissue samples collected in school include onion skin cells and blood smears.

Stain	Use
Methylene blue	Stains animal cell nuclei blue and enhances cell shape (see Figure F1.28).
H&E (haematoxylin and eosin)	Haematoxylin stains nuclei blue; eosin stains cytoplasm pink.
Crystal violet	Used in Gram staining to identify bacterial cells (see Figure F1.30).
Safranin	Highlights cell walls pink; used as a Gram counterstain (see Figure F1.30).

Table F1.4. Uses of different stains.

Using a stage microtome

A stage microtome cuts extremely thin sections from a specimen using a very sharp blade. The microtome is mounted on the microscope stage so that sections can be observed directly. This is ideal for building up a 3D reconstruction of a specimen, such as a tissue biopsy, to gain a better understanding of the sample.

A microtome can be particularly useful when preparing delicate or complex tissue samples. Sectioning using a microtome allows for direct observation to ensure that cuts are made in relevant locations within the structures. For instance, when preparing a sample of intestinal tissue for histological analysis, a microtome can reveal the fine structure of villi, by orientating the microtome to cut through the villi from the base to the tip, rather than the last to preserve its structure. This is critical for allowing accurate diagnosis of conditions.

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Figure F1.30. A microtome preparing extremely thin sections of

Recall questions

1. Describe how a coverslip should be placed on a slide. What technique is important.
2. Explain why a microtome may be useful when preparing a lung cancer biopsy, and how careful use of the microtome allows for the detail of delicate features.

The electron microscope

Electron microscopes use a beam of electrons, rather than visible light, to generate images of biological specimens. They have much higher resolution and magnification than light microscopes because of the shorter wavelength of electrons – up to $\times 500,000$ magnification and 0.2 nm resolution. This allows ultrastructure detail to be visible.

Types of electron microscope

There are two types of electron microscope: transmission and scanning:

- A transmission electron microscope (TEM) passes electron beams through thin sections of tissue stained with heavy metals. It produces a 2D image.
- A scanning electron microscope (SEM) bounces electrons off the surface of a specimen. The specimen is usually coated with gold. This allows the surface detail of larger specimens to be visible. It creates a 3D image.

Sample preparation

When samples are viewed in an electron microscope, they are placed in a vacuum to prevent the imaging beam from being scattered by air molecules in air. Specimens must be dehydrated to withstand the vacuum and the electron beam. For TEM samples, heavy metal staining provides contrast and highlights structures, but preparing samples is a complex and technical process. For SEM, fragile biological structures. The sample must be dehydrated then embedded in a resin. The microtome is used to stain for contrast.

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How images are formed

To create an image with a TEM, electrons pass through the specimen or interact with it. Electrons that pass through the specimen interact with the detector below, creating a negative: brighter areas correspond to transparent regions, while darker regions indicate more densely stained. These images are black and white, showing the presence or absence of colour in electron micrographs is added digitally to aid interpretation.

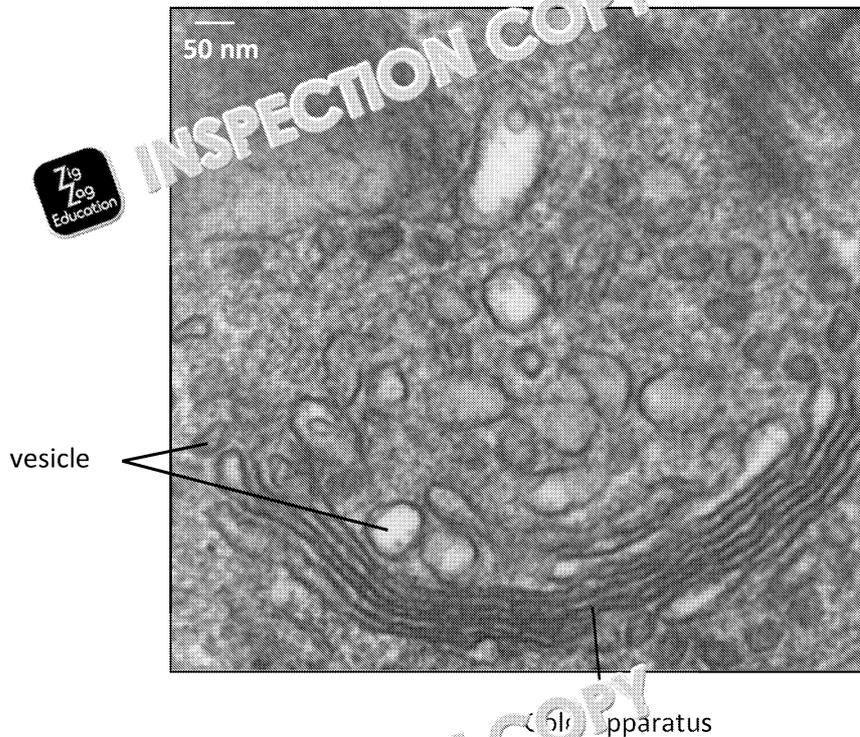


Figure F1.31. Human leucocyte showing a cross-section of Golgi apparatus, taken with a transmission electron microscope.

With a SEM, electrons interact with the particles on the surface of the sample: some dislodge electrons from the sample, known as secondary electrons. These are translated into a detailed 3D surface image. SEMs are especially good at obtaining views of larger specimens.



Figure F1.32. Scanning electron micrograph of a tardigrade *Milnesium tardigradum*.

Recall questions

1. Describe the main differences between the transmission and scanning electron microscopes.
2. Explain why biological samples must be stained with heavy metal salts and placed in a vacuum when observing using an electron microscope.

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Calculating magnification

Microscopes allow us to observe cells and subcellular structures at a much larger scale than they appear. Cell features are typically so small that they fall well below the resolution of the human eye. Therefore, magnification is essential for detailed study.

Key terms in magnification

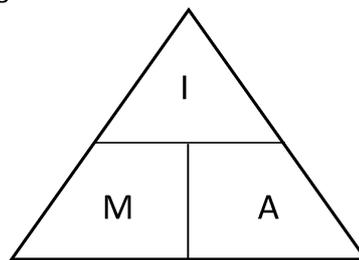
There are three measurements when interpreting microscope images:

- image size – the apparent size of the structure when viewed or measured
- actual size – the real size of the structure
- magnification – the number of times an image has been enlarged compared to the actual size

These variables are linked by the equation:

$$\text{magnification} = \frac{\text{image size}}{\text{actual size}}$$

You may prefer to use the equation triangle:



Common missteps and how to avoid them

While the formula is straightforward, applying it may be tricky. Avoid making the following common pitfalls:

- a) Being confused by terminology. Questions may use different phrasing for the terms 'image size' and 'actual size' or 'object diameter'. It can be tricky to correctly identify them. Carefully read the question to identify which values you are dealing with.

- b) Mismatching the units. Actual size is often given in micrometres (10^{-6} , μm) or nanometres (10^{-9} , nm), while magnification is usually measured in millimetres (10^{-3} , mm). Mixing these units leads to incorrect calculations.

Use powers of ten to convert between the units:

$$1 \text{ mm} = 1000 \mu\text{m}$$

$$1 \mu\text{m} = 1000 \text{ nm}$$

Tip!

There are 1000 nm in 1 μm , and 1000 μm in 1 mm.
 To calculate the number of μm in 1 mm, multiply mm by 1000.
 $3 \text{ mm} \times 1000 = 3000 \mu\text{m}$.
 To calculate the number of μm in a value given in nm, divide nm by 1000.
 $450 \text{ nm} \div 1000 = 0.45 \mu\text{m}$

Struggling to visualise a cm section of a ruler.
 In every cm there are 10 mm. In every mm there are 1000 μm .
 In every μm there are 1000 nm.
 So, if there are 775 μm , then there will be <1 mm (0.775 mm) because to reach 1 mm there must be 1000 μm , and this is only 775 μm .

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Tips for success

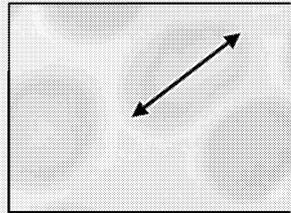
When calculating magnification, it is worth following these steps:

1. State the values you know from the question and label them clearly.
2. Convert units so they match before inserting into the formula.
3. Rearrange the equation if solving a different variable.
4. Show all your workings, including units at each step.
5. Double-check your answer by reversing the calculation.

Worked example 1: calculating magnification

An erythrocyte measures $7\ \mu\text{m}$ but appears to be $2800\ \mu\text{m}$ when viewed in a light microscope. Calculate the magnification of the microscope.

1. State the values that you know:
 $M = ?$ $I = 2800\ \mu\text{m}$ $A = 7\ \mu\text{m}$
2. State the equation: $M = I \div A$
3. Substitute in the numbers with their units:
 $M = 2800\ \mu\text{m} \div 7\ \mu\text{m}$
4. Solve the equation:
 $M = \underline{\times 400}$
5. Check your work:
 $A \times M = I$
 $7\ \mu\text{m} \times 400 = 2800\ \mu\text{m}$

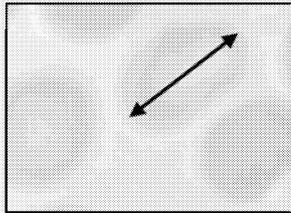


The first worked example is straightforward because it involves no unit conversions as both are in micrometres. Here is an example where unit conversions are involved.

Worked example 2: calculating magnification

An erythrocyte measures $7\ \mu\text{m}$ but appears to be $17.5\ \text{mm}$ when measured in the image below taken using a light microscope. Calculate the magnification of the image, with the microscope and the printing process.

1. State the values that you know and convert them to the same units:
 $M = ?$ $I = 17.5\ \text{mm} \times 1000 = 17\ 500\ \mu\text{m}$ $A = 7\ \mu\text{m}$
2. State the equation: $M = I \div A$
3. Substitute in the numbers with their units:
 $M = 17\ 500\ \mu\text{m} \div 7\ \mu\text{m}$
4. Solve the equation:
 $M = \underline{\times 2500}$
5. Check your work:
 $A \times M = I$
 $7\ \mu\text{m} \times 2500 = 17\ 500\ \mu\text{m} \div 1000 = 17.5\ \text{mm}$
 The erythrocytes in this printed image are 2500 times larger than their actual size.



The second worked example is more complex because the units of image and actual size are different and need to be converted. It does not matter which way you do this, as long as you perform the calculation correctly.

Your turn

1. A macrophage measures $0.4\ \text{mm}$ down a light microscope with a magnification of $\times 400$. Calculate the actual size of the cell, in micrometres.
2. An amoeba measures $2.4\ \mu\text{m}$ and is being viewed at medium power with a magnification of $\times 100$. Calculate the apparent size of the amoeba in micrometres.
3. A specimen of Ebola virus appeared to be $143.56\ \text{mm}$ under an electron microscope with a magnification of $\times 100\ 000$. Calculate the actual size of this virus in micrometres.

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Measuring cell size

The true magnification of each microscope lens varies and therefore each microscope lens must be calibrated separately. Once calibrated, the accurate measurement of specimen size can be made.

To calibrate a microscope, two pieces of equipment are required:

- **eyepiece graticule**
A transparent disc with a no-units scale that is inserted into the eyepiece lens, used for measuring microscopic structures.
- **stage micrometer**
A microscope slide with a very accurate known scale, used to calibrate the eyepiece graticule.

The eyepiece graticule has an arbitrary scale (e.g. 100 divisions), but its units do not have a known length. It must be calibrated against a stage micrometer at the magnification you plan to use. When the eyepiece graticule and stage micrometer are used, the calibration must be done separately for each lens.

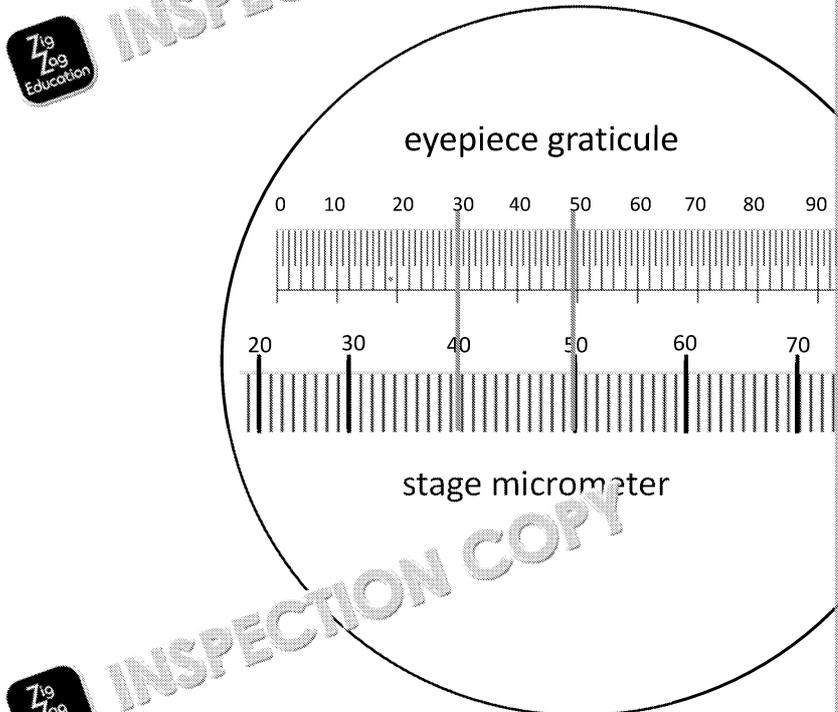
The stage micrometer is an exact length, usually 1 mm long, with ten larger divisions and each of these further divided into 0.01 mm / 10 μm divisions.

When used together, accurate measurements of microscopic structures can be made.

Calibration

To calibrate the eyepiece graticule using the stage micrometer:

1. **Align the scales:**
Put the stage micrometer on the microscope stage, and the eyepiece graticule in the eyepiece. Focus the micrometer scale at the desired magnification and align the scales.
2. **Compare scales:**
Count how many eyepiece divisions fit within an exact number of micrometer divisions. In the image, $50 - 30 = 20$ eyepiece divisions \equiv 10 micrometer divisions.



3. **Calculate the relative size of each eyepiece division:**
100 micrometer units = 1 mm, so
10 micrometer units = 0.1 mm
 $0.1 \text{ mm} \div 20 \text{ eyepiece divisions} = 0.005 \text{ mm}$, so
each eyepiece division is equal to 0.005 mm, or **5 μm**

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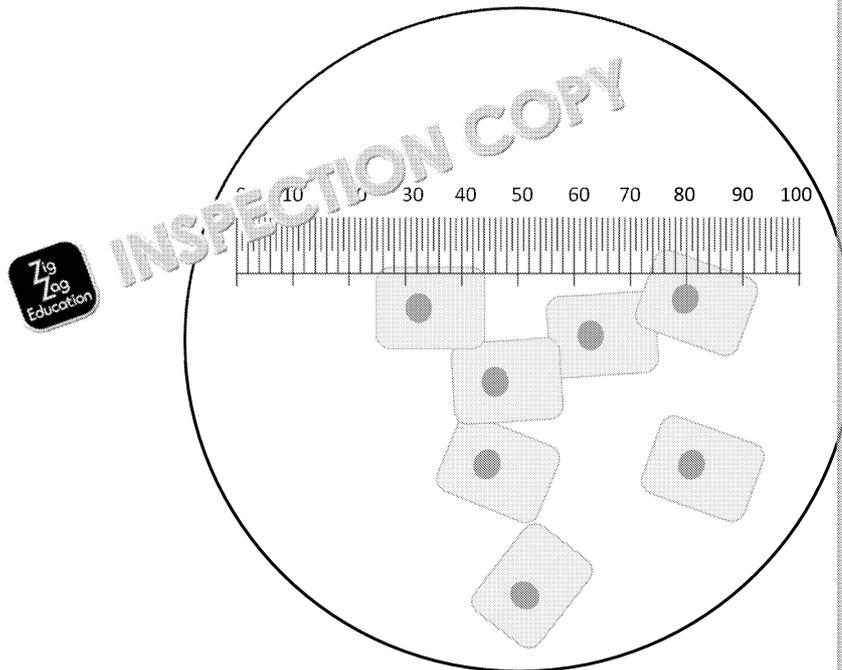
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Measuring specimen size

Having calibrated the eyepiece graticule, we now know the exact size of each division and its magnification. Next, we can measure a specimen against this known scale.

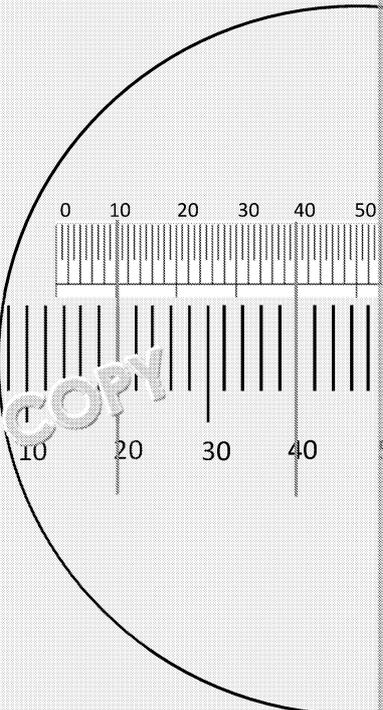
- Remove the stage micrometer and place the specimen slide on the stage.



- Focus at the same magnification used during calibration and align the specimen with the eyepiece graticule scale.
- Count the number of eyepiece divisions the specimen is equal to. In this example, the top-left cell spans from 25 to 95 divisions.
- Calculate actual size:
Each division = $5 \mu\text{m} \times 19 \text{ divisions} = 95 \mu\text{m}$
The cell is $95 \mu\text{m}$ wide.

Worked example: calculating actual size using an eyepiece graticule

- Compare the scales.
 $40 - 10 = 30$ eyepiece graticule divisions \equiv
 $40 - 20 = 20$ stage micrometer divisions
- Calculate the relative size of each eyepiece division.
100 micrometer units = 1 mm
20 micrometer units = 0.2 mm
 $0.2 \text{ mm} \div 30 \text{ eyepiece divisions} = 0.0067 \text{ mm}$, so each eyepiece division is equal to 0.0067 mm, or **$6.7 \mu\text{m}$**



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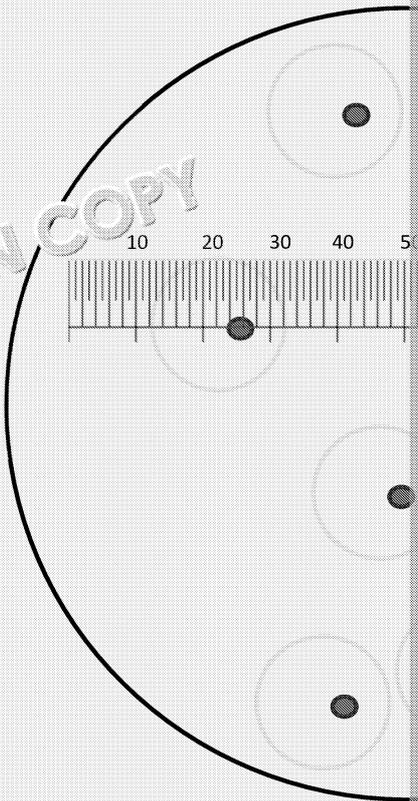
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Place specimen on stage.

- Count the number of eyepiece divisions the specimen is equal to:
 $32 - 12 = 20$ divisions

- Calculate the actual size:
 $6.7 \mu\text{m} \times 20 \text{ divisions} = 134 \mu\text{m}$



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Your turn

- Using the scale in the previous example, calculate the size of a red blood cell which is three divisions wide.



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Differential centrifugation

Differential centrifugation is a laboratory technique used to separate cellular components by density and size by rapidly spinning the sample at varying speeds in a centrifuge. Since organelles have different physical properties, sequential centrifugation at increasing speeds allows them to be progressively separated, from large, dense organelles, to small, light ones.

To centrifuge a cell sample for further analysis:

1. Homogenisation: the tissue or cell sample is broken down to release the cellular contents for separation. Homogenisation requires blending the tissue using a motorised homogeniser or a pestle and mortar to create a uniform suspension. Conditions must be carefully controlled. A cold, **isotonic buffered solution** is used to prevent enzyme activity and damage by osmosis or pH changes.
2. First centrifugation (low speed): the suspension is spun at low speed, causing large and dense organelles such as nuclei to settle as a pellet at the bottom of the vial.
3. Removal of supernatant: the supernatant (liquid layer above the pellet) is carefully removed and transferred into a new vial for further centrifugation.
4. Sequential spinning at higher speeds: this process is repeated at increasing speeds, separating progressively smaller organelles with each spin.

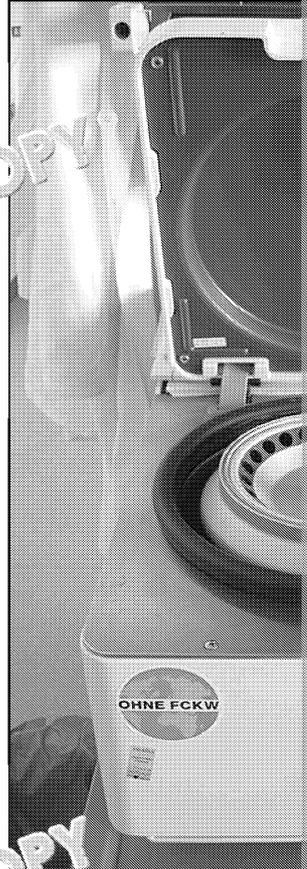


Figure F1.33. Top

Organelle isolation

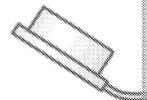
Pellets containing different organelles or cell components are removed after different centrifuge speeds.

Centrifuge speed	Cell components removed in pellet
Low	Nuclei
Medium	Mitochondria, lysosomes, peroxisomes
High	Microsomes, small vesicles
Ultra	Ribosomes, soluble proteins

Table F1.5. Cell components removed at different centrifuge speeds.

This technique allows scientists to study specific organelles in isolation – for example, analysing mitochondrial function or identifying enzyme activity within lysosomes.

Figure F1.34. During centrifugation, particles settle to the bottom of the tube and the rest remains suspended.



Pellet

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Recall question

1. State the purpose of the cold, isotonic buffered solution used in homogenisation.
2. Explain why different organelles can be separated using different centrifuge speeds.



Counting cells in a sample

Accurate cell counting is essential in biological investigations, diagnostics, and research. Two common tools used for estimating cell numbers in a suspension are the haemocytometer and the Coulter counter.

The haemocytometer

A haemocytometer is a specialised microscope slide which can hold a known volume of sample for the counting of cells. Once the number of cells in this defined volume is calculated, the original sample can be calculated. It is typically used for estimating red or white blood cell counts and microbial populations.

The haemocytometer has a finely etched grid, within a recessed chamber 0.1 mm deep. A coverslip rests above the chamber, creating a precisely known volume.

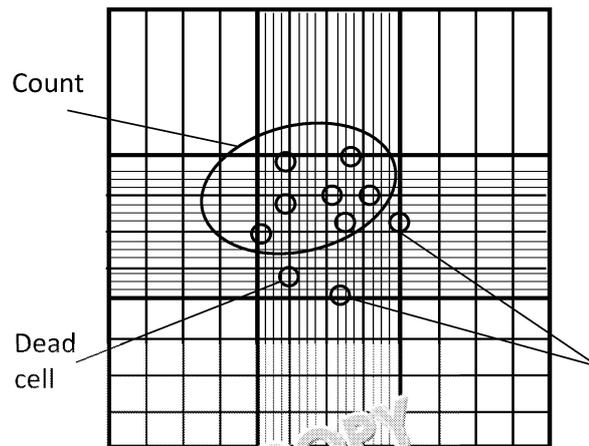


Figure 1.3.1 A haemocytometer can be used to count cells.

To use the haemocytometer, follow these steps:

1. Dilute the sample or cell suspension to a workable concentration.
2. Add a known volume of diluted sample into the chamber.
3. Count the number of cells under a microscope using the etched grid.
4. Calculate the concentration using the known volume, cell count and dilution factor.

The north-west rule (or 'top and left rule') can be used to determine whether a cell is counted. Cells touching the top (north) or left (west) boundary lines are included, while cells touching the right (east) or bottom (south) boundary lines are excluded. This method ensures accurate counting of cells and avoids double counting or artificially inflating or deflating the count.

Haemocytometry offers an effective method for determining cell population size.

Advantages	Disadvantages
<ul style="list-style-type: none"> • Known chamber volume allows a reliable estimate without calibration. • Inexpensive and portable. • Allows direct observation of other cell features, such as morphology. • Used for fieldwork and classroom settings. 	<ul style="list-style-type: none"> • Requires precise technique, which needs training. • Time-consuming and prone to inaccuracies and errors. • Accuracy declines at high cell concentrations. • Requires staining for some cell types.

Table F1.6. Advantages and disadvantages of haemocytometry.

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The Coulter counter

A Coulter counter is an electronic device used to count cells and estimate their size, based on their electrical resistance. A cell suspension is prepared in an electrolyte solution and is drawn through a small aperture between two electrodes. Each time a cell passes through, it displaces electrolyte, creating a pulse of electrical resistance. The amplitude of the signal indicates cell volume.

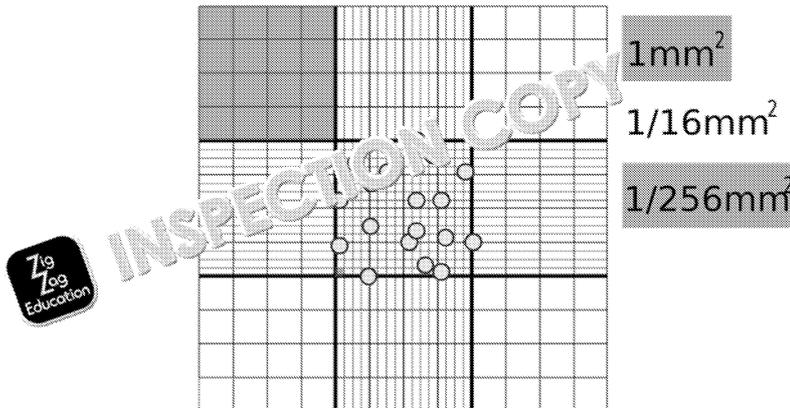
The Coulter counter can be used for very rapid cell counting. It can differentiate between cells based on their size and electrolyte displacement. This is useful when undertaking a part of a diagnosis, or monitoring cell size and growth in cultures.

Advantages	Disadvantages
<ul style="list-style-type: none"> • Rapid counting of large volumes. • Accurate and detailed: measures cell count and volume. • Versatile: can analyse diverse cells and particles. • Removes human error and fatigue. 	<ul style="list-style-type: none"> • Sample must be suspended in a fluid to promote cell clumping. • Tube diameter must match sample sizes can cause counting errors if cells pass through together and be counted as one. • Requires regular cleaning, mainly to prevent clogging.

Table F1.7. Advantages and disadvantages of the Coulter counter.

Your turn

1. Use the haemocytometer to count the number of valid cells within the central square.



2. Compare and contrast the haemocytometer to the Coulter counter, in particular:

- speed
- accuracy
- user training
- sample preparation
- cost

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Practice questions: Observing cells and organelles

- 1 Calculate, in μm , the width of the guard cells (green, indicated by pointer) in a *Tradescantia* leaf, where:
- 100 micrometer divisions = 1 mm
 - 10 micrometer divisions = 2 eyepiece divisions



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1.1.3. Link between organelle structure and function

Cells contain a variety of specialised organelles, each adapted for their specific function. The quantity and structure of organelles can vary depending on the functional demands of the cell. Organelles do not work in isolation: their coordinated interaction is essential for maintaining cell function.

Just as departments in a factory – production, packaging, and logistics – must operate in a coordinated manner, organelles like mitochondria, lysosomes, and vesicles. Disruption in this balance may lead to disease. That could prove detrimental, or even fatal, for the organism.

Coordination between organelles

Coordination between the nucleus and mitochondria

The nucleus and mitochondria share a tightly integrated relationship, rooted in evolutionary history (see Endosymbiotic theory, page 20). While mitochondria are able to synthesise some of their own mtDNA and mitoribosomes, the nucleus encodes more than 1000 mitochondrial proteins, which are synthesised in the cytoplasm and imported into the mitochondria. In return, mitochondria provide energy for energy-dependent cell processes, including transcription, translation, DNA replication, and cell division.

Some mitochondria are physically connected to the nuclear envelope, supporting **bilateral** communication. For instance, in response to cellular stress, mitochondria can signal to the nucleus to adjust gene expression, leading to reduced gene transcription or altered protein synthesis based on metabolic demand.

Organelle coordination in protein synthesis

Transcribing a gene in the nucleus into a protein in the cytoplasm is a complex, multi-step process involving several organelles.

1. Transcription in the nucleus.
The coding strand of the gene is transcribed into messenger RNA (mRNA) in the nucleus through nuclear pores into the cytoplasm.
2. Translation at the ribosome.
mRNA attaches to ribosomes, and its sequence of codons is used to place amino acids in a polypeptide chain. Ribosomes are made in the nucleolus but operate either free-floating in the cytoplasm or attached to the rough endoplasmic reticulum membrane.
3. Protein processing in the Golgi apparatus.
The polypeptide chain is modified and folded into its final shape by the Golgi apparatus.
4. Transport and final destination.
Proteins are packaged into vesicles or lysosomes, which deliver them to their specific locations or secrete them via exocytosis.

For efficient protein synthesis, organelles must be coordinated. For instance, excess amino acids leads to waste, as mRNA degrades quickly within the cytoplasm (typically within a few days). Conversely, overproduction of proteins can trigger inflammation or immune response if they are misfolded or unregulated.

Your turn

1. Create a review of organelles and their functions, highlighting how some organelles are intricately linked to others.
2. Outline the organelles involved in protein synthesis and describe how they influence each other to maintain cell function.

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1.1.4. The cell surface membrane

All cells are encased by the cell surface membrane that separates the internal surroundings. It is not a passive boundary, but rather a dynamic and highly selective barrier with a central role in controlling substance exchange, maintaining homeostasis, and

Structure of the cell surface membrane

The fluid mosaic model

The cell surface membrane, and indeed all membranes within living organisms (especially eukaryotic ones) are primarily made from phospholipids. The **amphipathic** nature of phospholipids means that they form as a **bilayer**, **hydrophobic** tails pointing inwards away from the water-based cytoplasm, and **hydrophilic** heads forming the membrane's inner and outer surface. Embedded within the phospholipid bilayer are many other components, including channel and carrier proteins, cholesterol, glycoproteins and glycolipids.

This arrangement is known as the fluid mosaic model and describes how cell membranes are assembled and function. This formation provides a flexible barrier which can be adapted to suit the specific cell and its function. For example, in nerve cells, the membrane's structure is crucial for the transmission of electrical signals, while in intestinal cells, it aids nutrient absorption.

The amphipathic nature of the membrane means that many substances are naturally prevented from moving through the membrane, either because they are too large to pass through the tightly packed phospholipid bilayer, or because they are charged and cannot pass through the hydrophobic middle. This enables the cell to control the entry and exit of substances.

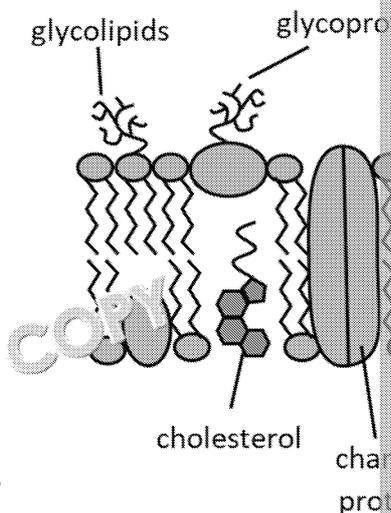


Figure F1.36. The fluid mosaic model of a cell membrane showing the phospholipid bilayer.

Components within the membrane

Many elements can be embedded within the cell membrane and provide a range of functions:

- enabling cell-to-cell recognition and communication – identifying the cell as self or foreign, and the binding of hormones
- adhesion between cells to form tissues – by forming a **glycocalyx**, gap junctions, and **desmosomes**
- providing channels to facilitate the movement of substances by, for example, diffusion, osmosis and active transport

To enable these functions, the cell surface membrane contains various components:

- **intrinsic proteins** (see Table F1.8):
 - channel proteins (do not change shape), and carrier proteins (do change shape to transport larger molecules that would otherwise be unable to pass through the membrane)
 - aquaporins (a specific form of channel protein, that transport water)
- **extrinsic proteins** (see Table F1.8):
 - present on the outer surface as receptor sites for hormones and other signalling molecules
 - present on the inner surface, involved in cell signalling
- **cholesterol** (see next)
- **glycoproteins** (proteins with carbohydrates attached) and **glycolipids** (phospholipids with carbohydrates attached) allow cell-to-cell communication, cell recognition and adhesion

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Intrinsic (integral)	Extrinsic (peripheral)
<ul style="list-style-type: none"> Span the bilayer. Amphipathic: hydrophobic and hydrophilic zones. Connect both sides of the membrane. 	<ul style="list-style-type: none"> Within one side of the bilayer. Loosely bound to the hydrophilic head of phospholipid. Do not enter the hydrophobic core.

Table F1.8. A summary of the key features of intrinsic and extrinsic membrane proteins.

	Glycoproteins	Glycolipids
Structure	Protein + carbohydrate	Phospholipid + carbohydrate
Location	External (extracellular) side of the membrane, including forming microvilli	External (extracellular) side of the membrane
Main functions	Cell signalling, recognition and adhesion, immune response, membrane transport	Cell signalling, recognition and adhesion, immune response, membrane transport
Examples	Antibody and hormone receptors	Blood group antigens

Table F1.9. A comparison of structure and function of glycoproteins and glycolipids.

The role of cholesterol in the membrane

Cholesterol is a steroid component of the cell surface membrane. The cell can adjust the amount of cholesterol present: the more cholesterol present, the greater the fluidity of the membrane that the membrane can remain flexible at a greater range of temperatures or be adapted to perform specific functions. For instance, some cells significantly change shape as part of their function when they are moving through narrow capillaries, and leucocytes when they move out of blood vessels into tissue spaces. Cholesterol in the cell surface membrane maintains fluidity to enable cells to change shape.

In addition to maintaining membrane fluidity, cholesterol plays a crucial role in the function of blood vessel endothelial cells. This is worth noting when considering the advantages and disadvantages of cholesterol in vessel endothelial membranes. Cholesterol is beneficial in these cell surface membranes because:

- It controls membrane fluidity, providing elasticity in response to blood flow and also in response to body-wide blood pressure changes.
- It provides signalling functions important when controlling vasodilation and constriction.

However, too much cholesterol in the blood vessel endothelial membranes can increase uptake and retention of **LDL** in the cell surface membranes, which can increase the formation of plaques and increase the risk of heart attack or stroke. These plaques can narrow or block arteries, leading to conditions such as atherosclerosis, which significantly increases the risk of cardiovascular diseases.

LDL (low-density lipoprotein) is often referred to as 'bad' cholesterol because it is found in plaque that can block cellular function, leading to heart disease, stroke and other conditions. Excess intake of cholesterol can lead to an increase in LDL.

Your turn

- Draw and annotate a labelled diagram of the fluid mosaic model to show the various components within the cell surface membrane and summarise their functions.
- Describe the role of cholesterol in the cell surface membrane, and outline its risks.
- Describe the importance of channel and carrier proteins in the cell surface membrane and why these are essential, referring to the structure and properties of the fluid mosaic model.

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Movement through the membrane

Some molecules can freely pass through the phospholipid bilayer; others cannot. Molecules that are required in higher concentrations inside the cell than they are present outside the cell have requirements that demand specialist transport through the cell surface membrane.

Bulk transport

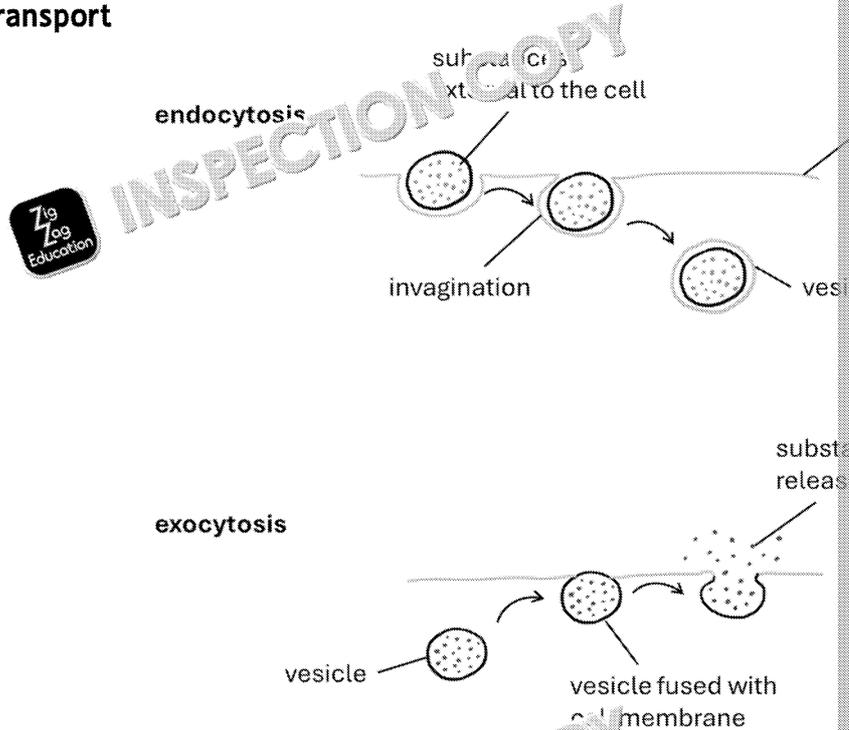


Figure F1.37. Diagrams that show the processes of endocytosis and exocytosis.

One method of transporting most types through the cell surface membrane is bulk transport. This is when many molecules need to be transported at once, or the substances to be transported are large. Bulk transport is through transport proteins. Endocytosis allows cells to intake essential nutrients while exocytosis enables the secretion of vital substances like hormones and enzymes. Exocytosis involves a part of a membrane (such as from the cell membrane or the Golgi apparatus) forming a vesicle and is crucial for maintaining cell homeostasis and facilitating various cellular processes.

Endocytosis involves the **invagination** of the cell surface membrane around a substance external to the cell, thus engulfing it and bringing it into the cell. Phagocytosis (used to engulf and destroy invading pathogens) and pinocytosis (used to transport liquids into the cell) are examples of this process.

Exocytosis involves part of an organelle's membrane budding off to form a vesicle. This transports carbohydrates, lipids, and proteins of the cell, such as in digestion or with antibodies.

Simple diffusion

Diffusion is the net movement of particles from an area of higher concentration to an area of lower concentration, due to the random movement of particles. Particles move in all directions, but the overall movement is down the concentration gradient. This movement continues until equilibrium is reached. This process does not require energy and is therefore considered passive.

Figure F1.38 shows oxygen diffusing through a cell surface membrane. For instance, oxygen molecules move across the cell surface membranes of the alveolar epithelial cells, the capillary endothelial cells, and the erythrocytes to bind to haemoglobin. This is possible because oxygen molecules and carbon dioxide are small and uncharged so are not restricted by the hydrophobic core of the phospholipid bilayer.

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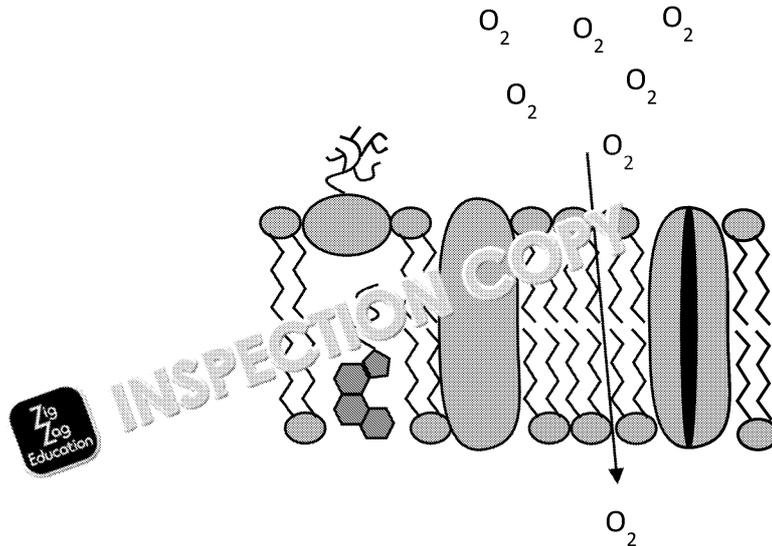


Figure F1.38. A simplified diagram showing how oxygen molecules can move across the cell surface membrane.

Facilitated diffusion

Facilitated diffusion is a refinement of simple diffusion: as with diffusion, particles move down a concentration gradient, but they move through a protein channel embedded within the membrane because of their size and/or charge.

Channel proteins facilitate the movement of small, charged ions, such as sodium or potassium ions, across the hydrophobic core of the bilayer.

Carrier proteins transport larger molecules like glucose across the membrane. They are another part of facilitated diffusion, which enables only the specific molecule to move through the membrane, with smaller particles getting through as well.

Channel and carrier proteins provide selective permeability: only certain substances can pass through the surface membrane.

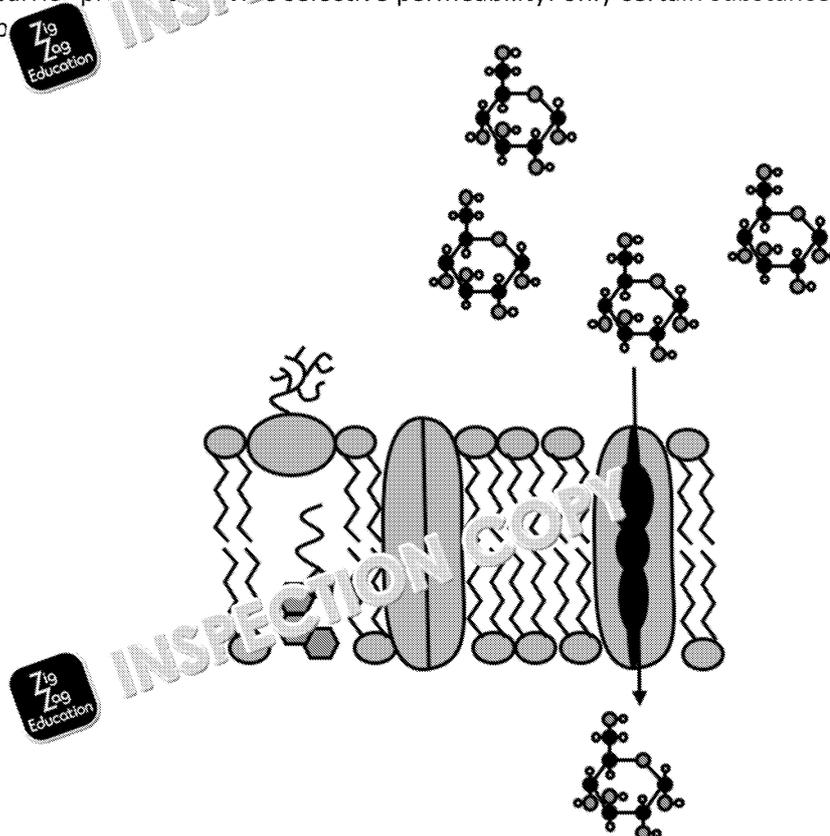


Figure F1.39. A simplified diagram showing glucose being moved through the cell membrane in the process of facilitated diffusion.

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Osmosis

Osmosis is a specialised form of diffusion – it is the net movement of water molecules from an area of higher water potential to an area of lower water potential, therefore down the water potential gradient, through a selectively permeable membrane.

The bilayer is partially hydrophobic because the fatty acid tails of the phospholipids prevent water from moving through the membrane. Instead, integral membrane proteins span the entire membrane and facilitate the movement of ions and molecules through the membrane.

Osmosis is important for maintaining water balance in animal cells in a process called osmoregulation.

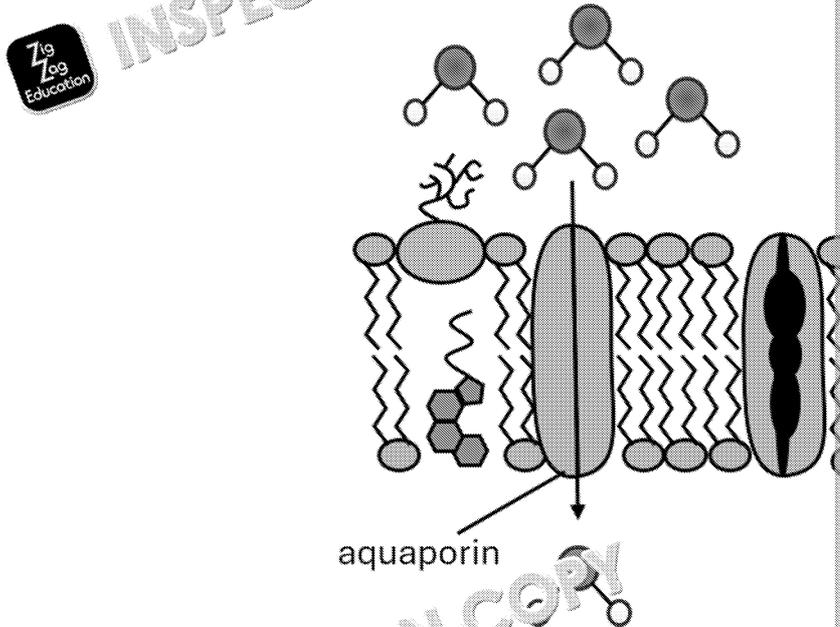


Figure F1.40. A simplified diagram to show how water moves through the cell surface membrane via aquaporin, which enables the polar water molecule to pass through the hydrophobic centre.

Active transport

Active transport is the net movement of particles against their concentration gradient. It occurs using intrinsic transport proteins and allows cells to maintain concentration gradients of molecules across the cell membrane.

For instance, cells in the stomach lining use ATP to actively transport H^+ ions into the stomach to create an acidic environment for digestion and defence against pathogens.

Recall questions

1. Describe how endocytosis and exocytosis enable bulk transport.
2. Explain the difference between diffusion, facilitated diffusion and active transport.

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Cell-to-cell communication

Cell-to-cell recognition

Cell-to-cell recognition occurs using extrinsic proteins, glycoproteins, and glycolipids on the surface of the cell. This includes identifying cells as self, and damaged and foreign cells that need to be destroyed.

This recognition is essential, and problems arise if it breaks down. Autoimmune diseases occur when the immune system mistakenly attacks its own cells. Examples include lupus, rheumatoid arthritis, and ulcerative colitis. Cancer cells evade detection, too, which is why they can proliferate.

In addition to autoimmune diseases, cell-to-cell recognition is an important factor with organ transplantation. The tissue or organ being transplanted will not have the same markers on the surface, and this will trigger the body to reject it as foreign or non-self, a response which causes tissue death and decay and can prove fatal, not only because the transplant was necessary for the patient, but because the rejection process can cause significant surrounding tissue damage.

When a transplant is being planned, one of the factors considered is how genetically similar the patient's tissues and blood are. The closer they are, the more likely the transplant will be accepted. This is why close family relatives are often good tissue matches. However, patients who have a transplant will then take immunosuppressants for the rest of their life to prevent organ rejection, no matter how close a tissue match they were. This is because the immune system will continue to see the organ as foreign and try to reject it. This is controlled by immunosuppressants, which reduce the immune response and reduce the chance of organ rejection. However, this increases the patient's risk of infections.

Role of extrinsic proteins as receptors

Extrinsic proteins face outwards from the cell membrane and facilitate cell-to-cell communication. One of these functions is as a receptor to hormones and chemical messengers from one part of the body to elicit a response in a different part of the body (see *Table F1.10*).

	Function
Insulin	Targets liver cells to increase uptake of glucose from the blood and convert it into glycogen for storage
Adrenaline	Targets vital organs to prepare the body for fight or flight
Testosterone	Development and maintenance of male characteristics
Oestrogen	Development of female characteristics and regulation of the menstrual cycle

Table F1.10. A summary of a few key hormones and their key functions.

When a hormone binds to a receptor, the receptor changes shape and triggers an action within the cell which alters tissue function. A specific example can be seen with antidiuretic hormone (ADH). ADH binds to the receptor on the surface of renal tubule epithelial cells, a chain reaction of events occurs, involving second messenger molecules and results in the positioning of aquaporins in the cell surface membrane. This increases the permeability of the membrane and water osmoses out of the tubule cells back into the blood. This reduces the volume of water excreted and concentrates urine in response to low water levels in the blood, which triggered ADH secretion from the posterior pituitary gland.

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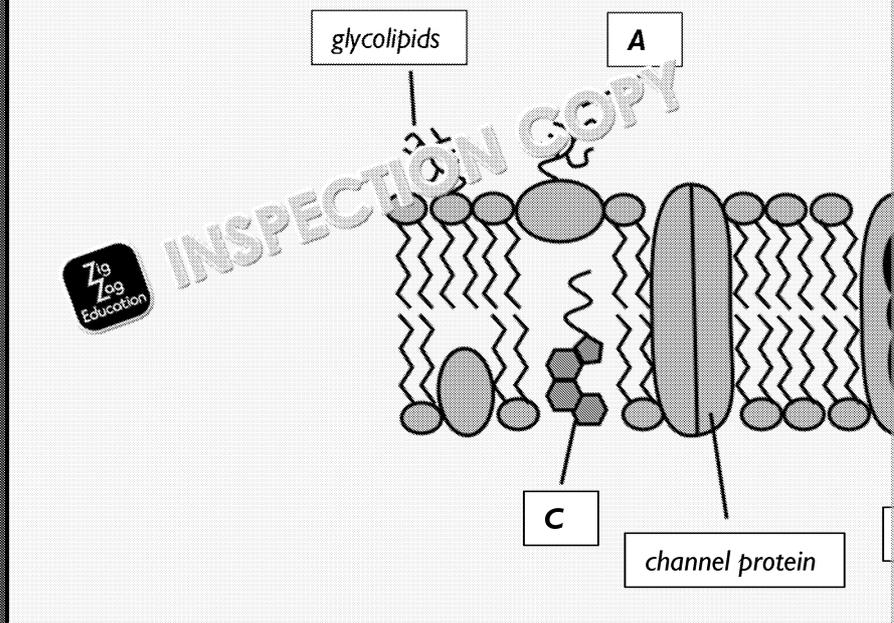
Apply your knowledge

1. Describe the role that cell-to-cell recognition has in the success or rejection of organ transplants.
2. Describe how extrinsic proteins are involved in hormone signalling.



Practice questions: The cell surface membrane

1 Below is a diagram of the cell membrane. Identify A, B and C from the diagram.



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1.1.5. Mitosis and meiosis

Mitosis and meiosis are forms of nuclear division used by eukaryotic cells, including plants and animals. Mitosis increases the number of cells within the organism's body, or replaces cells that have become infected or worn out. Meiosis is used to create gametes required for reproduction.

For nuclear division to occur, the cell must prepare itself for the process. This includes duplicating DNA, creating structures and frameworks to enable division and duplication of organelles, and ensuring there are enough organelles for division.

Not all cells can undergo nuclear division. Some cells are so complex and specialised that they cannot replicate. This section will explore the cell components required to enable division, such as cytoskeleton, microtubules, spindle fibres, and chromosomes, as well as the processes of mitosis and meiosis.



Chromosomes and DNA

Structure of chromosomes

Chromosomes are extremely long lengths of DNA, tightly coiled around histone proteins to form a complex called **chromatin**. Each chromosome contains a region called the **centromere**, which is essential when moving chromosomes during nuclear division.

During normal cell function (interphase) there is:

- one **chromatid** per chromosome
- one pair of each chromosome, one inherited from each parent, forming 23 homologous pairs

Homologous chromosomes are the same length, have the same centromere position, and carry genes for the same traits at the same position on the chromosome.

chromosome – a tightly coiled DNA molecule associated with proteins, which help in the movement of chromosomes within the nucleus.

chromatin – DNA associated with proteins.

centromere – the region of a chromosome that joins two sister chromatids together and attaches to spindle fibers during division.

chromatid – one of the two identical copies of a chromosome, joined together at the centromere.

homologous chromosomes – a pair of chromosomes in a cell, one from each parent. They have the same length and centromere position, and carry genes for the same traits at the same position on the chromosome.

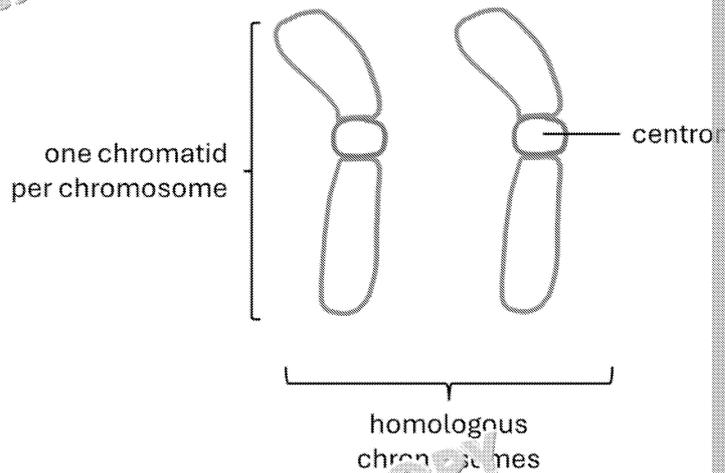


Figure F1.41. A diagram showing one chromatid per chromosome and one pair of homologous chromosomes.

In most human **somatic** cells, there are 23 pairs of chromosomes, a total of 46 chromosomes. The 22 pairs are called autosomes that contain genes for general body functions. The 23rd pair consists of the sex chromosomes, which determine biological sex: XX for females; XY for males. These cells are described as **diploid**, meaning they contain two sets of chromosomes, and their DNA content is denoted as 2n.



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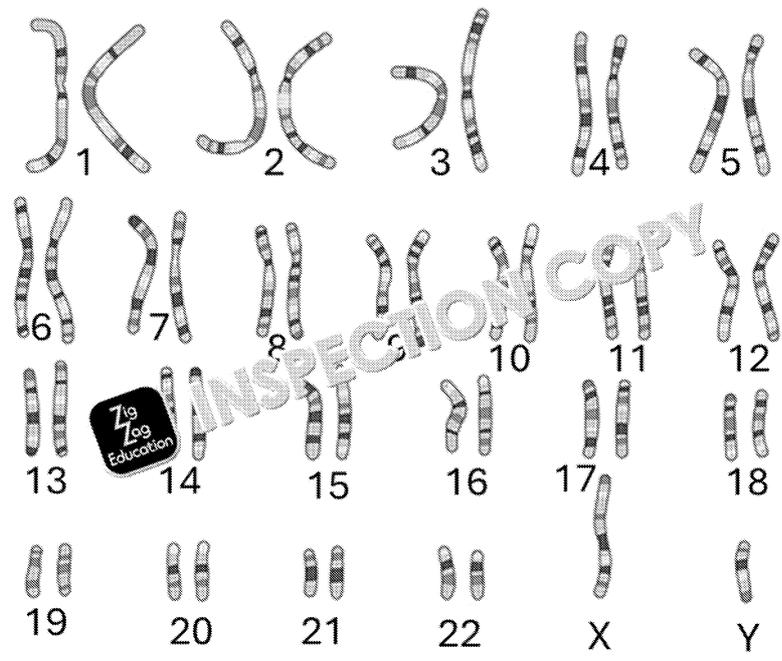


Figure F1.42. A karyotype of chromosomes from a human male, including the sex chromosomes. This type of karyotype is used to identify chromosomal abnormalities.

Molecular structure of DNA

DNA is a polymer containing many millions of repeated monomers: the nucleotide substructure, comprising of a phosphate group and a pentose sugar containing a nitrogenous base. The phosphate and sugar form the backbone, and one of four nitrogenous bases which contribute to the code.

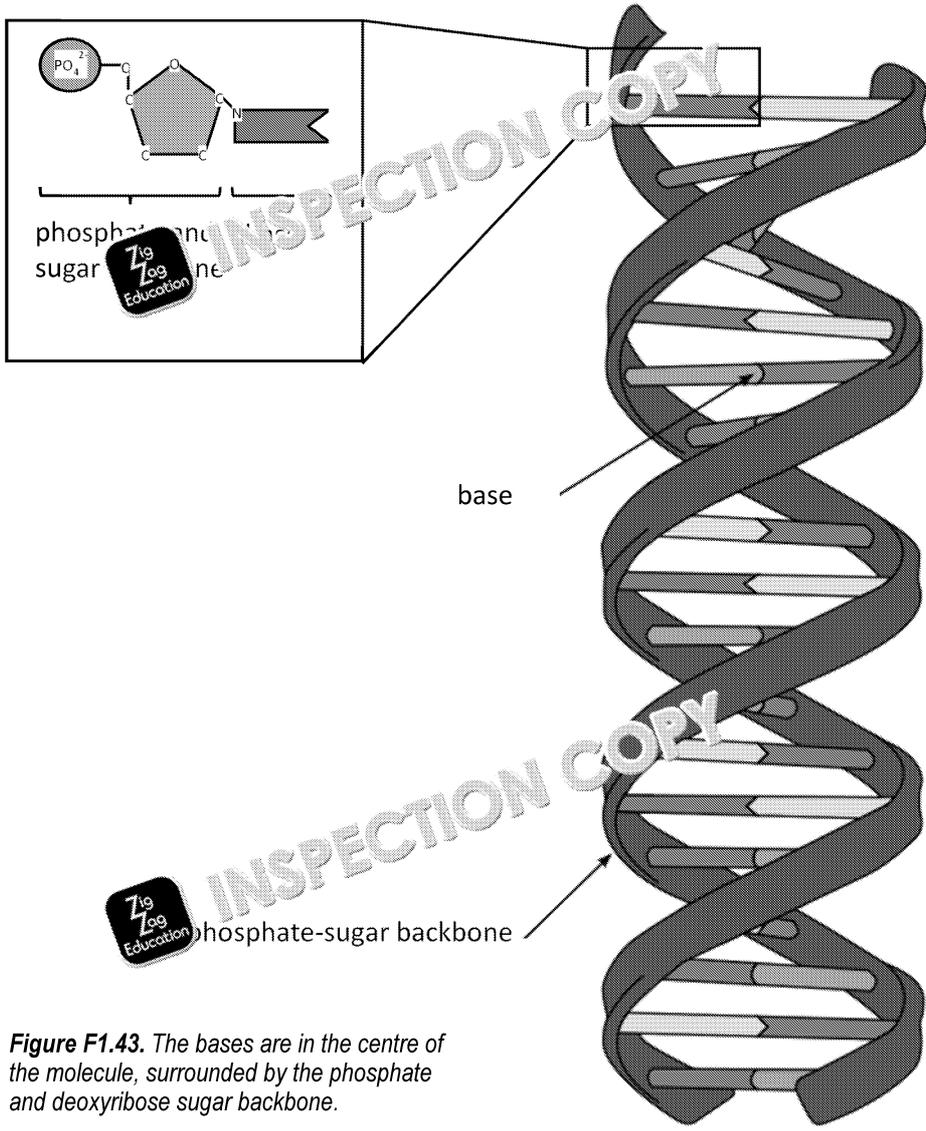


Figure F1.43. The bases are in the centre of the molecule, surrounded by the phosphate and deoxyribose sugar backbone.

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Four nitrogenous bases include guanine (G), cytosine (C), adenine (A), and thymine (T). Guanine and cytosine are purines and comprise a hexagonal unit joined to a pentagonal unit. Cytosine and thymine are pyrimidines and contain only the hexagonal unit.

Tip!

Remember that pyrimidines have a long name and a short structure, whereas purines have a short name and a long structure!

Across the double helix, the bases guanine and cytosine pair with each other, and adenine and thymine pair with each other. These bases pair with each other because three hydrogen bonds form between guanine and cytosine, and two hydrogen bonds form between adenine and thymine. In both cases, a purine is paired with a pyrimidine, maintaining a constant width along the double helix. As a result, if the quantity of each base is measured in a sample of double-stranded DNA, the number of guanine units will equal the number of cytosine units, and the number of adenine units will equal the number of thymine units.

Tip!

Remember the base pairing rules by remembering GoCAT! Ignore the 'o', then split these into two down the middle: G and C pair, and A and T pair. GoCAT is also really useful in other ways too:

G	3	C	A	2	T	= hydrogen bonds
Large		Small	Large		Small	= size of base

Note how the size and the number of hydrogen bonds decreases as you read across the bases.

Importance of base pairing

Base pairing is important because it creates a double-stranded DNA. One strand contains the code – the coding strand. The other strand contains the opposite side of the code – the template strand. The coding strand is the one that is used to produce the mRNA.

- The code – the nitrogenous bases (G, C, A and T) – is stored in the center of the double strand, offering maximum protection from chemical attacks and ionising radiation.
- There is implicit error checking because the two bases must match for a stable partnership and therefore less chance for error – mutation.
- When a gene is transcribed, the template strand is read so that the mRNA is the same as the coding strand.
- When DNA is being replicated, both strands are copied. The two new double helices contain one original strand and one copied strand, known as semi-conservative replication.

The molecular structure of a gene

A gene is a short length of DNA which codes for a particular protein. The order of bases within the gene is critical because the bases are read in order and transcribed onto the mRNA strand, which is then read by the ribosome and translated into equivalent amino acids. These are bonded together to form the polypeptide chain precursor of the protein.

Each amino acid is coded for by three bases: a **triplet**, and the triplets are non-overlapping. One triplet codes for one amino acid, but one amino acid may be coded for by several triplets, or **codons**: the DNA code is **degenerative**. This means that some changes to DNA bases can remain **silent**, resulting in no change to the amino acid that has been encoded.

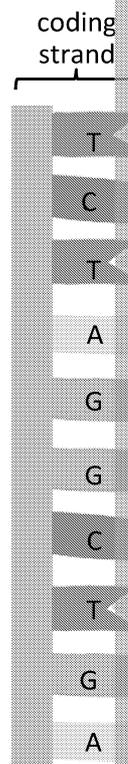


Figure F1.44. The DNA double helix is transcribed into mRNA, which is then translated into a protein. The sequence of three bases – a codon – codes for one amino acid.

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Each gene has a 'start' codon and a 'stop' codon, which define the length of the polypeptide. The start codon is ATG, which codes for the amino acid methionine and indicates where the ribosome starts. The stop codon is either TAA, TAG or TGA. No amino acid can be matched to these codons. The polypeptide is released from the ribosome.

Each gene codes for a particular protein, but there are different versions of all genes, and these are known as **alleles**. Alleles carry minor differences between them which affect protein structure because the polypeptide chain varies slightly between them. Understanding the role of alleles helps explain many genetic variations (our **genotype**) and the characteristics (our **phenotype**). For example, some characteristics are solely controlled by the alleles that we inherit from our biological parents; other characteristics are controlled by complex interplay between our alleles and the environmental influences external to us. Our combination of alleles is unique unless we have an identical sibling. Therefore, the order of the bases in our DNA is both a direct consequence of the DNA that our parents have, and a direct cause of our characteristics or phenotype.

triplet – set of three bases that code for one amino acid
codon – the three bases that code for one amino acid or instruction
degenerative – the fact that many amino acids are encoded by two or more different codons, meaning that some mutations do not affect the polypeptide of a protein
silent – a mutation that does not change an amino acid, or the structure of a protein
alleles – variations of a gene
genotype – the genetic make-up of a cell or organism, which determines its phenotype
phenotype – the characteristics of an individual as a result of their genotype and the environment

The Human Genome Project

The Human Genome Project began in 1990 and concluded in 2003. Its aim was to determine the sequence of the human genome, base by base, to produce a comprehensive catalogue of human DNA. It identified approximately 20,000 to 25,000 genes, and produced a catalogue that is freely available around the world.

It enhanced the development of technology and software used to read and analyse DNA. It has led to major advancements in genomics, such as understanding genetics, evolution, and identifying genes involved in inherited genetic diseases and cancers. Furthermore, it enabled the development of personalised medicine, such as those of emerging diseases like COVID-19, and is facilitating personalised medicine and targeted drugs.

The project also brought to light significant ethical, legal, and social issues related to genomics. These include concerns about privacy, consent, and the potential misuse of genetic information. Addressing these issues is crucial for ensuring that advancements in genomics are used responsibly.

It was a hugely successful international research programme that greatly accelerated our understanding of genetics. For instance, it has led to breakthroughs in diagnosing rare genetic diseases, the development of targeted cancer therapies, and the creation of personalised treatment plans based on an individual's genetic make-up.

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Your turn

- Using the rules and mnemonic to name a base, label:
 - the name of the four DNA bases
 - the base pair rules
 - the number of hydrogen bonds formed between base pairs
 - whether each base is a purine or a pyrimidine
- Draw a two-chromatid chromosome, then label the sister chromatids, the centromere, and the spindle fibres.
- Write a short news article summarising the importance and significance of the Human Genome Project.



The cell cycle

The only way to create a new cell is to duplicate an existing cell. To achieve this, the cell goes through a period of cell growth, before replicating DNA and dividing. One complete cycle of a cell is formed and ends once it has completed mitosis, although not all cells can or will complete the whole cell cycle.

The cell cycle is split into two main phases:

1. Interphase
2. M phase (nuclear division)

These phases are further divided into distinct subphases. M phase is much shorter than interphase. Some human cells can undergo mitosis within one hour but require a further 23 hours to be ready to divide again. The duration of these phases is crucial because it affects the rate at which cells proliferate. For example, in rapidly dividing tissues like skin or the digestive tract, a swift replacement of cells, essential for maintaining tissue health.

Interphase

Interphase is a highly active phase of the cell cycle. It is the part of the cell cycle when normal biochemical functions occur. It is divided into several stages, processes and checkpoints. A correct error-free copy of the cell is made during M phase and that a functioning cell exists in interphase.

For example:

- Some cells, once created from a stem cell, never proceed through interphase and instead **differentiate** then enter a period of **senescence**. Neurons and erythrocytes are examples. Neurons because they have an extremely complex structure; erythrocytes because they lack a nucleus, which stops them from dividing.
- Other cells may go through the cell cycle multiple times to replenish tissue that needs regular replacement. Skin, intestinal tract epithelia and hair follicles all require constant replacement. Tissue cells such as haematopoietic (create blood cells) and basal (create skin cells) are also examples.

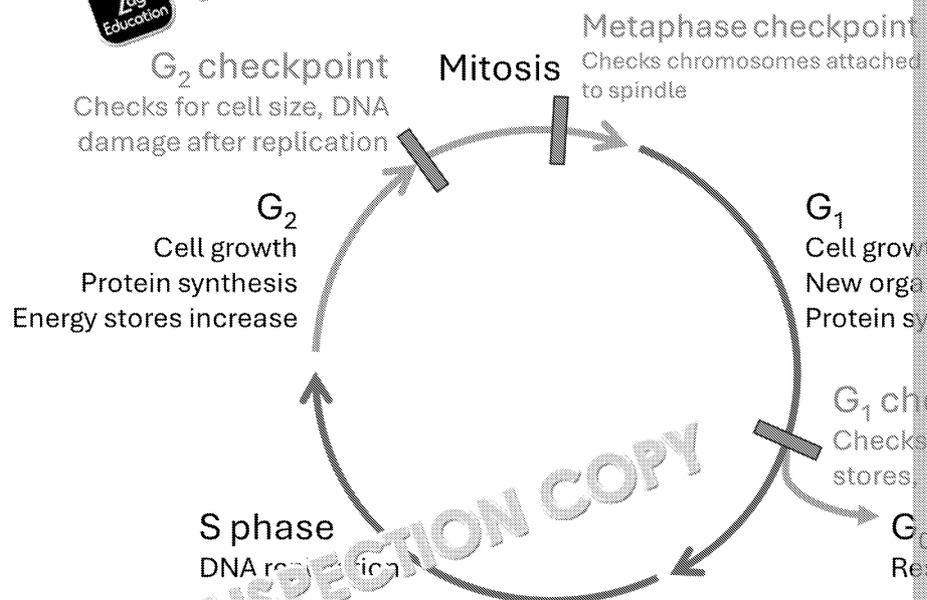


Figure F1.45. The cell cycle comprises several stages and three distinct checkpoints.

There are three gap phases and one synthesis phase within interphase. Each phase has a particular purpose but exit from gap phases 1 and 2 requires successful completion of checks. If the checkpoint is not passed successfully, the cell can either be fixed, or if not possible, placed into senescence and flagged for **apoptosis** (programmed cell death).

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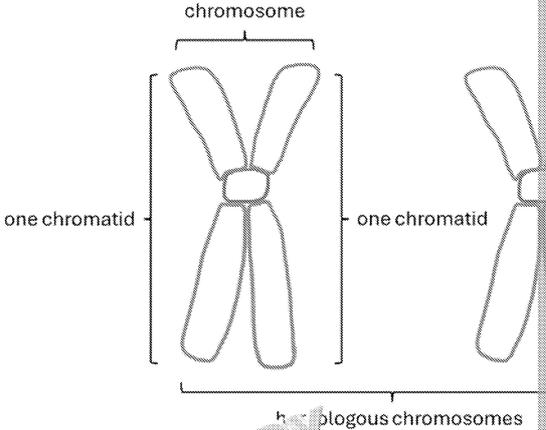
Phase	Processes completed
Gap phase 1 – G ₁	Cell grows and new organelles are made. Protein synthesis occurs. Checkpoint genes control exit.
Gap phase 0 – G ₀	Resting phase of variable duration (days, weeks, months, years), and some cells never leave this phase once entered. In this stage, cells may undergo apoptosis, differentiate, or become senescent. Neutrophils and mature erythrocytes are examples of cells that have entered. Cells enter this phase after entering G ₁ or S phase.
Synthesis phase – S phase	DNA replication: DNA in the nucleus is duplicated. Each chromosome now has two sister chromatids per chromosome.  <p>After DNA replication in S phase of interphase, chromosomes consist of two chromatids per chromosome. Cells are now committed to continuing with mitosis.</p>
Gap phase 2 – G ₂	Further cell growth and production of proteins necessary for cell division. Energy stores increase. DNA error checking.

Table F1.10. A summary of the phases of interphase and the processes completed.

Mitosis

Once a cell has successfully completed interphase and passed the checkpoints, it is ready to divide. This means that:

- DNA has been replicated, so each chromosome now contains two chromatids.
- DNA has been checked for errors to ensure accuracy.
- Sufficient cell structures have been built to enable cell division to occur successfully.
- Sufficient energy stores are available to facilitate the process of cell division.
- The cell is large enough for division to result in viable daughter cells.

Mitosis is the form of nuclear division which creates genetically identical, somatic cells. It is a complex process, and errors can result in mutations or malfunction.

To undertake cell division with accuracy and precision, mitosis has five key stages:

1. Prophase
2. Metaphase
3. Anaphase
4. Telophase
5. Cytokinesis

Remember
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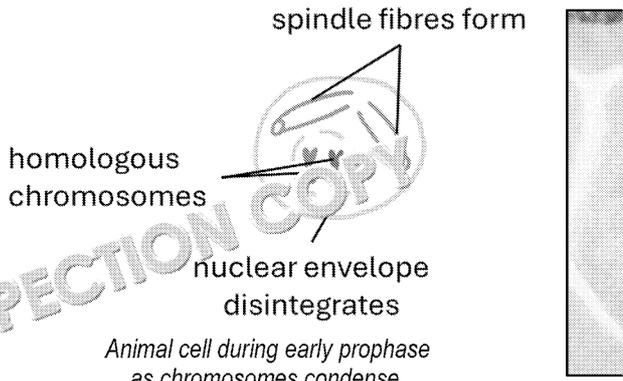
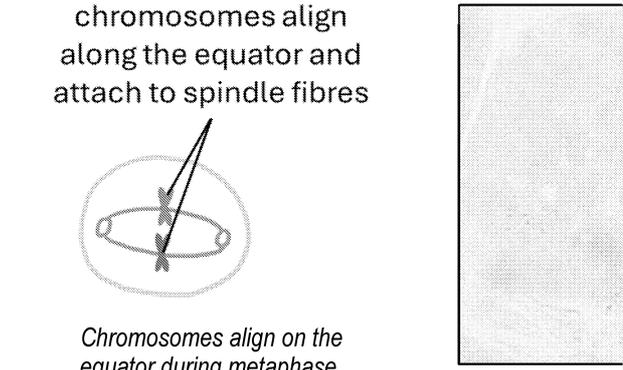
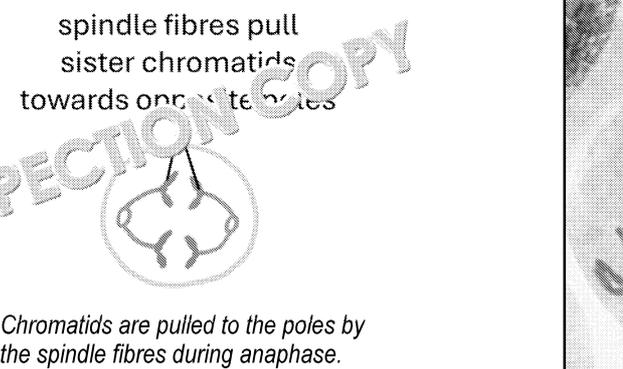
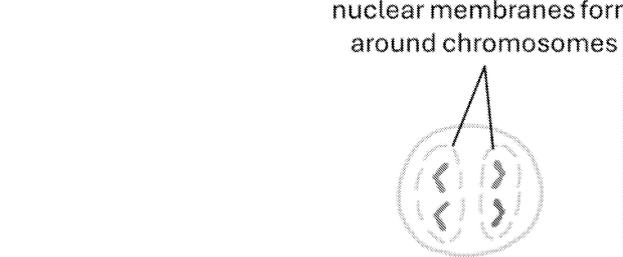
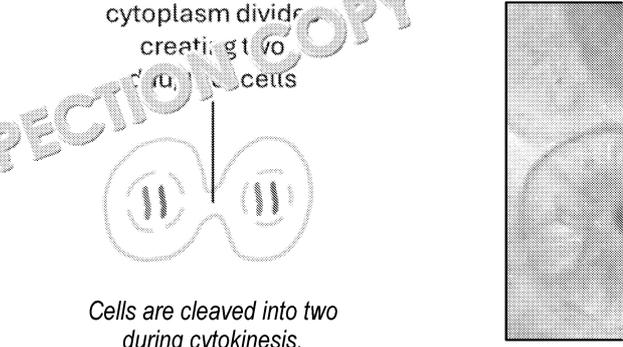
Stage of mitosis	Microscope image/diagram
<p>Prophase Chromatin condenses and forms chromosomes consisting of two sister chromatids joined at the centromere. Spindle fibres assemble. Nuclear membrane disintegrates.</p> 	<p>spindle fibres form</p> <p>homologous chromosomes</p> <p>nuclear envelope disintegrates</p> <p><i>Animal cell during early prophase as chromosomes condense.</i></p> 
<p>Metaphase Chromosomes align along the equator of the cell and attach to spindle fibres by the centromere.</p>	<p>chromosomes align along the equator and attach to spindle fibres</p>  <p><i>Chromosomes align on the equator during metaphase.</i></p>
<p>Anaphase Spindle fibres pull each sister chromatid in opposite directions towards the poles of the cell. Chromatids are now called chromosomes.</p> 	<p>spindle fibres pull sister chromatids towards opposite poles</p>  <p><i>Chromatids are pulled to the poles by the spindle fibres during anaphase.</i></p>
<p>Telophase Separated chromosomes reach the poles. New nuclear membranes form around each pole. Nuclear division is complete.</p>	<p>nuclear membranes form around chromosomes</p> 
<p>Cytokinesis The cytoplasm is divided by pinching the cell into two genetically identical daughter cells, each with its own nucleus. Also known as cleavage. Cell division is complete.</p> 	<p>cytoplasm divides creating two daughter cells</p>  <p><i>Cells are cleaved into two during cytokinesis.</i></p>

Table F1.11. Stages of mitosis.

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Prophase, metaphase, anaphase, and telophase are stages of nuclear division where duplicated DNA is separated to each pole and the nuclei are formed. Following this, cell division occurs during cytokinesis, where the other cell contents are divided into two new daughter cells and a cell membrane forms between them.

Check
you know
chromosomes

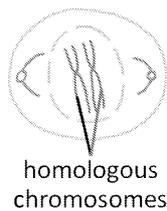
Meiosis

The process of meiosis is essential for creating genetic diversity in offspring. Meiosis is a form of cell division that produces gametes – sperm or ova – which are **haploid**: they contain only one set of chromosomes (n), rather than pairs of chromosomes as in most somatic cells, which are diploid (2n).

During fertilisation, two haploid gametes fuse to form a diploid zygote, restoring the full set of chromosome pairs.

Meiosis shares many similarities with mitosis in the mechanisms of nuclear division, but has key differences that enable the formation of haploid gametes. These include:

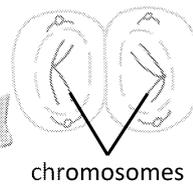
- Two successive divisions – meiosis I and meiosis II – that produce four genetically diverse daughter cells.
- Genetic variation in gametes, generated by crossing over at chiasmata during prophase I and independent assortment of homologous chromosomes during metaphase I.



Prophase I

Homologous chromosomes pair up, forming bivalents.

Non-sister chromatids exchange segments of DNA at chiasmata points in a process called **crossing over**.

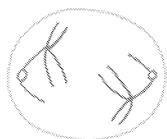
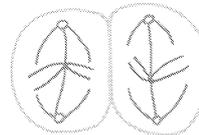


chromosomes



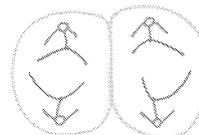
Metaphase I

Bivalents align on the equator randomly, in a process called **independent assortment**.



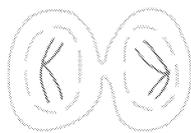
Anaphase I

Homologous chromosomes are pulled to opposite poles.



Telophase I

Nuclear envelope reforms.



Cytokinesis I

Cell divides into two cells, and the chromosomes are contained in two cells.

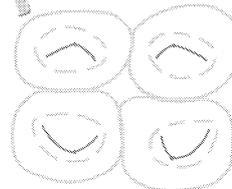


Figure F1.46. There are two phases of meiosis, which includes crossing over and independent assortment, leading to genetic variation in the four daughter cells.

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Creating genetic variation

Genetic variation occurs through two processes:

1. Crossing over.

This process occurs only once during prophase I. At this stage of meiosis, homologous chromosomes pair up to form **bivalents** and non-sister chromatids exchange segments of DNA at points called **chiasmata**. This process, known as crossing over, shuffles alleles from both parents, contributing to genetic variation.

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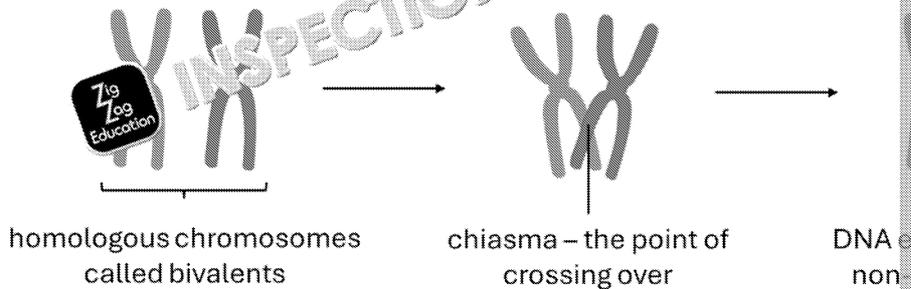


Figure F1.47. The process of crossing over involves the exchange of genetic material between homologous chromosomes, one paternal and the other maternal in origin.

2. Independent assortment.

This process occurs during metaphase I. Homologous chromosome pairs align in the equator of the cell. The orientation of each pair towards the poles is random and independent of other pairs, leading to independent assortment.

When the homologous chromosomes are separated during anaphase I, the random orientation of maternal and paternal chromosomes being sorted into daughter cells leads to independent assortment, contributing to genetic variation.

In metaphase II, sister chromatids separate independently. Although they are genetically identical, they may differ due to crossing over during prophase I, so their random separation also contributes to genetic variation.

Genetic variation produced by crossing over and independent assortment produces almost endless variety. In humans with 23 pairs of chromosomes, the number of possible combinations of maternal and paternal chromosomes in a gamete is 2^{23} , equivalent to 8,388,608 potential combinations of maternal and paternal chromosomes in a gamete! This is why siblings do not look identical to each other, nor their parents.

Comparing mitosis and meiosis

Mitosis and meiosis are both processes involved in cell division. There are a great many similarities between the two processes, but many significant differences too. The key features are compared in Table F1.12.

	Meiosis	
Homologous chromosomes	Homologous chromosomes form bivalents	Homologous chromosomes do not form bivalents
Chromosomes in daughter cells	Daughter cells are haploid	Daughter cells are diploid
Daughter cell genetics	Daughter cells are genetically different	Daughter cells are genetically identical
Crossing over	Crossing over occurs	No crossing over
Cell division of daughter cells	Cell divides twice, resulting in four daughter cells	Cell divides once, resulting in two daughter cells

Table F1.12. A comparison between mitosis and meiosis.

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Monohybrid crosses

When gametes fuse during fertilisation, the chromosomes present in the male gamete pair with the chromosomes in the female gamete. Each gene is present as a pair: one allele from the male, one from the female. Most genes have several alleles throughout the population, but every individual has only up to two of these available alleles.

Alleles may be **dominant** or **recessive** in their expression. Dominant alleles are always expressed in the phenotype, even if a recessive allele is also present. To express a recessive trait, two copies must be present. Dominant alleles are written with a capital letter (e.g. A) and appear before recessive alleles, which are written with a lower-case letter (e.g. a). A genotype with two identical alleles is either **homozygous** dominant (e.g. AA) or **homozygous** recessive (e.g. aa). A genotype with two different alleles is **heterozygous** (e.g. Aa).

If the parents' genotypes are known, then it is possible to predict the likelihood of offspring that they have. We can use a Punnett square with one gene to predict the outcomes of their children. If we consider the inheritance of tongue rolling, with RR (homozygous dominant: can roll tongue) and rr (homozygous recessive: can't roll tongue), the chances of offspring being able to roll their tongue can be calculated using a Punnett square, write the alleles from one parent across the top and the alleles from the other parent down the side. Then, complete the squares by combining the alleles from the top and the side to show the potential offspring:

♀ ♂	R	r
R	Rr	Rr
r	Rr	Rr

Every genotype in all offspring possibilities is Rr (heterozygous); therefore, 100% of offspring expressed as a decimal (1.0), or a phrase (four of four) will be able to roll their tongue as they are heterozygous for the characteristic.

If one of these children had their own children with someone else who is also heterozygous, what are the chances of their children being able to roll their tongue? Again, a Punnett square can be used:

♀ ♂	R	r
R	Rr	Rr
r	Rr	Rr

With this combination of genotypes, the chance of a child being able to roll their tongue is 75%. Only three of the four genotype outcomes contain the dominant allele as either heterozygous (Rr). The fourth possible outcome is homozygous recessive (rr) which is not able to tongue roll.

These are called **mono**hybrid crosses: meaning they deal with one gene only.

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Dihybrid crosses

Dihybrid crosses examine the inheritance patterns of two different genes simultaneously. These genes may be on the same chromosome or on different chromosomes and may influence each other's inheritance. By using a Punnett square, we can predict the expected ratios of various traits, although actual ratios may well vary due to factors such as natural skew in fertilisation and genetic linkage. Genes that appear on the same chromosome but are not separated by crossing over during meiosis are inherited together, and this will affect the actual ratio of inheritance.

Dihybrid crosses require consideration of two genes. Let's consider the potential outcomes for eye colour, together.

- Mother: blonde hair (hh), blue eyes (ee)
- Father: brown hair (HH), brown eyes (EE)

What genetic combinations exist for their gametes?

- Mother: h, h, e, e → he, he, he, he
- Father: H, H, E, E → HE, HE, HE, HE

As all the allele combinations are the same, we can simplify this to he and HE.

Now we know the allele combinations, we can combine this in a Punnett square and see the potential outcomes:

♀	he	he
♂ HE	HhEe	HhEe
HE	HhEe	HhEe

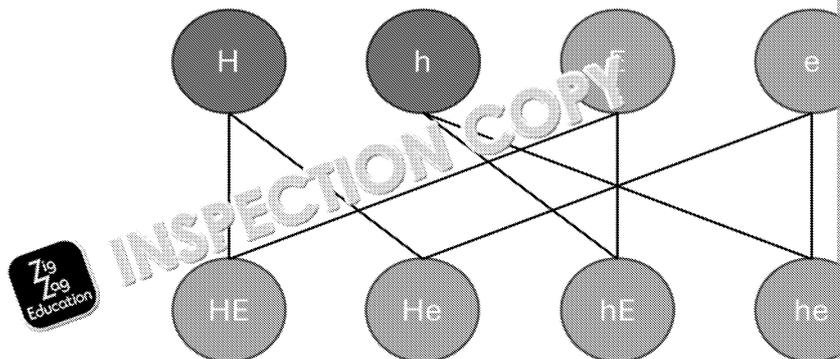
The same general rule applies: the dominant allele letter is written first, but the pairs are written together. The outcome is that all their children will have HhEe genotypes and therefore brown eyes phenotype.

How about one homozygous parent and one heterozygous parent?

- Mother: brown hair (Hh), brown eyes (Ee)
- Father: blonde hair (hh), blue eyes (ee)

Which combinations exist for their gametes?

- The father is straightforward as there are only recessive alleles, therefore h and e is the only option.
- The mother is more complex because the heterozygous alleles can be inherited together.



Therefore, the mother's genotypes include HE, He, hE and he.

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Putting these into a Punnett square results in the following outcomes:

♀ \ ♂	HE	He	hE
he	HhEe	Hhee	hhEe

Analysing the outcomes shows that:

- brown hair, brown eyes (HhEe) = 1 of 4 = 25 %
- brown hair, blue eyes (Hhee) = 1 of 4 = 25 %
- blonde hair, brown eyes (hhEe) = 1 of 4 = 25 %
- blonde hair, blue eyes (hhee) = 1 of 4 = 25 %

There is an equal chance of this couple having a child with brown or blonde hair

Let's consider an even more complex example – heterozygous parents:

- Mother: brown hair (Hh), brown eyes (Ee)
- Father: brown hair (Hh), brown eyes (Ee)

What are the allele combinations this time? For both parents, the allele combinations are:

- HE
- He
- hE
- he

In a Punnett square:

♀ \ ♂	HE	He	hE
HE	HHEE	HHEe	HhEE
He	HHEe	HHee	HhEe
hE	HhEE	HhEe	hhEE
he	HhEe	Hhee	hhEe

The chances of having a baby with the following phenotypes are:

- brown hair, brown eyes (HHEE, HhEE, HHEe, HhEe) = 9 of 16 = 56.25 %
- brown hair, blue eyes (HHee, Hhee) = 3 of 16 = 18.75 %
- blonde hair, brown eyes (hhEE, hhEe) = 3 of 16 = 18.75 %
- blonde hair, blue eyes (hhee) = 1 of 16 = 6.25 %

Tip!

Getting a dihybrid cross correct:

1. Organise the Punnett square so allele combinations follow a logical pattern.
2. Use the Punnett square to help identify one phenotype from another. Remember that some combinations will result in the same phenotype.
3. The total number of alleles should equal 16, so add them up to check (9 + 3 + 3 + 1 = 16).

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Mitochondrial inheritance

The inheritance features and patterns that we have considered so far refer exclusively to nuclear DNA. The nucleus provides almost all of the genomic content, but as discussed in section 1.1.1 (page 3), mitochondria have their own DNA of their own, known as mitochondrial DNA (mtDNA). mtDNA encodes 37 genes and is inherited from the maternal line via the egg cell. This is because the egg cell is about 10 million times larger than the sperm and must provide sufficient nutrients and ATP for the zygote to divide many times through which to get nutrients for growth and energy instead of sperm cells do contain mitochondria but these are only required to provide ATP for motility and are not passed onto the egg cell.

Your mitochondrial DNA was inherited exclusively and entirely from your biological mother. This is because that sufficient ATP can be provided for the energy-intensive processes involved in replication and the complex processes involved in the early stages of embryonic development, it is the mother's mitochondria and therefore genetic mutations within the mtDNA, they will all be passed on to the offspring. Each mitochondrion in the body has identical mtDNA. Mitochondria are organelles and components and are present in every living cell in the body. Therefore, harmful, defective mtDNA cause significant issues throughout the affected person's whole body but is most noticeable in tissues with high ATP requirements, such as muscle tissues, the brain and the eyes.

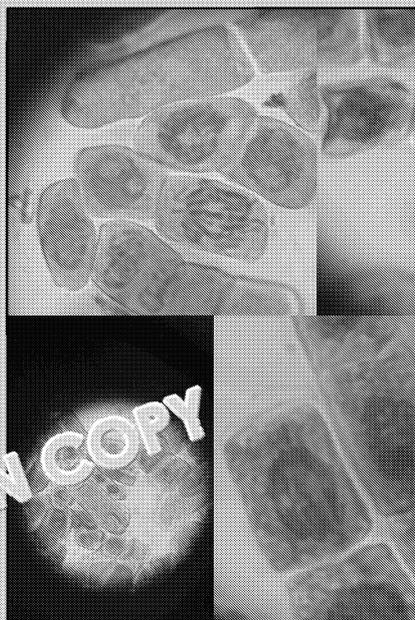
Research into mtDNA, inheritance and treatments for conditions caused by mtDNA has been ongoing for many years. One of the key treatment pathways requires diagnosing the mother. If a woman has a mitochondrial DNA condition, her unfertilised eggs can be harvested and the mitochondria removed from the egg cells. Mitochondria from a donor egg cell without mtDNA can be used to replace the mitochondria in the affected woman's eggs. This is known as mitochondrial replacement therapy. *In vitro* fertilisation is then used to create a fertilised embryo which is then transferred to the woman's uterus for her to continue with the pregnancy as normal.

The consequence of this procedure is that the baby technically has three, not two, 'parents' – the mother, the father and the female mtDNA donor. However, the 'third parent' has only a small number of the approximately 25,000 genes in the whole genome – approximately 0.15%.

Mitochondrial replacement therapy is a groundbreaking technique which offers a solution for people with mitochondrial diseases, but it is still undergoing regulatory scrutiny and ethical debate.

Apply your knowledge

1. The father has wet earwax (Ee) and can taste bitter substances (Tt). The mother has wet earwax (EE) and cannot taste bitter substances (tt). Predict the likely genotype and phenotype outcomes for their children using a dihybrid cross.
2. Describe the differences between mitosis and meiosis, including detailing the processes that lead to genetic variation.
3. Identify the stages of mitosis in the images, right, and describe the processes occurring at each stage.



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Practice questions: Mitosis and meiosis

- 1 Outline the role of checkpoints in the interphase phase of the cell cycle. (4)

1.2. Tissue structure and function

1.2.1. Tissues

Multicellular organisms are composed of various highly specialised cells. These cells perform complete specific functions, creating a working and efficient organism. Human adult female, there are about 28 trillion cells, grouped into more than 200 different cell types, which form part of approximately 60 different tissues, making up 11 major organs. To understand how these cells work together, we need to look at tissues.

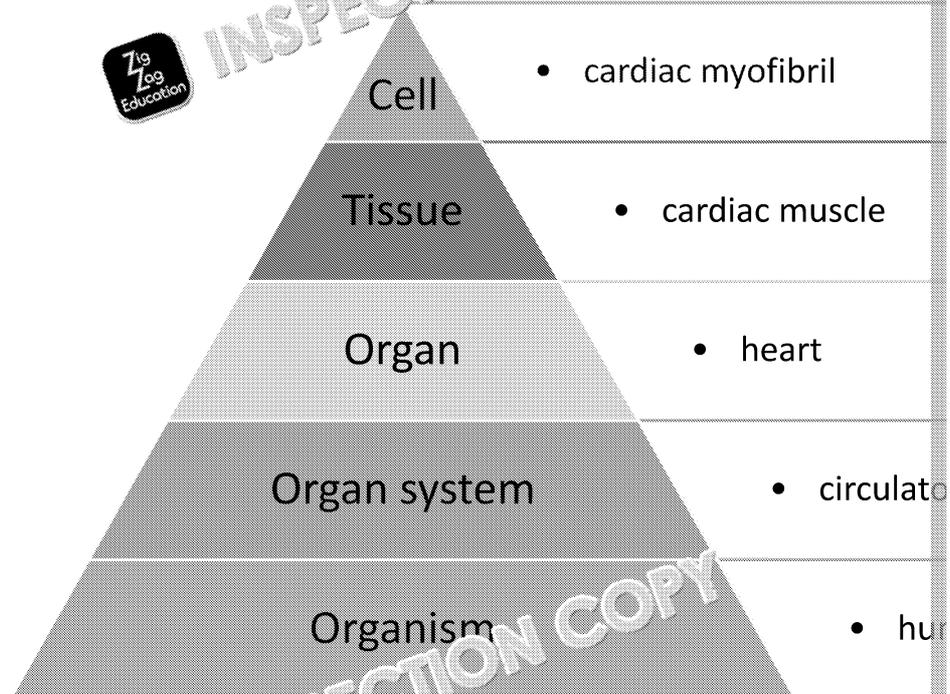


Figure 1.48: Multicellular organisms are constructed in a hierarchy, starting with cells as the basic unit.

So, what is a tissue? A tissue is a collection of similar cells working together for a common purpose.

Your turn

- Starting with renal tubule epithelial cell, create an organisation hierarchy, starting with the cell as the basic unit.

1.2.2. Tissue structure and function

There are four primary categories of tissues:

- Epithelial tissues – these include skin and digestive tract lining, forming linings.
- Connective tissues – these include bone, cartilage and blood, supporting and connecting other tissues together.
- Muscle tissues – these include skeletal, smooth and cardiac muscle, providing movement.
- Nervous tissues – these include neurons, which transmit electrical signals throughout the body.

Each category is further divided into subcategories of increasingly specialised cells. For example, epithelial tissues include ciliated and cuboidal epithelium.

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Epithelial tissue

Epithelial tissue forms linings and support (basement) membranes over other tissues. Epithelial tissue, and epithelium is found covering the inner and outer surfaces of all organs of the digestive system and brain.

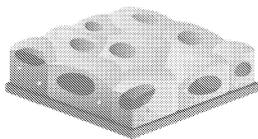
Types of epithelial tissue

There are several subcategories of epithelial tissue, including squamous, ciliated and cuboidal. These groups have pronounced differences in the shape of the cells, and this is reflected in their functions.

Squamous epithelial tissue is made of very flat and thin square-shaped cells. We have this in the alveoli of the lungs, forming a very thin layer through which diffusion of oxygen and carbon dioxide quickly occur (see Figure 1.1.1, page 16).

Ciliated epithelia are present in the trachea and the oviduct, as already discussed (see page 14). The cilia provide a functional role in wafting contents of the tract in the correct direction.

Cuboidal epithelial tissue is made of cube-shaped cells and is found in the kidney nephrons (see page 14). These cells control and adjust the water and mineral ion content of the blood and excrete products for excretion.



squamous epithelial



cuboidal epithelial



Figure 1.1.1: Comparison of squamous, cuboidal and columnar ciliated epithelia

The basement membrane

Epithelial tissue can be categorised by the number of layers it contains:

- Simple epithelium, such as found in the alveoli, is one layer thick. This is essential for the exchange of gases between the blood and lung cavities.
- Stratified epithelium is made of several layers of epithelial cells, mounted upon a basement membrane. The skin and the digestive tract are examples.
- Pseudostratified epithelium looks like it is made of several layers of cells, but every cell is attached to the basement membrane. The epithelium in the trachea is an example.

The basement membrane, present in stratified and pseudostratified epithelium, is made of large macromolecules, arranged in an extracellular matrix of glycoproteins including collagen and proteoglycans. This structure provides structural support for the epithelial cells to attach to. It also acts as a permeable barrier separating the epithelial cells from the underlying connective tissue to which they are attached. This restricts and regulates the interchange of substances such as nutrients and waste products between the two tissue layers. In addition, it forms a signalling layer which controls the differentiation of stem cells and releases growth factors which are required for the repair of the layer. Epithelial cells experience a great deal of wear and tear because of its location. Therefore, it needs to be regenerated constantly.



Apply your knowledge

1. Compare and contrast the three types of epithelial tissue described and give examples and roles within the body.

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Muscle tissue

As discussed in detail in section 1.1.1 from page 17, there are three types of muscle tissue: skeletal, smooth and cardiac. These tissues have different functions:

- Skeletal/striated muscle provides consciously controlled movement through interaction between the skeleton and the muscles. These cells are individual and **innervated**, allowing adjustment of the force generated. They are aligned in parallel muscle groups for maximum and coordinated force and appear striated because of this arrangement.
- Smooth muscle provides unconsciously controlled movement, such as the contraction of the gut. These muscles are innervated in groups and shaped as spindles, which allows them to use little energy expenditure. This is essential when keeping sphincter junctions closed for the digestive system.
- Cardiac muscle can innervate itself – is myogenic – which enables it to contract spontaneously. The cells are joined to other cardiac muscle cells via intercalated discs, which coordinate this contraction to provide a functional heartbeat.

Recall questions

1. Name the three types of muscle tissue and describe their structures and functions.

Connective tissue

Blood, bone and cartilage are all forms of connective tissue. Connective tissues in different sections of the body, provide support, and offer protection. For example, blood carries nutrients and oxygen around the body, bones provide structure and support, and cartilage cushions joints. Therefore, using these criteria, they are grouped as connective tissue.

Bone tissue

Bones provide structural support and enable movement (in conjunction with the skeletal muscles) of the brain, heart, and lungs.

Bones are made of specialised cells called osteocytes. These are embedded within a matrix and are regenerated by specialised stem cells which renew and repair the bone tissue. The marrow cavity is an inner chamber where bone marrow is stored. Bone marrow is a spongy tissue. Red marrow, which produces blood cells, and yellow marrow, which stores fat and can differentiate into bone and cartilage. In the femur (thigh bones), the red marrow contains stem cells which generate all types of blood cells (see Adult stem cells, page 8).

Cartilage tissue

Cartilage is smooth, strong, and flexible. There are three forms of cartilage which have different physical properties.

- Hyaline cartilage is found on the ends of bones at joints. It reduces friction and enables high-impact actions like jumping and landing heavily to occur without damage. It also forms the C-shaped supports in the trachea, keeping the airway open for breathing.
- Elastic cartilage provides flexible support for the ear pinna (external ear) and the epiglottis.
- Fibrous cartilage is found in the intervertebral discs and provides structural support by resisting compression.

Recall questions

1. State the role of red bone marrow and name the stem cells the femur contains.

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Nervous tissue

Nervous tissue is made of neurons: sensory, relay and motor (see page 13). All neurons have a cell body and long structures, and it is important to remember that one neuron is just one cell, and not a group of cells.

Sensory neurons have a centrally located cell body with relatively equal length axons and dendrites. This allows for efficient and fast communication between the sensory receptor at one end and the brain at the other.

Relay neurons have a central cell body through which dendrites and axons interact. This allows for multiple connections to be made between neurons, allowing the message to be relayed to multiple neurons, including motor neurons for a coordinated and specific response where necessary.

Motor neurons have very short dendrites and very long, myelinated axons. Myelination enables **saltatory conduction** (see page 139) to occur, significantly increasing the speed of transmission by up to 100 times. This is essential to enable effective, rapid muscular responses.

saltatory conduction is the process of nervous impulses jumping between nodes of Ranvier along the axon.

Recall questions

1. List the three types of neurons and state their functions.

Blood tissue

Blood is a special form of connective tissue due to its liquid state and its role in transporting oxygen and waste products throughout the body, unlike other connective tissues that provide structural support. Blood is unusual as it is one of only two types of tissue which is liquid, the other being lymph.

Composed of various cells, cell fragments and molecules suspended in plasma, blood includes leucocytes, erythrocytes and thrombocytes. Plasma is composed of water (about 90%), proteins (including antibodies and clotting factors), nutrients (like glucose and amino acids), waste products (such as urea), and ions. The liquid matrix supports the various cells suspended within it and makes up about 55% of blood volume.

Figure F1.50. Blood is comprised principally of plasma and erythrocytes (red blood cells), with a very small percentage of leucocytes (white blood cells) and thrombocytes (platelets).

Apply your knowledge

1. Explain why blood is considered a type of connective tissue and describe the main functions of its cellular components.

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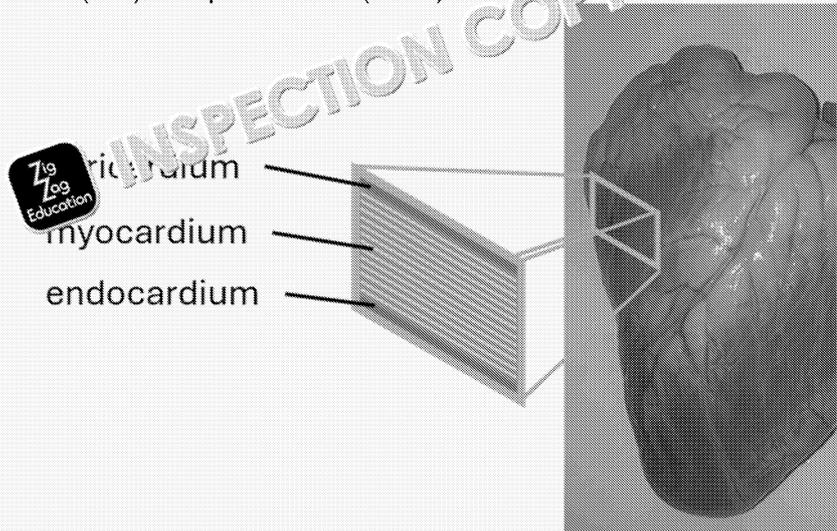




Practice questions: Tissue structure and function

1 The heart is an organ of the human body.

A cross section through the heart reveals three layers of tissue: the endocardium (inner), myocardium (mid), and pericardium (outer).



- State the meaning of the term 'tissue'. (1)
- Identify the specific type of tissue found in the myocardial layer of the heart. (1)
- Describe two adaptations of cardiac muscle cells and explain why these adaptations are important for their functions. (4)

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1.2.3. Use of tissues in research and development

Understanding how tissues function and interact with other tissues is crucial for discovering and developing effective treatment approaches. This knowledge helps researchers identify the underlying issues at the tissue level and create therapies that can address these issues.

Traditionally, this knowledge has been gained through animal laboratory models and dissections. As advancements in ethical standards, there has been a shift towards using *in vitro* human tissues. Organoids are miniature, simplified versions of organs, produced *in vitro* that mimic some of the structure and functions of real organs. They provide a more accurate model for studying human biology.

In vitro human tissues

In vitro human tissue cultures are grown in the laboratory rather than in a living organism such as a mouse or rabbit. This approach is ethically less controversial. While it has many benefits, there are limitations to the modelling it offers such as the inability to replicate complex interactions within a whole organism (see Table F1.13).

in vitro carried out in a laboratory

in vitro carried out in a laboratory

Benefits	Issues
<ul style="list-style-type: none"> Ethically less controversial than using whole animal models. Cheaper. Uses human tissues, so no differences between model and patients. Can be highly controlled and changed, leading to very precise research. Can be used for testing drug toxicity and efficacy, without causing death to the organism. 	<ul style="list-style-type: none"> Does not involve all the cells of the organism, so lacks detail. Cells have a limited life span and die differently when <i>in vitro</i> compared to <i>in vivo</i>. Tissue samples must be kept in a sterile environment as no immune system to fight against infection.

Table F1.13 Comparing the benefits and problems of *in vitro* human tissue cultures

To create an *in vitro* human tissue culture, cells must be grown in sterile conditions to prevent contamination, which can compromise the integrity of the culture and lead to inaccurate results. This is achieved by:

- using a flow hood
- sterilising equipment and reagents
- wearing gloves, a lab coat and face mask

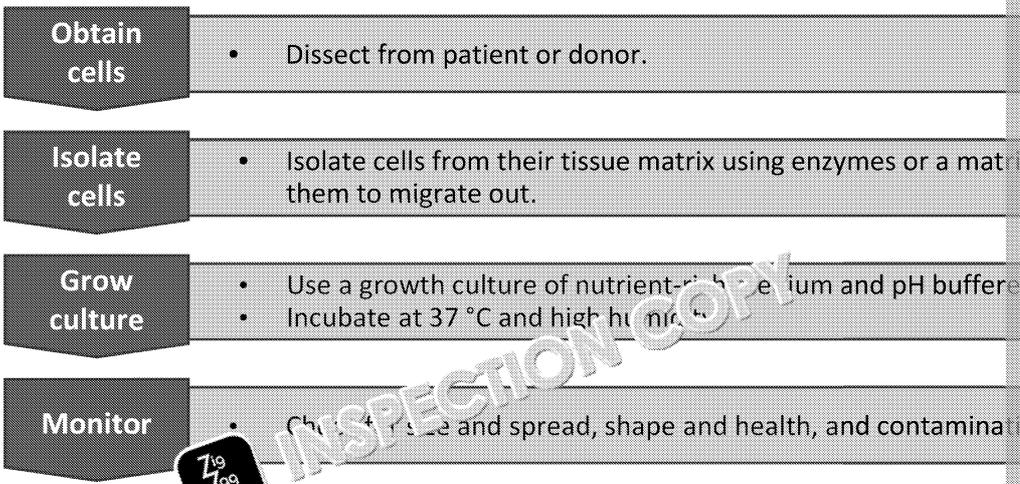


Figure F1.1. A flow chart showing the process of obtaining and growing an *in vitro* human tissue culture

Recall questions

- List some benefits and limitations of using *in vitro* human tissue cultures instead of animal models for research.

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Stem cell cultures

Stem cell cultures are extremely useful in developing models for diseases and in drug development. For instance, stem cell cultures have been used to develop organoids that mimic the human brain. Researchers with a live model to study neurological diseases such as Alzheimer's disease. Stem cells derived from stem cells have been used to test the toxicity of new drugs, offering a more accurate measure of toxicity and the unpleasant side effects caused. Stem cell cultures are also used to study diseases occurring during the development of the embryo.

Stem cells can be harvested from many different sources:

- From the patient or donor, such as from bone marrow or skin.
- From embryos. Embryos are a rich source of pluripotent stem cells.
- By reprogramming adult cells back to a pluripotent state, known as induced pluripotent stem cells (iPSCs).

As with human tissue cultures, using stem cells can mitigate several ethical concerns. For example, using animal models, including the welfare of animals and the applicability of animal data to humans. Using either from patient or donor, or using iPSCs, can also avoid the ethical issues related to the use of embryos.

However, stem cells must be cultured with great care to prevent them from naturally differentiating into specialised cells, or from becoming overcrowded or infected and dying.

Benefits	
<ul style="list-style-type: none"> • Human cells, so research is directly applicable. If using patient cells, then results are directly relevant to the patient too. • Environment can be highly controlled allowing for very specific research to be conducted. • Induced pluripotent and adult stem cell cultures do not have ethical issues that embryonic stem cells do. 	<ul style="list-style-type: none"> • Still only provide a simplified model of the organism such as a cell. Cells may spontaneously differentiate. Some cells are difficult to culture (e.g. neurons). • Embryonic stem cells have ethical issues over rights of embryos.

Table F1.14. Comparing the benefits and problems of human stem cell cultures.

The process of culturing stem cells is very similar to that of culturing human tissue. The culture medium is changed frequently to prevent differentiation, and this is done to ensure pluripotency is maintained.

Your turn

1. Create an information leaflet to explain to the public:
 - a. from where stem cells may be harvested
 - b. how they are used in research and development
 - c. some of the limitations that are posed

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Organoids in research

Organoids are miniature 3D models of human organs, grown from stem cells or tissue used to more accurately mimic conditions within the body, allowing researchers to study the environment and develop more effective treatments. Brain organoids have been used to study Alzheimer's and Parkinson's, while liver organoids have been used to test for drug toxicity.

An organoid has several characteristic features:

- 3D structure like the real organ
- a collection of different specialised cells and tissues, making it an 'organ'
- self-organising cells
- carries out functions like the organ
- developed from stem cells
- can survive, renew and expand over a long period of time
- is genetically identical to the donor

Organoids offer exciting potential for research and development because of the accuracy they provide, including matching patient genetics, and fewer ethical issues involved in their use. However, there are limitations, including the influence that the basement membrane may have on the cell behaviour and differentiation. Some tissue models are challenging to grow in this way, such as how nutrient diffusion works through the organoid (see *Table F1.15*).

Benefits	Limitations
<ul style="list-style-type: none"> • Are developed using patient cells, so are useful for developing personalised medicine. • Contain complex range of stem and specialised cells, so can self-organise into complex structures to provide a 3D model. • Can mimic real tissue structure and function. 	<ul style="list-style-type: none"> • Expensive to grow and require specialised techniques to create a model. • The models can be influenced by the basement membrane matrix only. • Not suitable for all tissue types.

Table F1.15 Comparing the benefits and problems of organoids in research and development.

Apply your knowledge

1. Define an organoid and describe how they are created and why they are valuable for studying diseases and developing treatments.



Practice questions: Use of tissues in research and development

1. State one possible source of stem cells. (1)

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Topic 2: Human physiology, organs and systems

2.1. Human physiology

2.1.1. The concept of human physiology

Understanding human physiology is a key requirement of professionals working in general wellbeing and sports settings. These professionals use their detailed knowledge of body function to assess the disease or malfunction that their patient is experiencing and recommend plans that will manage and improve their situation.

For some patients, care may focus solely on managing symptoms to ensure the patient is particularly in the context of life-limiting conditions. This approach is known as palliative care, to relieve suffering and support comfort, rather than cure the illness.

For others, treatment may involve lifestyle modifications to prevent further health issues. For example, in the case of sports injuries, this might include adjusting training routines or braces during healing, and applying therapeutic or medicinal interventions to the affected area.

In more complex or chronic conditions – such as diabetes or pulmonary disease – professionals provide education, guidance, and motivational support to help patients adopt and sustain lifestyle changes that improve health outcomes and quality of life.

Recall questions

1. List the three care options that may be considered for a patient with type 2 diabetes. Define the term 'palliative care' and describe how the different forms of treatment.

2.1.2. Organ structure and function

What is an organ?

When a collection of different tissues is grouped together and shares a common purpose, it is called an organ. For instance, the heart is an organ because it contains several different tissues that work together to perform a common purpose: cardiac muscle, nervous tissue, connective tissues and epithelial tissues that enable it to function.

Heart

The heart pumps blood around the body. An average adult has a **cardiac output** of between 5 and 6 litres per minute. Blood enters the heart from veins ('in'), with the exception of the pulmonary vein, which carries **oxygenated** blood to the heart. Blood is pumped to the lungs via the pulmonary artery so that carbon dioxide can be exchanged for oxygen, before it returns to the heart to be pumped again to the body via the aorta and other arteries. As a result of this, the human heart is called a double pump.

cardiac output is calculated by the left ventricle
stroke volume is calculated by the left ventricle
deoxygenated blood carries carbon dioxide to the lungs

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Gross heart anatomy

The heart has four chambers, divided vertically into the left and right side. The chambers at the top are called the atria (singular: atrium), and those at the bottom are called the ventricles. Blood enters the atria, then moves into the ventricles, then pumped out of the ventricles to the lungs or the body.

The right ventricle moves blood to the lungs for **gaseous exchange**. Blood must be at low pressure to prevent rupture of the blood vessels around the alveoli, so the right ventricle wall is much thinner (3–5 mm) than the left ventricle wall (10–15 mm) as little force is required.

gaseous exchange
oxygen into
carbon dioxide out of

The left ventricle pumps oxygenated blood to the body, including to the head. Therefore, it must pump against gravity, and to all parts of the body. To achieve this, the left ventricle wall is much thicker (10–15 mm) than the right, so more force is generated, and blood is pumped at high pressure.

The left and right sides of the heart are separated by a wall known as the central **septum**. The septum separates the deoxygenated and oxygenated blood.

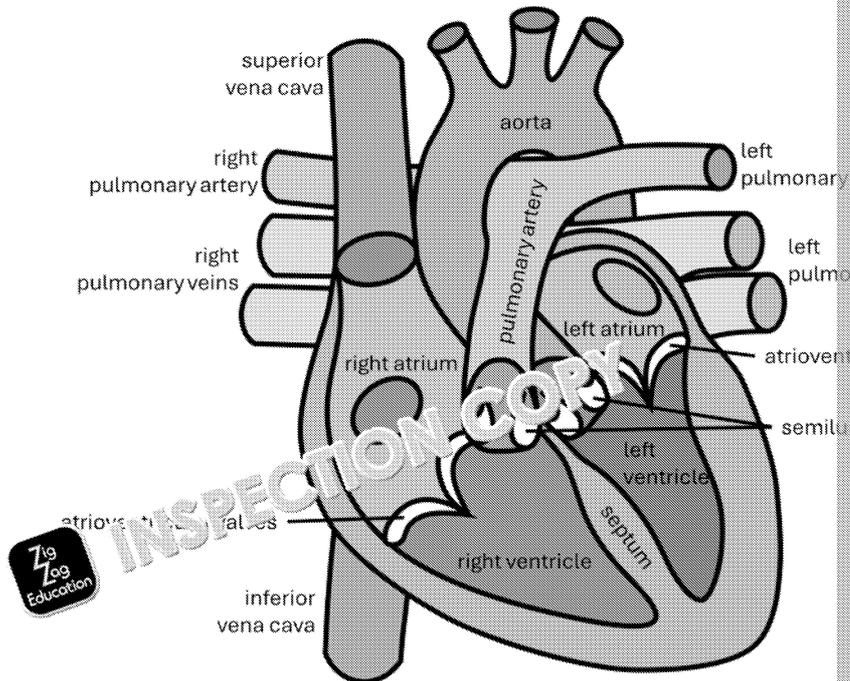


Figure F2.1. The internal anatomy of the heart, showing the blood vessels, chambers, valves, and septum.

Tip!

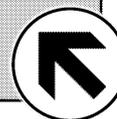
Remember the locations of the heart chambers by thinking about the shape of the capital letters. The Atria are at the top, just as the A joins at the top. The Ventricles are V-shaped, at the bottom of the heart, just as the V is joined at the bottom of the letter.

Blood enters and leaves the heart via veins and arteries. Veins transport blood toward the heart, and arteries transport blood away from the heart. The major blood vessels interacting with the heart are:

- Vena cava – the inferior and superior vena cava return deoxygenated blood from the body to the right atrium.
- Pulmonary artery – the only artery in the body to transport deoxygenated blood away from the heart to the lungs for gaseous exchange.
- Pulmonary vein – the only vein in the body to transport oxygenated blood. It returns blood from the lungs to the left atrium after gaseous exchange.
- Aorta – the largest artery in the body, transports oxygenated blood to the body.

Tip!

Remember that Arteries transport blood Away (A, A) from the heart, whereas veins transport blood 'tovvards' the heart (the double v = 'w').



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There are two groups of valves within the heart, which prevent backflow of blood. The atrioventricular valves are positioned between the atria and the ventricles, although may also be referred to as the mitral valve (left) and the tricuspid valve (right). The valves between the ventricles and the pulmonary artery are called the semilunar valves because of their shape, but may also be called the pulmonary (right) and aortic (left) valves.

The valves are attached to the inner walls of the heart by tendons called **chordae tendineae**. These are attached to muscles which contract and relax in time with the heartbeat to ensure the valves close and open in the correct direction. As the valves close they make a slapping sound which we hear as the heart beats. The first 'lub' sound is caused by the atrioventricular valves closing, followed by the second 'dub' sound which indicates the semilunar valves closing.

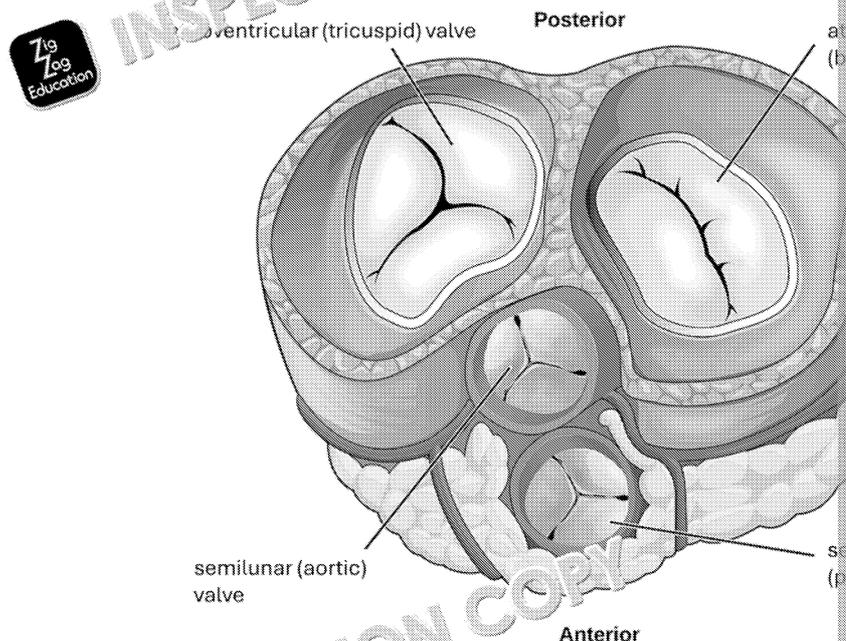


Figure 2.2 Cross section through the top of the heart, showing the valves.

Tip!

When viewing images and drawings of the heart, remember that you are looking at the body of someone facing you. Therefore, the left side of the heart in the diagram is on the right side of the page, and vice versa.

Heart function

Blood moves through the heart, lungs and body in a continuous flow so gases and nutrients are circulated:

1. Deoxygenated blood is returned to the heart from the body via the venae cavae.
2. It enters the right atrium.
3. It moves into the right ventricle via the atrioventricular valve.
4. It is pumped from the ventricle via the semilunar valve and passes through the lungs.
5. Gaseous exchange occurs at the lungs.
6. Oxygenated blood is returned to the heart via the pulmonary vein.
7. Blood enters the left atrium.
8. It is moved into the left ventricle via the atrioventricular valve.
9. It is pumped from the ventricle via the semilunar valve and passes through the body.

Heart histology

The heart tissue is composed of three distinct layers:

- Endocardium – a thin inner layer made of endothelial tissue.
- Myocardium – a thick middle layer made of cardiac muscle cells.
- Pericardium – a thin outer layer made of epithelial and connective tissue.

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The endocardium provides a smooth surface which reduces friction as blood moves through the heart. This prevents clots from forming. It also controls electrical conduction which is essential for the contraction of the heart.

The myocardium is composed almost entirely of cardiac muscle cells and therefore is responsible for the contractile force produced by the heart. The myocardium is thickest in the left ventricle, ensuring that blood is pumped at high pressure to the body. The muscle cells must contract in a coordinated manner and this is regulated by the **Purkinje fibres** and the **bundle of His**. (See cardiac cycle, next).

The pericardium protects the heart and produces a fluid which reduces friction between it and surrounding tissues. It also contains the coronary blood vessels which supply blood to the heart tissue itself. If these become blocked, the availability of oxygen to the heart muscles is restricted. The heart requires a constant supply of oxygen to maintain the metabolic rates required to produce enough ATP for its continuous function. Restricted blood flow can lead to myocardial infarction (heart attack), or other coronary heart diseases (CHDs) including angina and heart failure (reduced oxygen to parts of the heart muscle).

The cardiac cycle

The cardiac cycle is a sequence of events throughout one heartbeat. At rest, it lasts about 0.8 seconds, averaging 70 beats per minute. There are three stages to the cardiac cycle:

- Diastole – relaxation of the heart muscles.
- Atrial systole – contraction of the atrial muscles.
- Ventricular systole – contraction of the ventricular muscles.

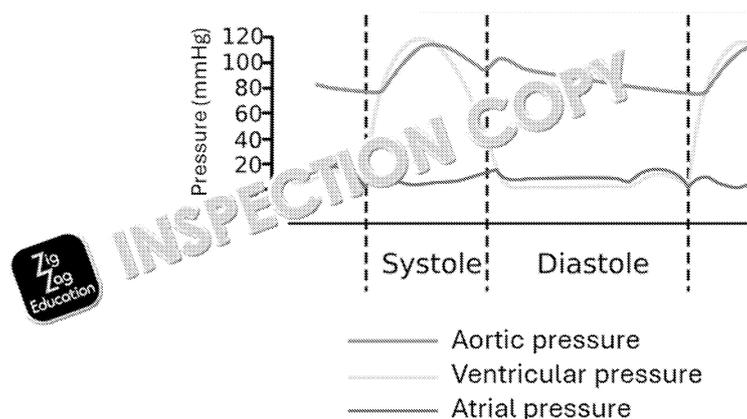


Figure F2.3. Heart pressure graph showing changes in pressure in the atria, ventricles and aorta.

Diastole is the longest phase of the heartbeat and involves the relaxation of the cardiac muscle. It occurs in all chambers simultaneously. It occurs after the heart has contracted and the start of diastole and refills with blood. We can therefore conclude that as blood enters the heart during diastole:

- Blood flows from the veins (vena cava and pulmonary) into the atria.
- The atrioventricular valves are open so blood flows passively from the atria into the ventricles.
- Atrial and ventricular blood volume is low and increases.
- Atrial and ventricular blood pressure is low and increases.
- The semilunar valves between the ventricles and the arteries (pulmonary and aorta) are closed so that blood is not leaving.

Atrial systole follows and involves atrial muscle contraction. Blood moves from the atria into the ventricles. Therefore, we can conclude that:

- Atrial blood volume decreases.
- Atrial blood pressure is low but increases as the heart muscles contract then decreases.
- Ventricular blood volume and pressure is low and increases as blood moves from the atria into the ventricles.
- The atrioventricular valves are open so that blood can flow from the atria into the ventricles.
- The semilunar valves between the ventricles and the arteries (pulmonary and aorta) are closed so that blood is not leaving.

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Ventricular systole follows next and involves ventricle muscle contraction. Blood is pumped out of the heart via the arteries to the lungs or the body. We can conclude that:

- The atrioventricular valves close to prevent backflow.
- Ventricular blood pressure increases rapidly as the heart muscles contract and blood is pumped from the heart.
- Ventricular blood volume reduces as blood leaves the heart.
- The semilunar valves are forced open by ventricular blood pressure, and blood is pumped out of the heart.

The cardiac cycle requires careful coordination, and this is controlled through the following:

- Cardiac muscle fibres – are striated (see Cardiac muscle cells, page 17), and contract rhythmically at approximately 60–500 times per minute without any stimulation. This allows a heart to contract without any external resources.
- Sinoatrial node (SAN) – acts as a pacemaker, stimulating contraction at a rate of approximately 100–150 times per minute.
- Relay components within the heart – include the atrioventricular node (AVN), bundle of His, and Purkinje fibres, which relay the electrical stimulation, initiated by the SAN, through the heart.

The SAN is located in the top right of the heart, above the right atrium and produces the electrical impulses that cause the atria to contract (atrial systole). This forces the atrioventricular valve to close and pushes the blood into the ventricles.

The impulses are blocked from travelling further by a band of non-conducting tissue called the atrioventricular node. This ensures that atrial systole occurs before ventricular systole, during which the ventricles fill with blood.

The atrioventricular node (AVN), located at the top of the septum between the atria, relays electrical signals through the bundle of His, which runs down the ventricular septum to the Purkinje fibres. As the electrical signal passes through the walls of the ventricles by the Purkinje fibres, they contract (ventricular systole) from the bottom of the heart up. This ensures that the ventricles contract from the bottom up, pushing the blood out of the heart, via the semilunar valves and through the arteries.

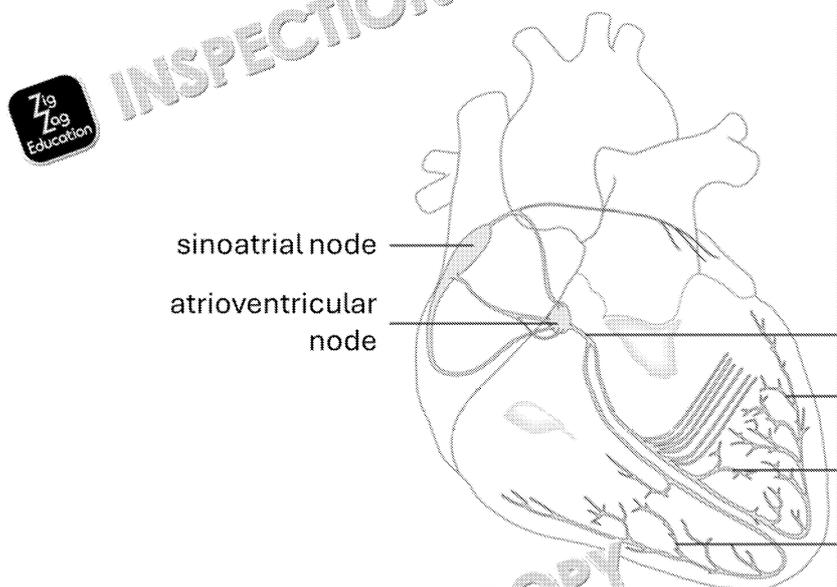


Figure F2.4. The locations of the SAN, AVN, bundle of His and Purkinje fibres.

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Your turn

1. State the function of the heart and its adaptations to enable this to occur.
2. Calculate your cardiac output: assume your stroke volume is 5.37 dm^3 and your heart rate is 70 beats per minute.
3. Create a flow chart of the sequence of blood flow through the heart, listing the chambers in order, and the oxygenation state of the blood.
4. Produce a table showing the stage of heart contraction or relaxation, changes in heart valves, and the electrical activity of the nodes or fibres.

Blood vessels

Blood is a tissue that is pumped around the body by the heart and moves through the blood vessels. Blood vessels run throughout the body and there are three main types:

- Arteries – carry blood away from the heart.
- Veins – return blood back to the heart.
- Capillaries – facilitate exchange of substances between blood and tissues.

In addition to these major vessels, there are also:

- Arterioles – smaller than arteries, they transport blood from arteries to capillaries.
- Venules – smaller than veins, they transport blood from capillaries to veins.

Therefore, as blood is transported around the body, it moves from the heart into an artery, through arterioles then into capillaries, before merging into venules then into veins, before returning to the heart.

All organs have an artery delivering oxygenated blood and nutrients to it, and a vein removing deoxygenated blood and waste products. For instance, the kidney is served by the renal artery and vein, which deliver blood to and from the kidney. Arteries, veins and capillaries each have specific structures to facilitate their function.

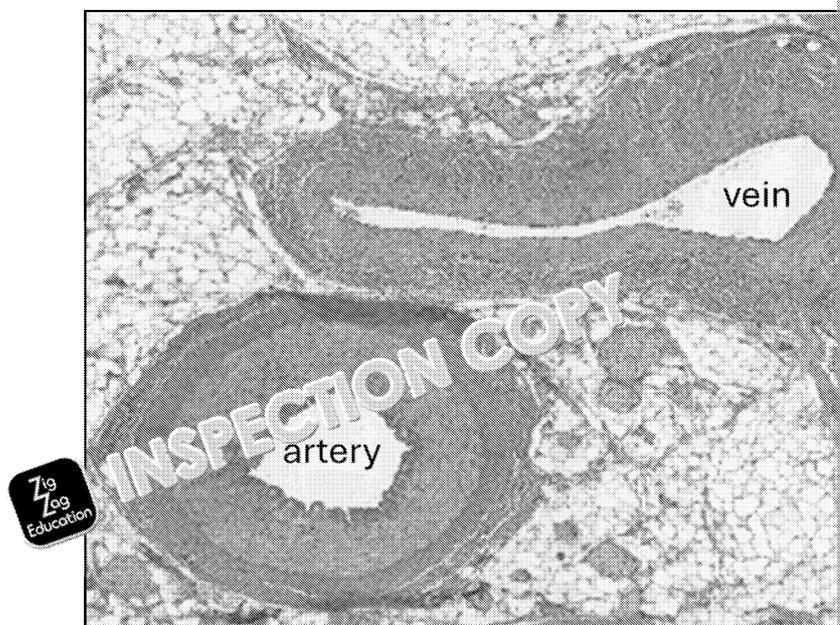


Figure F2.5. Light micrograph of a vein and an artery, showing the visibly different lumen sizes and diameters.

Arteries

Arteries are blood vessels that transport blood from the heart to the organs of the body. They carry oxygen-rich, having bound oxygen at the lungs. Only the pulmonary artery transports deoxygenated blood from the heart to the lungs.

Arteries must transport blood quickly to the organ, to provide sufficient levels of oxygen and nutrients to the tissues for their cell functions. For instance, mitochondria require a supply of oxygen and nutrients to create ATP via aerobic respiration, while other cell processes require other nutrients such as amino acids and glucose.

Arteries have a wall comprising three distinct layers, surrounding the **lumen** through which the blood flows:

- Endothelium – the inner layer, also known as the tunica interna, provides a smooth surface for the frictionless passage of blood through the artery.
- Smooth muscle and elastic fibres – these form a thick middle layer, called the tunica media, and can contract and relax to pump blood through the lumen. This is felt as the pulse at different points in the body.
- Connective tissue – the thin outer layer, the tunica externa, protects the tunica media and the artery into the surrounding tissue layer.

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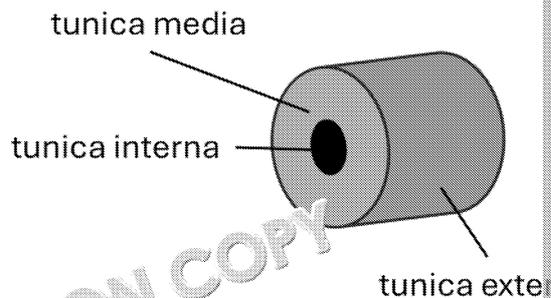


Figure F2.6. The structure of an artery, showing the three distinct tissue layers.

Distinct arteries have a narrow lumen and a thick tunica media. These features are adapted for high pressure and for that pressure to be maintained along the length of the artery. This is coordinated with the heartbeat by the brain.

Veins

Veins return blood from the organs of the body to the heart. Blood is usually rich with fewer nutrients and more waste products, although the pulmonary vein carries oxygenated blood from the lungs to the heart for further circulation.

Veins transport blood at a lower pressure and slower speed than arteries. This is because they carry blood with fewer nutrients and more waste products, which need to be processed at the organs.

Veins have a similar structure to arteries. The innermost layer is a smooth endothelium, providing a low-friction passage of blood. The next layer, the tunica media, comprises muscle fibres, so the diameter of the lumen can be adjusted. The outermost layer, the tunica externa, is made of connective tissue and anchors the vein in the surrounding tissue.

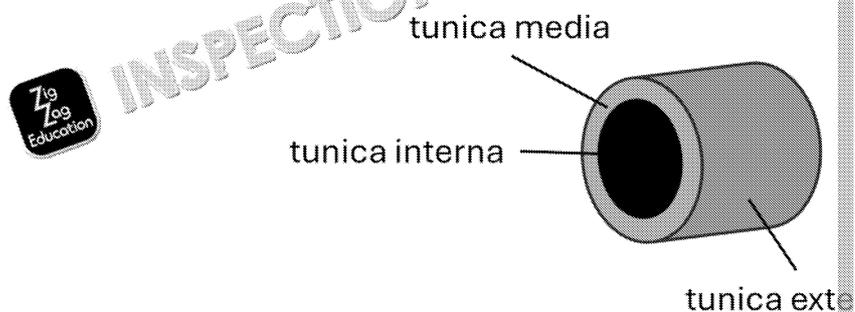


Figure F2.7. The structure of a vein, showing the three distinct tissue layers.

However, there are some key differences between arteries and veins:

- Veins transport blood at lower pressure than arteries, because the venous tunica media is much thinner.
- Some veins are very long and transport blood against gravity, such as those from the feet and ankles back to the heart. These veins have valves within them that prevent backflow of blood and ensure that blood returns to the heart. This is aided by the contraction of the muscles in the body.

Further your knowledge

Varicose veins are painful, swollen veins, usually within the legs. It most often affects people who stand for long periods of time with little movement, such as soldiers and police officers on sentry duty. Varicose veins are caused by the pooling of blood in pocket valves in the veins because of lack of movement. This causes the veins to stretch and lose their effectiveness.

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Capillaries

Capillaries facilitate the exchange of nutrients and waste products between the blood and the cells and tissue fluids of the organs. As blood moves through the capillaries, it delivers nutrients and gains waste products.

The capillaries are uniquely structured to facilitate the rapid exchange of nutrients and waste products between the blood and the tissues. Unlike veins and arteries, the capillary wall is only one cell thick, made of squamous endothelial cells that are extremely flat and thin. This creates a very short diffusion distance, ensuring rapid exchange and transport.

Furthermore, the capillaries are very narrow, and in some cases, it is narrower than the diameter of an erythrocyte. This slows the movement of red blood cells through the capillary, and they pass in single file, which increases the time for oxygen to diffuse and presses the walls of the erythrocytes against the capillary wall, reducing the diffusion distance even further.

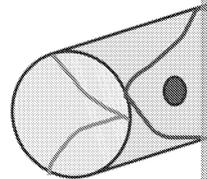


Figure F2.8. The structure of a capillary, showing the very thin wall.

Further your knowledge

Sickle cell anaemia is a genetic condition which causes the distortion of erythrocytes due to a mutation in a gene. It is a painful condition because the red blood cells do not move smoothly through narrow capillaries due to their sickle shape. This is particularly pronounced when heart rate increases at times of stress or increased physical activity.

Apply your knowledge

1. Name the three tissue layers of arteries and veins and describe their role in the blood vessel.
2. Describe how capillaries are specifically adapted for their function.
3. Describe the similarities and differences between arteries and veins.

Muscle

The term 'muscle' can refer to different biological structures: a muscle cell (myocyte), a muscle fibre (a long muscle cell), or a muscle organ (composed of multiple tissues). When we consider a skeletal muscle, it is a complex structure made of many tissues working together. Skeletal muscle consists of muscle tissue (collection of many myocytes working together), connective tissue (that encases different subsections of the muscle fibres, for instance), epithelial tissue (required to innervate the muscle fibres). Muscles are connected to bones by tendons and other non-contractile connective tissues.

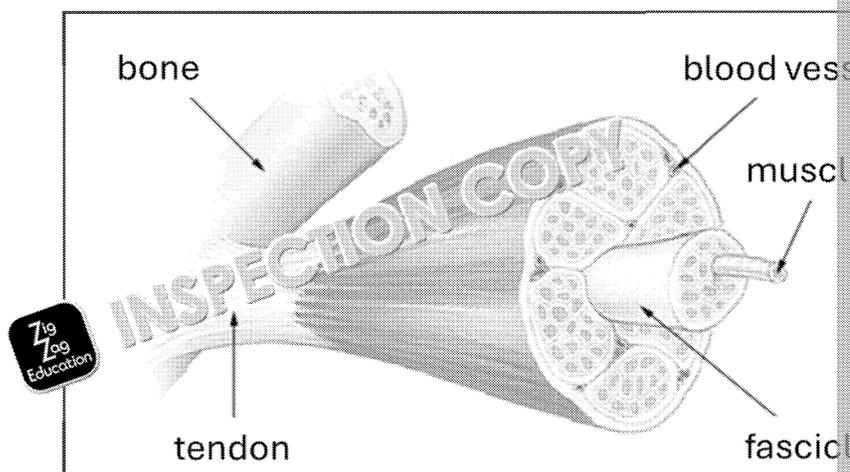


Figure F2.9. The structure of skeletal muscle, showing overall structure and attachment to bone and tendon.

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Muscles have a detailed macrostructure. A muscle organ is divided into fascicles containing capillaries and motor neurons, surrounded by an outer layer of epithelial tissue. Inside are arranged muscle fibres that maximise the force produced during muscle contraction. Each muscle fibre is made of myofibrils that contain many contractile filaments made of actin and myosin. Each muscle fibre is surrounded by a sarcolemma, equivalent to the cell membrane. Inside the fibre is the cytoplasm (like cytoplasm) and the nucleus. Beneath that is the sarcoplasmic reticulum, which stores calcium ions. This allows calcium to be released from the muscle fibre to the individual myofibrils to generate contraction.

An artery supplies blood to the muscle, and a vein returns the blood to the heart. Capillaries are dispersed throughout the muscle fibres. This ensures a rich supply of oxygen and nutrients for the production of ATP required for muscle contraction.

Your turn

1. Create a flow chart showing how myocytes are grouped into larger segments.
2. Explain why muscles require a rich blood and nerve supply.

Bone

Bone is both an organ and a tissue, which supports and protects the body, and stores minerals (see page 55 for more detail).

Bones are metabolically active; therefore, they have a good blood supply. They contain several specialised cells, including:

- fibrocytes – produce collagen fibres which give bone tensile strength (strength)
- osteoblasts – secrete a fluid called osteoid which hardens to form the calcified matrix
- osteocytes – maintain bone tissue

These specialised cells are embedded within a calcified matrix containing collagen fibres. The matrix is hard, while the fibres provide strength. This combination resists bones from snapping.

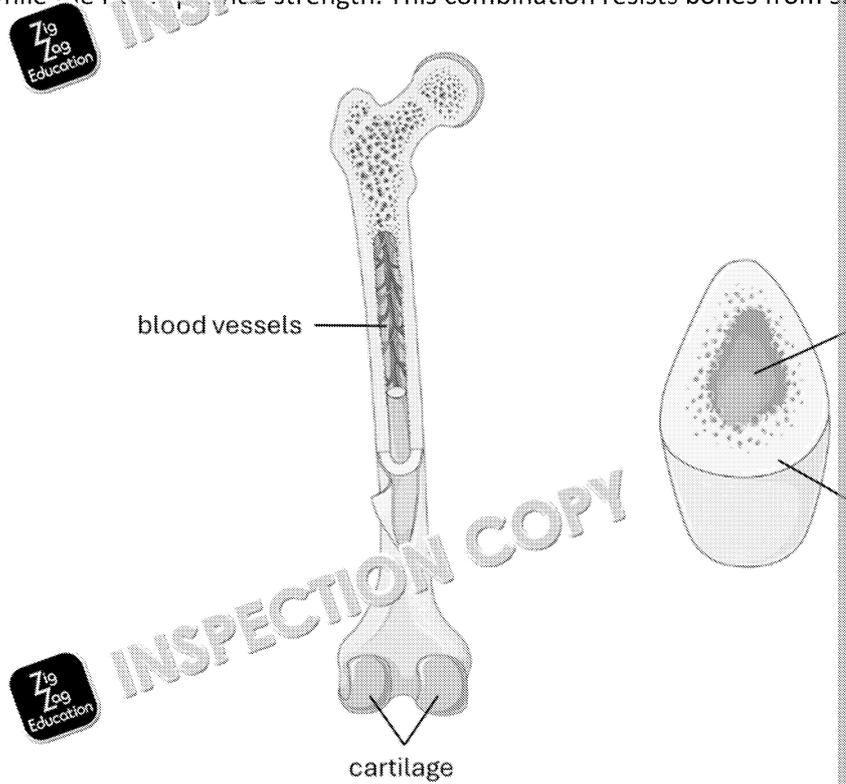


Figure F2.10. The structure of bone, showing the presence of a rich blood supply.

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If bones fracture, they can repair the damage. Bone repair requires a rich supply of blood for synthesis, oxygen for aerobic respiration, and calcium ions for matrix reconstruction, which involves many different specialised cells:

1. Upon fracture, blood vessels rupture and cause a blood clot to form. This invites platelets and, with osteocytes, produce signals to trigger repair.
2. Next, fibroblasts migrate to the site and lay down cartilage and fibrous tissue that bridge the two sections of the fractured bone.
3. Then, osteocytes recruit osteoblasts to move to the site and secrete osteoid which becomes a calcified matrix.
4. Finally, excess bone is reabsorbed by osteoclasts and collagen fibres are added to restore bone strength.

Osteocytes detect damage and recruit other cells into the site to repair the damage, and they also regulate the mineralisation process and maintain mineral balance.



Recall questions

1. Describe three roles that bones have within our body and explain how the structure of bones supports these functions.
2. Describe the role of red bone marrow.
3. Explain why bones require a good blood supply and list the components of blood.

Liver

The liver is the largest internal organ and is located within the upper abdomen, under the diaphragm and is covered by a thin layer of muscle. It is positioned on the right side of the body opposite the stomach and extends upwards above the stomach. It weighs approximately 5 % of a person's body mass – between 1.5 and 1.8 kg in an average adult.

The liver has many different vital functions, including detoxifying blood, metabolising drugs, producing bile to aid digestion of fat, storing glycogen and a range of other vitamins and minerals, and synthesising blood proteins and clotting factors. This explains its considerable size and complexity.

The liver receives blood from the hepatic artery from the heart (approximately 25 % of blood volume) and from the hepatic portal vein from the small intestines (approximately 75 % of blood volume). This ensures the liver with sufficient nutrients, energy and oxygen for the wide array of processes it performs. It also supplies the substances, or metabolites, to be processed, such as drugs and toxins which are broken down (breaking down), and glucose which may need anabolising (building up) into glycogen for storage.

The liver is formed from specialised cells called hepatocytes. These create channels called sinuses through which blood from the hepatic portal vein and the hepatic artery can mix. The proximity of the hepatocytes to this blood supply enables rapid and efficient processing of metabolites. It also enables effective absorption of substances from the blood supply for storage within the liver, or secretion of substances from the liver into the bloodstream for circulation.

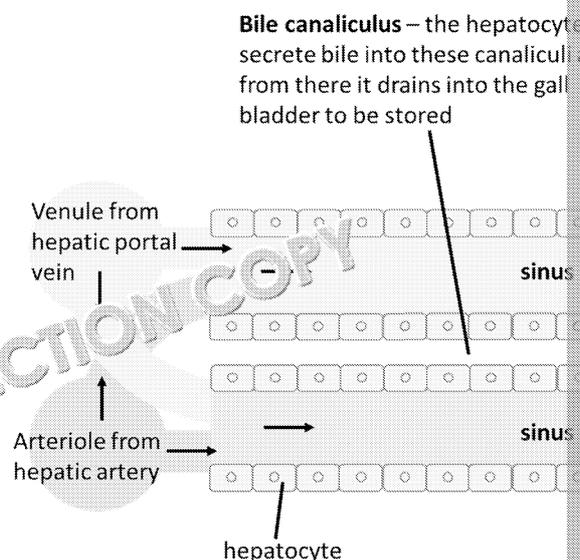


Figure F2.11. The structure of the liver involves drainage of blood and bile.

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Narrow channels called canaliculi (singular: canaliculus) are located on the other side of the hepatocytes. They secrete bile into the canaliculi. Bile drains into the gallbladder where it is stored until it is needed. Bile then flows into the duodenum: the first part of the small intestine.

Recall questions

1. List the essential functions of the liver and explain why it has a dual blood supply.
2. Describe the structure and function of hepatocytes and how their structure is related to their function.



Lungs

The lungs carry out gaseous exchange. Oxygen in the alveoli diffuses into the blood and carbon dioxide diffuses into the alveoli. The lungs provide an important interface between the

external environment and the internal environment. Gaseous exchange occurs deep within the lungs. Air is inhaled through the mouth and nose, passes through the pharynx and larynx, and then down the trachea. The trachea has a wide lumen, and the walls are reinforced with C-shaped cartilage to support the trachea and keep it open and unobstructed, and the gap in the ring is supported by the trachealis muscle. The trachea branches into the left and right bronchi, which enter the lobes of the lungs. The bronchi divide into many smaller bronchioles, which connect to the alveoli sac at the end.

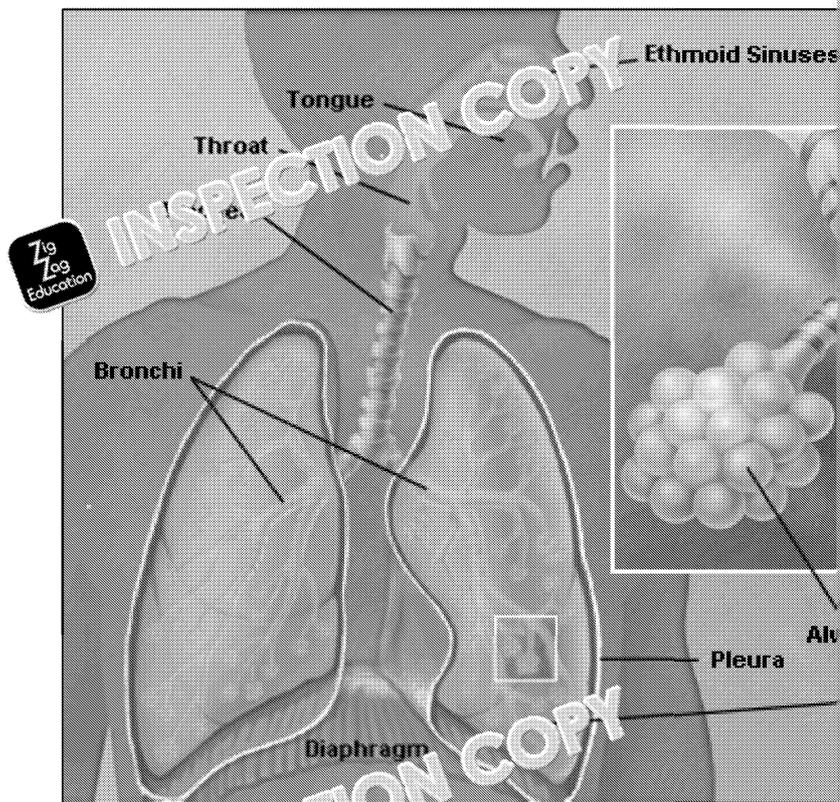


Figure F2.12. The anatomy of the lungs.

Gaseous exchange in the lungs must occur rapidly and efficiently. To achieve this, three factors are important:

1. A large surface area over which exchange can occur.
2. A short distance to move through.
3. A pathway that does not unnecessarily restrict the movement of substances.



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A large surface area is achieved by having more than 700 million alveoli in each lung and a dense capillary network. Alveoli enable half a tennis court's worth of surface area to fit in your chest! The surface area of each alveolus is maximised by its small, rounded bubble shape. If this shaping is lost and the alveoli become smoother. This reduces the surface area and causes the symptoms.

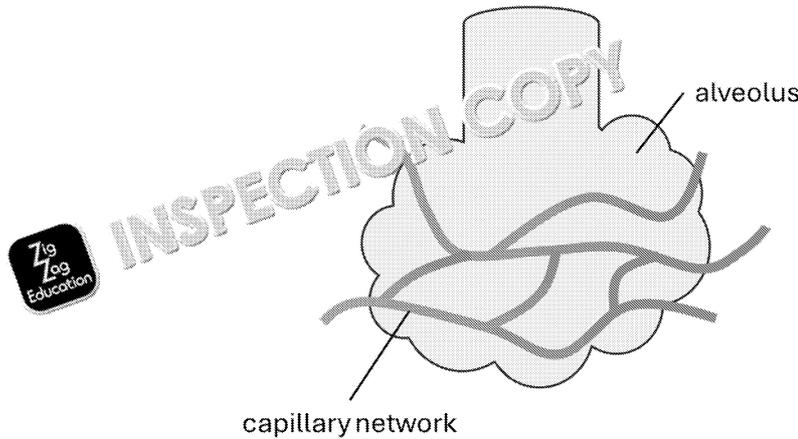


Figure F2.13. The alveolus has a rich capillary supply and a high surface area.

The diffusion pathway is short in part because both the alveoli and the blood capillaries have thin walls. In addition, the squamous epithelial cells in the alveoli, and the squamous endothelial cells in the capillaries are both extremely thin specialised cells (see section 1.1.1, page 16).

The movement of substances is unrestricted partly because the inner surface of the alveoli is coated with a liquid, known as surfactant, and diffuse more rapidly. In addition, the alveolar wall is extremely permeable to oxygen and carbon dioxide, so gases can move through the wall easily.

When gaseous exchange is impaired, or when the normal movement of air into and out of the lungs is restricted, symptoms including fatigue and shortness of breath quickly appear.

Recall questions

1. List the pathway through which inhaled air flows during inspiration.
2. Describe the structural features of alveoli that allow for efficient gas exchange.

Stomach

The stomach is positioned in the upper left section of the abdomen, opposite the liver and below the diaphragm.

Food enters the stomach through the cardiac sphincter between the end of the oesophagus and the stomach. The sphincter seals the stomach at the top and prevents reflux, a process whereby stomach contents move into the oesophagus and create an unpleasant burning sensation called heartburn.

The corpus, or body, of the stomach enables physical, enzymatic and chemical digestion. Physical digestion occurs as the stomach muscles contract and relax to churn the food over. Hydrochloric acid aids digestion by activating pepsinogen into the enzyme pepsin and lowering the pH to create optimum conditions for stomach enzymes to function.

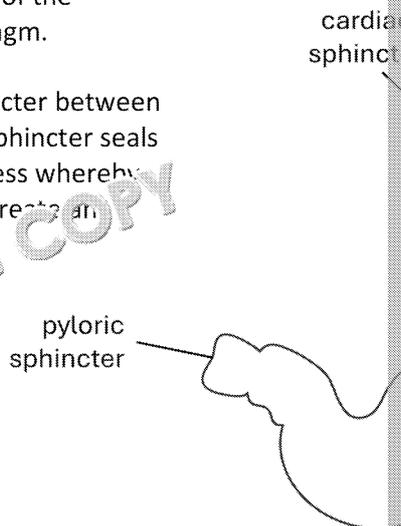


Figure F2.14. The stomach is divided into the corpus and the pylorus.

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The low pH also destroys pathogens that enter with the food and **denatures** enzymes made in the mouth, which must be remade in the small intestine.

The stomach wall contains gastric pits which are made of several specialised cells. These cells manufacture gastric secretions including hydrochloric acid, enzymes and mucus (see section 1.1.1, page 18). Mucus is crucial for providing a protective barrier and the digestive contents (see Stomach conditions, page 1892).

The pyloric sphincter separates the stomach from the duodenum. It is closed to regulate the movement of contents into the small intestine.

The stomach can absorb certain substances and not others because of the mucous membrane. Small molecules can pass through the stomach wall, and the quantity increases if the stomach is empty (low solute concentration and high water potential). Alcohol can be absorbed through the mucus barrier. This is especially problematic if the stomach is empty. Consumed, as this enables rapid absorption, causing the drinker to become quickly intoxicated. Ions and electrolytes can also be absorbed through the stomach wall, including aspirin.

The stomach has a rich blood supply via the gastric arteries and the portal vein. This provides oxygen and metabolic substrates required for ATP production, which is needed for the work required by the stomach.

Apply your knowledge

1. Describe how the gastric wall and the secretions it produces contribute to digestion.
2. Describe how the stomach protects itself from being digested and explain why it is important.

Intestines

The intestines digest and absorb nutrients and process waste ready for egestion. The stomach contents, now called **chyme**, enters the small intestines. The small intestine is the site of most digestion and absorb the products. Chyme then moves through the large intestine where water is reabsorbed and faeces are produced.

The small intestine

The small intestine is a long, narrow tube averaging 6–7 metres in adults. It occupies the lower right-hand side of the abdominal cavity, lying beneath the stomach and liver, and includes the duodenum and the ileum.

By the time partially digested food reaches the small intestine, it has been mixed with gastric secretions and is called chyme – a semi-liquid mixture of food particles and digestive secretions. The pyloric sphincter into the duodenum, where digestion resumes under very different conditions.

The stomach's highly acidic environment (pH 1.5–3.5) contrasts sharply with the alkaline environment (pH 6–8). This change is achieved through the secretion of bile and pancreatic juice into the duodenum, which neutralise stomach acid. As a result, stomach enzymes denature, while intestinal enzymes, including proteases such as trypsin, and carbohydrases including amylase and maltase, become active. The enzymes catalyse the breakdown of proteins, carbohydrates and lipids into their respective monomers: amino acids, glucose and other **monosaccharides**, and fatty acids and glycerol.

In the ileum, these monomers are absorbed through the intestinal wall into an extensive network of blood and lymphatic vessels. The mucosal surface of the small intestine is folded into villi, which greatly increase the surface area for absorption. Each villus is lined with epithelial cells which have dense arrays of microscopic, finger-like projections of the epithelial cell surface membrane that increase the absorbing surface by up to 600 times and form the brush border.

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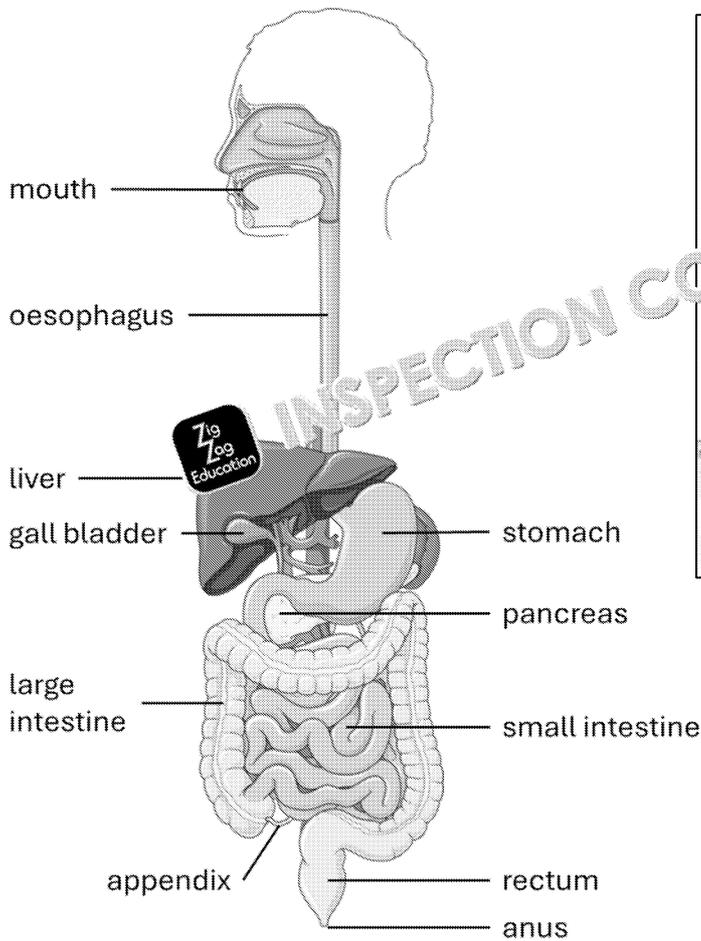


Figure F2.15. The organs of the digestive system.

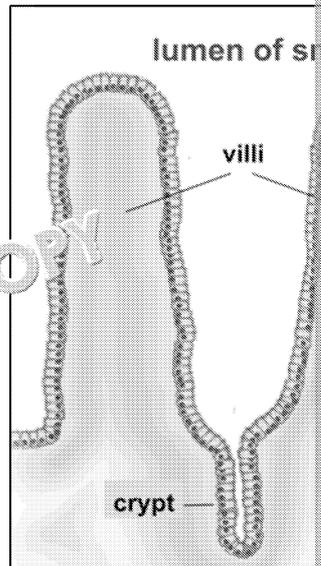


Figure F2.16. The lumen of the small intestine with surface area greatly increased by villi.

Microvilli have brush border enzymes including several carbohydrases that catalyse the breakdown of **disaccharides** into monosaccharides:

- Lactase – catalyses lactose into glucose and galactose.
- Sucrase – catalyses sucrose into glucose and fructose.
- Maltase – catalyses maltose into glucose.

These enzymes are embedded in the cell surface membrane, allowing immediate uptake by the same cell. A deficiency in lactase, for example, leads to lactose intolerance, due to inability to digest lactose effectively.

In addition, membrane-bound transporters facilitate the movement of nutrients from epithelial cells and on into the bloodstream. Once absorbed, nutrients travel to the liver, for processing, detoxification and distribution.

The large intestine

The large intestine borders the small intestine and while it is wider, it is also shorter and thicker. It consists of five main segments: the caecum, appendix, colon, rectum and anus. Its main functions are the final stages of digestion, water absorption, and faeces formation.

Chyme from the small intestine enters the caecum: a pouch-like region at the beginning of the large intestine. Here, excess water and salts are absorbed, starting the process of solidifying the chyme. Adjacent to the caecum is the appendix; a narrow finger-like projection. This plays a role in maintaining **gut flora** balance and supporting immune function, particularly after gastrointestinal infections.

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The partially dehydrated chyme then moves into the colon, the longest section of the large intestine. It continues to absorb water and electrolytes, gradually transforming chyme into faeces.

The caecum and colon host a dense **microbiome**, a complex ecosystem of microorganisms that:

- ferment undigested carbohydrates
- synthesise some vitamins, including vitamin K, which supports bone health
- outcompete pathogenic microbes, providing a critical layer of immune defence

However, broad-spectrum oral antibiotics can inadvertently reduce the biome diversity, leading to decreased fermentation and vitamin synthesis, and results in diarrhoea due to incomplete digestion.

Once faeces are formed, it reaches the rectum, it is temporarily stored. The rectal wall has sensory receptors that detect pressure build-up from faeces, triggering the urge to defecate. During defecation, the anus, which is regulated by two sphincters:

- internal anal sphincter – involuntarily controlled
- external anal sphincter – voluntarily controlled, allowing conscious regulation of defecation

The movement of chyme and faeces throughout the large intestine is driven by **peristalsis**: the coordinated, rhythmic contractions of smooth muscle. The consistency of faeces depends upon water balance – dehydration can lead to hard, dry faeces that are more difficult to pass.

Apply your knowledge

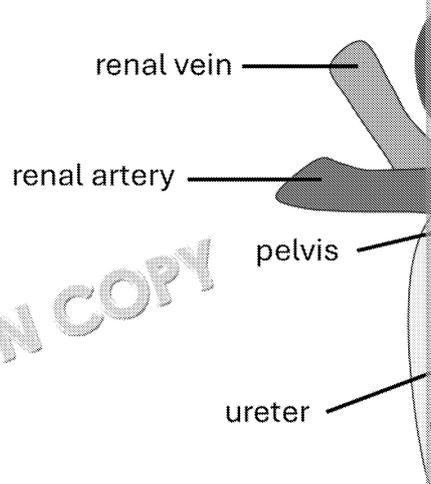
1. Describe the role of the microbiome in digestion and overall health.
2. Describe the differences between the small and large intestines and the adaptations for their different functions.
3. Explain how the presence of villi and microvilli enhance digestion.

Kidney

The kidneys are vital organs that filter blood, to remove waste products of metabolism such as urea, and regulate water and electrolyte balance. Humans have two kidneys, located in the lower back. Blood enters each kidney via the renal artery and exits through the renal vein.

The kidney macrostructure comprises:

- The outer capsule, which encases the kidney.
- The cortex, the outer area that interlocks with the medulla.
- The medulla, on the inner side of the cortex, contains renal pyramids, which converge onto central calyces (singular: calyx).
- The calyces drain into the renal pelvis, which leads to the ureter, which transports urine to the bladder for storage.



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Figure F2.17. The kidney has...

Filtration and reabsorption

Blood filtration occurs in the **nephrons** of the kidney: specialised structures which span the medulla and cortex. For filtration to occur, blood enters under high pressure, aided by differences in the lumen diameter of the inbound (afferent) and outgoing (efferent) arterioles. This pressure, combined with selective permeability of the **glomerular cells**, generates **ultrafiltration**. All small molecules, except proteins and blood cells, are pushed into the kidney tubules to form filtrate.

As the filtrate passes through a series of tubules, it interacts closely with surrounding capillaries so that:

- Glucose, some electrolytes and water are reabsorbed into the bloodstream.
- Urea, excess electrolytes, and surplus water are retained in the tubules and excreted as urine.

The tubules converge into collecting ducts, which drain into the bladder. Final adjustments are controlled by the hormone ADH (antidiuretic hormone):

1. When blood water concentration is low, ADH secretion increases.
2. ADH stimulates the insertion of aquaporins (water channels; see section 1.1.4, p. 10) into the collecting ducts.
3. Water diffuses into surrounding tissues and re-enters the bloodstream.
4. This produces concentrated urine, a common response in hot conditions or dehydration.

Normal function can be maintained with just one kidney, enabling transplant from a donor.

Recall questions

1. Outline the structural adaptations of the kidney that enable it to filter blood efficiently and regulate water balance.
2. Describe what happens to the different filtrates as they pass through the collecting ducts.
3. Describe how the hormone ADH influences urine concentration and why this will be important when dehydrated.

Pancreas

The pancreas is a long, tapering organ located behind the stomach. It has both exocrine and endocrine functions.

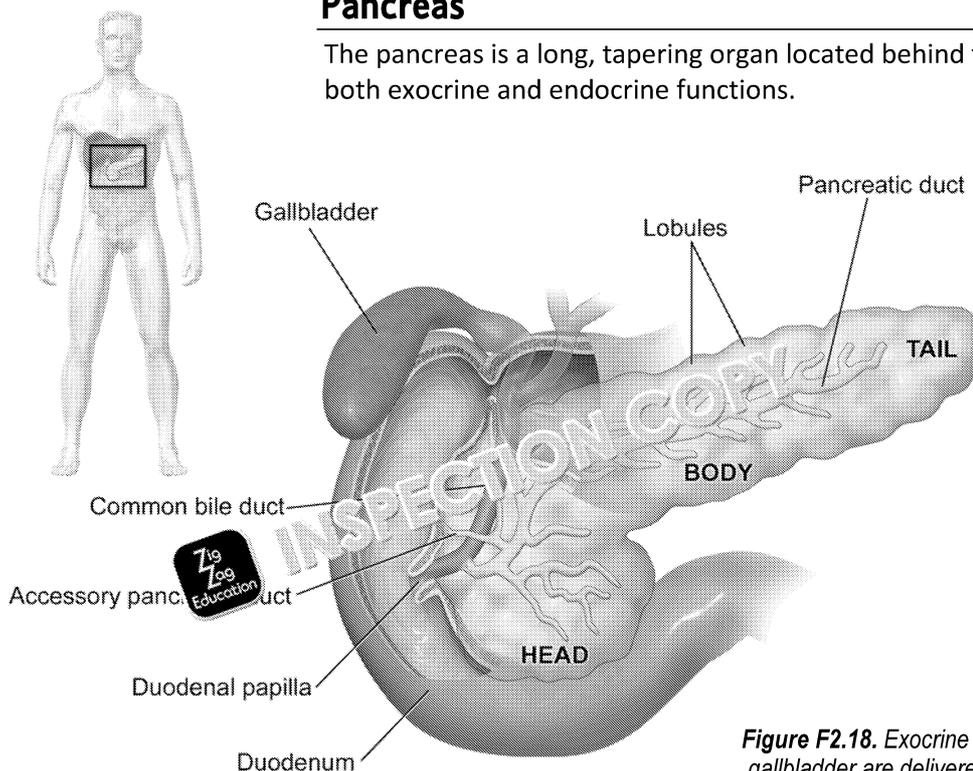


Figure F2.18. Exocrine secretions from the pancreas and gallbladder are delivered directly to the duodenum.

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Exocrine function

The pancreas aids digestion by secreting enzymes into the duodenum. These enzymes include:

- pancreatic amylase – catalyses starch to maltose
- proteases (e.g. trypsin) – catalyse proteins into amino acids
- pancreatic lipase – catalyses lipids into fatty acids and glycerol

These enzymes are produced by specialised cells called acini, arranged in clusters. Secretions flow out through the pancreatic duct, which merges with the duodenum.

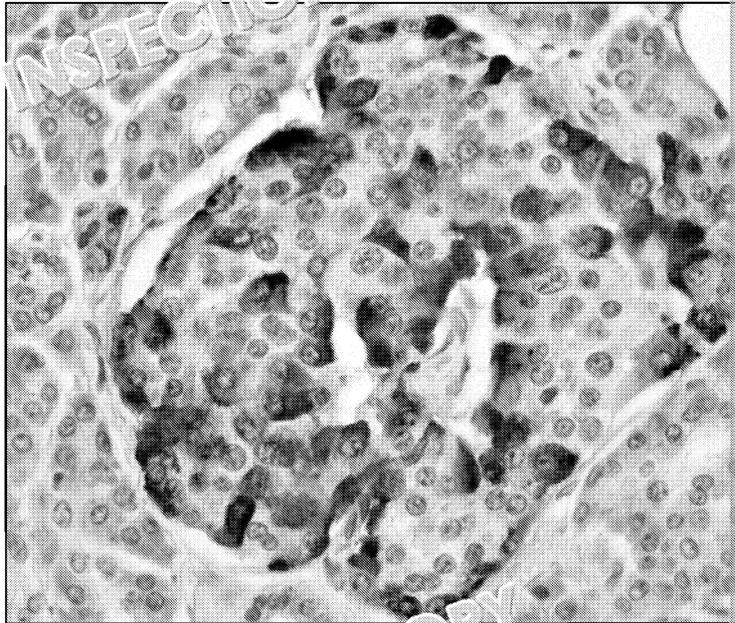


Figure F2.19. Light micrograph of pancreatic cells. Brown-stained cells in the islets of Langerhans, surrounded by blue acini cells.

Endocrine function

The endocrine pancreas regulates blood glucose concentration by producing hormones. The endocrine cells are called islets of Langerhans, embedded throughout the exocrine tissue. In the islets, there are:

- Insulin, released by β (beta) cells when blood glucose levels are high, promotes the uptake of glucose by cells in the liver and muscles and its conversion to glycogen for storage, lowering blood glucose levels.
- Glucagon, secreted by α (alpha) cells when blood glucose levels are low, stimulates the liver to release glucose, increasing blood glucose concentration.

Recall questions

1. State which cells release insulin and glucagon and describe the function of these hormones.
2. Describe the functional differences between the acini cells and the islets of Langerhans.
3. Describe how the pancreas contributes to exocrine and endocrine functions in the digestive system.



Practice question on organ structure and function

1

Describe how low ADH levels in the kidneys adjust when blood water concentration is low.

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2.1.3. Disease and organ failure

Diseases may be classified as either communicable or non-communicable, depending on their causes and transmission routes. Communicable diseases are caused by pathogens, such as bacteria, viruses and protists. These illnesses can be spread from one person to another, and examples include influenza (viral), typhoid (bacterial) and malaria (protist).

Most non-communicable diseases (NCDs) are not transmissible and typically result from a combination of genetic and environmental factors. They fall into two broad categories:

- Genetic disorders – conditions inherited from parents through genes, including type 1 diabetes, some cancers and asthma.
- Lifestyle-related diseases – conditions influenced by habits and behaviours. Risk factors include smoking, alcohol consumption, poor diet, lack of exercise. Diseases include type 2 diabetes, some cancers and heart disease.

Organ failure occurs when an organ loses its ability to perform its normal function effectively. This may result from:

- chronic disease progression (e.g. liver failure from cirrhosis)
- genetic defects (e.g. kidney failure)
- lifestyle factors (e.g. heart failure due to long-term hypertension or poor diet)

This section explores a range of non-communicable diseases, both inherited and lifestyle-related, and the mechanisms that contribute to organ failure.

Heart defects

The heart is a vital organ that contracts rhythmically to circulate blood throughout the body. It ensures unidirectional flow and prevents backflow during contraction.

The right side of the heart receives deoxygenated blood from the body and pumps it to the lungs for exchange. The left side receives oxygenated blood from the lungs and circulates it to the rest of the body.

Septal structure

The right and left sides of the heart are separated by an impervious muscular wall called the septum. It comprises two sections:

- the atrial section (upper portion)
- the ventral or ventricular septum (lower portion)

After birth, small openings in these septa normally close. However, if these remain open, septal defects develop – **congenital abnormalities** classified by location and symptoms.

Ventral septal defect (VSD)

A ventral, or ventricular, septal defect (VSD) is an opening in the ventricular septum. It can take two common forms:

- muscular VSD – located lower in the ventricular wall
- perimembranous VSD – located higher in the heart valves where the septum is thin

The left ventricle generates higher pressure than the right ventricle, so that blood can be pumped to the rest of the body. However, if a VSD is present, blood may be shunted from the left to the right ventricle, reducing the amount of blood going to the lungs. This leads to excess blood volume (pulmonary hypertension) in the lungs. This can cause heart failure, especially if the hole is large.

Small VSDs are often asymptomatic and may heal themselves but larger defects require surgery.

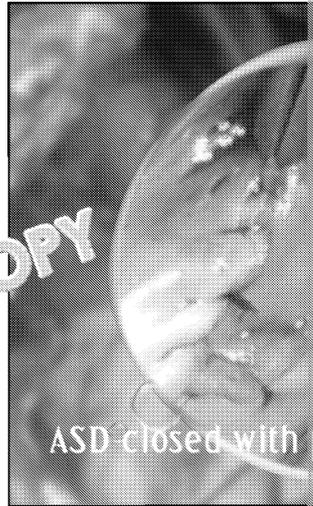


Figure F2.20. Septal defect

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Atrial septal defect (ASD)

An atrial septal defect (ASD) is an opening in the atrial septum, with three main types:

- secundum ASD – occurs in the centre of the septum and is most common
- primum ASD – occurs in the lower region near the valves
- sinus venosus ASD – occurs in the upper region near the major veins

ASDs cause left-to-right shunting of blood, down the pressure gradient, which can lead to the following symptoms:

- pulmonary hypertension
- stroke
- arrhythmias (irregular heart rhythms, including atrial fibrillation)

Small ASDs may be asymptomatic and close on their own, but larger holes usually require surgery.



Valve malfunction

The atrioventricular and semilunar valves maintain one-way blood flow and produce the familiar ‘lub-dub’ sound when closing. They can become damaged and malfunction, and this can be detected via **auscultation** using a **stethoscope**.

auscultation
internal
stethoscope
auscultation

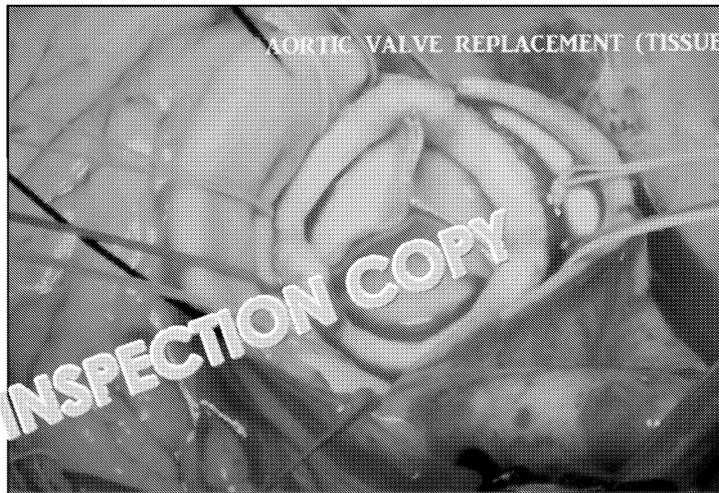


Figure F2.21. Faulty valves can be replaced surgically.

There are three types of valve malfunction:

- stenosis – a narrowing of the valve which restricts blood flow and makes the heart work harder
- regurgitation or incompetence – the valve does not close properly, and blood flows back
- prolapse – the valve leaflets bulge backwards, which can lead to regurgitation

These malfunctions may cause an array of clinical symptoms, including:

- shortness of breath, especially during exercise or when lying flat
- fatigue, dizziness or fainting
- chest pain or ‘pressure’
- heart arrhythmia or palpitations
- oedema (swelling) in the ankles, feet or abdomen



Recall questions

1. State what ventricular septal defects (VSD) and atrial septal defects (ASD) are and list the symptoms in each.
2. Describe how these heart malfunctions affect blood flow.
 - a. Stenosis
 - b. Regurgitation
 - c. Prolapse

Fundamentals of Human Biology
Internal
position
Stethoscope
valves
and
position
used

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Atherosclerosis

Atherosclerosis is a progressive disease in which fatty plaques (atheroma) accumulate. These plaques are made of cholesterol, lipids and cell debris, and gradually narrow the artery and harden over time. The result is restricted blood flow, which can lead to serious complications such as heart attack and stroke.

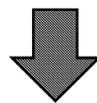
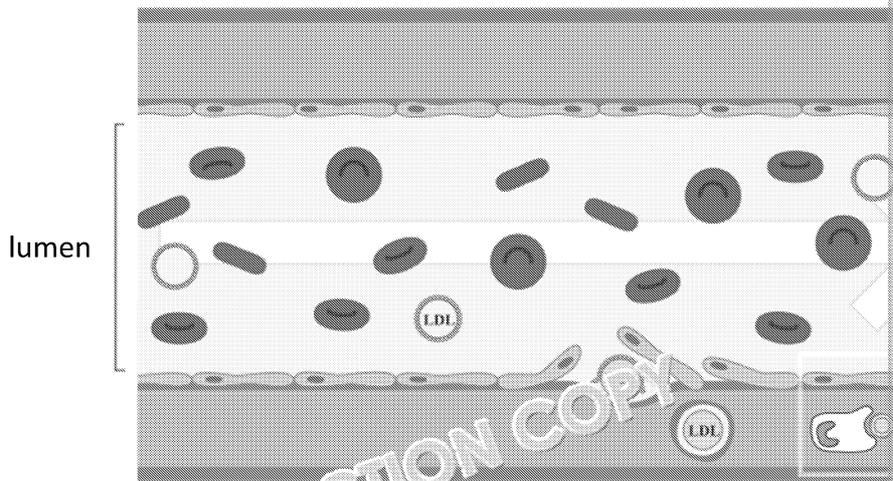
Plaque development

Plaque formation usually begins with damage to the arterial wall, caused by natural wear and tear (such as smoking or high blood pressure). Once damaged, the site traps cell debris and there are elevated levels of LDL (low-density lipoprotein) cholesterol, triglycerides and

These trapped molecules attract other molecules, forming the plaque that grows and narrows the artery further, impairing blood flow to dependent organs.



STEP 1: Damage to the arterial wall



STEP 2: Lipid-laden macrophages accumulate in early plaques

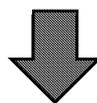
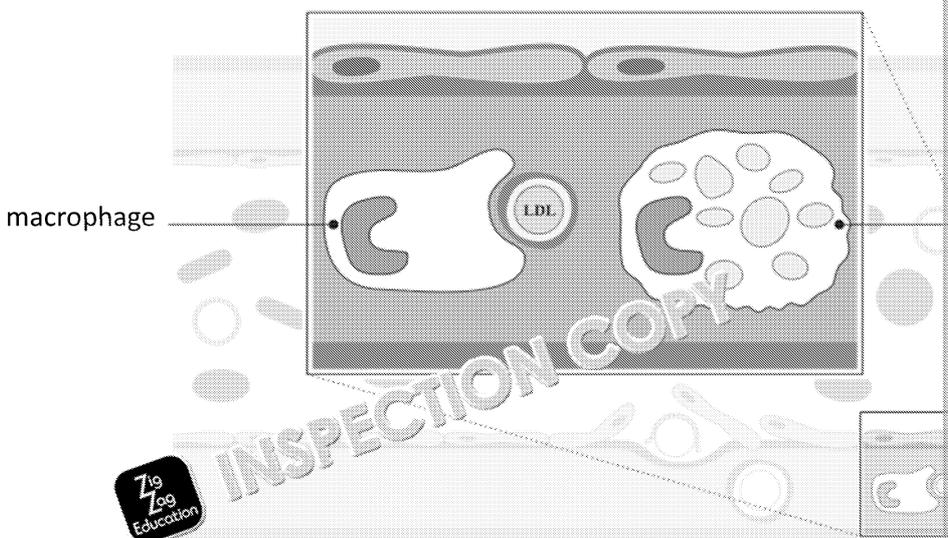


Figure F2.22A. Steps 1 and 2 of the formation of an atherosclerotic plaque, and its rupture to

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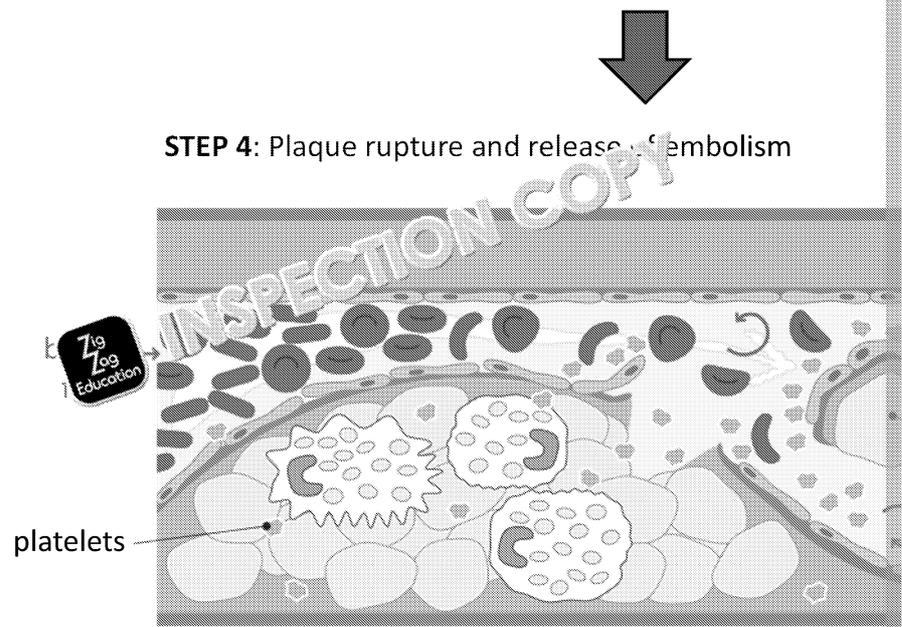
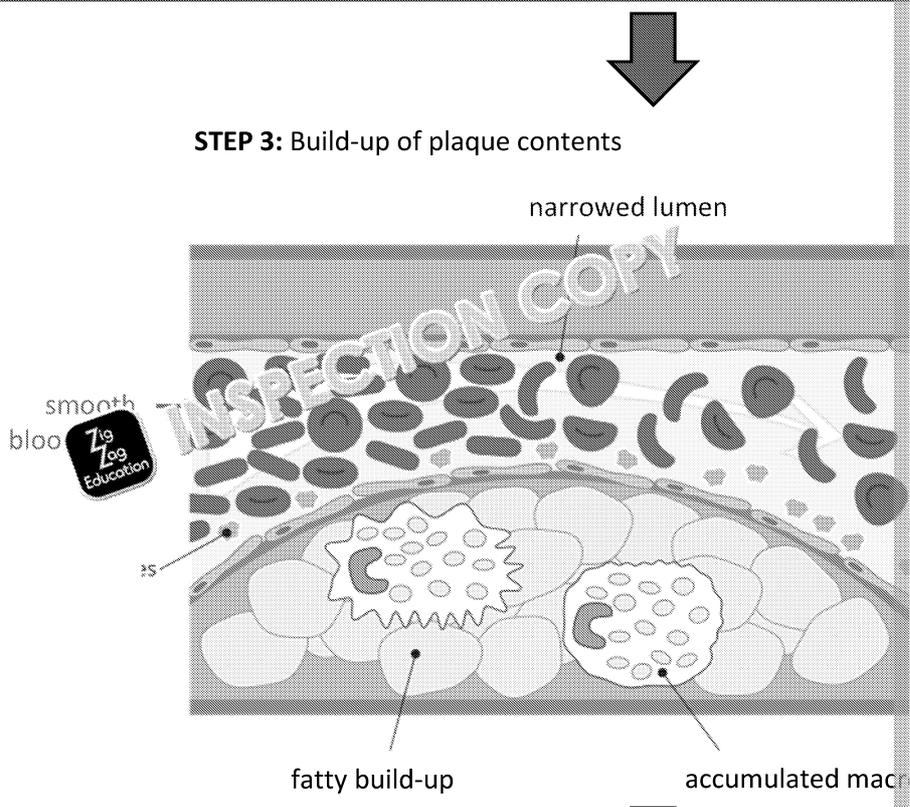


Figure F2.22B. Steps 3 and 4 of the formation of an atherosclerotic plaque, and its rupture.

Embolism

If a plaque ruptures, its contents may enter the bloodstream as an **embolus** – a circulating mass that can lodge in smaller arteries, causing blockages in vital organs. This can have catastrophic effects if the embolus becomes lodged in the heart, lungs or brain (see Table F2.1).

Organ affected	Embolism type	Resulting condition
Heart	Cardiac embolism	May trigger heart attack
Lungs	Pulmonary embolism	Often a result of a deep vein thrombosis Causes breathing difficulties
Brain	Cerebral embolism	Can cause stroke

Table F2.1. A summary of the conditions caused by embolisms lodging in the body.

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Causes and risk factors

Lifestyle choices increase the risk of developing atherosclerosis, including a poor diet and sugars, lack of exercise, and smoking.

These may lead to conditions such as diabetes, obesity, high blood pressure, and high cholesterol, which increase the risk of developing atherosclerosis further.

Family history is important too as some genetic factors also increase the risk.

Symptoms

Atherosclerosis may be asymptomatic for years, and when symptoms do arise, they are at the site of the atherosclerosis but may include:

- shortness of breath
- fatigue, dizziness and confusion
- chest pain and angina
- pain in limbs during exercise

Your turn

1. Create a flow chart or cartoon to show the development of a plaque and its rupture and the formation of an embolism. Add as much detail as possible.
2. Describe the causes and risk factors for atherosclerosis and the symptoms that may arise.

Aneurysms

An aneurysm refers to the abnormal dilation or bulging of an artery wall, caused by the weakening of its structural proteins. This can result from **chronic** pressure or **degenerative** changes.

A **thrombus** may form within an existing aneurysm and increase its risk of rupture. Because arteries transport blood under high pressure, a ruptured aneurysm can lead to catastrophic internal bleeding and may prove fatal if not treated promptly.

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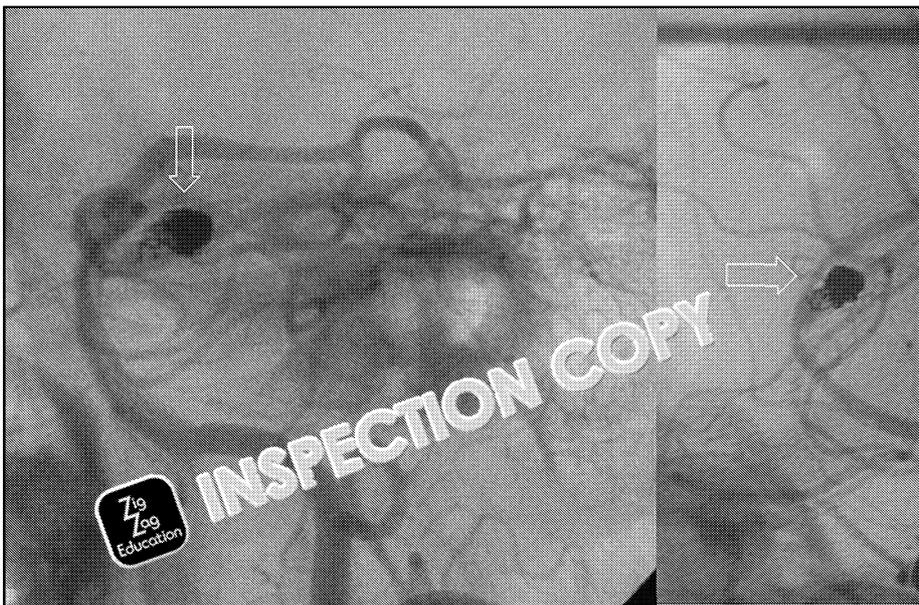


Figure F2.23. Saccular aneurysm visible in a patient under X-ray, due to the injection of a contrast agent.

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Classification

Aneurysms can also be classified by how much wall is involved:

- True aneurysm – involves dilation through all three arterial wall layers (tunica intima, tunica media, and tunica externa; see section 2.1.2, page 65).
- False aneurysm (pseudoaneurysm) – involves blood leaking through the tunica intima and tunica media; not all wall layers are involved.

Dissection or rupture of the aneurysm

An aneurysm may break. The extent to which this happens affects the severity of the condition. The extent of the dissection involved will determine the interventions required and the damage caused.

Dissection in an aneurysm describes a tear developing in the inner endothelial layer of the vessel wall. This allows blood to split the vessel wall layers, which may progress through the vessel wall and widen the lumen.

A rupture is a full thickness tear of the arterial wall: all three layers give way, causing blood to leak into the surrounding tissues. If the affected artery is substantial, the body can go into shock. A ruptured cerebral aneurysm causes a stroke, while a ruptured aortic aneurysm causes internal bleeding.

Aortic aneurysms

The aorta, the main artery leaving the heart, can develop aneurysms in two key locations:

- Abdominal aortic aneurysm (AAA, or triple A) – located in the lower aorta; may cause back pain and rupture.
- Thoracic aortic aneurysm (TAA) – located near the heart; may cause chest pain and rupture.

There are several risk factors for aortic aneurysms, including atherosclerosis, high blood pressure, smoking, genetic disorders (e.g. Marfan syndrome), and age. If an aortic aneurysm ruptures, it is a medical emergency and essential to prevent death from rapid internal bleeding.

Pulmonary aneurysms

A pulmonary aneurysm forms in the artery transporting deoxygenated blood from the heart to the lungs. It is a rare condition but can be life-threatening.

It is caused by high blood pressure in the lungs (pulmonary hypertension), infection, trauma, congenital heart defects and connective tissue disorders.

Rupture leads to bleeding on the lungs, severely impairing breathing and gas exchange.

Apply your knowledge

1. Define the term aneurysm, list the different types of aneurysm, and describe the difference between a dissection and a rupture.
2. Explain why a ruptured aneurysm is considered a medical emergency and describe the consequences of a rupture.
3. Identify three or more risk factors for developing a thoracic aortic aneurysm and explain how they contribute to the condition.

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Muscle deterioration

Muscle deterioration, or muscle **atrophy**, refers to the loss of muscle mass, strength and function. It primarily affects skeletal muscles and can occur due to various biological and lifestyle factors.

Causes

Muscle atrophy is a progressive disease which may develop slowly or rapidly depending on the cause.

- Ageing – after the age of 40, muscle mass and strength decline naturally due to changes in metabolism. This process is known as sarcopenia.
- Lack of use (disuse) – a sedentary lifestyle or prolonged immobility from bed rest or surgery limits muscle use and atrophy.
- Malnutrition – inadequate protein intake or poor nutrient absorption impairs muscle growth.
- Neurologic disorders – conditions like multiple sclerosis and spinal muscular atrophy damage neurons, interrupting muscle innervation.
- Genetic conditions – disorders such as muscular dystrophy weaken muscle fibres due to inherited structural defects.
- Endocrine disorders – hormonal imbalances, including hyperthyroidism and Cushing's disease, affect protein metabolism and muscle maintenance.
- Autoimmune and inflammatory disorders – chronic illnesses such as AIDS can lead to muscle inflammation and muscle wasting.

Symptoms

As muscle fibres progressively deteriorate, patients experience muscle weakness and loss of muscle mass and tone. This leads to difficulty in daily activities such as walking and climbing stairs, and impaired balance and strength, increasing the risk of falls.

Recall questions

1. List four common causes of muscle atrophy and explain how they affect muscle mass and strength.
2. Describe the main symptoms of muscle atrophy and explain how they affect daily life.

Osteoporosis

Osteoporosis is a progressive condition in which bone mineral density decreases, leading to fragile bones. It often affects post-menopausal women, although it is not exclusive to women. It can remain undetected until a fracture occurs, sometimes from minor incidents such as a fall.

Causes and risk factors

Bones are living tissues which undergo constant remodelling. This balance is maintained by the activity of osteoblasts, which build bone, and osteoclasts, which break down bone. In osteoporosis, the rate of bone breakdown exceeds the rate of bone formation, reducing bone density, causing porous, brittle bones which are more likely to fracture. Osteoporosis commonly affects weight-bearing bones, such as the spine, hips and wrists, which absorb the most stress.

While osteoporosis is associated with older women, there are several other risk factors, in addition to age and sex, including:

- low sex hormone levels – reduced oestrogen (in women) or testosterone (in men)
- sedentary lifestyle and lack of weight-bearing exercise
- smoking and excessive alcohol consumption
- long-term steroid use – steroids (e.g. prednisolone) are used to treat a wide range of conditions, including asthma and eczema
- poor nutrition, including lack of calcium and vitamin D, low body mass index (BMI) or eating disorders
- family history of osteoporosis

Further your knowledge

Vitamin D enables calcium absorption and is produced by the body using UV radiation. Vitamin D is also found in some foods. Calcium is present in dairy products and leafy green vegetables like kale and broccoli.

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Diagnosis

Osteoporosis is diagnosed and monitored using DEXA (Dual-Energy X-ray Absorptiometry). This imaging technique uses two low-dose X-ray beams at different energy levels to measure bone density. It measures how much radiation is absorbed by bone compared to soft tissue.

DEXA provides two bone density scores:

- T-score – compares bone density against a healthy young adult
- Z-score – compares bone density against others of the same age, sex and ethnicity

T-score range	Diagnosis
Above -1	Normal
-1 to -2.5	Osteopenia (early bone loss)
Below -2.5	Osteoporosis

Table F2.2. The T-score range compares bone density of the patient to that of a healthy young adult.

DEXA scans are routinely offered to women over the age of 65 and men over the age of 70. For postmenopausal women with known risk factors, and individuals who are on long-term corticosteroid therapy or with a history of fractures, may also be offered scans at a younger age.

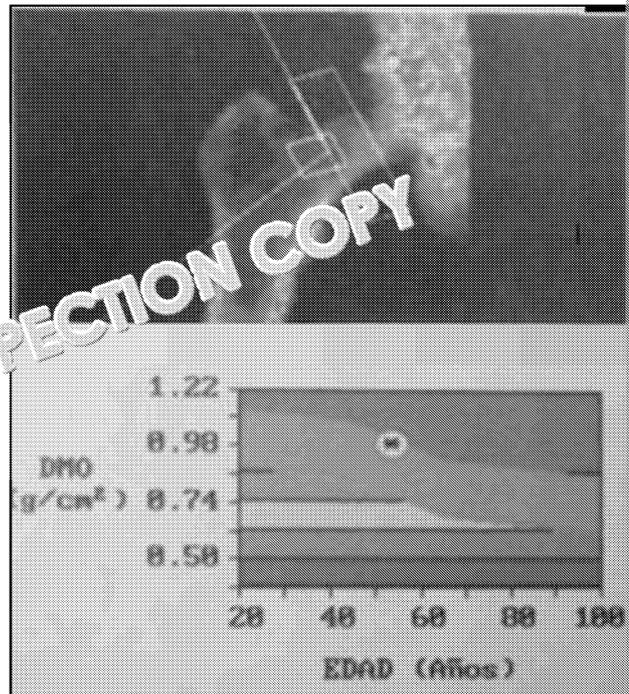


Figure F2.24. Bone density image and reference graph from a female femur. Areas in red indicate low bone density.

Recall questions

1. List some common risk factors associated with the development of osteoporosis.
2. Describe how the DEXA scan is used to diagnose and monitor osteoporosis. What do the T-score and Z-score represent?

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Liver cirrhosis

Liver cirrhosis is a chronic condition where long term damage leads to the gradual replacement of healthy tissue with scar tissue (**fibrosis**). This disrupts normal digestive and metabolic processes, such as bile production (for lipid digestion) and blood detoxification (see section 2.1.2, page 69). As fibrosis advances, liver function becomes increasingly impaired, potentially resulting in liver failure.

Causes

The most common cause of cirrhosis is chronic alcohol misuse. However, other factors causing progressive liver damage include:

- non-alcoholic fatty liver disease (NAFLD) – associated with obesity; fat accumulation eventually causes inflammation and fibrosis
- chronic viral infections – hepatitis B or C
- autoimmune liver conditions – e.g. autoimmune hepatitis
- genetic disorders – e.g. Wilson’s disease (causes copper accumulation), haemochromatosis (causes iron overload)
- toxic substances and medications – long-term exposure increases detoxification burden, leading to chronic inflammation

These conditions cause hepatocytes to become inflamed and damaged over time. Repeated damage leads to scarring.

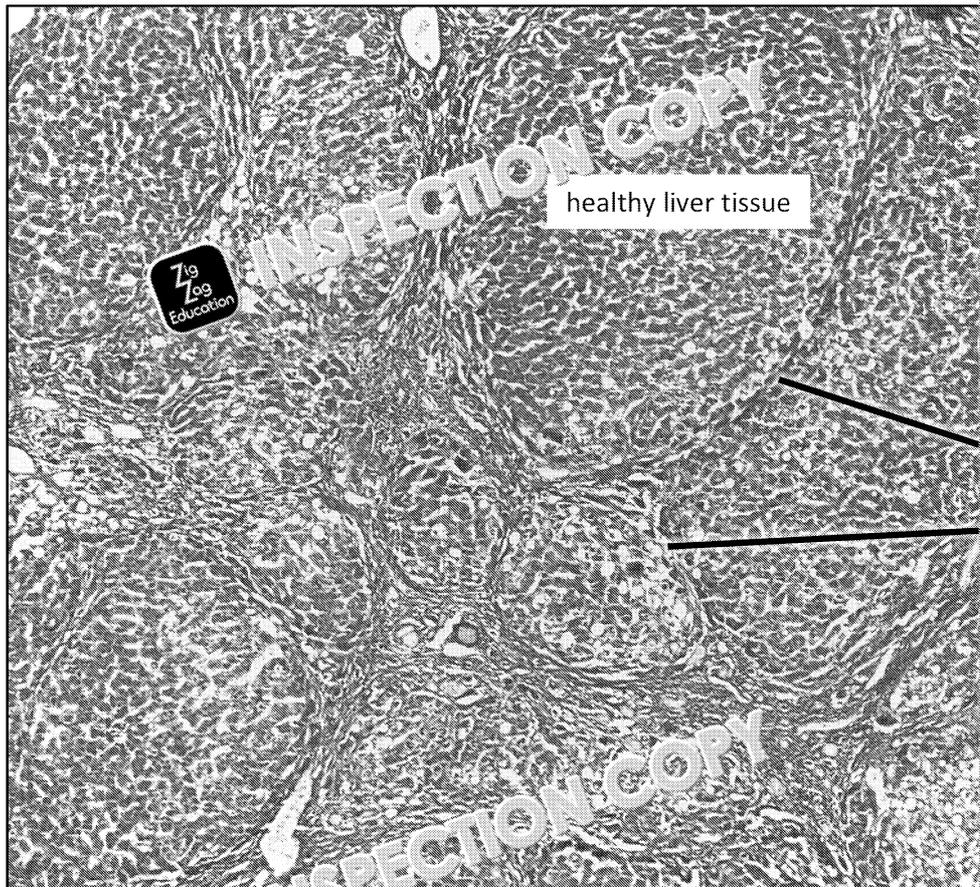


Figure F2.25. Fibrosis clearly visible in this light micrograph of cirrhotic liver tissue. The fibroids are the deep blue bands running through the purple healthy tissue, causing scarring and distortion of the liver's structure.

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Symptoms

In early stages, cirrhosis may be asymptomatic. As damage progresses, symptoms and toxin accumulation within the bloodstream, including:

- fatigue, weakness and loss of appetite
- jaundice – yellowing of skin and eyes, due to impaired processing of bilirubin (when erythrocytes break down)
- itchy skin – often linked to bile salt accumulation
- abdominal swelling and liver enlargement
- vascular changes – spider-like blood vessels under the skin, red palms, easy bruising
- cognitive symptoms – confusion, poor concentration
- internal bleeding – vomiting blood, black faeces



Recall questions

1. List the primary causes of liver cirrhosis and how they lead to the development of fibrosis.
2. Describe the symptoms associated with liver cirrhosis and how they occur in affected individuals.

Lung conditions

The lungs are a vulnerable target for disease and infection. They form an essential interface between the external and internal environments, are moist to enhance diffusion, and have a large surface area which contribute to the possibility of developing issues.

Asthma

Asthma is a chronic respiratory condition, characterised by **acute** episodes of inflammation, airway narrowing and swelling, muscular contraction (bronchospasm), and excess mucus production. These factors lead to the narrowing of the bronchi and bronchioles. This restricts airflow and causes symptoms such as characteristic wheezing, coughing, chest tightness and shortness of breath, especially during physical activity.

Causes

Asthma is a genetically influenced condition, with symptoms often triggered by environmental factors. Triggers include airborne allergens, irritants, dust or infections. Exercise, especially in cold weather, and emotional responses such as stress, laughter and crying which change breathing patterns are also triggers. Some medications are also triggers, including non-steroidal anti-inflammatory drugs (NSAIDs) and beta blockers (for hypertension).

Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a progressive lung condition characterised by chronic inflammation, narrowing of the airways and damage to the alveolar surface. COPD includes both chronic bronchitis and emphysema.

Chronic bronchitis

Chronic bronchitis is defined by persistent inflammation of the bronchi and bronchioles for at least three months per year for two or more consecutive years. Inflammation stimulates the production of mucus, narrowing the airways and restricting air flow. Epithelial cilia are also damaged, and retaining particles and debris in the airways, increasing the risk of infection. This reduces the efficiency of gaseous exchange and can lead to hypoxia.

Symptoms of chronic bronchitis include a persistent productive cough (smoker's cough) coupled with wheezing, shortness of breath, fatigue and frequent chest infections. In severe cases, individuals may have bluish lips and nails (cyanosis) from poor oxygenation, ankle swelling from poor circulation, and crackling sounds when breathing indicating mucus or fluid in the lungs.

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Emphysema

Emphysema involves progressive damage to the alveoli (air sacs responsible for gas exchange) which reduces oxygen uptake, causing breathlessness and leading to long-term respiratory issues.

When the alveoli become damaged, the walls break down, and they lose their structure and merge into larger, less efficient air spaces, which reduces the surface area available for gas exchange. This also traps air, making it difficult to exhale completely. Over time, this leads to chronic hyperinflation (hyperinflation), laboured breathing, and in severe cases, the risk of lung infection, chronic air and reduced clearance.

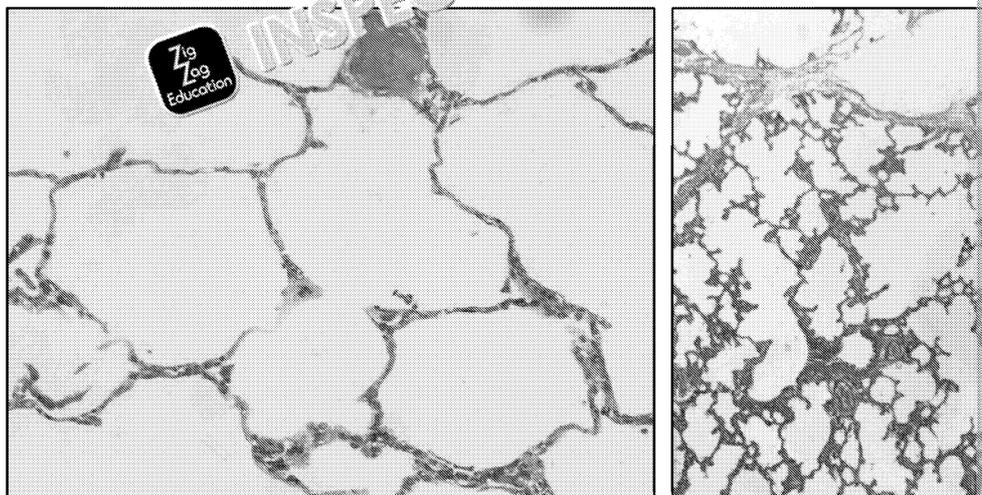


Figure F2.26. Light micrograph on left shows normal lung alveoli, showing high surface area compared to emphysematous tissue on right, which has enlarged alveoli and substantial loss of surface area.

Causes and risk factors

The leading cause of COPD is smoking, including passive smoking. Smoke contains various chemicals that damage lung tissue, leading to irreversible structural changes. Other contributing factors include:

- age – the disease usually develops in individuals over the age of 40
- occupational exposure – to air pollution or chemical fumes

Lung cancer

Cancer is a disease caused by uncontrolled cell division. Lung cancer is one of the most common worldwide and the leading cause of cancer-related death because it progresses quickly and tends to be diagnosed at an advanced stage, making treatment complex.

There are three types of lung cancer:

- Non-small-cell lung cancer (NSCLC) – most common subtype; includes adenocarcinoma, squamous cell carcinoma and large-cell carcinoma.
- Small cell lung cancer (SCLC) – more aggressive, meaning it progresses quickly and is more likely to **metastasise** (migrate).
- Secondary lung cancer – occurs when cancerous cells metastasise to the lungs from another organ in the body via the bloodstream.

Unlike COPD and asthma, where impairment is due to narrowed airways or damaged cilia, lung cancer disrupts function through abnormal cell growth.

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Causes and risk factors

The primary cause of lung cancer is smoking, which accounts for around 70 % of cases. Lung cancer also has several other risk factors, including:

- air pollution – in particular, PM2.5 particles (airborne particulates < 2.5 µm) that reach the lungs; this includes soot, sulfates and nitrates released in vehicle exhaust
- occupational hazards – such as exposure to asbestos, diesel fumes or industrial dust
- radiation exposure – X-rays and CT scans
- family history of lung cancer and inherited mutations

These risk factors increase the risk of lung cancer, like blood but do not guarantee that the disease will develop. Lung damage accumulates over time.

Symptoms

Early stages of lung cancer are often asymptomatic, which delays diagnosis. Symptoms can be similar to other lung conditions, and include a persistent cough, often with blood-tinged sputum, fatigue and chest pain. Sudden, unexplained weight loss, hoarseness and recurrent infections are also observed. These stem from impaired gaseous exchange leading to reduced aerobic capacity, reduced blood flow to the tumour, and local tissue invasion by the tumour, with associated inflammation.

Recall questions

1. List the main causes and symptoms of asthma and describe how a severe asthma condition is diagnosed.
2. Describe the differences between chronic bronchitis and emphysema.
3. Describe the major risk factors for developing lung cancer.

Stomach conditions

Stomach ulcers

Stomach ulcers are open sores on the stomach lining. They are caused by the erosion of the gastric lining due to the absence of the protective mucus layer. The mucus layer is produced from degeneration by acid, and its absence causes damage by burning from the acid.

Causes

There are two main causes of stomach ulcers:

- *Helicobacter pylori* (*H. pylori*) infection – a bacterium which disrupts the mucus layer, allowing stomach acid to interact with the stomach lining.
- Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) – include aspirin, which can make the lining more vulnerable to acid.

However, there are other risk factors which increase the likelihood that these conditions will develop, including smoking, excessive alcohol consumption and stress.

Symptoms

Not all stomach ulcers are painful. Typical symptoms include a burning or gnawing pain in the upper abdomen; indigestion, heartburn and acid reflux; and nausea, bloating and feeling full. Vomiting blood, iron in the faeces, and a sudden, sharp abdominal pain may indicate a perforation or bleed.

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Stomach cancer

Stomach cancer occurs when abnormal cells in the stomach lining divide uncontrollably to form a tumour. This can impair digestive processes, reduce nutrient absorption, and occupy space in the stomach. These cancers are relatively uncommon in the UK but are medically serious, often diagnosed late due to non-specific early symptoms which are similar to ulcers and gallstones.

Risk factors and symptoms

There are several factors which increase the risk of developing stomach cancer. The risk increases due to abnormal exposure of stomach epithelial cells to corrosive gastric secretions. Helicobacter pylori infections therefore increase the risk because the protective mucus lining is damaged, and by increasing the likelihood of a genetic mutation occurring in the underlying cells of the stomach lining.

Smoking and excessive alcohol consumption increase the risk because of carcinogenic effects. Interestingly, a diet high in salt, or smoked or pickled foods, also increases the risk. Other risk factors include older age (over 50), family history, pernicious anaemia, and blood group A. These risk factors may lead to malignant cells, increase inflammation, cause **oxidative stress**, or cause damage to DNA.

Stomach cancers are often diagnosed at a late stage because early symptoms are vague and non-specific, such as indigestion, ulcers or gallstones. Persistent heartburn, indigestion, bloating, abdominal pain, loss of appetite and feeling full quickly are symptoms common to stomach ulcers and cancer. Other symptoms include unexplained weight loss, common to many cancers due to redirected energy to the tumour and systemic nutrient deficiency; difficulty swallowing (dysphagia) due to obstruction; and blood or black faeces, which indicates internal bleeding.

Recall questions

1. List the primary causes and risk factors of stomach ulcers and their diagnosis.
2. Compare the risk factors for stomach ulcers and stomach cancer.

Bowel conditions

Inflammatory bowel disease (IBD)

Inflammatory bowel disease (IBD) is a group of chronic disorders which affect the gastrointestinal tract, characterised by persistent inflammation. The two main forms are ulcerative colitis and Crohn's disease. They share typical symptoms including abdominal pain, diarrhoea and fatigue, but differ in their location and the depth of tissue involvement.

Condition	Area affected	Inflammation
Ulcerative colitis	Colon and rectum only	Inner lining
Crohn's disease	Anywhere between mouth and anus, but most commonly in the intestine	Full thickness

Table F2.3. Location and depth of inflammation for ulcerative colitis and Crohn's disease.

Unlike irritable bowel syndrome, which involves no inflammation, IBD involves chronic inflammation which damages GI tissues.

Symptoms

Symptoms are caused by inappropriate immune-mediated inflammation, which disrupts digestion, nutrient absorption, water balance and faecal processing. They often follow a relapsing-remitting pattern, with acute episodes triggered by diet, stress or infection.

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During an acute episode, symptoms may include:

- diarrhoea, often with blood or mucus – symptomatic of inflammation
- abdominal pain and cramping
- urgency to defaecate
- fatigue, loss of appetite, and weight loss
- fever – a result of inflammation

Causes and risk factors

IBD is an autoimmune disease involving the immune system wrongly attacking several where the exact cause is unknown; however, there is evidence to suggest infection, coupled with a genetic predisposition, can lead to chronic immune inflammation. Other factors may also act as a trigger for the disease, including smoking, infections, use of **NSAIDs**, and changes to the gut microbiome, including from substantive dietary changes or the use of oral antibiotics. Age is also a factor: patients are most often diagnosed with IBD between the ages of 15–30 and 50–70.

Foods that often trigger an acute episode vary but are linked specifically to those that irritate the gut wall. This includes high-fibre foods like grains and raw vegetables, coffee, alcoholic drinks, and artificial sweeteners. Therefore, avoiding these foods during an acute episode, is well advised.

Stress is also a trigger, due to hormonal effects on gut function, and because lifestyle factors often include reduced diet quality (for instance, increased consumption of caffeinated or alcoholic drinks) and less exercise.

Cancer of the colon

Colon cancer is caused by the uncontrolled cell division of abnormal epithelial cells in the lining of the large intestine, forming a **malignant** tumour. When the rectum is also affected, the term colorectal cancer is used instead. These cancers often start as polyps – small, **benign** growths on the inner mucosal lining – which can become cancerous if not detected and removed early.

Symptoms and causes

Colon and colorectal cancer symptoms may be absent until the tumour is large depending on its location, size and degree of spread. Symptoms typically include:

- blood in the faeces
- changes in bowel habits – persistent diarrhoea or constipation
- abdominal pain, bloating or cramping
- fatigue and unexplained weight loss
- feeling of incomplete bowel movement

Risk factors include both genetic and lifestyle factors. A family history or pre-existing disease (IBD) increases the risk of developing colorectal cancer. Lifestyle factors include smoking, alcohol consumption, obesity, and type 2 diabetes, low levels of fibre or processed meats and low in fibre intake, because these factors may inflict damage on the gut and mucosal health, which contribute to chronic inflammation and can lead to cancer with age.

Recall questions

1. List the lifestyle factors that increase the risk of developing inflammatory bowel disease and colon cancer.
2. Describe the main differences between ulcerative colitis and Crohn's disease.

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Kidney failure

Kidney failure is a condition where one or both kidneys are unable to effectively filter and regulate fluid and electrolyte balance, or maintain homeostatic control. The failure can be due to the ultrafiltration membrane, nephron tubules, or impaired water and ion reabsorption.

Causes and symptoms

There are many causes of kidney failure, including:

- infections – inflammation and damage to nephrons reduce filtration efficiency
- hypertension – increased pressure damages ultrafiltration membranes, allowing the filtrate to pass back into the blood
- polycystic kidney disease – cysts (fluid-filled sacs) displace tissue and compress nephrons
- genetic conditions, e.g. diabetes insipidus (inability to produce ADH) – causes conditions which can lead to nephron damage

Symptoms of kidney failure are often systemic due to the kidney's role in homeostasis:

- hypertension – from fluid retention and increased blood volume
- proteinuria or haematuria – presence of protein or blood in the urine because of damaged filtration membranes
- anaemia and fatigue – reduced erythropoietin secretion (a hormone produced by the kidney that stimulates bone marrow to manufacture erythrocytes, see page 123) leads to low red blood cell production (anaemia), resulting in reduced oxygen transport and reduced aerobic capacity
- bone pain and joint stiffness – linked to impaired calcium/phosphate ion regulation
- fracture risk – chronic kidney disease alters bone metabolism, causing weakened bones

Recall questions

1. Outline the main causes and symptoms of kidney failure.

Pancreatic conditions

Diabetes mellitus

Diabetes mellitus is a chronic condition where the body fails to effectively regulate blood glucose levels due to impaired insulin production or insulin function. There are two types – type 1 and type 2 – and causes different defects.

Type	Defect	Cause	Risk factors
Type 1	Pancreatic β cells unable to produce insulin	Autoimmune destruction	Family history, genetic triggers
Type 2	Insufficient insulin produced or target cells become resistant to insulin	Metabolic dysregulation	Obesity, poor diet, sugar intake

Table F2.4. The defects, causes and risk factors for types 1 and 2 diabetes.

Type 1 diabetes

Type 1 diabetes typically develops during childhood or adolescence, although it can arise at any age. It is caused by autoimmune destruction of pancreatic β cells, leading to complete insulin deficiency, and requires lifelong insulin therapy.

Symptoms include the sudden onset of excessive thirst, frequent urination and unexplained weight loss. **Hyperglycaemia** may lead to confusion and behavioural changes. **Hypoglycaemia** may cause slurred speech, drowsiness and disorientation. Both extreme states can lead to coma or death if left untreated.

To manage the condition, patients require lifelong insulin therapy via injections to regulate blood glucose concentration. In addition, they must frequently monitor their blood glucose levels to avoid hyperglycaemic episodes.

Ongoing research into stem-cell-based therapies is exploring the possibility of growing new β cells. Successful transplant would restore insulin production and not be vulnerable to rejection by the patient's own cells.

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Type 2 diabetes

Type 2 diabetes is usually diagnosed in adulthood, but incidences are rising in children due to changes in dietary habits and increased obesity. It occurs when either the pancreas cannot produce enough insulin or the target cells become resistant to insulin, so reducing glucose uptake by cells.

The primary cause of type 2 diabetes is obesity, due to overconsumption of refined carbohydrates. Many of these have been processed to remove fibre, vitamins and minerals, leaving behind refined sugars. Examples include white bread, pizza dough, sugary cereals, bagels, waffles, fruit juices and fizzy drinks.

Symptoms include the gradual onset of persistent thirst, fatigue, blurred vision and frequent urination.

Due to its chronic nature, the main treatment involves lifestyle modification: weight loss, a diet of low-calorie foods, and regular physical activity. In some cases, and often initially as a temporary effect, medications are required to either stimulate insulin production or reduce insulin resistance. In advanced or unresponsive cases, insulin injections may be required. Studies have shown that type 2 diabetes can be reversed if significant lifestyle changes are sustained, especially if caught early.

Pancreatic cancer

Pancreatic cancer typically presents at a late stage, resulting in a poor prognosis.

The pancreas contains two functional types of cells: endocrine cells that secrete hormones into the bloodstream; and exocrine cells that secrete digestive enzymes into the small intestine.

Most pancreatic cancers occur in the exocrine cells and are classified as adenocarcinomas. Neuroendocrine tumours (NETs) can also occur from hormone-producing cells.

Symptoms

Pancreatic cancer often remains asymptomatic until advanced stages. Symptoms may include abdominal pain, jaundice, weight loss, and changes in stool. If symptoms resembling other gastrointestinal conditions such as indigestion, gallstones or IBD, making early diagnosis difficult. If they appear, they may include:

- dull and persistent abdominal pain
- jaundice – a yellowish tint to the skin caused by bile duct blockage caused by abnormal growth in the pancreas
- steatorrhea – fatty, pale faeces caused by poor fat digestion due to obstruction of the pancreatic duct
- loss of appetite or unexplained weight loss
- new-onset or worsening diabetes
- nausea, vomiting and fatigue

Causes and risk factors

As with many cancers, there are several prevalent risk factors, notably smoking. Cigarettes contain many carcinogens which damage DNA, and obesity or poor diet can also contribute to the disease and promotes inflammation, causing damage to tissues and DNA.

Ongoing conditions like pancreatitis and diabetes also increase the risk of pancreatic cancer. Pancreatitis involves persistent inflammation which causes repeated tissue damage and may also contribute to the disease. Diabetes puts stress on the body's metabolism and creates inflammation that can lead to tissue damage.

Age is also a factor, due to the accumulation of cells with damaged DNA through time. Most cases of pancreatic cancer are diagnosed in patients over the age of 65 years.

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Apply your knowledge

1. Describe the main differences between type 1 and type 2 diabetes mellitus with respect to their causes and treatment approaches.
2. Describe the types of lifestyle modifications that can be effective in managing type 2 diabetes.
3. Explain why pancreatic cancer is often diagnosed at an advanced stage.



Practice questions: Disease and organ failure

1 A 53-year-old male presents with the following history, background and symptoms:

Medical history	Background	Symptoms
Recent <i>H. pylori</i> infection, but all cleared Mother died of breast cancer Father had long-term stomach ulcers	Smoker Drinks 4-7 pints per week Has increased exercise in last 2 months about 20 mins per day of light workouts and ~8000 steps per day Consumes 2-3 portions of fruit/veg per day, recently improved Sleeps well	Blurred vision Recurrent fatigue Mild weight gain Frequent urination General weakness

Using this patient history:

- State one lifestyle changes that the patient could make immediately (1 mark)
- Outline one possible diagnosis for the patient and explain your reasoning (3 marks)



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2.1.4. Transplanted and artificial organs

The human body consists of highly specialised organs and systems that interact. When organ function becomes impaired, either through disease, damage or congenital conditions, it can significantly reduce quality of life. In many cases, corrective surgery or organ transplantation can replace lost function. This section explores key interventions across major organs, their advantages and limitations.

Transplants and corrective surgery

Heart

Surgical interventions are often needed when electrical conduction fails, valves become faulty or cardiac muscle is damaged. Each of these issues can be addressed using corrective surgery.

Main problem	Caused by	Surgical intervention
Uncoordinated contraction	Damage to sinoatrial node (SAN) or atrioventricular node (AVN)	Pacemaker
Antidirectional blood flow	Septal defects	Surgical repair
	Faulty valves	Valve replacement (mechanical or biological)
Coronary artery blockage	Atherosclerosis in coronary artery	Coronary artery bypass grafting (CABG)

Table F2.5. Surgical interventions for heart issues.

For end-stage heart failure, a heart transplant may be required, replacing the patient's heart using a heart from a recently deceased donor.

Lungs

Surgical solutions address recurrent collapse, airway obstruction, or localised disease.

Main problem	Caused by	Surgical intervention
Recurrent collapse of the thorax	Lung collapse caused by air leakage into the pleural (lung) cavity	Pleurodesis
Permanent airway obstructions	Structural weakness or collapse	Stent placement or reinforcement
Localised disease	Various causes including infection, tumour, trauma	Lobectomy or removal

Table F2.6. Surgical interventions for lung issues.

In chronic, widespread conditions such as cystic fibrosis and COPD, lung transplantation may be considered.

Liver

Corrective surgery targets ducts, blood vessels and tumours.

Main problem	Caused by	Surgical intervention
Bile duct damage	Gallstones	Repair tears
Portal hypertension	Blocked blood vessels causing increased blood pressure	Shunts fitted
Tumours	Malignant growth	Liver resection

Table F2.7. Surgical interventions for liver issues.

Liver transplants are offered for end-stage liver disease or large malignant tumours. Partial transplants are also possible.

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Stomach

Corrective surgery may be offered for structural or functional complications.

Main problem	Caused by	Surgical intervention
Ulcers	Damage to the mucosal layer	Gastrectomy
Cancer	Malignant growth	the stomach
Reflux	Weak cardiac sphincter	Fundoplication using the fundus
Gastric outlet obstruction	Restriction of the pyloric duct	Pyloroplasty of the pyloric canal

Table F2.8. Surgical interventions for stomach issues.

Stomach transplants are rare and usually performed as part of a multivisceral transplantation involving the intestines, liver and pancreas.

Intestines

Surgical corrections are common in Crohn's disease, diverticulitis, or intestinal failure.

- bowel resection and anastomosis – removal of the diseased segments and reconnection
- stoma creation – diverts waste into an external bag when anastomosis isn't possible
- stricturoplasty – widens strictures (narrowed sections of bowel) to improve movement

Multivisceral transplants may be offered for conditions like short bowel syndrome or

Kidney

Corrective surgery on kidneys can be used to address obstructions, tumours and calcifications.

Main problem	Caused by	Surgical correction
Obstruction	Narrowing of collecting ducts or ureter	Ureteroplasty: reconstruction
Tumour	Malignant growth	Nephrectomy: partial or total
Kidney stones	Crystallisation of salts	Lithotripsy: ultrasound to fragment stones Surgical removal

Table F2.9. Surgical interventions for kidney issues.

Kidney transplantation is the most common solid organ transplant and can be performed using donor tissue, as function can be maintained with only one kidney.

Bone and spine

Orthopaedic surgery addresses fractures, joint degeneration, spinal deformities and

Main problem	Caused by	Surgical intervention
Fractures	Trauma, osteoporosis	Internal fixation with plates and rods
Joint damage	Cartilage erosion, injury	Joint replacement
Deformity	Abnormal growth, congenital defect, e.g. scoliosis, spondylitis	Spinal rods, osteotomy (cutting and reshaping), retractor systems
Spinal instability	Prolapsed disc, vertebral collapse	Spinal fusion to stabilise

Table F2.10. Surgical interventions for bone and spine issues.

Bone grafts (not whole bones or joints) may be harvested from the patient's femur or iliac crest, especially in the case of fusion and reconstructive surgeries.

Apply your knowledge

1. Outline the main surgical interventions available for treating diseases of the heart, lungs, intestines, kidneys, and spine.
2. Describe when a transplant might be preferred over corrective surgery.
3. Explain how bone grafts contribute to the healing process in reconstructive and spinal surgery.

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Organ rejection

Organ rejection occurs when the recipient's immune system recognises the transplanted organ as foreign and initiates an immune response to eliminate it. This response is triggered by differences in antigens of the host and transplanted tissues. These markers are genetically unique to each individual. The immune system uses these molecular identifiers to distinguish between self and foreign cells.

Transplanted tissues carry foreign antigens, even if donor and recipient are the same. The presence of T lymphocytes which destroy the cells, triggers antibody production, and ultimately leads to organ and tissue damage. To prevent rejection, patients are given immunosuppressant drugs to reduce immune activity and maintain the function of the transplanted organ.

In graft versus host disease (GvHD), donor immune cells are transplanted with the organ. The donor immune cells recognise the recipient's cells as foreign and attack them. This is most common in bone marrow transplants, because this tissue contains haematopoietic stem cells that produce lymphocytes. However, it can also affect skin, liver and gastrointestinal tract grafts. GvHD can lead to complications including sepsis and multi-organ failure if not managed effectively.

Recall questions

1. Compare and contrast organ rejection with graft versus host disease.
2. Explain how organ rejection and GvHD involve the immune system.

Artificial organs

Artificial organs are man-made and replicate the function of biological tissues. They can be made from metals or biologically derived materials such as animal tissue, or may be lab grown. Artificial organs are increasingly used in surgery, including joint replacements and prosthetics. While cell-derived organs show potential, they are still largely used within research and development.

Deciding between donor and artificial organs involves multiple considerations, including ethical concerns, longevity of use, and resource availability and accessibility.

	Donor organs	Artificial organs
Advantages	<ul style="list-style-type: none"> • High biological functionality • Integration with body systems 	<ul style="list-style-type: none"> • Longer average lifespan: ~15 years • No need for immunosuppression
Disadvantages	<ul style="list-style-type: none"> • Limited availability • Organ rejection or failure without lifelong immunosuppression • Average lifespan ~5-10 years 	<ul style="list-style-type: none"> • Reduced or specialised functionality • Limited to certain types and replacement frequency • High development costs

Table F2.11. Surgical interventions for bone and spine issues

Decisions around organ replacement involve many considerations:

- Ethical issues – including consent, allocation priority and fairness.
- Moral dilemmas – such as animal-derived vs man-made materials, and allocation of resources.
- Medical risks – for example, surgical complications, organ failure, immune rejection.
- Financial costs – including long-term care, cost of research and development.

Artificial organs may reduce waiting lists and avoid immune rejection but may not be as effective as whole organ replacement is essential for fully functioning, complex systems such as the heart and lungs.

Recall questions

1. Describe the key differences between donor organs and artificial organs.
2. Outline the factors considered when deciding between a donor organ and the use of an artificial organ.



Practice questions: Use of tissues in research and development

- 1 Explain the limitations of creating a heart organoid that could be used for research.

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2.2. Systems in the human body

2.2.1. Organ systems

We have examined how specialised tissues work together as an organ for a specific purpose. In this section, we will review further by identifying that a collection of different organs working together form an organ system. For example, the circulatory system has many different tissues and organs working together. The blood vessels and the heart are organs within this system.

The eleven different organ systems present within the human body are:

1. Urinary or excretory system
2. Digestive system
3. Respiratory system
4. Immune system
5. Nervous system
6. Circulatory system
7. Musculoskeletal system
8. Endocrine system
9. Reproductive system
10. **Integumentary system** (hair, skin and nails)
11. Lymph system

Remember the eleven human organ systems with the mnemonic U D R

Recall questions

1. Describe how an organ differs from an organ system.

2.2.2. System structure and function

There are eleven different organ systems within the human body. This chapter will explore the structure and function of these systems and consider their components, structures and adaptations.

Blood circulatory system

The circulatory system is a critical support system that moves blood throughout the body. It is essential for survival. It includes the following organs:

- heart
- blood
- blood vessels

Blood carries many substances either dissolved or suspended in plasma, including:

- oxygen – delivered to all cells for aerobic respiration
- nutrients – including glucose, amino acids, vitamins and minerals, necessary for cell growth and repair
- waste products – including carbon dioxide and urea for excretion
- immune system components – antibodies and lymphocytes that provide defence against pathogens
- hormones – regulating homeostatic mechanisms and coordinating responses

Blood also plays an important role in thermal regulation, i.e. distributing heat evenly throughout the body, maintaining a stable internal temperature.

The circulatory system works closely with other body systems to supply essential substances to cells, remove metabolic waste for processing and disposal, and transmitting chemical messages.

Chemical communication through the circulatory system complements the nervous system. Chemical signals to enable effective communication and coordination across the body.

Recall questions

1. List the organs in the blood circulatory system.
2. Explain why the blood circulatory system interacts with all other body systems.

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Lymphatic system

The lymphatic system acts as a secondary drainage system and immune network, complementing the circulatory system by returning excess tissue fluid to the bloodstream and defending against infection.

Tissue fluid that does not re-enter capillaries drains into lymphatic capillaries – blind-ended tubes that form a network throughout body tissue. The fluid, now called lymph, flows through a series of larger vessels by compression caused by skeletal muscle contraction. As with blood vessels, lymph vessels have valves that ensure unidirectional flow and prevent backflow. Lymph is eventually returned to the bloodstream via veins located under the clavicle (collar bone).

Lymph is similar to blood plasma, except it has higher levels of fatty acids and lower concentrations of nutrients and oxygen. It is enriched with lymphocytes, which collect at the lymph nodes and detect pathogens. At the lymph nodes, bacteria are phagocytosed by macrophages, and B lymphocytes produce antibodies that are passed into the bloodstream. During an infection, the lymph nodes often become swollen because of increased immune cell activity. This is why doctors palpate (examine by touch) lymph node sites, such as in the armpits, groin or neck.

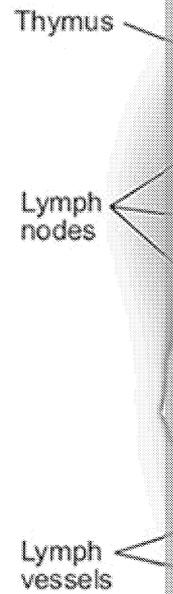


Figure F2.27. The network of vessels

Comparing the lymphatic and circulatory systems

The lymphatic and circulatory systems have notable structural and functional differences.

	Lymphatic system	Circulatory system
Type of system	Open-ended: lymph drains from the tissues	Closed
Vessels	Lymph capillaries, vessels and ducts	Arteries and veins
Movement caused by	Muscle contraction	Heart
Organs involved	Lymph nodes, spleen, thymus, tonsils	Heart, lungs
Transports	Lymph: tissue fluid with lymphocytes and fatty acids	Blood: oxygen, nutrients
Waste removal	Removes cell debris, bacteria and toxins	Removes carbon dioxide from the lungs and waste from the body
Immune role	Filters pathogens via the lymph nodes	Transport and antibodies

Table F2.28. Comparison of the lymphatic and circulatory systems

In conclusion, the circulatory system delivers nutrients and removes waste to maintain homeostasis. In contrast, the lymph drains excess tissue fluid, monitors the immune system, and returns fluid to the bloodstream. Together, they maintain fluid balance and operate as a

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Recall questions

1. Outline the key differences between the blood circulatory system and the lymphatic system.
2. Explain why the lymphatic system is not a circulatory system.

Musculoskeletal system

The musculoskeletal system includes bones, skeletal muscles, and the connective tissue and tendons, that support, stabilise and coordinate movement. Ligaments are tough bone, providing joint stability. Tendons are fibrous cords that attach muscle to bone, muscles contract.

The musculoskeletal system has three key roles:

1. Movement and coordination: achieved by muscle contraction acting on the skeleton
2. Posture and balance control: using receptors in the joints that detect change in position
3. Protection of internal organs: the skull protects the brain; the ribcage protects the heart and lungs; the pelvis protects the reproductive organs and the lower GI tract.

Other roles of bones

Bone tissue provides a major calcium reservoir. This is essential for the structural integrity of the skeleton and the activation of muscles at the neuromuscular junction.

Long bones, such as the femur, have a spongy inner matrix called bone marrow which is the site of production of some stem cells and the storage of fat (see Bone tissue, page 58).

Other roles of muscles

Muscles are important for blood glucose homeostasis: they provide a substantial store of glycogen. They provide useful reservoirs of amino acids, which can be mobilised during fasting and immune support. They are also significant in thermoregulation: shivering generates heat through muscle contraction, which is essential when body temperature has dropped due to exposure to cold.

Recall questions

1. Outline the role of bones and muscles within the musculoskeletal system.
2. Explain why bones, muscles and bones are required to enable movement.

The homeostatic system refers to a collection of linked biological processes that work together to maintain the internal environment despite external fluctuations: homeostasis. This is essential for life and is required for cell function, enzyme activity and overall survival.

Key processes involved in homeostasis include:

- thermoregulation – regulates body temperature
- blood glucose regulation – maintains blood glucose concentration
- osmoregulation – controls water balance and solute concentration

Role of the hypothalamus

Homeostatic processes are coordinated by the hypothalamus, a specialised region in the brain that acts as a regulatory hub, constantly monitoring the composition of blood flowing through it and initiating changes away from normal levels.

The hypothalamus detects changes in a wide range of conditions, including:

- blood water potential (osmolarity)
- core body temperature
- salt (electrolyte) concentration
- blood pressure
- blood oxygen and carbon dioxide levels

Responses are communicated via neuronal pathways for rapid changes, and hormonal pathways for longer-lasting effects.

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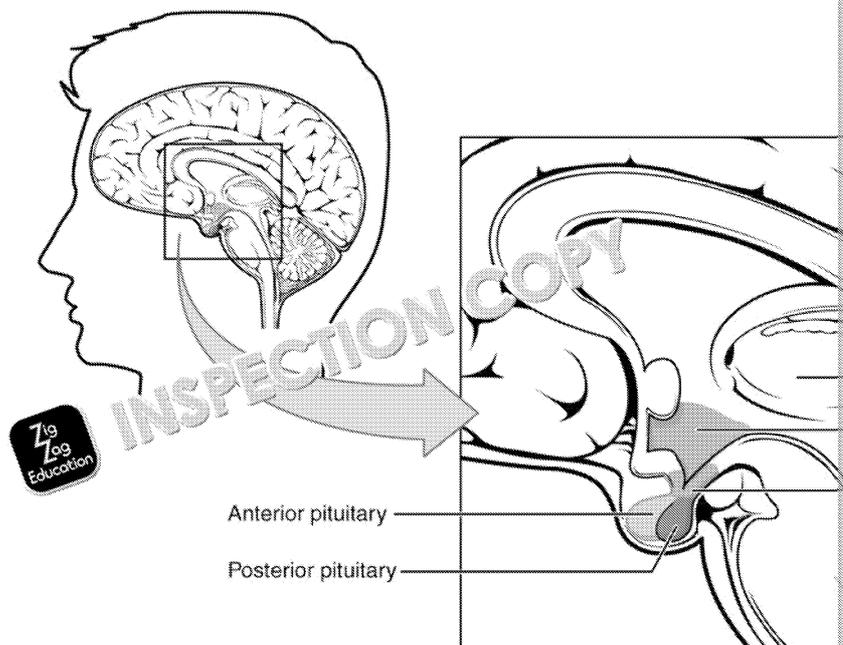


Figure F2.28. The hypothalamus is nestled alongside the pituitary.

Recall questions

1. Outline the location and roles of the hypothalamus.
2. Briefly describe how the hypothalamus causes change in response to changes in internal conditions.

Gastrointestinal system

The gastrointestinal (GI) system, also known as the digestive tract, is a continuous tube through our body. It facilitates ingestion, mechanical and chemical digestion, nutrient absorption, and elimination and water reabsorption. These processes are vital for ATP production.

The GI system includes the following major regions, in order that food passes through:

1. Buccal cavity (mouth).
Site of ingestion and initial mechanical digestion through mastication (chewing). Salivary enzymes (e.g. amylase) begin carbohydrate breakdown.
2. Oesophagus.
Muscular tube that moves food to the stomach via peristalsis.
3. Stomach.
Secretes gastric juices that contain hydrochloric acid and pepsin for protein digestion.
4. Small intestine.
Includes the duodenum and ileum.
Primary site for chemical digestion and nutrient absorption.
Receives enzymes from the pancreas and bile from the gallbladder to aid digestion.
5. Large intestine.
 - Colon. Reabsorbs water and electrolytes. Compacts undigested material into faeces. Supports gut microflora, some involved in vitamin synthesis and production.
 - Rectum and anus. Store and expels waste during defecation.

The GI system includes other organs which are not part of the digestive tract, including the gallbladder (which stores bile ready for secretion), and the pancreas.

Recall questions

1. List the organs and organ systems linked directly to the GI system.
2. Outline the role of the digestive organs in digestion.

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Excretory system

The excretory system removes metabolic waste products from the body to maintain and prevent the accumulation of harmful substances. There are two organ systems in kidneys and the skin.

Renal excretion

The kidneys are the primary excretory organs. They filter blood to remove metabolic substances in excess, including:

- Urea – nitrogenous waste product derived from amino acid deamination (decomposition). Urea is formed in the liver and enters the ornithine cycle.
- Excess salts and ions – including sodium, potassium and calcium.
- Water – removing excess blood volume and pressure.
- Toxins and drugs – metabolised by the liver.

Urea combines with water to form urine, which passes through ureters for storage in the bladder for eventual elimination via the urethra.

Cutaneous excretion

The skin also contributes to excretion via the production of sweat from glands in the skin. Sweat contains water, salts, especially sodium and chloride ions, urea and uric acid, present in lower concentrations than in blood.

Sweating is therefore involved in excretion but also forms an important part of thermoregulation. The evaporation of sweat removes heat thus cooling the surface of the skin and enabling the body to maintain its internal body temperature.

Apply your knowledge

1. Describe the similarities and differences between renal and cutaneous excretion.
2. Explain why cutaneous excretion is important.

Respiratory system

The respiratory system, also known as the gaseous exchange system, carries out inspiration (inhalation) and expiration (exhalation) of air, enabling uptake of oxygen from the atmosphere, and removal of carbon dioxide from the bloodstream. It consists of a series of specialised structures that support and optimise gaseous exchange.

The system comprises:

- Trachea.
A single, hollow tube, reinforced with C-shaped cartilage rings that keep the airway open. It moves air from the mouth and nasal cavity toward the lungs.
- Bronchi.
The trachea divides into left and right primary bronchi (singular: bronchus), each of which then branches again into secondary and tertiary bronchi, feeding air deep into the lungs.
- Bronchioles.
Many fine, progressively narrowing branches of the bronchi that lead to the alveoli. They control airflow to the alveoli and improve the efficiency of gaseous exchange by increasing the surface area available for ventilation.
- Alveoli.
Tiny air sacs surrounded by capillaries, where gaseous exchange occurs. Oxygen diffuses into the blood; carbon dioxide diffuses out.
- Lungs.
Composed of bronchioles, alveoli and connective tissue.

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- Ribcage.
Skeletal framework that protects the lungs and provides a structure for breathing.
- Intercostal muscles.
Located between the ribs.
The external intercostal muscles contract to lift ribs up and out during inspiration.
The internal intercostal muscles contract to draw ribs down and in during expiration.
- Diaphragm.
A large, dome-shaped skeletal muscle beneath the lungs.
Contracts and flattens during inspiration – increases chest volume and decreases pressure.
Relaxes and returns to dome shape during exhalation – reduces chest volume and increases pressure.

Your



1. List the parts of the respiratory system that air does not pass through and which parts are essential to the functioning of the system.



Practice questions: System structure and function

- 1 Identify two organ systems involved in the involuntary response of shivering.

2.2.3. Measuring system activity

Comparing a patient’s organ system function against established reference ranges can help identify abnormalities, concerns and guide further medical investigation and treatments. To support this, various diagnostic technologies have been developed to accurately monitor organ system activity.

This chapter explores several common clinical medical devices and techniques, the conditions they investigate, how data is collected and interpreted, and the benefits of using this technology in clinical practice.

Sphygmomanometer



A sphygmomanometer is a clinical device used to measure arterial blood pressure, usually at the brachial artery in the upper arm. It is used to diagnose and monitor **hypertension**, **hypotension**, and other conditions where blood pressure regulation is disrupted, such as sepsis, heart failure or renal disease.

hypertension – high blood pressure.
hypotension – low blood pressure.

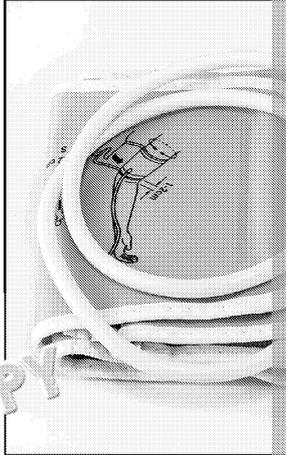


Figure F2.29.

Sphygmomanometers may be manual or digital, and typically consist of the following pieces of equipment, which may be separate or combined.

- Inflatable cuff – fitted around the upper arm to temporarily restrict blood flow.
- Pressure gauge – measures the pressure inside the cuff.
- Bulb and valve (manual models) – used to manually inflate and deflate the cuff.
- Pump (digital models) – electronic device which automatically inflates and deflates the cuff.
- Stethoscope (manual use) – positioned over the brachial arterial to hear blood flow sounds, which indicate systolic and diastolic pressure.

There are several types of sphygmomanometer, including mercury, aneroid and digital.

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Method of use

To use a manual sphygmomanometer:

1. Fit the cuff securely around the patient's upper arm.
2. Position the stethoscope over the brachial pulse and listen for the Korotkoff sounds.
3. Inflate the cuff until no Korotkoff sounds are heard – the artery is fully **occluded**.
4. Slowly release the pressure until the first Korotkoff sound is heard – this is systolic pressure.
5. Continue releasing the pressure until the sound disappears – this is diastolic pressure.

Korotkoff sounds are caused by turbulent blood flow through the brachial artery, as the cuff pressure reduces, altering the degree of arterial occlusion. The sounds occur in five distinct phases:

- Phase I, the first tapping sound, indicates systolic pressure when blood begins to compress.
- Phase V, when all sounds disappear, indicates diastolic pressure when blood flow is fully restored.

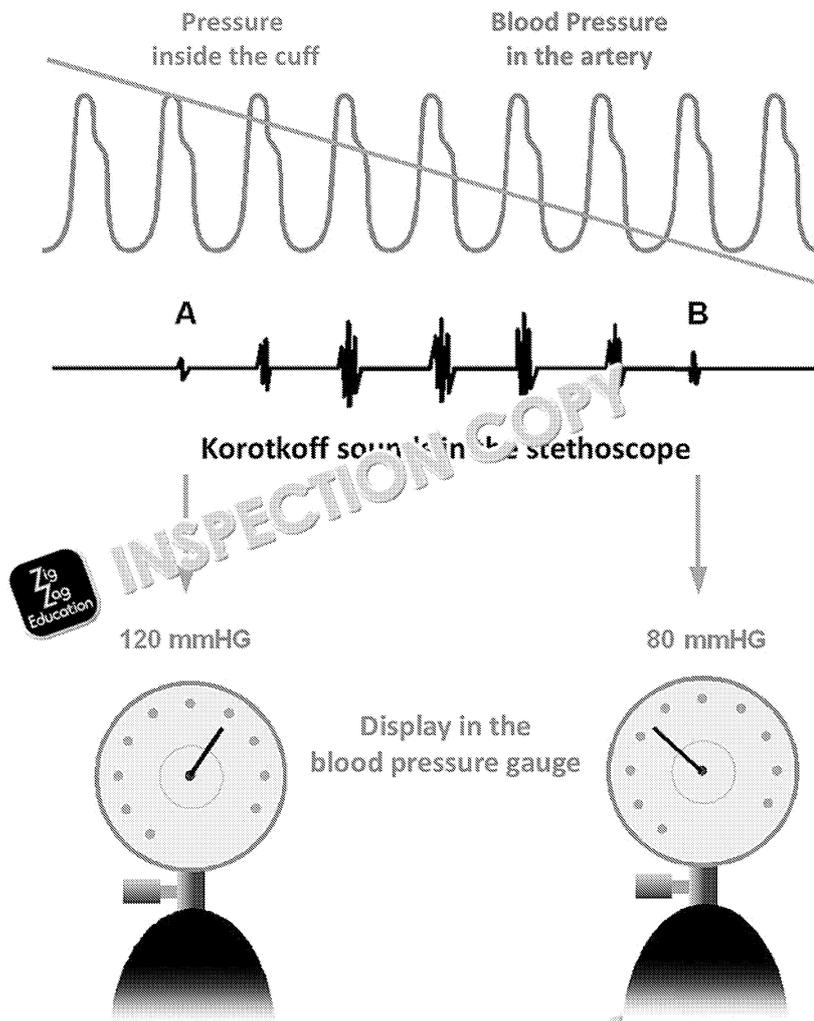


Figure F2.30. Korotkoff sounds relate to the pressure in the cuff and blood pressure in the artery.

Blood pressure is recorded as:

systolic pressure
diastolic pressure

Average blood pressure for a healthy adult is < 120/80 mmHg. Hypertension is considered when pressures are over 130/80 mmHg, and hypotension is diagnosed with pressures < 90/60 mmHg. These values vary depending on baseline measurements.

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Benefits and limitations of the sphygmomanometer

Manual and digital sphygmomanometers accurately measure arterial blood pressure. It provides important information to clinicians on the general health of patients to inform diagnoses and treatment or management plans.

Type	Description	Advantages	Limitations
Mercury 	Column of mercury and scale to read pressure	<ul style="list-style-type: none"> • Very accurate • Portable • Reliable • Can be used on most patients 	<ul style="list-style-type: none"> • Costly • Can be difficult to read • May be hazardous • Requires observer • Requires training
Aneroid	Mechanical dial with metal spring	<ul style="list-style-type: none"> • Portable • Safe as mercury-free • Can be used on most patients 	<ul style="list-style-type: none"> • Requires training • Less accurate • Mechanical parts may wear • May require calibration • Requires observer • Requires training
Digital (oscillometer)	Uses sensors and algorithms	<ul style="list-style-type: none"> • Safe as mercury-free • Portable • Good reliability • Can be used on most patients 	<ul style="list-style-type: none"> • May be costly • Requires observer • Requires training
Automated spot-check device 	Uses sensors and algorithms	<ul style="list-style-type: none"> • Safe as mercury-free • Light weight • Compact • Portable • Easy to use • No observer bias 	<ul style="list-style-type: none"> • May be costly • Requires observer
Wrist device	Uses sensors and algorithms	<ul style="list-style-type: none"> • As with spot-check device, but increased patient comfort 	<ul style="list-style-type: none"> • As with spot-check device • Requires training • Reliability may be lower • Less accurate • Requires observer • Requires training
Finger device	Uses sensors and algorithms	<ul style="list-style-type: none"> • As wrist device 	<ul style="list-style-type: none"> • As with spot-check device • May be costly • Requires observer • Requires training

Table F2.13. Advantages and limitations of various types of sphygmomanometers.

Blood pressure varies naturally throughout the day, and may rise temporarily due to emotional stress (including stress of being medically examined), or environmental factors such as loud noises and temperature extremes. These variations must be considered when drawing clinical conclusions.

Apply your knowledge

1. Compare and contrast the aneroid and digital sphygmomanometers and state when each is most appropriate.
2. Describe how phase I and phase V Korotkoff sounds relate to blood and cuff pressure.

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Radial pulse readings

Pulse points are locations where an artery lies close to the skin and it is possible to feel the contraction and relaxation of muscles in arterial walls due to pressure changes in the cardiac cycle (the pulse at the wrist) is most commonly assessed in routine practice.

Clinical importance

Monitoring pulse rate gives an indication of cardiac function and shows physiological responses to exertion, stress, cardiac interventions like pacemaker use, and whether arrhythmias are present.

The pulse can be characterised by:

- rate – beats per minute
- rhythm – regular or irregular
- strength – normal, weak, bounding
- equality – compare left and right pulses

How to take a reading

To take the radial pulse:

1. Ensure the patient is seated and relaxed.
2. Position the index and middle fingers lightly over the radial artery, located on the wrist, just below the thumb side of wrist crease.
3. Count the number of pulses felt over 60 seconds (or 30 seconds \times 2 if rhythm is regular).

Never use the thumb – it has its own pulse and will interfere with measurements.

The normal pulse range for adults is 60–100 bpm. This is higher in children and decreases with age. Bradycardia describes heart rates $<$ 60 bpm, whereas tachycardia is seen in pulses $>$ 100 bpm.

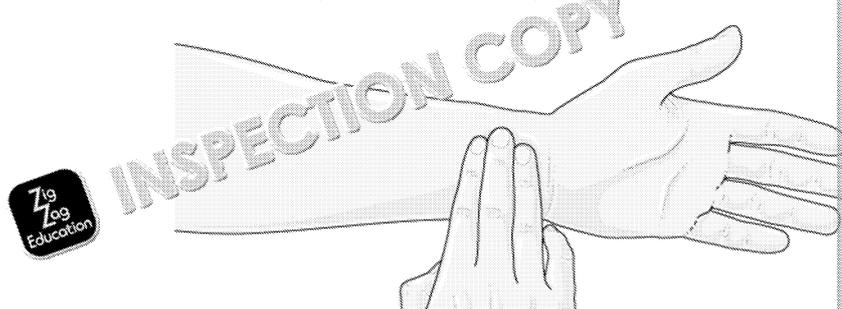


Figure F2.31. Taking a radial pulse.

Benefits and limitations of taking the radial pulse

Taking a pulse provides a good indication of cardiac health. As with all techniques, there are benefits and limitations to the procedure.

Benefits	Limitations
<ul style="list-style-type: none"> • Non-invasive, quick. • Useful for assessing general heart health. • Minimal equipment required (stopwatch). • Easily repeated to monitor trends. 	<ul style="list-style-type: none"> • May be difficult to locate in some individuals. • Pulse rate can be elevated by anxiety or pain. • Radial pulse is weaker than carotid pulse. • Does not reveal arrhythmias.

Table F2.14. Advantages and limitations of taking the radial pulse.

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Your task

1. Describe the four characteristics of a pulse, and the way a pulse would be recorded in a conscious patient, an infant, and a collapsed patient.
2. Outline the limitations of taking a radial pulse reading.
3. Record your or your peer's pulse rate, noting the key characteristics.

Electrocardiogram (ECG) readings

An electrocardiogram (ECG) is a diagnostic tool that measures electrical activity of the heart over time. It is used to detect cardiac abnormalities, including:

- arrhythmias – irregular heart rhythms
- **myocardial infarction** (heart attack) – heart muscle damage from ischaemia (restricted blood flow to heart muscle)
- fibrillation – rapid, irregular, and uncoordinated contraction of muscle fibres
- other cardiac conditions, including conduction defects, electrolyte imbalances, and chamber enlargement

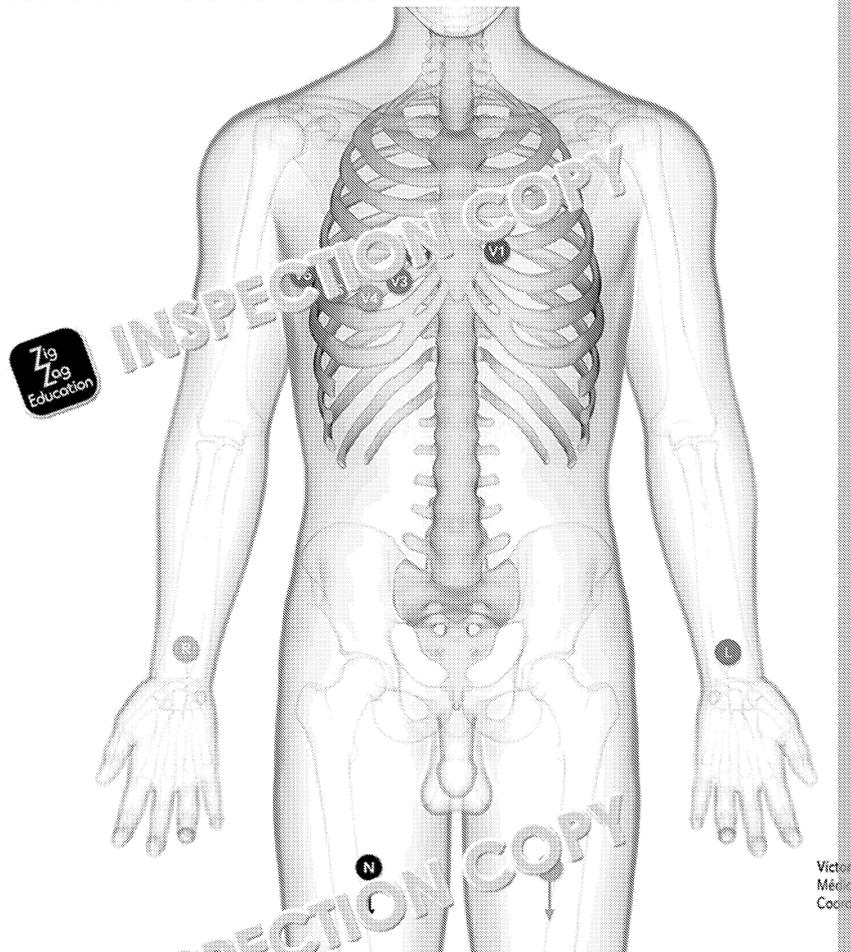
During the heart's normal rhythm, changes in electrical impulses are detected by the ECG machine. Electrodes are attached to the skin.



Taking an ECG

To take an ECG:

1. Prepare the patient:
 - a. Lie them flat on the bed, arms by their side and legs uncrossed.
 - b. Remove jewellery and ensure skin is clean and dry.
 - c. Expose the chest and limbs.
 - d. Clean the skin where electrodes will be placed (shave chest hair for better contact).
2. Place the four limb and six chest electrodes.



Victor
Médica
Coop

Figure 2.32. The 10 electrodes should be placed on specific parts of the body.

3. Record the trace:
 - a. Connect leads to ECG machine and ensure good contact.
 - b. Instruct the patient to lie still and breathe normally.
 - c. Start recording – check trace for clarity, and adjust calibration if required.
 - d. Print or save trace.



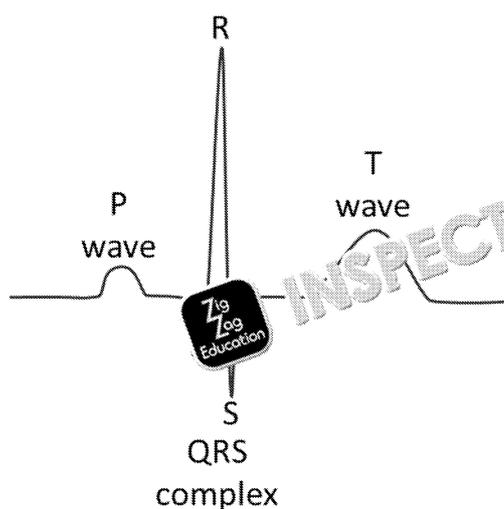
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Interpreting the trace

Typical ECG readings present as follow:



The trace is made up of the following:

- P wave – atrial depolarisation
- PR interval – conduction time
- QRS complex – ventricular depolarisation
- ST segment – ventricular repolarisation
- T wave – ventricular repolarisation

Figure F2.33. Typical ECG trace.

Changes in the shape of the trace indicate cardiac abnormalities. For instance, a widened QRS complex, absent P waves or erratic rhythms may suggest **fibrillation**, **tachycardia** or **bradycardia**, **ischemia** or **infarction**. The ST segment should be flat, and depression may indicate ischemia, while elevation may indicate infarction (damage across the full thickness of the heart wall).

Benefits and limitations of an ECG

As with all medical procedures, there are benefits and limitations.

Benefits	Limitations
<ul style="list-style-type: none"> • Rapid, non-invasive and inexpensive. • Provides view of electrical activity in real time. • Assists in diagnosis and monitoring. 	<ul style="list-style-type: none"> • Requires specialist equipment. • Requires training in interpretation. • May not detect all structural changes. • Can be affected by stress, anxiety, or poor contact.

Table F2.15. Benefits and limitations of an ECG.

Your turn

1. Draw and label the typical, healthy ECG trace and what each part indicates.
2. Describe the uses of an ECG and outline the procedure involved in taking an ECG.
3. Explain how prolonged ischemia could progress to infarction.

Ultrasound scans

Ultrasound is a non-invasive imaging technique that uses high-frequency sound waves to create images of internal body structures. It is most often used to monitor foetal development but can also be used to:

- detect fluid-filled cysts or solid masses in breast tissue
- assess structures in the neck, such as the thyroid or lymph nodes
- visualise abdominal organs, including the liver, gallbladder and GI tract

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How ultrasound works

The machine emits sound waves from a hand-held **transducer**, which are directed into the body. These waves reflect off tissues based on their density and **acoustic properties**. Soft tissues, bone and fluids all reflect sound waves differently. The pattern of reflected waves is translated into a diagnostic image on the screen.

Ultrasound does not use ionising radiation, so it is safer than X-rays or CT scans, especially when used during pregnancy or for paediatric care.

How to perform an ultrasound scan

To take a basic ultrasound scan:

1. Prepare the patient:
 - a. Position the patient to best view the part of the body to be scanned.
 - b. Apply a water-based gel to the target area to enhance sound transmission to the skin.
2. Conduct the scan:
 - a. Place the transducer against the skin, using firm, steady pressure.
 - b. Move the transducer methodically to capture various views.
 - c. Use the machine to take screenshots or videos. The device can also print images.
3. Clean up:
 - a. Remove gel from patient's skin and transducer.
 - b. Print or save images.

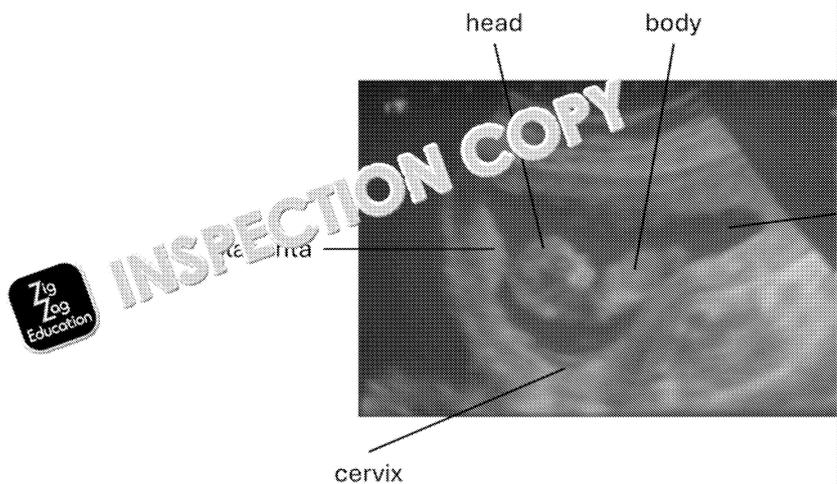


Figure F2.34. An ultrasound of a 20-week foetus, clearly showing head, body and cervix.

Benefits and limitations of ultrasound

Ultrasound offers a non-intrusive, inexpensive and quick imaging method.

Benefits	Limitations
<ul style="list-style-type: none"> • Safe – no radiation – suitable for foetal and paediatric imaging. • Real-time images. • Inexpensive, quick and easy to use. • Useful in initial pregnancy assessment. 	<ul style="list-style-type: none"> • Image clarity can vary. • Image quality depends on accuracy of transducer. • Training required to operate. • May require other imaging for more detail.

Table F2.16. Benefits and limitations of ultrasound.

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Recall questions

1. Describe how ultrasound works and the benefits this offers to patients such as pregnant women.
2. Explain why a gel is applied to the skin before scanning.

Colonoscopy

Colonoscopy is a diagnostic procedure used to examine the inner lining of the large intestine by inserting a long, flexible instrument called a colonoscope, with a camera and light at the end, into the rectum and through the colon.

It is a useful medical procedure, used to investigate the cause of symptoms such as changes in bowel habit and unexplained weight loss; screen for and monitor conditions such as polyps and inflammatory bowel diseases (IBDs); and remove polyps and take biopsies.

Taking a colonoscopy

Colonoscopy is an invasive procedure that can cause discomfort and requires careful preparation in advance to ensure the visibility of the colon wall.

For a successful colonoscopy:

1. Prepare the patient.
 - a. A low-fibre diet must be followed for 2–3 days before the procedure.
 - b. A strong laxative is taken the day before to clear the colon of faecal matter.
 - c. On the day, the patient fasts and may only consume clear fluids.
2. Perform the colonoscopy.
 - a. The patient lies on their left side with knees tucked up into a curled position.
 - b. A sedative or gas and air is administered to sedate the patient.
 - c. The colonoscope is inserted via the anus.
 - d. Carbon dioxide gas is used to inflate the colon to improve visibility.
 - e. Examination of the colon and the collection of biopsies and removal of polyps.

The procedure usually leaves the patient feeling bloated and uncomfortable, due to the inflation of the colon. It can cause bleeding, especially after biopsy or polyp removal, and these can, on rare occasions, require surgical repair.

Benefits and limitations of colonoscopy

This invasive and substantial procedure has several benefits and limitations.

Benefits	Limitations
<ul style="list-style-type: none">• Detailed examination of colon wall.• Enables biopsy and polyp removal.• Crucial for cancer screening and monitoring.	<ul style="list-style-type: none">• Requires specialist facilities.• Invasive, uncomfortable and time-consuming.• Requires substantial patient preparation and procedure recovery.

Table F2.17. Benefits and limitations of colonoscopy.

Apply your knowledge

1. Describe the preparations the patient must do in advance of a colonoscopy to ensure the procedure is successful. Explain why these are important.
2. Describe some of the risks and issues with a colonoscopy and why these might arise.

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Urinalysis

Urinalysis refers to the analysis of urine's chemical composition, physical appearance and contents. Because urine reflects many systemic changes – especially those affecting kidney function – urinalysis serves as a valuable tool for assessing general health and

Tests within urinalysis

Urine can be analysed:

- visually – to check colour, clarity and odour for immediate indicators
- chemically – to detect substances such as glucose, proteins and ketones
- microscopically – to identify cells, crystals, casts and microorganisms under a microscope

Visual analysis

Visual inspection of urine can reveal signs of disease:

- colour – pale yellow to amber is normal; red or brown indicates blood or infection
- clarity – clear is normal; cloudy suggests infection or high protein content
- odour – sweet smell signals diabetes; foul odour indicates urinary tract infection (UTI); other unusual smells may offer diagnostic indicators

Chemical analysis

A chemical dipstick test uses reagent strips that change colour when exposed to various substances, like litmus paper changes colour to indicate pH. Based on visual inspection of the urine sample, plus the patient history, clinicians select dipsticks to test for

Test	Normal	Indicative
pH	Typically, pH 6.0, but within range of pH 4.5–8.0	Acidic: pH < 4.5 <ul style="list-style-type: none"> infection metabolic imbalance
Protein	Negative/trace (≤ 30 mg/dL)	Persistent elevation: > 30 mg/dL <ul style="list-style-type: none"> chronic kidney disease diabetes hypertension-related damage
Glucose	Negative/trace (≤ 15 mg/dL)	> 15 mg/dL: <ul style="list-style-type: none"> diabetes mellitus
Ketones	Negative	> 20 mg/dL: may indicate: <ul style="list-style-type: none"> diabetic ketoacidosis alcohol-related ketoacidosis prolonged vomiting/illness starvation or malnutrition
Blood	0–3 cells per high power field (HPF)	> 3–4 cells per HPF may indicate: <ul style="list-style-type: none"> infection kidney stones trauma (including sexual activity) medications (e.g. aspirin, antibiotics, blood thinners) chronic conditions (polycystic kidney disease, sickle cell disease, haemophilia, bladder/kidney cancer, enlarged prostate)

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Test	Normal	Indicative	Notes
Leucocyte esterase and nitrites	Both absent: no likely infection	Both present: <ul style="list-style-type: none"> likely bacterial urinary tract infection (UTI) Leucocytes present, nitrites absent: <ul style="list-style-type: none"> inflammation without bacteria Leucocytes absent, nitrites present: <ul style="list-style-type: none"> early infection or immune suppression 	Leucocyte esterase – enzyme released by inflammatory cells Nitrites – especially (see page 110) into nitrite
Bilirubin and urobilinogen	Bilirubin: negative Urobilinogen: 0.1–1.8 mg/dL	Bilirubin present: <ul style="list-style-type: none"> liver disease obstructive jaundice (e.g. gallstones) impaired bile flow (bile or leaks into bloodstream) Urobilinogen low/absent: <ul style="list-style-type: none"> bowel obstruction antibiotic use liver failure Urobilinogen high: <ul style="list-style-type: none"> liver disease (e.g. hepatitis) haemolytic anaemia 	Bilirubin is released by erythrocytes, processed in the liver and excreted in bile Urobilinogen is formed when intestinal bacteria convert bilirubin to urobilinogen, which is reabsorbed in the gut and excreted in urine.

Table F2.18. Details of various dipstick tests.

Microscopic examination

Microscopic analysis after differential centrifugation reveals particles not visible to the naked eye. Key findings include:

- cells:
 - erythrocytes (> 4 cells/HPF) – requires further investigation
 - leucocytes – indicates infection or inflammation
 - epithelial cells – normal: 0–5 cells/HPF; if > 5 cells/HPF:
 - squamous – from outer urethra or genital area; usually due to sample contamination
 - transitional – from bladder, ureters or renal pelvis; indicates bladder irritation
 - renal tubular – from kidney tubules; signals kidney damage or disease
- microorganisms – bacteria, yeast and parasites – requires further investigation to confirm; suggest appropriate treatment
- structures – requires further investigation:
 - casts – proteinaceous structures from kidney tubules
 - crystals – calcium oxalate kidney stones

Benefits and limitations of urinalysis

Urinalysis is a useful diagnostic tool that can aid diagnosis or suggest further areas for investigation.

Benefits	Limitations
<ul style="list-style-type: none"> Non-invasive and easy to perform. Rapid results in minutes for quick screening. Cost-effective: ideal for routine screening. Useful for chronic conditions monitoring. Enables home testing with dipsticks. 	<ul style="list-style-type: none"> Accuracy depends on timing and sample collection. May produce false positives/negatives due to contamination (e.g. from menstruation). Dipstick methods are qualitative not quantitative. Limited specificity: suggest further testing. Cannot diagnose all conditions; better for screening.

Table F2.19. Benefits and limitations of urinalysis.

Despite its limitations, urinalysis is an essential diagnostic tool because it is quick, accessible and supports clinical interpretation.

Apply your knowledge

- Summarise the different types of tests that can be conducted through urinalysis and include what each test is able to reveal about the patient.
- If a patient presents with signs of an infection or inflammation, which tests would confirm this?

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Blood glucose levels

Measuring blood glucose levels is essential for diagnosing and managing conditions such as diabetes, gestational diabetes (which occurs during pregnancy), and identifying developing prediabetes. A variety of tests can assess current levels, fluctuations, and long-term control of blood glucose.

Test	How it works	Use
Finger prick	Small sample of blood is taken from fingertip and analysed on a hand-held device (glucometer).	Monitoring blood glucose levels in diabetes.
Fast glucose	Venous or capillary sample after 8+ hours without food.	Diagnosis or monitoring of diabetes using glucose levels.
Oral glucose tolerance test (OGTT)	Fasting sample followed by glucose drink; blood tested at intervals over 2 hours.	Diagnosis of type 2 diabetes.
HbA1c test	Laboratory test of glycated haemoglobin (haemoglobin-bound glucose in erythrocytes) from venous blood. Provides average blood glucose over past 2–3 months, because of average lifespan of red blood cells (8–12 weeks).	Assessing and monitoring long-term blood glucose control (e.g. retirement, cardiovascular health).
Continuous glucose monitoring (CGM)	Wearable sensor tracks glucose levels in real time via interstitial (tissue) fluid.	Continuous monitoring of blood glucose levels to prevent hypoglycaemia. Especially useful for people with insulin-dependent diabetes to help prevent hypoglycaemia.

Table F2.20. Details of various blood glucose tests

Oral glucose tolerance test (OGTT)

The oral glucose tolerance test (OGTT) is used to assess how efficiently the body uses insulin. It is commonly used to detect gestational diabetes, type 2 diabetes and prediabetes.

Method

- Preparation.
Patient fasts for 8–12 hours before the test – only water is allowed.
Patient should avoid smoking and certain medications which may affect blood glucose levels.
- Baseline measurement.
A venous blood sample is taken to measure fasting blood glucose levels.
- Glucose challenge.
Patient drinks a solution containing 75 g glucose (100 g for pregnancy screening).
- Monitoring.
Blood samples are taken at 30-minute intervals over 2 hours.

Interpreting results

Elevated blood glucose levels may indicate:

- insulin resistance, where cells like hepatocytes, myocytes and adipocytes do not respond to insulin secreted by the pancreas
- glucose intolerance, the effect of insulin-resistant cells, indicated by high blood glucose levels

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Elevated glucose levels are classed as prediabetic – not high enough to be classified as diabetic but above normal levels. It is possible to have insulin-resistant cells but not be glucose intolerant as the body overcompensates by producing more insulin. However, glucose intolerance is almost always associated with a degree of insulin resistance.

It can also be used to diagnose gestational diabetes between 24 and 28 weeks of pregnancy. The results influence care decisions, including delivery method such as induction or Caesarean section.

Time point	Normal range	Prediabetic range
Fasting	< 5.6 mmol/L	6.1–6.9 mmol/L
2 hours	< 7.8 mmol/L	7.8–11.0 mmol/L

Table F2.21. Ranges of glucose levels in normal, prediabetic and diabetic patients when fasting.

Benefits and limitations of testing blood glucose levels

The different approaches to blood glucose monitoring and assessment offer varying degrees of convenience and accuracy.

Test	Benefits	Limitations
Finger prick glucometer	<ul style="list-style-type: none"> Quick, easy to use and inexpensive. Portable and widely available. Useful for spot checks and insulin dosing. 	<ul style="list-style-type: none"> Requires frequent testing. Only provides a single reading – no data trends. Accuracy depends on strip quality.
Lab-based tests (OGTT, HbA1c)	<ul style="list-style-type: none"> Provides long-term glucose control data. Useful for diagnosis and treatment planning. No sensor or in measurement. 	<ul style="list-style-type: none"> Not suitable for frequent testing. Requires venous blood and lab processing. Doesn't reflect real-time glucose levels.
Continuous glucose monitoring (CGM)	<ul style="list-style-type: none"> Real-time glucose tracking (> 288 readings per day). Trends and fluctuations detected – enables proactive management. Can alert for hypo/hyperglycaemia. Reduces need for finger prick tests. 	<ul style="list-style-type: none"> Expensive. May require calibration. Slight lag between interstitial and blood glucose levels (slightly delayed). May cause skin irritation. Not suitable for all patients.

Table F2.22. Benefits and limitations of testing blood glucose levels.

Recall questions

- Outline the procedure for an oral glucose tolerance test and when this might be necessary.
- Compare the finger prick and continuous monitoring tests and their use in managing diabetes.

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Thermometer

Core body temperature is one of the four vital signs – alongside pulse, breathing and blood pressure – and can be assessed using a thermometer to evaluate a patient's physiological status.

Accurate temperature monitoring is crucial for the early detection of illness, as it may indicate infection, inflammation or systemic disease. It also helps track treatment, assess the effectiveness of antibiotics, or ensure a patient's recovery after surgery or by infection.

Types of thermometer

There are several types of thermometer, used for different purposes and with different sites.

- Digital – used orally, rectally or axillary (under the arm); high accuracy.
- Infrared – used temporally (forehead) or tympanically (ear canal); provide with moderate to high accuracy depending on device positioning.
- Mercury – used orally, rectally or axillary; high accuracy but rarely used because of mercury.
- Gallium – used orally, rectally or axillary; high accuracy; alternative to mercury.
- Strip – used temporally; low accuracy as measures skin temperature only and changes colour with temperature.

Rectal digital or gallium thermometers offer the highest clinical accuracy, especially for infants. The infrared thermometer used temporally, or the tympanic thermometer offer moderate accuracy for measurements.

Methods of taking temperature

There are many sites from which the body temperature can be assessed.

Site	Recommended technique	Accuracy
Oral	Wait 30 minutes after eating/drinking. Place probe under tongue and keep mouth closed.	High ($\pm 0.1^\circ\text{C}$)
Rectal	Use a lubricant and gently insert probe into rectum.	Very high
Axillary	Ensure armpit skin is dry, and thermometer is in full contact. Hold arm in snugly against the body.	Moderate to high
Tympanic	Pull ear up and back to straighten the canal. Insert thermometer carefully, aiming towards the eardrum.	High if correctly positioned
Temporal	Sweep thermometer across the forehead and down the neck (if required by probe).	Moderate to high
Infrared	Hold 1–2 inches from the skin on forehead or wrist. Adjust to readings for oral equivalent.	Variable

Table F2.23. Details of the sites from which body temperature can be assessed.

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The normal range varies depending on site, and the threshold for determining a fever accordingly and considered in context with other clinical signs.

Site	Reference range (°C)	Fever threshold
Oral	36.4–37.5	≥ 37.6
Rectal	36.6–38.0	≥ 38.0
Axillary	34.9–37.3	≥ 37.4
Tympanic	36.1–38.0	≥ 38.0
Temporal	35.8–37.6	≥ 37.7

FIGURE 17.1 Normal temperature ranges at various sites for taking body temperature.



Benefits and limitations

The choice of thermometer and measurement site depends on how important accuracy is and the setting that it is being measured in. For example, infrared thermometers suit speed and convenience, while rectal digital devices offer superior accuracy for critical care. Tympanic thermometers are inexpensive, widely available and easy to use.

Apply your knowledge

1. Outline the advantages and disadvantages of digital, infrared and gallium thermometers and state which each thermometer might be used.
2. Compare and contrast rectal and oral methods of taking body temperature and state which would be most appropriate.

Spirometry

Spirometry is a diagnostic test used to assess lung function by measuring the volume of air that can be inhaled and exhaled. It plays a vital role in diagnosing and monitoring respiratory conditions such as chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis, as well as in monitoring disease progression, treatment effectiveness, and readiness for surgery or return to work.

Taking measurements

A spirometer records several key respiratory parameters:

- Tidal volume (TV)
 - Volume of air inhaled or exhaled during normal breathing.
- Forced vital capacity (FVC)
 - Total volume of air exhaled forcefully after full inhalation.
- Forced expiratory volume in 1 second (FEV₁)
 - Volume of air exhaled in the first second of forced breath.
- Peak expiratory flow rate (PEFR)
 - Maximum speed of exhalation.

Using these values, additional calculations can be made:

- FEV₁/FVC ratio
 - < 0.7 indicates airway obstruction, possibly obstructive lung disease.
- Pulmonary ventilation rate (PVR)
 - $PVR (L/min) = \text{breathing rate (breaths/min)} \times \text{tidal volume (L)}$



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To perform spirometry:

1. The patient sits upright and wears a nose clip.
2. They take a deep breath and exhale forcefully into a mouthpiece.
3. The test is repeated two to three times to ensure accuracy.
4. In some cases, a bronchodilator is administered, and spirometry is repeated to assess reversibility of airway obstruction.

Patient takes a deep breath and blows as hard as possible into tube

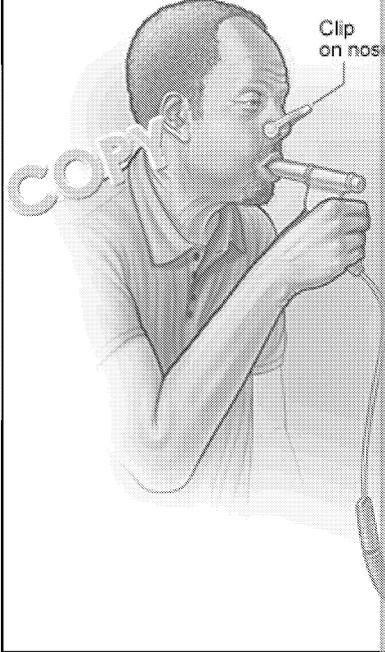


Figure F2.35. Taking measurements

Assessing Reversibility

Reversibility testing helps distinguish between different respiratory conditions by measuring lung function before and after administering a bronchodilator (medicine that dilates the bronchioles). If there is a significant improvement in airflow, and especially in the FEV₁ reading, it suggests that a reversible condition such as asthma is most likely. If there is no significant improvement, it may indicate a chronic non-reversible condition such as COPD,

Interpreting results

Spirometry results reveal two key patterns:

- Obstructive pattern (e.g. asthma or COPD)
 - Reduced FEV₁
 - Normal or reduced FVC
 - Reduced FEV₁/FVC ratio (< 0.7)
- Restrictive pattern (e.g. fibrosis or neuromuscular disease):
 - Reduced FEV₁ and FVC
 - Normal or increased FEV₁/FVC ratio

Benefits and limitations

When interpreted alongside symptoms and patient history, spirometry provides a valuable tool for diagnosing and monitoring respiratory health. However, it has some benefits and limitations.

Benefits	
<ul style="list-style-type: none"> • Quick, non-invasive and repeatable. • Identifies and monitors respiratory conditions. • Tracks disease progression and treatment response. • Supports pre-operative and workplace assessments. 	<ul style="list-style-type: none"> • Not suitable for all patients. • Requires patient cooperation and correct technique. • Unsuitable during acute respiratory infections. • May not detect intermittent asthma between attacks.

Figure F2.35. Benefits and limitations of spirometry

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Apply Your Knowledge

1. Calculate the pulmonary ventilation rate for a 10-year-old child with a suspected asthma attack. The breathing rate is 37 breaths per minute and tidal volume is 0.175 L.
2. Describe how an obstructive pattern differs from a restricted pattern, and what conditions can cause each.
3. Describe the differences between the forced exhalation volume in 1 second (FEV₁) and the forced vital capacity (FVC), and what the relationship between these two values can indicate.

Pulmonary ventilation rate changes

Pulmonary ventilation rate (PVR) represents the volume of air exchanged between the environment per minute. It provides a useful baseline for assessing lung function and responses to exercises, illness or training.

It can be calculated using:

$$\text{PVR (L/min)} = \text{breathing rate (breaths/min)} \times \text{tidal volume (L)}$$

For a healthy adult at rest, normal values are:

- Tidal volume (TV): ~0.5 L (volume of air per breath).
- Breathing rate (BR): ~12 breaths per minute.

Therefore, the average adult is:

$$\begin{aligned} \text{PVR} &= \text{BR} \times \text{TV} \\ &= 12 \times 0.5 \\ &= \sim 6.0 \text{ L/min} \end{aligned}$$

Well-trained athletes typically exhibit a higher tidal volume and lower resting breathing rate, enhanced respiratory efficiency due to cardiovascular adaptation.

Changes in pulmonary ventilation rate

PVR varies according to physiological demands or medical conditions.

Understanding this requires linking pulmonary ventilation (movement of air in the lungs) to cellular respiration, especially in muscle cells (myocytes), which require oxygen to generate ATP.

During exercise

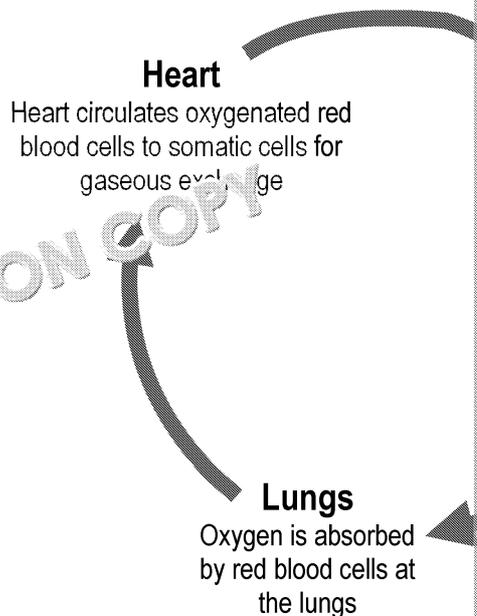
During exercise, cell energy requirements increase sharply, increasing demand for oxygen. To fulfil this demand, breathing rate, tidal volume, and heart rate all increase.

If oxygen demand exceeds supply, an oxygen debt forms. The body shifts from aerobic to anaerobic respiration, producing lactic acid, which leads to muscle fatigue.

After exercise, elevated ventilation and heart rate continue temporarily to repay the oxygen debt delivered to muscles to oxidise lactic acid and remove carbon dioxide.

In cardiovascular disease

In cases of heart disease or congenital defects, the heart's reduced pumping efficiency affects oxygen delivery to tissues. To compensate, PVR increases – both breathing rate and tidal volume rise – to maintain oxygen uptake even if systemic circulation is limited.



Apply your knowledge

1. Explain why breathing rate, tidal volume and heart rate all increase on exercise, and why they remain elevated for a few minutes after exercise has ceased.
2. Use the equation to calculate your pulmonary ventilation rate, assuming a lung volume of 0.5 L. How would you expect this value to change if you completed one minute of high-intensity activity?

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Peak flow readings

Peak flow readings assess how quickly air is forcefully exhaled from the lungs (PEFR) – using a hand-held peak flow meter. This test is especially useful in asthma to detect asthma attacks early, track lung function changes and guide treatment.

Using a peak flow meter

A patient's highest recorded reading during a symptomatic period becomes the reference point for future measurements. Regular daily readings can detect an asthma attack and help to identify triggers, such as pollen or exercise.

Lower readings indicate narrowed airways and may indicate an asthma or COPD attack. In such cases, bronchodilators may be prescribed. Further monitoring can assess treatment response or signal the need for hospital care, such as nebuliser therapy.

To use a peak flow meter:

1. Reset meter to zero.
2. Stand or sit upright.
3. Take a deep breath in.
4. Seal lips around the mouthpiece.
5. Blow out as hard and fast as possible.
6. Repeat three times and record highest value.

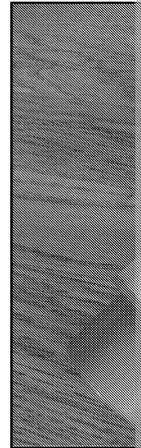


Figure 52.1

Interpreting results

Results are interpreted as a percentage of the normal reading:

- Green zone (80–100 %) – normal lung function.
- Yellow zone (50–80 %) – possible airway narrowing; caution advised.
- Red zone (< 50 %) – possible asthma attack; urgent medical attention needed.

For instance, if your normal reading is 400 L/min then:

- Green: 320–400 L/min
- Yellow: 200–319 L/min
- Red: < 200 L/min

Measurements should be taken in the morning and evening, before medication, using the same technique. This supports pattern recognition and identification of trends. Effective management adjustments are.

Benefits and limitations

The peak flow meter is a simple device that can be used at home to monitor COPD. As with all procedures, there are benefits and limitations.

Benefits	
<ul style="list-style-type: none"> • Simple, inexpensive and portable. • Enables personalised tracking of lung function. • Supports early intervention and treatment planning. • Encourages self-management through daily monitoring and independence. 	<ul style="list-style-type: none"> • Accuracy depends on technique. • Only measures airflow; minor airways can be affected. • May miss subtle changes. • Less reliable if not used consistently.

Table 52.1 Benefits and limitations of the peak flow meter

Though not a substitute for spirometry function testing, peak flow meters offer valuable information consistently and interpreted alongside clinical signs.

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Apply your knowledge

1. Describe how to use a peak flow meter and when this might be useful.
2. A patient's normal reading is 360 L/min. Calculate their green, amber and red zones.

Fractional exhaled nitric oxide (FeNO) test

The fractional exhaled nitric oxide (FeNO) test is a fast, non-invasive procedure used to measure airway inflammation, which is particularly helpful in diagnosing and managing allergic asthma when spirometry results are inconclusive, allowing clinicians to differentiate asthma from other respiratory conditions.

Nitric oxide (NO) is produced by epithelial cells lining the airway. Elevated levels of NO are associated with airway inflammation caused by eosinophils – a type of leucocyte involved in immune responses to allergens, parasites and infection. This form of inflammation is linked to allergic asthma that typically responds to inhaled corticosteroids.

The FeNO test

To complete a FeNO test:

1. The patient inhales deeply through the mouth.
2. The patient then exhales slowly and steadily into the mouthpiece of a hand-held device.
3. The test is repeated for accuracy.

To avoid false readings, patients should avoid smoking, exercise, hot drinks and nitrates (found in spinach) at least 1–3 hours before testing.

The monitor measures FeNO concentration in parts per billion (ppb).

Interpreting results

Result ranges are interpreted as follows:

	FeNO level (ppb)		Interpretation
	Adults	Children	
Low	< 25	< 20	Airway inflammation unlikely
Intermediate	25–50	20–35	Consider clinical history and other tests
High	> 50	> 35	Significant inflammation; allergic asthma likely

Table F2.27. Interpretations of FeNO levels in adults and children

Apply your knowledge

1. Describe how to complete a FeNO test and the conditions required to avoid false readings.
2. A child presents at a doctor's surgery with intermittent shortness of breath, particularly during exercise such as running, and asthma in the family history on both sides. A FeNO test is performed and the result is high. State your asthma diagnosis with reasons.

Practice questions: Measuring system activity

1. State the test to use in these clinical scenarios.
 - a. 8-year-old with intermittent shortness of breath
 - b. Pregnant woman with suspected gestational diabetes

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Topic 3: Endocrinology, neurobiology and reproduction

3.1. Key concepts of endocrinology

3.1.1. The endocrine system and homeostasis

To survive and function effectively, the human body relies on constant communication between its tissues and organs. Internal conditions – such as temperature, blood content and pH – must be carefully regulated in response to both internal activity and environmental changes. This regulation is known as homeostasis.

One of the key systems involved in coordinating these responses is the endocrine system. It uses chemical messengers called hormones, which are released by specialised glands into the bloodstream to travel to target tissues and trigger changes that help maintain internal balance.

In this chapter, we will explore how the endocrine system functions, how hormones work, and how the system works both independently and in partnership with the nervous system and the immune system – to support homeostasis and regulate the body's responses.

The endocrine system

The endocrine system coordinates responses using hormones: chemical messengers that travel through the bloodstream by specialised glands. These hormones allow distant tissues to respond to internal or external environment and help maintain homeostasis.

The endocrine system consists of:

- endocrine glands – specialised organs that act as coordination centres by producing hormones in response to signals from other organs, and releasing hormones into the bloodstream
- hormones – chemical messengers secreted by endocrine glands and transported through the bloodstream to target tissues
- target cells – cells with specific receptors that detect and respond to particular hormones, leading to physiological changes

Endocrine signals may act across the whole body – systemically (e.g. thyroxine) or locally (e.g. ADH).

Speed and duration of hormonal responses

The endocrine system communicates more slowly than the nervous system because hormones travel through the bloodstream, then must interact with cell surface membrane receptors to initiate a response. This results in responses taking from minutes to hours to initiate and resolve.

Hormonal responses can vary greatly in duration. Some are short-lived, lasting minutes, such as insulin reducing blood glucose or ADH adjusting water balance. Others are long-lived, such as steroid hormones, which involve changes to gene expression and cellular specialisation. These long-term responses typically reshape tissues and influence behaviour over months to years.

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Hormones of the endocrine system

Many hormones are involved in the endocrine system, each triggering different actions.

Hormone	Functions	Released from
Adrenaline	Initiates fight or flight response	Adrenal glands (above kidneys)
Thyroxine (T ₄)	Regulates metabolic rate	Thyroid gland (stimulated by TSH from pituitary gland)
Somatostatin	Inhibits growth hormone and other hormones	Hypothalamus, pancreas, GI tract
Erythropoietin	Stimulates red blood cell production	Kidneys (renal cortex interstitial cells)
Calcitonin	Lowers blood calcium levels	Thyroid gland (C cells)
Insulin	Lowers blood glucose	Pancreatic β cells (islets of Langerhans)
Anti-diuretic hormone (ADH)	Regulates water reabsorption	Hypothalamus, then stored and released from posterior pituitary gland

Table F3.1. Details of hormones involved in the endocrine system.

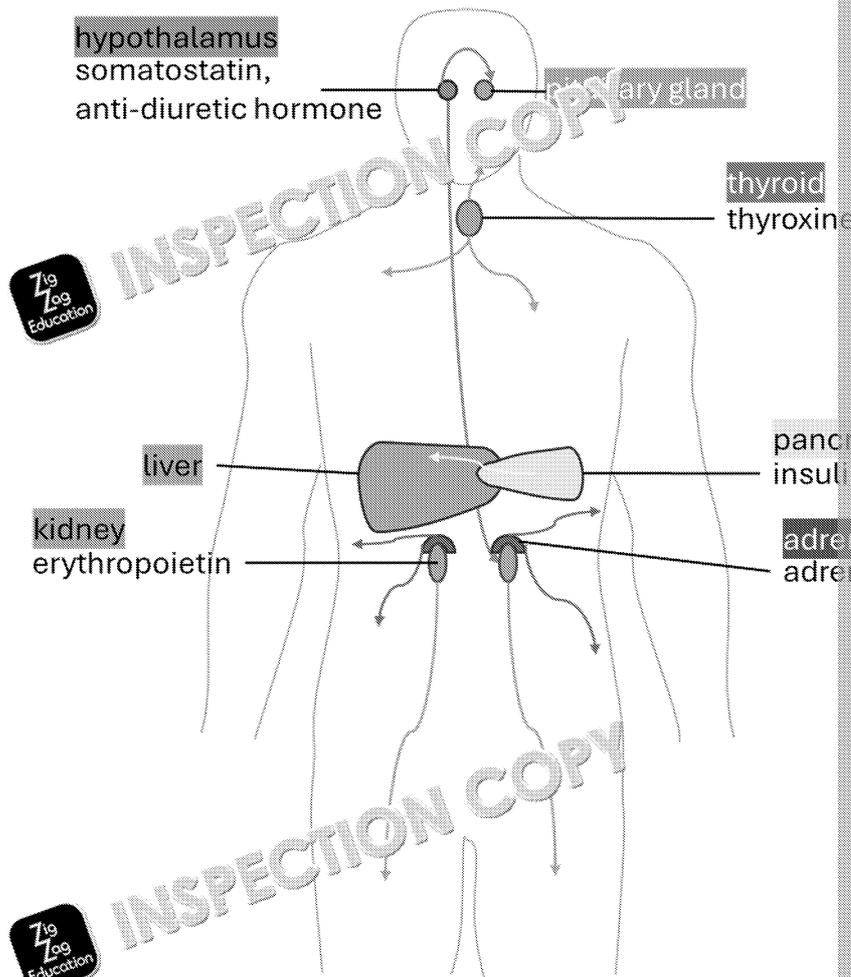


Figure F3.1. A visual representation of the organs that release specific hormones and approximate areas where these hormones have their effect.

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Adrenaline

Adrenaline, also called epinephrine, is a hormone secreted by the adrenal gland and the kidneys. It is released in response to stress, excitement or danger, such as fear or the elation after public speaking. It triggers the body's rapid-response mechanism or 'fight or flight' response.

Adrenaline plays a central role in preparing the body to react quickly, by affecting several systems simultaneously:

- eyes: pupil dilation – enhances visual acuity to better detect threats
- lungs: increased ventilation in rib cage and airway dilation – improves oxygen availability for aerobic respiration
- heart: increased heart rate – increases delivery of oxygen and nutrients to tissues
- intestines: reduced digestive activity – diverts blood away from the gut to other organs
- pain suppression – temporarily dampens pain perception to prevent distraction during emergency responses
- enhanced blood flow to muscles and brain – supports fast motor reactions
- greater energy availability – stimulates the breakdown of glycogen into glucose so that cells can generate ATP quickly

Adrenaline also has important medical applications. It is used in emergency treatment of severe allergic reactions, such as anaphylaxis. Devices like EpiPens deliver adrenaline by rapidly reversing airway constriction and supporting cardiovascular function.

Thyroxine

Thyroxine, also known as T_4 , is a hormone produced by the thyroid gland, located in the neck. It is a systemic hormone, meaning it affects nearly all cells in the body. Its primary function is to regulate the metabolic rate (BMR) – the rate at which cells use energy for aerobic respiration to produce ATP. It also influences the pace of all cellular processes.

Thyroxine has several key effects:

- increases metabolic activity – increases rate of aerobic respiration
- regulates body temperature – respiration releases heat energy, so thyroxine helps maintain a constant temperature
- adjusts protein synthesis – promotes both the synthesis and breakdown of proteins to meet energy requirements
- affects cardiovascular and digestive systems – elevated levels increase heart rate and speed up the passage of food through the gut

Thyroxine secretion is tightly regulated by a multistage negative feedback loop involving the hypothalamus and pituitary gland (see *Figure F3.2* on the following page).

Hypothyroidism is a condition where thyroxine levels are suppressed. This causes symptoms of fatigue, weight gain, cold intolerance and bradycardia (slow heart rate). It is typically treated with synthetic thyroxine (e.g. levothyroxine) to restore normal levels.

Hyperthyroidism (including Grave's disease) involves elevated thyroxine levels, leading to symptoms such as an elevated heart rate, anxiety, weight loss, heat intolerance and fatigue. Many treatments involve medications that suppress TSH or thyroxine production. In more severe cases, radioactive iodine is used to destroy overactive thyroid tissue, or a thyroidectomy may be performed. Patients often require lifelong thyroid hormone replacement therapy.

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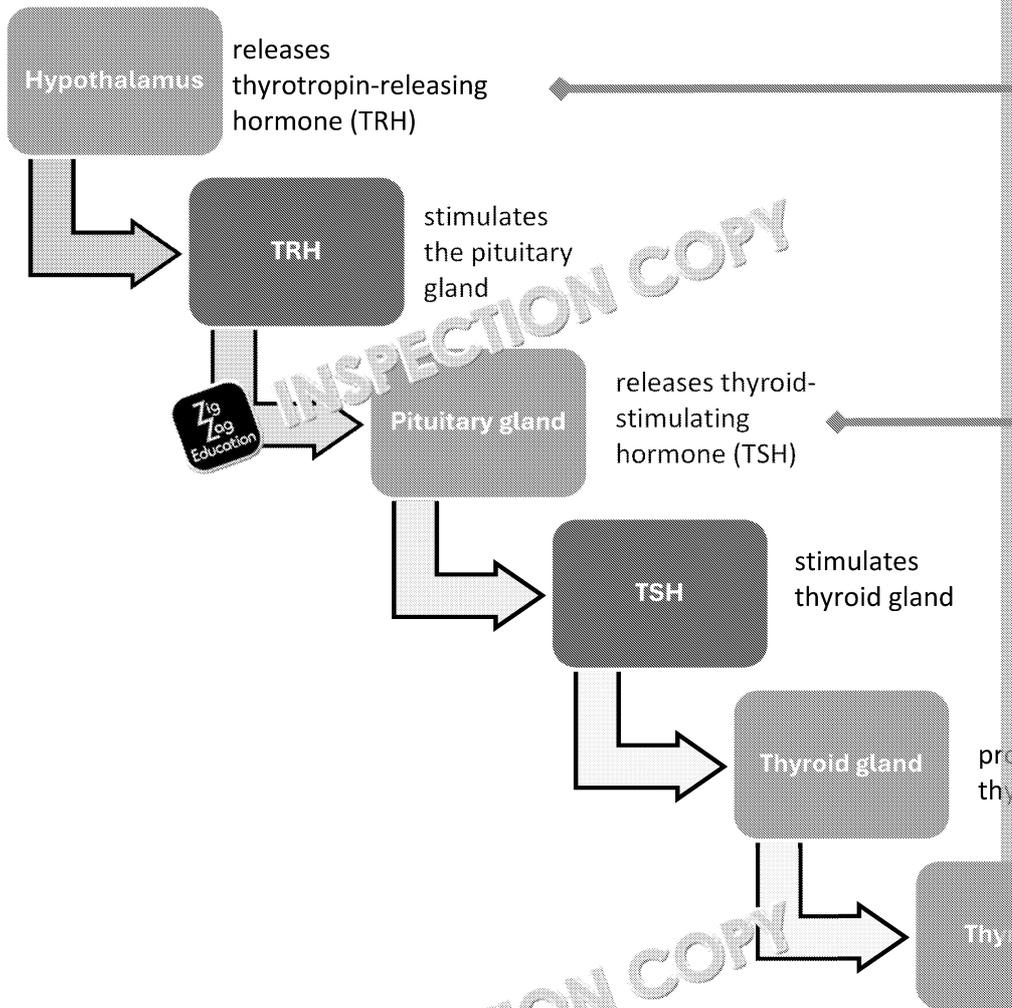


FIGURE 12.10 Multistage negative feedback loop for thyroxine secretion.

Somatostatin

Somatostatin is a hormone that plays a critical inhibitory role in various physiological multiple tissues, including the hypothalamus, pancreas and gastrointestinal (GI) tract suppressing the release of other hormones or slowing digestive activity.

Its site-specific functions include:

- hypothalamus – inhibits release of growth hormone (GH) and TSH from anterior regulate growth and metabolism
- pancreas (delta (δ) cells) – suppresses insulin and glucagon secretion, contributing to glucose levels
- GI tract – slows digestion by reducing hydrochloric acid secretion, inhibiting pancreatic enzyme release, delaying stomach emptying, and slowing intestinal peristalsis. This controls the rate of food passage through the digestive system.

Somatostatin is involved in several negative feedback loops, where its release prevents responses that could disrupt homeostasis. This self-regulating mechanism maintains blood sugar and digestive systems.

Synthetic somatostatin analogs are used therapeutically to treat hormone-secreting tumours and acromegaly, a syndrome, a rare condition caused by tumours of the nervous and hormone systems, leading to symptoms like diarrhoea. It is also used to control gastrointestinal bleeding, particularly resulting from oesophageal varices.

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Erythropoietin

Erythropoietin (EPO) is a hormone primarily produced by the kidneys in response to **hypoxia**. Its main function is to stimulate erythropoiesis – the production of erythrocytes in the bone marrow, thus increasing the oxygen-carrying capacity of the blood.

As erythrocyte numbers rise, more haemoglobin becomes available to transport oxygen, helping to correct hypoxic conditions. EPO production notes both the proliferation and differentiation of red blood cell precursors, making it vital when oxygen requirements are high.

EPO secretion is regulated via a negative feedback loop:

1. In hypoxic conditions, such as anaemia, high altitude, chronic lung disease or heart failure, hypoxic conditions activate the EPO gene.
2. This causes increased synthesis and secretion of EPO, increasing erythropoiesis.
3. As oxygen levels improve, hypoxic conditions decline, reducing EPO gene expression of EPO, slowing erythrocyte production.

This feedback mechanism ensures that red blood cell numbers remain within a normal range, preventing blood from thickening.

Synthetic EPO (e.g. epoetin alfa) is used to treat anaemia in patients with chronic kidney disease or those undergoing chemotherapy.

However, EPO has also been used illegally by athletes to enhance performance. Such misuse can lead to dangerous side effects including increased blood clots.

Calcitonin

Calcitonin is a hormone secreted by C cells of the thyroid gland. Its main function is to lower blood calcium levels (Ca^{2+}) when they become elevated, helping to maintain calcium ion homeostasis.

Calcitonin achieves this through several mechanisms, including:

- inhibiting osteoclast activity – osteoclasts break down bone tissue, releasing calcium into the bloodstream; suppressing their activity limits bone reabsorption and prevents calcium release
- increasing renal calcium ion excretion – promotes the loss of calcium ions from the body through the kidneys

Calcitonin secretion is inhibited by somatostatin, and together they modulate these functions, calcitonin has limited physiological impact in humans, because levels of calcitonin (e.g. post-thyroidectomy) usually remain asymptomatic.

However, synthetic calcitonin (e.g. salmon calcitonin) can be used therapeutically to reduce the risk of bone fracture, manage hypercalcaemia, alleviate symptoms caused by bone metastases and provide relief from osteoporotic fracture pain.

Calcitonin is also used as a diagnostic marker, since elevated levels may indicate hyperparathyroidism, a condition characterized by excessive growth of calcitonin-secreting cells.

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Insulin

Insulin is a hormone produced by β cells within the islets of Langerhans in the pancreas. It maintains glucose homeostasis by stimulating cells – particularly in the liver, muscles and adipose tissue – to take up glucose from the bloodstream. Excess glucose is converted to glycogen for storage or used in cellular respiration.

Insulin has several inter-related functions:

- facilitates cellular glucose uptake, especially in liver, fat and muscle tissues
- promotes glycogenesis, the conversion of glucose to glycogen for storage
- inhibits gluconeogenesis and glycogenolysis – the production of new glucose and the release of stored glycogen
- enhances lipogenesis, the storage of energy through the synthesis of triglycerides
- supports protein synthesis – increases amino acid uptake and anabolic activity

Insulin secretion is primarily triggered by elevated blood glucose levels, for instance as seen in type 2 diabetes mellitus, and is impaired in type 1 diabetes mellitus, due to immune destruction of β cells, and type 2 diabetes mellitus, due to insulin resistance (see page 91).

Synthetic insulin (e.g. insulin lispro) is manufactured using genetically engineered bacteria. It is critical in managing type 1 diabetes and is sometimes required in advanced type 2 diabetes. Formulations include rapid-, short-, and long-acting forms, each tailored to reflect different physiological effects.

ADH (anti-diuretic hormone)

Anti-diuretic hormone (ADH), also known as vasopressin, is a hormone vital for maintaining blood pressure and concentration of solutes in the plasma. It is produced by the hypothalamus and stored in the posterior pituitary gland, from where it is released in response to low water levels or high osmolarity in the blood.

ADH targets cells in the collecting ducts of the kidney (see pages 74–75), causing aquaporins to be inserted into the cell membranes. These channels increase the collecting ducts' permeability to water, allowing for increased reabsorption into the bloodstream and reducing water loss in urine.

When ADH levels are high (as during dehydration), the kidneys produce small volumes of concentrated urine. Conversely, low levels result in increased water loss.

Changing water balance affects the concentration of solutes in the plasma, blood volume and pressure, which in turn affects ADH secretion. An increase in osmolarity (reduction in water potential causing increased solute concentration) or a reduction in blood volume or pressure all lead to increased ADH secretion. Conversely, a decrease in osmolarity has the opposite effect as it inhibits ADH secretion, leading to increased volumes of dilute urine.

Insufficient or excessive ADH secretion is clinically significant. Diabetes insipidus is caused by insufficient secretion by the hypothalamus or pituitary gland (called central DI) or kidney insensitivity to ADH (called nephrogenic DI). It is characterised by excessive urination and dehydration. Conversely, inappropriate ADH secretion (SIADH) is caused by excess ADH. Water retention increases blood volume, leading to hyponatraemia (dilution of sodium ions in the blood) and lower haemoglobin concentration, causing anaemia and cell swelling, particularly in brain tissue.

Synthetic ADH (e.g. desmopressin) is used to treat central diabetes insipidus, nocturnal enuresis (bedwetting beyond childhood), and certain bleeding disorders because of ADH's role in enhancing platelet aggregation.

Apply your knowledge

1. State three physiological effects that adrenaline causes during the 'fight or flight' response.
2. Outline the main functions of insulin and describe the result if the body cannot produce insulin.
3. Describe how the endocrine system is involved in maintaining homeostasis.
4. Compare and contrast the action of hormones with electrical signals in the nervous system.

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Homeostasis

Homeostasis is the maintenance of optimum internal conditions, essential for all and biological systems. It includes the regulation of water balance, blood glucose and temperature, among many others.

Deviations from these ideal conditions impair cell function:

- Enzyme activity reduces or enzymes denature, slowing metabolic reactions.
- Substrate concentrations are no longer optimal, limiting reaction efficiency.
- Gene expression and protein synthesis are reduced, affecting cell performance.
- Active transport and intracellular signalling no longer function effectively.
- Cell signalling is impaired, causing damage to cell structure.

Maintaining homeostasis

To restore balance when internal conditions fluctuate:

1. The endocrine and nervous systems detect changes using specialised receptors.
2. These changes trigger hormonal release or nervous impulses, coordinated by the brain or pancreas.
3. The signals are relayed to effectors, such as muscles or glands, which respond.

Negative feedback mechanisms

Homeostasis operates through negative feedback loops, where a rise in one hormone and promotes the opposite response. The two responses counterbalance each other and return levels back to the optimum.

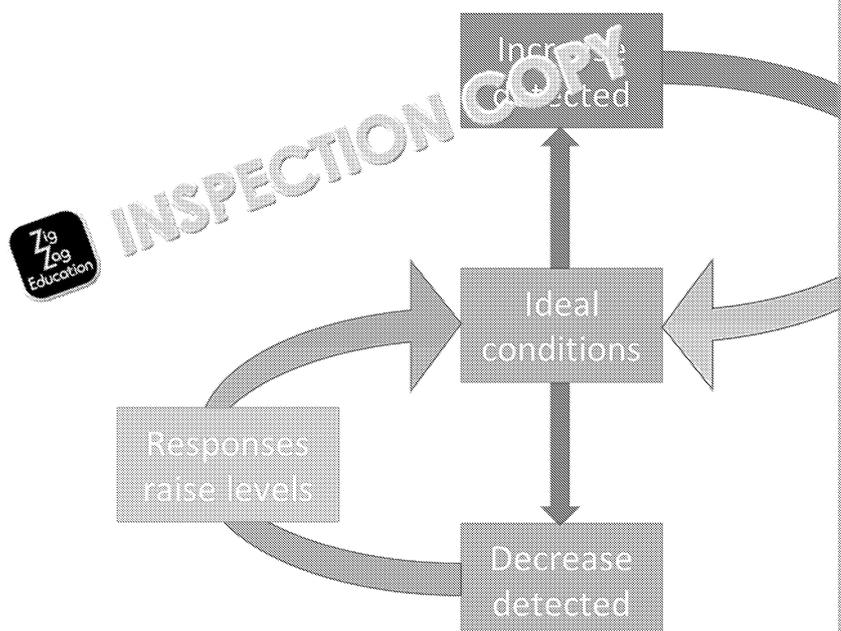


Figure F3.3. An overview of how negative feedback mechanisms help to maintain homeostasis.

Recall questions

1. List the three components essential for the maintenance of homeostasis.
2. Explain how negative feedback mechanisms work, with reference to the diagram.
3. Explain why homeostasis is so important for good cell function.

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Thermoregulation

Thermoregulation is the process of maintaining a stable internal body temperature, in healthy adults. This is critical for enzyme function, as lower temperatures slow enzyme activity and higher temperatures risk enzyme denaturation, disrupting metabolic processes.

Detection and coordination

Changes to core temperature are detected by the thermoregulatory centre in the hypothalamus, which continuously monitors blood temperature. The hypothalamus then interacts with the autonomic nervous system and endocrine system to coordinate appropriate physiological responses via nervous and hormonal pathways.

Responses to increased core temperature

To promote heat loss, the following responses are coordinated, including:

- vasodilation of arterioles in skin surface – increases blood flow nearer skin surface to radiate away heat; skin appears pink and flushed
- sweating – enhances heat loss through evaporation of water from the skin
- relaxation of erector pili muscles – body hair lies flat, reducing insulation and allowing heat to be lost more easily
- reduced metabolic rate – lowers aerobic respiration, generating less internal heat

Responses to decreased core temperature

To conserve and generate heat, the following responses are triggered:

- vasoconstriction of arterioles in skin surface – restricts blood flow near the skin surface; skin appears pale
- shivering – involuntary, rapid muscle contractions generate heat via increased aerobic respiration
- contraction of erector pili muscles – body hair stands upright, trapping a layer of air to reduce heat loss
- increased metabolic rate – increases respiration to generate more internal heat

Negative feedback

Regulating core body temperature relies on negative feedback mechanisms to prevent deviations and maintain stable internal conditions. This process works as follows:

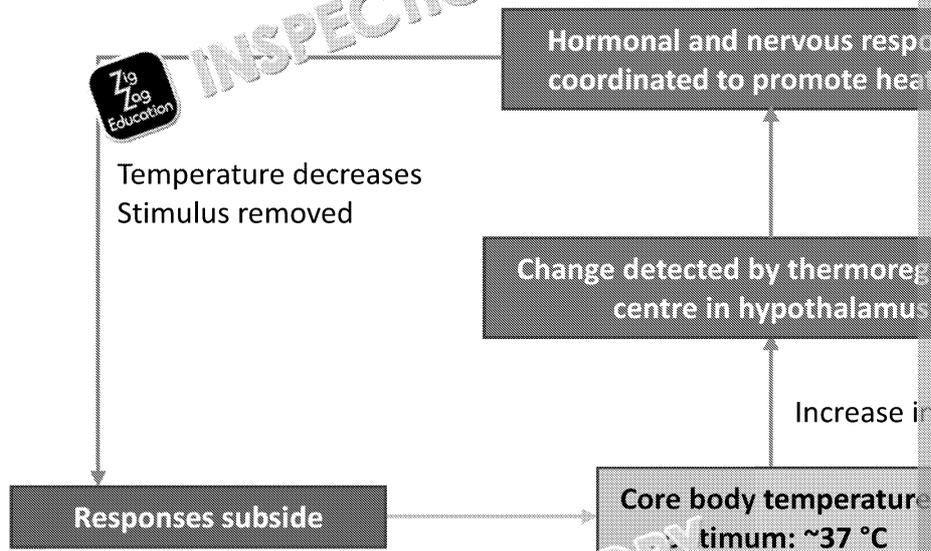


Figure F3.4. Negative feedback mechanism for regulating core body temperature

The same feedback loop applies in the opposite direction:

- A decrease in core temperature triggers responses that increase core temperature.
- Once the temperature returns to normal, these responses are suppressed.

Apply your knowledge

1. Compare the physiological responses to increases and decreases in core temperature.
2. Explain why maintaining a constant core body temperature is essential for health.

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Osmoregulation

Osmoregulation is the control of the balance of water and dissolved electrolytes, such as sodium, potassium and chloride, within body fluids. This regulation ensures a stable internal environment for cell function and homeostasis.

Effects of plasma tonicity

Hypotonic blood plasma causes water to move into cells by osmosis, causing swelling and potential **lysis**. Conversely, **hypertonic** blood plasma causes water to move out of cells by osmosis, leading to **crenation** and shrinkage.

Detection and regulation

The osmoregulatory centre of the hypothalamus contains osmoreceptors that monitor plasma water potential and solute concentrations. Deviations from the optimum trigger corrective responses, primarily involving the hormone ADH (anti-diuretic hormone).

Response to hypertonic conditions

Hypertonic conditions are caused by water loss or electrolyte gain and can be corrected by retaining water. In these conditions, ADH, stored in the posterior pituitary gland, is secreted into the bloodstream and binds to receptors on cells in the kidneys' collecting ducts.

ADH activates an intracellular signalling cascade that inserts aquaporin channels into the cell membrane. As filtrate passes through the collecting ducts, water molecules are reabsorbed. They move into the interstitial fluid and then into the bloodstream, conserving water.

The kidneys produce small volumes of concentrated urine because less water is available. Dry mouth and thirst pathways stimulate thirst, promoting behavioural modification leading to fluid intake.

Response to hypotonic conditions

In hypotonic conditions, there is excess water and insufficient electrolytes, which can lead to cell swelling. The osmoregulatory centre detects this change and causes the pituitary gland to release less ADH. Fewer aquaporins are inserted into the cell membrane of the kidney tubules and collecting ducts. Larger volumes of dilute urine are produced to eliminate excess water.

Additional control

Changes in blood **plasma osmolarity** also affect blood volume, which alters blood pressure. These shifts are detected by baroreceptors in the aorta and carotid arteries (in the neck), influencing ADH release. Low pressure or volume leads to an increase in ADH, while high pressure or volume suppresses ADH release.

plasma
concentration
blood
electrolyte
glucose
potential
plasma
concentration

Negative feedback

Responses to changes in osmolarity rely upon negative feedback mechanisms.

- A stimulus (increase in plasma osmolarity) is detected by osmoreceptors in the hypothalamus, leading to the posterior pituitary gland to increase release of ADH. ADH acts on kidneys to increase water reabsorption, reducing plasma osmolarity. ADH secretion is reduced.

Recall questions

1. Define what is meant by a negative feedback pathway.
2. Outline the roles of ADH and aquaporins in maintaining water balance.
3. Outline the negative feedback pathway that is triggered by changes in plasma osmolarity.
4. Describe how changes in water balance are detected.

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Glucose regulation

Glucose is the primary molecule used in aerobic respiration. It enters the bloodstream in capillaries and is transported to cells throughout the body. However, excessive glucose can disrupt osmotic balance:

- High blood glucose concentration causes water to move out of cells by osmosis, risking cell shrinkage.
- Low blood glucose concentration causes water to move into cells by osmosis, risking cell swelling.

Maintaining optimal blood glucose levels is essential to protect cell integrity and ensure energy is available for respiration.

Detection and Coordination

Normal blood glucose concentration lies between 4–6 mmol/dm³ (or 90 mg / 100 cm³) before eating and 7.8 mmol/dm³ in the two hours after eating. Deviations from this range are detected by β cells of Langerhans in the pancreas.

These cells secrete hormones into the bloodstream, targeting liver (hepatocytes), muscle (myocytes), and fat tissue (adipocytes). The hormones bind to specific receptors and initiate responses that regulate glucose levels.

Response to increased glucose levels

Increased glucose levels stimulate β cells to secrete insulin, which binds to receptors on hepatocytes, myocytes, and adipocytes and:

1. Promotes GLUT4 transporter insertion into membranes, increasing glucose uptake by cells.
2. Stimulates glycogenesis (conversion of glucose to glycogen for storage).
3. Inhibits gluconeogenesis and glycogenolysis in the liver.
4. Enhances lipogenesis (production of lipids) and protein synthesis.

Together, these actions reduce blood glucose concentration, returning levels to normal.

Response to decreased glucose levels

Low glucose levels stimulate α cells to secrete glucagon, which restores levels via:

- reduced glucose uptake by cells
- increased glycogenolysis – breakdown of stored glycogen into glucose
- increased gluconeogenesis – synthesis of glucose from amino acids and glycerol
- increased lipolysis – breakdown of lipids into fatty acids and glycerol for aerobic respiration

These processes release glucose into the bloodstream, correcting the deficit.

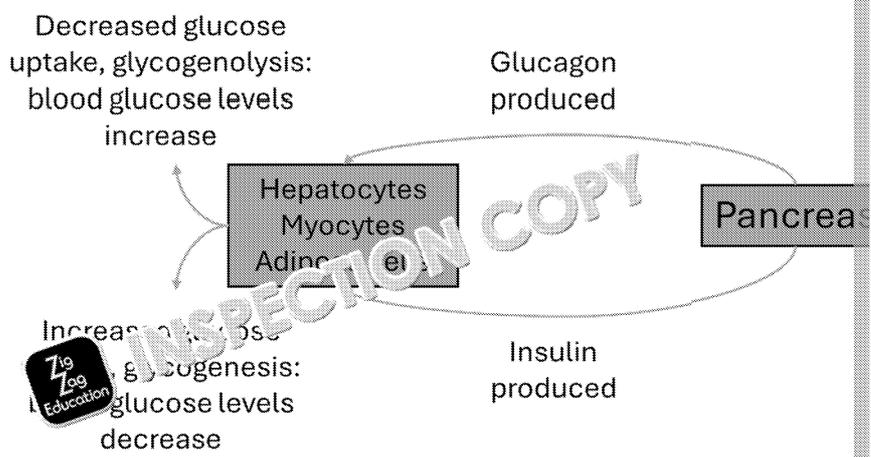


Figure F3.5. A schematic overview of blood glucose regulation.

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Negative feedback loops

Blood glucose regulation relies on a negative feedback loop:

- rising glucose → insulin release → absorption and storage → glucose falls
- falling glucose → glucagon release → mobilisation and synthesis → glucose rises

Your turn

1. Outline the processes involved in decreasing and increasing blood glucose levels.
2. Create a detailed flow chart of the components and stages involved in the regulation of blood glucose levels after eating a large meal. Include the target blood glucose concentration and how this is controlled through a negative feedback loop.



Practice questions: The endocrine system and homeostasis

- 1 Complete the table to match the hormone to the regulatory pathway.

Hormone	Regulatory pathway
A.	Osmoregulation
Insulin	B.
C.	Metabolic regulation
Calcitonin	D.



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3.1.2. Monitoring homeostasis

Failure in homeostatic systems can lead to serious health consequences. This chapter discusses disrupted regulation and how health professionals can assess and manage these imbalances.

Malfunctioning thermoregulation

Maintaining a stable core body temperature is vital for the rate of metabolism and enzyme activity. Thermoregulation is coordinated by the hypothalamus and involves both the nervous and endocrine systems.

When internal temperature deviates significantly from the optimum (~37 °C), the body can experience either hypothermia (low temperature) or hyperthermia (high temperature), both of which have serious clinical consequences.

Symptoms of poor thermoregulation

Hypothermia

Hypothermia occurs when core body temperature drops below 35 °C and the body is unable to generate enough heat. It is a medical emergency, potentially affecting organ function, consciousness, and heart rate.

Common causes of hypothermia include:

- prolonged exposure to cold conditions without adequate protection (e.g. mountain climbing)
- cold indoor environments, particularly for elderly or vulnerable individuals
- medical conditions that impair thermoregulation, such as hypothyroidism, malnutrition, and alcoholism
- substance use, including alcohol or sedatives which suppress thermal responses

Symptoms worsen as severity increases:

Severity	Core temperature (°C)	Symptoms
Mild	32–35	Shivering, pale skin, confused speech, fatigue
Moderate	28–32	Delirium, slowed reflexes, bluish skin, unconsciousness
Severe	< 28	No shivering, coma, absent respiratory failure

Table F3.2. Symptoms at different severities of hypothermia.

Infants may have cold, red skin, be floppy and unusually quiet and refuse to feed.

Treatment includes moving the patient to a warm, dry location, removing wet clothing, covering with blankets, and warming with warm non-alcoholic drinks or warmed intravenous (IV) fluids.

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Hyperthermia

Hyperthermia occurs when core body temperature rises above 40 °C, overwhelming normal thermoregulatory mechanisms. Unlike fever, which is a regulated response, hyperthermia is uncontrolled.

Hyperthermia has several contributing factors, including:

- prolonged exposure to heat, including during heatwaves and high humidity
- strenuous activity in hot conditions or inappropriate clothing
- disorders affecting thermoregulation, such as hyperthyroidism, stroke or brain injury
- medications and drug reactions, including from diuretics or when used during surgery

Symptoms of hyperthermia vary as core temperature increases:

	Core temperature (°C)	Symptoms
Heat stress	~37.5–38.5	Thirst, headache, dizziness
Heat exhaustion	~38.5–40	Heavy sweating, nausea, rapid heart rate
Heat stroke	> 40	Dry skin, delirium, seizures

Table F3.3. Symptoms at different stages of hyperthermia

Treatment includes relocating to a cool environment and removing excess clothing. Severe cases may require intravenous saline with electrolytes, and active cooling using ice packs applied to the neck, groin and armpits (axillae), cool water immersion or fans.

Comparing hypothermia and hyperthermia

The symptoms of hypothermia and hyperthermia reflect opposing thermoregulatory responses as the body's attempt to restore core temperature.

In hypothermia, the body strives to conserve heat through vasoconstriction, shivering and symptoms like confusion and decreased alertness which indicate metabolic slowing. Shivering is a thermoregulatory mechanism, producing warmth through involuntary muscle contraction.

Conversely, in hyperthermia, the body works to dissipate excess heat. Responses include vasodilation, increased breathing and heart rate. Delirium and seizures may occur when vasodilation drive heat loss but lead to electrolyte depletion, so treatment often involves fluid therapy, typically administered via IV fluids.

Monitoring core temperature

The accurate measurement of core temperature is essential for diagnosis and treatment.

Method	Accuracy	Uses
Rectal thermometer	Very high	Emergency and clinical assessment
Oral/Tympanic	Moderate – High	Convenient and non-invasive
Oesophageal probe	Very high	Surgical and critical care; intensive care

Table F3.4. Accuracy and uses of different methods of monitoring core temperature

Other methods are also available (see Table F3.1), and selection depends on the required precision and the patient condition.

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1. List the primary causes and symptoms of hypothermia.
2. Describe the physiological responses that the body exhibits to maintain core temperature during extreme cold and heat.
3. Compare the use cases and accuracy of the rectal thermometer and the oesophageal probe.

Malfunctioning osmoregulation

Water balance is critical to cell health, blood pressure, and overall fluid homeostasis. The movement of water and electrolytes, ensuring plasma osmolarity remains within a narrow range, is essential for maintaining these functions.

When osmoregulation fails, the body's ability to maintain water and electrolyte balance can lead to cell dysfunction, fluid imbalance and serious clinical consequences, depending on whether water is being retained or lost excessively.

Symptoms of poor osmoregulation

Excessive water retention

A key condition involving excessive water retention is the syndrome of inappropriate ADH secretion (SIADH). SIADH results in persistent ADH secretion, causing excessive water reabsorption in the kidneys.

Common symptoms include:

- hyponatraemia (low plasma sodium ion concentration)
- headache, nausea and lethargy
- muscle cramps, confusion and **ataxia**
- cerebral **oedema** in severe cases

Neurons reduce excitability in low plasma sodium ion concentrations, causing neurological symptoms. Excess water retention also dilutes plasma solutes, so it becomes hypotonic and water enters cells via osmosis.

Treatment includes restricting fluid intake, then salt tablets or hypertonic saline for moderate cases, and ADH antagonists for resistant or severe cases.

Excessive water loss

Conditions where excessive water is lost include diabetes insipidus, excessive alcohol consumption, and post-operative diuresis. Symptoms include:

- excessive urination
- excessive thirst
- dehydration, with dry mucous membranes, such as eyes, mouth and throat
- hypotension and tachycardia (elevated heart rate) due to reduced blood volume
- hypernatraemia (increased plasma sodium ions)
- fatigue, dizziness and confusion

Reduced water retention increases plasma osmolarity, drawing water out of cells by osmosis, which can impair cellular function, especially in the brain.

Treatment includes drinking plenty of water daily. In more severe cases, synthetic ADH can be used to improve water retention, and a low sodium diet may be helpful to reduce electrolyte imbalance and plasma osmolarity.

ataxia – a lack of coordination that results in unsteady gait, slurred speech, and other symptoms.

oedema – the accumulation of fluid in tissues, causing swelling, especially in the feet, ankles, and hands.

antagonist – a substance that blocks or opposes the actions of another substance.

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Monitoring blood osmotic potential

Blood osmotic potential can be monitored using several methods, including:

Method	Description	Advantages
Direct lab measurement	Uses freezing point to assess solute concentration.	Highly accurate
Calculated osmolarity	Estimates levels of sodium ions, glucose and urea in the blood. Blood is collected, allowed to clot and the clot removed before testing.	Rapid Accessible
Blood pressure	Provides an indication of blood volume. Can infer potential osmotic imbalance, particularly in cases of dehydration or fluid overload.	Rapid Non-invasive
Urine analysis	Measure volume and solute concentration. Can distinguish between types of water imbalance (e.g. SIADH vs diabetes insipidus).	Fast Practical May indicate

Table F3.5. Methods of monitoring blood osmotic potential

Recall questions

1. List the main symptoms of excessive water retention and dehydration.
2. Describe the treatment options for conditions like dehydration.
3. Describe the methods used to monitor blood osmotic potential and the advantages and disadvantages of each.
4. Explain how the body responds to excessive water intake.

Malfunctioning glucose regulation

Glucose is the body's primary energy source, essential for aerobic respiration and powers cell processes. Its concentration in the bloodstream must be carefully regulated while avoiding osmotic imbalance and vascular damage.

Poor regulation of blood glucose is characteristic of type 1 and type 2 diabetes. Type 1 diabetes results from autoimmune destruction of β cells in the pancreatic islets of Langerhans, preventing glucose uptake by cells (see page 91).

Type 2 diabetes involves reduced insulin sensitivity or β cell exhaustion, leading to high blood glucose despite the presence of insulin (see page 92).

In both cases, poorly managed diabetes can result in hypoglycaemia (low blood glucose) or hyperglycaemia (high blood glucose), each with distinct symptoms and risks.

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Symptoms of hypoglycaemia and hyperglycaemia

Hypoglycaemia

Hypoglycaemia is defined when blood glucose levels drop below 4.0 mmol/L. Symptoms include energy and osmotic changes affecting cell balance.

Early symptoms include shaking or tremors, sweating, **palpitations**, hunger, anxiety or irritability and tingling lips.

Later symptoms include confusion and poor concentration, blurred vision, slurred speech, drowsiness, seizures and loss of consciousness.

Treatment for mild cases includes fast-acting carbohydrates such as glucose tablets or fruit juice. In severe cases, intravenous glucose and rehydration with emergency care may be required.

Hyperglycaemia

Hyperglycaemia occurs when blood glucose levels exceed 7.0 mmol/L at fasting, or 12.0 mmol/L after a meal.

Symptoms often develop slowly and may include increased thirst, frequent urination, blurred vision. If sustained, unintentional weight loss, recurrent infections and slow wound healing may occur.

In severe cases, rapid breathing, fruity-smelling breath, confusion and drowsiness are observed.

High blood glucose creates a hypertonic environment, causing water to leave cells by osmosis. Excess glucose increases abnormal metabolic activity. Mild increases in blood glucose can be managed with hydration, exercise and dietary adjustments. Persistent increases require insulin therapy. In emergency cases require hospitalisation for the administration of IV fluids to correct dehydration. In severe cases require insulin therapy to reduce blood glucose levels.

Lifestyle changes

Long-term complications of untreated hyperglycaemia include neuropathy (nerve damage), nephropathy (kidney damage) and cardiovascular disease. However, lifestyle adjustments can help manage most severe symptoms and help prevent daily adjustments. These include:

- Consuming foods with a low glycaemic index to promote gradual release of glucose into the bloodstream. These foods include whole grains, legumes and fruits.
- Regular, moderate exercise, timed to avoid after-eating (postprandial) spikes in blood glucose and good cardiovascular function.
- Minimising alcohol consumption to avoid glucose fluctuations.
- Avoiding smoking, which exacerbates cardiovascular risk and inflammatory damage.

Monitoring glucose levels

Blood glucose levels can be monitored using several methods (see page 111), including self-monitoring of blood glucose (SMBG), continuous glucose monitors (CGMs) and HbA1c blood tests for long-term control.

Recall questions

1. Describe the causes of type 1 and type 2 diabetes.
2. Describe the symptoms of hypoglycaemia and explain the immediate treatment steps for a mild episode.
3. Explain how hyperglycaemia leads to dehydration and outline long-term complications if it is not managed properly.

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Practical questions: Monitoring homeostasis

1. An otherwise healthy young man becomes stranded in the African outback and is not found for several days. They are found at about 2am in the open savannah. Temperature is 10 °C at night to 42 °C during the day.

Name one regulatory malfunction he may be suffering from.

3.2. Key concepts of neurobiology

3.2.1. The nervous system

The nervous system produces rapid, short-lived responses by transmitting electrical impulses. It plays a fundamental role in enabling fast reactions to sudden internal or external changes. Interactions between the nervous and endocrine systems allow a wide range of responses, which are rapid and sustained over varying durations.

Organisation of the nervous system

The nervous system is divided into two major components:

- The central nervous system – consists of the brain and spinal cord and controls the rest of the body.
- The peripheral nervous system – comprises all the neural structures and components outside the central nervous system.

The peripheral nervous system is further subdivided into:

- The somatic nervous system – responsible for all voluntary actions under conscious control (e.g. movement, sensory perception).
- The autonomic nervous system – regulates involuntary processes such as heart rate, blood pressure and respiratory function.

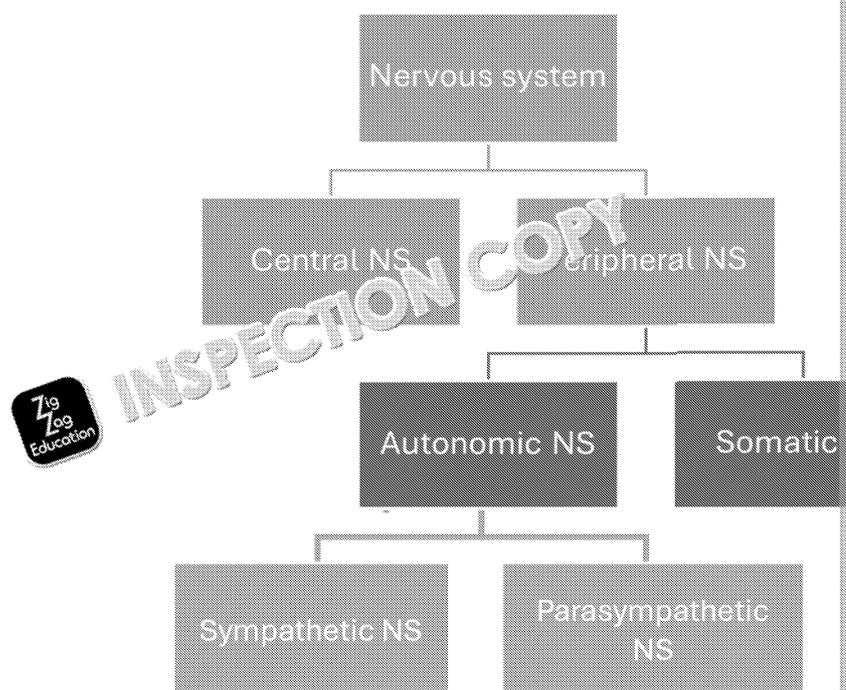


Figure F3.6. The overall organisation of the nervous system and its components.

The somatic nervous system

The somatic nervous system enables conscious perception and control. Sensory receptors (e.g. eyes, ears, nose, tongue, skin) detect stimuli (e.g. light, sound, pressure, pain) and signals are transmitted via sensory neurons to the brain. A response is coordinated and relayed through motor neurons to effectors (skeletal muscles).

The autonomic nervous system

The autonomic nervous system (ANS) controls involuntary responses, such as digestion and heart rate. It receives information through internal sensors that detect changes in body state. Signals are sent to control centres, usually in the brain, spinal cord or pancreas. Effectors, including smooth or cardiac muscles, or glands, carry out the adjustments.

Many autonomic responses involve interaction between nervous and endocrine systems. The two systems often interact between the two systems or integrate the response across both, depending on the situation.

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Sympathetic and parasympathetic divisions

The ANS is divided into two antagonistic systems:

- The sympathetic nervous system – activates ‘fight or flight’ response, such as increasing heart rate and releasing adrenaline.
- The parasympathetic nervous system – promotes ‘rest and digest’ functions, including slowing heart rate, encouraging digestion, and sleep.

Together, they coordinate a response followed by a return to balance through opposite actions.

Pathway through the nervous system

All nervous responses follow a predictable pathway:

1. A stimulus is detected by a receptor.
2. The signal travels via a sensory neuron to a control centre (usually the brain or spinal cord).
3. Within the CNS, the signal is processed by relay neurons.
4. The response is transmitted via a motor neuron to an effector (muscle or gland), which carries out the action.

Your turn

1. State by which part of the nervous system the responses of yawning and sneezing are controlled.
2. Suggest why most body functions and processes are controlled autonomically.
3. Create a flow chart of the signalling pathway through the nervous system.

Nerve function

Structure and function of neurons

Neurons are highly specialised cells with unique structural adaptations that enable them to communicate across the nervous system. There are three main types of neuron – sensory, relay and motor – each tailored to a specific function (see pages 12–13).

One key feature of motor neurons, and some sensory neurons, is the myelin sheath – an insulating layer formed by Schwann cells along the axon. Interrupting this sheath at regular intervals are gaps known as nodes of Ranvier, each approximately 20 nm wide. These nodes are essential for saltatory conduction, a process that enables the electrical impulse to ‘jump’ between nodes. This greatly increases transmission speed – up to 100 times faster than conduction along unmyelinated axons. Conduction is disrupted in conditions such as multiple sclerosis and motor neuron disease.

Features of nerve impulse transmission

The transmission of a nerve impulse along an axon relies on a wave of **depolarisation** followed by **repolarisation**, which occurs in a rapid, sequential manner along the axon membrane.

Resting potential

When a neuron is at rest, the membrane is polarised, with a resting potential of approximately -70 mV. This electrical gradient is maintained by differences in ion distribution across the membrane, particularly involving sodium ions (Na^+) and potassium (K^+) ions.

Action potential and depolarisation

A stimulus, such as activation of a sensory receptor, triggers a depolarisation event. This causes Na^+ ions to enter the neuron, making the inside of the axon less negative than the outside. As the membrane potential increases to about $+40$ mV, generating an action potential that travels down the axon.

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Repolarisation

Once the peak voltage is reached, K^+ ions move out of the neuron, restoring the potential to the resting potential – a process known as repolarisation. The potential falls back towards -70 mV.

Hyperpolarisation

During repolarisation, the membrane potential briefly drops below the resting potential, a state known as hyperpolarisation. The neuron then stabilises back to its resting potential, ready to receive another impulse.

Reading a nerve impulse from a potential difference graph

A typical nerve impulse can be visualised on a membrane potential graph, showing potential, depolarisation, repolarisation and hyperpolarisation. These changes are the result of ion channel opening and closing during transmission of the nervous impulse along the axon.

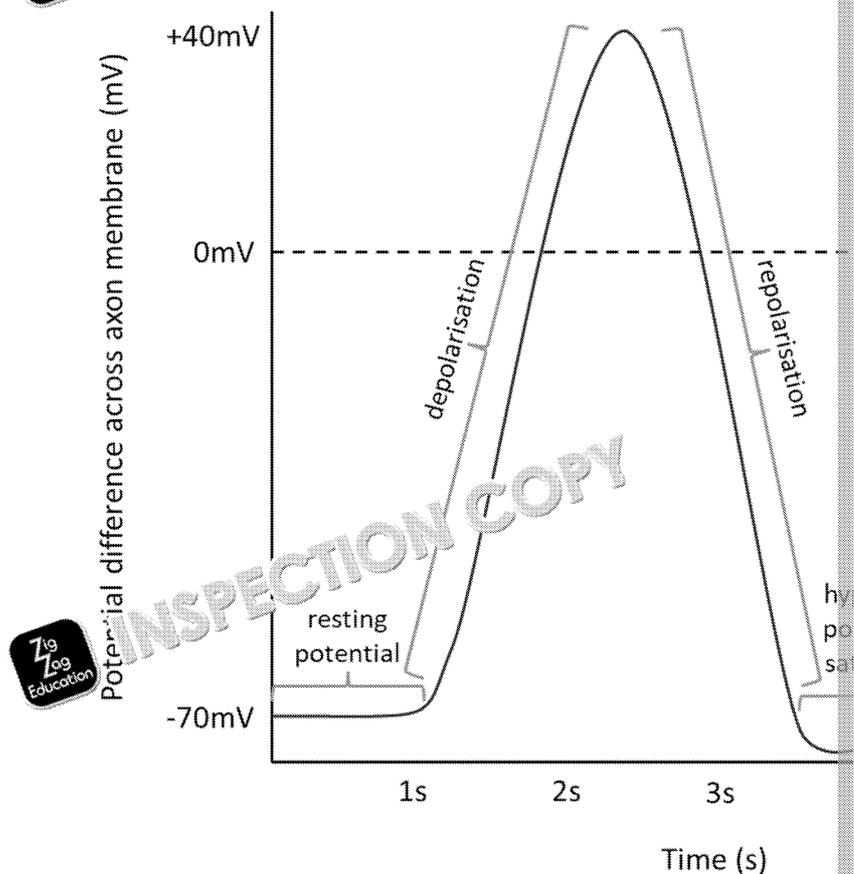


Figure F3.7. A potential difference graph showing depolarisation, repolarisation and hyperpolarisation.

Saltatory conduction

Saltatory conduction is the rapid transmission of electrical impulses along a myelinated neuron. In unmyelinated neurons, where depolarisation and repolarisation must occur continuously along the axon, myelinated neurons allow ion exchange only at the nodes of Ranvier.

At a depolarised node, positive charges enter the axon, while the adjacent resting node remains negatively charged (at resting potential). This establishes a local current causing the impulse to 'jump' from node to node. The myelin sheath acts as an **insulator**, preventing ion movement across it. This allows the impulse to travel along axon segments and vastly increases conduction speed.



This is essential for the rapid transmission of long-distance motor and sensory impulses, allowing for coordinated movement.

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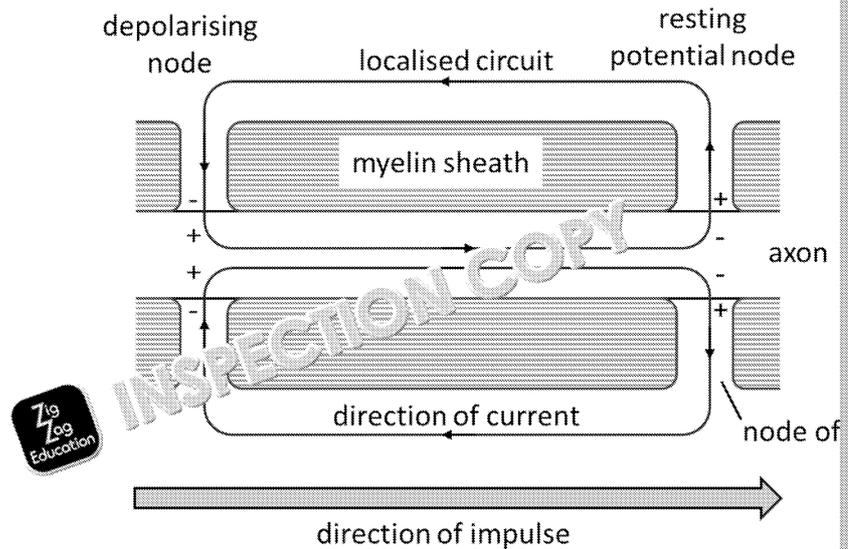


Figure F3.8. The myelin sheath insulates the neuron membrane, and each sheath is next to the next, leaving a gap called the node of Ranvier. This allows currents to create localised electrical impulses that jump along the axon, vastly increasing its speed.

Recall questions

1. State the neuron resting potential and describe how the membrane potential of the neuron changes during depolarisation, repolarisation and hyperpolarisation.
2. Explain the roles of the myelin sheath and the nodes of Ranvier.

The reflex arc

The reflex arc uses a shortened neural pathway to produce an extremely rapid, automatic response. It is vital in situations where conscious processing would take too long, potentially leading to delayed protection, such as withdrawing from a hot surface or a sharp object.

The basic principle of neuronal transmission still applies:

stimulus → receptor → sensory neuron → relay neuron → motor neuron → effector → response

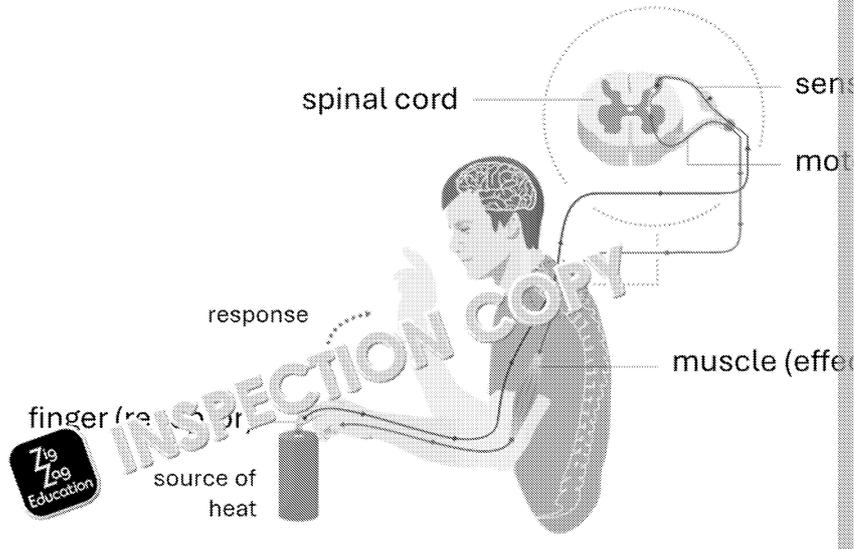


Figure F3.9. The reflex arc.

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However, reflex actions bypass conscious thought. Unlike typical voluntary responses, the brain, reflexes are hard-wired anatomically. The stimulus is detected by receptor sensory neurons to the spinal cord, where relay neurons connect directly to motor neurons for an immediate response from the effector (usually a muscle).

At the same time, a secondary signal is sent to the brain for processing, but this takes time to reach the brain. This is why your body moves to protect you before you are consciously aware of the speed of reaction over awareness of response.

Recall questions



1. Explain why the reflex arc leads to rapid, involuntary responses. Why is this an important survival response.
2. Describe how the brain is updated as part of the reflex arc. Why is it not included in the initial response.

Multiple sclerosis

Multiple sclerosis (MS) is a chronic, potentially life-limiting neurological condition of the central nervous system (CNS), specifically the brain and spinal cord, and the optic nerve. The immune system mistakenly attacks the myelin sheath, the protective insulating layer protecting nerve fibers. This leads to demyelination, inflammation and ultimately, to irreversible nerve damage.

Causes and risk factors

Although the exact cause is unknown, MS is believed to result from a combination of genetic and lifestyle factors, including:

- Autoimmune dysfunction: T cells and B cells target and damage myelin and neurons.
- Genetic predisposition: It is not directly inherited, but ~200 gene variants may increase susceptibility.
- Environmental triggers: Low Vitamin D levels due to reduced sun exposure, Epstein–Barr virus infection, and obesity are associated with increased risk.

Symptoms

MS symptoms vary depending on which regions of the CNS are damaged by the disease. However, symptoms may be grouped into functional categories:

Category	Common symptoms
Sensory	Numbness, tingling, burning, electric-shock sensations
Motor	Muscle weakness, spasms, tremors, difficulty walking
Visual	Blurred or double vision, optic neuritis (inflammation of the optic nerve)
Cognitive	Memory issues, poor concentration, slowed thinking
Autonomic	Bladder and bowel dysfunction, sexual problems, fatigue
Emotional	Depression, anxiety, mood swings, pseudobulbar affect (emotional outbursts unrelated to genuine feelings, and impaired emotional expression neural pathways)

Table F3.6. Common MS symptoms.

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Course and classification

MS is a condition involving the immune system. Symptoms may improve (remission) when immune activity and worsen (relapse) when inflammation escalates. The most common form is relapsing-remitting MS (RRMS) and follows this pattern of worsening symptoms followed by periods of remission.

Impact on saltatory transmission

Damage to the myelin sheath disrupts saltatory conduction. In MS, demyelination will force impulses to travel via slower non-saltatory conduction along parts of the axon. Fewer impulses 'jump' effectively between nodes, and the speed of transmission reduces. This leads directly to motor, sensory and cognitive symptoms, depending on which nerves are affected.

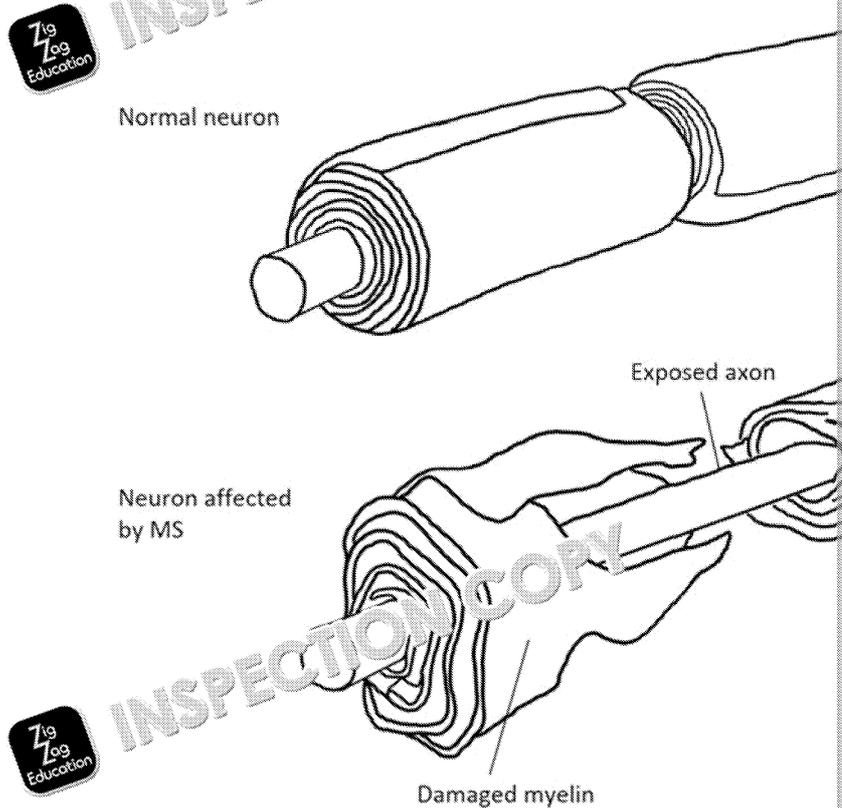


Figure F3.10. Multiple sclerosis is caused by damage to the myelin sheath which impairs saltatory conduction.

Recall questions

1. Describe the symptoms of multiple sclerosis depending on the extent of nerve damage and the different forms this illness may take.
2. Explain why damage to the myelin sheath causes these symptoms.

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Practice questions: The nervous system

1. The transmission of signals from the eye to the brain occurs extremely quickly along myelinated neuron axons. The distance is approximately 5.5 cm and the time taken is approximately 0.001 s.
 - a. Calculate the speed of transmission in metres per second (m/s). Give your answer to 2 significant figures.
Use the equation $speed = distance \div time$
 - b. Describe how a myelinated axon is structured [3].



3.2.2. The brain and spinal cord

The brain and spinal cord are the primary structures of the central nervous system, coordinating responses and maintaining communication across the body. Together, they form the central nervous system, which is the control centre for sensory processing, motor function, homeostatic regulation and reflex actions.

The brain contains distinct functional regions, each specialised for tasks such as sensory processing, interpretation, motor coordination, and memory formation. The spinal cord is part of the central nervous system, connecting the brain and the peripheral nervous system, and acting as a pathway for spinal reflex arcs.

This chapter explores the structure and function of the CNS, adding additional details to your understanding of the human body.

Structure and function of the brain

The brain contains an estimated 86 billion neurons, each forming connections with other neurons, creating a densely interconnected network. This makes anatomical interpretation of the brain a complex task, often requiring magnification.

Regions of the brain

The brain is divided into the left and right hemispheres, which are connected by the corpus callosum. Key functional areas include:

- **Cerebrum (cerebral hemispheres):**
The largest region; divided into lobes (frontal, parietal, temporal and occipital). Controls conscious thought, sensory perception, memory, emotions and voluntary movement.
- **Cerebellum:**
Located beneath the cerebrum. Coordinates balance, posture and fine motor control.
- **Medulla oblongata and brain stem:**
Includes midbrain, pons and medulla; forms the lower brain to spinal cord. Regulates vital functions, including breathing and heart rate, core body temperature and blood pressure.

Key regulatory centres include:

- **Hypothalamus:**
Monitors internal conditions such as blood pressure, core temperature and integrates signals from the nervous and endocrine systems.
- **Pituitary gland:**
Often referred to as the 'master gland', which responds to signals from the hypothalamus and secretes hormones that regulate growth, metabolism, reproduction and stress response.

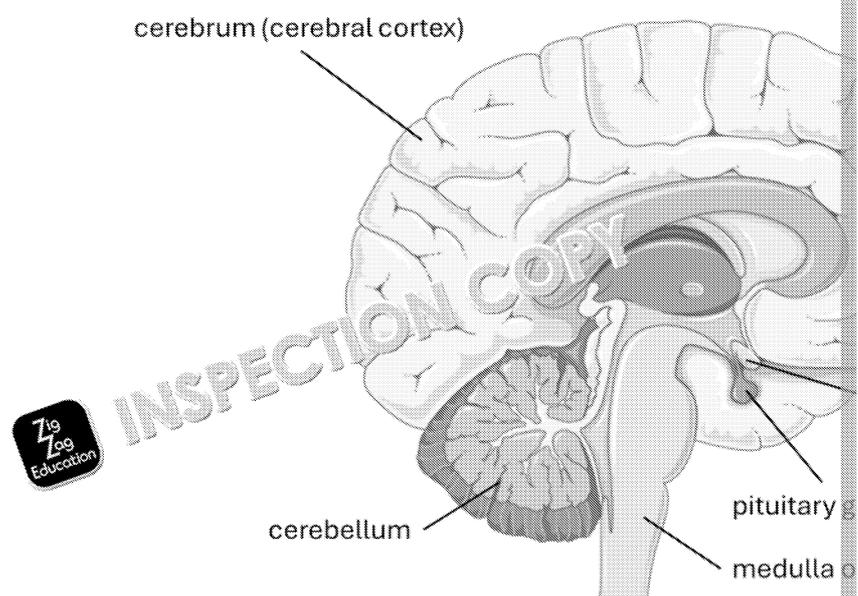


Figure F3.11. The areas of the brain.

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Protection and internal structures

The brain is encased within three protective membranes that also surround the spine collectively as the meninges. These layers prevent mechanical damage and infection, meningitis, which is why this is a medically critical condition.

The brain contains four interconnected cavities called ventricles that produce and circulate cerebrospinal fluid (CSF). This fluid cushions the brain against trauma, delivers nutrients and removes waste, regulates intracranial pressure and maintains chemical stability throughout the CNS.

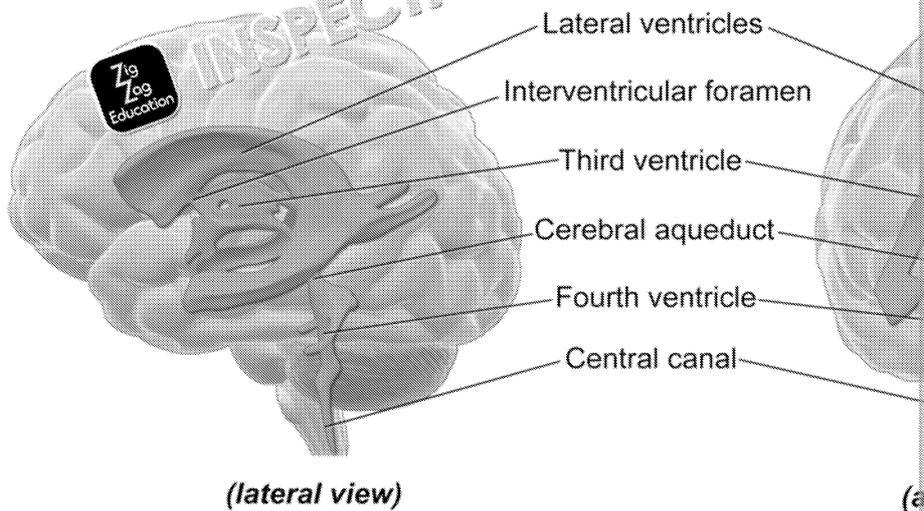


Figure F3.12. The brain has four interconnected ventricles that are filled with cerebrospinal fluid.

Interpreting brain scans

MRI or CT scans produce cross-sections of the brain that reveal internal brain structures.

In vertical sections (VS), slices are taken front-to-back, as if facing the patient. Early slices reveal the cerebral cortex, while deeper cuts reveal the cerebellum and brainstem near the base of the skull.

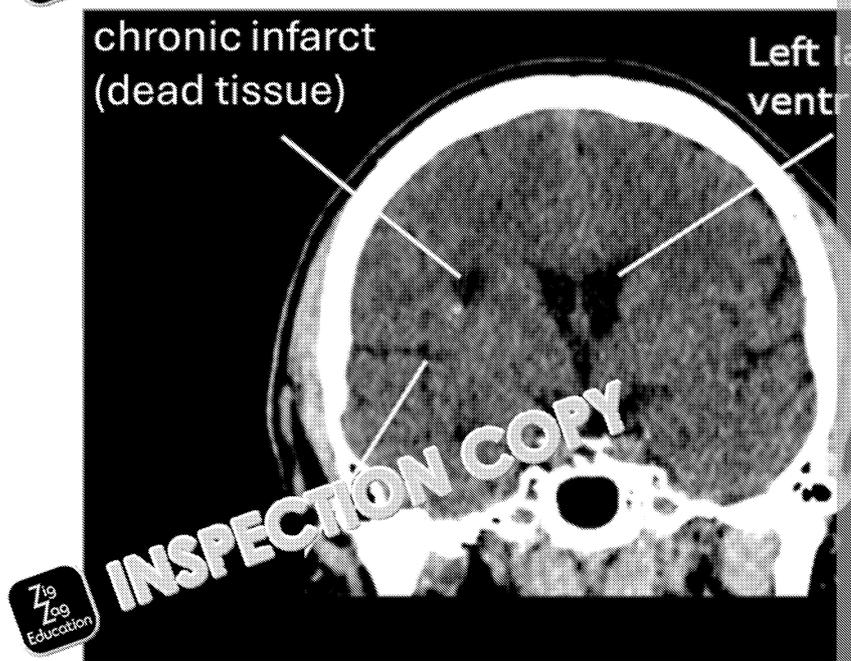


Figure F3.13. CT scan of brain showing a chronic infarct, as seen in a vertical section.

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In transverse sections (TS), images are taken from top-to-bottom, from crown to base of the cerebral cortex, followed by structures like the hypothalamus and pituitary, and so on. Deeper levels reveal the cerebellum then the medulla.

lesion (abnormal change or damage)

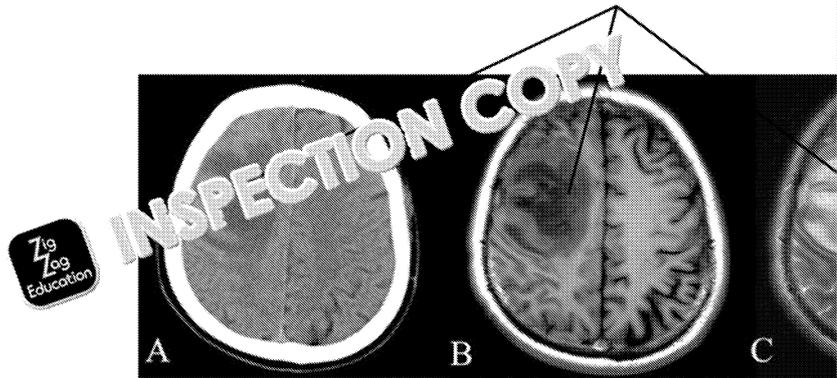


Figure F3.14. CT (image A) and MRI scans (images B and C) showing a lesion in the brain.

Understanding how anatomical regions appear in imaging supports clinical diagnosis of the structure of the brain.

Recall questions

1. State the regions of the brain and their overall functions.
2. Outline the protective internal structures of the brain and how they prevent damage.
3. Describe the difference between images taken of vertical and transverse sections of the brain.

Structure and function of the spinal cord

The spinal cord is a long, thin, tubular column of nervous tissue containing approximately 31 segments. It extends from the medulla oblongata at the base of the brain, down to the lumbar region of the vertebral column. As the central part of the CNS, it is the main route for sensory input, motor output, and coordination between the brain and the rest of the body.

Organisation

In adults, the spinal cord is protected by 31 vertebrae, grouped into five regions:

Region	Number of vertebrae	Location
Cervical (C)	8	Neck
Thoracic (T)	12	Upper back
Lumbar (L)	5	Lower back
Sacral (S)	5	Lower back/pelvis
Coccygeal		Coccyx

Figure F3.17. Details of the five regions of vertebrae.

Internal anatomy

A transverse section of the spinal cord reveals distinct features. The outer layer is the meninges, which contains myelinated axons grouped into ascending sensory, and descending motor tracts.

The central section is known as grey matter. This region contains neuron cell bodies. The dorsal (posterior, rear) horns for sensory processing, ventral (anterior, front) horns for motor processing, and lateral (side) horns for autonomic neurons in the thoracic and lumbar regions.

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Running through the grey matter is the central canal, which circulates cerebrospinal fluid and nourishes the spinal cord.

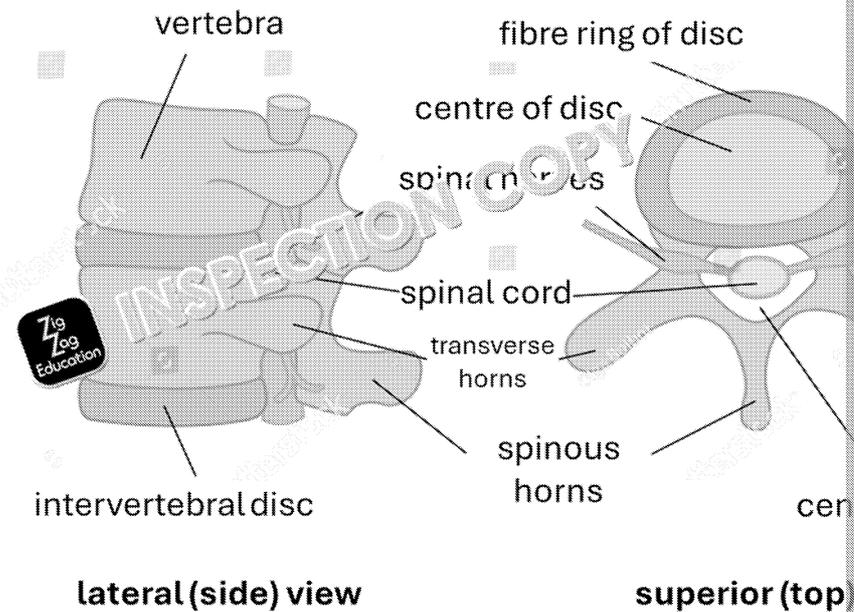


Figure F3.15. Spinal cord anatomy showing the vertebrae, nerves and intervertebral discs.

Protective structures

The spinal cord is protected by the vertebral column. This is a flexible, articulated bony structure that surrounds the spinal cord and protects it.

It is also protected by the meninges, which continue down the spinal column from the brain.

Interpreting spinal cord imaging

MRI and CT scans offer different cross-sectional views of the spinal cord.

In vertical sections, the spinal cord is viewed from front-to-back. This shows organs (e.g. lungs) plus spinal structures. It will show spinal cord anatomy, including white and grey matter, central canal, and vertebrae.

In transverse sections, the spinal cord is viewed from top-to-bottom, so images will show slices of the body, alongside bones, muscles and other soft tissues.



Figure F3.16. A cervical spine vertical MRI section showing a C4 fracture and spinal cord compression.



Figure F3.17. A transverse MRI section through the spinal cord.

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Sampling cerebrospinal fluid

Lumbar puncture is the primary method for obtaining cerebrospinal fluid (CSF) between the L3–L5 vertebrae, below the end of the spinal cord, to avoid damage to the spinal cord.

CSF testing can reveal neurological conditions that are not evident in blood or other body fluids because it crosses the blood–brain barrier. Therefore, it can support diagnosis of:

- Infections
 - Meningitis (inflammation of the meninges)
 - Encephalitis (inflammation of the brain)
 - Tuberculosis and other CNS infections
- Autoimmune disorders
 - Multiple sclerosis
 - Guillain-Barré syndrome (where the immune system attacks peripheral nerves)
- Bleeding
- Neurodegenerative and other conditions
 - CNS cancers
 - Alzheimer's disease

Recall questions

1. State the organisation and internal anatomy of the structures that protect the brain.
2. List some of the diseases that lumbar puncture can be used to diagnose. Describe how this procedure is completed.



Practical questions: The brain and spinal cord

1 Label the sections of the spinal column in the diagram. (4)

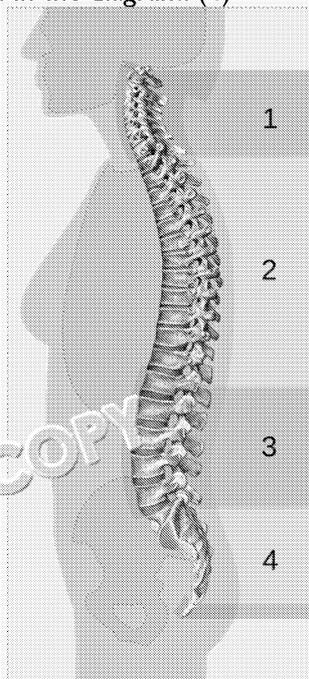


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3.3. Key concepts of reproduction

3.3.1. The reproductive system

Reproduction is the biological process by which genetic material is passed from one generation to the next. In humans, this occurs via sexual reproduction, where genetic information from two parents is combined to produce genetically diverse offspring. This diversity plays a crucial role in evolution and adaptation.

Successful reproduction involves several interconnected steps:

- The production of gametes (sperm in males and ova in females) – via meiosis, a process that halves the chromosome number.
- The union of gametes during sexual intercourse, leading to fertilisation.
- The specialised structures of the male and female reproductive systems, which facilitate the transport and fertilisation.
- In females, the ability to nurture the developing embryo and facilitate childbirth.

This chapter explores the anatomical features and physiological functions that underpin the processes of reproduction, laying the foundation for understanding fertility, pregnancy and developmental biology.

Female reproductive system

The female reproductive system matures during puberty. It typically remains reproductively active from the late teens to around age 50–55, between puberty and menopause – a period of roughly 30–35 years.

This system includes several highly adapted organs, each with specialised roles:

- ovaries – produce and release ova (egg cells); secrete reproductive hormones
- oviducts (fallopian tubes) – link ovaries to uterus for fertilisation
- uterus – muscular organ where foetal development occurs
- cervix – connects the uterus to the vagina; regulates access between internal and external environments
- vagina – muscular canal for intercourse and childbirth
- vulva – the external genital structures providing protection and sensory functions

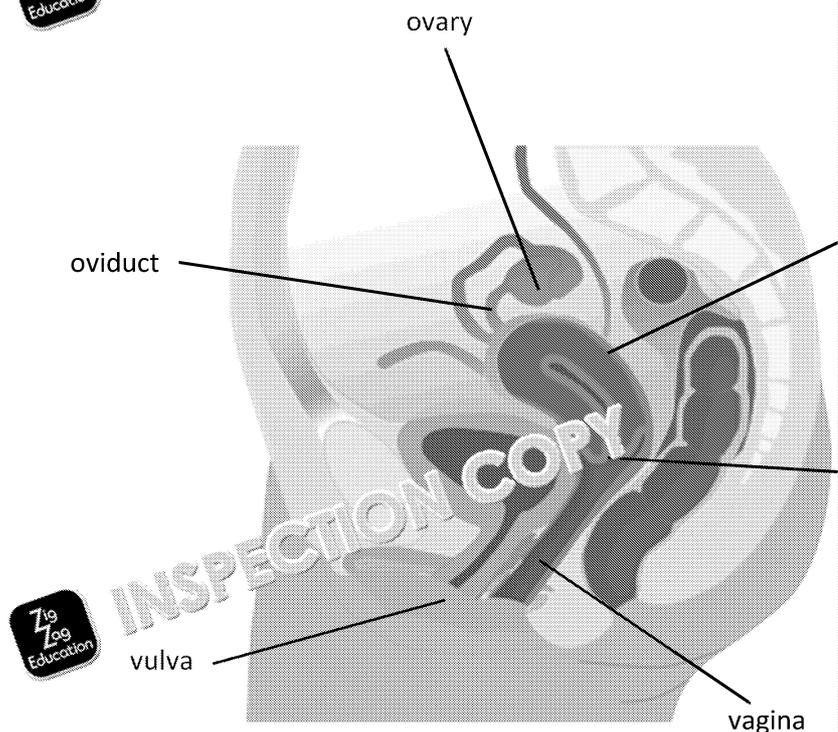


Figure F3.18. The female reproductive system.

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Ovaries

At birth, the ovaries contain approximately 1 million immature ova. From puberty, one typically matures per cycle and is released into the oviduct during ovulation.

The ovaries are also endocrine glands, secreting oestrogen and progesterone – the hormones of the menstrual cycle, support pregnancy and influence secondary sexual characteristics.

Oviducts (fallopian tubes)

Each oviduct is lined with ciliated columnar cells that assist in moving the ovum. Fertilisation usually occurs here, allowing the zygote to divide and develop into a blastocyst ready for implantation.

Uterus

The uterus is a muscular, pear-shaped organ capable of significant expansion during pregnancy. As it develops a thickened lining to support potential implantation. If fertilisation does not occur, hormonal changes trigger the shedding of this lining as menstrual blood flow.

Cervix

The cervix acts as a sphincter-like gateway between the uterus and vagina, regulating the flow of internal organs. During pregnancy, it remains tightly closed to maintain and protect the developing foetus. During labour, the cervix dilates to enable birth. It also produces mucus which change throughout the menstrual cycle to either hinder or enable sperm entry.

Vagina

The vagina is a highly elastic muscular canal that accommodates the penis during intercourse, allowing sperm to be deposited near the cervical opening. It is also the birth canal, stretching during childbirth. The vaginal environment is acidic, maintained by beneficial microbes.

Vulva

The vulva comprises the external genitalia, including the protective skin folds (labia) that contribute to sexual sensation, and plays a role in guiding the penis during intercourse.

Recall questions

1. Describe how the parts of the female reproductive system work together to enable the development of an embryo.
2. Explain how the vagina protects the other parts of the female reproductive system from pathogens.
3. Explain how the cervix maintains pregnancy and how it changes during labour.

Male reproductive system

The male reproductive system is responsible for the production, storage and delivery of sperm. It also functions as part of the endocrine system, producing testosterone, the male sex hormone.

The system matures during puberty and remains active throughout adult life. Sperm production, as spermatogenesis, continues from puberty until death, although both sperm count and motility decline with age.

Fertility also depends on successful sperm delivery to the female reproductive system, which can be affected by ageing, illness or hormonal factors.

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The male reproductive system comprises several key organs and glands, including:

- testes – produce sperm and secrete testosterone
- epididymis – sperm maturation and storage
- vas deferens – transports sperm to the ejaculatory ducts
- seminal vesicles – secrete fructose-rich fluid to nourish and add volume to semen
- prostate gland – adds enzymes and alkaline fluid to semen
- urethra – carries semen and urine out of the body
- penis – delivers semen into female reproductive tract during intercourse

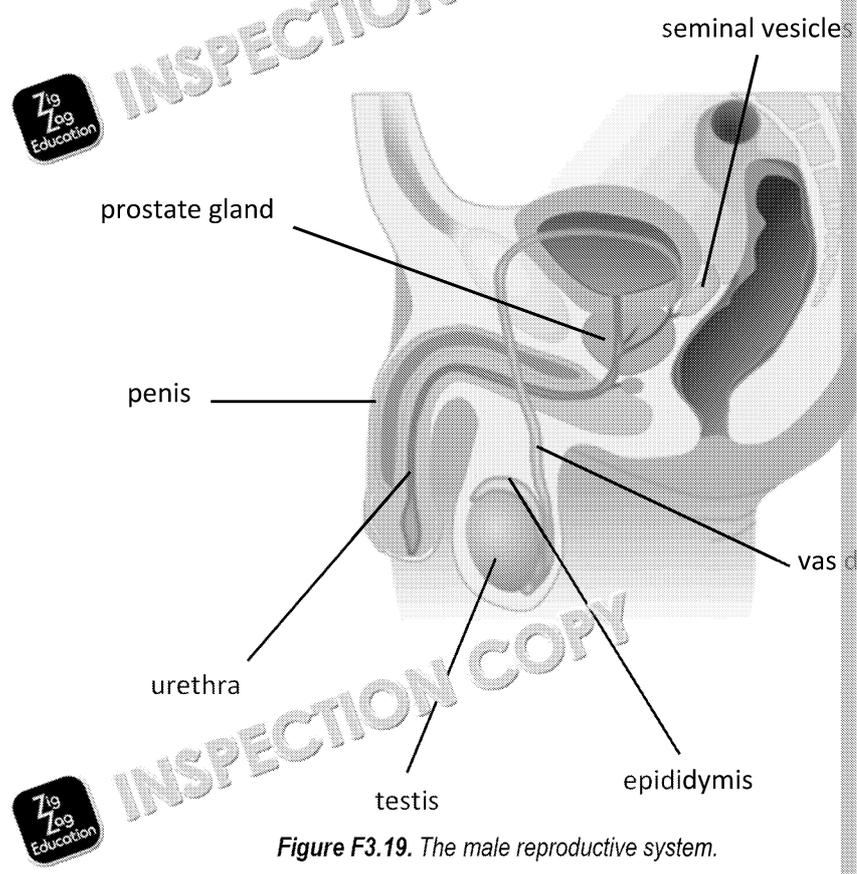


Figure F3.19. The male reproductive system.

Semen is the fluid ejaculated during sexual intercourse, and it consists of two main components:

- Sperm – makes up 5–10 % of the total semen volume.
- Accessory fluids – comprises the remaining 90–95 % of semen and includes secretions from the seminal vesicles and prostate gland. This:
 - provides nutrients (e.g. fructose) for aerobic respiration for sperm motility
 - creates an alkaline environment to neutralise vaginal acidity
 - adds enzymes and mucus to aid sperm transport and survival

Testes

The testes (singular: testis) contain tightly coiled seminiferous tubules where sperm are produced. Surrounding these are interstitial (Leydig) cells, which secrete testosterone. This hormone maintains male characteristics and maintains sperm production.

The optimum temperature for sperm production is 2–3 °C lower than the body's average 37 °C. This is because higher temperatures can impair sperm count, motility and survival. The testes are located outside the body in the scrotum to maintain a cooler environment.

Epididymis

Immature sperm, called spermatids, travel from the seminiferous tubules into the epididymis, a long, thin, coiled tube located behind each testis. Sperm mature and are stored here until ejaculation.

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Vas deferens

The vas deferens is a thick-walled duct made of smooth muscle that moves sperm towards the urethra using peristaltic contractions (similar to contractions through ejaculation).

Seminal vesicles

The seminal vesicles are glands that secrete a fructose-rich fluid that enables sperm movement and contributes significantly to semen volume. These secretions mix with the prostate.

Prostate gland

The prostate gland adds enzymes and alkaline fluid to semen, which enhances sperm motility and the survival of sperm in the acidic environment of the vagina and optimising conditions for sperm survival.

Urethra

The urethra is a shared passageway for urine and sperm, but not simultaneously. Mechanisms prevent urine flow by closing off the bladder neck, ensuring only sperm can pass.

Penis

The penis is an external organ composed of erectile tissue. During arousal, it becomes erect, and enables penetration of the vagina to deposit sperm near the cervix. The centre of the penis and ejects semen at high speed during ejaculation.

Recall questions

1. Describe the contents of semen and the process and hormones involved in order to create it.
2. Describe the functions of the hormone testosterone.
3. Explain why the testes hang outside the body.

Intersex individuals

Intersex individuals are born with biological sex characteristics, such as chromosomal variations, hormone levels or external genitalia, that do not fit the typical definitions of male or female. They may be visible at birth, emerge during puberty, or remain undetected without medical intervention.

Intersex variation reflects the natural diversity of human development and maps onto the following categories:

- chromosomal variation, where individuals have unusual chromosomal patterns
- ovary or testes (gonads) differences
- genital anatomical alterations
- hormonal pattern differences

Chromosomal variations

These involve atypical combinations or structures of sex chromosomes, including:

- XXY – Klinefelter syndrome
Individuals typically have small testes and undescended testicles. They have reduced fertility and may experience hormone imbalances.
- XO – Turner's syndrome
Affects females, who have a single X chromosome. Common features include short stature, and distinct physical features such as a webbed neck, low-set ears, and usually impaired hearing.
- Mosaicism – some cells XY, some XX, or other combinations
This arises through errors in mitosis after fertilisation and can result in a variety of hormonal outcomes.

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Gonad differences

Gonad differences may include a combination of ovarian and testicular tissue (ovotestes), undescended or absent testes, or underdeveloped or non-functional gonads. Gonad structure influences hormone production and reproductive potential.

Genital anatomical differences

These may present as ambiguous genitalia, such as an enlarged clitoris, or micropenis, which involve the atypical placement of the urethra. In the condition hypospadias, the urethra is located on the underside of the penis, rather than at the tip.

Some individuals may have internal reproductive structures that differ from their external genitalia. For instance, in androgen insensitivity syndrome, individuals with XY chromosomes develop female external genitalia but internally possess undescended testes, and lack a uterus or ovaries. In Müllerian duct syndrome, individuals with male external genitalia may retain female internal structures such as a uterus and oviducts.

Hormonal pattern differences

These involve disruptions in hormone production or receptor function. Androgen insensitivity syndrome occurs when the body does not respond to male hormones (androgens), leading to feminized characteristics. Congenital adrenal hyperplasia develops when there is excess androgen production, which can lead to masculinized characteristics and may cause external genitalia to have masculine features.

Sex, gender and developmental complexity

Sex refers to biological traits, such as chromosomes, hormones and anatomy that an individual has, whereas gender refers to identity and social roles that the individual adopts, which may or may not align with their biological sex. Intersex individuals may identify as male, female, non-binary or as a combination of these, while non-intersex people do not.

Human reproductive development is a complex, multi-step process. All embryos begin to develop both male and female anatomy. The presence of testosterone promotes male development, while its absence leads to the formation of female structures. Therefore, disruptions in hormone production, sensitivity or gene expression can lead to mixed or atypical development pathways, resulting in intersex variations.

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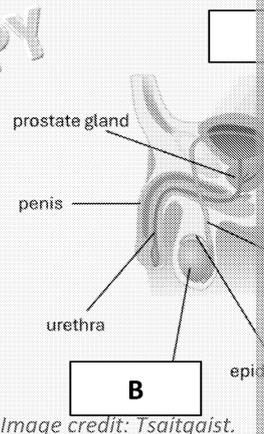
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Recall questions

1. List the main types of intersex variations, and describe how they relate to an individual's chromosomes, gonads, and external genitalia.
2. Describe how androgen insensitivity syndrome influences the development of sex characteristics in individuals with XY chromosomes.
3. Describe the difference between biological sex and gender, and how these concepts relate to the experiences of intersex individuals.

? Practice questions: The reproductive system

1. Add the missing labels to the male reproductive organ diagram. (3)



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3.3.2. Hormonal control of gametogenesis

Gametogenesis is the biological process by which gametes – ova and sperm – are produced. Its core mechanism involves chromosomal reduction, gametogenesis is also a cyclical process, influenced by signals from multiple endocrine glands.

In females, this regulation is orchestrated by four key hormones – follicle-stimulating hormone (FSH), luteinising hormone (LH), oestrogen and progesterone. These hormones follow a cyclical pattern of concentrations, guiding the maturation of ova, ovulation, and the preparation of the uterine lining for potential embryonic development.

In males, testosterone plays a dominant role in maintaining spermatogenesis and contributing to the development and maintenance of secondary sexual characteristics. FSH and LH also play roles in male reproductive health.

This chapter explores the interplay between hormones and gamete production mechanisms, physiological changes, and the hormonal basis of reproductive health.

Role of hormones in female reproduction

During foetal development, approximately 1 million immature ova (primary oocytes) enter prophase I, remaining dormant until puberty. From the onset of the menstrual cycle, a regular hormonal cycle causes the maturation of ova, ovulation, and preparation for implantation and embryonic development.

Hormonal control during puberty

The onset of puberty is driven by increased secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus, which stimulates the pituitary gland to release FSH and LH. These hormones then stimulate the ovaries to produce oestrogen and progesterone.

Oestrogen promotes the development of secondary sexual characteristics including:

- development of breasts
- widening of hips
- production of pubic and axillary (armpit) hair
- initiation of menstrual cycle

Progesterone supports the maturation of the uterus.

Hormonal regulation of the menstrual cycle

The menstrual cycle is governed by the interplay of four key hormones:

Hormone	Source	Function
Follicle-stimulating hormone (FSH)	Pituitary gland	Stimulates follicle development and oocyte production
Luteinising hormone (LH)	Pituitary gland	Triggers ovulation and formation of the corpus luteum
Oestrogen	Developing follicles in the ovary	Thickens uterine lining and stimulates LH surge
Progesterone	Corpus luteum	Maintains uterine lining for implantation

Table F3.8. Source and functions of the four key menstrual hormones.

This hormonal feedback creates a cyclical process, typically resulting in the release of one ovum per cycle, and the development of a thickened uterine lining that is suitable for implantation.

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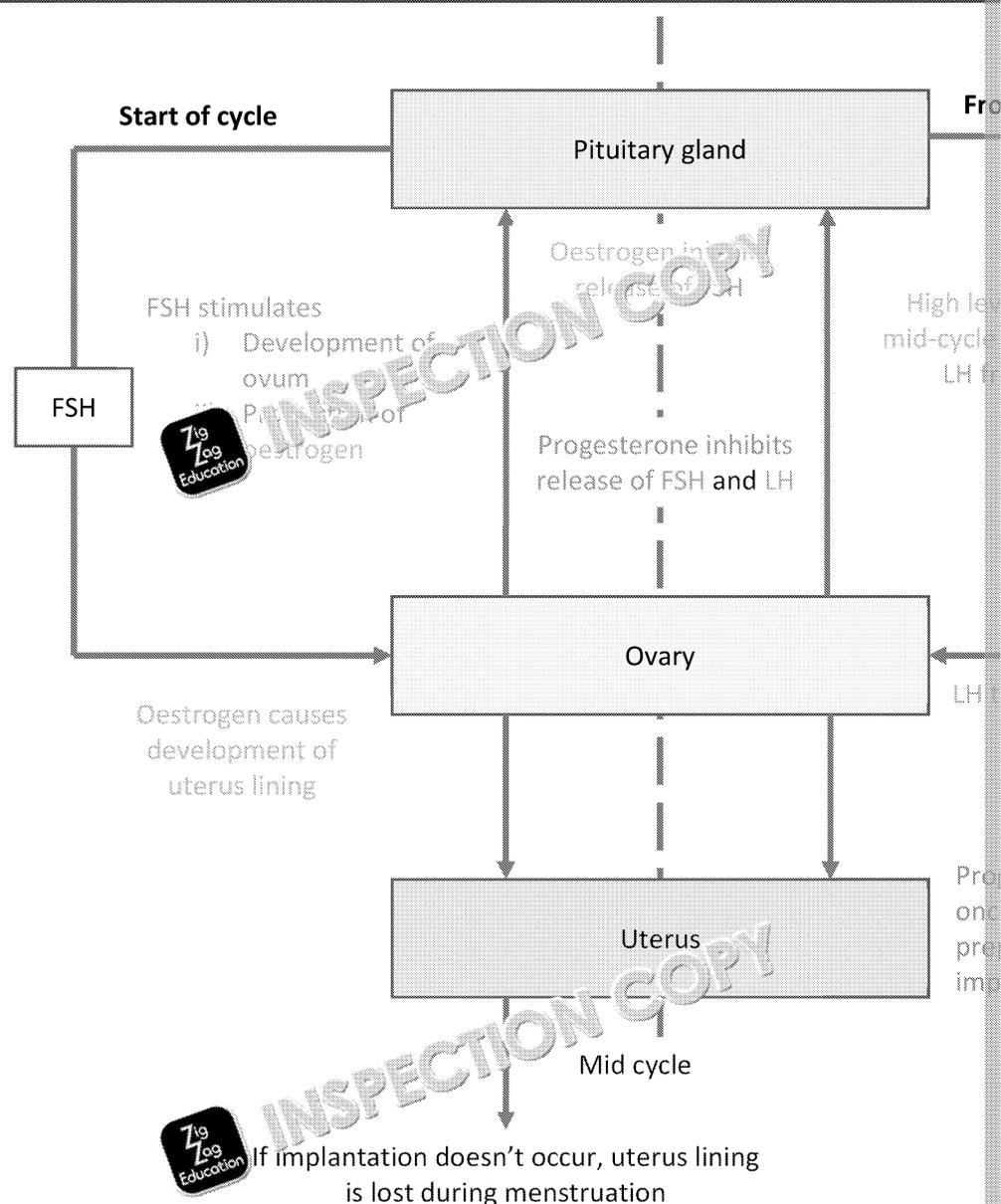


Figure F3.20. Hormonal regulation of the menstrual cycle.

Follicle-stimulating hormone (FSH)

FSH is released from the start of the menstrual cycle by the pituitary gland. It stimulates **follicle** maturation and the secretion of oestrogen.

Oestrogen

Release of oestrogen from the maturing follicle is stimulated by FSH. Oestrogen promotes development of the uterine lining, but as oestrogen levels increase, it inhibits FSH.

Luteinising hormone (LH)

High levels of oestrogen at mid-cycle cause a surge of luteinising hormone (LH) from the pituitary gland. This induces ovulation and corpus luteum formation.

Progesterone

Progesterone is initially secreted by the ovaries and then by the corpus luteum – the structure that remains after ovulation. Progesterone inhibits the release of both FSH and LH which maintains the uterine lining for implantation.

If fertilisation does not occur, progesterone levels decline, leading to menstruation.

However, if implantation does occur, progesterone levels remain high to support pregnancy and further ovulation.

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Role of hormones at fertilisation

During fertilisation, progesterone is released by cells that surround the ovum. It attracts sperm to the ovum. Progesterone also enhances motility by attaching to channels in the sperm, which is crucial for successful penetration.

Once a sperm has attached to the ovum, enzymes in the sperm acrosome digest the zona (see Ova, page 10). Granules in the ovum release enzymes to prevent multiple fertilisation (polyspermy). Fertilisation triggers mitotic division, which forms a ball of cells called a morula, which implants into the uterine lining a few days after fertilisation.

Hormonal regulation during pregnancy

Through pregnancy, levels of progesterone remain high. This maintains the corpus luteum and LH production, preventing further ovulation.

Other hormones are essential for successful pregnancy. Human chorionic gonadotropin (hCG) is produced by the developing placenta. This maintains the corpus luteum during early pregnancy progesterone production; both hormones are essential for maintaining the uterine lining. hCG is also used in pregnancy tests as it is present from very early pregnancy in detectable quantities.

Oestrogen stimulates uterine expansion and prepares the body for labour and **lactation**. Human placental lactogen (hPL) supports mammary gland development, critical for lactation after birth, and adjusts maternal metabolism to support foetal development.

Lastly, once the placenta is formed, placental growth hormone replaces maternal growth hormone to support foetal development.

Hormonal control during birth

Towards the end of pregnancy, progesterone levels decline, which removes inhibition on uterine contractions.

Another hormone, oxytocin, released from the posterior pituitary gland, causes positive feedback during the birth cycle, causing contractions to intensify as labour progresses.

In addition, the hormone relaxin is produced by the placenta and the corpus luteum, which loosens ligaments in the pelvis, facilitating birth.

Evolutionary reasoning for periodic ovulation

In mammals, ovulation occurs at regular intervals, and in humans this typically occurs every 28 days. This periodicity reflects evolutionary compromises, balancing the need for regular reproduction against the substantial metabolic and physiological costs of reproduction.

Female reproduction requires the coordinated action of multiple hormones, signalling pathways, and tissue development to support follicle maturation, ovum release and uterine preparation. This coordination ensures that these processes are only activated when conditions are favourable.

Furthermore, embryonic survival depends not only on ovum availability but also on the internal environment. Cyclical coordination between ovulation and the development of the uterine lining can occur under optimal conditions, improving reproductive efficiency.

In species with long **gestation** periods and postnatal care, like humans, continuous ovulation would increase the risk of simultaneous pregnancies. This is unsustainable because of the physical demands of carrying a foetus and the high level of care required after birth for the baby.

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Periodic ovulation also influences behavioural patterns. In humans and several other species, changes around ovulation slightly alter mood, scent and physical appearance, which helps to attract mates and increase mating success.

Humans have evolved to produce fewer offspring with a higher probability of survival. This strategy is supported by controlling the number of ova released, restricting the period of availability, and regulating hormones to align maturation with oestrus, lactation and so on. These features maximise the success of each reproductive event while conserving biological resources.

Recall question



1. List the four key reproductive hormones and state where they are produced and their main roles.
2. Describe how the four key hormones interact to regulate the menstrual cycle and ovulation in females.
3. Describe how hormones support pregnancy and how they change during gestation at each stage.
4. Describe the evolutionary advantages that periodic ovulation provides.

Role of hormones in male reproduction

The process of spermatogenesis starts at the onset of puberty and continues throughout life. It is regulated by the interaction of hormones from the hypothalamus, pituitary gland and testes.

Hormonal control during puberty

Puberty begins when the hypothalamus increases secretion of gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

FSH and LH act on the testes, which then secrete testosterone, initiating the development of male sexual characteristics:

- deepening of the voice due to growth of the larynx (voice box)
- production of pubic, axillary and facial hair
- enlargement of the penis and testicles
- increased muscle mass and bone density
- broadening of the shoulders

Hormonal role in spermatogenesis

Spermatogenesis requires the coordinated action of FSH, LH and testosterone:

- FSH stimulates cells in the seminiferous tubules to support sperm cell maturation. These cells release a hormone called inhibin, which provides negative feedback, inhibiting production of FSH, thus regulating FSH levels.
- LH stimulates Leydig cells to produce testosterone. Testosterone promotes spermatogenesis and maintains sex drive and secondary sexual characteristics.

To produce sperm, stem cells lining the seminiferous tubules of the testes undergo mitotic divisions to expand their population. Some of these cells then differentiate into primary spermatocytes, which enter meiosis:

- Meiosis I forms two primary spermatocytes (23 chromosomes).
- Meiosis II forms four spermatids, each genetically unique due to crossing over and independent assortment.

Spermatids travel to the epididymis, where they transform into mature spermatozoa. They are stored for up to several weeks.

This process produces large quantities of sperm, each genetically distinct from each other.

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Evolutionary reasoning for continuous sperm production

Continuous sperm production reflects an evolutionary strategy where sperm production (egg cell production), requires less energy, fewer nutrients and fewer hormones to produce millions of sperm daily throughout adult life.

Male fertility benefits from being unrestricted by reproductive cycles. In human reproduction is regulated by female physiology, due to the greater demands of postnatal care – the majority of resources are invested in the female.

As a result, the male strategy of continuous sperm production increases the likelihood that males can father multiple offspring.

This evolutionary pattern has further selected traits such as high sperm counts, competitive behaviour, and secondary sexual characteristics, including muscular development and hair, which shape sexual selection and competition for mates.

Together, these adaptations reflect a reproductive model adapted for maximising reproductive success while minimising resource and energy requirements per gamete.

Recall questions

1. List the main hormones involved in male sexual development, where they are produced and their main roles.
2. Describe how these hormones work together to regulate male sexual development.
3. Describe the process of spermatogenesis and explain why sperm production is significant.
4. Outline the evolutionary advantages that continuous sperm production offers males in terms of reproductive success.

Role of hormones in intersex individuals

Hormones play a central role in shaping the development and physiology of intersex individuals. The effects of hormones depend not only on their levels, but also on the existing gonad structure and receptor sensitivity. In intersex individuals, the type and responsiveness of gonadotropin receptors and how they act (see page 148).

Recall questions

1. Describe why the hormones produced and the effects of these hormones differ in intersex individuals.

3.3.3. Reproductive changes during ageing

Ageing brings a range of physiological changes, including slower tissue repair, and changes in hormone regulation. As the body becomes less capable of supporting gestation in females, biological mechanisms have evolved to limit reproduction to the most favourable conditions.

In females, menopause marks the end of natural fertility, reflecting a shift towards survival over continued ovulation. This enables females to support others in pregnancy and childcare.

Male reproductive function also declines with age, though less abruptly. Changes in hormone levels, lower testosterone levels, affecting sex drive and sexual function, and enlargement of the prostate gland, which can impair both ejaculation and urination.

This chapter explores how reproductive systems change through ageing and how these changes contribute to overall biological and evolutionary fitness.

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Menopause

Menopause is defined as the permanent ending of menstruation, diagnosed after 12 months without a period. It typically occurs between the ages of 45 and 55, with an average age of 51.

It is caused by ovarian ageing and hormonal changes. Specifically, a decline in the number of ovarian follicles, and the reduction in secretion of oestrogen and progesterone.

Symptoms of menopause vary, but include hot flushes and night sweats, vaginal dryness, joint pain and osteopenia, thinning hair and skin. These symptoms can be managed by lifestyle changes, including hormonal, non-hormonal and surgical approaches.

Hormone replacement therapy (HRT) replaces declining oestrogen and progesterone, which can help with hot flushes, vaginal dryness and mood changes. It also helps prevent osteoporosis but may increase the risk of breast cancer, blood clots and stroke, depending on the type of therapy and for how long it is used.

Non-hormonal therapies include antidepressants to help control mood and hot flushes, and vaginal lubricants for dryness.

Surgical responses seek to preserve and reimplant ovarian tissue, thus delaying menopause and hormone production, but is experimental.

Lifestyle interventions like a well-balanced diet, sufficient exercise, and stopping smoking can help delay the timing of menopause and the severity of symptoms.

Your turn

1. State the average age at which menopause typically occurs and the conditions that must be met for menopause to be diagnosed.
2. Describe the main physical and hormonal changes that occur during menopause and how they affect the body.
3. Discuss the benefits and potential risks associated with hormone replacement therapy for the management of menopause symptoms.

Pregnancy later in life

In Britain, the trend over recent decades has been towards delayed parenthood. The average age of mothers in the UK has risen from approximately 23 years in the 1950s, to 29.2 years in 2014. In 1950, the average number of children per woman was around 2.4, but this has fallen to 1.7 in 2014. This pattern is mirrored across many developed nations.

Risks associated with later pregnancy

Pregnancy at older maternal ages is associated with increased risks, including:

- reduced fertility due to declining egg quality and quantity
- higher chance of miscarriage
- increased likelihood of complications during pregnancy, such as gestational diabetes, preeclampsia and foetal chromosomal abnormalities (e.g. Down's syndrome)
- greater chance of delivery by Caesarean section, which carries greater risk than vaginal birth, and a longer recovery time and temporary impairment of mobility and function while the surgery heals
- lower energy levels, which can affect day-to-day caregiving

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Advantages of later parenthood

Despite the risks, later-life parenting offers several potential benefits:

- emotional maturity and a greater psychological readiness
- stable relationships and increased likelihood of co-parenting support
- financial security, which makes childcare, education and enrichment activities easier to manage
- life experience, which may enhance resilience and problem-solving in parenting
- cognitive stimulation, which may lead to improved verbal memory and executive functions, helping to manage the demands of parenting

Recall questions



Describe some potential advantages and disadvantages of becoming a parent later in life, and how this might impact family dynamics.

Changes in the male reproductive system

As males age, the reproductive system undergoes gradual structural and functional changes. Similar to the hormonal shifts of female menopause, male reproductive ageing is typically slow and does not significantly affect fertility, sexual function, and urinary health.

One notable change is a reduction in testicular volume and the number of Leydig cells, leading to lower levels of testosterone. From around the age of 30, testosterone levels decline at an average rate of 1% per year, contributing to several effects. Along with fewer germ cells (cells that give rise to sperm), declining testosterone slows spermatogenesis, leading to reduced sperm count and motility.

Damaged DNA in sperm increases with age, raising the risk of miscarriage and chromosomal abnormalities such as Achondroplasia (unusually short stature), autism spectrum disorders, and Down syndrome. This risk is also associated with increased paternal age.

Declining testosterone levels may reduce libido and impair sexual function. Additionally, decreased blood flow to the penis, which also increases ejaculation time, can contribute to these issues.

In addition, the epididymis and vas deferens lose elasticity, reducing the efficiency of sperm transport. This, along with reduced semen volume, contributes to reduced fertility.

Prostate hypertrophy

Benign prostatic hyperplasia (BPH) affects about one in every two men over the age of 50. It is characterized by hypertrophy (excessive growth) of prostate tissue, leading to enlargement of the prostate gland. This enlargement can compress the urethra, resulting in urinary symptoms such as difficulty starting urination, a weak urine stream and incomplete bladder emptying, causing more frequent urination.

An enlarged prostate may also reduce semen flow, or cause dry ejaculation, where little or no semen is released. Additionally, it may increase the risk of urinary tract infections, due to the bacteria that can colonise the urethra. In severe cases, this can lead to kidney complications, as urine backs up into the bladder and ureter.

Recall questions



1. State the population frequency and approximate age of onset of benign prostatic hyperplasia (BPH).
 2. Describe the symptoms and possible complications of BPH in ageing males.
- Explain how age-related changes in the male reproductive system affect fertility and sexual function.



Practice questions: Reproductive changes during ageing

1. Analyse the advantages and disadvantages of becoming a parent later in life.

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Topic 4: Basics of microbiology

4.1. Microbes

4.1.1. Features of bacteria found in human

Certain species of bacteria can colonise various niches of the human body, sometimes causing disease. However, not all bacteria are harmful, and many have essential roles in digestion and maintaining a healthy microbiome.

A deeper understanding of bacterial structure and function helps us to interpret how bacteria cause disease, how to diagnose after infection, and determines which treatments are likely to be most successful. This section explores the key features of bacterial cells and how they are classified.

Cell components of bacteria

Bacterial cells consist of several components, although not all features are present in all bacteria. Each component has a specific role in the survival, adaptation, and reproduction of the cell.

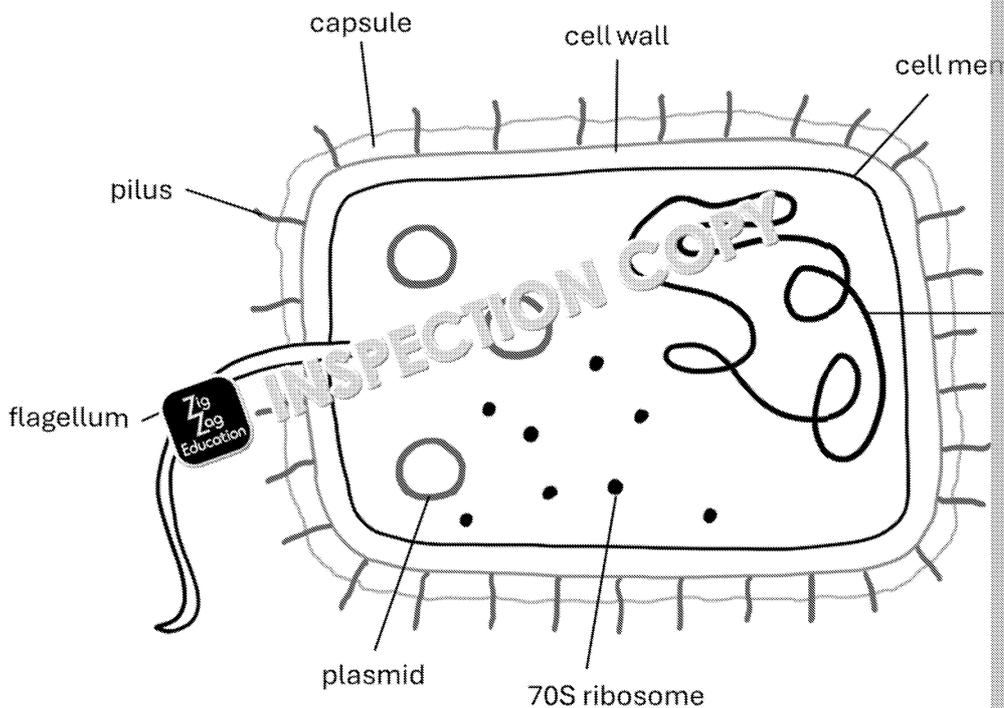


Figure F4.1. Prokaryotic subcellular structure.

Capsule / Slime layer

Some bacteria produce an outer capsule or slime layer. This provides protection against immune responses and helps adhere to surfaces.

Peptidoglycan cell wall

The bacterial cell wall, made up of peptidoglycan, provides mechanical strength. It protects against environmental fluctuations in pH, water availability and salinity. Gram-positive (pages 158–159) bacteria differ in wall thickness and membrane structure.

Cell surface membrane

Located beneath the cell wall, this phospholipid bilayer contains embedded proteins that facilitate nutrient uptake, waste removal, and intercellular signalling. It also facilitates attachment to host cells.

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Cytoplasm

The cytoplasm is the site of metabolic activity. It contains water, dissolved solutes, and enzymes. It is the site of many reactions, including respiration and biosynthesis.

70S ribosomes

Bacterial ribosomes, which are smaller (70S) than those in eukaryotes (80S), catalyze the translation of mRNA into polypeptides. Their similarity to 80S ribosomes found in eukaryotes supports endosymbiotic theory.

DNA loop

Bacterial DNA forms a single circular chromosome located in the nucleoid region of the cell. Genes are arranged in loops for transcription and replication.

Plasmids

Plasmids are small circular DNA fragments carrying non-essential but advantageous genes, such as antibiotic resistance. They are widely used in genetic engineering due to their ease of manipulation.

Mesosomes

Mesosomes appear as membrane infoldings in electron micrographs but are likely to be **artefacts** from sample preparation. Historically, they were considered functional structures, but their existence and function are now debated.

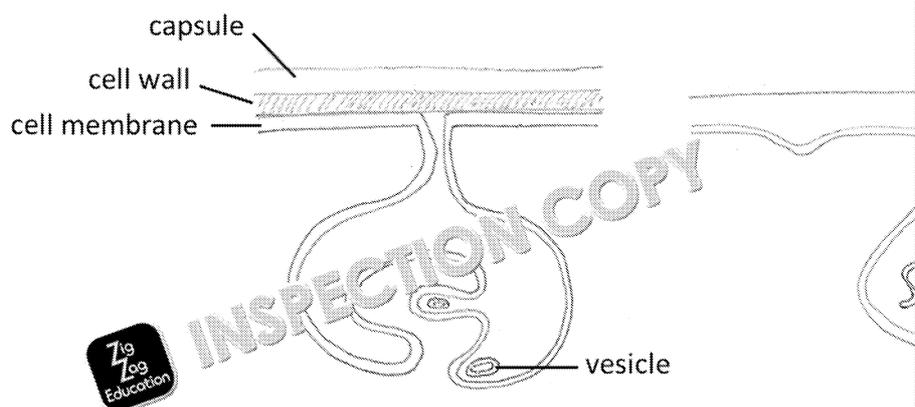


Figure F4.2. Mesosomes appear as membrane infoldings but are likely to be artefacts from sample preparation.

Rotary-like flagellum

Flagella are very fine threads called filaments, driven by a rotatable motor embedded in the cell wall, which enables motility without the 9+2 microtubules structure seen in eukaryotic cilia and flagella.

Gram staining

Gram staining is a staining technique used to classify bacteria based on the cell wall structure. Gram-positive and Gram-negative bacteria differ in their appearance under the microscope and their susceptibility to antibiotics.

Gram-positive bacteria

Gram-positive bacteria have a thick peptidoglycan-rich cell wall with very little lipid content. This retains the crystal violet stain, causing the cells to appear purple or blue under a light microscope. These bacteria are usually susceptible to the antibiotic penicillin, which inhibits peptidoglycan synthesis. Common examples include *Bacillus*, *Clostridium*, *Staphylococcus* and *Streptococcus*.



Figure F4.3. A micrograph of *Bacillus anthracis* bacteria.

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Gram-negative bacteria

Gram-negative bacteria have thinner peptidoglycan walls, but a high lipid content in membrane, similar to the inner cell membrane.

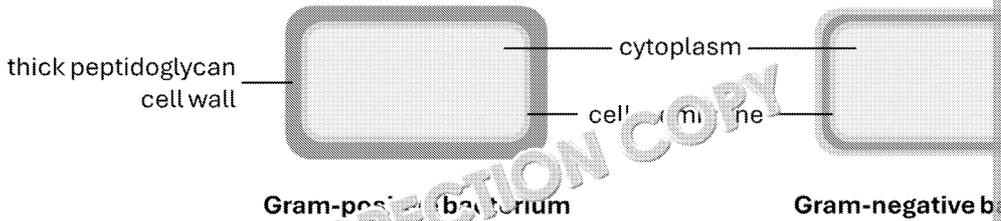


Figure F4.4. Diagram illustrating the differences in the cell wall and membranes of Gram-positive and Gram-negative bacteria.

As a result, the crystal violet stain is lost during alcohol wash, and a second counterstain, typically safranin, is used to stain them red or pink (see Staining specimens, page 22). These bacteria are resistant to penicillin because of their cell wall so other antibiotics must be considered. Examples include *Salmonella*, *Escherichia* and *Azotobacter*.

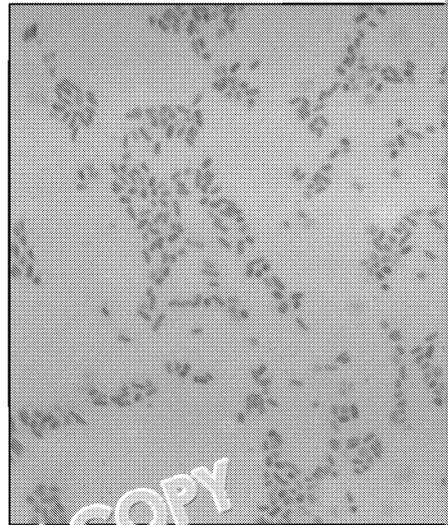


Figure F4.5. A photomicrograph of *Bacteroides fragilis* ss. *vulgatus*.

Classification of bacteria

Bacteria are classified based on their **morphology**, specifically the shape and arrangement of their cells:

- Coccus (plural: cocci) – spherical or oval
- Bacillus (plural: bacilli) – rod-shaped
- Spiral – twisted or curved

This allows identification and understanding of their environmental adaptations and behaviour, and to quickly determine their pathogenic significance.

Cocci

Cocci bacteria are spherical or oval, and may be arranged individually (*Monococcus*), in pairs (*Diplococcus*), in chains (*Streptococcus*), or in clusters (*Staphylococcus*) like grape bunches.

These bacteria are often involved in respiratory, skin and bloodstream infections, and include *Streptococcus pneumoniae*, which causes pneumonia, and *Staphylococcus aureus*, responsible for many infections including skin infections, sepsis and toxic shock syndrome (a rare but serious condition often associated with prolonged use of menstrual tampons).

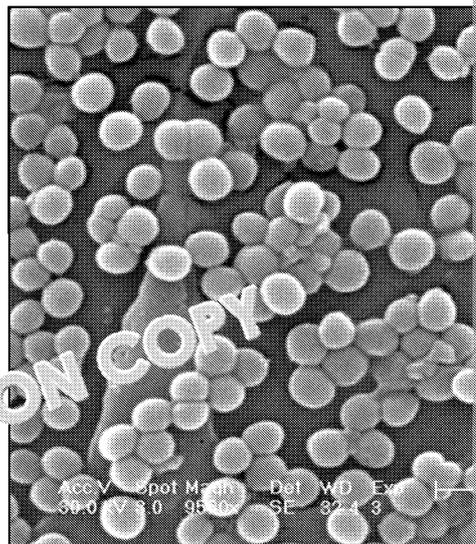


Figure F4.6. Scanning electron micrograph of *Staphylococcus aureus* (MRSA) bacteria.

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Bacilli

Bacilli bacteria are rod-shaped and may be found individually or in chains. They are found in gut flora (*Bacillus subtilis*), but some species cause food poisoning (*Escherichia coli*) or anthrax (*Bacillus anthracis*).

Spiral

Spiral bacteria may form rigid spirals with external flagella (*Spirillum*) or flexible spirals with internal flagella (*Coccobacillus*), or comma-shaped (*Vibrio*).

These bacteria are often motile because of the presence of flagella, and are associated with chronic infections, such as syphilis (*Treponema pallidum*) and cholera (*Vibrio cholerae*).

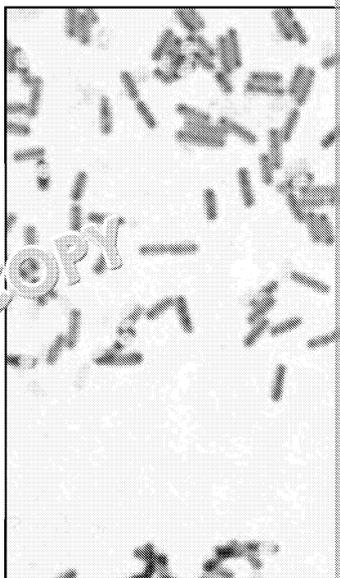


Figure F4.7. Light micrograph of bacteria.

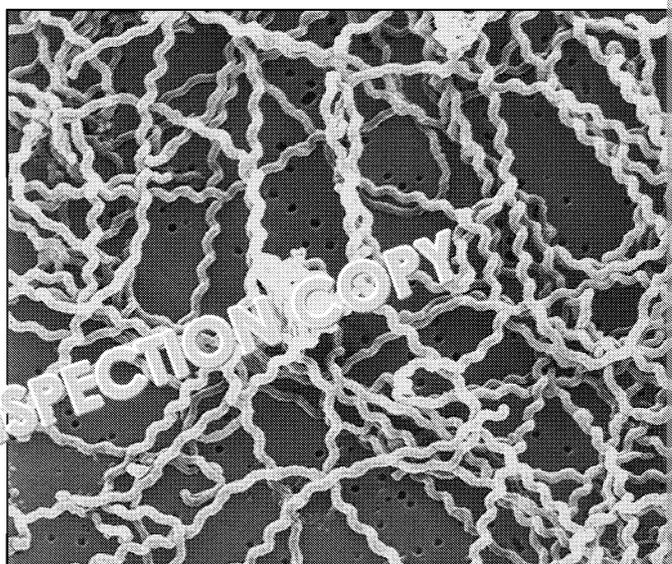
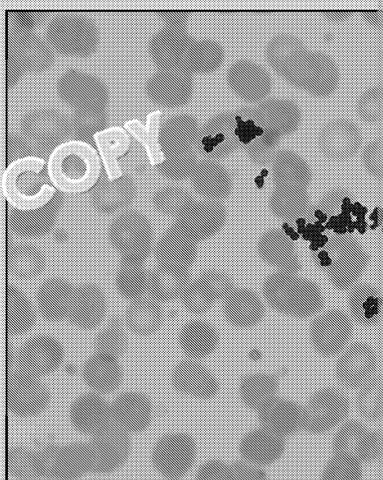


Figure F4.8. Scanning electron micrograph of *Leptospira* sp. bacteria, a type of spiral bacterium.

Apply your knowledge

1. State what a plasmid is.
2. Describe how Gram staining distinguishes between Gram-positive and Gram-negative bacteria and how structural differences in their cell walls leads to this.
3. Describe the different bacteria's flagella used for classification and provide an example of a disease condition associated with each type.
4. Use classification information to identify the type of bacteria in the image of a blood smear.



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Practice questions: Features of bacteria found in humans

- 1 The bacteria in the image below is commonly found within the gut microbiome collected from the environment, such as soil or water.



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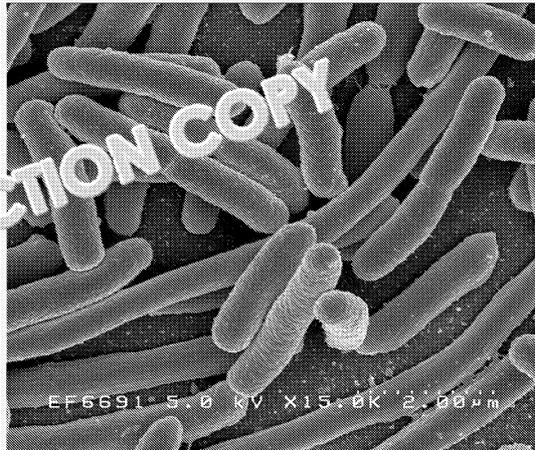


Image credit: National Institute of Allergy and Infectious Diseases (NIAID)

Classify the bacteria according to its shape [1].



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4.1.2. Features of fungi found in humans

Fungi may be unicellular or multicellular eukaryotic organisms, and they play various roles as pathogens and symbionts. They digest organic material extracellularly using secreted enzymes and absorb nutrients across their cell surfaces.

This chapter explores the cellular structure and function of fungal components and common fungal infections relevant to human biology.

Structure and function of fungal components

Fungal cells share several distinctive components, each with specialised roles for survival, growth, and reproduction.

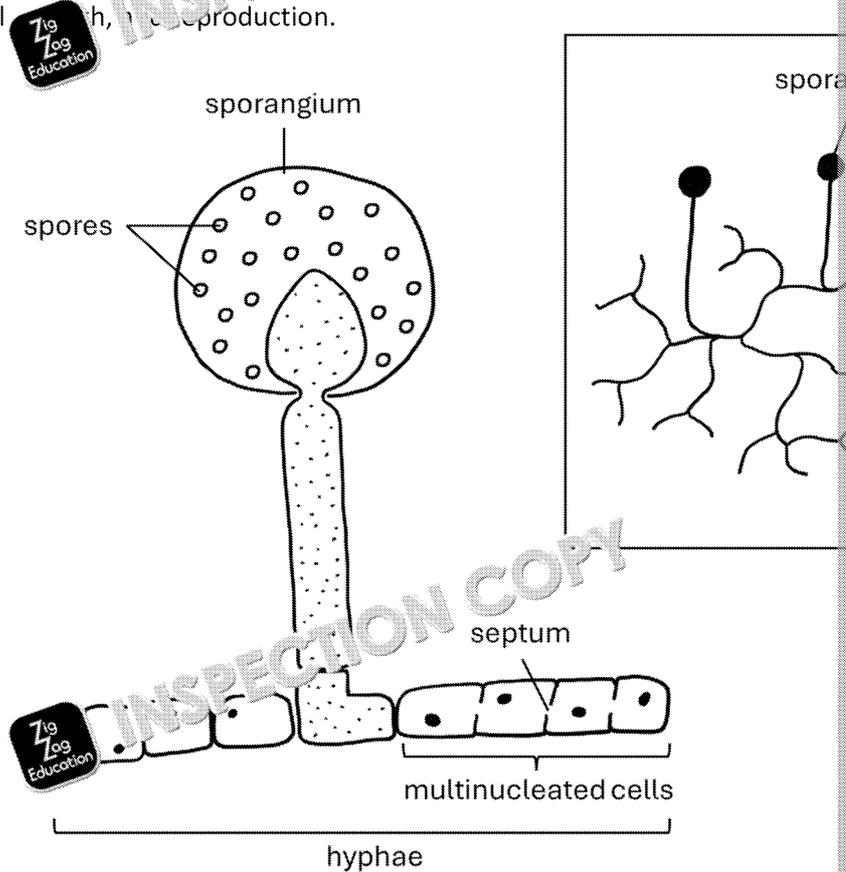


Figure F4.9. The parts of a fungus in overview and close-up.

Cytoplasm

The cytoplasm contains essential organelles such as nucleus, mitochondria and Golgi apparatus, and is involved in energy production, nutrient processing and intracellular transport, while also helping to maintain osmotic balance and perform other metabolic functions.

Chitin cell wall

Fungal cell walls are primarily composed of chitin, a tough polysaccharide also found in the exoskeletons of insects. This provides rigidity, structural integrity, and protection from environmental factors such as desiccation, pH, and availability and salinity.

Septum

Septa (singular: septum) are internal cross-walls that separate hyphae into compartments. They allow cytoplasm to move between cells (called cytoplasmic streaming), enabling the transport of organelles, molecules, and ions. They also enable the isolation of damaged regions of the fungal network.

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Hypha

Hyphae (singular: hypha) are thread-like filaments that form the basic structure of many fungi. They can grow and colonise substrates, secreting hydrolytic enzymes to digest organic matter, which is then absorbed.

Hyphae may be septate (divided) or aseptate (undivided).

Mycelium

A mycelium (plural: mycelia) is a dense, interconnected network of hyphae. It forms the vegetative part of a fungus and provides a large surface area for enzymatic digestion and nutrient absorption. It is made up of many individual hyphae and serves as a base for spore production.

Spores

Spores are specialised reproductive units, produced sexually or asexually. They are often small and can be dispersed by wind or animals. The spore's outer layers protect it from extreme conditions, increasing survival and enabling colonisation in new habitats.

Recall questions

1. State the main role of chitin in fungal cell walls.
2. Describe the function of hyphae and explain how they contribute to the survival of fungi in their environment.
3. Explain how septa benefit fungi.

Types of fungi

Fungi may be parasitic or saprophytic:

- Parasitic fungi – live off a living host:
 - endoparasitic – living inside the host and derive nutrients from host tissues
 - ectoparasitic – living outside the host, colonising external surfaces of the body
- Saprophytic fungi – decompose and digest dead organic matter, sometimes on dead bodies.

However, classifications overlap, for example *Candida albicans* is both saprophytic and parasitic, depending on context.

Type of fungus	Location in/on body	Key characteristics
Endoparasitic	<ul style="list-style-type: none"> • Deep tissues • Bloodstream • Lungs 	<ul style="list-style-type: none"> • Invasive growth • Causes systemic (body-wide) infections • May evade immune detection
Ectoparasitic	<ul style="list-style-type: none"> • Skin • Nails • Hair 	<ul style="list-style-type: none"> • Digest keratin • Cause superficial infections • Often transmissible by contact
Saprophytic	<ul style="list-style-type: none"> • Skin surfaces • Mucous membranes 	<ul style="list-style-type: none"> • Normally harmless • Can become pathogenic when immune defences are low

Table 1.1: Details of endoparasitic, ectoparasitic and saprophytic fungi.

Recall questions

1. Use the key characteristics of fungal type to explain why ectoparasitic fungi are less harmful than endoparasitic fungi.
2. Explain why people taking immunosuppressant drugs or with weakened immune systems may succumb to a saprophytic fungal infection.

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Common fungal diseases

Fungal infections in humans vary in severity and location, ranging from superficial skin conditions to life-threatening systemic illnesses.

Aspergillosis

Aspergillosis refers to a group of diseases caused by inhaling spores from *Aspergillus* moulds commonly found in soil, compost, decaying vegetation and dust. These spores are usually harmless to healthy individuals but may opportunistically colonise the respiratory system in immunocompromised conditions or weakened immune function.

Common symptoms include a persistent cough which may include blood or thick sputum, fever, fatigue, and weight loss.

Allergic bronchopulmonary aspergillosis (ABPA)

ABPA results from an allergic reaction to inhaled spores and primarily affects those with asthma.

Chronic pulmonary aspergillosis (CPA)

CPA is a long-term lung infection that may lead to cavity formation or fibrosis (scarring) in the lungs, particularly in those with COPD or a history of tuberculosis.

Aspergilloma

This condition results from a fungal ball growing in a pre-existing lung cavity. It typically affects those with other past lung infections.

Invasive pulmonary aspergillosis (IPA)

IPA occurs when a lung infection spreads into lung tissue and beyond. It is a life-threatening condition that generally affects immunocompromised individuals, such as those receiving chemotherapy or immunosuppressed post-transplant.

Vaginal candidiasis

Vaginal candidiasis, also known as vaginal thrush, is a very common fungal infection caused by the yeast *Candida albicans*. Usually, this fungus exists harmlessly as part of the vaginal microbiome, but it can overgrow and cause infection if the balance is disturbed. Antibiotics, hormonal changes, and immunosuppression may all cause disruption.

Symptoms include itching and soreness of the vulva and vagina with a thick, white discharge that is usually odourless. Individuals can experience a burning sensation during urination, and there may be redness or swelling in more severe cases.

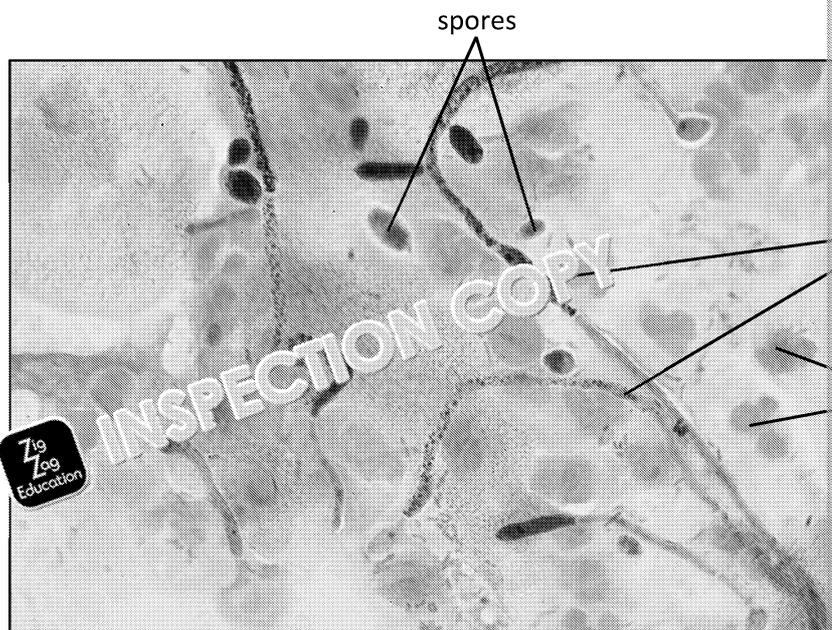


Figure F4.10. A high-powered light photomicrograph of *Candida albicans* from a vaginal swab.

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Athlete's foot

Athlete's foot, or tinea pedis, is a highly contagious skin infection, caused by the *Tinea* in damp, warm environments, and digest keratin. It is common in individuals who frequently use communal areas like gyms, pools or changing rooms.

It is spread by direct skin contact or contact with contaminated surfaces such as shoes.

Symptoms include an itchy, white or red scaly rash, with cracked or peeling skin. It may affect the feet or toenails, and in severe cases cause blisters.

Recall question



1. Describe the factors that can increase an individual's risk of aspergillosis and explain how the various forms of this condition differ in severity.
2. Describe the causes and typical symptoms of vaginal candidiasis, and explain why this infection might occur even in healthy individuals.
3. Explain how athlete's foot is spread among people and describe the conditions that make transmission more likely.

4.1.3. Bacteria of the human body and beyond

Recognising the normal distribution of bacteria within the human body is crucial for diagnosing infection. Equally, being aware of where bacteria are in our surroundings, air, and water, helps us minimise exposure to harmful strains.

This chapter explores the locations of bacteria found around the human body and how they are collected and cultured from the external environment. By the end, you will appreciate how microorganisms are essential to human biology and impact our environment, and key microorganisms that cause disease.

Bacteria in the human body

The human body hosts trillions of bacteria, collectively known as the human microbiome. These communities are essential for digestion, immune function and protection against pathogens. Some are harmless or beneficial, but disruption can lead to infection or disease.

Skin surface

The surface of the skin is colonised mainly by Gram-positive bacteria, including *Staphylococcus* and *Cutibacterium acnes*. They are adapted to dry, salty and acidic conditions. The skin's natural acidic pH acts as a competitive barrier that prevents colonisation by harmful bacteria. Imbalances in the microbiome contribute to skin conditions such as acne.

Conjunctiva

The conjunctiva forms the surface of the eye and provides an important barrier between the external environment and the delicate internal eye structures. It is hostile to microbes due to the presence of tears and mechanical cleaning by blinking.

However, some bacteria, including *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*, can colonise the conjunctiva. Disruption to the microenvironment can lead to conditions such as conjunctivitis (inflammation of the cornea).

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Mucous membranes

Mucous membranes are present in the mouth, nasal passages, respiratory tract. These surfaces are covered in mucus which traps pathogens and supports antimicrobial activity. Mucous membranes have specific adaptations:

- oral cavity – saliva contains enzymes and antimicrobial peptides
- nasal passages – lined with hairs which filter incoming particles
- trachea – lined with ciliated epithelial cells which sweep mucus up to the throat
- vagina – acidic environment (~pH 4.5)

These adaptations are enhanced by the microbiome – rich in *Lactobacillus*, *Streptococcus* and *Veillonella* species which out-compete potential pathogens for space and nutrients.

Teeth and oral cavity

The teeth and mouth are constantly exposed to microbes from food, air or contact. Saliva incorporates pH buffers which resist changes in pH and contains antimicrobial enzymes.

However, bacteria persist as **biofilms** called dental plaque, which contain *Streptococcus mutans*, *Lactobacillus* and *Actinomyces*. These bacteria quickly colonise teeth and gums because carbohydrates from food provide energy for bacterial metabolism, which leads to acid production, causing dental decay.

Gastrointestinal tract (colon)

The colon hosts one of the densest microbiomes in the body, including *Bacteroides*, *Clostridium*, *Firmicutes* and *Lactobacillus*. These have essential functions, including breaking down carbohydrates, synthesising some vitamins (e.g. the B and K groups), and supporting the immune system to identify pathogens.

Disruption in the microbiome is linked to inflammatory bowel diseases and gas production.

Reproductive tract

The vagina contains a protective microbiome dominated by *Lactobacillus*. The bacteria produce lactic acid which keeps the vaginal pH at around pH 4.5. This environment discourages pathogens with organisms like *Candida* and *Gardnerella*. The flora composition fluctuates throughout the menstrual cycle and sexual activity.

Renal tract

The renal tract is normally sterile from the kidneys to the bladder, although the bladder has low numbers of harmless bacteria. Urinary tract infections (UTIs) usually involve *Klebsiella* species of bacteria and their presence is normally indicated by a burning sensation when urinating coupled with increased frequency and urgency.

Your turn

1. List the types of bacteria that commonly colonise the skin surface.
2. Describe the role that skin bacteria play in protecting against harmful microbes.
3. List the adaptations that the oral mucous membranes defend against pathogens.
4. Explain the importance that the oral microbiome has on dental health.
5. Explain how the composition of the vaginal microbiome changes and why this is important for maintaining a healthy environment.

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Bacteria in the external environment

Bacteria inhabit virtually all environments on Earth, including some of the most extreme. Many are pathogenic, many have essential ecological roles such as nutrient cycling and decomposition.

Air

Most airborne bacteria actually spend most of their life in water, the soil or attached to surfaces. They travel attached to dust particles, skin cells or droplets. Common bacteria include *Micrococcus*, *Staphylococcus* and *Bacillus*. Airborne transmission can spread respiratory diseases like tuberculosis, caused by *Mycobacterium tuberculosis*.

Water

Aquatic bacteria are found in freshwater, seawater or wastewater, and are used in bioremediation. They are involved in nutrient cycling, nitrogen fixation, and the breakdown of pollutants (called bioremediation), and include *Pseudomonas* and photosynthetic *Cyanobacteria* (blue-green algae).

Pathogens like *Vibrio cholerae* may cause gastrointestinal infections marked by severe diarrhea.

Soil

Soil is one of the richest and biologically diverse habitats in the world, containing billions of bacteria. Soil bacteria support plant growth, nitrogen fixation, nutrient cycling, decomposition and detoxification. *Rhizobium* species attach to legume root nodules in nitrogen-fixing plants, but many others exist in soils, including *Actinomyces*, *Streptomyces* and *Bacillus*.

Clostridium species are anaerobic that can survive harsh conditions. Some are notable pathogens like *C. botulinum* that causes botulism, *C. tetani* that develops into tetanus, and *C. perfringens* that causes food poisoning and gas gangrene.

Plant surfaces

Leaves and roots host epiphytic bacteria. They often work symbiotically with the host to assist nutrient uptake (like rhizobias at root nodules), protect against pathogens or support growth. Common species include *Pseudomonas*, *Agrobacterium* and *Erwinia*.

Animal surfaces

All animals host harmless or symbiotic bacteria on their feathers, fur, skin, or mucous membranes. Bacteria only become pathogenic if displaced – for instance, gut bacteria on the conjunctiva can cause eye infections.

Zoonotic pathogens such as *Salmonella*, *Campylobacter* and *Brucella* can be transferred between animals and humans through direct contact or contaminated materials.

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Your turn

1. Create a summary table comparing the habitats, general roles and pathogenic potential of different bacteria.



Collecting environment bacterial samples

When analysing bacteria from the environment, samples must be collected and stored carefully to avoid:

- contamination by microorganisms not present at the sampling site (e.g. pollution when the soil is the environment being sampled)
- exposure to potentially pathogenic organisms, especially anaerobic species during culture

Therefore, to protect the reliability of the sample and to reduce the risk to health, samples must be collected, stored and transported carefully and thoroughly applied.

Collecting samples

To collect samples from the environment:

Sample source	Collection method	Storage
Water	Use a sterile pipette or sampling syringe to transfer the water into a sterile screw-cap tube (e.g. McCartney bottle or Falcon tube)	<ul style="list-style-type: none"> • Ensure clearly labelled • Transport promptly
Surfaces	<ul style="list-style-type: none"> • Wipe the surface using a sterile cotton swab in firm strokes • Avoid touching other objects 	<ul style="list-style-type: none"> • Place in sterile container • Refrigerate promptly
Soil	Use a sterile corer or spatula to extract a soil sample from beneath the surface layer	Store in sterile container, avoid exposure if anaerobic

Table F4.2. Methods for collecting samples from water, surface

Aseptic technique in sampling

Aseptic means without contamination. Aseptic techniques aim to prevent the introduction of microorganisms to the sample other than those that were present within the environment originally, thus not contaminating the sample.

The key principles of aseptic technique when sampling are:

- Using sterilised equipment, including all tools (swabs, tubes, pipettes, corers)
- Good personal hygiene, including wearing disposable gloves, tying back hair, and avoiding touching sample areas unnecessarily.
- Accurate sample labelling and storage, including labelling with date, location and sampling method, and transporting the sample promptly back to the laboratory to prevent overgrowth or death of **fastidious species** that have complex and specific requirements.

Advantages and disadvantages of sampling bacteria from the environment

Sampling bacteria from the environment can be challenging but provides useful information.

Advantages	Disadvantages
<ul style="list-style-type: none"> • Helps study biodiversity and ecological roles of microbes • Supports identification of pathogenic or beneficial species • Enables monitoring of pollution levels and microbial contamination • Provides data for bioremediation, antibiotic research or soil science 	<ul style="list-style-type: none"> • Environmental variables are often difficult to control • Some species cannot be cultured under laboratory conditions • Risk of culturing fastidious or anaerobes • May require special media to sustain growth

Table F4.3. Advantages and limitations of sampling bacteria from the environment

Recall questions

1. List the key steps and precautions required to maintain aseptic technique when collecting bacterial samples from different environments.
2. Identify and explain two advantages and two disadvantages of sampling bacteria from the environment.

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4.1.4. Reproduction and culture of bacteria

Microorganisms reproduce extremely quickly, sometimes in as little as 20 minutes, and grow in large numbers. Understanding how bacteria replicate and exchange genetic information is essential for studying growth, antibiotic resistance, and industrial culturing practices.

In this chapter, we explore binary fission and asexual reproduction in bacteria, and how environmental conditions influence growth dynamics. We also explore horizontal gene transfer, an important evolutionary mechanism that allows bacteria to share survival-enhancing traits. These concepts underpin laboratory techniques such as culturing bacterial cells on agar and liquid media, and are fundamental to microbiology, biotechnology, and medical diagnostics.

Bacterial reproduction

Bacteria reproduce asexually through a process called binary fission. Unlike mitosis in eukaryotes, binary fission is simpler but still involves DNA replication, cytokinesis and cell separation. Binary fission results in two genetically identical offspring, unless mutation occurs during DNA replication.

The steps of binary fission are:

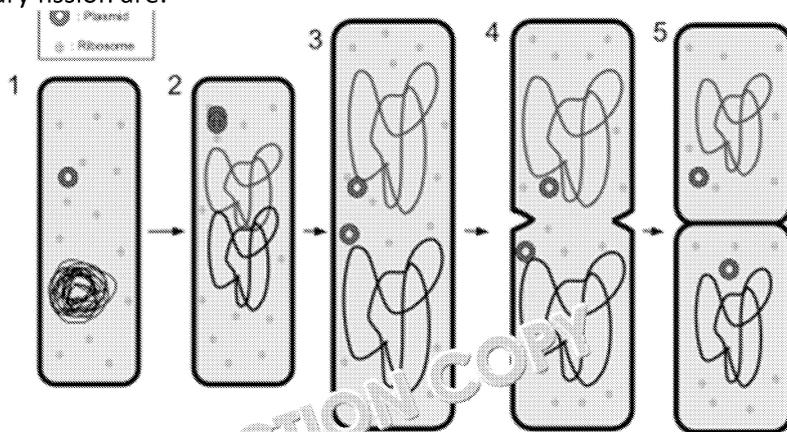


Figure F4.11. The steps of binary fission.

1. Bacterial cells contain DNA stored as a circular nucleoid and in plasmids.
2. The circular DNA molecule replicates once; plasmids replicate at least once.
3. The copies of the circular DNA molecule move to opposite poles of the cell. Plasmids move randomly between the poles.
4. Cell elongates and the membrane pinches inwards.
5. A new cell wall forms between the two DNA molecules.
6. Cytoplasm divides into two roughly equal daughter cells, containing the same DNA and plasmids.

Estimating population size

If each bacterium divides at regular intervals, we can estimate future population size.

$$\text{number of bacteria} = 1 \times 2^n$$

where n = number of divisions

Worked example:

A bacterium takes 1 hour to reproduce. Calculate the population size after 9 hours.

1. Calculate number of divisions:
 $9\text{-hour window} \div 1\text{-hour reproductive period} = 9$
2. Calculate population size:
 $1 \times 2^9 = 512$

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Sex pili and conjugation

Although binary fission is asexual, bacteria evolve quickly due to high replication and horizontal gene transfer (conjugation). Mutations may have no effect on survival, reduce viability or cause cell death, or be beneficial and enhance survival, such as antibiotic resistance.

Some Gram-negative bacteria, such as *E. coli*, possess sex pili (singular: pilus) or hair-like appendages that enable horizontal gene transfer of usually plasmids, by a process called conjugation.

Conjugation involves several stages:

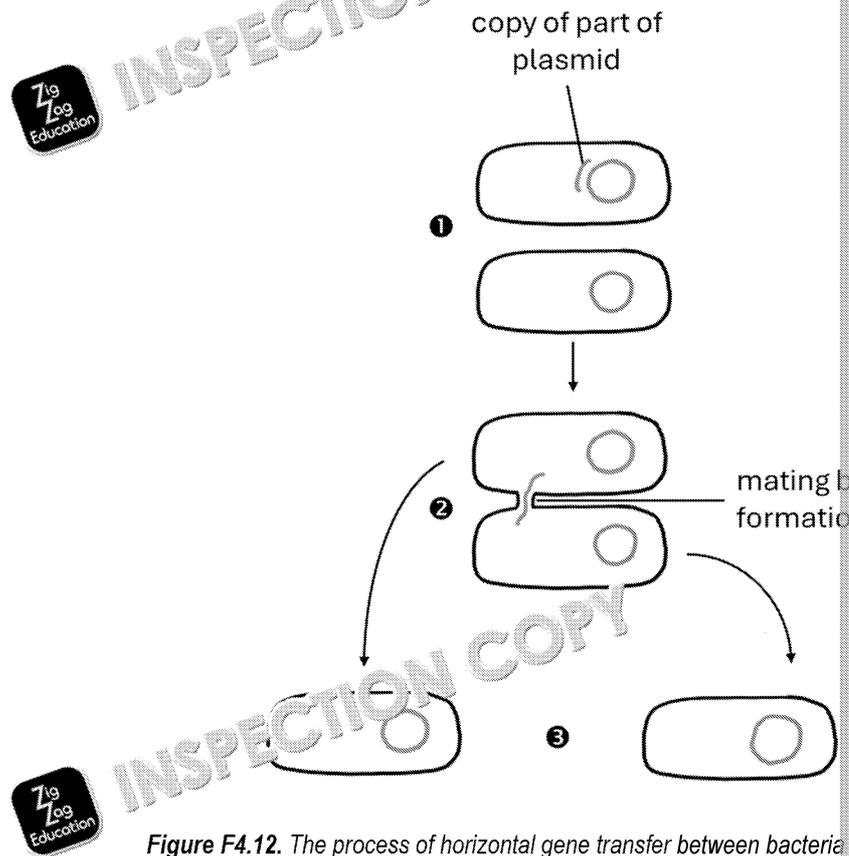


Figure F4.12. The process of horizontal gene transfer between bacteria.

1. Donor cell replicates part or all of a plasmid.
2. Mating bridge forms between the two bacteria with a pilus. The copy of the plasmid is transferred from donor to recipient.
3. The recipient now contains a copy of the plasmid, and both cells can go on to reproduce.

This allows bacteria to share adaptive traits, such as antibiotic resistance, virulence factors, and metabolic capabilities. Conjugation causes genetic diversity without reproduction, sexual reproduction, or mating between different species of bacteria, making it an important factor in microbiology.

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Apply your knowledge

1. Estimate the bacterial population size after 10 days with a reproductive rate of 2.
2. Outline the stages in binary fission and explain how conjugation serves a different purpose than binary fission.



Culturing bacteria in the lab

Bacterial populations can be cultured in the laboratory using agar plates or nutrient broths. These media provide essential nutrients for growth and allow controlled observation of colony development.

- Agar is a solid medium formed from seaweed-derived polysaccharides. It has a gel-like consistency with carbon, nitrogen and trace minerals. It provides a stable surface for growing bacterial colonies.
- Nutrient broth contains similar ingredients but remains liquid, supporting growth of planktonic (free-floating) or aquatic bacteria. It is ideal for studying population density, turbidity, and metabolic activity.



Figure F4.13. An agar plate with bacterial culture (streak) and a bacterial broth culture.

Phases of population growth in culture

Bacterial growth in a closed system (e.g. nutrient broth) follows a predictable pattern:

- lag phase – bacteria are metabolically active but not dividing; adapting to new conditions
- exponential phase – rapid cell division; population doubles at regular intervals
- stationary phase – nutrient depletion and waste accumulation slow growth; cell death equals cell formation
- death phase – cell death exceeds cell formation because resources have been used up

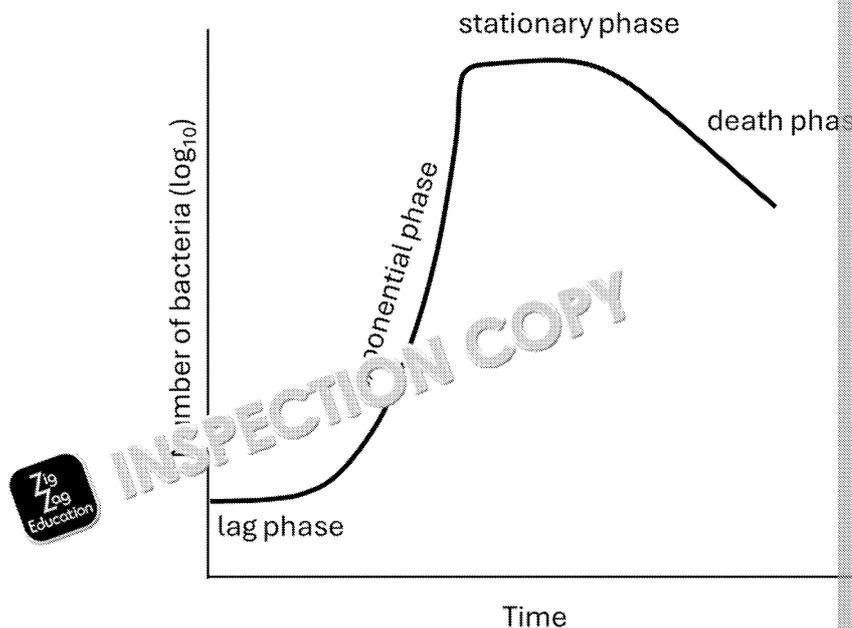


Figure F4.14. A graph outlining bacterial growth phases.

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Environmental factors affecting growth

The phases of cultured bacterial growth are affected by various environmental factors that can be adjusted and controlled within the lab.

Factor	Effect on growth
Temperature	Affects enzyme activity so can restrict or promote growth Optimal range varies by species
pH	Influences enzyme function and cell membrane stability Most bacteria prefer pH 6.5–7.5
Salinity	High salt concentrations cause osmotic stress as water is usually harmful to growth Halophiles thrive in salty environments
Nutrient availability	Key nutrients include carbon, nitrogen and trace minerals Lack of nutrients limits population expansion
Oxygen levels	Aerobes require oxygen; anaerobes may be harmed Some bacteria tolerate both

Table F4.5. Details of environmental factors and the effect they have on bacterial growth.

Bacterial species require specific growth conditions. *E. coli*, *Bacillus subtilis* and *Clostridium perfringens* are commonly studied:

Species	Temperature range (°C)	Optimal pH	Oxygen requirement	Growth media
<i>Escherichia coli</i>	20–48 (optimum ~37)	6.5–7.5	Facultative anaerobe	LB broth/agar, nutrient agar
<i>Bacillus subtilis</i>	18–43 (optimum 30–37)	6.8–7.4	Obligate aerobe	Nutrient broth, LB broth, molasses + yeast extract
<i>Clostridium perfringens</i>	12–50 (optimum 3–47)	6.0–7.0	Obligate anaerobe	Cooked meat medium, thioglycolate broth

Table F4.6. Specific growth conditions for various species of bacteria.

Obligate – bacteria that must live in the condition stated, e.g. an obligate anaerobe must live in oxygen-poor air.

LB broth – lysogeny broth – a nutrient-rich medium which provides bacteria with amino acids needed for growing many forms of bacteria.

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Aseptic technique

Aseptic technique prevents contamination of cultures and protects the handler from infection. It involves sterile handling procedures before, during and after sample collection and culture.

Obtaining bacterial samples

When obtaining bacterial samples from patients or the environment (see page 167):

- use sterilised swabs or pipettes
- label and repackage samples immediately
- wear disposable gloves and avoid touching non-sterile surfaces

Working within the laboratory

When working in the laboratory to grow or observe cultures, aseptic techniques include:

- Sterile handling:
 - Open containers only when needed.
 - Avoid talking, coughing or sneezing near open materials.
 - Use a flame or alcohol wipes to sterilise surfaces, especially in the laboratory.
 - Use autoclaved equipment, sterile water, and gloves.
- Environmental controls:
 - Work near a Bunsen burner or in a **laminar flow cabinet** where possible.
 - Keep windows closed to minimise airborne contamination.

Creating bacterial suspensions

Aseptic techniques necessary when creating bacterial suspensions include:

- working near a Bunsen burner or in a laminar flow hood
- closing windows and minimising air movement
- using autoclaved equipment, sterile water, and gloves

Creating streak plates

When streaking agar plates, aseptic techniques to observe include:

- flame-sterilising the inoculating loop before and after use
- avoiding getting the loop into the agar
- keeping Petri dish lid ajar but covered during streaking to limit airborne contamination
- securing lid with tape in an X-shape to allow airflow while preventing accidental opening
- labelling with name, date, sample, and type of growth medium

Incubation and disposal

The incubation and destruction of bacterial cultures must be carried out with care to ensure controlled growth, and responsible disposal.

Aerobic or facultative anaerobic bacterial samples should be incubated at 25 °C in conditions of high oxygen availability. This helps prevent the unintended growth of pathogenic species, which grow at body temperature (37 °C).

Obligate anaerobic bacteria must be incubated at 25 °C in airtight containers or anaerobic chambers and maintain appropriate atmospheric conditions. Anaerobic packs can be used to allow for anaerobic growth. Some clinical samples may need culturing at human body temperature (35–37 °C) for accurate results.

Cultures are typically incubated for no more than 7–8 days to prevent overgrowth and contamination. After incubation, cultures, media and equipment must be sterilised using a high temperature (e.g. 121 °C for 15–20 minutes under pressure) before disposal. Disposed contents must be recorded, in line with biosafety protocols.

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Health and safety recording

Maintaining comprehensive health and safety records protects personnel and

A complete aseptic procedure record should include:

- date and results of mandatory staff training
- maintenance logs for laminar flow hoods and autoclaves
- sample and culture details, including organism, incubations, disposal methods

Benefits and limitations

There are benefits and limitations of aseptic techniques:

Benefits	Limitations
<ul style="list-style-type: none"> • Prevents contamination from external microbes • Protects microbiologists from exposure to unknown or pathogenic strains • Ensures integrity of experimental results • Reduces risk of laboratory-acquired infections 	<ul style="list-style-type: none"> • Requires careful control of environment • May require expensive sterilisation procedures • Human error (missed steps) can compromise the culture • Enhanced protection for high-risk samples

Table F4.7. Benefits and limitations of aseptic techniques

Recall questions

1. Outline the key steps involved in aseptic techniques in the laboratory and explain why each step is important.
2. Describe the main phases of bacterial population growth and explain the factors that influence each phase.
3. Compare the growth requirements and characteristics of *Clostridium perfringens*.



Zig Zag Education

Practice questions: Bacteria of the human body and beyond

1. a. Plot the data of bacterial growth in a flask and draw a smooth line of best fit to show the pattern of growth. (2)

Time (hours)	Population
0	1×10^5
2	1.2×10^5
4	5×10^5
6	2×10^6
8	8×10^6
10	1×10^7
12	1×10^7
14	5×10^6
16	1×10^6
18	2×10^5

- b. Label the phases of growth on your graph. (4)

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Zig Zag Education



4.1.5. Viruses

Viruses are often described as biological contradictions. They possess genetic material but lack the cellular structures and metabolic machinery required for independent life. For example, the influenza virus contains only eight genes, yet it can cause devastating disease.

Because viruses cannot carry out metabolism or replicate on their own, they do not count as living organisms; however, they are capable of infecting living cells, destroying cells with extreme efficiency.

Structure and classification of viruses

Viruses consist of a protein shell, called a capsid, which is surrounded by a lipid bilayer membrane. The capsid is often covered in glycoprotein spikes that aid attachment to specific receptors on host cells. They have a central core containing either DNA or RNA, which may be single- or double-stranded.

Most viruses are extremely small, typically 20–300 nm, far smaller than bacteria, and only visible under an electron microscope.

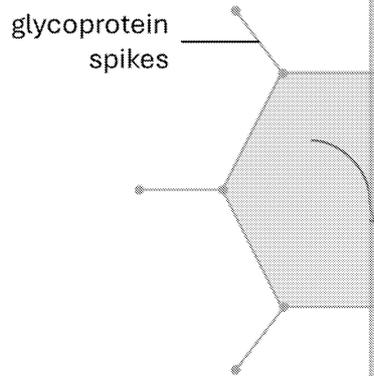


Figure F4.15. A

Bacteriophages

Bacteriophages, or simply phages, are viruses that infect and replicate within bacterial cells. In addition to the capsid which holds the viral genome, they have a tail that penetrates the cell wall to inject genetic material, and tail fibres that recognise specific receptors on the bacterial cell surface and confer high specificity – phages usually target only one species of bacteria, even down to the strain.

Phage reproduction may occur lytically or lysogenically. In the lytic cycle, the phage invades the bacterial cell, uses the machinery to replicate the virus, then lyses the cell to release new phages. Lysogenic reproduction involves DNA integration with the host genome to form a prophage, which then replicates passively until it is triggered into the lytic cycle.

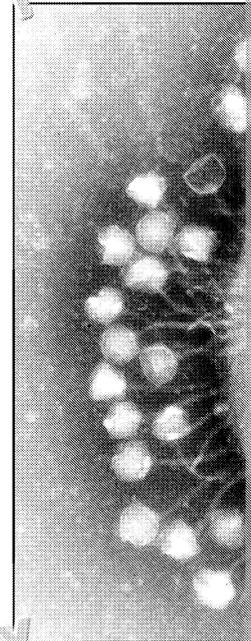


Figure F4.16. Electron micrograph of bacteriophages attached to a bacterial cell wall, at approximately 100,000x magnification.

Recall question



1. Describe the structure of a typical virus.
2. Describe how phages reproduce in bacterial cells and explain why this is essential for their survival.

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Viral reproduction in eukaryotic cells

Viruses reproduce by invading host cells and using their biochemical machinery.

1. Attachment – viral glycoproteins bind to specific host cell receptors
2. Penetration – virus enters the cell via endocytosis or membrane fusion
3. Use of host machinery
 - Inhibits normal cell functions
 - Replicates viral genetic material and synthesises viral proteins
 - May direct host to produce hormones or modify immune signals
4. Assembly and release – new viruses are assembled and released by lysis (cell membrane bulges and breaks off with virus inside, in a process similar to viral budding)

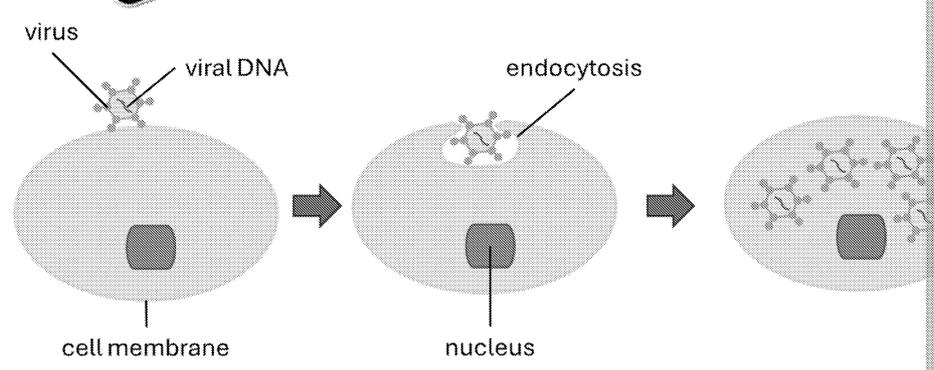


Figure F4.17. Viral replication in eukaryotic cells.

Living or not living?

Viruses differ fundamentally from cells and tissue because they lack a cell membrane, organelles or enzymes for metabolism, cannot reproduce without a host, and do not live in their environment.

However, because they carry genetic material and evolve over time, they are considered particles, rather than living organisms.

Your turn

1. Describe viral replication in eukaryotic cells and explain why using host cell machinery is essential for this process.
2. Discuss whether viruses should be considered living organisms or remain non-living particles.

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4.2. Beneficial microbes

The human microbiome is a vast community of microorganisms, including bacteria, and protozoa, that live in and on the human body. They inhabit nearly every surface, forming complex ecosystems that are essential for our health, development, and physiological functions.

The human microbiome

The many microbial communities throughout the human body contribute actively to digestive and metabolic efficiency. They can influence our mood, behaviour, and neurological health when imbalanced.



Site	Role
Gut, especially colon	Digestion, vitamin synthesis, immunity
Skin	Barrier protection, pH regulation
Oral cavity	Enzymatic activity, pathogen defence
Respiratory tract	Immunity
Urogenital tract	pH maintenance, protection against infection
Conjunctiva	Antimicrobial defence

Table F4.8. Details of the site and role of microbial communities in the body.

Benefits of the human microbiome

The human microbiome performs essential functions. In many sites, the microbiome acts through destruction of pathogenic bacteria through the production of antimicrobials, killing invading bacteria, and preparing the immune system.

Within the digestive system, the microbiome is essential for breaking down undigested fibres, and for synthesising vitamins that contribute to energy metabolism and nervous system function (vitamin B12), or blood clotting and bone health (vitamin K).

The microbiome can also influence mood and brain function, and the balance of microbes is essential for overall health. When the balance is disrupted, conditions like inflammation, obesity, diabetes mellitus, autoimmune diseases, and mental health disorders may occur.

Maintaining and enhancing the human microbiome

Microbiome composition is shaped by our diet, environment, medications, lifestyle, and genetics. As microbiome balance is vital, it is possible to enhance our microbiome to improve microbial diversity.

Probiotic foods

Eating a healthy, balanced diet is important for maintaining a good gut microbiome, and probiotic foods and active cultures that can increase our gut microbiome if consumed in sufficient quantities.

Common probiotic-rich foods include yoghurt and kefir, milk-based drinks, fermented kimchi and miso, and aged cheeses. These typically contain *Lactobacillus* or *Bifidobacterium* species that support digestion, strengthen immune defences and increase the variety of microbes.

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Rectal probiotic implants

Rectal probiotic implants, or probiotic enemas, deliver beneficial microbes directly to the lower (GI) tract, bypassing digestive enzymes and acids that may degrade oral probiotics.

Implants are typically administered after colonic hydrotherapy and involve inserting live *Lactobacillus* or *Bifidobacterium* species into the colon.

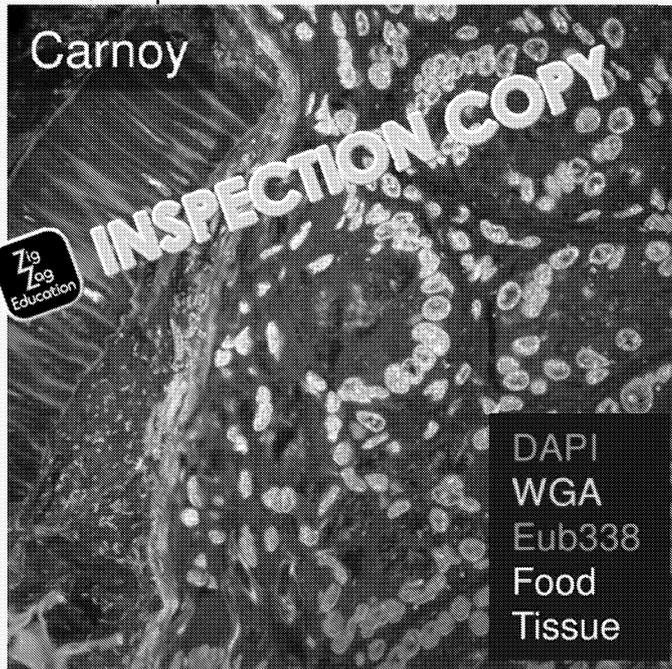
They have been shown to improve the colon microbiome and form part of a treatment for obese or have disorders of the GI tract, such as ulcerative colitis. However, it is important that they should only be implemented by qualified professionals.



1. List three microbiome sites in the human body and describe the types of microorganisms at these locations.
2. Describe everyday activities that can be easily completed to improve the gut microbiome.
3. Explain how medical interventions can be used to improve the gut microbiome.

? Practice questions: Beneficial Microbes

1 The gut microbiome is one of the densest microbiomes in the human body, containing billions of bacteria, viruses, and protists.



The image shows mucus, microbes, host tissue, and food in an area of the large intestine.

- a. Name two bacteria commonly found within the large intestine microbiome.
- b. Describe the essential roles that the microbiome has within the gut.



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