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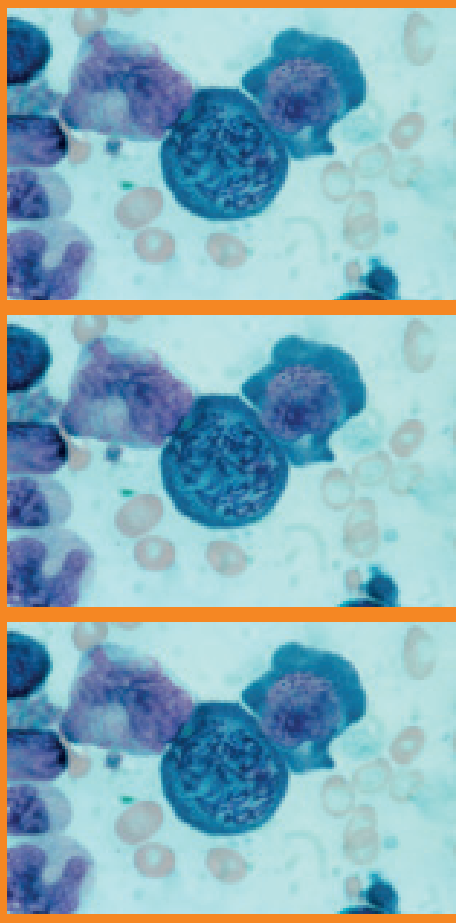
BTEC Level 3 National Extended Certificate in

Applied Human Biology



Unit 1

Principles of Applied Human Biology

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How to use this document

Welcome to your Applied Human Biology course.

A BTEC National in Applied Human Biology will give you the opportunity to develop a range of skills that will prepare you for the world of work, or for continued study at a higher level.

The number of units in your BTEC National qualification varies depending on the size of qualification you are taking. Unit 1 Principles of Applied Human Biology is a mandatory unit (one you must do) for the Certificate and the Extended Certificate.

This document supports the official specification and associated assessment guidance, it does not replace it and should not be used in place of it. Teachers should use their expertise and judgement regarding the teaching and delivery of this course and ensure that all areas of content are taught to learners in sufficient depth in preparation for the external assessment. Every effort has been made to cover as much of the specification as possible. This document does not in any way indicate topics, question types or activities that may come up in the external assessment and no member of the examination team has been involved in its creation.

Features of this document

There are a number of different features in this document, designed to help you learn about the topics in your course in different ways and understand it from multiple perspectives. Together these features:

- explain what your learning is about
- help you to build your knowledge
- help you to reflect on and evaluate your learning.
- make you think beyond what you are reading about
- help you make connections between your learning and real word workplace environments.

In addition, each feature has a specific purpose designed to support your learning.

Features that explain what your learning is about

Getting to know your unit

This section introduces the unit and explains how you will be assessed. It gives an overview of what will be covered in the unit.

Features that help you build your knowledge

Worked example

The worked examples show the process you need to follow to solve a problem, such as a maths or science equation. This will help you to develop your understanding and your numeracy and literacy skills.

Key points

Concise and simple definitions are provided for key words, phrases and concepts. This will allow you to have, at a glance, a clear understanding of the key ideas in the unit.

Features connected to your assessment

Assessment practice

These features give you the opportunity to practice some of the skills you will need when you are assessed on your unit. They do not fully reflect the actual assessment tasks but will help you get ready for them.

Features to help you reflect on and evaluate your learning

Pause point

Pause points give you the opportunity to review and reflect on your own learning. The ability to reflect on your learning is a key skill you'll need to develop and use throughout your life.

Hint and Expand
These also give you suggestions to help cement your knowledge and indicate other areas you can look at to expand it.

Case study

Case studies are used in the unit to allow you to apply the learning and knowledge from the unit to a scenario f A workplace or industry scenario. Case studies include questions to help you consider the wider context of a topic.

Think future skills

This section includes a case study of someone working in the industry. They talk about the job role they do and the skills they need. This comes with a Focusing your Skills section, which gives suggestions for how you can begin to develop the employability skills and experiences needed to be successful in a career in your chosen sector. This is an excellent opportunity to build up your employability skills.

Getting to know your unit

Assessment You will be assessed through a 90- minute written exam worth 80 marks, which is set and marked by Pearson	All biologists need to understand the core science concepts which underpin knowledge of health and disease. Understanding cells and biological molecules helps medical professionals to understand the effect of disease on the human body, the development of symptoms and the impact of different treatments. Understanding how the different organ systems in the body function and the cellular and tissue level, helps scientists keep us healthy and to develop new diagnostic techniques and treatments for human diseases.

How you will be assessed

The external assessment consists of one exam lasting 90 minutes. The paper contains 80 marks. It will include a range of different question types including multiple-choice questions, calculations, short and longer answer questions. The short answer or longer open response generally assess discrete knowledge and understanding of the content in this unit.

You need to be able to apply and synthesise knowledge from this unit. The questions on the paper will be contextualised in order for you to show you can do this.

Unit 1 has four Assessment Outcomes (AO), which will be included on the external assessment. These are:

- AO1: Demonstrate understanding of human biology, health and disease facts, terms, definitions
- AO2: Demonstrate understanding of human biology, health and disease concepts, procedures, processes and techniques and their application
- AO3: Analyse, interpret and evaluate information and data relating to human biology, health and disease to make judgements and reach conclusions
- AO4: Make connections, use and integrate different areas of knowledge and understanding of human biology, health and disease concepts, procedures, processes or techniques.

A Fundamental development and function

It is important to understand the relationship between the structure, function and activities in cells. In this section we look at biological molecules, cellular ultrastructure, the transport of substances in and out of cells, cell specialisation and tissue structure and function.

A1 Cells, tissues and biological molecules

Every living organism is built from different chemical elements. When these elements combine, they make carbohydrates, proteins and lipids. We will look at the structure and function of these molecules and their importance in living organisms.

Structure and function of biological molecules

Carbohydrates

Carbohydrates are an essential part of the diet. They are essential for all living organisms, they act as an energy source, energy store and are used for structure. Carbohydrates contain the elements:

- carbon,
- hydrogen and
- oxygen.

Carbohydrate means 'hydrated carbon.' The formula is Cn(H2O)n, (where n is the number of carbon atoms). Therefore, for every carbon atom there is an equivalent water molecule.

Carbohydrates are used in the body for:

- ATP production
- energy storage
- structural support
- lipid metabolism.

Monosaccharides

Monosaccharides are the simplest carbohydrate. They are monomers. When two monosaccharides bond together a disaccharide is formed an example of this is sucrose. When more than two monosaccharides bond together, they form a more complex carbohydrate called a polysaccharide examples include starch and glycogen.

Monosaccharides all have similar properties for example they:

- are soluble in water
- form crystals
- taste sweet.

Monosaccharides are classified according to the number of carbon atoms they have (Table 1.1 below).

Table 1.1: Types of monosaccharide sugars

Number of carbons	Type of sugar
3-Carbon	Triose
5-Carbon	Pentose
6-Carbon	Hexose

Key points

Monomer - single small molecule that can be joined together to form a polymer.

Monosaccharide - a single carbohydrate molecule.

Disaccharide - two monosaccharides bonded together by a glycosidic bond.

Polymer - a single large molecule made from repeating units of monomers.

Glucose

Glucose is the main source of energy for many organisms. It is described as a hexose monosaccharide, as it contains six carbons, and the formula of glucose is $C_6H_{12}O_6$.

In the molecular structural diagram, the carbons are numbered clockwise, starting with the carbon to the right of the oxygen atom within the ring.

Figure 1.1 shows the structure of alpha (α) glucose, the OH group at carbon 1 is below the plane of the ring. Figure 1.2 shows the structure of beta (β) glucose and the OH group on carbon 1 is above the plane of the ring.

Glucose molecules are polar and soluble in water because hydrogen bonds can form in between the hydroxyl group and the water molecule.

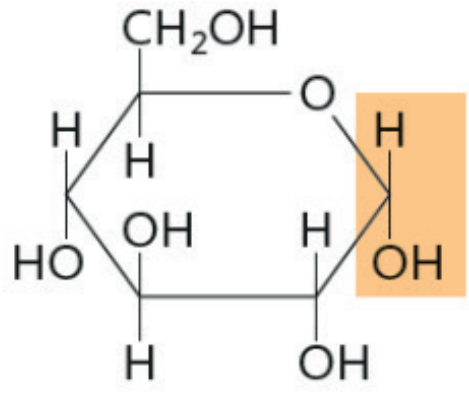


Figure 1.1: Structure of alpha glucose

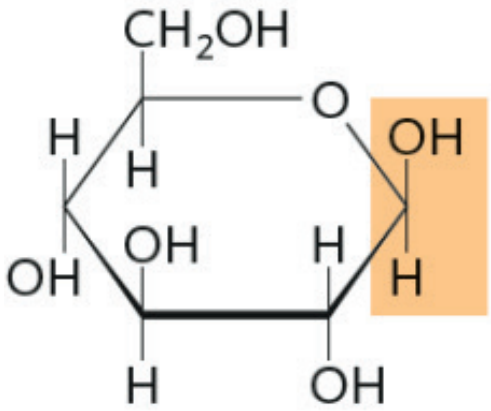


Figure 1.2: Structure of beta glucose

Both glucose molecules have different functions as well as structures. Alpha glucose is used in respiration in plants and animals, this is because the enzymes involved in these processes have active sites complementary to the shape of alpha glucose and not beta glucose. Beta glucose molecules join to form a polymer called cellulose; this is an essential polysaccharide used in the structure of plants.

Disaccharides

A disaccharide is formed when two monosaccharide's bond together during a condensation reaction, where water is eliminated. A new covalent bond, called a glycosidic bond, is formed, for example this could be between carbon 1 of one glucose molecule and the carbon 4 of another glucose. The bond formed is called a 1,4 glycosidic bond. This bond can be broken by adding water, this is called a hydrolysis reaction and makes two monosaccharides again. Common disaccharides are maltose, lactose and sucrose the formation of these are shown in Figure 1.3 below.

- maltose
- lactose
- sucrose.

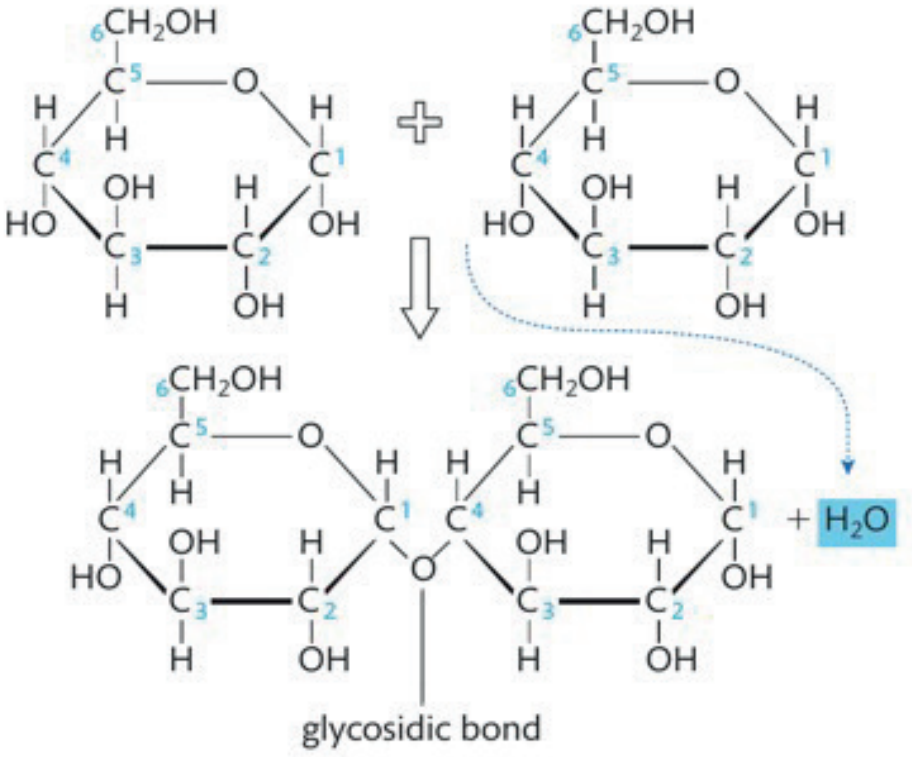


Figure 1.3: Disaccharide (maltose) forming when two monosaccharides (lactose and sucrose) bond together.

Case study

Disruption to living organisms - lactose intolerance

Jackson is lactose intolerant and has been since he was born. Lactose intolerance is a very common problem with the digestive system. Lactose is a disaccharide made from two monosaccharides; galactose and glucose. This sugar is usually found in milk and dairy products. The body is normally able to digest lactose because it produces an enzyme called lactase. This enzyme is essential in breaking down the lactose in milk and other dairy products into monomers so that they can be easily absorbed into the blood stream.

However, people who suffer from lactose intolerance are unable to produce enough lactase to break down lactose. The lactose stays in the digestive system and is fermented by bacteria. This produces lots of gas and causes symptoms such as stomach cramps, bloating and diarrhoea.

There is no cure for lactose intolerance. It is normally controlled by making changes to diet and avoiding foods that contain high concentrations of lactose. There is also medication available in the form of drops or tablets, these can be taken just before or during a meal to help digest the lactose present in the meal, but these must be taken with all meals to have an effect.

Check your knowledge

1. What is lactose?
1. Where is lactose commonly found?
1. What does the body make to digest lactose?
1. What happens in people who suffer from lactose intolerance?
1. What are some of the symptoms of lactose intolerance?

Polysaccharides

Polysaccharides are produced when a large number of monosaccharides form glycosidic bonds. Polysaccharides are known as polymers because they are made from many repeating units of monosaccharides. Amylose, amylopectin, glycogen and cellulose are important polysaccharides.

Key points

Polysaccharide - polymers of monosaccharides. They consist of thousands of monosaccharide monomers bonded together to form a single large molecule.

Energy storage and production

Amylose is composed of unbranched chains of glucose monomers connected by alpha 1,4 glycosidic linkages. Amylose. Figure 1.4 is a polysaccharide that is shaped like a coiled spring because of the position of the 1,4-glycosidic bonds).

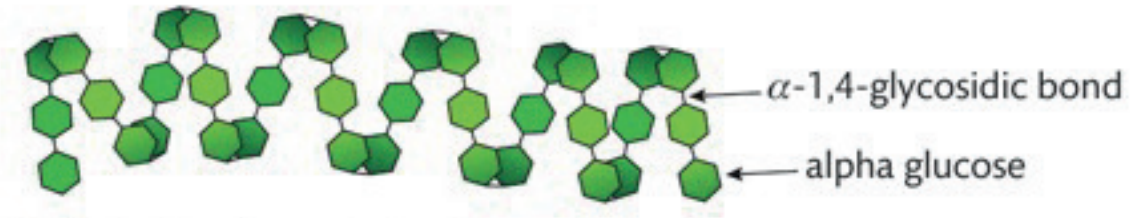


Figure 1.4: Amylose Structure shaped like a coiled spring

Cells get energy from glucose. Plants store excess glucose in the form of starch. Plants use enzymes to break down starch to release glucose. Starch is a mixture of two polysaccharides, amylose, a long, unbranched chain of alpha glucose and amylopectin another long, branched alpha glucose. Amylopectin (Figure 1.5) consists of 1,4 glycosidic bonds as seen in disaccharides and also 1,6 glycosidic bonds. 1-6 glycosidic bonds are created by a condensation reaction occurring between carbon 1 on one alpha glucose molecule and carbon 6 of another. The glucose chains in amylopectin form a helical structure.

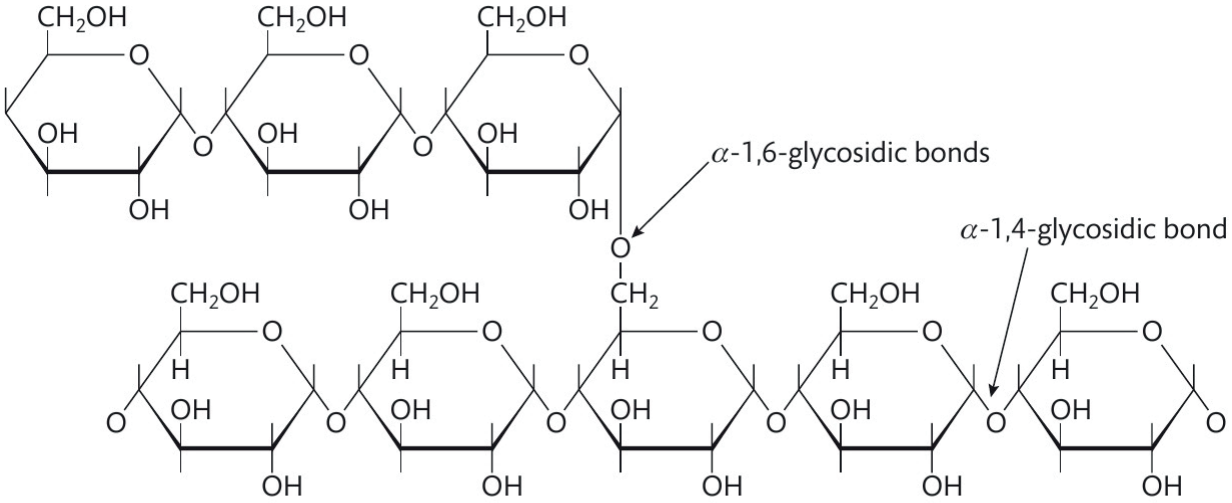


Figure 1.5: Amylopectin, branched carbohydrate with 1,4-glycosidic bonds and 1,6-glucosidic bonds

Animals store excess energy in the form of a polysaccharide called glycogen; glycogen is mainly stored in the liver and skeletal muscles. Glycogen is a polysaccharide of alpha-glucose. Glycogen has a similar structure to amylopectin but with many more side branches; the 1, 6 glycosidic bonds between glucose allow glycogen to be branched. Glycogen molecules are very compact making them ideal for energy storage and their branched structure means that stored glucose can be released very quickly. Since glycogen is broken down from the free ends of the branches, the more branches that exist, the more glucose that can be released at once.

Glycogenolysis

When blood glucose levels drop, glycogenolysis occurs. Glycogenolysis (glycogen breakdown) is coordinated by the action of two enzymes, glycogen phosphorylase, which releases glucose-1-phosphate by untangling the alpha 1,4-glycosidic linkages, and glycogen debranching enzyme that detaches the branch points and releases free glucose. Glucose-1-phosphate is converted into glucose-6-phosphate, a form that can enter the glycolytic pathway to be oxidised for energy.

Pause point

Can you describe the structure and explain the function of carbohydrate molecules?

Hint

Close the book, try to describe the structure and explain the function of carbohydrate molecules.

Extend

Describe the difference in structure of alpha and beta glucose.

Proteins

Proteins are large polymers made of long chains of amino acids and they are involved with nearly all your cellular functions. The cells in your body are 50% protein. Proteins are extremely important for growth and repair of your tissues and tissues. All proteins within the body have a specific job. For example, some are structural, such as collagen in connective tissue, bones and tendons, or proteins in muscle and within cell membranes. Others, fold into specific shapes and function as enzymes, antibodies, receptors, channels for transporting ions across membranes, and haemoglobin that transports oxygen to cells. Some hormones are small proteins (peptides). Some proteins act as buffers, because when they dissolve in water they ionise.

Amino acids are the monomers of proteins. Amino acids are made from the elements below:

- carbon.

Protein accounts for 10 – 30% of cell mass. Fibrous proteins, such as collagen, are the basic structural material of the human body providing mechanical support and tensile strength. Globular proteins such as enzymes, haemoglobin in red blood cells and contractile proteins in muscle also play a vital role in almost all biological processes.

All proteins contain carbon, oxygen, hydrogen and nitrogen; many also contain phosphorus and sulphur.

The monomers of protein are called amino acids (Figure 1.6). Humans use 21 different types in order to function and grow. All amino acids consist of a central carbon atom linked to an amine group (-NH2), a carboxyl group (-COOH), a hydrogen atom and variable side chains (R groups). The different R groups allow each protein to function differently within the body.

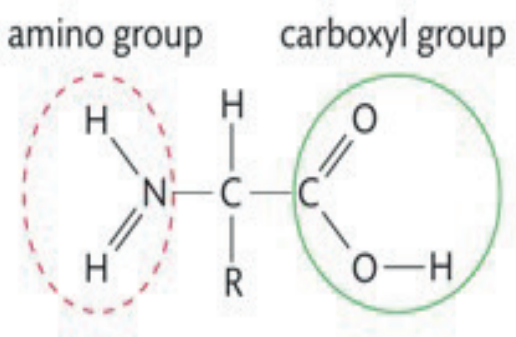


Figure 1.6: Molecular structure of an amino acid

Key points

Carboxyl group (-COOH) – carbon atom double bonded to an oxygen atom and single bonded to a hydroxyl (OH) group.

Amino group – the -NH2 group present in an amino acid.

There are 21 different amino acids each with a different R group (Figure 1.7). All the proteins in the human body are made from different combinations of these amino acids.

Proteins exist in four different structural levels:

- Primary structure – the specific sequence of amino acids forms a polypeptide chain
- Secondary structure – the primary chain forms spirals (α-helices) and sheets (β-sheets)
- Tertiary structure – α-helices and/or β-sheets are folded to form a compact globular molecule held together by intramolecular bonds
- Quaternary structure – two or more polypeptide chains, each with its own tertiary structure, combine to form a functional protein.

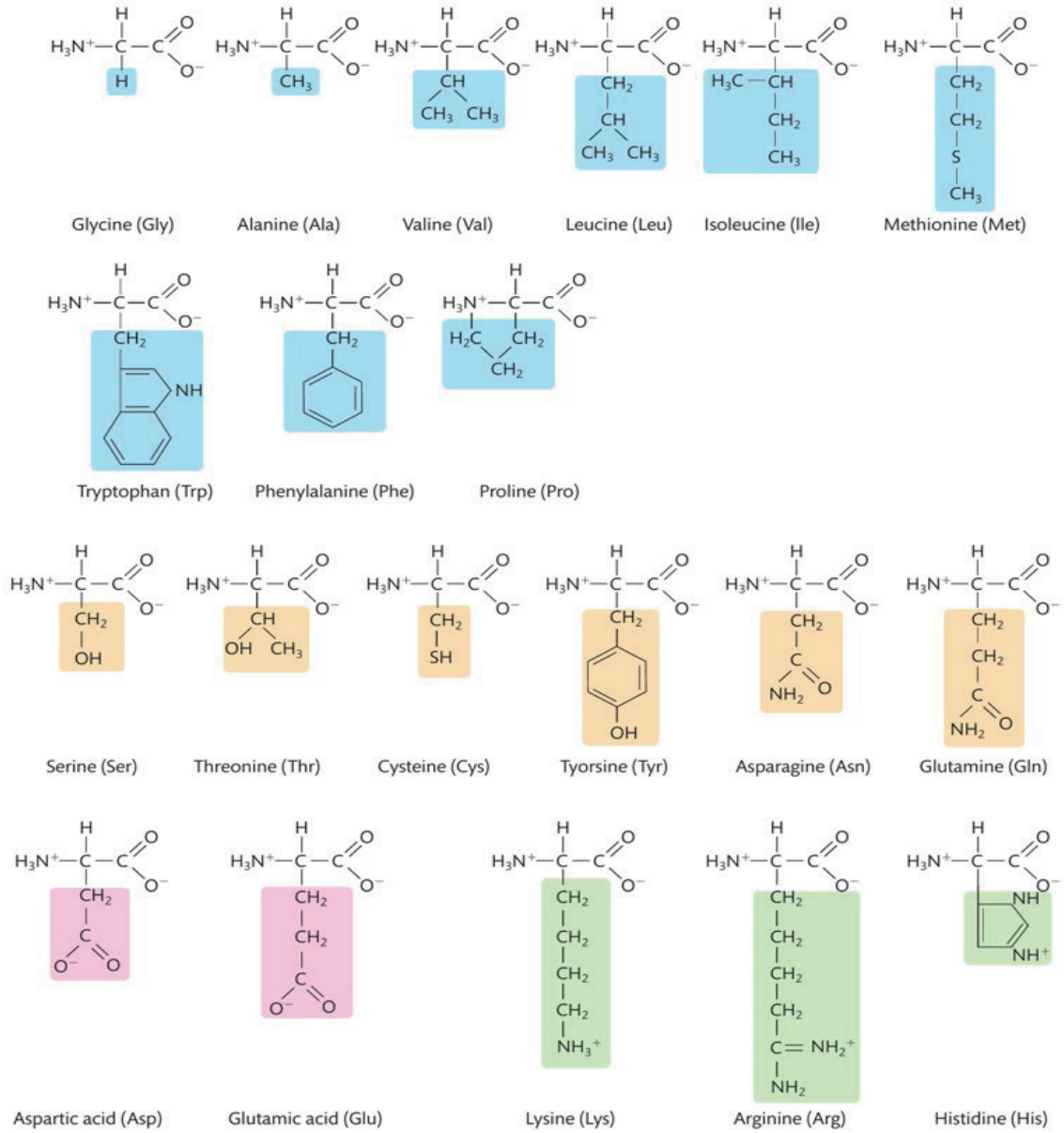


Figure 1.7: Twenty different amino acids

Primary structure

The simplest level of the protein structure is called the primary structure. It consists of a unique sequence of amino acids that make up a **polypeptide**. The function of each protein depends on this unique sequence of amino acids.

Amino acids bond together when a condensation reaction occurs between the carboxyl group of one amino acid and the amino group of another amino acid. A covalent bond is formed between the two amino acids and a water molecule is produced. The bond that forms between the two amino acids is called a **peptide bond**. The new molecule produced is called a **dipeptide**.

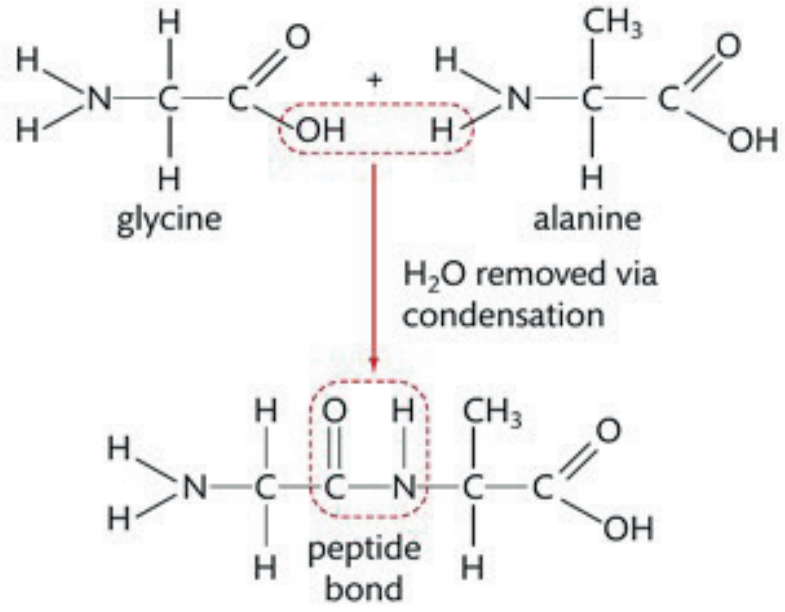


Figure 1.8: A dipeptide forming when two amino acids undergo a condensation reaction

As more amino acids form bonds with each other the chain of amino acids gets bigger. A polypeptide is produced with many peptide bonds. Each peptide bond can be broken during a hydrolysis reaction.

Secondary structure

A protein's secondary structure forms because this unique chain of amino acids (primary structure) either coils to form an alpha helix or folds to form beta **pleated sheets**. Regions of alpha helix and beta pleated sheets can exist within the same polypeptide chain. The secondary structures are held in shape by hydrogen bonds. Each bond is a weak force of attraction between a lone pair of electrons on an oxygen atom and a hydrogen atom attached to a nitrogen atom.

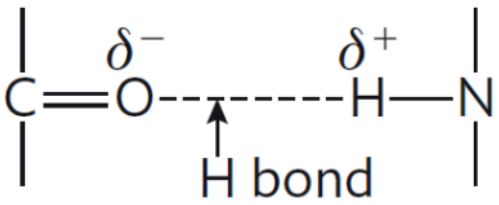


Figure 1.9: Hydrogen bonding between an oxygen atom and a hydrogen atom that is attached to a nitrogen atom

In the secondary structure, the hydrogen bonds are a type of intramolecular force. This means that they are forces of attraction between different parts of the same molecule.

An alpha helix (α helix) is formed when the polypeptide chain coils into a spring shape (Figure 1.10). It is held together by hydrogen bonds, although each bond is only a weak force there are so many hydrogen bonds that their combined effect results in a strong structure.

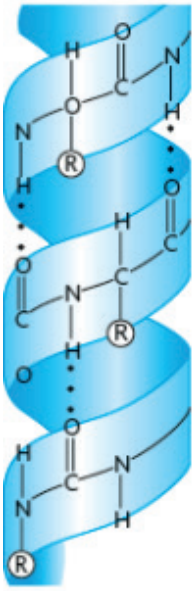


Figure 1.10: Alpha helix in the secondary structure of a protein

Key points

Polypeptide – polymer consisting of a large number of amino acids bonded in a chain.

Covalent bond – a chemical bond formed when two atoms share one or more pairs of electrons.

Peptide bond – a covalent bond formed between two amino acids.

Alpha Helix (α-helix) – a right-handed coiled formation in the secondary structure of a protein.

Beta pleated sheet (β-sheet) – the folding of the primary structure that consists of parallel polypeptide chains.

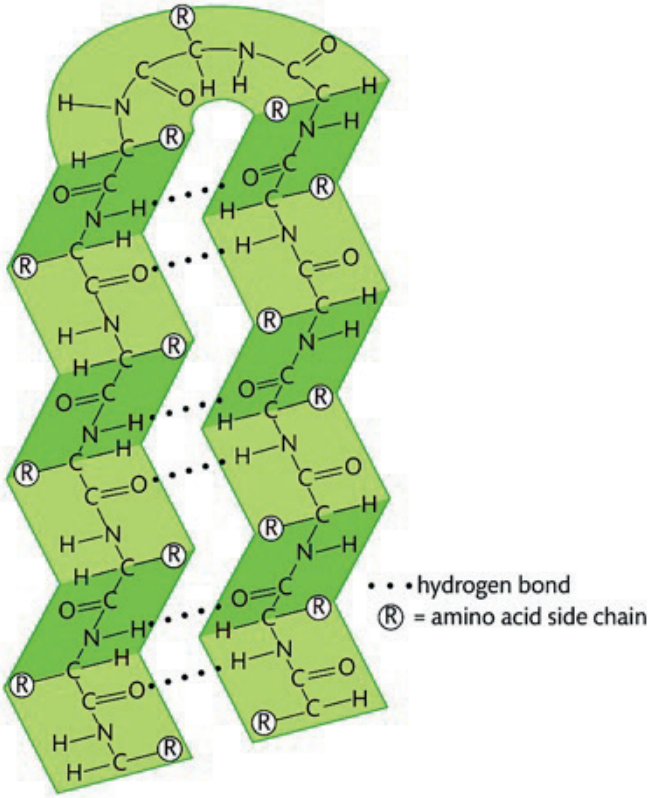


Figure 1.11: Beta peated sheet in the secondary structure of a protein

In a beta (β) pleated sheet (Figure 1.11) the polypeptide chains are folded so that they run next to each other. This structure is also held together by hydrogen bonds.

Tertiary structure

The tertiary structure is formed when the secondary structure coils and folds. The protein becomes a three-dimensional (3D) structure held in place by a number of different bonds and interactions between the R groups (see Figure 1.12) of amino acids, which are now adjacent to each because of the secondary structure.

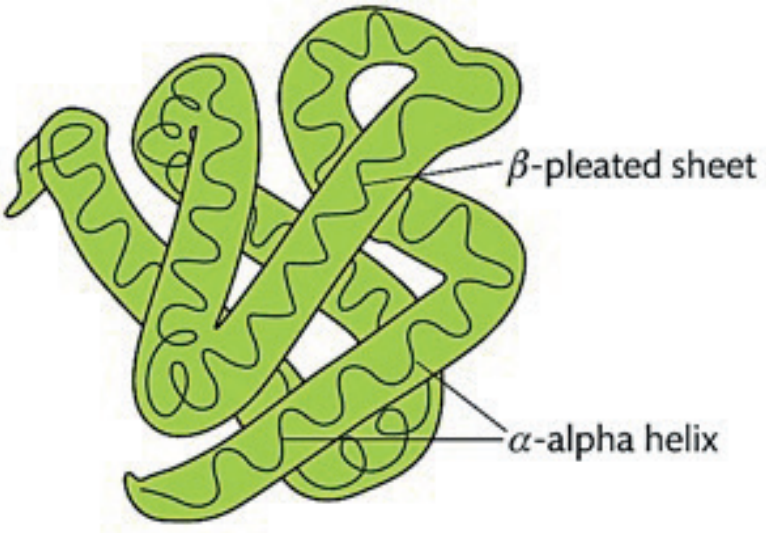


Figure 1.12: Tertiary structure of a protein

Disulphide bridges (Figure 1.13) **(or S-S links)** occur between two sulphur atoms. Sulphur atoms are present in the R group of the amino acids' cysteine and methionine, so when there are two close together a covalent bond forms between the two sulphur atoms. These bonds are the strongest intramolecular bonds in the proteins

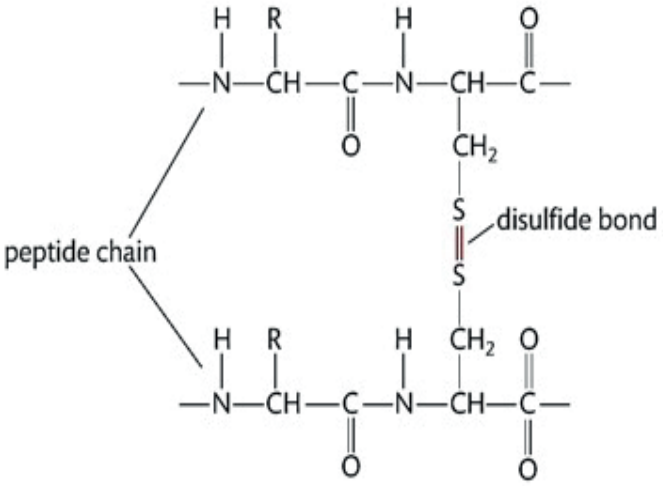


Figure 1.13: Disulphide Bond between sulphur atoms in R groups

Ionic bonds form between R groups if they carry opposite charges (Figure 1.14). For example, proteins containing the amino acid aspartic acid and lysine when oppositely charged amino acids are close together an ionic bond will form. These are weaker than disulphide bonds but stronger than hydrogen bonds.

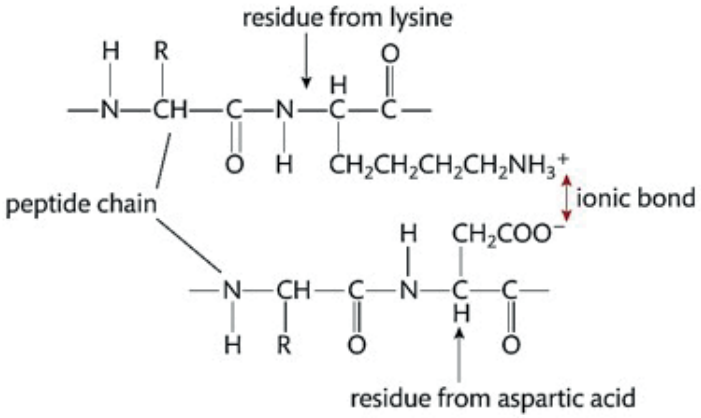


Figure 1.14: Ionic bonds in the protein tertiary structure

Hydrogen bonds will occur where there are slightly positively charged hydrogen ions in R groups close to slightly negatively charged groups.

Finally, **hydrophobic** and **hydrophilic interactions** occur in a protein tertiary structure. Amino acids with hydrophobic R groups tend to be found in the centre of the globular protein and amino acids with hydrophilic R groups are found on the outside of the protein.

Van der Waals forces are weak interactions that also occur in the tertiary structure. They form between nearby atoms, when temporary charges occur, due to the movement and fluctuation of electrons. They are not specific to any particular group.

Key points

Hydrophilic – associates with water molecules easily.

Hydrophobic – does not mix with water.

Quaternary structure

Some proteins are made from more than one **polypeptide chain**. This is the quaternary structure. These proteins sometimes contain essential functional groups, known as prosthetic groups. This is the non-protein part of the protein structure and is essential for the functioning of the protein. An example of a protein with a quaternary structure and a prosthetic group is haemoglobin. This is found in red blood cells.

Globular proteins

Haemoglobin is a soluble globular protein that consists of four globular sub-units arranged in a roughly spherical structure, each with a prosthetic group called haem. Haem contains an Iron (Fe) ion (Figure 1.15). Oxygen binds to the prosthetic group, which is bonded within the quaternary structure.

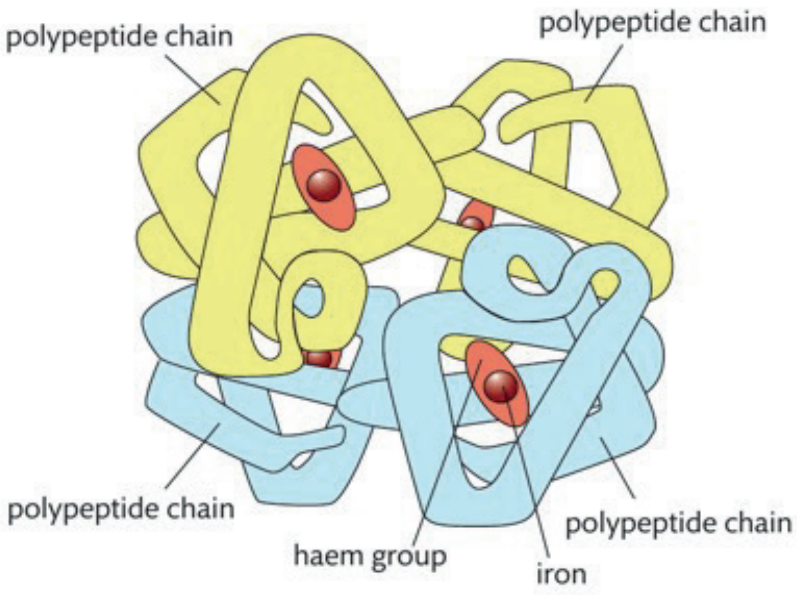


Figure 1.15: Haemoglobin with the haem prosthetic group

Fibrous proteins

Insoluble, fibrous proteins (Figure 1.16) like collagen consist of different protein strands coiled around each other in an alpha helix. The helix forms in collagen because of the regular repeating amino acid sequence of glycine-proline-X (X can be any amino acid) in the strands. Fibrous proteins normally have a structural function. Collagen is present in large quantities in the body's connective tissue and provides ligaments and tendons with tensile strength, supporting organs and bones. Collagen is made up of three polypeptide chains wound around each other. Each of the three chains is a coil made of around 1000 amino acids. It is very strong as hydrogen bonds form between the chains.

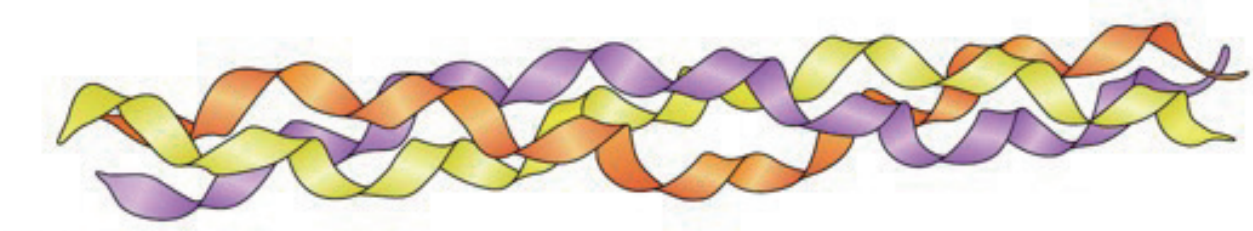


Figure 1.16: Structure of a collagen

Glycoproteins

Carbohydrates can be covalently attached to amino acid R groups to form glycoproteins. The carbohydrate chains attach to either the oxygen atom in the R group of the amino acids threonine or serine (O-Linkage) or the nitrogen atom in the R group of the amino acid asparagine (N-Linkage). Glycoproteins are always found on the outside of the plasma membrane with the carbohydrate facing out. Glycoproteins have many functions such as structure, reproduction, immune response, hormone and protection of cells. Their hydrophilic nature means they can function in aqueous environments. Cell surface glycoproteins are also very important for cross-linking cells and proteins, for example, collagen to add strength to the tissues.

Assessment activity 1.1

1. Draw the structure of an amino acid.
2. Label the amino, carboxyl and R groups.
3. Describe the primary structure.
4. Describe the secondary structure.
5. Explain the bonding that exists in the tertiary structure.
6. Explain the structure and function of collagen.

Triglycerides

Triglycerides are a type of lipid (fat). They are mainly used as energy storage but can also be used as an energy source. They are vital as a component of cell membranes and play an important role in insulating the body. Lipids are made from the elements:

- carbon
- hydrogen
- oxygen.

The common terms for lipids are fats, wax and oil.

Triglycerides are made up of three fatty acid chains and a glycerol molecule. Glycerol contains three –OH functional groups which bond to the three fatty acids chains by removing three molecules of water in a condensation reaction, forming a triglyceride. The bond that forms between the glycerol and a fatty acid is called an ester bond. Three ester binds are formed in a triglyceride. All fatty acids have a carboxyl functional group on one end and a large hydrocarbon chain on the other end.

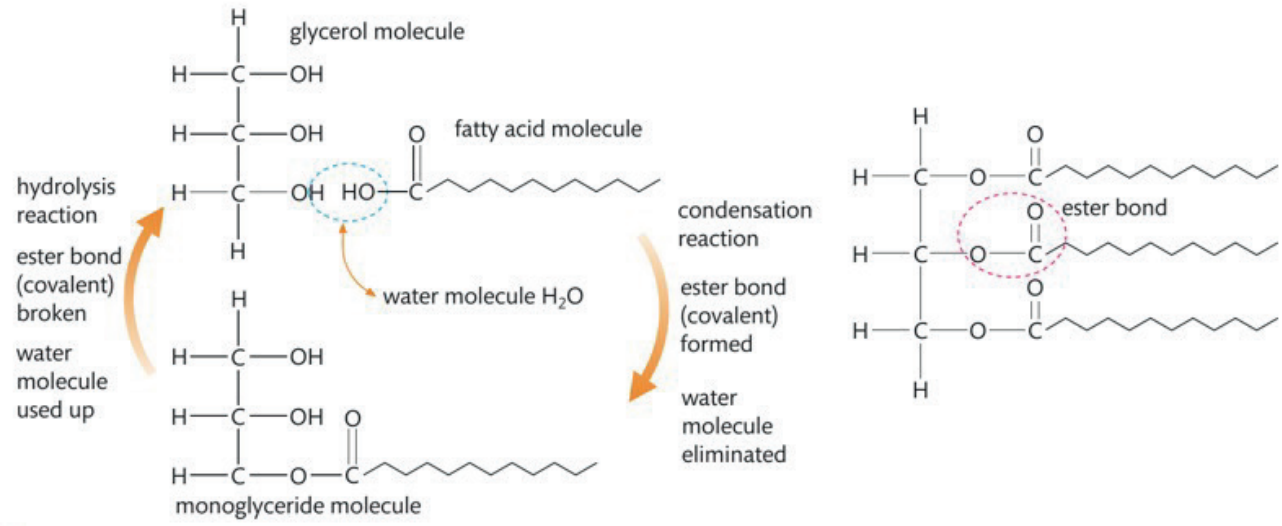


Figure 1.17: Image showing the formation of a triglyceride after a condensation reaction.

There are different types of triglyceride, the main types are saturated fat and unsaturated fat. These have different types of hydrocarbon chain.

Saturated- contains just carbon-carbon single bonds (C-C) (see Figure 1.18).

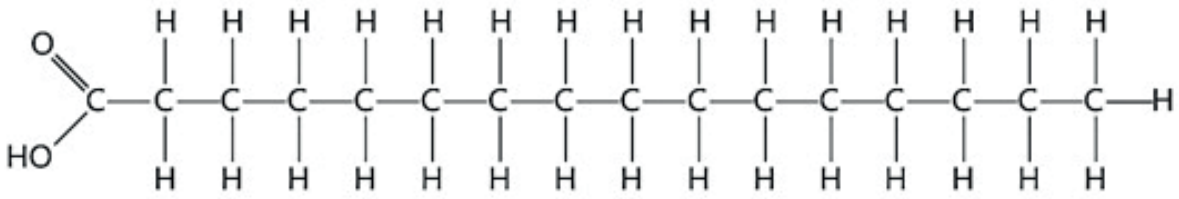


Figure 1.18: Structure of palmitic acid, a saturated fat

Unsaturated- contains carbon-carbon double bonds (C=C) (see Figure 1.19)

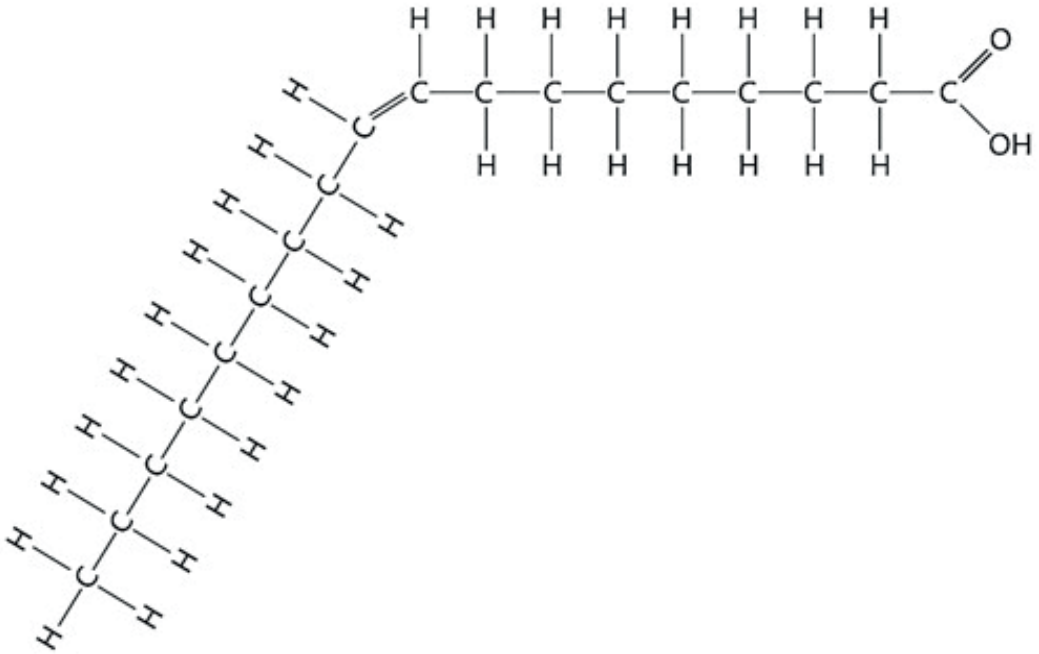


Figure 1.19 Structure of oleic acid, an unsaturated fat

Saturated fats

These form straight chains. They can line up against each other more easily than molecules that have branched chains and all the molecules form attractions. A lot of energy is required to overcome these attractions, and this means that saturated fatty acids have high melting points and tend to be solid at room temperature. Any lipids containing saturated fatty acids will have high melting points, e.g., waxes.

Unsaturated fats

These form chains with kinks due to the double bonds. Their shape means that they push away from each other and attractions are not formed as strongly as saturated fats. Any lipids containing unsaturated fatty acids will have low melting points and tend to be liquid at room temperature, e.g., oil.

Phospholipids

Phospholipids (Figure 1.20) are similar to triglycerides, but they do vary in structure and function. Whilst triglycerides have a glycerol and three fatty acid chains, phospholipids consist of two hydrophobic fatty acid chains and a phosphate group which is hydrophilic, these are joined together by a glycerol. Phospholipids are a major component of all cell membranes. They can form lipid bilayers, made of two layers of phospholipids due to their hydrophilic and hydrophobic properties (Figure 1.21).

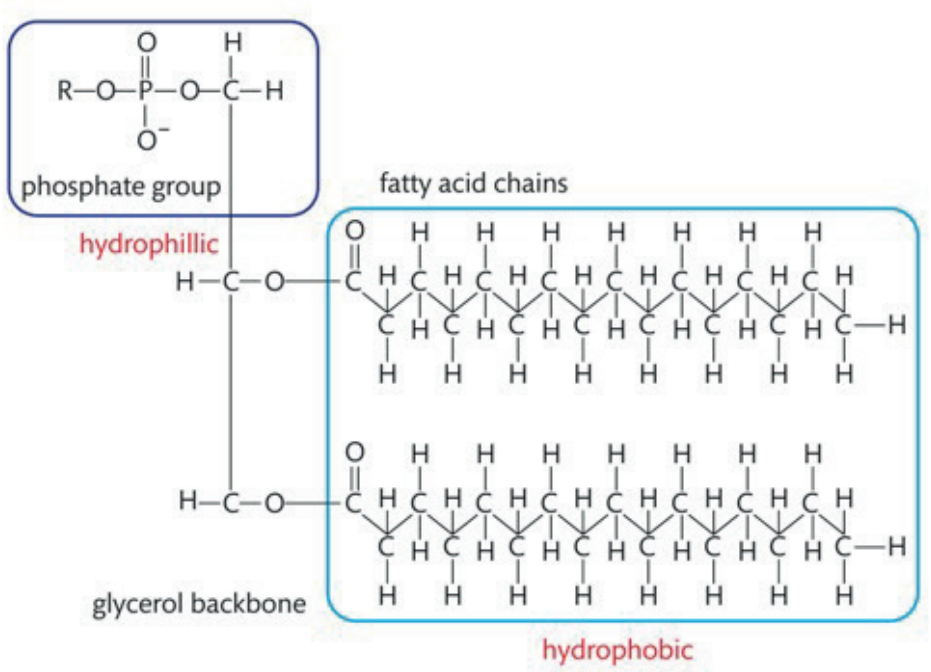


Figure 1.20: Structure of a phospholipid

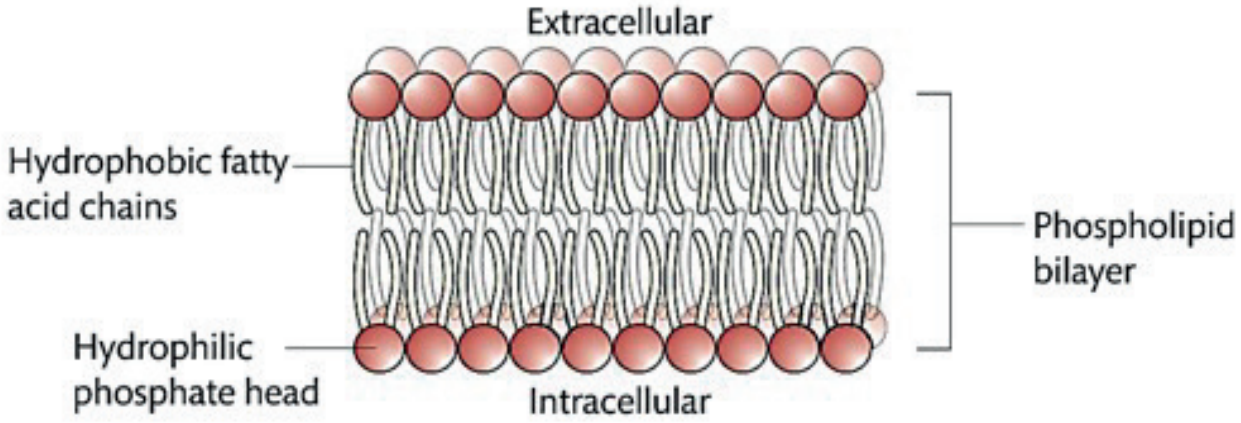


Figure 1.21: A phospholipid bilayer

Cellular ultrastructure and function

A cell is a basic unit of life. You will need to be able to recognise eukaryotic cell ultrastructure when using a light microscope and when observing images from electron microscopes.

There are two types of cell:

- **Eukaryotic:** these cells make up multicellular organisms such as plants and animals. They are complex cells with a nucleus and membrane-bound organelles.
- **Prokaryotic:** these cells are single-celled organisms. They are simple structures and do not have a nucleus or any membrane-bound organelles.

Eukaryotic animal cells

Eukaryotic animal cells are approximately 10-100 μm and the ultrastructure can be seen using an electron microscope. Chemical reactions occur in the **cytoplasm** of a cell. The cell surface membrane or the **plasma membrane** separates the cell cytoplasm from the external environment. Inside the cell cytoplasm there are a number of different structures called organelles. Figure 1.22 shows the ultrastructure of a eukaryotic animal cell.

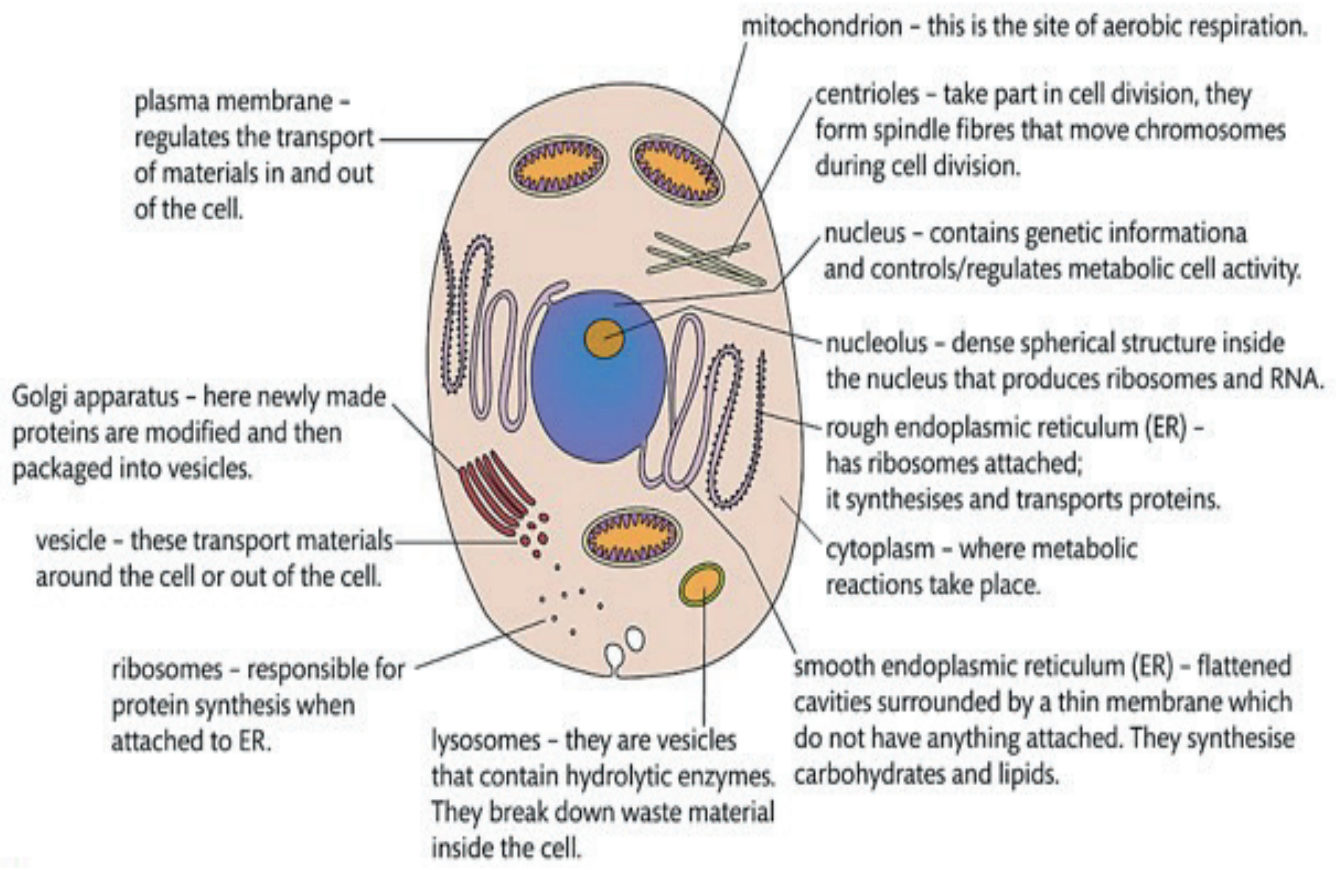


Figure 1.22: Ultrastructure of an animal cell

Table 1.2 describes each eukaryotic animal cell structure and explains its function

Table 1.2: Structure and function of a eukaryotic cell

Organelle	Structure	Function
Plasma membrane	Composed of a phospholipid bilayer, with proteins embedded in the layer.	The membrane is selectively permeable and regulates the transport of materials into and out of the cell. Separates cell contents from the outside environment.
Cytoplasm	Cytoplasm is a thick, gelatinous, semi-transparent fluid.	The cytoplasm maintains cell shape and stores chemicals needed by the cell for metabolic reactions.
Nucleus	The nucleus is the largest organelle and is surrounded by a nuclear envelope. The envelope has nuclear pores which allow the movement of molecules through it. The nucleus contains chromatin.	The nucleus controls/regulates cellular activity and houses genetic material called chromatin, DNA and proteins from which comes the instruction for making proteins.
Nucleolus	Dense spherical structure in the middle of the nucleus.	The nucleolus synthesises RNA and ribosomes
Rough endoplasmic reticulum (RER)	Network of membrane bound flattened sacs called cisternae studded with ribosomes.	Protein synthesis takes place on the ribosomes and the newly synthesised proteins are transported to the Golgi apparatus.
Smooth endoplasmic Reticulum	Network of membrane bound flattened sacs called cisternae. No ribosomes.	Responsible for synthesis and storage of lipids and carbohydrates.
Golgi apparatus	A stack of membrane bound flattened sacs.	Newly made proteins are received here from the rough ER. The Golgi apparatus modifies them and then packages the proteins into vesicles to be transported to where they are needed. Lysosomes are produced here too.
Vesicles	Small spherical membrane bound sacs with fluid inside.	Transport vesicles are used to transport materials inside the cell and secretory vesicles transport proteins that are to be released from the cell, to the cell surface membrane.
Lysosomes	Small spherical membrane bound sacs containing hydrolytic enzymes.	They break down waste material including old organelles.
80s ribosomes	Tiny organelles attached to rough ER or free floating in the cell. They consist of two subunits and they are not surrounded by a membrane.	Protein synthesis occurs at the ribosomes.
Mitochondria	They have two membranes. The inner membrane is highly folded to form cristae. The central part is called the matrix. They can be seen as long in shape or spherical depending on which angel the cell is cut at.	They are the site of the final stages of cellular respiration.
Centrosomes	They are made from two small microtubules called centrioles and a complex of protein fibres	They form spindle fibres during cell division.

Microscopy

A microscope is an instrument that magnifies objects hundreds and thousands of times. Before microscopes were invented, people knew very little about cells. Microscopes have given us the power to see the intracellular structure of cells in microscopic detail.

Light microscopy

Light microscopes were first developed in the 16th century and continue to be improved and developed. There are limitations to using light microscopes because they have a lower magnification and **resolution** than other more advanced microscopes. However, light microscopes do allow us to observe some intracellular structures, known as **organelles**. A light microscope magnifies cellular organelles such as the cell **nucleus**, **mitochondria**, and chloroplasts in plant cells. Ribosomes are too small to see with a light microscope but can be viewed using an electron microscope. The image below shows a human cheek cell observed down a light microscope.

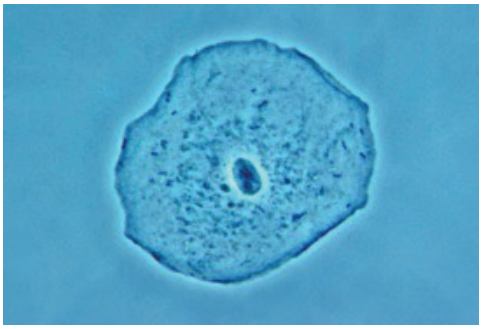


Figure 1.23: Human cheek cell seen under a light microscope

Key points

Resolution – the ability to distinguish between objects that are close together.

Organelles – specialised structures found within a living cell.

Nucleus – an organelle found inside a cell containing genetic information.

Mitochondria – an organelle where aerobic respiration takes place.

Electron microscopy

Electron microscopes were first developed in the 20th century. They use a beam of electrons with a wavelength of less than 1nm to illuminate the specimen. They allow much more detail of cell ultrastructure to be observed and produce images called electron micrographs, with a magnification of x 500,000 and higher resolution.

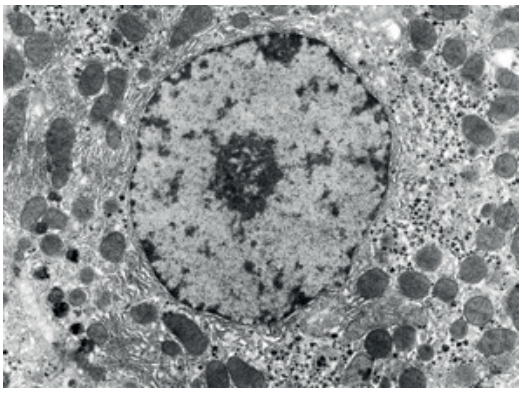


Figure 1.24: Animal cell electron micrograph

Calculating magnification

We can use the calculation below to work out magnification:

$$\text{Magnification (M)} = \frac{\text{size of image (I)}}{\text{actual size (A)}}$$

The equation can also be represented by an equation triangle (Figure 1.25).

Figure 1.25: Magnification equation triangle

The size of the image refers to the length of the image when you measure it with a ruler. Ensure that you always measure in millimetres. You will usually be given the magnification or the actual size in the exam question so you will therefore have one unknown and you can rearrange the equation to work out the unknown answer. Always include units in your answer and place your answer on the given line in the exam question. Finally, make sure you show your working out, including the equation above.

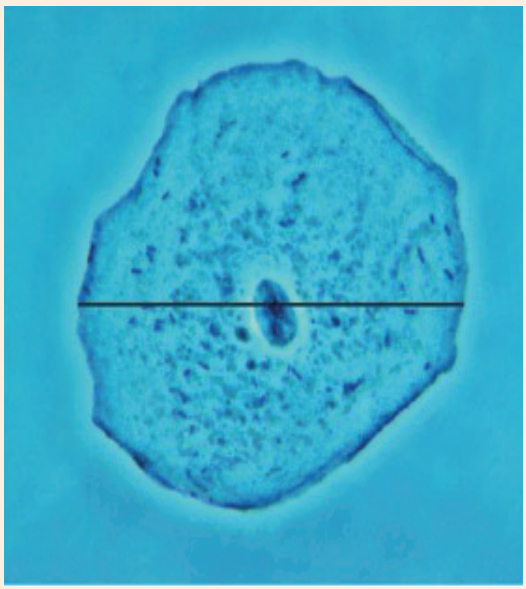
Worked example

Calculate the magnification of this image. Use the calculation above to work out the magnification.

Remember to convert all units to make them the same.

1000 nanometres (nm) = 1 micrometre (µm)

1000 micrometres (µm) = 1mm



1000 mm = 1 m

1. Imagine the line through the centre of the cell is 50 mm
2. The actual size of the image is 50 µm.

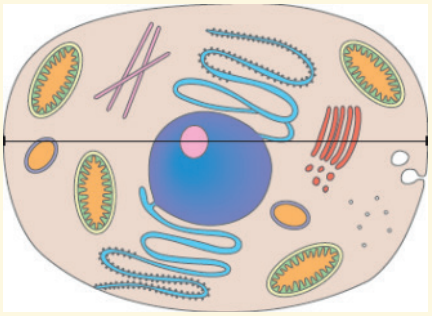
You need to convert this to mm so they are both in the same units.

= 0.05mm

3. Magnification = 50 /0.05
4. 50/ 0.05 = 1000
5. Magnification = x 1000

Figure 1:26: Magnification calculation activity

Assessment activity 1.2



Work out the magnification for the diagram.

The actual size of the cell is 200 µm.

1. Use your ruler to measure the size of the cell shown in the image in mm.
2. The actual size is 200 µm. You need to convert this into mm so they are both in the same units.
3. Put both figures into the magnification equation and work out magnification.

Fluid mosaic model and transport of substances into and out of cells

Cell membranes have a specific structure to enable the movement of substances from one place to another, e.g.,, glucose.

The term fluid mosaic model, proposed by Singer and Nicholson, is used to describe the arrangement of biological membranes. Fluid mosaic membranes consist of:

- the phospholipid bilayer, which forms the basic structure
- protein molecules, which are present within the phospholipid bilayer
- extrinsic proteins, which are embedded on the surfaces of the membrane
- intrinsic proteins, which completely span the bilayer.

Key points

Fluid mosaic model – description of the cell membrane structure, a phospholipid bilayer with proteins floating in it.

Phospholipid bilayer

Phospholipid molecules consist of a phosphate head and two side-by-side chains of fatty acids that form the lipid tails (Figure 1.27). The phosphate head is negatively charged making it hydrophilic (water-loving), the phosphate head is attracted to intracellular and extracellular water molecules. The two fatty acid chains are uncharged making them hydrophobic (water-fearing); a hydrophobic molecule repels, and is repelled by, water.

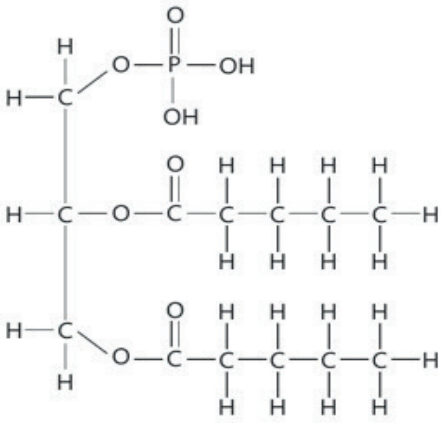


Figure 1:27: Phospholipid structure

Key points

Hydrophilic – associates with water molecules easily.

Hydrophobic - repels water.

When a phospholipid molecule is spread onto a watery surface, it forms a bilayer with hydrophilic heads facing into the water and hydrophobic tails tucked inside (Figure 1.28).

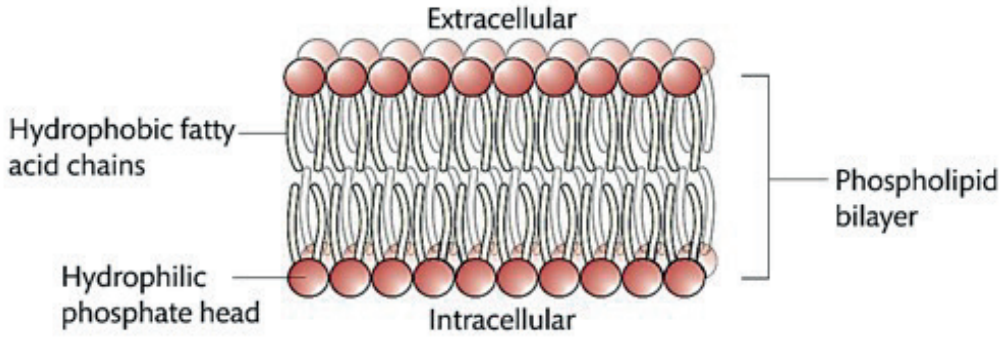


Figure 1:28: Phospholipid bilayer

All biological membranes are made from a double layer of phospholipid molecules. One layer is formed from hydrophilic, polar heads (glycerol and phosphate molecules) and the other from hydrophobic, non-polar tails (fatty acid chains). The phospholipids are arranged in a bilayer with the polar heads facing the intracellular and extracellular fluids and the lipid tails facing inwards (away from fluids). All membranes are semipermeable and allow water to pass through the bilayer by processes of diffusion and osmosis. The two main pathways for plasma-membrane water transport are diffusion through the lipid bilayer and via aquaporins, which are specialised channel proteins that allow water to rapidly pass through the cell membrane.

Methods of transport

Diffusion

Diffusion is the movement of molecules from an area of high concentration to an area of lower concentration, down a concentration gradient. Molecules possess kinetic energy which keeps them moving so they can be passively transported across biological membranes. Diffusion is therefore known as a passive process, as they only rely on kinetic energy and a concentration gradient for movement, they do not use energy from the cell.

Key points

Concentration gradient – the difference in the concentration of a substance in two different regions.

Lipid based molecules

Fat soluble molecules such as steroid hormones can simply pass through the phospholipid membrane because the bilayer consists of fatty acid tails. They passively diffuse down a concentration gradient through the membrane and into the cell.

Small molecules

Oxygen, carbon dioxide and fat-soluble vitamins are small enough to pass through the spaces in the phospholipid bilayer by simple diffusion; where a concentration gradient exists, passive diffusion will occur.

Facilitated diffusion

Larger and charged molecules

Large molecules such as glucose and other sugars, some amino acids and small charged particles (ions) are not able to passively diffuse through the phospholipid bilayer. They need help to cross the membrane; they move by **facilitated diffusion**. There are two types of proteins present in the membrane that facilitate diffusion:

- Channel proteins: these form pores, for example sodium and calcium ions in the membrane, they are shaped to allow particular molecules/ions to pass through. Many are 'gated' meaning they can be open and closed.
- Carrier proteins: these have a specific shape complementary to a specific molecule for example glucose and amino acids, when this molecule binds to the protein, the protein changes shape to allow the molecule to pass across the membrane.

Key points

Ion – atom that carries a positive or negative charge -formed when atoms gain or lose electrons.

Facilitated diffusion – the movement of molecules down their concentration gradient, across a membrane with the help of carrier proteins. Energy is not required.

Active transport

Active transport is the movement of molecules from a lower concentration to a higher concentration, against a concentration gradient, across a membrane. Carrier proteins in the membrane act as pumps to carry large and charged molecules across the membrane. The shape of the protein is complementary to the molecules they carry, which they carry one way across the membrane. As the molecule moves through, the shape of the protein changes so as the molecule exits, it cannot enter again because the protein shape is no longer complimentary. These protein pumps use metabolic energy in the form of Adenosine triphosphate (ATP) to transport molecules across the membrane. This process of active transport is much faster than diffusion.

Key points

Active transport – the movement of molecules from a lower concentration to a high concentration, against a concentration gradient, across a bi membrane. Energy in the form of ATP is required.

Endocytosis and exocytosis

Endocytosis and exocytosis are types of active transport. Sometimes large quantities of materials need to be moved into cells by endocytosis, or out of cells, by exocytosis both require the expenditure of energy. Vesicles are membrane bound organelles used to transport bulk material for example insulin. They easily fuse with membranes and can separate from existing membranes by 'pinching off.

There are different types of endocytosis but all result in a pocket forming around a targeted particle, this pocket pinches off, creating a newly formed vesicle containing the particle.

Phagocytosis

Phagocytosis is a type of endocytosis. During this process cells engulf a target particle and the membrane forms around it to produce vesicles called phagosomes. This normally happens when the body is trying to destroy something like a virus.

Key points

Endocytosis – movement of bulk material into a cell.

Exocytosis – movement of bulk material out of a cell.

Osmosis

Osmosis is diffusion of water molecules across a partially permeable membrane from an area of higher water potential (higher concentration of water molecules) to an area of lower water potential (lower concentration of water molecules). Water potential refers to the likelihood of water molecules to diffuse into or out of a solution. If two solutions have the same water potential, they are isotonic and there will be no net movement of water molecules between the two solutions. In situations where there is a higher water potential outside of a membrane than inside, the solution is hypertonic and water molecules will move toward the area of lower concentration. Pure water has a water potential of zero.

Assessment activity 1.3

1. Draw and label a phospholipid bilayer.
2. Describe the structure of a biological membrane.
3. Produce a table to compare and contrast the different methods of transport across membranes.

Stages involved in respiratory pathways

Respiration activities of cells

Metabolism refers to the thousands of chemical reactions that are taking place in body cells. These reactions can be **catabolic** (e.g.,, respiration) or **anabolic** (e.g.,, photosynthesis).

Key points

Catabolic – reactions that involve the breakdown of a molecule.

Anabolic – reactions that produce a molecule.

ADP – adenosine diphosphate, an important organic compound in metabolism.

Pi – inorganic phosphate, the appropriate concentration of intracellular inorganic phosphate (Pi) is required for cellular metabolism.

Inorganic– does not contain carbon.

Respiration is the release of energy from food, usually from glucose, although fats and amino acids can be respired. The energy stored in these complex macromolecules comes originally from sunlight, trapped during the process of photosynthesis. Respiration takes place in a series of metabolic pathways, each consisting of several stages so the energy is released in small manageable amounts that will not damage cells. This released energy is used to make ATP from **ADP** and **Pi**. Respiration is an extremely important process, because the end-product is chemical energy in the form of Adenosine triphosphate (ATP), that we rely on to keep our cells alive.

ATP is a small soluble molecule that can diffuse easily within a cell, it consists of adenine, ribose and three phosphate groups. The bonds between the two phosphate groups on the right-hand side (see Figures 1.29 and 1.30) can be broken easily by an enzyme, ATPase, causing ADP to be hydrolysed. This immediately releases small amounts of energy to drive anabolic reactions. ATP becomes Adenosine diphosphate (ADP) and an **inorganic** phosphate.

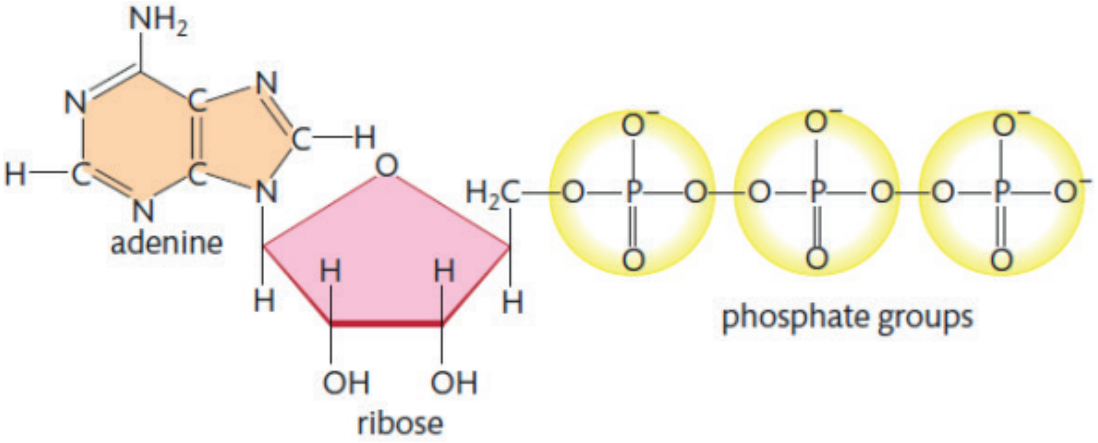


Figure 1.29: Structure of ATP

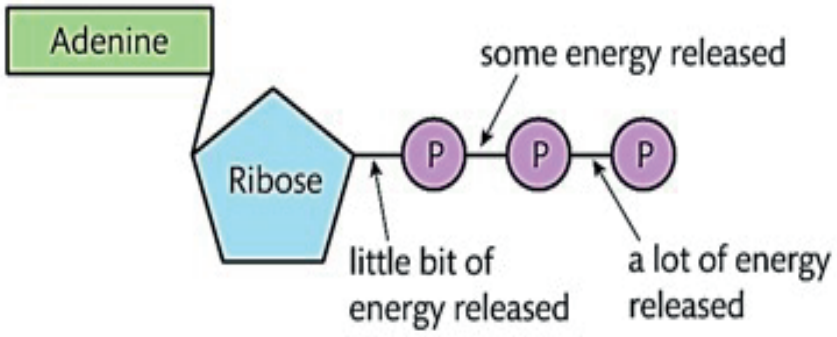


Figure 1.30: Energy release from ATP

Biological processes requiring energy from the hydrolysis of ATP include:

- active transport
- endocytosis – the transport of large substances into a cell
- exocytosis – the transport of large substances out of a cell
- synthesis of polymers and macromolecules
- DNA replication
- protein synthesis
- cell division
- movement.

Respiration can be shown in a word equation:

glucose + oxygen → carbon dioxide + water (+energy)

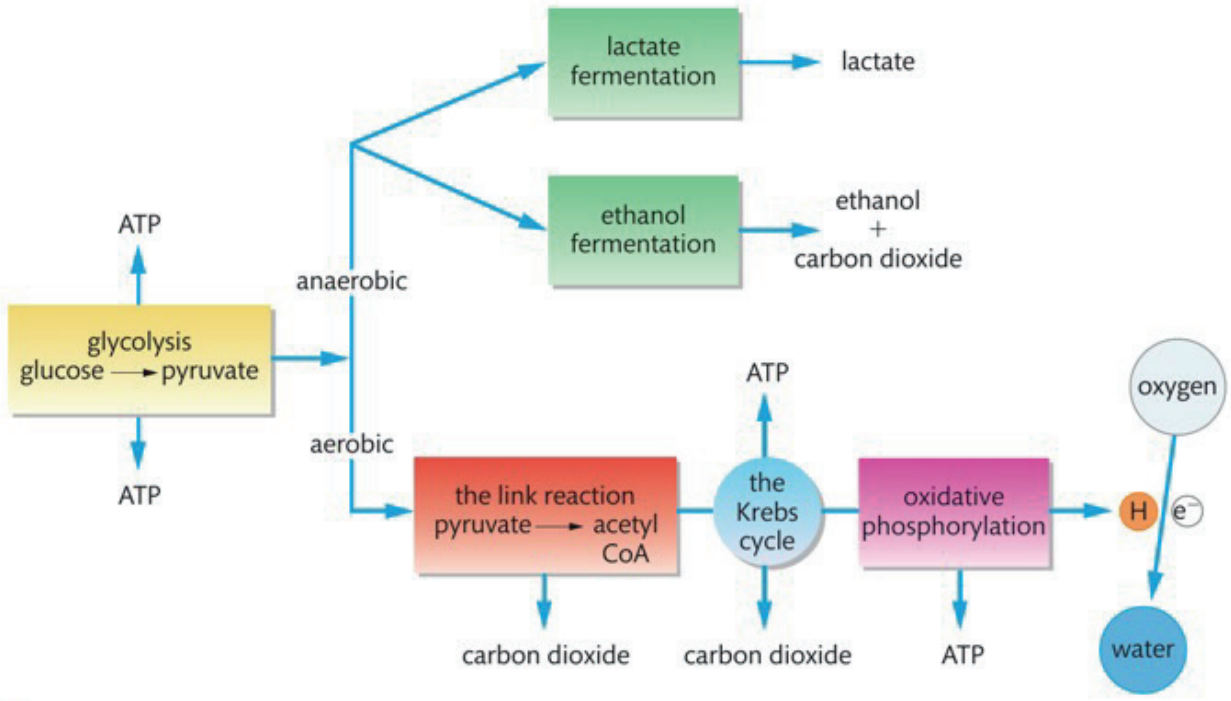


Figure 1.31: Summary of the stages of respiration

Respiration is a series of complex metabolic pathways that incorporates more than 30 different steps. Figure 1.31 above is a summary of the stages of respiration.

It is typically broken down into four stages. Stage 1 does not require oxygen and is described as **anaerobic**. Stages 2, 3 and 4 do require oxygen, they are **aerobic**.

Key points

Anaerobic – does not require oxygen.

Aerobic – requires oxygen.

Respiration stage 1: glycolysis

Glycolysis (sugar splitting) takes place inside the cytoplasm of cells. Glycolysis is a -step enzymes-controlled process that results in the conversion of one molecule of glucose into four molecules of ATP, two molecules of NAD and two molecules of pyruvate.

Glucose is a 6- carbon compound and pyruvate is a 3- carbon compound. This stage does not require any oxygen and can therefore occur during anaerobic conditions, providing the cell with some energy even when there is no oxygen. Within the four stages of glycolysis, there is a sequence of reactions, each catalysed by a different enzyme. Glycolysis only produces two molecules of ATP but the pyruvate is used to form more ATP in stages 2 and 3 of respiration.

Phosphorylation is the first stage of glycolysis (see Figure 1.32), this refers to the addition of a phosphate group to activate a glucose molecule so that it can be split:

- An ATP molecule is hydrolysed and a phosphate group is released. This phosphate group attaches to carbon 6 of a glucose molecule to produce, glucose 6-phosphate. The enzyme hexokinase catalyses this reaction.
- Glucose 6-phosphate turns into Fructose 6-phosphate. The enzyme glucose phosphate isomerase catalyses this reaction.
- Another ATP molecule is hydrolysed and the phosphate group that is released attaches to carbon 1 of Fructose 6-phosphate. This becomes Fructose 1,6-biphosphate. The enzyme phosphofructokinase catalyses this reaction.

Phosphorylation uses two molecules of ATP and a molecule of glucose and produces fructose 1,6-biphosphate.

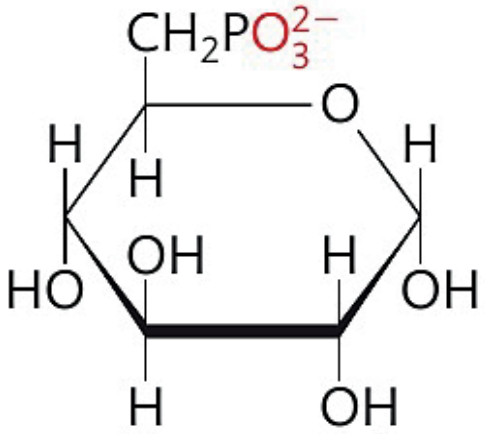


Figure 1.32: Diagram of step 1 of phosphorylation

The second stage of glycolysis involves splitting Fructose 1,6-biphosphate to enable the products to form ATP:

- Fructose 1,6-biphosphate is split into two molecules. The enzyme fructose diphosphate aldolase catalyses this reaction.
- The enzyme triose phosphate isomerase produces two molecules of glyceraldehyde 3-phosphate

By splitting fructose 1,6-biphosphate, two molecules of glyceraldehyde 3-phosphate are produced.

The third stage of glycolysis is oxidation whereby glyceraldehyde 3-phosphate loses electrons:

- Two hydrogen atoms are removed from each glyceraldehyde 3-phosphate to produce two molecules of 1,3 bisphosphate glycerate. This reaction is catalysed by glyceraldehyde phosphate dehydrogenase, but this enzyme also needs another molecule to work called a co-enzyme. It requires two molecules of nicotinamide adenine dinucleotide (NAD). These molecules act as electron acceptors. They accept the hydrogen atoms and, in this reaction, two NAD molecules become reduced NAD or NADH.

Oxidation requires, two glyceraldehyde 3-phosphate and two NAD co-enzymes and produces 2 reduced NAD (NADH) and two 1,3 bisphosphate glycerate.

The fourth stage of glycolysis is conversion of 1,3 bisphosphate glycerate to produce pyruvate:

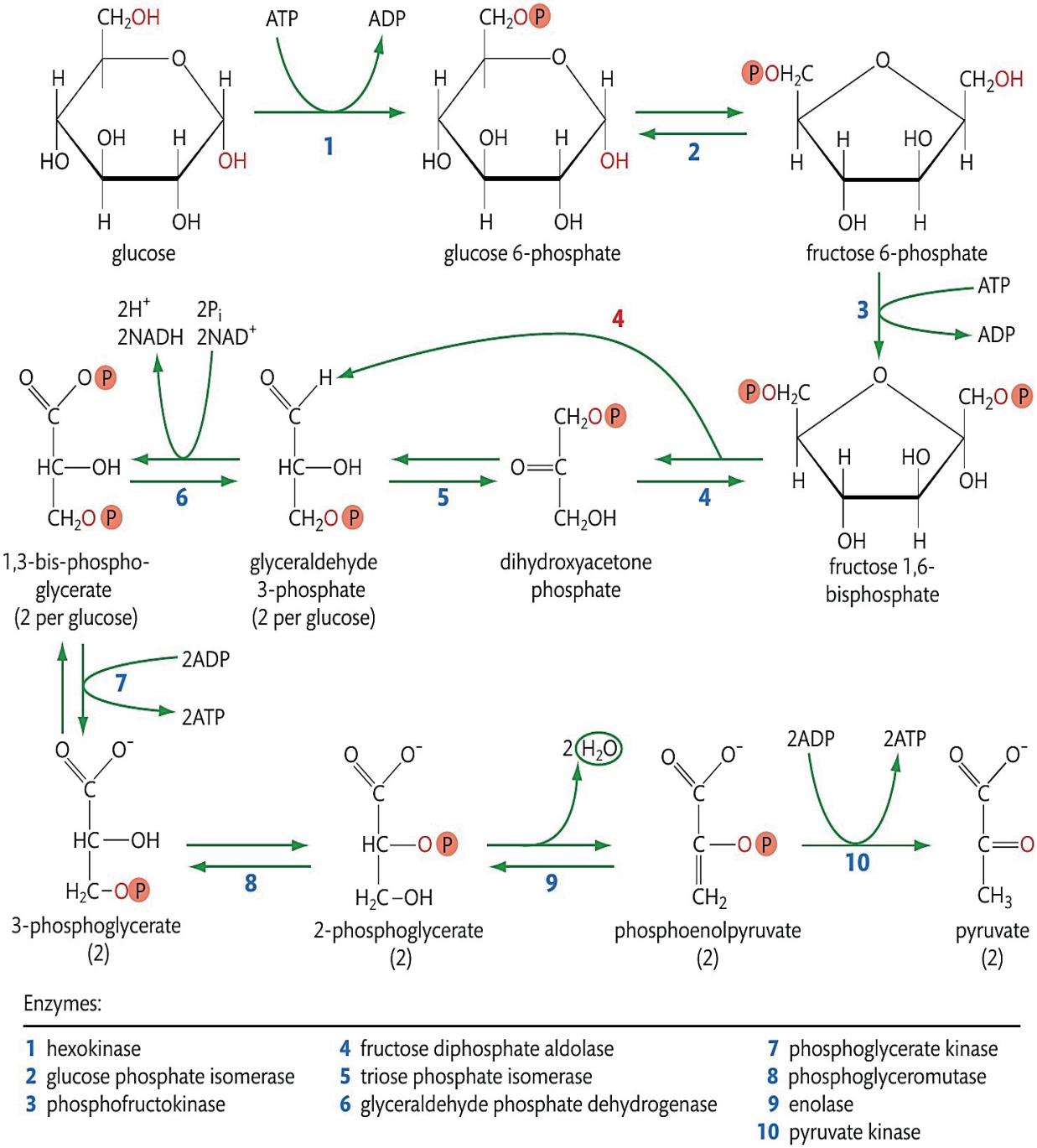
- Four different enzymes are used to convert both molecules of 1,3 bisphosphate glycerate into pyruvate, this produces two ATP per molecule of 1,3 bisphosphate glycerate so four overall by adding an inorganic phosphate to ADP during phosphorylation.
- The conversion of two molecules of 1,3 bisphosphate glycerate produces two pyruvate and four ATP.

Overall glycolysis produces four molecules of ATP per glucose. However, it uses two ATP during phosphorylation. So, for every glucose molecule, two molecules of ATP, two molecules of NADH and two molecules of pyruvate are produced (see Figure 1.33 on the next page).

Key points

Phosphorylation – production of ATP from ADP and Pi.

Oxidation – removal of hydrogen atoms or removal of electrons from substrate molecules.



Enzymes:

1. hexokinase
2. glucose phosphate isomerase
3. phosphofructokinase
4. fructose diphosphate aldolase
5. triose phosphate isomerase
6. glyceraldehyde phosphate dehydrogenase
7. phosphoglycerate kinase
8. phosphoglyceromutase
9. enolase
10. pyruvate kinase

Figure 1.33: Ten-step enzyme catalysed reactions to show the chemical changes taking place during glycolysis to produce pyruvate

Pause point

Can you state the products of glycolysis?

Hint

Do you know the four distinct stages?

Extend

Can you explain the four stages? Try drawing small diagrams to help you explain.

Respiration stage 2: the link reaction

This stage of respiration takes place inside the matrix of the mitochondria (Figure 1.34).

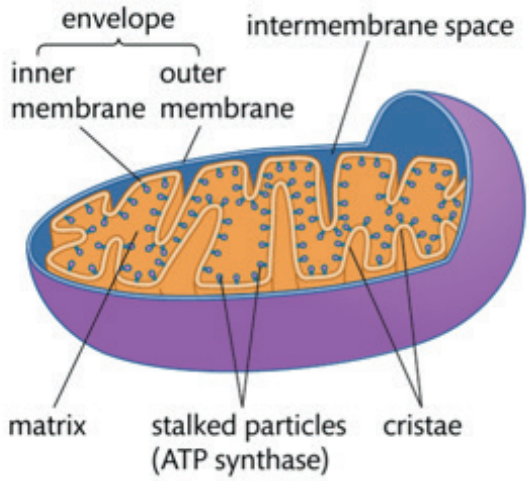


Figure 1.34: Structure of mitochondria

If oxygen is present, the pyruvate produced during glycolysis is changed into acetate during the link reaction (Figure 1.35).

Pyruvate is a 3-carbon molecule. Both molecules of pyruvate produced during glycolysis are decarboxylated (CO2 is removed) and it is dehydrogenated (2 hydrogen atom is removed) during this stage of respiration. Enzymes are needed for this to occur.

The carbon dioxide is a product of respiration and diffuses into the bloodstream from where it is breathed out via the lungs.

NAD accepts the hydrogen atoms and becomes reduced NAD (NADH).

A 2 carbon compound called acetate is produced. The acetate joins to a co-enzyme called co-enzyme A (coA) and forms acetyl co-enzyme A.

For every two molecules of pyruvate, two NADH are made. No ATP is made during this reaction however the two molecules of acetyl co enzyme A and the NADH are used in stage 3.

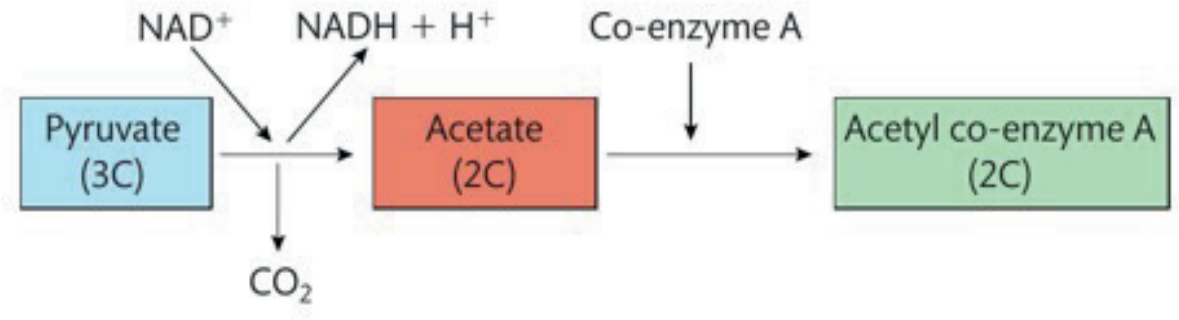


Figure 1.35: The link reaction showing two molecules of pyruvate being converted into acetyl co enzyme A

Respiration stage 3: Krebs cycle

The next stage of respiration also occurs in the mitochondrial matrix and requires oxygen. This stage consists of five enzyme catalysed reactions.

- The acetyl co-enzyme A molecule from the link reaction releases the acetate. This reacts with oxaloacetic acid to form citric acid. Citric acid is a 6-carbon compound
- Citric acid is then decarboxylated (CO_2 is removed) and it is dehydrogenated (2 hydrogen atoms are removed) NADH and H+ is produced. A 5-carbon compound is now produced.
- This 5- carbon compound is decarboxylated and dehydrogenated, NADH and H+ is produced. A 4-carbon compound is made, this is then turned into another 4-carbon compound and 1 molecule of ADP is phosphorylated (addition of inorganic phosphate) producing one molecule of ATP.
- This 4-carbon compound is changed into another 4-carbon compound. This 4-carbon compound is dehydrogenated except this time a different co-enzyme called flavin adenine dinucleotide (FAD) accepts the hydrogen atoms and becomes reduced FAD or FADH2.
- This 4-carbon compound is dehydrogenated, reduced NAD is produced again and oxaloacetic acid is formed. This goes on to accept the acetate again from the link reaction.

The Krebs Cycle produces one molecule of ATP per acetate. One glucose molecule produces two pyruvate and each pyruvate goes on to produce one acetate (so two per glucose). So, this cycle happens twice per glucose molecule hence two ATP are produced per glucose.

The Krebs cycle also produces six reduced NAD per glucose (three per acetate) and two reduced FAD per glucose (one from each acetate).

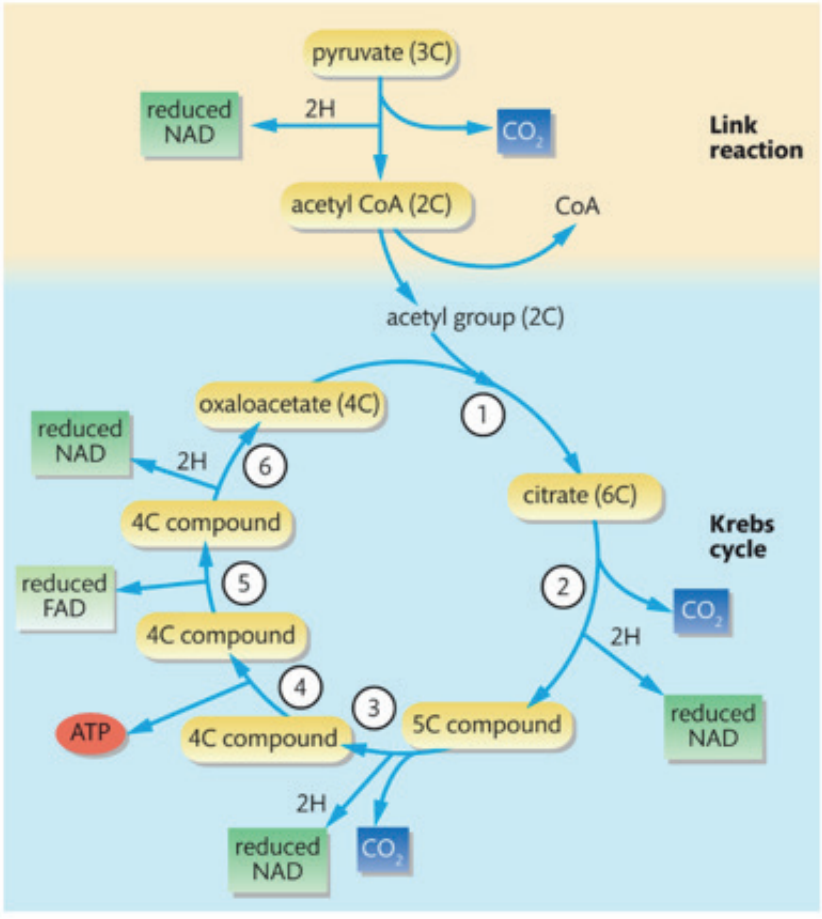


Figure 1.36: Krebs cycle diagram

Assessment activity 1.4

Produce a comparison table to show the products of glycolysis, the link reaction and the Krebs cycle.

Respiration stage 4: oxidative phosphorylation

Oxidative phosphorylation is the final stage of respiration. It occurs across the inner mitochondrial membrane. The inner mitochondrial membrane contains four large protein complexes: I, II, III and IV (referred to as the cytochrome system of carriers in the cristae of the mitochondria). These are used throughout the stage of oxidative phosphorylation. During this stage (see Figure 1.37 below) hydrogen atoms from all the reduced NAD that has been produced from stages 1,2 and 3 release their energy to produce ATP.

- Reduced NAD (NADH) molecules bind to complex I and release their hydrogen atoms as protons (H+) and electrons (e-) into the matrix of the mitochondria. The reduced NAD returns to NAD and can be used again in the Krebs cycle.
- Reduced FAD molecules made during the Krebs cycle bind to complex II and release their hydrogen atoms as protons (H+) and electrons (e-) into the matrix.
- The H+ ions stay in the matrix while the electrons pass along all the protein complexes. This is known as the electron transport chain (ETC).
- In complexes I, II and IV (found in the membrane) the electrons release some of their energy. This energy is used to pump the protons from the matrix across the inner mitochondrial membrane to the space between the inner and outer membrane. The protons are pumped by complexes I,III and IV.
- In complex IV, the electron combines with protons and oxygen to form water, another product of respiration. This is the only stage that uses oxygen but, without it respiration does not occur. Four electrons, four protons and one molecule of oxygen are needed to make two molecules of water. Oxygen is therefore known as the final electron acceptor.
- Because protons have moved from the matrix to the intermembrane space, this has created a proton gradient, where there are more protons in the intermembrane space than in the matrix. This is a store of potential energy and is used to generate ATP.
- The protons cannot move back across the inner mitochondrial membrane without being pumped. However, the ATP synthase enzyme has a channel for the protons to move through. This movement of protons across a membrane due to a proton gradient is called chemiosmosis.
- When the protons move from the intermembrane space back to the matrix, through the ATP synthase enzyme, the energy physically spins part of the enzyme which in turn cause phosphorylation of ADP to produce ATP.

Therefore, the stage of oxidative phosphorylation, uses all the reduced NAD and reduced FAD produced in stages 1 to 3 to produce ATP. All the reduced NAD and FAD comes from glucose molecules, so the energy that is stored in the glucose molecule is used to produce ATP (see Figure 1.37 below).

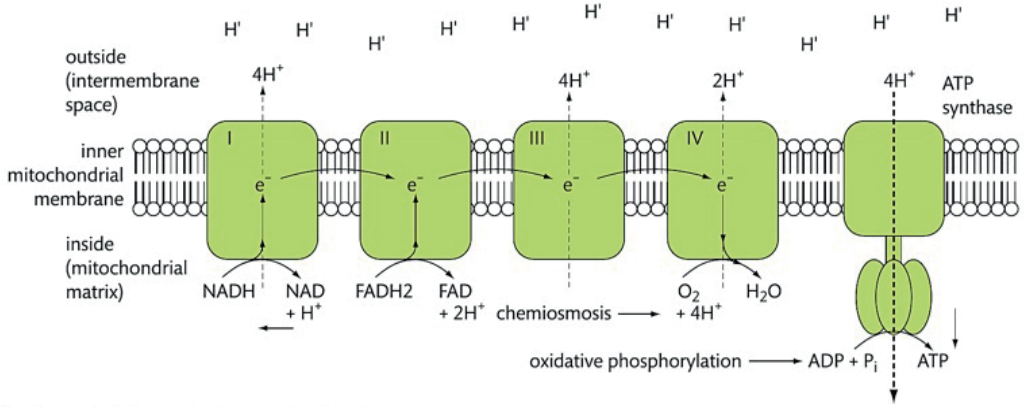


Figure 1.37: The electron transport chain and chemiosmosis

Key points

Chemiosmosis – the movement of ions across a semi-permeable membrane, down an electro-chemical gradient.

The table below show the estimated number of ATP molecules made for each molecule of glucose. It is approximately 2.5 molecules of ATP made per reduced NAD and 1.5 molecules of ATP per reduced FAD.

Table 1.3: Estimated ATP molecules for each molecule of glucose

Stage of respiration	Molecules used/produced	Total ATP produced after oxidative phosphorylation
Glycolysis	-2 ATP +4 ATP +2 reduced NAD	2 5
Link reaction	+2 reduced NAD	5
Krebs Cycle	+2 ATP + 6 reduced NAD +2 reduced FAD	2 15 3

The total yield of ATP for each glucose molecule respired is approximately 32. However, this is rarely achieved so is more realistically approximately 30 because:

- Protons can leak across the inner mitochondrial membrane which reduces the number remaining in the cytoplasm. So, there are less protons available to move through the ATP synthase enzyme and cause phosphorylation of ADP to produce ATP.
- Some ATP produced is used to actively transport the pyruvate into the mitochondria as it is made in the cytoplasm.
- Some ATP is also used to transport the reduced NAD (made in the cytoplasm during glycolysis), into the mitochondria.

Key points

Yield -– the amount produced.

Pause point

Can you explain oxidative phosphorylation?

Hint
Can you explain why the proton gradient is a source of potential energy?

Extend
Produce a table to show the molecules that are needed in each stage and state what is produced in each stage.

Anaerobic lactic acid cycle

As you have just seen, oxygen acts as the final electron acceptor during oxidative phosphorylation. However, if oxygen is not present the electron transport chain stops and so do the Krebs cycle and the link reaction.

This means the only source of ATP is through glycolysis because this does not require oxygen. The reduced NAD produced during glycolysis needs to be re-oxidised so that glycolysis can keep happening. No more than two ATP are produced during this stage, but it does mean that glycolysis can continue.

Lactate fermentation

This is the process that happens in human tissue during vigorous activity such as sprinting to sustain muscle contraction. The enzyme lactate dehydrogenase is responsible for both oxidation of NAD and reduction of pyruvate. During lactate fermentation the following happens:

- Reduced NAD produced during glycolysis must be re-oxidised to NAD+
- Pyruvate (the product of glycolysis) acts as the hydrogen acceptor (accepting H from reduced NAD)
- Pyruvate becomes reduced and forms lactate
- NAD is now re-oxidised and available again to accept more hydrogen atoms from glucose
- Glycolysis can therefore continue generating more ATP.

The lactate produced is carried away from muscles in the blood to the liver, until oxygen becomes available again. When there is more oxygen the liver will convert the lactate back into pyruvate, which can then enter the Krebs cycle in the muscles and continue to generate more ATP.

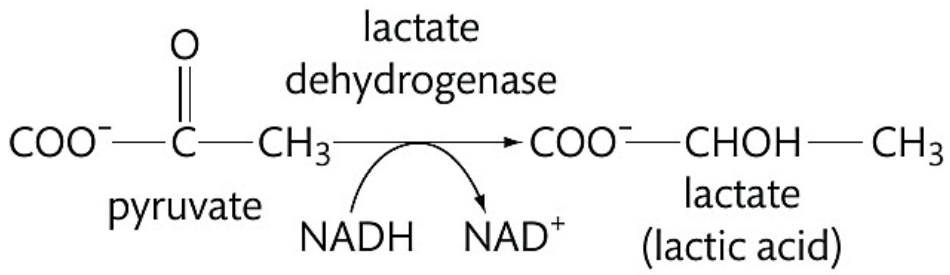


Figure 1.38: Lactate fermentation chemical equation

Pause point

Can you explain anaerobic respiration?

Hint

Draw the chemical equation for lactate fermentation.

Extend

Can you explain why NAD needs to be re-oxidised and why this is important for mammals.

Cellular activities

The cell cycle

Cells reproduce by splitting into two cells. The new cells produced are genetically identical to the parent cell and are referred to as daughter cells. To prepare for division, a cell must duplicate all of its contents, this includes the DNA in the nucleus and all of the cellular organelles. To prepare for division, the cell goes through a sequence of events called the **cell cycle**.

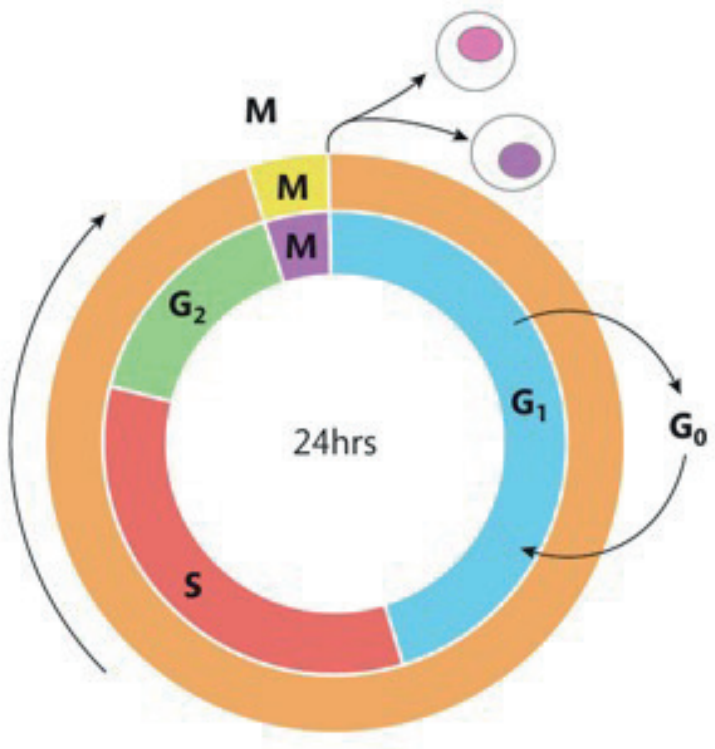


Figure 1.39: The cell cycle in eukaryotic cells showing the different phases of cell preparation (Interphase) and division (M phase) to produce genetically identical daughter cells by cytokinesis

Key points

The cell cycle –the sequence of events that take place in a cell to prepare for cell division.

Interphase – the phase of the cell cycle in which the cell is preparing for division.

Mitosis – the division of a nucleus into two genetically identical nuclei.

Cytokinesis – the division of the cytoplasm and organelles to produce two genetically identical daughter cells.

Phases in the cell cycle

Mitosis (M phase) – during this phase the nucleus of the cell divides into two. At the beginning of M phase, the nucleus contains two copies of each chromosome as these are replicated in the synthesis phase (see below). This means that after division of the nucleus, each newly produced nucleus contains a full set of chromosomes

Cytokinesis – following mitosis, the cytoplasm of the cell divides to produce two genetically identical daughter cells. Each daughter cell produced contains a full set of chromosomes in the nucleus and organelles needed to carry out cellular processes.

Interphase – when the cell is not dividing, the cell cycle phases are collectively known as interphase. During interphase processes take place to prepare the cell for mitosis and cytokinesis.

Interphase is made up of four phases:

- Gap 1 phase (G1) – during G1, the cell prepares for division by growing and increasing in size. Protein synthesis takes place and the cellular organelles are duplicated.
- Synthesis phase (S) – in this phase, the DNA in the cell nucleus is duplicated. The chromosomes are replicated so that each one consists of a pair of identical sister chromatids.
- Gap 2 phase (G2) – during G2 the cell grows further. The cell also prepares the materials in the cytoplasm that are needed for mitosis and cytokinesis.
- Go is the fourth stage of the cell cycle that is not part of replication but is known as a resting phase. The term resting phase can be misleading however as the cell is still active during this phase even though it is not dividing. G0 can be entered immediately following G1. It can be reversible or irreversible. Some cells once they have become differentiated to perform a specific function, stay in Go and do not divide further. An example of one such cell is a neurone. Cells with DNA damage are prevented from dividing by irreversibly entering Go, this stops the cell from replicating and passing on the damage. Other cells enter G0 before returning to the cell cycle in response to external signals.

Cell cycle checkpoints

There are two main places in the cell cycle where control mechanisms ensure that the cell is able to divide properly. These are called the cell cycle checkpoints. The system of cell cycle control ensures that the correct amount of time is spent in each phase and detects errors that might occur during the different processes. There is a checkpoint at the start of G1 and the start of G2. The checkpoints can detect errors in DNA replication and chromosome production. If errors are detected the cell cycle is stopped from progressing until the damage is repaired or the cell enters G0 permanently. The cell cycle control system uses a different regulatory protein called cyclins to promote or prevent cell cycle progression.

Cancer and the cell cycle

The cause of some cancers has been linked to malfunctions in the cell cycle control system. In these cases, cancer can be caused by loss of cell cycle control. This leads to abnormal replication of cells which contain DNA damage. These cells replicate at a faster rate than usual and form a tumour. Often the DNA damage is in the form of a mutation (change to DNA) in a gene which produces cell cycle regulatory proteins. The protein cannot be produced correctly, and so cell cycle checkpoints are not performed properly. Cancers are not usually inherited but inheriting a mutation in a gene involved in the cell cycle can increase the risk of certain types of cancer developing. Other cancers develop because the damage to the DNA of cell cycle control genes occurs during a person's lifetime.

Case study

Cancer and the cell cycle

Rebekah has a history of breast cancer in her family, both her mother and grandmother developing the disease. She read about genetic tests which are available to some people to test for mutations (DNA changes) in a set of genes called BRCA1 and BRCA2. These mutations can be passed down from parents and research shows that having a mutation in a single copy of either gene can increase the risk of breast and ovarian cancers. Both genes are known to produce proteins which are involved in the complex processes that take place during the cell cycle checkpoint at the start of G2. During the genetic test, Rebekah's relative with cancer would be tested to find out the DNA sequence of her BRCA1 and BRCA2 genes. Following this, Rebekah's genes would also be sequenced and compared to the sequence of her mother's genes. This will allow scientists to identify if Rebekah has the same faulty gene and to assess whether she has increased risk of breast and ovarian cancers. If increased risk is found, Rebekah will have different options to minimise the risk of cancer including regular screening, lifestyle changes, medications and surgery.

Check your knowledge

1. What events happen in the different phases of interphase?
2. Why are cell cycle checkpoints important?
3. Suggest how a faulty BRCA1 or BRCA2 gene may lead to a tumour forming.
4. Explain why Rebekah's gene sequences would be compared to that of her mother.

Haploid and diploid cells

Humans have cells that contain 23 pairs of chromosomes in the nucleus. These cells contain a full set of DNA and make up most of the cell types in the human body. They are known as diploid cells. Cells that make up the different tissues and organs in the body are diploid. There are two types of cell that do not fit into this category: red blood cells and sex cells. Red blood cells (erythrocytes) do not have a nucleus and so do not contain any chromosomes. Sex cells, also known as **gametes**, sperm and ova, have nuclei which contain 23 individual chromosomes (one copy from each pair). These are known as haploid cells. It is important that sex cells only contain one copy of each chromosome, so that when the gamete nuclei fuse during fertilisation, a diploid **zygote** is produced which will then develop into an embryo.

Key points

Haploid - having only one set of chromosomes, represented by n.

Diploid - having two sets of chromosomes, represented by 2n.

Gamete – a sex cell, in animals, these are sperm and ova.

Zygote – a fertilised ovum.

Embryo – an unborn child in the process of development.

Somatic cells - a cell in the body which is not a gamete or undifferentiated stem cell.

Cell potency

Cell potency refers to a cell's ability to differentiate into other cell types. Differentiation is the process that cells go through to obtain a specific function. Different cells are able to carry out different functions because they have specialised structures. During differentiation genes are switched on which coordinate a series of complex processes leading to the development of different structures and different functions. A stem cell is a cell with the ability to develop into cells with specific structure and function. Cell specialisation leads to structural variation. For example, muscle cells make large amounts of actin and myosin, liver and phagocytic cells produce more lysosomes; this development of specific and distinctive features in cells is called cell differentiation.

Stem cells are found in embryos and adult bone marrow. Table 1.4 describes the potency of different types of stem cell.

Table 1.4: Potency levels of stem cells

Relative potency	Description	Found in
Totipotent	These cells are also called omnipotent and can differentiate into any other cell type	Zygote, placenta, umbilical cord
Pluripotent	These cells have the potential to differentiate into many other cell types	Embryo and foetus
Multipotent	These cells develop into a limited number of cell types usually of the same tissue type. They have a designated fate	Bone marrow

Assessment activity 1.5

1. Draw a diagram of the cell cycle.
2. Label the different phases.
3. Describe what happens in each phase.
4. Describe what happens in G0.
3. Explain the need for cell cycle checkpoints.
4. Explain what can happen if the cell cycle is not regulated properly.

Chromosome formation and nuclear division

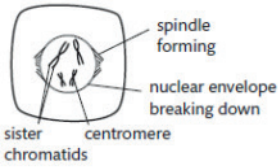
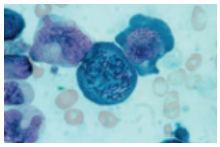
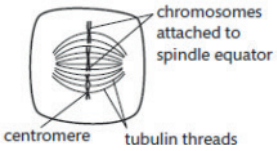
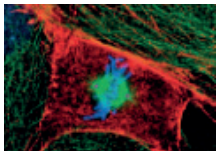
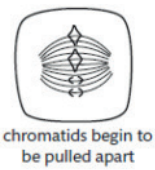
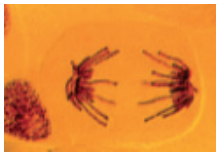
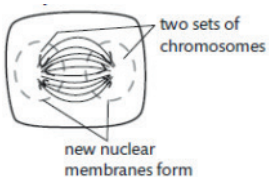
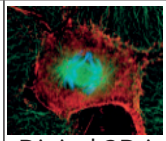
Mitosis

Figure 1.39 showing the cell cycle included a phase called mitosis. Mitosis is a type of nuclear division that results in two daughter cells which are genetically identical to each other. The new cells each contain a nucleus with a full set of chromosomes (23 pairs). In humans, the purpose of mitosis is for growth of the organism and repair of damaged tissue. Mitosis has four main stages, they are called prophase, metaphase, anaphase and telophase.

Exam tip

An easy way to remember the order of the stages of mitosis is to use a mnemonic. You could make up your own or use 'Please Make Another Two'.

Table 1.5: Events taking place during each stage of mitosis

Stage of mitosis - diagram	Stage of mitosis - photo	Events occurring during the stage
Prophase  	 Prophase of mitosis in white blood cells. The condensed chromatin is visible as chromo-somes	• The chromosomes that have replicated during the S phase of interphase, and now consist of two identical sister chromatids, now shorten and thicken as the DNA supercoils. • The nuclear envelope breaks down. • The centriole divides and the two new daughter centrioles move to opposite poles (ends) of the cell. • Cytoskeleton protein (tubulin) threads form a spindle between these centrioles. The spindle has a 3D structure and is rather like lines of longitude on a virtual globe. In plant cells the tubulin threads form from the cytoplasm.
Metaphase  	 Digital 3D immunofluorescent light micrograph of a section through a mammalian cell during metaphase of mitosis. The tubulin microtubules of the spindle are coloured green, the chromosomes blue and the two centrioles are pink. [Magnification × 500.]	• The pairs of chromatids attach to the spindle threads at the equator region. • They attach by their centromeres.
Anaphase  	 Light micrograph of anaphase of mitosis in a bluebell cell.	• The centromere of each pair of chromatids splits. • Motor proteins, walking along the tubulin threads, pull each sister chromatid of a pair, in opposite directions, towards opposite poles. • Because their centromere goes first, the chroma-tids, now called chromosomes, assume a V shape.
Telophase  	 Digital 3D immunofluorescent light micrograph of anaphase of mitosis. The chromatids (blue) of each chromsome have separat-ed and been pulled to opposite ends of the cell.	• The separated chromosomes reach the poles. • A new nuclear envelope reforms around each set of chromosomes. • The cell now contains two nuclei, each genetically identical to each other and to the parent cell from which they arose.

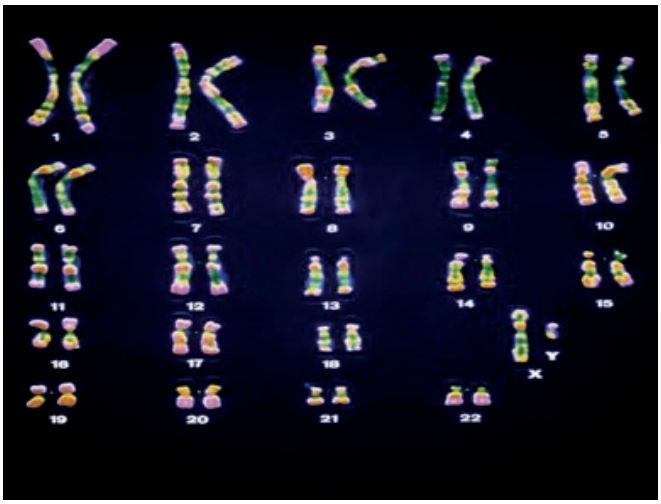
Cytokinesis

Once mitosis is complete, the cell cytoplasm divides into two so that two new genetically identical daughter cells are produced, each containing its own nucleus. In animal cells, the plasma membrane folds inwards and 'nips in' the cytoplasm. In animal cells, and end plate forms where the equator of the spindle was, and new plasma membrane and cellulose cell wall material is laid down either side along this end plate.

Homologous chromosomes

Somatic cells contain 23 pairs of chromosomes. Each pair consists of one maternal chromosome (from the mother) and one paternal chromosome (from the father). The chromosome making up a pair are known as homologous chromosomes. The chromosomes contain the same genes in the same places on the chromosomes (loci). Each chromosome of a homologous pair will contain the same genes but may contain different variants of the gene – different alleles. This leads to variation in an individual.

a)



b)

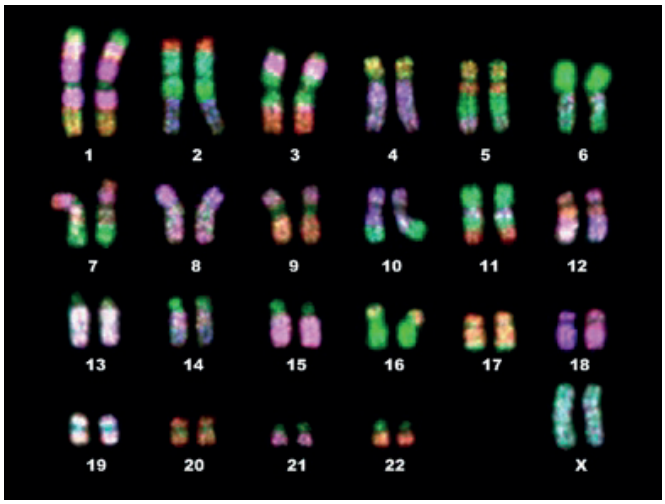


Figure 1.40: A karyotype - the pairs of homologous chromosomes in a human somatic cell. You can see 22 pairs of autosomal chromosomes and one pair of sex chromosomes which determine whether the person is male or female. a) male and b) female.

Meiosis

Mitosis is the process that produces diploid cells that are required for growth of the organism or repair of tissues. Mitosis and differentiation produce somatic body cells. However, a different process called meiosis is used in the production of gametes. Gametes are haploid cells as they do not have a full set of chromosomes in their nucleus. Rather than having 23 pairs of chromosomes (2n) like somatic human cells, human gametes contain 23 individual chromosomes (n). Meiosis is crucial for sexual reproduction to take place. Sexual reproduction increases genetic variation in populations as it involves the combining of genetic material from two (usually) unrelated individuals. During fertilisation, the nucleus of the sperm combines with the nucleus of the ova. This then produces a diploid zygote, with a full set of chromosomes, which can then develop through mitosis and differentiation into a person.

Key points

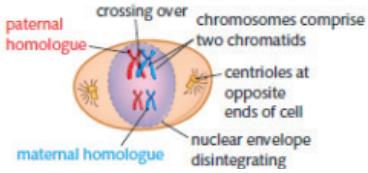
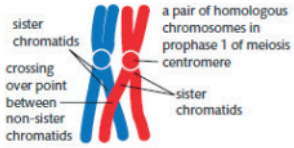
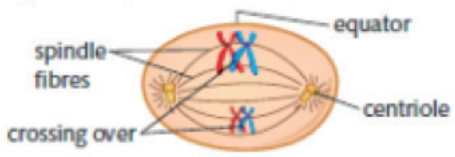
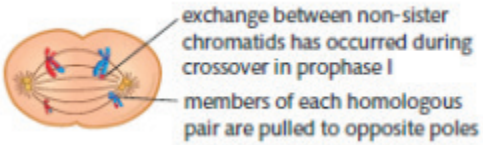
Fertilisation – the union of two gametes/gamete nuclei, to produce a zygote.

Zygote – diploid cell produced by the union of two gametes.

The stages of meiosis

Meiosis takes place in the ovaries and testes of eukaryotic organisms. Cells that divide by meiosis are diploid at the start of the process but produce four haploid cells (with half the original number of chromosomes) that are genetically different from each other; these cells are called gametes. As in mitosis, meiosis is preceded by DNA replication. Meiosis takes place in two stages, during the first stage (meiosis I, Table 1.6) the phases are prophase 1, metaphase 1, anaphase 1 and telophase 1. During telophase I, the chromosomes are enclosed in nuclei. The cell now undergoes a process called cytokinesis that divides the cytoplasm of the original cell into two daughter cells. The second stage, meiotic division (meiosis 2II, Table 1.7) which may take place immediately or following a short gap. This round also has four phases called prophase 2, metaphase 2, anaphase 2 and telophase 2. Finally, during telophase II, the chromosomes are enclosed in nuclear membranes. Cytokinesis follows, dividing the cytoplasm of the two cells. After progressing through the phases of meiosis and cytokinesis, the product is four haploid cells, each genetically different from the original cell.

Table 1.6: Events taking place during the first phase of meiosis (meiosis I)

Stage of meiosis 1	Events during the stage
Prophase 1  Prophase 1 may last for days, months or years depending on the species and type of gamete (male or female) being formed  Crossing over	• The chromatin condenses and each chromosome supercoils. In this state they can take up stains and be seen with a light microscope. • The nuclear envelope breaks down and spindle threads of tubulin protein form from the centriole. • The chromosomes come together in their homologous pairs. • Each member of the pair consists of two chromatids. • Crossing over occurs where non-sister chromatids wrap around each other and may swap sections so that alleles are shuffled.
Metaphase 1  Homologous pairs of chromosomes, still in their crossed-over state, on the equator of the spindle	• The pairs of homologous chromosomes attach along the equator of the spindle. • Each attaches to a spindle thread by its centromere. • The homologous pairs are arranged randomly with the members of each pair facing opposite poles of the cell. This arrangement leads to independent assortment – the way they line up in metaphase determines how they will segregate independently when pulled apart during anaphase.
Anaphase 1  	• The crossed-over areas separate from each other, resulting in swapped areas of chromosome and allele shuffling. • The members of each pair of homologous chromosomes are pulled apart by motor proteins that drag them along the tubulin threads of the spindle. • The centromeres do not divide and each chromosome consist of two chromatids.

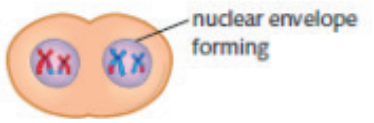
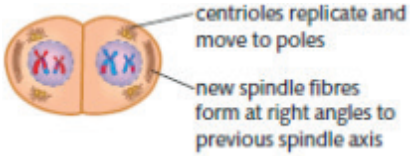
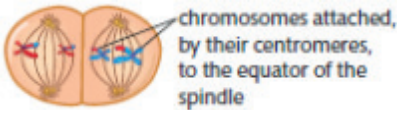
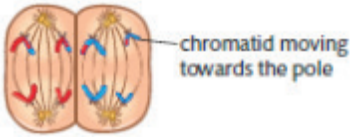
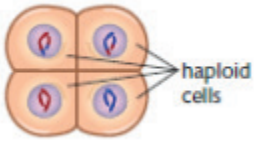
Telophase 1  	• In most animal cells two new nuclear envelopes form around each set of chromosomes and the cell divides by cytokinesis. There is then a short interphase where the chromosomes uncoil. • Each new nucleus contains half the original number of chromosomes, but each chromosome consists of two chromatids. • In most plant cells the cell goes straight from anaphase 1 into prophase 2.

Table 1.7: Events taking place during the second stage of meiosis

Stage of meiosis 2	Events during the stage
Prophase 2  	• If the nuclear envelopes have reformed they now break down. • The chromatids of each chromosome are no longer identical due to crossing over in prophase 1 • Spindles form
Metaphase 2  	• The chromosomes attach, by their centromere, to the equator of the spindle. • The chromatids of each chromosome are randomly arranged. • The way they are arranged will determine how the chromatids separate (independent assortment) during anaphase.
Anaphase 2  	• The centromeres divide. • The chromatids of each chromosome are pulled apart by motor proteins that drag them along the tubulin threads of the spindle, towards opposite poles. • The chromatids are therefore randomly segregated.
Telophase 2  	• Nuclear envelopes form around each of the four haploid nuclei. • In animals the two cells now divide to give four haploid cells. • In plants, a tetrad of four haploid cells is formed.

Pause point

Produce a table to distinguish between mitosis and meiosis

Hint

Include the type and number of daughter cells produced, whether the nuclei produced are haploid or diploid, the number of rounds of division, the names of the phases and the purpose of the division.

Extend

Discuss how cells are prepared for nuclear division in the other stages of the cell cycle and describe what happens following nuclear division to produce daughter cells.

Homeostasis

Homeostasis is the process of keeping the internal body environment in a steady state. Reactions that take place inside the body are catalysed by enzymes. For enzymes to work at their optimum rate, the body must keep several factors in a steady state. Body temperature is one of the factors that is tightly maintained by homeostatic mechanisms. Normal body temperature is around 37°C; even a few degrees change above or below can have serious consequences for the body. Blood glucose concentration and blood water potential are two other examples of states maintained by homeostasis.

All mechanisms of homeostasis rely on negative feedback (Figure 1.41). Negative feedback means that when there is a change away from the normal set point, corrective processes take place to return the change back to normal. All negative feedback mechanisms involve:

- a receptor which detects the change away from normal
- an input pathway which sends signals to the control centre
- a control centre which coordinates a response to reverse the change
- an output pathway which takes signals from the control centre to the effector
- an effector which carries out a response to reverse the change.

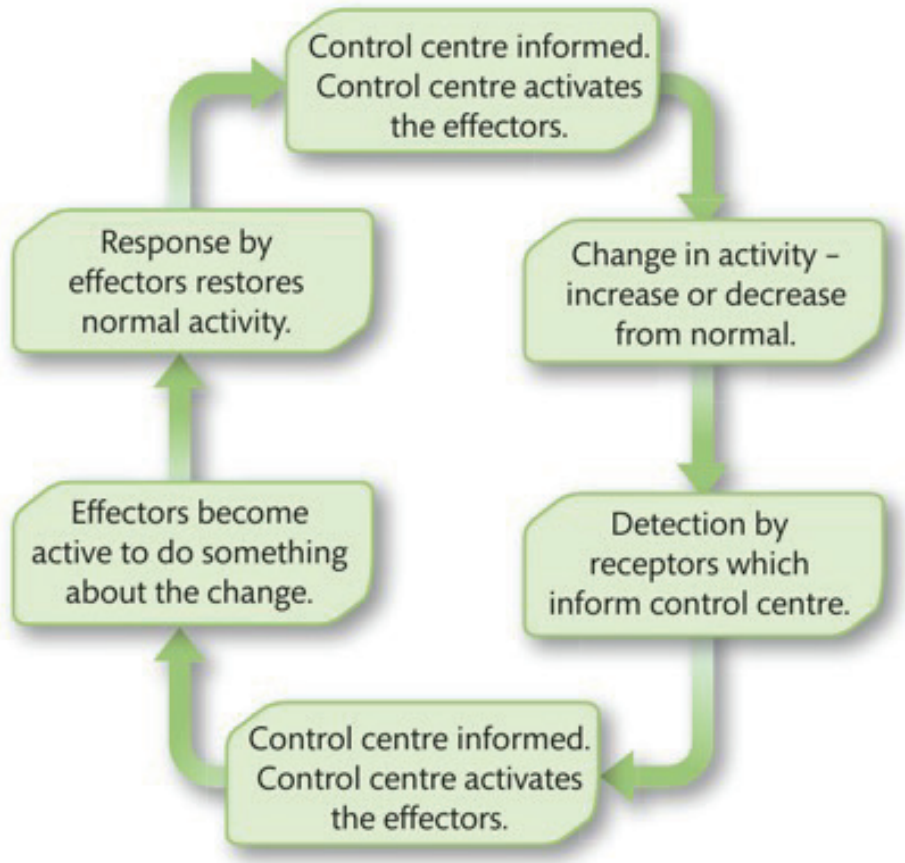


Figure 1.41: A negative feedback loop is used to maintain homeostasis in the human body

Key points

Homeostasis – process of maintaining a constant internal environment, despite external changes.

Thermoregulation – maintenance of normal body temperature – around 37oC.

Control of body temperature

Maintenance of normal body temperature of around 37oC is called **thermoregulation**. Failure of this system can lead to hyperthermia (abnormally high body temperature). Several factors can lead to high body temperature, these include: heat exhaustion where severe dehydration and reduced sweating causes the temperature to rise excessively and fluid loss caused by medications such as diuretics. Prolonged exposure to temperatures above 40oC can result in heat stroke. Heat stroke disrupts thermoregulation because compensatory mechanisms such as sweating are lost and the core body temperature soars. This is an extremely serious condition which causes blood pressure to fall and respiratory function to weaken. If the body temperature remains high, neurological damage will occur causing confusion, delirium and eventually, coma. Urgent steps must be taken to reduce the core body temperature otherwise death will result.

Body temperature control is coordinated by the thermoregulatory centre in the hypothalamus of the brain. The thermoregulatory centre receives input signals from two sets of receptors which detect changes in temperature. These are called thermoreceptors. The hypothalamus itself contains thermoreceptors which monitor the temperature of the blood as it passes through the brain thus monitoring the body's core temperature. Thermoreceptors in the skin monitor the temperature of peripheral regions of the body. The thermoregulatory centre sends signals to a range of different effectors in response to increased or decreased temperatures. The heat loss centre of the hypothalamus is stimulated when you get too warm (heat needs to be lost) and the heat gain centre of the hypothalamus is stimulated when you get too cold (heat needs to be gained).

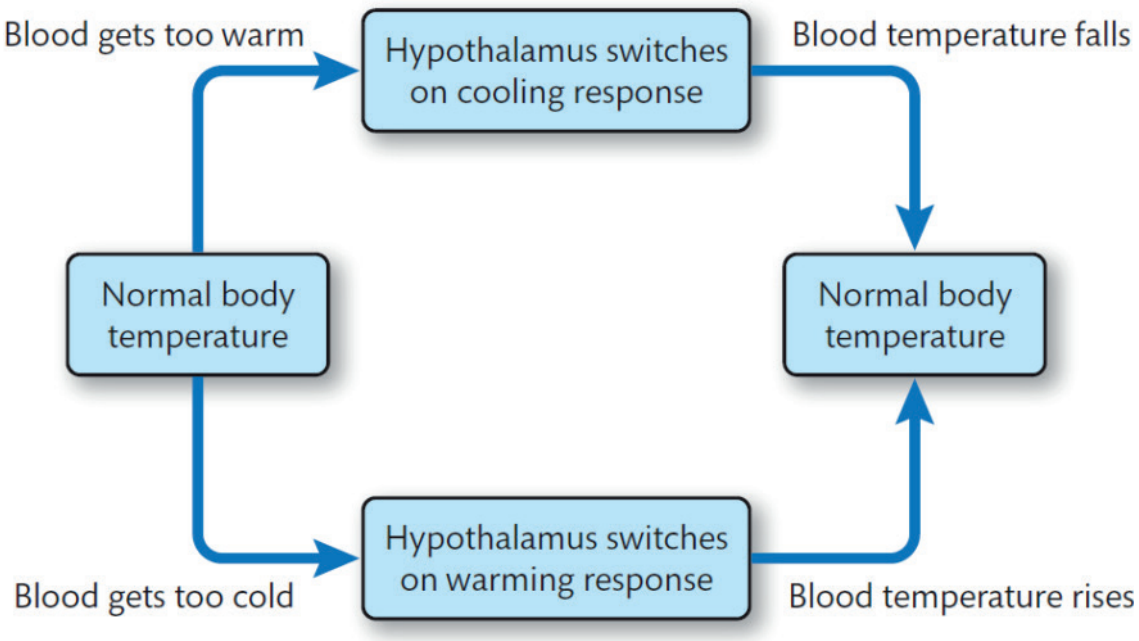


Figure 1.42: Negative feedback control of body temperature

Responses to changes in temperature

The first response to a change in temperature is a voluntary behavioural action. If it gets too cold, you may put on a jumper or move indoors. If it gets too warm, you may take layers of clothing off or move to the shade. If these corrective mechanisms are not enough, then the thermoregulatory centre will act to initiate appropriate responses.

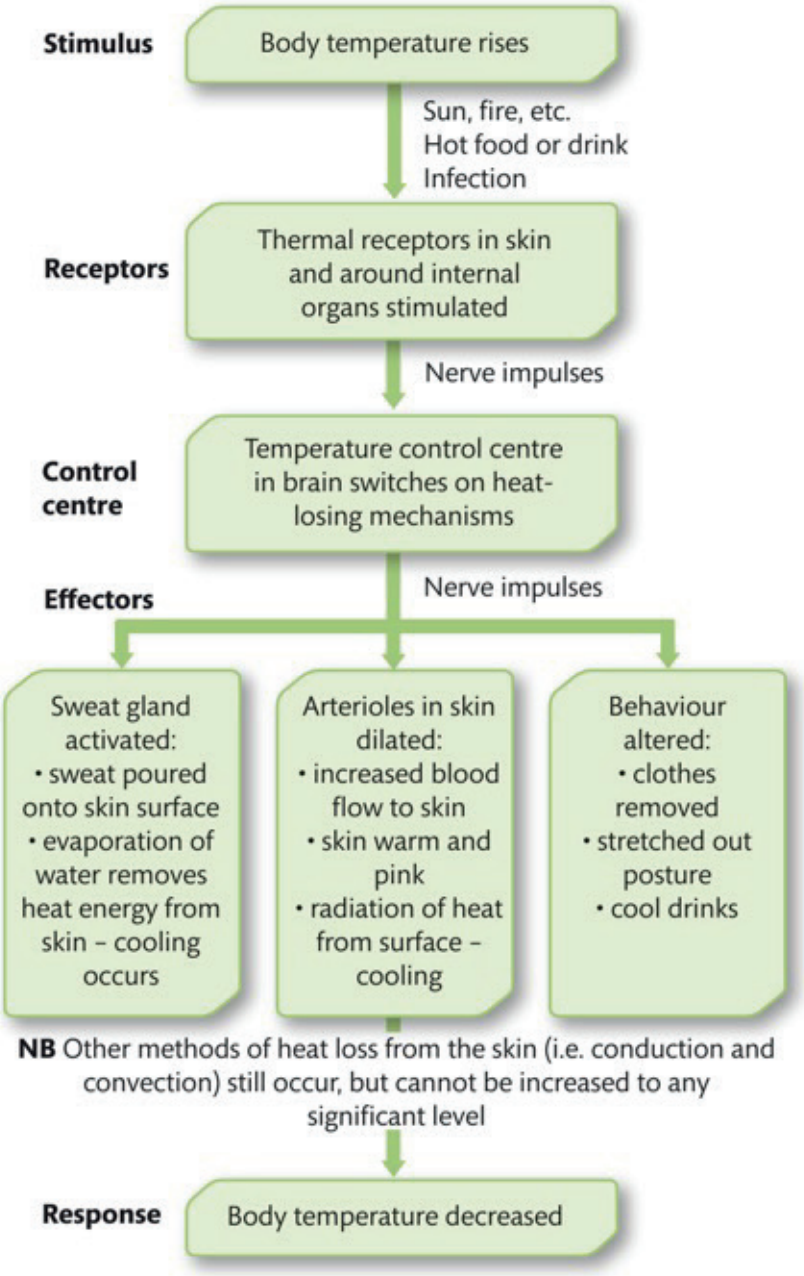


Figure 1.43: Homeostatic control of an increasing body temperature

Arteries divide into smaller blood vessels called arterioles. Arterioles contain a layer of smooth muscle (tunica media) which allows the arterioles to dilate and constrict and therefore alter the diameter of the lumen in order to regulate the flow of blood into capillary beds in the tissues. When this smooth muscle contracts, the lumen of the blood vessel is constricted (the blood vessel narrows) and less blood flows through the body tissues; this is called vasoconstriction. When body temperature falls, vasoconstriction occurs meaning that less heat is transferred away from the body core and so less heat is lost. When body temperature rises, the opposite occurs. The smooth muscle in the arteriole walls relaxes and vasodilation occurs. More heat is carried from the core to the surface of the body where it can be lost to the external environment.

- Sweat glands – when body temperature increases, sweat glands in the skin secrete sweat onto the skin where it evaporates. The evaporation of water requires a relatively large amount of energy and so sweating is an effective way of cooling down.
- Erector pili muscles in the skin – the hairs that can be found covering the surface of the skin have muscles attached to them. When body temperature falls, signals from the heat gain centre cause these muscles to contract. This causes the hairs to stand on end, allowing them to trap an insulating layer of air close to the skin. This is not an effective heat gain mechanism in humans since much of the body hair has been lost through evolution.
- Skeletal muscle – when you are cold, the heat gain centre of the hypothalamus can send signals to skeletal muscles to cause them to contract and relax repeatedly. This is shivering. Heat is generated from the increased rate of respiration needed to supply the ATP for the contractions to take place.
- Adrenal and thyroid glands – the adrenal gland is responsible for the secretion of the hormone adrenaline. The thyroid gland is responsible for the secretion of the hormone thyroxine. Secretion of both hormones by their respective gland is increased to raise the body's metabolic rate. This generates heat. When the body temperature decreases the glands stop secreting adrenaline and thyroxine.

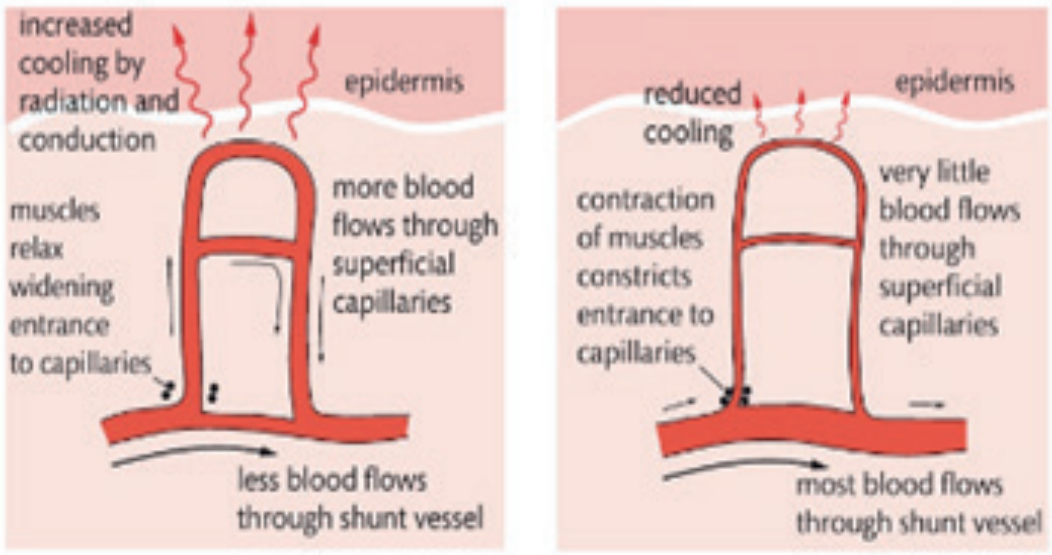


Figure 1.44: The role of blood vessels in thermoregulation

Extremes of temperature

When the body temperature changes, the hypothalamus works to restore temperature to normal. However, the homeostatic mechanisms are not able to cope with extreme changes in temperature.

If body core temperature falls below 35°C hypothermia occurs. Hypothermia can be caused by exposure to a cold environment or from something that causes decreased heat production or increased heat loss such as alcohol intoxication or low blood sugar. Hypothermia can cause shivering, drowsiness, unconsciousness and ultimately death if left untreated. Other cold related conditions that can occur at the same time as hypothermia include:

- chilblains – cold causes permanent damage to the small blood vessels in the skin resulting in redness and itching
- frostbite – tissue, usually of the extremities including fingers and toes, freezes and is destroyed. This can result in permanent nerve damage and gangrene. Often amputation of the affected area is needed to prevent gangrene from spreading which can be fatal.

If body core temperature increases greater than 37.5 – 38.3 °C, hyperthermia occurs. Hyperthermia is also known as heat stroke. It occurs when there is an excess production of heat due to exercise, an increase in the temperature of the environment or ineffective heat loss. It occurs when the body is unable to cool down using the normal homeostatic mechanisms. Symptoms include sweating, rapid breathing, vomiting, headaches, unconsciousness, organ failure and eventually death if left untreated. Excess heat can also cause injury to the skin resulting in burns. Depending on the extent of damage, burns can heal within a few days or weeks or can require amputation or even result in death.

Pause point

Produce a diagram to show the homeostatic mechanism of temperature control.

Hint

Start off with normal body temperature and add arrows for increase and decrease. Include how changes are detected, how the response is co-ordinated and give a description of the different responses that restore normal body temperature.

Extend

Discuss how failure to regulate body temperature can have serious consequences for the body.

A2 Nervous system

The central and peripheral nervous systems

The central nervous system (CNS) consists of the brain and spinal cord. The peripheral nervous system (PNS) consists of sensory and motor neurones. Sensory neurones receive information from **receptors**, e.g., ears, and take this information to the CNS. The brain processes the information, then motor neurones take the information from the brain to the **effector**, e.g., muscle.

Neurones

The nervous system is made up of two types of cells, one of which is **neurons**. Neurones are cells that receive and facilitate nerve impulses, or action potentials, across their membrane to the next neurone. They consist of a large cell body called a soma with small projections called dendrites and an axon. The end of the axon is called the axon terminal. It is separated from the dendrite of the following neuron by a small gap called a synaptic cleft.

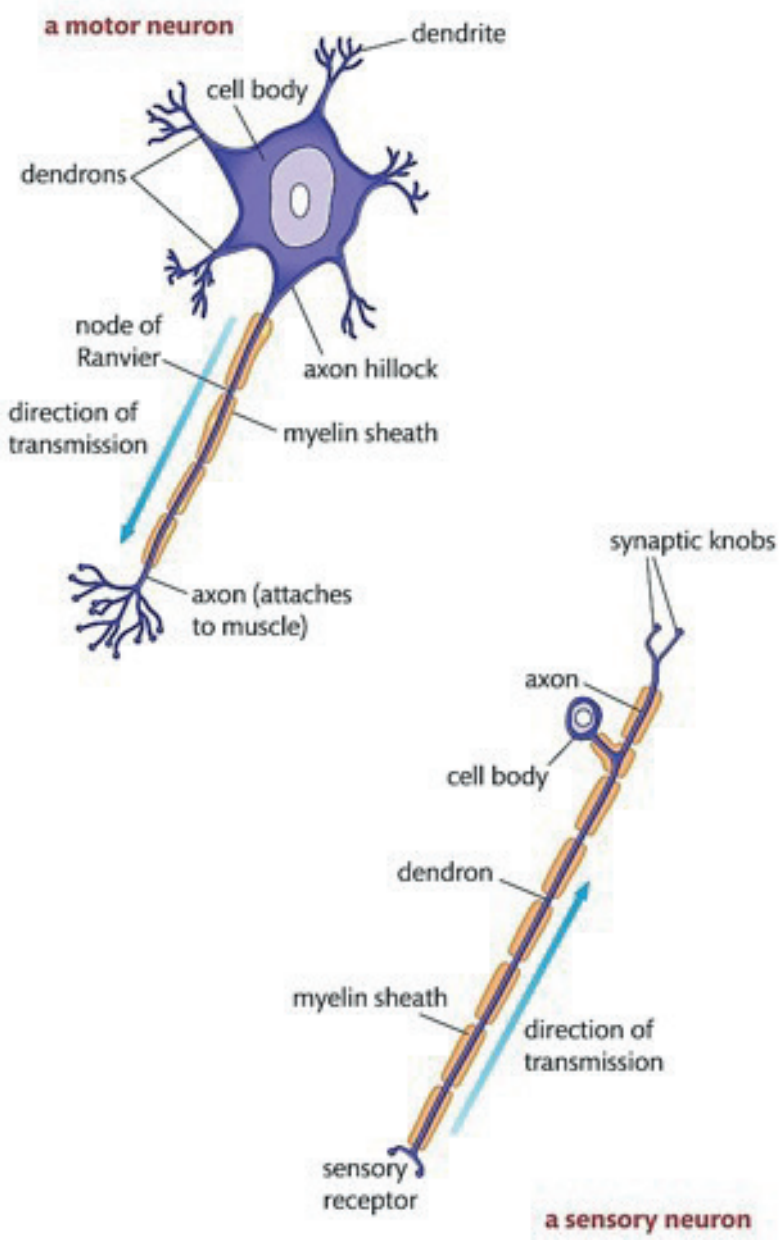


Figure 1.45: The structure of a motor neuron and a sensory neuron

Information travels along neurones in the form of electrical signals called nerve impulses. A nerve impulse is scientifically known as an **action potential**. Action potentials arise from a change in the ion balance in the nerve cell which spreads rapidly from one end of the neuron to the other. Neurones are bundled together to form nerves and these nerves form a network all around the body. When the action potential travels along the axon, to the axon terminal, neurotransmitters (chemicals) are released across the synaptic cleft and bind to receptors on the post-synaptic membrane, regenerating the action potential on the next neuron so the nerve impulse continues. Glial cells provide support for the neuron by digesting dead neurons and manufacturing the components of neurons.

Key points

Receptor – a specialised cell or group of cells that respond to changes in the surrounding environment.

Effector – a muscle, organ or gland that is capable of responding to a nerve impulse.

Neuron – a cell that transmits electrical impulses and is located in the nervous system.

Action potential – the change in electrical potential along the membrane of a nerve or muscle cell. More commonly known as a nerve impulse.

Glial cell – cells that provide support for neurons such as manufacturing neuron components and digesting dead neurons.

Resting potential and action potential

There is a potential difference across the membranes of neurons, in the resting state, the interior of the cell is negative compared to the exterior. Potassium ions (K+) are in higher concentration in the cells than outside, and sodium ions (Na+) are in higher concentration outside the cell than inside. This creates a concentration gradient which ions flow down when the appropriate voltage-gated ion channels are open. Once the potential difference reaches a threshold voltage (around -55mV), the reduced voltage causes hundreds of sodium gates in the membrane to open briefly. Sodium ions flood into the cell and depolarise the membrane. This causes more voltage-gated ion channels to open in the adjacent membrane and a wave of depolarisation travels along the cell creating an action potential.

When a neuron is in its resting state, its membrane is polarised – the electrical charge on the outside of the membrane is positive and the electrical charge inside the membrane is negative. An action potential (nerve impulse) is caused by a brief change in the voltage across a membrane due to the flow of ions into and out of a neuron. The resting potential of a neuron is around -70mV.

A nerve impulse is initiated when a neurone is stimulated. In everyday situations a stimulus can be chemical, mechanical, thermal or electrical and a stimulus is detected by receptor cells.

Depolarisation

Depolarisation occurs when there is a change in the membrane potential relative to the resting potential – the inside of the membrane becomes less negative. An action potential is generated when a stimulus changes the permeability of the neuron's membrane by opening specific voltage-gated channels on the axon. These channels open and close in response to changes in membrane potential. Depolarisation occurs when sodium channels are opened allowing Na+ to diffuse into a cell causing the interior to become progressively less negative (moving from -70mV to +30mV).

Repolarisation

Repolarisation occurs when Na+ channels are inactivated and K+ channels open allowing K+ to rush out of the cell thus restoring the internal negativity of the neuron. The electrical resting potential is restored but repolarisation does not restore the ionic conditions. Ion redistribution is accomplished by the sodium-potassium pump which moves Na+ and K+ against the concentration gradients by active transport – two K+ are moved into the cell and three Na+ are moved out of the cell into the extracellular fluid.

Hyperpolarisation

The potassium ion channels are slow to close and too many potassium ions diffuse out of the axon across the membrane. The membrane potential falls too low, past -70mV. The membrane is described as hyper-polarised. The time taken for the membrane to return to resting potential is known as the refractory period, during this time an action potential cannot be generated.

Hyperpolarisation occurs when there is an 'overshoot' of the interior membrane potential, the potential increases and becomes more negative than the resting potential e.g., a change from -70Mv to -75mV is hyperpolarisation. In hyperpolarisation, some K+ channels remain open and Na+ channels reset. The period of increased K+ permeability lasts longer than is needed to restore the membrane to the resting state (-70mV). As a result of excessive K+ efflux, hyperpolarisation prevents the neuron from receiving another stimulus during this time; this is important in preventing any stimulus already sent up an axon from triggering another action potential in the opposite direction. In other words, hyperpolarisation assures that the signal is proceeding in one direction only.

Key points

Depolarisation – when the axon is stimulated, channels in the axon membrane open. This allows sodium ions to diffuse into the axon. This creates a positive charge on the axon and causes the action potential.

Diffuse – movement of particles from a region of high concentration to a region of low concentration.

Sodium potassium pump – carrier proteins in the cell membrane that transport sodium ions in opposite directions across the cell membrane.

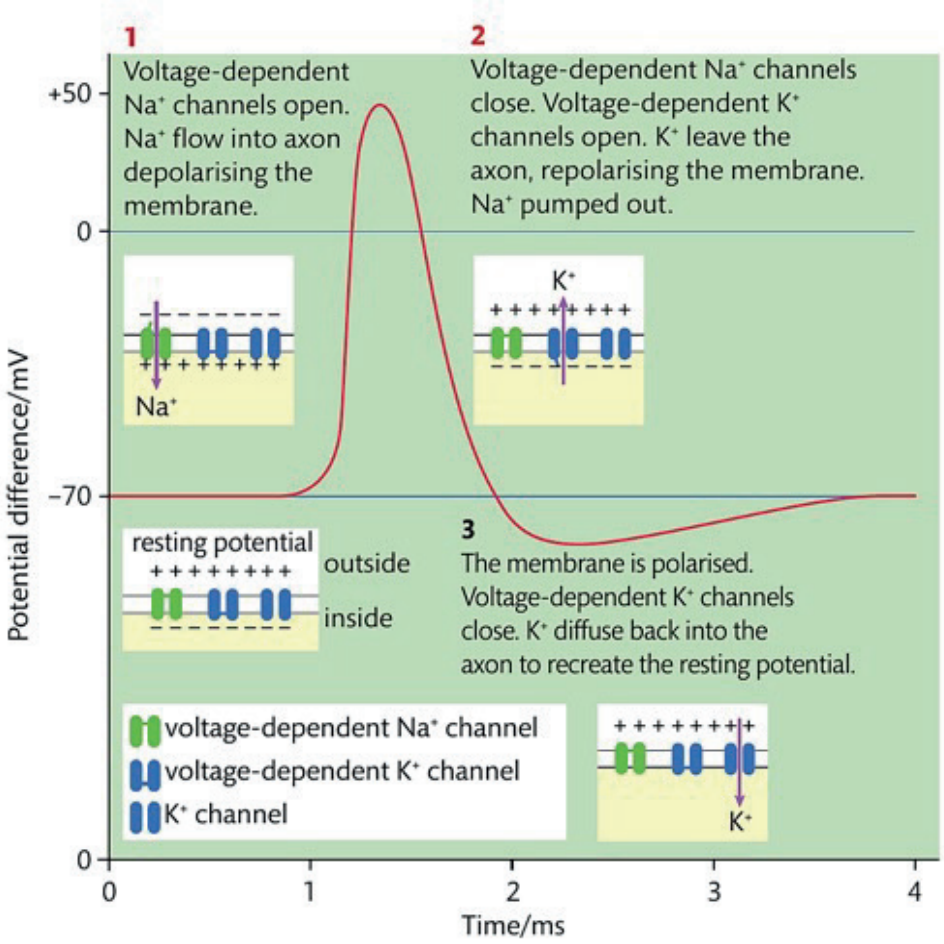


Figure 1.46: A graph showing the change in membrane potential during the generation of an action potential

The speed of an action potential in humans

The speed at which a nerve impulse travels in humans is 1–3 m/s in unmyelinated fibres and 3–120 m/s in myelinated fibres. The conduction depends on:

- Axon diameter – the larger the axon, the faster the conduction
- Myelination of neurone – the nerve impulse travels faster if the neurone is myelinated
- Number of synapses involved – the fewer synapses there are to cross, the faster the communication.

Myelinated neurones and saltatory conduction

Some neurones have an axon covered with a fatty sheath called myelin. Myelin is made from flattened layers of specialised cells called Schwann cells. These cells wrap around the axon and form a lipid insulating layer around the neurone called the myelin sheath. Myelin insulates the axon and makes the action potential travel faster. In between Schwann cells are areas where the axon is exposed these areas are called 'nodes of Ranvier, this is where ion exchange occurs.

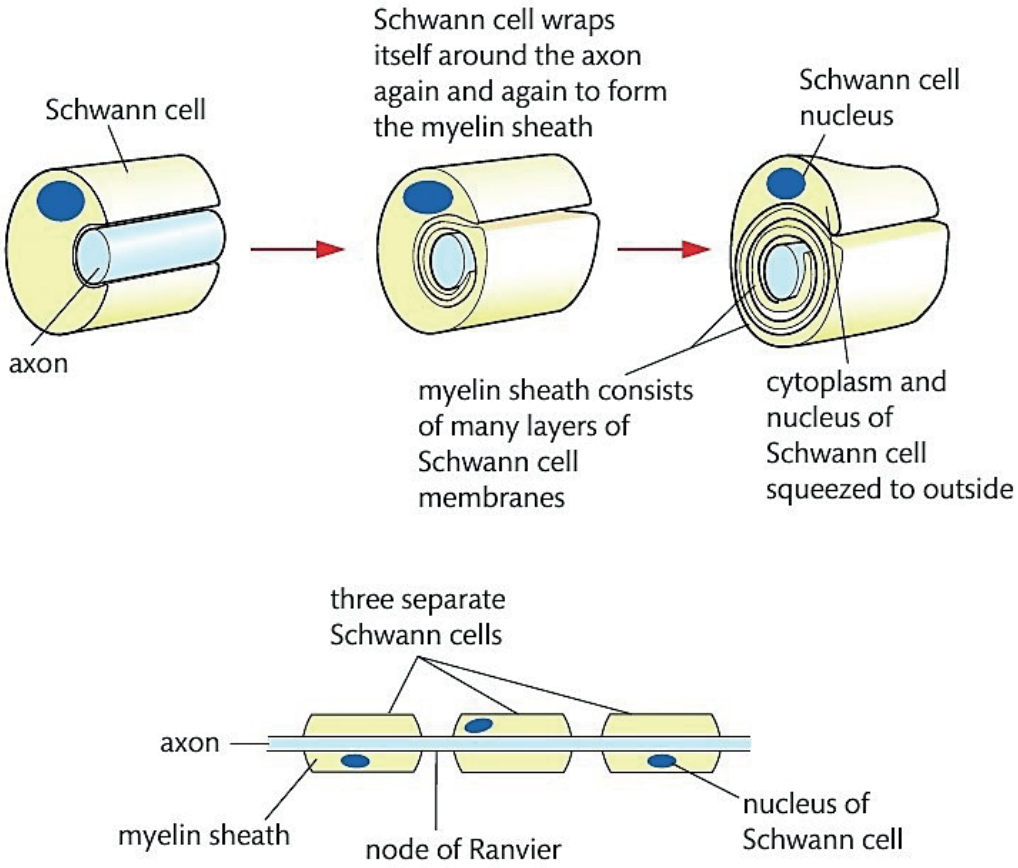


Figure 1.47: The myelin sheath, the insulating layer that grows as a result of Schwann cells around the axon

Saltatory conduction is the process of the signal jumping from node to node (saltatory comes from the Latin saltare, meaning 'to dance'). When the action potential reaches a node of Ranvier, sodium ions diffuse into the axon membrane. They displace the potassium ions down the axon because they are both positively charged, and like charges repel. The movement of the potassium to the node further down the axon makes the next node more positive and depolarises it until the threshold is reached. The impulse appears to jump from node to node very quickly, making the action potential quicker therefore the speed of conduction is faster. Only a small part of the axon is being used, so less ATP is needed, and fewer ions are being exchanged.

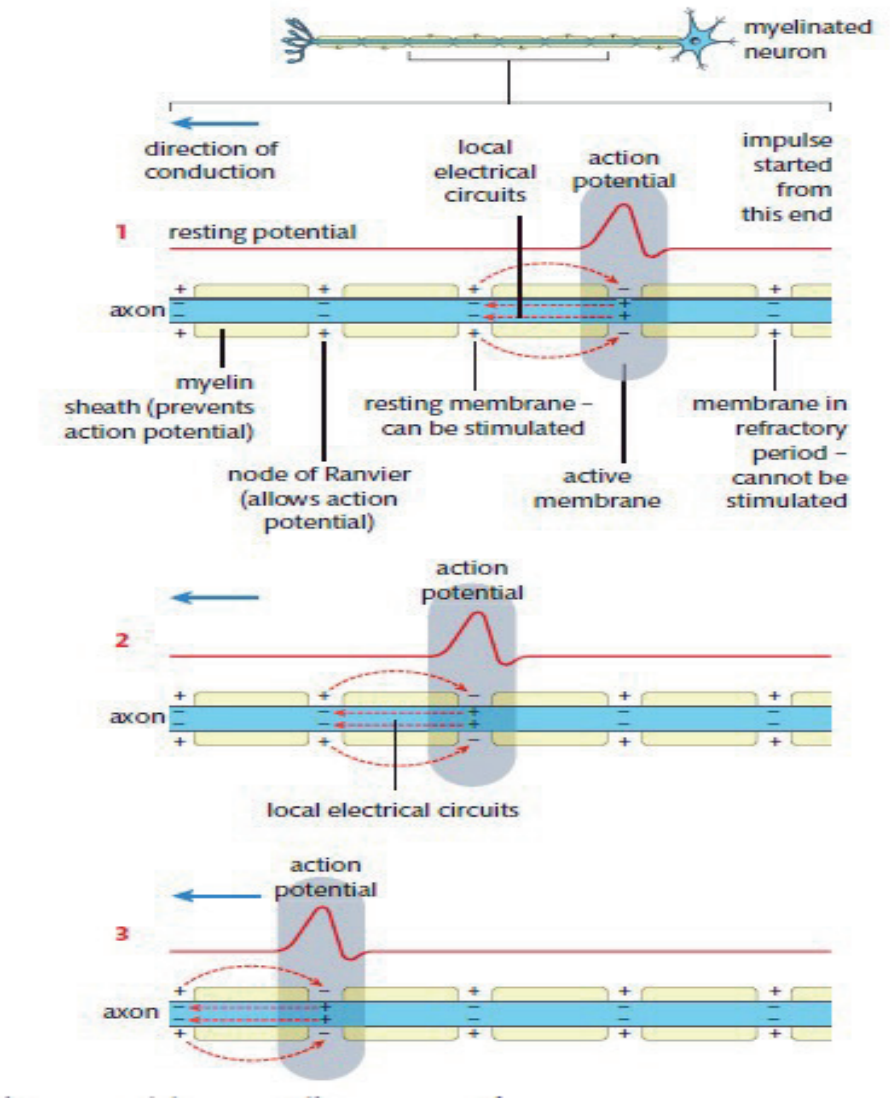


Figure 1.48: Saltatory conduction. By 'jumping' node to node along a myelinated nerve fibre, the nerve impulses in vertebrate neurons can travel very quickly along narrow nerve fibres – allowing for the development of the nervous system.

Key points

Saltatory conduction – in myelinated neurons the impulse appears to jump along the axon between nodes. The action potentials are propagated from one node of Ranvier to the next node, which increases conduction velocity of action potentials.

Synapses

The junction where two neurons meet is called a synapse. At the synapse, the neurons do not touch and are separated by a narrow gap called the synaptic cleft. The neuron carrying the impulse to the synaptic cleft is called the presynaptic neuron and the one receiving the impulse and carrying it away is termed the post synaptic neuron.

Information crosses the synaptic cleft in the form of neurotransmitters. These are the chemical molecules used by the nervous system to transmit messages between neurons, or from neurons to muscles. When the nerve impulse reaches the dendrites at the end of one axon, called the axon terminal, the neurotransmitters diffuse across the synaptic cleft and bind with receptor molecules on the membrane of the adjacent postsynaptic neuron. When the neurotransmitters bind to the receptors, it stimulates the second neuron and this journey is repeated onto the next neuron. There are hundreds of neurotransmitters, a common neurotransmitter responsible for muscle contraction is acetylcholi

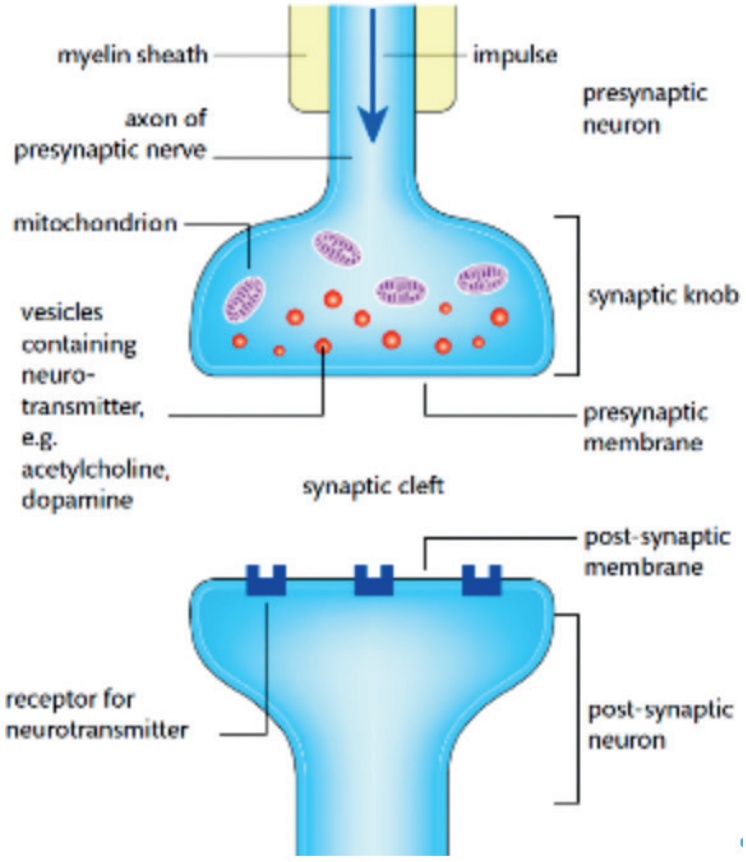


Figure 1.49: Structure of the synapse

Key points

Presynaptic membrane – the axon terminal membrane of the neuron carrying the impulse to the synapse.

Axon terminal – the axon of a neuron ends in a swelling called the axon terminal. It contains mitochondria which provide energy for synaptic transport, and synaptic vesicles which release the neurotransmitter into the synaptic cleft.

Postsynaptic membrane – the membrane of the cell body or dendrite or the neuron carrying the impulse away from the synapse. It contains a number of channels to allow ions to flow through, and protein molecules which act as receptors for the neurotransmitter.

Threshold level – the point at which increasing stimuli trigger the generation of an electrical impulse.

Step-by-step: chemical transmission across the synapse

1. The action potential arrives at the end of the axon known as the pre-synaptic membrane.
2. Calcium ion channels open in the presynaptic membrane and calcium ions (Ca+2) diffuse across the pre-synaptic membrane into the axon due to a concentration gradient.
3. As the calcium ion concentration increases in the axon, vesicles containing neurotransmitters move towards the membrane.
4. These vesicles fuse with the pre-synaptic membrane and release the neurotransmitter into the synaptic cleft.
5. The neurotransmitters diffuse across the synaptic cleft from a high concentration to a low concentration, down a concentration gradient, to the post- synaptic membrane.
6. The neurotransmitters bind to receptors on the post-synaptic cell membrane
7. Sodium ion channels in the post-synaptic membrane open, causing sodium ions to diffuse into the next axon. This depolarises the membrane of the post-synaptic cell, triggering an action potential on the post synaptic membrane and the wave of depolarisation continues along the next neurone.
8. The neurotransmitter will be recycled, enzymes in the synaptic cleft with break down neurotransmitters and they will diffuse back across the synaptic cleft to the pre-synaptic membrane. They will be taken back across this membrane and repackaged into vesicles to be used again.
9. Between impulses, neurotransmitters molecules are removed from the synaptic cleft to prevent continuous stimulation of postsynaptic neurons. Removal occurs by two methods; re-uptake in which the neurotransmitter is reabsorbed into the presynaptic neuron ready to be used again and by enzyme degradation in which the neurotransmitter is broken down by an enzyme. The inactive products of enzyme degradation are then reabsorbed by the presynaptic neuron where they are resynthesised into active neurotransmitters.

The minimum level of neurotransmitter required to produce a postsynaptic action potential is called the **threshold level**.

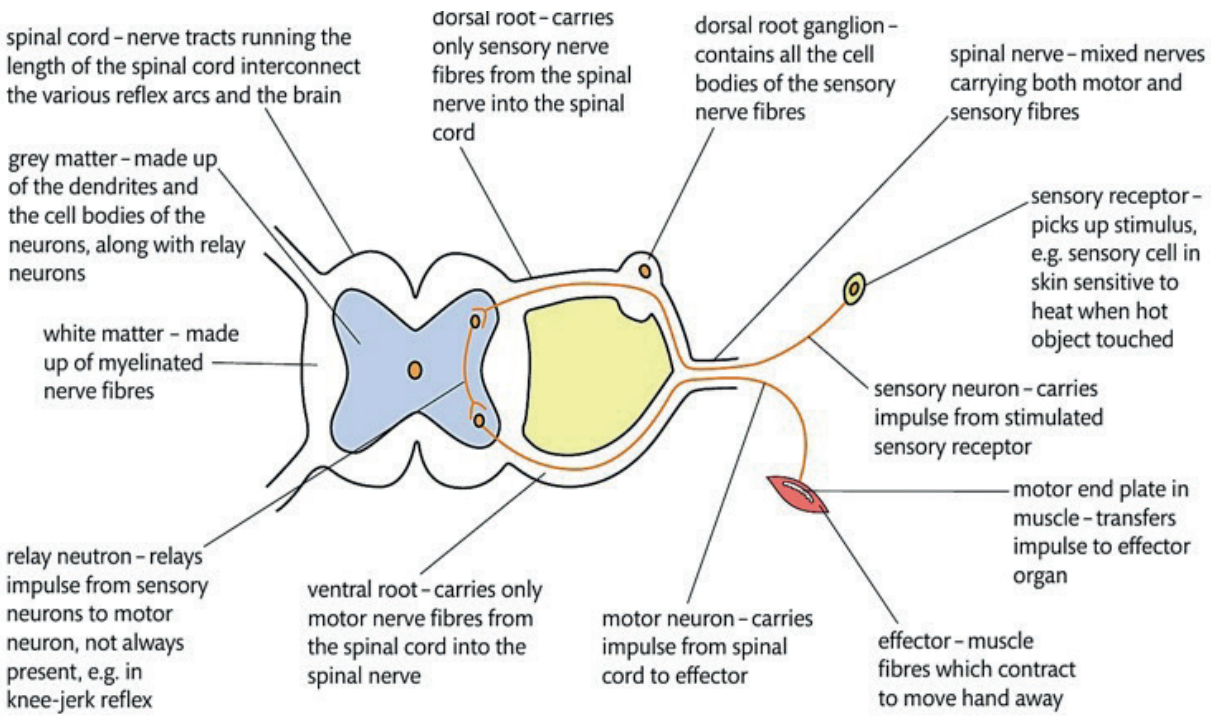


Figure 1.50: The reflex arc showing the structures and sequence of events involved in a reflex action

Assessment activity 1.6

1. Describe the structure of the myelin sheath.
2. Explain why the speed of conduction is faster in myelinated neurones compared to non-myelinated neurones.
3. Explain the changes in membrane potential during depolarisation and repolarisation ensure you reference the changes in membrane permeability of sodium and potassium ions.
4. Explain what happens to neurotransmitters after they have completed their function.

A3 Cardiovascular and respiratory system

The respiratory system

The respiratory system is made up of the lungs and associated airways. The function of the respiratory system is ventilation and gas exchange between the atmosphere and the blood. Through the mechanism of ventilation (breathing in and out) air enters the body. Oxygen from the air can then diffuse into the bloodstream to be transported to cells. All cells in the body require oxygen for aerobic respiration. This process is needed for cells to stay alive. Aerobic respiration produces carbon dioxide as a waste product. This must be removed from the body as it is toxic. Carbon dioxide is removed in the air you breathe out.

Humans have two lungs which can be found in the chest cavity. Air enters the respiratory system through the nasal passage or mouth and then travels down the trachea. The trachea branches into two bronchi, the left and right bronchus, each of which take air into one of the lungs. The bronchi branch into smaller and smaller tubes called bronchioles. Each of the smallest bronchioles, ends in an air sac called an alveolus. There are millions of alveoli in the lungs. The alveoli are the site of gas exchange between the air and the blood.

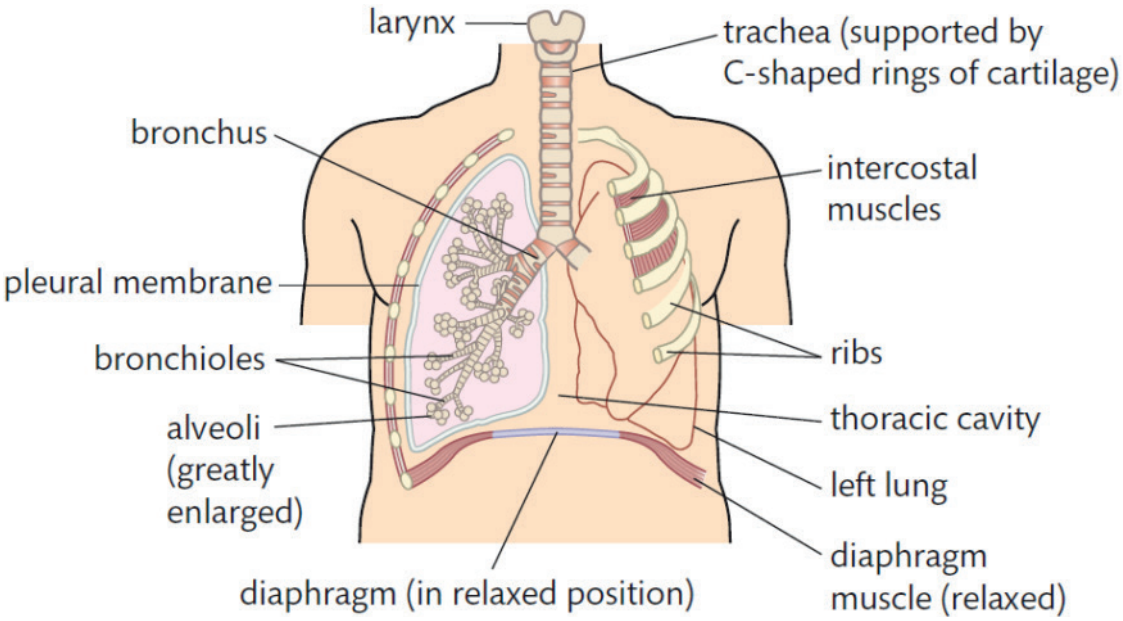


Figure 1.51: The respiratory system

Lungs have a spongy feel to them and are lined on the outside by a thin, moist membrane known as the pleura. The pleura continues around the inner thoracic cavity so the that the two pleural layers slide over one another with ease and without friction. The **surface tension** of the pleura allows the two layers to slide, meaning when the chest wall moves when breathing, the lungs can move with it. The lungs are protected by the ribcage which is made up of rib bones. The rib bones are held together by antagonistic muscle pairs called the intercostal muscles. Each rib has an internal and an external intercostal muscle. A sheet of muscle called the diaphragm separates the chest cavity from the abdominal cavity. The action of the intercostal muscles and the diaphragm causes ventilation.

Key points

Surface tension – a thin elastic skin of a liquid that allows it to resist an external force.

Structure of the respiratory system

The trachea

The trachea is supported by c-shaped rings of cartilage to provide support and keep the airway open. The inside of the trachea is lined with ciliated epithelial tissue. This tissue contains many hair-like projections called cilia that are able to move in a synchronised pattern. This movement wafts mucus up the trachea and away from the lungs. The mucus is produced by cells found in the walls of the trachea called goblet cells. Mucus traps pathogens and the wafting of mucus by cilia, prevents these pathogens from entering the respiratory system.

The bronchi

The bronchi have a similar wall structure to the trachea. However, as you get further into the lungs, the c-shaped rings of cartilage are replaced by irregular blocks of cartilage.

The bronchioles

Larger bronchioles have blocks of cartilage in their walls but as the bronchioles branch into narrower and narrower tubes, cartilage is no longer present. The bronchiole walls contain smooth muscle and elastic fibres. The smooth muscle can contract to constrict the diameter of the bronchioles. This can help regulate air flow to the alveoli.

The alveoli

Gases pass by diffusion through the walls of the alveoli. Oxygen diffuses from the air in the alveoli into the blood whereas carbon dioxide diffuses in the opposite direction. The alveoli are small and highly folded, this increases the surface area for gas exchange. There are a large number of alveoli in the lungs which results in a large total surface area for gas exchange. The walls of the alveoli consist of a one cell thick layer of squamous epithelium. The alveoli have thin walls so that gases only have a short distance to diffuse across. Each alveolus is also close to a blood capillary network, increasing the efficiency of diffusion. The alveoli are lined by a thin layer of moisture for the gases to dissolve in. Surfactant produced by the lungs coats the internal surface of the alveoli. Pulmonary surfactant reduces the surface tension within the alveoli through hydrophilic and hydrophobic forces, a process which prevents alveoli from collapsing.

When you exercise, the internal intercostal muscles contract to reduce the volume of the chest cavity further. This further increases the pressure in the chest cavity creating a larger pressure gradient between the air in the lungs and atmospheric air. As a consequence, a greater volume of air can be breathed out with each breath. This allows you to eliminate the extra carbon dioxide produced by a higher rate of respiration in muscle tissue during exercise.

Ventilation

Ventilation is the mechanism of breathing. Breathing in is called inspiration.

Inspiration occurs in the following steps:

- The external intercostal muscles contract
- The rib cage moves up and out
- The diaphragm contracts and moves down
- Both of these actions increase the volume in the chest cavity
- As a result, the pressure inside the chest cavity decreases
- Air moves in down the trachea, bronchi, bronchioles and into the alveoli down the air pressure gradient. Air moves from high atmospheric air pressure to low chest cavity air pressure.

Breathing out is called expiration.

Expiration occurs in the following steps:

- The external intercostal muscles relax
- The rib cage moves down and in
- The diaphragm relaxes and moves up
- Both of these actions decrease the volume in the chest cavity
- As a result, the pressure inside the chest cavity increases
- Air moves out of the lungs down the air pressure gradient. Air moves from high chest cavity air pressure to low atmospheric air pressure
- The elastic recoil of alveoli assists in the process of exhalation

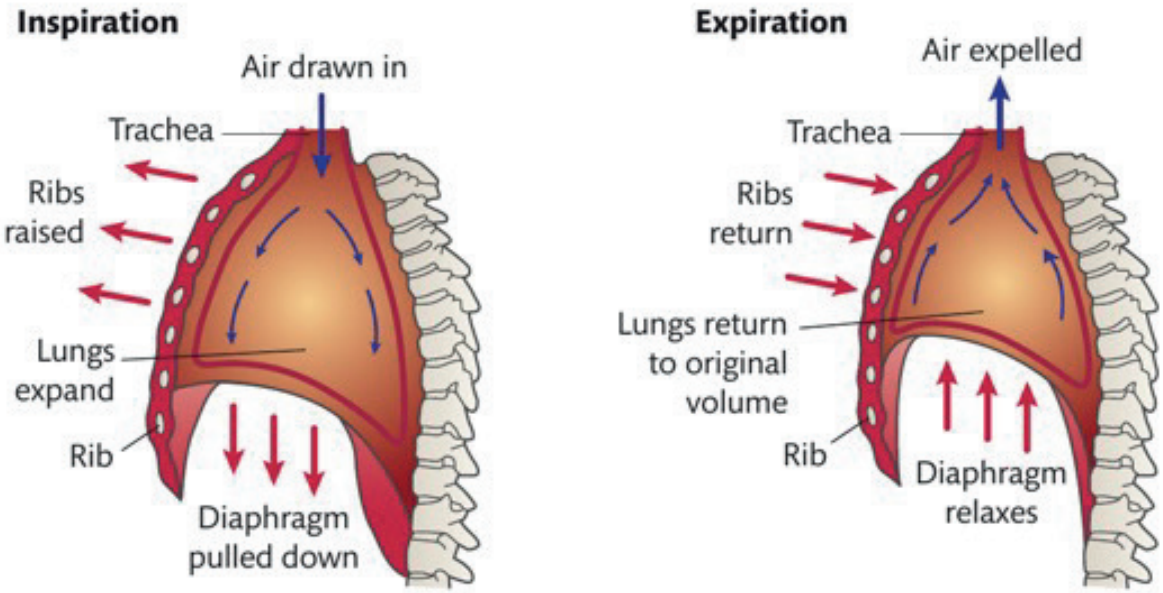


Figure 1.52: Changes in the thorax during inspiration and expiration

Assessment activity 1.7

1. Draw a labelled diagram of the respiratory system.
2. Describe the structure of the trachea, bronchi, bronchioles and alveoli.
3. Describe the process of ventilation.
4. Describe how ventilation during exercise is different.
5. Explain why it is necessary to change ventilation during exercise.

The cardiovascular system

The cardiovascular system is made up of the heart, blood vessels and blood. The heart is a muscular pump which pumps blood around the body in blood vessels. Nutrients, oxygen and waste material are transported around the body using blood.

All of the cells in the body require oxygen and glucose for aerobic respiration. Aerobic respiration produces ATP which is the universal energy carrier. Cells require ATP for all cellular processes. Oxygen is taken into the body by the respiratory system and glucose is absorbed into the bloodstream by the digestive system. Both are transported to all body cells via the blood. Respiration produces waste carbon dioxide; this has to be removed from the body as it is toxic. Carbon dioxide moves from cells into the blood and is transported back to the lungs where it is exhaled. Other substances including amino acids and hormones are also carried in the blood.

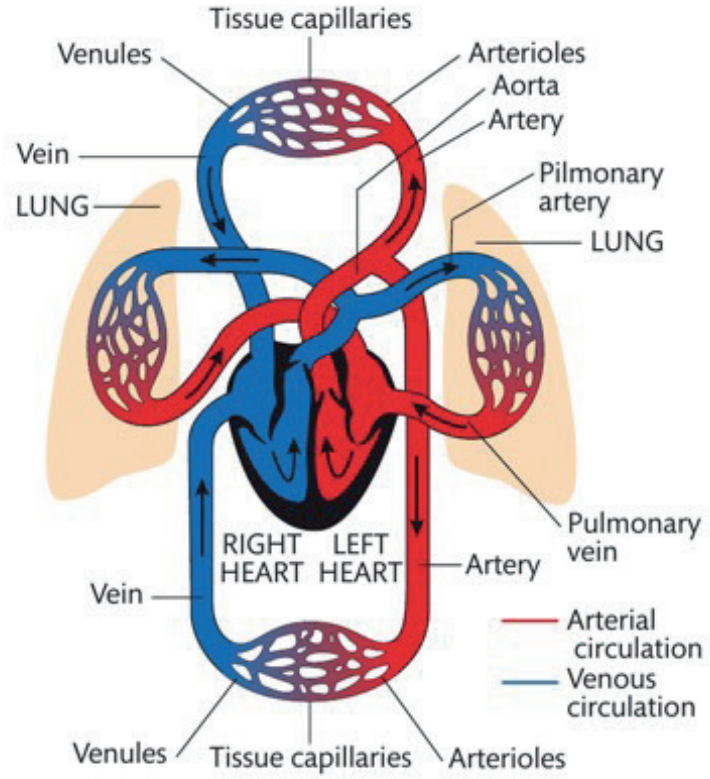


Figure 1.53: The cardiovascular system structure

Circulatory systems

Blood does not leave blood vessels. The blood vessels and the heart make up a closed transport system which starts and finishes at the heart. The human circulatory system is a double circulatory system because there are two separate circulations. The heart acts as a link between the two systems, moving blood around the different blood vessels in a unidirectional pathway.

The heart, lungs and blood vessels make up the pulmonary circulatory system. The heart pumps blood to the lungs where it picks up oxygen to become oxygenated blood. At the lung capillaries, carbon dioxide also diffuses out of the blood to be breathed out. The blood then returns to the heart using veins.

The heart and blood vessels of the rest of the body make up the systemic circulatory system. The heart pumps blood so that it flows along arteries and arterioles, eventually reaching body capillaries. At the capillaries, oxygen diffuses out of the blood and carbon dioxide produced by respiration, diffuses in. The deoxygenated blood is then transported back to the heart using blood vessels called venules and veins.

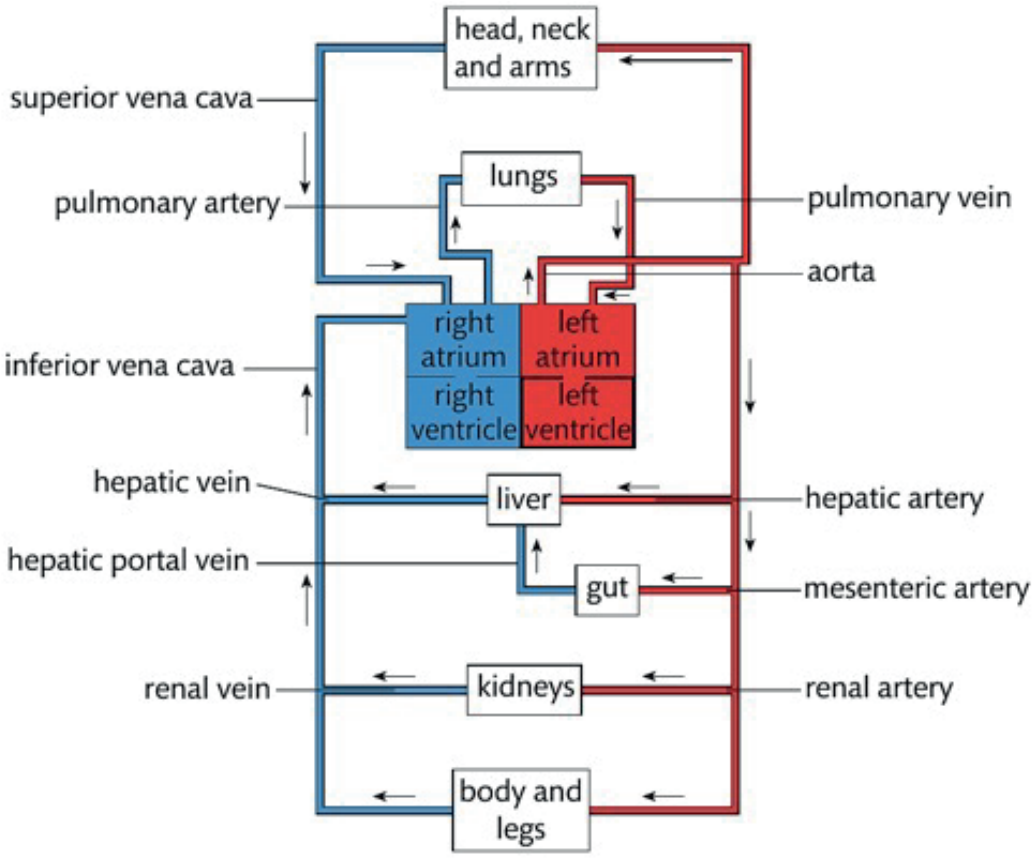


Figure 1.53: The main blood vessels and direction of blood flow around the cardiovascular system

Key points

Pulmonary circulatory system – the heart, lungs and all associated blood vessels that circulate blood to and from the lungs.

Systemic circulatory system – blood circulation around the body.

Structure and function of the heart

The heart is located in the chest cavity (the thoracic cavity), behind the breastbone. It is a muscular pump that is divided into the left and right side. The left side deals with oxygenated blood and the right-side deals with deoxygenated blood.

External heart structure

The heart is made from cardiac muscle. Lying across the surface of the cardiac muscle are small blood vessels called coronary arteries. These supply oxygenated blood to the heart muscle so that it can contract. When the heart muscle contracts, the blood inside the heart chambers if put under pressure. At the top of the heart there are four major blood vessels. The veins carry blood into the heart and into the top chambers, the atria. These veins are called the pulmonary vein and the vena cava. Arteries carry blood away from the bottom chambers, the ventricles. These arteries are called the pulmonary artery and the aorta.

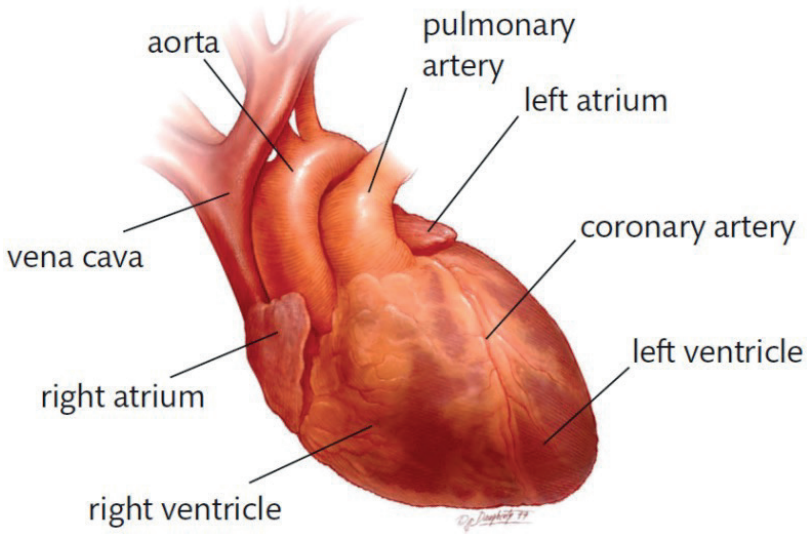


Figure 1.54: The external view of the heart

Internal heart structure

The heart contains four chambers. The upper chambers are called the left and right atria, the bottom chambers are called the left and right ventricles. The left side of the heart pumps oxygenated blood and the right side of the heart pumps deoxygenated blood.

Exam tip

To help you label all of the structures of the heart, try to understand the pathway of blood around the circulatory system.

In the lungs, blood picks up oxygen. This oxygenated blood travels from the lungs and enters the left atrium of the heart via the pulmonary vein. Deoxygenated blood travels from the body, where oxygen has been used up, and enters the right atrium of the heart via the vena cava.

When the atria contract, blood is forced from the atria into the ventricles through the atrioventricular valves. The valves are attached to the walls of the heart by tendinous cords which prevent the valves from turning inside out.

When the ventricles contract, blood leaves the heart. Oxygenated blood leaves the left ventricle via the aorta. This carries blood to a number of arteries that supply all parts of the body. Deoxygenated blood leaves the right ventricle via the pulmonary artery. This vessel carries blood to the lungs, where it picks up oxygen and loses carbon dioxide.

At the base of the aorta and the pulmonary artery. There are valves called semi-lunar valves. These prevent blood from flowing back into the ventricles when the heart relaxes.

A wall of muscle separates the ventricles from each other. This is called the septum. The role of the septum is to ensure that oxygenated and deoxygenated blood do not mix.

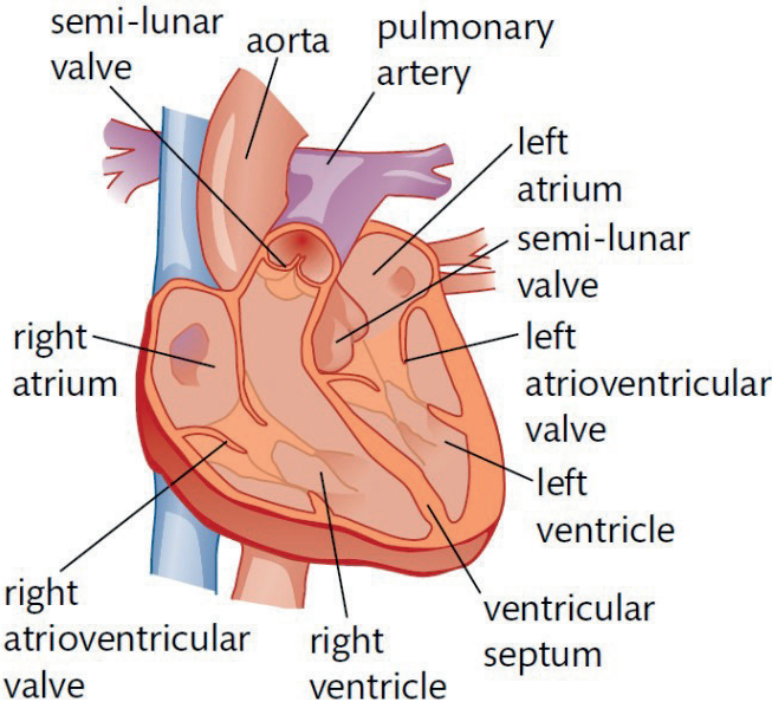


Figure 1.55: The internal structure of the heart

Key points

Atria – the two top chambers of the heart.

Ventricles – the two bottom chambers of the heart.

Vena cava – large vein carrying deoxygenated blood into the right atrium.

Atrio ventricular valve (AV) – structure found between the atrial and ventricular chambers of the heart to prevent blood flowing back into the atria when the ventricles contract.

Tendinous cords – fibrous cords that attach the papillary muscle to the atrioventricular valves, preventing backflow of blood during the cardiac cycle.

Aorta – large artery carrying oxygenated blood from the left ventricle.

Semi-lunar valve - structure found at the base of the aorta and pulmonary artery which prevent blood flowing back into the ventricles when the heart relaxes.

Pause point

Label the structure of the heart.

Hint

Use the internet to find an unlabelled diagram of the heart. Start by labelling the left and right sides. Add which side deals with oxygenated and deoxygenated blood.

Extend

Draw a flow diagram to show the pathway of blood through the heart and the circulatory systems.

The cardiac cycle

The heart beats in a rhythmic cycle:

1. First, the atria relax and fill with blood from the pulmonary vein and vena cava, this is called **atrial systole**.
2. The atria contract and force the atrioventricular (AV) valves open. Blood flows into the ventricles and they fill up; this is ventricular diastole.
3. The AV valves close when pressure in the ventricles rises above the pressure in the atria to prevent backflow of blood into the atria.
4. The ventricle walls contract and increase pressure in the ventricles. This forces the semi-lunar valves to open and blood flows to the pulmonary artery and aorta.
5. When the pressure in the aorta and the pulmonary artery rises, the semi-lunar valves close to pre vent backflow of blood into the ventricles. After this there is a short delay before **ventricular systole**. This is where the ventricles contract at the same time. There is then a short period of time where all chambers of the heart relax and fill. This is called **diastole**.

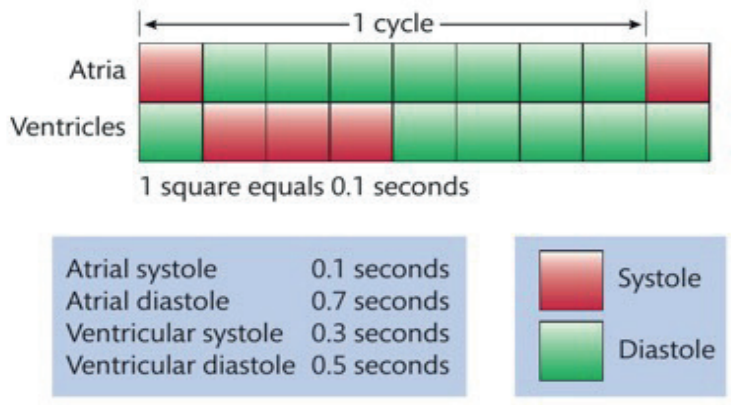
Control of the cardiac cycle

It is important that the cardiac cycle is co-ordinated to ensure that the chambers empty fully before the next stage of the cycle. The heart is made of cardiac muscle. This muscle is myogenic as it can initiate its own contraction without stimulation from the nervous system. However, the heart has a conduction system to help control this contraction.

There is a patch of specialised tissue in the wall of the right atrium known as the **sino-atrial node (SAN)**. It is this node that generates the initial electrical activity to initiate a coordinated wave of excitation, it is effectively the 'pacemaker' of the heart. Once the SAN has generated a wave of excitation, it quickly spreads across the walls of the atria using the cardiac muscle. This causes both atria to contract simultaneously, emptying their blood into their respective ventricles. This is called **atrial systole**.

When the wave of excitation reaches the base of the atria, it meets a band of non-conductive tissue and cannot simply carry onto the ventricles. The wave of excitation is instead picked up by another specialised region of tissue in the septum called the **atrioventricular node (AVN)**. The wave is excitation is delayed here allowing the atria to fully empty into the ventricles.

The AVN sends the wave of excitation down a bunch of conductive fibres in the septum called the Bundle of His. These carry the wave of excitation to the apex of the heart (the bottom of the ventricles). Once the wave of excitation reaches the apex, it then travels up the ventricle walls in Purkinje fibres. As the excitation spreads up the ventricles, the ventricles contract simultaneously, from the base upwards. This is ventricular systole. The muscle making up the walls of the chambers then relaxes, to prepare for



the cycle to start again. This is known as **diastole**.

Figure 1.56: Coordination of the cardiac cycle

Key points

Systole – time in heartbeat when cardiac muscle contracts.

Diastole – time in heartbeat when the cardiac muscle relaxes.

Sino-atrial node (SAN) – specialised muscle cells in the right atrium that start the cardiac cycle by sending impulses across atria walls. This is often called the heart's pacemaker as these cells control the speed of the cardiac cycle.

Atrio ventricular node (AVN) – specialised muscle cells in the junction of the atria and ventricles that receive impulses from the SAN and send impulses across the ventricle walls.

Regulation of heart rate

The ability of cardiac muscle to contract is intrinsic; it does not depend on the nervous system. Electrical excitation of the heart is initiated by the sino-atrial node (SAN). The SAN is a specialised cell mass located within the wall of the right atrium close to the junction with the superior vena cava. The SAN acts as the heart's natural pacemaker by automatically generating regular, spontaneous action potentials.

The wall of the aorta and the carotid artery (the main artery in the neck) contain receptors called chemoreceptors. These receptors detect changes in pH. When blood carbon dioxide levels rise, the blood pH falls. This is detected by the chemoreceptors. A nerve impulse (action potential) is generated which travels along sensory neurones to the cardiovascular centre in the medulla oblongata in the brain.

Heart rate is under the involuntary control of two branches of the autonomic (involuntary) nervous system. The sympathetic nervous system and the parasympathetic nervous system. The sympathetic nervous system releases neurotransmitters (catecholamines - epinephrine and norepinephrine) to accelerate the heart rate. The parasympathetic nervous system (vagus nerve) releases the hormone acetylcholine to decrease the heart rate.

Baroreceptors in the aorta and carotid artery also act in a similar way. They detect changes in blood pressure. The cardiovascular centre acts to reduce heart rate when blood pressure rises and increase heart rate when blood pressure falls.

Although the SAN initiates the rhythm of the heartbeat, there are occasions we need the output of the heart to change, for example during exercise. Changes to the **cardiac output** are regulated by the autonomic nervous system. The ANS sends signals from the brain to release more noradrenaline to stimulate the SAN, this increases the frequency of signals from the pacemaker region, so the heart beats more quickly. Branches of the sympathetic nerve also pass into the ventricles, so they increase the force of contraction.

Key points

Baroreceptors – stretch receptors found in the blood vessels that respond to changes in blood pressure in the blood vessels.

Cardiac output – heartbeat rate multiplied by stroke volume.

Regulation of blood pressure

When the heart contracts, it places the blood in the chambers under pressure. During ventricular systole, the left ventricle creates the highest blood pressure this is because the blood has to travel furthest around the body and the high pressure enables the blood to overcome the resistance of the systemic circulatory system. When the heart relaxes, the blood pressure falls again. The pressure created by the heart contracting and relaxing can be measured using the pressure changes in the arteries close to the heart. Blood pressure is usually taken using an inflatable cuff around the upper arm arteries and a stethoscope. Normal blood pressure is approximately 120 / 80 mmHg (this can vary from person to person). 120 refers to the pressure in the artery when the ventricles contract and is the systolic pressure. 80 refers to the pressure in the artery when the heart relaxes and is the diastolic pressure.

The cardiovascular centre in the medulla oblongata of the brain also plays a role in regulating blood pressure. The cardiovascular centre transmits nerve impulses to constrict the size of blood vessels called arterioles (much like vasoconstriction in thermoregulation) in response to low blood pressure. Constricting the blood flow causes the blood pressure to increase. The cardiovascular centre can also cause vasodilation to decrease blood pressure when rises in blood pressure are detected by baroreceptors.

The kidneys also play a role in the regulation of blood pressure as they control the water volume in the body. If an increased volume of water is lost from the body in urine, then blood pressure decreases. If more water is conserved (so less is excreted in urine), then blood pressure increases. This involves hormones called angiotensin II and aldosterone.

Blood vessels

Blood flows around the circulatory system in blood vessels. There are different blood vessels that are adapted for their role. Arteries carry blood away from the heart, all arteries except the pulmonary artery carry oxygenated blood. As the blood gets further away from the heart, arteries branch into numerous smaller vessels called arterioles. Arterioles branch into capillaries. All of the cells in the body are in close proximity to a capillary network called a capillary bed. At the capillary bed, exchange of substances between the blood and the tissue surrounding the body cells occurs. After capillaries, the blood flows in small vessels called venules. These fill larger blood vessels called veins. Veins return blood to the heart. The vena cava is the main vein which carries deoxygenated blood into the right atrium. The pulmonary vein is the only vein to carry oxygenated blood, it transports blood from the lungs to the left atrium.

Structure of blood vessels

All blood vessels have an inner single layer of cells called the endothelium but then the wall structure varies for each vessel. The walls of most blood vessels have three distinct layers called tunics. The tunics surround a central space called the lumen through which the blood passes. The inner layer (tunica intima) is the thinnest layer, formed from a single continuous layer of endothelial cells and supported by a layer of connective tissue. Surrounding the tunica intima is the tunica media, which is made up from smooth muscle cells and elastic and connective tissues arranged circularly around the vessel.

Blood leaves the heart via arteries which have thick walls to withstand the high blood pressure; the tunica media is thicker in arteries than in veins as this layer contains more elastic fibres. Arteries have narrow lumens surrounded by large amounts of muscle and elastin fibre. Artery walls expand and recoil with the heartbeat; this serves to keep the blood under continuous pressure.

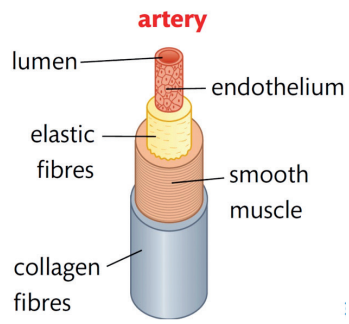
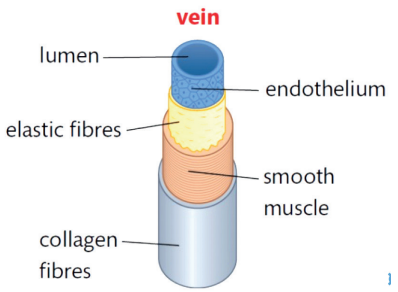
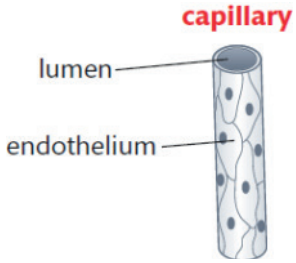
Large arteries divide to form smaller muscular arteries, these carry blood to the body organs. The tunica media within muscular arteries contains less elastic tissue and more smooth muscle.

The muscular arteries further divide to form arterioles, these are small vessels with a layer of smooth muscle wrapped around the inner endothelial layer. Dilation of arterioles allows more blood to flow into the capillaries.

The smallest blood vessels are called capillaries. Capillaries are made up from a single layer of endothelial cells. The lumen of a capillary so small that it only allows erythrocytes (red blood cells) to pass through in single file. Capillaries form capillary networks/capillary beds where plasma is forced out through gaps in the cell walls delivering oxygen and nutrients and removing waste from the tissues.

Capillaries join up to form venules which have small diameters and very thin walls. Venules join to form veins which have the same three layers as arteries but are much thinner. Veins have little smooth muscle or elastin but the tunica externa is often thicker to prevent them from collapsing. The blood pressure in veins is low. Veins have valves to prevent the backflow of blood.

Table 1.8: The structure and function of blood vessels

Arteries	Veins	Capillaries
		
• Carry blood away from the heart • Thick muscular walls • Large amount of elastin in walls • Small lumen (inner open space within the vessel) • High blood pressure • Rapid blood flow • Pulse • No valves	• Carry blood back to the heart • Thin muscular walls • Small amount of elastin in walls • Large lumen • Low pressure • Slow blood flow • No pulse • Valves to prevent backflow of blood	• Form networks in the tissues of the body • Link arterioles and venules • Walls are made up of a single layer of endothelium cells • No elastin fibres or muscle • Small lumen, just enough to allow blood cell to pass through • Little pressure • Slow blood flow • No pulse • No valves
Function Carry fast-flowing blood under high pressure away from the heart. Elastic walls enable the vessel to stretch and recoil to keep the blood flowing.	Function Carry slow-flowing blood under low pressure back to the heart. There is sufficient pressure to force valves in the veins to open, and backflow of blood causes the valves to close, therefore keeping blood flow in one direction.	Function Networks of tiny, thin blood vessels in the tissues of the body that supply blood to all tissues and cells of the body. Thin walls create a short diffusion pathway to enable rapid diffusion of substances between the tissues and the blood.

Blood composition

Blood is the fluid transported in veins. It is made up of a liquid called plasma in which different blood cells are found. Plasma also contains dissolved substances including oxygen, carbon dioxide, glucose, amino acids and hormones. The cells found in blood are red blood cells (erythrocytes) and white blood cells (leukocytes). Blood also contains cell fragments called platelets (thrombocytes). Table 1.9 describes the function of the different blood cells

Table 1.9: The role of blood cells

Name of blood cell	Function
Red blood cells (erythrocytes)	Contain a pigment called haemoglobin which temporarily binds oxygen to transport it around the body.
White blood cells (leukocytes)	White blood cells play a role in the immune response. Some types produce antibodies (lymphocytes) whilst others engulf and digest foreign material such as bacteria (phagocytes).
Platelets (thrombocytes)	The main function of platelets is blood clotting. When there is an injury to a blood vessel, platelets gather at the site of injury and from a blood clot.to prevent further blood loss.

Pause point

Produce a table to distinguish between the different type of blood vessels.

Hint

Include the type of blood being transported, the direction of transport, the structure of the wall, the size of the lumen and whether exchange between the blood and tissue fluid takes place.

Extend

Discuss the composition of blood and explain why it is needed.

Exchange of substances between blood and tissues

Exchange of substances between the blood and tissues occurs at the capillaries. In the tissues of the body, substances such as oxygen, glucose, and amino acids move out of the blood so that they can move into cells to be used in metabolic processes such as respiration. These processes produce useful products such as hormones and waste materials such as carbon dioxide that move back into the blood to be transported around the body.

Cells are bathed in a fluid called tissue fluid. Tissue fluid has a similar composition to blood plasma but it does not contain most of the cells or plasma proteins that are found in blood. When substances move out of the blood in the blood capillaries, they first move into the tissue fluid. From the tissue fluid, the substances then move into cells usually by diffusion. The reverse happens for substances moving from the cells to the blood.

Formation of tissue fluid

Tissue fluid is formed by the leakage of plasma from capillaries. Capillaries have a wall made of a one cell thick layer of flattened endothelial cells. There are tiny gaps between the cells that plasma can move through. As blood plasma leaks from the capillary, it carries the small dissolved substances such as oxygen, glucose and hormones with it. This occurs at the arterial end of the capillary bed and creates tissue fluid. At the venous end of the capillary bed, the tissue fluid returns to the blood capillary. Useful and waste products from metabolism will be carried back into the capillary dissolved in the tissue fluid.

Formation of tissue fluid

- Blood enters a capillary bed from an arteriole. This end of a capillary bed is referred to as the arterial end as before the arteriole, the blood was contained in an artery. At the capillary bed, tissue fluid is formed and exchange of substances between the blood and cells of the tissues occurs. The blood flows from the capillary bed into a venule and then eventually into a vein. This end of the capillary bed is referred to as the venous end.
- At the arterial end of the capillary bed, the blood is at a relatively high hydrostatic pressure. This pressure pushes plasma (and dissolved substances) out of the tiny gaps in the capillary wall to form tissue fluid. Most of the cells and the plasma proteins remain in the blood as they are too large to pass through the gaps in the capillary wall.
- Once in the tissue fluid, substances can move into cells. Waste substances can also leave cells and enter the tissue fluid. The exchange can occur by diffusion, facilitated diffusion and active transport.
- The **hydrostatic pressure** of the blood at the venous end of the capillary bed is much lower. This causes some of the tissue fluid to drain back into the capillary carrying dissolved waste products with it.

Oncotic pressure

Hydrostatic pressure is not the only pressure that influences the formation and drainage of tissue fluid at the capillary beds. Both plasma and tissue fluid have pressure created by the osmotic effect of the substances dissolved in them. This is called oncotic pressure. Oncotic pressure causes plasma to move in the direction of where the most solutes are (the lowest water potential). This can cause movement in the opposite or same direction as movement caused by hydrostatic pressure.

At the arterial end:

- The hydrostatic pressure of the blood is high and causes fluid to move out of the capillary and into the tissues
- Oncotic pressure of the blood tends to cause fluid to move back into the capillary
- However, as the hydrostatic pressure is greater than the oncotic pressure, the overall effect is that **plasma** moves out of the capillary bed and forms tissue fluid.

At the venous end:

- The hydrostatic pressure of the blood is low. Fluid moves back into the capillary from the tissues
- Abundant plasma proteins in capillary blood cause oncotic pressure to develop. Oncotic pressure increases along the length of the capillary because the filtering fluid leaves proteins behind leading to an increase in protein concentration.
- The overall effect of these forces is that fluid moves back into the capillary bed.

Formation of lymph

At the capillary bed, not all of the fluid re-enters the blood at the venous end. Some of the tissue fluid is directed into another body system called the lymphatic system. Excess tissue fluid drains out of the tissues and forms lymph fluid. This travels through lymphatic vessels and lymph nodes before returning to the blood in the subclavian vein in the chest. Lymph has a similar composition to tissue fluid except that it contains more of a type of white blood cell called lymphocytes. This is because lymphocytes pass into the lymph from the lymph nodes where they mature.

The lymphatic system contains:

- Lymphatic vessels – transport lymph fluid.
- Lymphatic organs – lymph nodes, spleen and thymus gland.
- Lymphatic nodules found in the digestive system – tonsils, Peyer's patches in ileum and appendix.
- Bone marrow – produces lymphocytes.

Key points

Hydrostatic pressure – the pressure that a fluid exerts when pushing against the sides of a vessel.

Oncotic pressure – the pressure created by the osmotic effect of dissolved substances.

Plasma – the liquid part of the blood.

Tissue fluid – fluid surrounding cells and tissue.

Lymph – fluid formed from excess tissue fluid that is transported in lymphatic vessels to be returned to normal blood circulation.

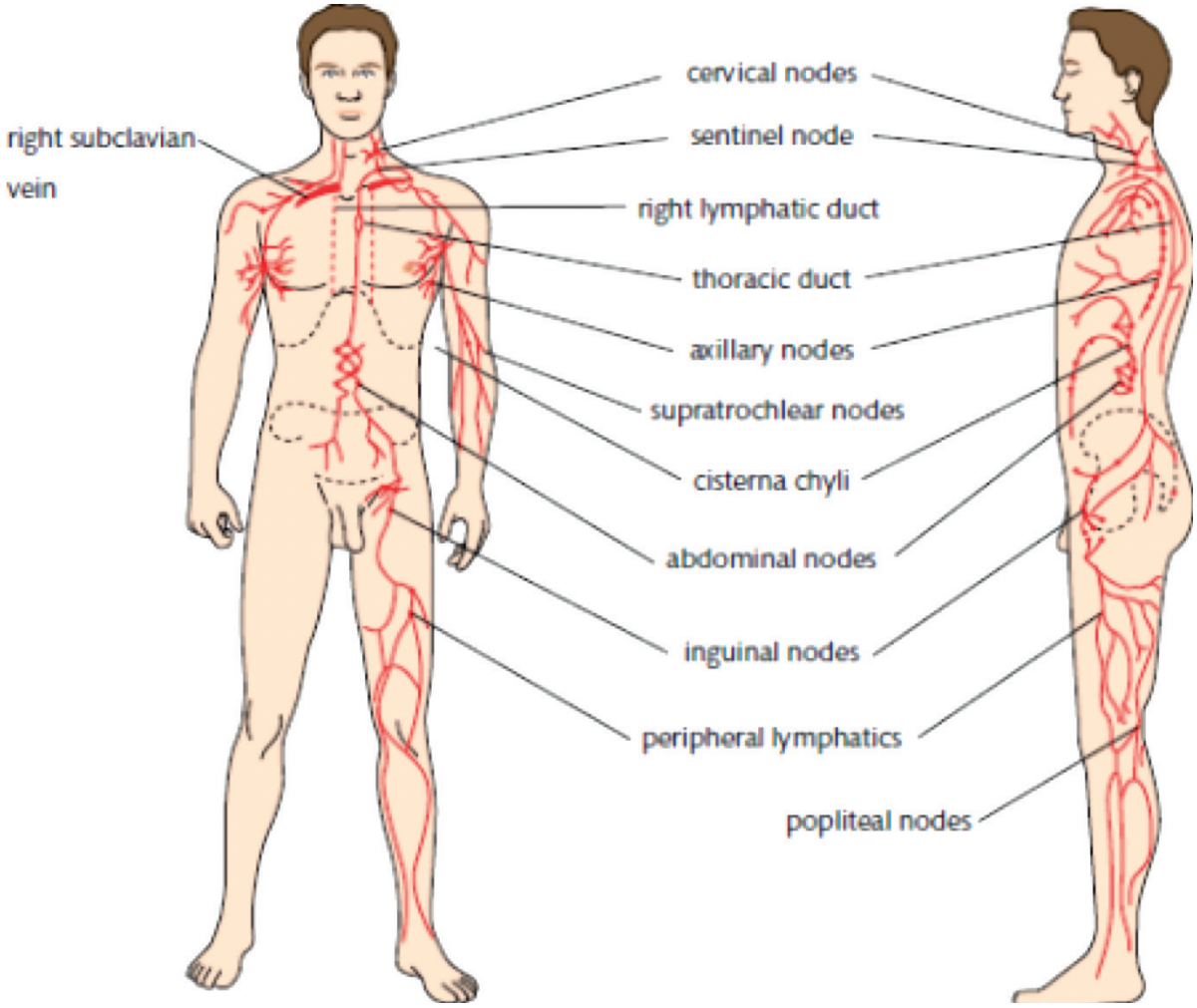


Figure 1.57: The lymphatic system

Assessment activity 1.8

1. Draw and label the structure of the heart.
2. Describe how contraction of the heart is coordinated.
3. Explain how heart rate and blood pressure are regulated.
4. Describe the structure of different blood vessels and explain how their structure is related to their function.
5. Describe the formation of tissue fluid.

Medical conditions affecting the respiratory and cardiovascular systems

There are a range of medical conditions that can affect the respiratory system, the cardiovascular system or both. These include hypertension, hypotension, coronary heart disease (CHD), stroke and chronic obstructive pulmonary disease (COPD). Table 1.10 describes the risk factors (something that may increase the chance of developing a disease) and symptoms of each of these.

Table 1.10: Risk factors and symptoms affecting the respiratory system

Medical condition	Description	Risk factors	Symptoms
Hypotension	Hypotension is also known as low blood pressure. Normal blood pressure readings are 120 / 80 mmHg. Blood pressure readings below 90/60mmHg are defined as hypotension.	Being fit and healthy can cause low blood pressure. Some people may also have low blood pressure due to their genetics. Hypotension can also be caused by: Pregnancy Medical conditions such as diabetes Some medications Blood loss Severe dehydration.	Low blood pressure does not often cause symptoms, but it can lead to: Feeling lightheaded or dizzy Feeling sick Blurred vision Confusion Fainting.
Hypertension	Hypertension is known as high blood pressure. Normal blood pressure is 120 / 80 mmHg. Persistent blood pressure readings above 140 / 90 mmHg are defined as hypertension	The following factors can increase the chances of developing high blood pressure: age, over 65s are most likely to have hypertension being overweight lack of exercise smoking high salt diet high consumption of alcohol or caffeine-based drinks	Hypertension itself does not usually have any symptoms but if left untreated, it can contribute to coronary heart disease, heart attacks and strokes.
Coronary heart disease (CHD)	CHD is caused by blockages in the coronary arteries that supply blood to the heart muscle. The blockages restrict blood flow to the heart and prevent it from contracting properly.	The following factors can increase the chances of developing CHD: age, risk of CHD increases with age smoking hypertension diabetes high levels of cholesterol in the blood.	The symptoms of CHD are: Chest pain (angina), a tight, dull or heavy sensation in the chest which may spread to the left arm, neck, jaw or back Heart attack(s) Heart failure.

Table 1.10: Risk factors and symptoms affecting the respiratory system continued

Medical condition	Description	Risk factors	Symptoms
Stroke	A stoke is caused by restricted blood flow to the brain. A blood clot in a blood vessel carrying blood to or in the brain is usually the main cause. Strokes can also be caused by the bursting of a weakened blood vessel (haemorrhage) that usually carries blood to or in the brain.	Any factor that increases you chance of blood clots, increases the chances of strokes. These factors include: smoking hypertension being overweight diabetes high levels of cholesterol in the blood excessive alcohol intake.	The main symptoms of a stroke can be remember using the acronym FAST: Face – the face may droop on one side. Arms – the person may not be able to lift both arms and keep them there Speech – the persons speech may be slurred, or the person may not be able to talk at all Time – it is important to call 999 immediately if a person has any of these symptoms even if they appear to go away over time. Other symptoms include: paralysis loss of or blurred vision confusion loss of consciousness.
Chronic obstructive pulmonary disease (COPD)	COPD is the name for a group of conditions that affect the lungs and cause breathing problems. The conditions include emphysema (damage to alveoli) and chronic bronchitis (long-term inflammation of the bronchi). The breathing problems get worse over time and can limit normal everyday activities.	COPD occurs when the lungs and airways become damaged. Things that can increase the risk of COPD are: smoking exposure to fumes exposure to dust air pollution genetic deficiency of a protein that is usually produced to protect the lungs. The protein called alpha-1-antitrypsin.	Symptoms of COPD include: increasing breathlessness. At first a person may only experience shortness of breath following exercise but over time, this develops to being breathless even when asleep persistent chesty cough frequent chest infections persistent wheezing.

Pause point

Produce a patient information leaflet for each of the medical conditions of the cardiovascular and respiratory system.

Hint

Include a description of the disease, the symptoms and risk factors.

Extend

In each leaflet, add some advice to the patient which tells them how they could modify their lifestyle to reduce the risk factors of each disorder.

A4 Digestive and excretory system

The digestive system

The function of the digestive system is to break down the food you eat into smaller, soluble molecules which can then be absorbed into the blood stream or lymphatic system. Waste parts of food are passed out of the body as faeces. The digestive system itself consists of several organs which the food comes into contact with during the digestion process. There are also some accessory organs that produce and secrete chemicals which are necessary for digestion, but the food does not come into contact with these organs.

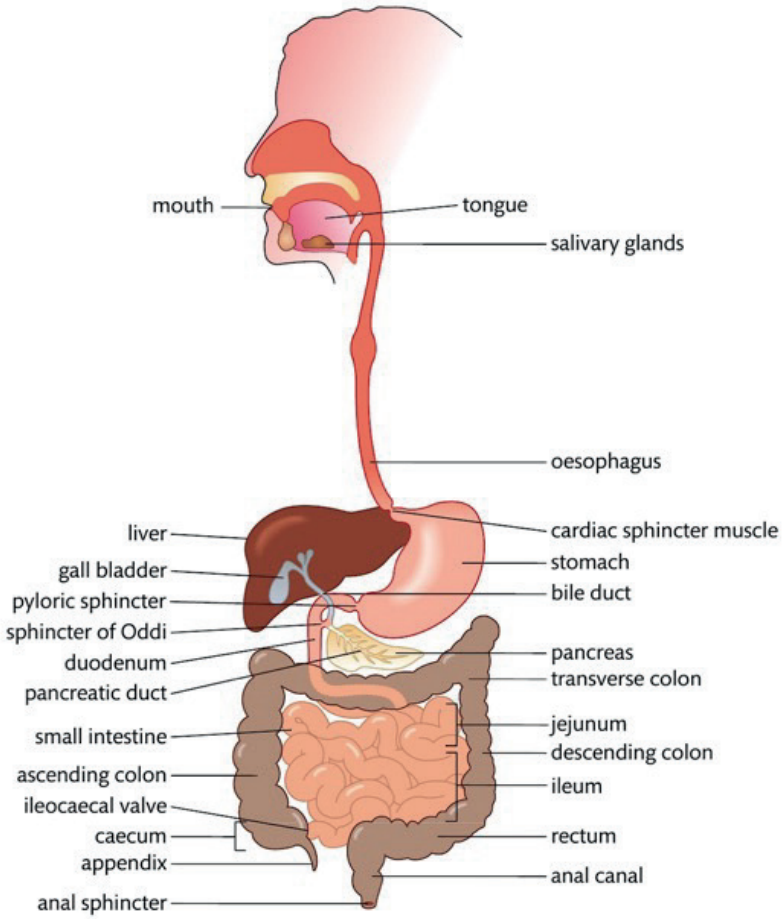


Figure 1.58: The digestive system and accessory organs

Mouth

Digestion begins in the mouth. Ingested food is broken down mechanically by the teeth and mixed with saliva. Saliva contains salivary amylase, an enzyme that begins the chemical digestion of starch. The tonsils filter bacteria from food. The tongue forms the chewed food into a bolus which is then moved toward the pharynx. The food is pushed to the back of the throat by the tongue and the roof of the roof of the mouth to the pharynx where swallowing occurs as an autonomic cranial reflex. The epiglottis closes over the glottis to prevent food entering the airway (trachea). The bolus then moves into the oesophagus.

Oesophagus

The oesophagus is a muscular tube which is about 25cm long, 2.5cm in diameter. It connects the throat to the stomach allowing food to pass down to the stomach once it has been swallowed. The wall of the oesophagus is made up of four layers:

- mucous membrane to secrete mucus for the smooth movement of food
- submucosa which holds the mucous membrane in its position
- thick layer of muscle that causes peristalsis. Peristalsis is the alternate contraction and relaxation of the muscle layers to push the food down into the stomach
- outer protective covering.

Stomach

The stomach is a muscular bag that is found in the upper part of the abdomen, just below the diaphragm. The role of the stomach is to churn the food and mix with stomach acid and enzymes. The wall of the stomach is made up of a thick layer of muscle. The muscle consists of longitudinal, circular and oblique smooth muscle fibres, lined with epithelial cells. Epithelial cells produce gastric juice containing acid and enzymes. The muscular wall of the stomach generates peristaltic movement to churn the food and mix it with enzymes to form chyme. Food remains in the stomach for 1-3 hours.

Small intestine

Duodenum

At the end of the stomach, the chyme causes the sphincter muscle to relax. The duodenum is the first part of the small intestine. Food passes in small quantities from the stomach into the duodenum. The duodenum is around 25cm long, with a diameter of about 2.5cm and is fixed to the dorsal abdominal wall. It consists of layers of smooth muscle cells. The interior of the duodenum is lined with epithelium tissue. Pancreatic juice with hydrolytic enzymes and bile from the liver are added to the duodenum. These secretions enter the duodenum at the sphincter of Oddi.

Jejunum and ileum

After the duodenum, food passes into the next part of the small intestine called the jejunum which is about 2.5m long and has a diameter of 3.8cm. From the jejunum, food passes into the last part of the small intestine, the ileum. The ileum is the longest part of the small intestine at around 3.6m long. The products of digestion are absorbed across the walls of the ileum and into the bloodstream or lymphatic system. The walls of the ileum contain epithelial tissue with finger like projections (villi) that protrude into the lumen of the tube. This makes the walls highly folded and gives a large surface area for absorption. Jejunum and ileum are supported on a membrane called the mesentery.

Pancreas

The pancreas is a soft pink gland supported by mesentery, within the loop of the duodenum. The pancreas itself has both endocrine and exocrine functions. The exocrine function is to produce and secrete pancreatic juice containing digestive enzymes directly into the duodenum via the pancreatic duct to aid the digestion of all food types. Pancreatic juice is produced by clusters of cells in the pancreas called the acini cells. These cells contain large amounts of rough endoplasmic reticulum, golgi apparatus and vesicles to allow the cells to produce digestive enzymes. Epithelial cells lining the pancreatic ducts secrete hydrogencarbonate ions that make the pancreatic juice alkaline.

The endocrine function is to produce the hormones insulin and glucagon. Scattered among the acini cells are islets of Langerhans. Beta cells in these islets secrete insulin, in response to increased blood glucose levels. glycogen is secreted by alpha cells in the islets in response to lowered blood glucose levels.

Gall bladder

The gall bladder is small muscular sac around 10cm in length. The gall bladder stores bile which is made in the liver. Bile is released from the gall bladder into the duodenum via the bile duct when food moves from the stomach into the duodenum at the sphincter of Oddi. Bile contains salts to emulsify fats, increasing their surface area for digestion. It also contains hydrogen carbonate ions to neutralise stomach acid.

Liver

The liver is a large gland in the abdomen, in front of the stomach. It consists of hexagonal shaped liver lobules, inside which are hepacytes. Oxygenated blood enters the liver from the hepatic artery and nutrient rich blood comes from the ileum via the hepatic portal vein. Deoxygenated blood leaves the liver in the hepatic vein. Hepacytes make bile that enters canaliculi and passes to the gall bladder where it is stored until it is needed.

Bile contains salts that emulsify fats to increase their surface area for digestion; hydrogencarbonate to neutralise acid chyme; bilirubin and biliverdin which are the products of broken-down red blood cells and cholesterol.

The liver also stores glycogen, helps regulate blood glucose levels, makes plasma proteins, stores fat-soluble vitamins and metabolises alcohol, drugs and other toxins. It breaks down excess amino acids to make urea for removal at the kidneys.

Large intestine

Branching out from that is the appendix which contains lymphoid tissue and bacteria that may help recolonise gut microbiota. The colon makes up the majority of the large intestine and has four parts: ascending colon, transverse colon, descending colon and sigmoid colon. Colon mucosa consists of columnar epithelial cells, no villi or folds and few to no digestive enzyme-secreting cells. The colon wall has a membrane of goblet cells that secretes mucus to protect the wall from the acids and gases produced by bacteria that live in the colon. Gut bacteria are essential for production of vitamins B and K. In the colon, water and minerals are absorbed from the undigested food into the blood. The undigested food residues that remain produce faeces. Faeces containing undigested food residue, gut bacteria, sloughed off epithelial cells and other excretory products such as bilirubin, pass into the rectum to be stored. More water is then absorbed, and the faeces pass into the anal canal to be expelled.

Anus

Stretching of the rectum wall initiates the defaecation reflex and forces faeces into the anal canal. Impulses reach the brain and we make voluntary decisions as to whether or not we open the external anal sphincter.

Key points

Peristalsis – involuntary contraction and relaxation of smooth muscles of the intestine creating wave like movements that push forward the contents of the canal.

Chyme – semi-fluid mass of partly digested food formed in the stomach.

Sphincter muscle – circular muscle that surrounds an opening and acts as a valve.

Mesentery – double layered extension of the peritoneum able to support organs within the ab-dominal cavity.

Gut microbiota – all the microbes that live in the human gut.

Digestion, absorption and assimilation

While food is in the gut, large molecules undergo **hydrolysis** and are digested into smaller molecules that can be absorbed across the gut wall into the blood stream. **Assimilation** is the process that takes the products of digestion such as glucose, amino acids, fatty acids and glycerol into the body cells after the food has been digested and absorbed. The nutrients are then used for body processes. Amino acids are used to build proteins such as hormones and enzymes or are deaminated by the liver to form ammonia then urea which is excreted in urine. Glucose is used for cellular respiration or is converted into glycogen that is stored in the liver. Fatty acids are used as part of cellular membranes, insulation or stored body fat.

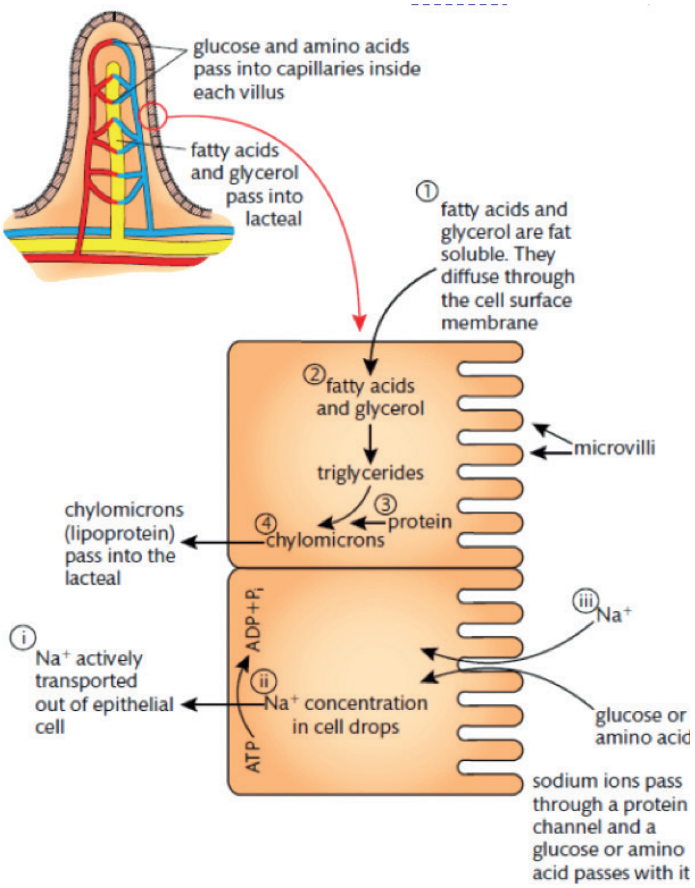


Figure 1.59: How the products of digestion are absorbed in the ileum

Key points

Hydrolysis – chemical reaction that splits large molecules into smaller molecules, by adding water.
Assimilation – the movement of the products of digestion into the cells of the body where they are used.

Mechanical and chemical digestion

When you bite and chew food, large pieces are broken down into smaller ones. This is mechanical digestion. The action of the stomach-churning food is another example of mechanical digestion.

Enzymes that hydrolyse macromolecules are also present in saliva, gastric juice, enteric juice and pancreatic juice. This hydrolysis of macromolecules to smaller molecules is chemical digestion.

Nutrient absorption

Some small molecules such as glucose may be absorbed from the stomach. However, the main site of nutrient absorption is the ileum. The ileum has a large surface area for absorption because it long, folded and the epithelium of the ileum contain villi. The villi also have projects of microvilli, which increase the surface area even more.

Some of the absorption in the ileum is by **diffusion**, some by **facilitated diffusion**, and some by **active transport**.

Glucose and amino acids are absorbed into the bloodstream by active transport using a cotransporter mechanism. Firstly, sodium ions are actively transported out of the epithelium cells lining the villi and into the ileum lumen. This uses energy from ATP and decreases the concentration of sodium ions in the epithelium cells. Sodium ions diffuse back down their concentration gradient across the cells lining the walls of the villi. To do this they use protein channels in the epithelial cell surface membrane. When they move into the epithelial cell, they carry glucose or amino acids with them.

Glycerol and fatty acids are fat-soluble and can move by diffusion though the cell surface membrane of the epithelial cells of the villi. Inside the epithelial cells, they are combined to form triglycerides by the smooth endoplasmic reticulum. The triglycerides are then modified by the addition of a protein coat to form a chylomicron. Chylomicrons diffuse out of the epithelial cells and into a lymphatic vessel.

Inorganic ions pass through the epithelial cells of membranes by facilitated diffusion. Water passes down its water potential gradient by osmosis.

Key points

Diffusion – movement of molecules down their own concentration gradient. This may or may not be through a partially permeable membrane. It uses only the kinetic energy of molecules and does not use energy from ATP.

Facilitated diffusion – diffusion that is enhanced by the presence of carriers or channels made of protein in the cell surface membrane.

Active transport – movement of molecules into or out of cells against their concentration gradient. It uses carrier proteins in the cell surface membrane and energy from ATP.

Cotransporter – a type of transport protein that transports two or more substances at the same time across a cell membrane.

Control of blood glucose levels

One of the products of digestion is glucose. Glucose is transported from the ileum where it is absorbed into the blood stream and transported to all of the cells in the body. Excess glucose is stored in the liver and muscles as glycogen. All of the cells in the body require glucose for respiration. Respiration produces ATP which is required for cellular processes. Having a supply of glucose to cells is crucial in keeping you alive. The body uses a negative feedback mechanism to ensure that glucose levels in the blood are maintained within strict parameters. Normal blood glucose levels are between 4 and 7 mmol L-1. Excess blood glucose is stored as glycogen in the muscle and liver cells. If blood glucose levels fall, glycogen can be converted back to glucose to increase blood glucose levels back to normal. This mechanism requires two hormones that work antagonistically to control blood glucose levels. These hormones are called insulin and glucagon. Both hormones are produced by cells in a region of the pancreas called the Islets of Langerhans. Insulin is produced by beta cells (β-cells) and glucagon is produced by alpha cells (α-cells). The regulation of blood glucose levels can be seen in figure 1.60 below.

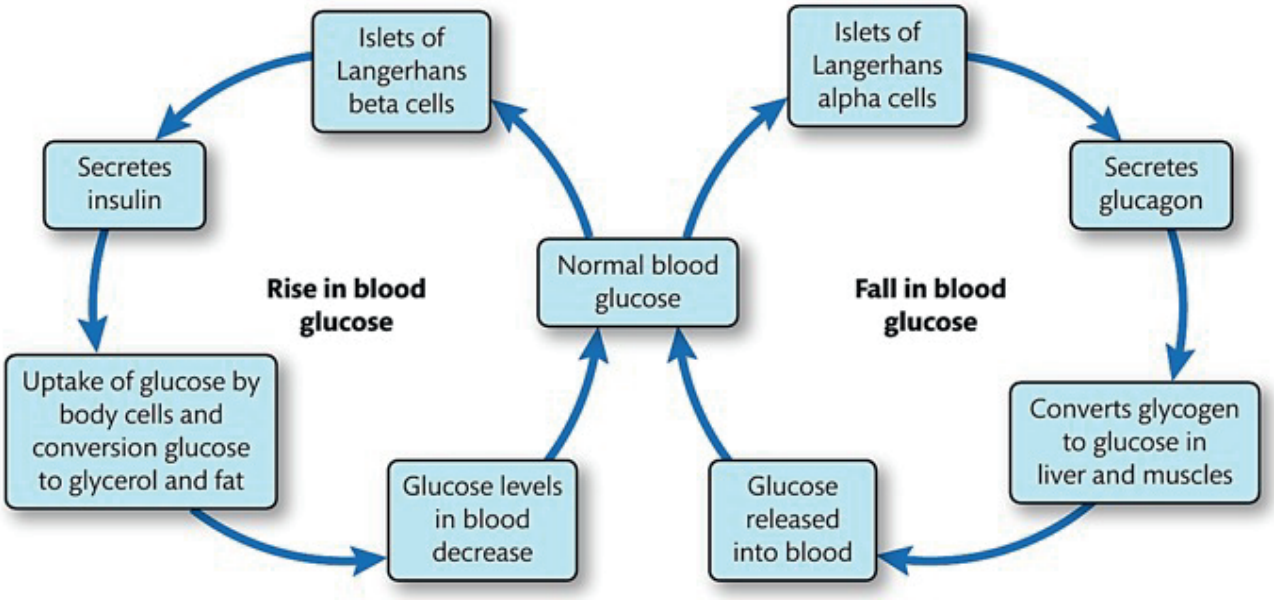


Figure 1.60: The regulation of blood glucose levels by negative feedback

Alpha cells and glucagon

If blood glucose levels fall below the normal range, this is detected by the alpha cells of the Islets of Langerhans. A fall in blood glucose can be due to an extended period of time without eating or exercise. In response, the alpha cells secrete glucagon into the bloodstream. Glucagon binds to receptors on the plasma membrane of liver cells. This causes glycogen which is stored in the liver to be converted to glucose which is then secreted into the blood. This brings the blood glucose levels back to normal. This process is called **glycogenolysis**. Glucagon also stimulates an increase in the rate of **gluconeogenesis**. This is a process where glucose is synthesised from non-carbohydrate sources such as protein or fat.

Beta cells and insulin

If blood glucose levels rise below the normal range, this is detected by the beta cells of the Islets of Langerhans. A rise in blood glucose is caused by the digestion of food. In response, the beta cells secrete insulin into the bloodstream. Insulin binds to receptors on the plasma membrane of muscle and liver cells. This causes a series of events that causes the cells to take up glucose. This brings the blood glucose levels back to normal. Increasing the rate of uptake of glucose increases the rate of respiration in cells. Excess glucose is also stored as glycogen. This process is called **glycogenesis**. Excess glucose can also be converted to fat which is stored as adipose tissue.

Key points

Glycogenolysis – the breakdown (lysis) of glycogen to release glucose.

Gluconeogenesis – the formation (genesis) of glucose from non-carbohydrate sources such as protein.

Glycogenesis – the formation (genesis) of glycogen from glucose.

Diabetes mellitus

Diabetes mellitus is a condition where the body is unable to regulate blood glucose levels properly.

There are two main types of diabetes mellitus, type 1 diabetes and type 2 diabetes, Table 1.11 summarises the most common symptoms of diabetes mellitus and explains their causes.

Table 1.11: Symptoms of diabetes mellitus and their underlying causes

Symptom	Cause
Weight Loss	There is insufficient insulin to increase the permeability of the cell membranes to glucose. The cells are therefore starved of fuel and have to respire using fats and proteins instead. Insulin also acts as an anabolic (body building) hormone and lack of it leads to muscle wasting.
Thirst	High levels of glucose in the blood cause a decrease in water potential in the blood.
Lack of energy and tiredness and craving for sweet foods	Cells are starved of the glucose they require for respiration to release energy.
Presences of glucose in the urine (glycosuria)	The kidneys are unable to reabsorb the high levels of glucose filtered into the tubules.

Type 1 diabetes

Type 1 diabetes is most commonly diagnosed in young or adolescent people. It is also known as insulin-dependent diabetes or juvenile onset diabetes. It is caused when the body's own immune system attacks the beta cells in the Islets of Langerhans in the pancreas. This stops the cells from being able to produce insulin. The consequence of this is also hyperglycaemia (high blood glucose levels). Type 1 diabetes has to be managed by regular blood glucose testing (before and after food) injections of insulin, careful management of a balanced diet and exercise.

A person with type 1 diabetes must be careful to inject the correct amount of insulin according to the food that they are eating, their overall health and the amount of exercise they do. Failure to take these factors into consideration, may lead to too much insulin being injected. If this happens the person can experience hypoglycaemia. Hypoglycaemia is low blood glucose and can be dangerous. Brain cells require glucose for respiration and so lack of glucose can lead to unconsciousness, coma and death. The first aid treatment for hypoglycemia is to have a sugary drink, snack or dextrose tablets.

Type 2 diabetes

Type 2 diabetes is most commonly diagnosed later in life. It is known as insulin-independent or late onset diabetes. It occurs when insulin is still being produced by the beta cells of the pancreas, but the body and liver cells gradually lose their response to insulin. This can have the effect of causing the beta-cells to reduce insulin secretion. The consequence of this is also hyperglycaemia (high blood glucose levels).

People with type 2 diabetes can often control their blood glucose levels with regulation of diet and exercise, but some people may require injections of insulin. Studies have shown that being overweight, lack of exercise and high sugar diets can increase the risk of type 2 diabetes.

Hyperglycaemia

In the short-term hyperglycaemia can lead to symptoms of increased thirst, increased frequency of urination, headaches, blurred vision, tiredness and difficulty concentrating. Elevated blood glucose levels over a long period of time can damage organs and tissues. Long-term damage can lead to necessary amputation of extremities such as toes or fingers. It can also lead to nerve damage, kidney damage and loss of sight.

Pause point

Produce a diagram to show the homeostatic mechanism of blood glucose control.

Hint

Think about cell size. Start off with normal blood glucose levels and add arrows for increase and decrease. Include how changes are detected, how the response is co-ordinated and a description of the different responses that restore normal blood glucose.

Extend

Discuss how failure to regulate blood glucose levels can have serious consequences for the body.

Diet and dietary needs

You have seen that a poor diet can increase the risk of type 2 diabetes, but a poor diet can also increase a person's risk of hypertension and cardiovascular and respiratory diseases. Humans need a balanced diet to maintain health. A balanced diet should include the correct amount of macronutrients and micronutrients. Macronutrients include carbohydrates, fats and proteins. Micronutrients include vitamins and minerals. We obtain the nutrients we need by ingesting and digesting food.

Tables 1.12 and 1.13 below show sources and role of different macronutrients and micronutrients required for good health.

Table 1.12: Macronutrient sources and their roles

Nutrient	Examples of sources	Use in body	Result of deficiency or excess
Carbohydrate • Starches • Sugars	Starches: Potatoes, rice, maize, quinoa, sorghum, bread, cereals, muscle meat (glycogen) Sugars: Fruit, honey, milk, table sugar, processed foods with added sugar; fizzy drinks, fruit squashes and juices	Makes up the staple/main part of diet; energy source	As carbohydrate foods are usually cheap and plentiful, you are unlikely to suffer from a deficiency. Too much carbohydrate may lead to weight gain. Too much sugar can lead to tooth decay or type 2 diabetes.
Lipids (fats_	Meat, oily fish, oils, nuts, butter, cream, cheese, margarine	Energy source; stored in body as energy store, and for protection of internal organs and under skin for insulation; source of fat soluble vitamins; some fatty acids are essential to make cell membranes and nerve tissue; cholesterol needed to make sex hormones and to strengthen membranes	Deficiency of fat-soluble vitamins (A, D and E). Too much saturated fat may lead to weight gain/obesity, fatty plaques in artery walls (atherosclerosis) and increased risk of heart attack and stroke.

Nutrient	Examples of sources	Use in body	Result of deficiency or excess
Proteins	Meat, fish, cheese, eggs, milk, soya beans, nuts, beans, quinoa, tofu, yoghurt	Growth and body structures such as bone, muscle, skin, internal organs; enzymes, haemoglobin, antibodies, neurotransmitters	Lack of protein can lead to kwashiorkor – stunted growth, muscle wasting and tissue oedema.
Fibre	Fruit and vegetables, porridge	Soluble fibre can lower blood cholesterol level; fibre adds bulk, prevents constipation and encourages growth of bacteria in the gut	Lack of fibre can lead to: • constipation • potentially bowel cancer, due to increased time faeces spends in the large intestine • lack of desirable bacteria in the gut microbiota.
Water	Water, drinks such as coffee and tea, milk	To make body fluids such as gastric juice; to remove excretory waste products such as urea in urine; keeps body hydrated; keeps eye surface moist; blood plasma; provides medium for metabolic reactions within cells; helps regulate body temperature (sweat); humans are about 80% water	Lack of water leads to dehydration – disruption of electrolyte (ions) balance. Loss of water from blood leads to osmotic imbalances and water leaving body and blood cells; enzyme-catalysed reactions cannot take place in dehydrated cells; sweat cannot be produced so leads to hyperthermia.

Table 1.13: Micronutrient sources and their roles

Nutrient	Examples of sources	Use in body	Result of deficiency or excess
Vitamin A (retinol) and beta carotene	Liver Carrots, sweet potatoes, squash, pumpkin, spinach, green vegetables, apricots, mango, egg yolks, peppers	Colourful vegetables supply beta carotene that the body changes to retinol. Vitamin A is needed for rod cells in the retina of the eye, healthy epithelial cells, resisting infections, growth and acting as an antioxidant reducing risk of cancer	Lack of beta carotene and vitamin A leads to poor night vision, xerophthalmia (dry hard cornea) and eventually blindness; severe deficiency is fatal. Excess vitamin A can lead to nerve disorders and during pregnancy can lead to abnormal development in the fetus.
Vitamin D	Formed in skin when exposed to UV light; a form of cholesterol in the skin is changed to vitamin D Milk, salmon, tuna, mackerel and herrings, egg yolks, liver	Is a hormone and regulates calcium phosphate deposition in bone; also helps protect against heart disease, cancer, multiple sclerosis, depression and schizophrenia	Too much in the diet by supplements can lead to calcium deposits in kidney, brain, heart and muscle, and learning difficulties in children. Negative feedback prevents formation of too much in skin. Lack leads to rickets in children, osteomalacia in adults and may contribute to osteoporosis.
Vitamin E	Nuts, prawns, wholemeal bread, sweet potatoes, oils	Antioxidant so may help reduce risk of cancer and heart disease	Deficiency very rare – poor nerve transmission, muscle weakness and degeneration of retina.

Nutrient	Examples of sources	Use in body	Result of deficiency or excess
Vitamin K	Green leafy vegetables; made by gut microbiota bacteria	Needed to help blood clot during injury	Lack leads to easy bruising and internal bleeding.
Vitamin C (ascorbic acid)	Fruits and green vegetables, potatoes, kiwi fruits, blackcurrants and green peppers are very good sources	Helps body make collagen protein – important for muscles, bone, blood vessel walls and cartilage; aids absorption of dietary iron; is an antioxidant – by becoming oxidised itself it protects molecules such as DNA from damage due to oxidation by free radicals	Excess is passed out in urine. Lack leads to scurvy – poor bone and teeth development; delayed wound healing; weakened blood vessels and increased haemorrhaging, tender sore gums, loss of teeth and hair; painful joints due to internal bleeding. Death if untreated.
Vitamin B group B, thiamine	Bran, rice husks, meat, peas	Activates enzymes in respiration	Lack leads to mental confusion, Beriberi.
Vitamin B group B, riboflavin	Green vegetables, meat	Activates enzymes used in respiration	Lack leads to decreased growth, cracked dry skin.
B3 Niacin	Meat, fish, brown rice	Activates enzymes used in respiration	Lack leads to pellagra – depression and confusion; dementia and death.
B6	Meat, fish, green vegetables, bananas	Activates enzymes used in protein metabolism	Lack leads to large irregularly shaped red blood cells.
Folic Acid	Dark green vegetables	Activates enzymes for DNA replication and protein synthesis	Lack leads to pernicious anaemia.
B12	Meat and fish	Activates enzymes involved in making nerve, blood and other cells	Lack leads to confusion and dementia-like symptoms. Pernicious anaemia, if caused by autoimmunity, leads to vitamin B12 deficiency as the cells making intrinsic factor are destroyed and vitamin B12 cannot be absorbed from the gut even if it is present in the diet.
Iron	Meat, soya beans, fish, whole wheat bread, prunes, plums	To make haemoglobin and myoglobin	Lack leads to anaemia.
Iodine	Seafood, iodised salt, egg	To make the hormone thyroxine	Lack leads to goitre; during pregnancy can lead to mental and physical development abnormalities in fetus – cretinism.
Calcium	Milk, cheese, yoghurt, ice cream, cream, green vegetables	Bones, muscle contraction, blood clotting, nerve function	Lack leads to problems with bone density and muscle contraction.

Nutrient	Examples of sources	Use in body	Result of deficiency or excess
Magnesium (Mg), Sodium (Na), Phosphorus (P) Potassium (K)	Milk, meat, seeds, vegetables, Salt Tuna, potatoes Bananas, avocado, fish	Maintaining electrolyte balance for body fluids; nerve function (Na+); bone formation (Mg2+ and P); heart function (K+)	Lack leads to nerve and heart dysfunction.

Calorific value of food

The energy content of most foods is stated on the packaging as part of the nutrition label. The energy content is often given in kcals, which is short for kilocalories, and also in kJ, which is short for kilojoules. Kilojoules are the metric measurement of calories. Food packaging usually displays this information as kilocalories per 100g of food; 1 kilocalorie is 1000 calories. To convert the calorie content in kilojoules, multiply the calorie figure by 4.2.

The average woman needs to consume around 2,000 kcal per day (8,400kJ) and the average man needs to consume around 2,500 kcal per day (10,500kJ). Energy requirements however do vary from person to person.

The recommended intake of calories/kilojoules per day depends on:

- general health
- level of physical activity
- weight
- height
- body shape composition.

Consuming more than the recommended daily calories or more calories than the body requires based on your level of physical activity in the long term, leads to weight gain. Consuming less than the recommended daily calories or less calories than you need based on your level of physical activity leads to weight loss.

Exclusion and calorie-controlled diets

Calorie-controlled diets can help people to lose weight if they are overweight. The British Dietetic Association recommends that consuming no more than 1400 kcal a day for a woman and 1700 kcal a day for a man will lead to on average a 0.5 to 1.0 kg weight loss per week. Calorie controlled diets for weight loss are based on the principle that consuming less calories than are required for daily activity will lead to weight loss. It is for this reason that exercise is also recommended to increase levels of activity.

Calorie-controlled diets can also help people gain weight. Special calorie dense drinks can be given to those who need to gain weight. This can be due to an eating disorder, other illnesses such as cancer, and to older people who need additional help to increase their calorific content. In this type of diet, the underlying principle is that consuming more calories than are required for daily activity will lead to weight gain.

Exclusion diets are diets that are designed to identify the source of an allergy or intolerance. They typically involve removing one type of food from a diet for a period of time (2 to 8 weeks) and seeing if the symptoms from the allergy or intolerance go away. The food can then be reintroduced gradually to see if the symptoms come back. If an allergy or intolerance is found, the person would be advised to eliminate the food from their diet altogether. Common examples of food that can cause allergy or intolerance are eggs, milk, fish, nuts and gluten.

Dietary and nutritional problems

Body mass index or BMI is a measure that can be used to indicate whether you are a healthy weight. It is calculated by dividing the weight of an adult (in kilograms) by their height (in metres) squared. The formula looks like this:

$$\text{BMI} = \frac{\text{Weight in Kg}}{(\text{Height in m})2}$$

For most adults an ideal range for BMI is 18.5 to 24.9. Being below this can indicate that you are underweight and being above can indicate that you are overweight.

However, some people can have a BMI that is outside of the normal range and still be healthy. For example, muscle is much denser than fat and so weight trainers and athletes may have a high BMI despite being a healthy weight. Figure 1.610 below shows a chart that can be used to find out which category a person's BMI falls into. For example, a person who weights 65kg and is 170cm tall will have a BMI that falls into the healthy weight category. A person who weighs 100kg and is 170cm tall will have a BMI which falls into the obese category.

Figure 1.61: A BMI chart that can be used to find out which category a person's BMI falls into, based on height and weight

The table below is another way of presenting how a BMI could be interpreted.

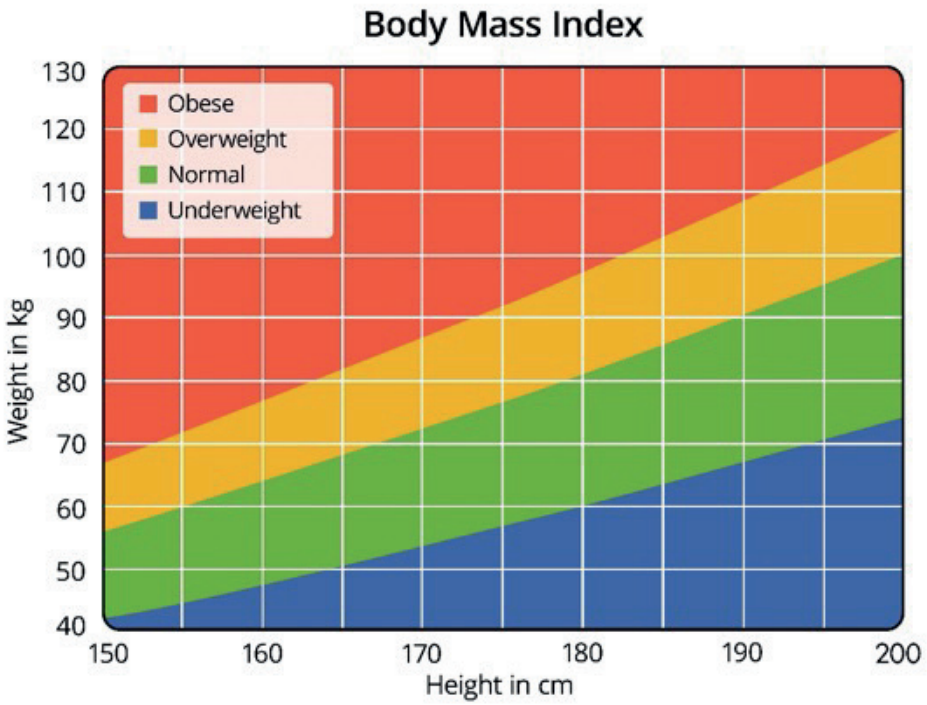


Table 1.14: This table is used by the NHS, be aware that different organisations may use slightly different BMI ranges.

BMI	Meaning
Less than 18.5	Underweight
Between 18.5 and 24.9	Healthy weight
Between 25 and 29.9	Overweight
Between 30 and 34.9	Obese
Between 35 and 39.9	Severely obese
40 or above	Morbidly obese

Assessment activity 1.9

1. Draw and label a diagram of the digestive system.
2. Describe the process of digestion, stating where each stage takes place.
3. Describe how blood glucose levels are regulated by the hormones insulin and glucagon.
4. Explain the consequences of a failure to regulate normal blood glucose levels.
5. Explain why diet is important in maintaining a heathy BMI.

The excretory system

The urinary system plays a role in dealing with some of the waste products of metabolism by producing urine. It is also responsible for osmoregulation and maintaining the balance of electrolytes in the body.

Key points

Osmoregulation – maintenance or regulation of normal osmotic concentration of body fluids by adjusting salt and water levels.

Electrolytes – ions found in the blood including Na+ (sodium), K+ (potassium). Cl- (chlorine) and H2CO3- (bicarbonate).

The renal (urinary) system

The renal system consists of the kidneys, ureters, urinary bladder and urethra. The kidneys are small bean-shaped organs found each side of the spine at the back of the abdominal cavity just above the waist. Most people have two kidneys, the left and right kidney. Each kidney is supplied with blood by branches of the renal artery. Blood is taken away from each kidney by branches of the renal vein. The function of the kidneys is to filter blood and produce urine. The urine produced is carried in the ureters, one from each kidney, to the urinary bladder where it is stored. At an appropriate time of release, urine is released from the urinary bladder and travels down the urethra and out of the body.

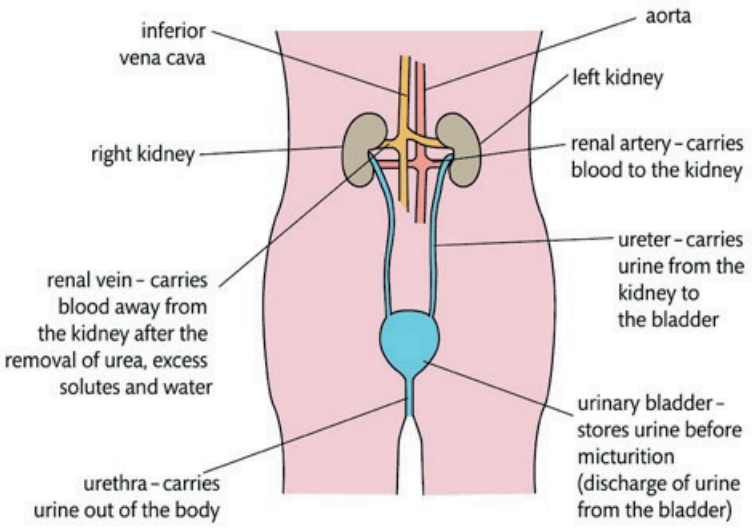


Figure 1.62: Structure of the urinary system

The ureters

The ureters are muscular tubes made of smooth muscle fibres. They transport urine from the kidneys to the urinary bladder.

The urinary bladder

The urinary bladder is a hollow muscular organ that stores urine produced by the kidneys until it is released into the urethra. The urinary bladder has a sphincter muscle at the exit to the urethra. This ring of muscle can be opened under conscious control to release urine into the urethra and out of the body.

The urethra

The urethra carries urine from the bladder and out of the body. The urethra is a hollow tube lined with a layer of epithelial cells and contains glands which secrete mucus to prevent the tube being damaged by acidic urine. The wall of the urethra also contains smooth muscle. In males, the urethra also carries sperm out of the body.

The kidneys

In addition to filtering waste products and excess water from the blood, the kidneys also conserve and return vitamins, amino acids, glucose, hormones and other vital substances into the bloodstream. The kidneys are surrounded by a strong capsule. If you dissect a kidney, inside you will see that they consist of three distinct regions, the outer cortex, the inner medulla and the central renal pelvis. The renal pelvis drains into the ureter. Kidneys contains around 1 million individual functional components called nephrons. It is the nephrons that filter the blood and produce urine.

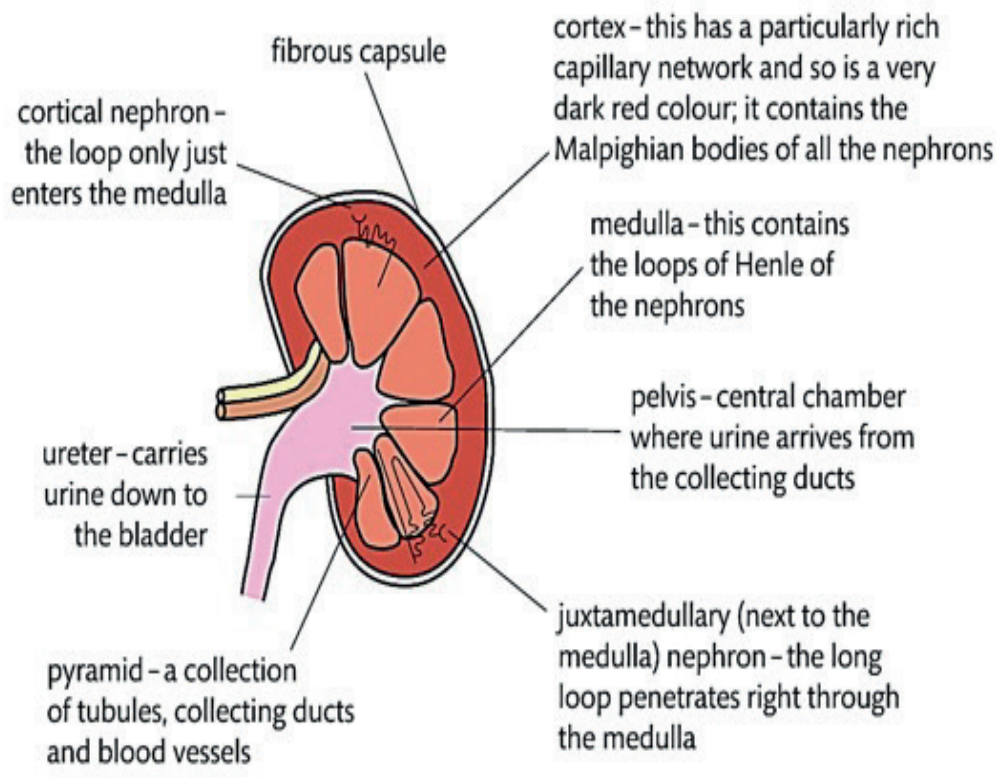


Figure 1.63: The structure of a kidney. The two main types of tubule have been superimposed.

Nephrons

Nephrons are microscopic structures found in the kidneys. They are the functional units of the kidney. Blood enters the kidney in a branch of the renal artery and then travels into smaller arterioles before reaching capillaries. Substances can be filtered out of the blood of the capillaries and into the nephrons. As the fluid produced travels around the nephron its composition is altered until eventually urine is produced. This urine then drains into the renal pelvis before draining into the ureter to be transported to the urinary bladder.

The nephrons have five distinct parts:

1. Bowman's capsule
2. Proximal convoluted tubule
3. Loop of Henle
4. Distal convoluted tubule
5. Collecting duct.

Each nephron starts in the cortex of the kidney. Here, the blood capillaries from the renal artery form a knot of capillaries known as the glomerulus. This sits inside the first part of the nephron, the Bowman's capsule. This is where the blood is filtered to remove waste.

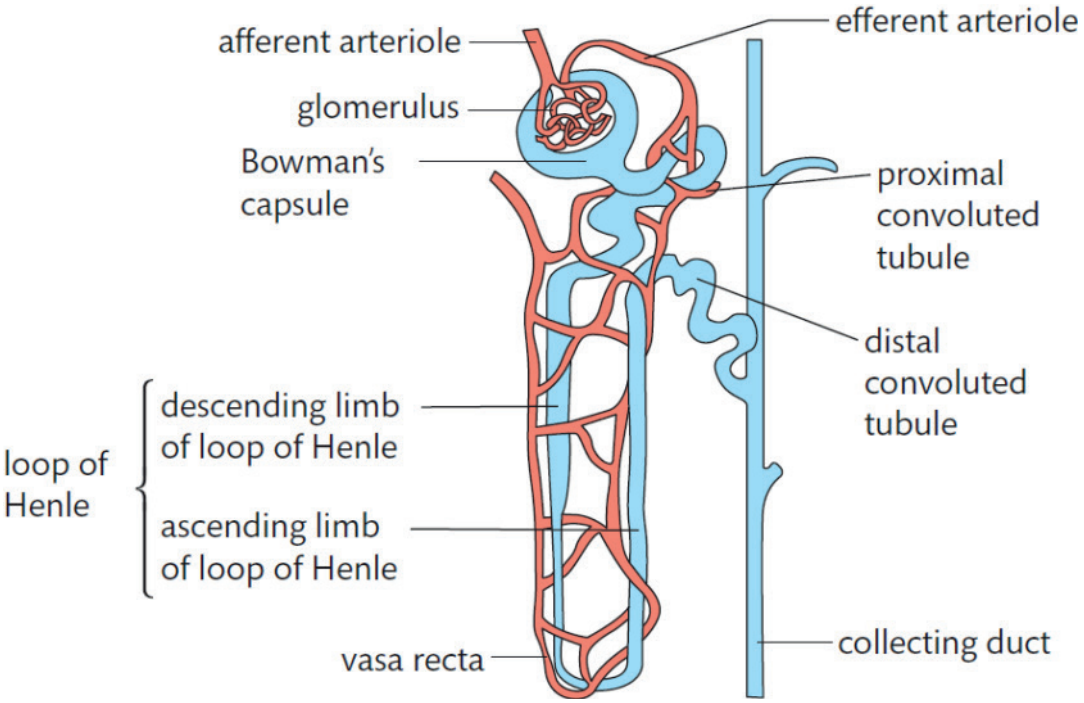


Figure 1.64: The structure of a nephron

Bowman's capsule

Blood is supplied to the kidney by the renal artery which branches to form arterioles. Each Bowman's capsule receives blood from an arteriole, called the afferent arteriole. The arteriole branches into a dense capillary network inside the Bowman's capsule called a glomerulus. The capillaries join up to form the efferent arteriole which takes blood away from the capsule.

Bowman's capsule is the site of ultrafiltration. This is the process by which small molecules are filtered out of the blood under pressure in the capsule. This forces fluid out of the blood and into the Bowman's capsule. The fluid pushed out contains water, amino acids, glucose, waste urea, and inorganic ions (electrolytes). These substances are small enough to fit through the small gaps in the glomerulus wall. Cells and proteins remain in the blood as they are too large to pass into the Bowman's capsule.

Loop of Henle

The loop of Henle runs through the medulla and back up to the cortex of a nephron. Its function is to create an area of high solute concentration in the medulla through which the nephron collecting duct flows. This allows for a large amount of water to be reabsorbed from the collecting ducts by osmosis.

The first part of the loop is the descending limb and the second part is the ascending limb. The ascending limb is more permeable to salts and less permeable to water.

As the filtrate passes along the loop, sodium and chloride ions move into the descending limb by diffusion, and water leaves it. As a result, the concentration of the filtrate increases as it moves down the loop, until it is hypertonic to the blood. When the filtrate reaches the bend in the loop of Henle, it is at its most concentrated. As the filtrate moves up the ascending limb, chloride and sodium ions are pumped out, increasing the sodium chloride concentrations in the tissue of the medulla. The concentration of the filtrate reduces as it moves up the ascending limb, making it increasingly hypotonic to the blood. This mechanism is called a counter-current multiplier mechanism.

Distal convoluted tubule

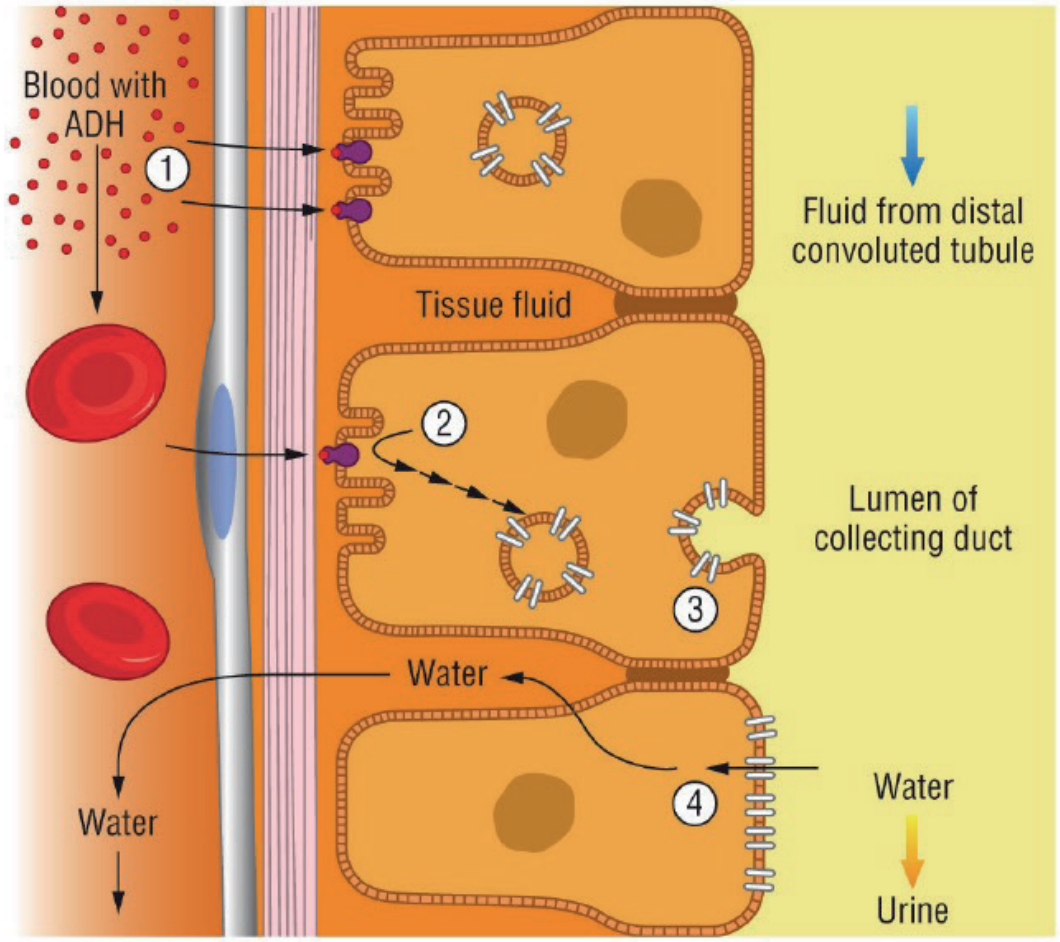
At the top of the ascending limb, is the distal convoluted tubule. Active transport is used to adjust the concentration of ions in the filtrate before it passes into the collecting duct. The removal of sodium ions is controlled by a hormone called aldosterone. When low blood pressure is detected by the baroreceptors in the carotid artery, one of the responses is an increase in the secretion of aldosterone by the adrenal glands. Aldosterone causes the distal convoluted tubule to increase reabsorption of sodium ions. This in turn causes increased water to be reabsorbed from urine which increases blood pressure.

Collecting duct

The final part of the nephron is the collecting duct which controls the volume of water in urine. The collecting duct passes through the medulla to the pelvis, passing through the region of high solute concentration. Water moves across the walls of the collecting duct and into the medulla tissue by osmosis. From the medulla tissue, water enters the blood capillaries to be returned to normal circulation. This results in the formation of concentrated urine. The amount of water that is reabsorbed from urine depends on the permeability of the walls of the collecting duct. This is controlled by a hormone called ADH (antidiuretic hormone); when ADH is present, the collecting duct becomes permeable to water. This promotes reabsorption of water back into the bloodstream and therefore, prevents dehydration.

Key points

Counter-current multiplier – a counter-current system (a system that maintain s a concentration gradient along its length) that uses energy to actively transport substances across a membrane to create a diffusion gradient.



1. ADH detected by cell surface receptors
2. Enzyme-controlled reactions
3. Vesicles containing water-permeable channels (aquaporins) fuse to membrane
4. More water can be reabsorbed

Figure 1.65: Effect of ADH on the collecting duct wall

A5 Cellular injury and repair

Cell injury is a result of stress where cells are no longer able to adapt or when they are exposed to damaging chemicals. Cells expand in size and this may occur due to cellular hypoxia or lack of oxygen to that particular region. At a cellular level, injury can cause a reduction in ATP, beginning the process of anerobic respiration increasing the intracellular pH cells, affecting enzyme activity. ATP dependent sodium-potassium pumps in the cell membranes are damaged and therefore unable to function, and this causes an influx of sodium and potassium ions, resulting in increasing amounts of water entering the cell by osmosis. The initial result of this process is inflammation, also known as swelling, in the affected area.

Cell damage can be reversible, depending on the extent of injury, whether the damaging stress or stimulus can be removed, and the cellular response may be adaptive and therefore, homeostasis can be restored. However, damage can be irreversible and result in cell death, this happens when the severity of the injury is too much, and the cell is unable to repair itself.

Cell adaptations

Cellular adaptations are defined as changes made by a cell in response to environmental changes. Types of adaptations include: hyperplasia, hypertrophy, atrophy and metaplasia. The table below compares the different cellular adaptations.

Table 1.15: Cell responses to injury

Cellular adaptation	Response to injury
Hyperplasia	Cells increase in number as a result of increased mitosis.
Hypertrophy	Cells increase in cell size and volume, and if enough cells in an organ hypertrophy the whole organ will increase in size.
Atrophy	Cells decrease in size and if enough cells in an organ undergo atrophy the entire organ will decrease in size.
Metaplasia	Cells of a certain type are replaced by another type of cell which may be less differentiated.

Tissue response to injury

Swelling and bruising

The first response of soft tissue when an injury occurs is inflammation. Bruising within the tissues will be noticeable due to bleeding, this causes swelling and pain as the pressure increases. If inflammation doesn't decrease and blood and swelling is left in the injured area this can delay the natural healing process. A bruise is a type of hematoma (localised bleeding) of tissue. It is caused when capillaries are damaged due to trauma resulting in localised bleeding into the tissue.

Burst blood vessels

Blood vessels normally burst as a result of an injury. A small amount of blood escapes from blood vessels when they burst. This may be visible under the surface of the skin. It can appear as small dots called petechiae or in large flat patches called purpura.

Blood clotting and scab formation

Blood clotting also known as coagulation occurs to stop excess blood leaking from the body following a break in the surface of the skin. If a blood vessel (a capillary, vein or artery) is damaged bleeding occurs until a clot forms. If a blood clot does not form it will result in uncontrolled bleeding known as a haemorrhage. These can be life threatening.

Blood clotting occurs in a number of stages:

Stage 1:

- When the blood vessel wall is broken, thrombocytes (platelets) in the blood disintegrate and release an enzyme called thromboplastin.
- Thromboplastin converts a protein in the blood plasma called prothrombin into an active enzyme called thrombin. Calcium is needed for this process to work.
- The platelets become sticky and bind directly over the site of injury.

Stage 2:

- Thrombin changes another plasma protein called fibrinogen into fibrin.
- Fibrin is insoluble and forms a netlike covering across the damaged vessel.

Stage 3:

- As blood tries to flow through the net, red and white blood cells and platelets are trapped and form a clot. When the clot dries and hardens it forms a scab. Once the site of injury has healed, the blood clot will naturally dissolve.

Health consequences of tissue injury

Injury to cells and tissue can cause many different health consequences.

Ischemia

Ischemia is a vascular disease where there is restriction in blood supply to tissues, this leads to hypoxia (reduced oxygen) or anoxia (absence of oxygen) and results in lack of oxygen necessary for cellular respiration. Ischemia is caused by blockages in blood vessels which results in damage of tissues lining the vessels. If untreated it can lead to cell death. In extremely metabolically active tissues such as the brain, irreversible cell damage can occur after 3-4 minutes.

Pressure sores most commonly develop in people who are unable to move about and pressure is applied to soft tissue, causing ischemia. It is localized skin and soft tissue damage. The main way to prevent pressure sores is to redistribute the pressure by regularly moving or re-positioning.

Necrosis

Necrosis is a form of cellular injury, caused by factors external to the cell such as trauma or damage to blood vessels. The trauma causes unregulated digestion of cellular components and this results in the premature death of cells. Necrosis results in loss of cell membrane integrity resulting in uncontrolled release of products of cell death into extra cellular space.

Key points

Hypoxia – deficiency in the amount of oxygen reaching the tissues.

Anoxia – absence or severe deficiency in the amount of oxygen reaching the tissues.

Pause point

Do you now the four cellular adaptations and their response to injury?

Hint
Think about cell size.

Extend
Can you explain the result of cellular injury on ATP production?

A6 Diagnostic techniques

Diagnostic techniques can be used to determine whether a person's health is normal. Abnormal results of diagnostic tests can give medical professionals information to produce a diagnosis or can indicate that further tests may be needed. Diagnostic tests can involve taking a sample from the body. Common samples taken from the body are blood, urine and faeces. Other diagnostic tests involve taking measurements of an organ or body system. These include measurements of blood pressure, temperature and ECG (electrocardiogram) which measures the electrical activity of the heart. Measurements can be made manually (by a person) or can be automated (made by a machine).

Techniques to determine normal and abnormal function in humans

To check the health of a person, often the first tests carried out are the observation and measurement of vital signs. Vital signs include heart rate, blood pressure, respiratory rate and temperature. When a patient is in hospital, vital sign measurements or observations would be taken regularly, every few hours. They provide a baseline as records will show a patient's normal range. Changes away from the normal range can indicate deterioration or improvement in a patient's condition.

Key points

Vital signs – measurements of the body's most basic functions.

Heart rate

Heart rate or pulse rate is the number of heart beats per minute. The units are usually given as bpm (beats per minute). It can be taken manually by placing the first (index) finger and the middle finger of one hand on the inside of the wrist of the other hand. The fingers are pressed lightly until the pulse is felt. The number of beats per minute can be counted. It is important that pulse rate is taken when a person is resting. If they have been exercising or have exerted themselves, you should wait five minutes before taking their pulse. Most adults have a resting heart rate between 60-100bpm. A high heart rate is called tachycardia. A slow heart rate is called bradycardia. Heart rate can also be measured using a pulse oximeter or some types of blood pressure machine (sphygmomanometer).

Blood pressure

Blood pressure is a measure of the force that the heart creates to pump blood around the body. It is measured using millimetres of mercury (mmHg) and expressed using two figures. Normal blood pressure is typically 120 / 80 mmHg. This is read as "120 over 80".

- The top number (e.g., 120) represents the pressure in the main arteries created when the heart contracts. It is known as the systolic pressure.
- The bottom number (e.g., 80) represents the pressure that exists in the main arteries when the heart is relaxing. It is known as the diastolic pressure.

A device called a sphygmomanometer is used to measure blood pressure. The equipment used usually consists of a stethoscope, arm cuff, pump and dial. More modern devices are automatic and use sensors to measure blood pressure and display the results digitally.

Step-by-step: manual blood pressure measurement

Ensure that the patient is relaxed before taking the reading. The patient should sit upright with their upper arm positioned so that it is level with the upper chest. Ensure feet are flat on the floor and that there is no clothing restricting the blood flow to the arm.

- Wrap the blood pressure cuff around the patient's upper arm ensuring the tubing of the sphygmo manometer is connected to the gauge.
- Use the index and middle fingers to feel for the brachial pulse on the inner side of the patient's elbow and position the diaphragm of the stethoscope on this spot.
- Inflate the blood pressure cuff whilst reading the pressure gauge on the sphygmomanometer. Inflate the cuff until the gauge reads above the expected systolic pressure.
- When the cuff has inflated to above systolic pressure, use the stethoscope to listen to the brachial artery. Because the inflated cuff has squeezed the artery closed there will be no blood flowing in the artery and so no pulse sounds in the stethoscope.
- Use the air release valve to slowly deflate the cuff whilst listening for the return of pulse sounds in the brachial artery. When you hear the first pulse sounds as blood flow returns, record the reading on the gauge, this is the patient's systolic blood pressure.
- Continue to listen as the cuff deflates. Record the reading on the gauge at the point when pulse sounds can no longer be heard, this is the patient's diastolic blood pressure.

Automatic sphygmomanometers consist of a blood pressure cuff that is placed around one of the upper arms above the brachial artery. The cuff automatically inflates when a button is pressed, and the machine detects and displays the systolic and diastolic blood pressure measurement. The machine usually also displays the heart rate.

Ideal blood pressure is between 90 / 60 mmHg and 120 / 80 mmHg depending on age. High blood pressure (hypertension) is diagnosed with persistent pressures of 140 / 90 mmHg or higher. Repeated blood pressure readings taken over 24 hours are usually used to diagnose hypertension. A diagnosis would not be made based on a single measurement as other factors such as stress or anxiety can temporarily cause raised blood pressure. Low blood pressure (hypotension) is considered to be lower than 90 / 60 mmHg.

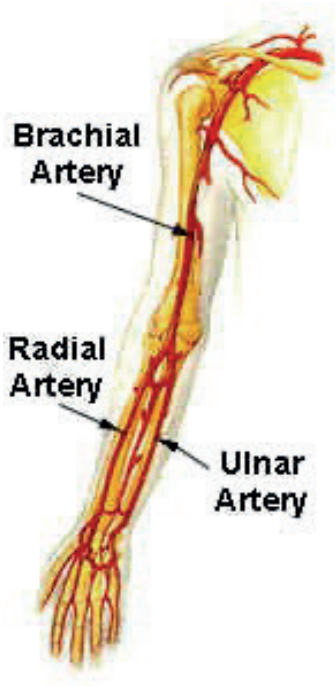


Figure 1.66: Location of the brachial artery used for blood pressure measurements

Respiratory rate

Respiratory rate (breathing rate) is the number of breaths taken per minute. The rate is measured when a person is at rest and simply involves counting the number of breaths taken in one minute by counting how many times the chest rises. The typical resting rate of a healthy adult is between 12 and 20 breathes per minute. Changes in the normal baseline respiratory rate can be an important indicator of a change in the person's health status. For example, fast, shallow breathing (tachypnoea) may indicate asthma, pulmonary embolism, pneumonia, cardiac failure, fever or anxiety. An abnormally slow respiratory rate (bradypnoea) could indicate brain injury, use of opioid drugs, carbon monoxide poisoning or alcohol intoxication.

Temperature

Temperature is taken using a thermometer or temperature probe usually placed under the tongue. Temperature can also be taken using a temperature probe inserted into the ear canal or rectum. Normal body temperature is between 36.5 °C - 37.5 °C but it is noted that elderly people often have a slightly lower body temperature. A body temperature above 37.5°C can indicate that a patient has fever, this usually a response to an infection which may require antibiotics or other medication. A low temperature, below 35°C can be a sign of hypothermia.

Tissue perfusion

If a patient is taken into hospital in an emergency situation, tissue perfusion tests can give medical professionals an indication of whether there is normal blood flow to different areas of the body. Perfusion refers to the flow of blood through blood vessels. Restricted blood flow to an extremity such as an arm, leg, hand or foot can be dangerous. Restricted blood flow can lead to damage and death of tissues which could result in necessary amputation.

Tissue perfusion is performed by applying pressure to the skin of the patient's limb using the thumbs. When doing this, the skin should turn white as blood flow to the area is restricted. You would then remove your thumbs to allow the blood to flow again. If the time taken for the colour to return to the site is longer than expected, then there may be problems with blood flow. Further tissue perfusion tests can be performed using ultrasound.

Blood oxygen saturation

Haemoglobin is the protein found in red blood cells (erythrocytes). The function of haemoglobin is to carry oxygen. Oxygen is needed by all of the tissues in the body for aerobic respiration. Each molecule of haemoglobin (Hb) has the capacity to bind four molecules of oxygen (O2) to form oxyhaemoglobin (HbO8). The oxygen saturation of the blood in the arteries can be measured using a pulse oximeter. A pulse oximeter is a small device that is clipped to the fingertip or ear lobe. The oximeter emits light which passes through the fingertip or ear lobe and is then detected by the other side of the oximeter. Blood oxygen saturation is expressed as a percentage with 100% being the maximum possible oxygen saturation. For someone who is healthy, normal blood oxygen saturation levels will be between 94 and 99%. If oxygen saturation is below this a patient may need oxygen treatment. A blood test to measure oxygen levels in arterial blood would be performed to confirm this. Low "sats" (oxygen saturation) can be an indication of a lung problem such as pneumonia.

Figure 1.67: A pulse oximeter measuring blood oxygen saturation

Electrocardiograms (ECG)

An electrocardiogram (ECG) measures the electrical activity of the heart. During the test, several sensors (electrodes) are attached to the skin of various parts of the body. Typically, the torso, arms and legs are used but different ECGs have different numbers and locations of electrodes. The electrodes detect tiny changes in electrical activity that have spread from the heart as it contracts and relaxes. The electrical signal is converted to a trace which can be seen on a screen or printed onto paper to be interpreted by a medical professional.

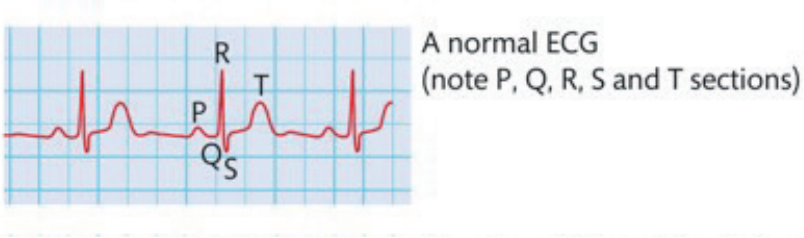


Figure 1.68: A normal ECG trace

A normal trace consists of a series of waves with a particular shape (Figure 1.68):

- P wave shows excitation of the atria when they contract and therefore represents atrial systole
- QRS complex shows excitation of the ventricles when they contract and therefore represents ventricular systole
- T wave represents diastole, when the heart chambers are relaxing.

ECGs can be used to detect different problems with the heart or its electrical system. Table 1.16 describes some common heart problems that can be detected by an ECG.

Table 1.16: Common heart problems that can be picked up by an ECG

Heart problem	Description	Indicative ECG trace
Bradycardia	Slow heart rate, under 60 beats per minute.	The trace has a normal shape with a normal P wave, QRS complex and T wave. The P waves have even spacing between them. but they are further away from each other than they should be.
Tachycardia	Fast heart rate, over 100 beats per minute.	The trace has a normal shape with a normal P wave, QRS complex and T wave. The P waves have even spacing between them, but they are closer together than they should be.
Arrhythmia	A variation in the rhythm of the heartbeat.	The trace has a normal shape with a normal P wave, QRS complex and T wave. The P waves have uneven spacing between them.
Coronary heart disease	A coronary artery supplying blood to the heart becomes blocked restricting the blood flow and oxygen supply to the heart muscle.	Stable coronary heart disease does not produce an abnormal resting ECG trace. However, an ECG performed during exercise can have small T waves. These can be seen on a resting trace of a person with severe coronary heart disease.

Table 1.16: Common heart problems that can be picked up by an ECG continued

Heart problem	Description	Indicative ECG trace
Myocardial infarction – also known as a heart attack.	Oxygen supply to the heart muscle is completely blocked. The heart muscle cannot contract.	The part of an ECG trace between S of the QRS complex and the T wave is called the ST segment. When a person is or has experienced a heart attack, this segment is elevated. The T wave may also be inverted.

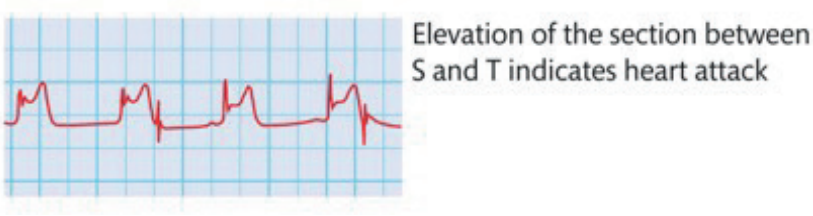


Figure 1.69: An ECG trace following a myocardial infarction. The trace shows an elevated ST segment

Use of ECG to calculate heart rate

One method of calculating heart rate from an ECG tracing is to look at the duration between consecutive waves e.g., between one R wave and the next. Count the number of large squares between two successive R waves and divide by 300 to obtain heart rate.

Reflex testing

Reflex arcs involve at least two neurons, an afferent (sensory) neurone and an efferent (motor) neuron. The afferent neurone carries information from a receptor to the central nervous system (CNS) while the efferent neurone transmits nerve impulses from the CNS to the effector. Medical professionals use reflex tests to investigate functioning of the patient's central and peripheral nervous system. A typical example of this test is the 'knee-jerk reflex test' in which a reflex hammer is used to deliver a sharp tap to the patellar tendon that attaches the kneecap (patella) to the shinbone (tibia). Tapping the tendon slightly stretches the quadriceps muscle which should result in contraction of the muscle and automatic 'kicking out' of the lower leg. A decreased or absent knee jerk reflex may mean that there is nerve compression or damage in the L2, L3, or L4 lumbar vertebrae. A similar test on the Achilles tendon indicates functioning of the S1 and S2 sacral nerves. Hyperreflexia is a condition in which the muscle will repeatedly contract when stimulated. Hyperreflexia usually indicates an interruption of corticospinal and other descending pathways that influence the reflex arc. Having no response to a reflex test is called hyporeflexia. Certain medical conditions including multiple sclerosis, diabetes, vitamin deficiency and certain cancers can lead to poor reflex reactions.

Step-by-step: testing the knee reflexes

1. Position the patient so that they are sitting on a chair with knees and lower leg hanging over the edge of the seat.
2. Locate the patellar tendon which is located just below the knee cap. The tendon feels like a tight strip of tissue under the surface of the skin.
3. Make sure the patient has relaxed their leg muscles and there is nothing obstructing movement of the lower leg.
4. Using a reflex hammer, lightly tap the tendon using one swift stroke.
5. Observe how long it takes for the lower leg to raise.

Key points

Hyperreflexia – overactive or overresponsive reflexes.

Hyporeflexia – absent or diminished reflex response. Nerve conduction tests

Nerve conduction tests

Nerve conduction tests are used to determine how well electrical impulses spread down nerves. They measure the speed of an impulse as it travels down a nerve. Nerve conduction tests are typically performed when it is suspected that a person has peripheral neuropathy. Peripheral neuropathy develops when the nerves in the hands, feet or arms are damaged. Damage can be caused by diabetes, physical injury, shingles, excessive alcohol consumption and some medication. During a nerve conduction test, a machine that emits a small electrical pulse is attached to the fingers or toes. An electrode which detects the electrical impulse is also placed at the wrist or ankle. The machine generates an electrical impulse which travels to the electrode. The time taken for the impulse to travel is recorded. The normal speed of conduction is between 50 – 60 metres per second (ms-1).

Pause point

Produce a reference table for a health professional that describes the different diagnostic techniques used when assessing patients.

Hint

Include the method of testing and an indication of normal and abnormal results.

Extend

Can you think of symptoms a patient may experience if their results indicate abnormalities?

Haematology

Haematology is the branch of medical science that involves the use of blood to diagnose and treat different disorders. Blood tests are routinely taken from patients as the first clue in helping to diagnose a disease.

Full blood counts

A full blood count or FBC is one of the most commonly performed tests. The test gives information about the different cells in the blood, including their characteristics and numbers. It is used to check for disorders including anaemia, infections and some cancers. Most full blood counts are performed by an automated machine in modern haematology laboratories. Machines can make multiple measurements reducing the chances of the result being affected by the sample size used. However, some abnormalities in blood cells may not be correctly identified by a machine and haematologists may need to review the sample manually using microscopes and other equipment.

FBC can be used to:

- count red blood cells
- count platelets
- measure mean corpuscular volume
- count white blood cells.

Table 1.17: Normal references ranges for full blood count

Test	Normal Range for Healthy Adult Male	Normal Range for Healthy Adult Female
Red blood cell count	4.7 to 6.1 million cells per µL of blood	4.2 to 5.4 million cells per µL of blood
Platelet count	150 to 450 x 109 per µL of blood	
Mean corpuscular volume	80 – 100 fL	
Haemoglobin test	14 – 18 g / dL	12 – 16 g / dL
Lymphocyte count	20-40% of total white blood cells	

Autoantibodies

Antibodies are produced by types of white blood cells called B lymphocytes as part of the body's normal immune response. Antibodies are produced in response to antigenic material found on pathogens such as bacteria or viruses. The immune system recognises these antigens as foreign material (non self) in the body and this triggers an immune response. The body cells of your own tissues have proteins on their cell surface membranes that also act as antigens. These are recognised as your own and do not normally trigger an immune response. There are regulatory mechanisms that prevent an immune response against your own body cells. Sometimes, these mechanisms fail, and antibodies are produced in response to a specific tissue in the body. This leads to destruction of the affected tissues which causes problems depending on which tissues are targeted. The antibodies are called autoantibodies.

Testing blood for the presence of autoantibodies is a way of diagnosing different autoimmune diseases such as:

- coeliac disease
- rheumatoid arthritis
- myasthenia gravis
- Graves' disease.

Real-life example: coeliac disease

Coeliac disease is a condition where the immune cells produce autoantibodies when a person eats gluten. Gluten is found in pasta, bread, cereals and cakes. Ingesting gluten causes diarrhoea, stomach-ache, bloating, indigestion and constipation. The production of autoantibodies causes damage to the surface of the intestines which can affect the absorption of the products of digestion. Coeliac disease can be diagnosed using a blood test which measures the presence of autoantibodies, particularly anti-tissue transglutaminase antibodies (tTGA) and endomysial antibodies (EMA). Before the test, the patient must eat a gluten-containing diet for six weeks. This ensures that autoantibodies would be present if the patient has coeliac disease. Diagnosis of coeliac disease is usually confirmed by taking a biopsy (sample of tissue) from the intestine. This is because some patients do not produce autoantibodies even though they suffer from coeliac disease.

C-reactive protein (CRP)

Proteins of the immune system include C-reactive protein (CRP) that is synthesised by the liver. C-reactive protein is released into the blood in response to infection, acute tissue inflammation, cancer or trauma. Raised blood concentrations of CRP can be found following events such as heart attack, sepsis, accidental trauma or surgical trauma. CRP levels can rise a thousand-fold in response to tissue inflammation and therefore, measuring blood CRP levels provides useful information which, when used in conjunction with other medical tests, can help doctors to diagnose and monitor inflammatory disease processes. Testing for C-reactive protein involves a simple blood test. Test results showing a concentration of CRP above 10mg/L indicate active inflammation, results below 10mg/L indicate that the patient has no clinically active inflammation.

Blood grouping

Key points

Blood group – refers to the antigens present or not present on the surface of red blood cells.

Blood transfusion – when blood, or it's components, from one person, are given to another person.

Donor – a person who donates blood or an organ to another person.

Recipient – a person who receives blood or an organ from another person.

There are many antigens attached to the cell membrane of red blood cells; three of these determine an individual's blood group as A, B, AB or O. Each group can be either rhesus D (RhD) positive or RhD negative. The rhesus factor is a protein antigen attached to the red blood cell, if this protein is present, the blood group is RhD positive, if it is absent, the blood group is RhD negative.

Sometimes it is necessary for patients to receive blood transfusions. A blood transfusion is when blood, or the components of blood from a person (the donor) is given to another person (the recipient).

A person might require a blood transfusion if they have:

- experienced trauma resulting in major blood loss, e.g., car accident
- experienced major blood loss due to surgery
- experienced major blood loss due to childbirth
- have a blood disorder such as sickle cell anaemia
- leukaemia.

In an emergency situation, where there is insufficient time to determine the recipient's blood group, group O rhesus D negative (RhD-) will be given to the patient. Blood group O RhD- is known as the universal donor. This is because the red blood cells of blood group O do not have any A, B or D antigens on their surface. This means that there is unlikely to be any transfusion reaction.

Receiving blood from the wrong ABO group can be life threatening. For example, if someone with group A blood is given group B blood, the recipients anti-B antibodies will attack the group B cells causing agglutination (clumping) of the red blood cells which could be fatal.

Table 1.18: The different blood groups and the antigens present or absent for each group

Blood Groups	Antigen on red cells	Antibodies in plasma	Compatible blood groups
A	A	Anti-B	A and O
B	B	Anti-A	B and O
AB	AB	None	All groups
O	None	Anti-A and Anti-B	O

Assessment activity 1.10

1. Describe the different tests that can be performed to measure a patient's vital signs including what the normal results should be.
2. Draw and label a normal ECG trace, include a description of what the different parts of the trace represent.
3. Explain how the blood test for coeliac disease works.
4. Describe the blood grouping system.
5. Explain why it is important that compatible blood be given to a patient requiring a blood transfusion.

B Immune response, dysfunction and treatment of immune disorders

B1 Immune response

Organisms that can cause disease are called pathogens. Pathogens can be bacteria, viruses, fungi or protozoa. Bacteria are small single-celled organisms that have no nucleus or membrane-bound organelles. Pathogenic bacteria are able to reproduce quickly in the body and give off toxins which can damage tissues, for example inflammation, which can appear as swelling, redness, and feel hot and painful. Viruses are acellular, they are not true cells, they contain nucleic acid surrounded by a protein coat. Viruses reproduce by entering the cells of other living organisms where they use the host cellular mechanisms to replicate. Newly created viruses are released from the host cell by causing the cell to break apart or by budding through the cell membrane. Fungi are eukaryotic organisms which produce a mycelium that can grow under the skin surface, invade tissues and disrupt their function. Protozoa are small, single-celled organisms that generally attach to the lining of the host's small intestine, where they prevent the host from fully absorbing nutrients.

Before organisms can cause disease, they must enter the body. Once they have entered the body, they can cause damage to cells. The immune system responds to pathogens to try and prevent disease from occurring.

The immune system can distinguish between body cells (self) and foreign materials (non-self). Body cells possess unique surface molecules that identify them as 'self' and, in normal health, the immune system will not react to the body's own cells. Pathogens are recognised as 'non-self' and instigate an immune response. There are many mechanisms that act to defend the body from pathogenic (disease-causing) organisms. The innate (non-specific) and the adaptive (specific) defence systems work independently and cooperatively to protect the body from pathogens.

Table 1.19: Transmission routes of various pathogens

Method of transmission	Examples
Direct contact – fomites are objects or substances that can carry infecting agents and transfer them from one person to another. They include computer keyboards, doo knobs, operating tables, towels, bedding, hair and money.	Many hospital acquired infections, such as MRSA and norovirus are transmitted by items of hospital equipment or health personal clothing. Viral infections such as colds and flu can be spread by hand shaking. Foodborne infections can be spread via preparation surfaces and utensils.
Body fluids	HIV/AIDS, Ebola, hepatitis B, CMV (cytomegalovirus).
Airborne	Measles, colds, influenza, anthrax, smallpox (eradicated but samples still exist), TB.
Foodborne	Bacillus cereus in rice, Salmonella, Campylobacter and E. coli food poisoning. Listeria, typhoid fever, cholera (shellfish), Creutzfeldt-Jakob disease, norovirus, hepatitis A, ergotism. Undercooked infected mean may contain work parasites or protoctists such as Entamoeba histolytica that causes amoebic dysentery. Cholera can also be spread by infected food.

Waterborne	Travellers' diarrhoea, cryptosporidium, dysentery, cholera, typhoid fever, hepatitis A. Parasitic infections such as schistosomiasis (bilharzia) can be acquired by swimming in infected water.
Vector borne	Malaria (protozoan spread via female Anopheles mosquitos), dengue fever (virus spread be female Aedes aegypti mosquitos), Lyme disease (bacteria spread by ticks), yellow fever (virus spread by Aedes mosquitos), bubonic plague (bacteria spread by fleas), sleeping sickness (protozoan spread by tsetse flies).
Transplacental	CMV, HIV, syphilis, gonorrhoea, Chlamydia, herpes simplex, human papilla virus, rubella, toxoplasmosis, hepatitis C, parvovirus.

Innate immunity

Innate immunity is present from birth and includes first line and second line defences.

First line defences – surface membranes and barriers:

- intact skin forms a mechanical barrier to prevent entry of pathogens
- skin secretions (sweat, sebum) make the epidermal surface acidic which inhibits bacterial growth
- intact mucous membranes form a mechanical barrier to prevent pathogens entering the body
- mucus traps microorganisms in respiratory and digestive tracts
- nasal hairs filter air and trap microorganisms
- cilia propel debris and mucus away from respiratory passages
- lacrimal secretions (tears) continuously lubricate and cleanse the eyes, contains lysozyme an enzyme that destroys microorganisms
- saliva lubricates and cleanses the mouth, contains lysozyme an enzyme that destroys microorganisms
- gastric juice contains hydrochloric acid and protein-digesting enzymes that destroy pathogens in the stomach
- urine is normally slightly acidic and this inhibits bacterial growth
- vaginal acidity inhibits growth of bacteria and fungi in the reproductive tract.

Second line (internal) defences – innate cellular and chemical defences.

The second line of defence is activated if the first line of defence is breached, for example if a pathogen is able to enter the body and cause tissue damage, then the body's secondary defences act to try and destroy it before it is able to reproduce and cause further damage e.g., the skin is broken.

Phagocytes

Phagocytes are a type of white blood cell that engulf and ingest pathogens, dead cells and other foreign materials that have entered the body. **Neutrophils** are the most common type of phagocyte. Neutrophils are released in large numbers when there is an infection. They carry out phagocytosis to destroy invading pathogens. They do this by having large numbers of lysosomes which contain digestive enzymes. Figure 1.70 demonstrates the process of phagocytosis and the role played by the lysosomes inside the neutrophils.

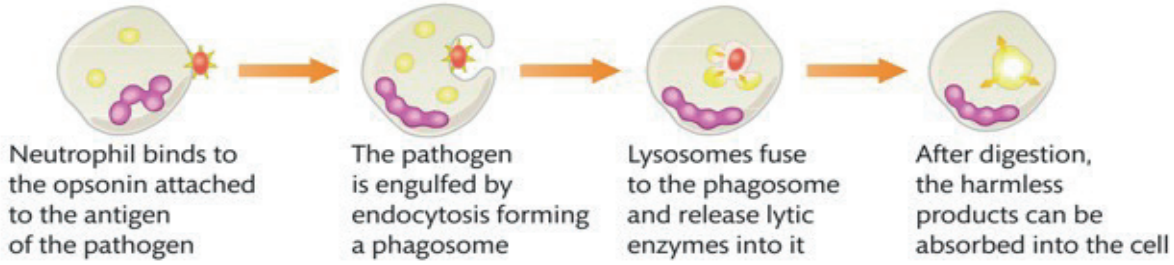


Figure 1.70: The process of phagocytosis

Macrophages are another type of phagocyte. These cells travel in the blood as immature cells called monocytes. When they reach lymph nodes, they mature into macrophages. Macrophages carry out phagocytosis but as a result also turn into antigen-presenting cells. When a macrophage engulfs a pathogen, it is not fully digested. The antigen from the pathogen is moved and placed on the cell surface membrane of the macrophage itself. This produces an antigen-presenting cell which displays the antigen so cells of the immune system can recognise it without the pathogen being allowed to reproduce and cause further damage to your body. It allows the adaptive (specific) immune response to be triggered. Table 1.15 describes some other biological defences present in the body.

Table 1.20: Biological defences in the body

Name of leukocyte	Function
Neutrophils	Respond to a breach in the skin by attaching to walls of blood vessels and preventing pathogens from entering the bloodstream. Carry out phagocytosis of engulfed pathogens.
Monocytes	Monocytes travel in the bloodstream and mature into macrophages when there is an active infection. Macrophages carry out phagocytosis of any type of dead cell in the body. This can be a dead cell that has been destroyed by a pathogen or a neutrophil that has carried out phagocytosis of a pathogen.
Eosinophils	Involved in combating allergies and parasitic worm infections. They move to inflamed areas and trap substances. Work by releasing enzymes from the granules in the cytoplasm to kill pathogens. High eosinophil counts are seen in allergic reactions. In some conditions, the cells move outside the bloodstream to build up organs and tissues.
Lymphocyte	Natural killer cells. Concentrated in the lymphatic system, B Cells (in bone marrow) and T Cells (in the thymus). Bind to antigens and help remove them from the body. Some B Cells become antibody cells other B Cells act as 'memory cells' for the immune system. T Cells are either cytotoxic (bind and kill infected cells and cancer cells); regulatory (control immune reactions) or memory cells (those that stimulate B cells into plasma cells).
Basophils	A type of white blood cell responsible for coordinating immune responses such as the release of heparin (to prevent blood clotting too quickly), and histamine causing vasodilation. Significant changes in the number of basophiles can contribute to anaphylaxis, asthma, dermatitis and hay fever.
Mast cells	First line of defence for the immune system due to its location in mucosal and epithelial tissues throughout the body, for example under the skin, in the surfaces of the gut and lungs and clustered along blood vessels. Detects microorganisms and foreign substances and initiates local inflammatory responses. Mast cells play an active role in parasitic infection and allergic reactions.

Adaptive immunity

The innate and adaptive immune systems work together to defend the body. Adaptive immunity is also known as acquired or specific immunity. Whilst the innate immune response is immediate, the adaptive response takes considerably more time to be effective.

The adaptive immune response refers to the production of long-term immunological memory against specific antigens. When B-lymphocytes divide, they differentiate into plasma cells which produce antibodies, also known as immunoglobulins, and B-memory cells, which are involved in the adaptive secondary immune response. When T-helper cells divide, they differentiate into T-killer cells, and T-memory cells. T-helper cells also activate B-cells.

B plasma cells are covered in proteins (antibodies) that bind to virus-specific antigens to form an antigen-antibody complex. There are circumstances when the B cell can be activated by T-independent antigens and respond to an antigen independently of a T cell. However, T dependant antigens can stimulate the B cell to become activated, but they have to bind with T helper cells to stimulate and secrete cytokines to respond to an antigen. In both situations, pathogens and abnormal cells are destroyed before they can cause illness. This explains why there are many diseases which are only usually caught once, e.g., measles, mumps, rubella.

B plasma cells secrete antigens for weeks after activation, circulating between the blood and the lymph on the lookout for antigens to bind to and destroy. B memory cells remain in the bone marrow, tonsils and spleen for many decades if necessary. T memory cells flow through the lymphatic system in the same manner as B cells but only have short-term life spans of months in comparison.

The adaptive immune system is usually very effective in protecting the body from a wide range of infectious agents and abnormal cells. However, when the system fails, the system can begin to attack 'self' cells and autoimmune diseases such as rheumatoid arthritis and lupus can develop.

Passive immunity

Passive immunity occurs after receiving antibodies that have been produced by another organism. There are two types of passive immunity:

- natural passive immunity – babies gain immunity through antibodies received from the mother through the placenta and from breast milk.
- artificial passive immunity – immunity gained after injection with antiserum containing antibodies produced by another person or animal. This provides immunity to a specific disease such as rabies.

Active immunity occurs when the immune system produces antibodies in response to an antigen. There are two types of active immunity:

- natural active immunity – the body produces antibodies in response to exposure to a pathogenic infection
- artificial active immunity – developed in response to the administration of a vaccine. Antigenic material (dead or weakened live pathogens or deactivated toxins) are injected to bring about an immune response. When the antigenic material is injected it stimulates the adaptive immune response. Memory B and memory T cells are produced which then remain in the blood for a number of years. If the actual antigen enters the body, the memory cells quickly become activated, divide and differentiate into the cells required to produce the appropriate response.

Antibodies

A different shaped antibody is produced for each different antigen. Figure 1.71 shows three ways in which antibodies work.

Antibodies can act as:

- Opsonins – bind to dangerous antigens so that they can be easily recognised by antibodies or complement receptors on phagocytic cells. This neutralises the pathogen and stimulates phagocytosis.
- Agglutinins – these antibodies bind to multiple antigens at once. This groups pathogens together, preventing them from spreading through the body and makes it easier for phagocytes to engulf a number of pathogens at the same.
- Anti-toxins – these antibodies bind to the toxins produced by pathogens. Toxins can be harmful and make you feel ill, anti-toxins neutralise the toxin, preventing it from working.

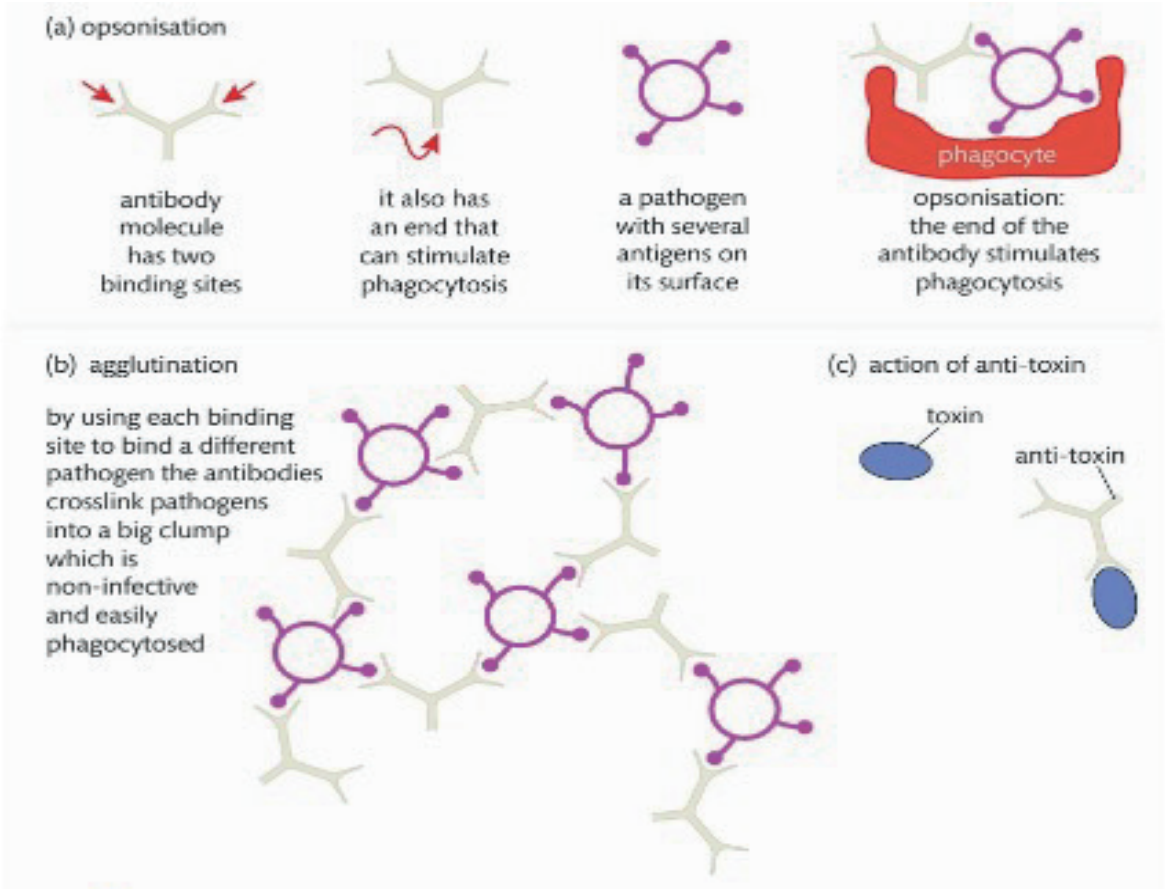


Figure 1.71: How antibodies work

Key points

Artificial immunity – immunity that is achieved through medical intervention, such as vaccines.

Natural immunity – immunity achieved through normal processes.

Passive immunity – immunity that is achieved when antibodies are passed to another through breastfeeding or injection.

Adaptive immunity – when the immune system is activated, and antibodies are produced.

B2 Immune dysfunction

Autoimmune diseases

Autoimmune diseases occur when the immune system malfunctions and attacks a part of the body. Autoimmune diseases occur when antibodies are produced against antigens on specific types of body tissue. This leads to damage and destruction of the tissue. Table 1.20 describes different autoimmune diseases, their cause, symptoms and treatment.

Table 1.2:1 Autoimmune diseases, causes, symptoms and treatments

Autoimmune disease	Description	Cause	Symptoms	Treatment
Diabetes mellitus (type 1)	Insulin is not produced resulting in high blood glucose levels (hyperglycaemia)	Antibodies are produced against beta cells in the Islets of Langerhans in the pancreas. These, insulin producing cells, are destroyed.	Increased thirst Frequent urination Fatigue Blurred vision Lack of concentration Unconsciousness Coma Death	Careful monitoring of blood glucose levels, Balanced diet and exercise. Regular injections of insulin
Multiple sclerosis (MS)	Condition affecting the brain and spinal cord	The immune system attacks the myelin sheath in the brain and spinal cord. The myelin sheath becomes inflamed and disrupts nerve transmission	Fatigue Difficulty walking Vision problems Loss of bladder control Numbness in the limbs Muscle stiffness Balance and coordination problems	Steroids Treatment or alleviation of the symptoms such as exercise, avoiding painkillers that cause fatigue and mobility aids.
Crohn's disease	Inflammation of the bowel	The immune system attacks the cells of the intestines	Diarrhoea Stomach aches Blood in the faeces Fatigue Weight loss	Steroids to reduce inflammation Liquid diet Medication to suppress the immune system Surgery to remove small sections of the bowel
Rheumatoid arthritis	Condition that causes pain, swelling and stiffness in the joints.	The immune system attacks the tissue that lines the joints. This tissue, the synovium, becomes sore and inflamed. Chemicals released by inflamed tissue causes further damage to the bones, cartilage, tendons and ligaments of the joint.	Pain Stiffness Swelling Inflammation Tiredness Weight loss	Tablets can be taken to reduce the effects of the chemicals released during inflammation Pain killers Non-steroidal anti-inflammatory drugs Steroids Physiotherapy

Primary and secondary immunodeficiency diseases

Immunodeficiency diseases result from the impairment of the immune system. Primary immunodeficiency diseases are caused by inherited genetic defects. Secondary immunodeficiency diseases are caused by environmental factors such as pathogens.

Severe combined immunodeficiency disease (SCID)

Severe combined immunodeficiency disease (SCID) is a very rare but very serious immune disease. It can be caused by mutations in several different genes that are inherited from a parent. SCID is an example of a primary immune disease. The most common type of SCID is caused by a mutation which is inherited on the X chromosome. Mutations result in the malfunction of a protein which is required for normal immune system development. SCID is usually diagnosed in the first year of life, a child with SCID will have very few T cells and reduced numbers of B cells. The result of this are symptoms including frequent infections such as coughs and colds, persistent thrush of the mouth and / or nappy area, poor feeding, chronic diarrhoea and failure to gain weight (failure to thrive). Without treatment SCID is usually fatal before the age of 1. Children diagnosed with SCID must be kept away from sources of infection as much as possible. Often, they will need to stay in hospital in air-filtered rooms away from other children and with restricted adult visitors. Antibiotic, antiviral and antifungal medication can be given to help prevent infection. The child may also receive antibody treatment and blood transfusions. All of these treatments aim to prevent infections which with reduced numbers of T or B cell, would be potentially fatal. There are also potential cures for SCID, including stem cell transplantation. During stem cell transplantation, stem cells are obtained from healthy bone marrow of a donor and given by transfusion into the vein of a child with SCID.

HIV

HIV (Human Immunodeficiency Virus) damages the cells in the immune system and impairs the body's ability to fight everyday infections. HIV can be transmitted through unprotected sex, sharing infected needles or from mother to baby during pregnancy, childbirth or breast feeding. The virus infects and destroys a type of T lymphocyte called T CD4 cells. It is an example of a secondary immune disease. Most people who have HIV, develop symptoms similar to flu around 2 to 6 weeks after infection. Symptoms include increased temperature (fever), sore throat, tiredness, muscle pain and a rash. Symptoms usually last for 2 weeks but then disappear. An infected person may not experience any further symptoms for up to 10 years despite having an active viral infection. Over time, more and more CD4 cells are destroyed and the person's ability to fight off other infections decreases. A person with HIV will have regular blood tests to measure their CD4 counts. When the CD4 count falls below 400 per microliter of blood, the person is diagnosed with AIDS. AIDS stands for Acquired Immunodeficiency Syndrome and is used to describe the point in HIV infection where the immune system is no longer able to defend against usually minor infections. Once the immune system has become damaged, a patient may experience weight loss, night sweats, skin problems and recurrent infections. Patients may begin to develop opportunistic infections such as tuberculosis, thrush, chronic diarrhoea and meningitis. To slow down the progression of HIV and avoid the development of AIDS for as long as possible, patients are prescribed antiretroviral medication. Antiretroviral medication stops the virus from replicating in the body. Over time one antiretroviral drug will stop working as HIV develops resistance. For this reason, patients are given a combination of different drugs and closely monitored so that the medication can be changed if there are signs of resistance developing.

Immunodeficiency due to chemotherapy

Chemotherapy is a type of cancer treatment where medication is given to a patient to kill cancer cells. There are lots of different types of medication that can be used to treat a range of different types of cancer. Chemotherapy is usually given intravenously (into a vein) or as a tablet. Chemotherapy does however have side effects including tiredness, feeling sick and vomiting, hair loss and dry skin. Chemotherapy also causes immunodeficiency which can lead to more frequent infections such as coughs and colds. Chemotherapy directly damages the bone marrow. The bone marrow is a source of stem cells which differentiate into white blood cells. So, a patient undergoing chemotherapy may produce less

white blood cells leading to reduced immune function. Patients are advised to avoid contact with people with infections and can be given antibiotics, antivirals and antifungals if required.

Immunodeficiency due to organ transplants

Organ transplants are when a recipient receives an organ from another person, the donor. The purpose of an organ transplant is to replace an organ that has severely reduced or no function. Organs can sometimes come from living donors, e.g., kidney or liver but can also come from deceased donors, e.g., heart, lung and pancreas. Rejection of the transplanted organ can occur when the immune system detects non-self-antigens on the transplanted organ tissue. Doctors try to avoid this as much as possible by ensuring that transplanted organs are a tissue match for the recipient, but even then, there is still a chance of the organ being rejected. Rejection triggers a response which will result in damage and destruction of the transplanted organ. Immunosuppressant medication is also given to the recipient to minimise the risk of rejection. Immunosuppressant medication is non-specific in that it reduces the function of the whole immune system. This can make the recipient more vulnerable to infections and cause other side effects such as high blood pressure, reduced kidney function, diabetes mellitus and increased risk of cancer. People taking immunosuppressant medications must take them for the rest of the life of the transplanted organ. Due to the immunodeficiency caused, those taking immunosuppressant drugs are advised to avoid contact with people with infections and can be given antibiotics, antivirals and antifungals if required.

Allergies and Allergens

An allergy is an abnormal reaction to a particular food or substance. The substance causing the allergy is known as an allergen. The allergen triggers an immune response in a person which would not normally take place. This can be a nuisance e.g., hay fever or can be more severe e.g., anaphylaxis. It is not known why some people's immune system reacts to usually non-harmful substances but the number of people suffering from allergies in the UK is increasing year by year. Table 1.22 describes three examples of allergies.

Table 1.22: Allergies, cause, symptoms and treatments

Allergy	Description	Cause	Symptoms	Treatment
Allergy-induced asthma	Chronic disease that affects the airways. The smooth muscle in the trachea, bronchi and bronchioles becomes inflamed in response to an allergen and the lumen of the airways is reduced	Pollen Dust mites Pet fur and dander	Tightness in the chest Difficulty breathing Wheezing Coughing Itchy and watery eyes Sneezing Runny nose	To treat the symptoms of asthma patients are usually given an inhaler which contains muscle relaxant to widen the airways. A daily tablet can be taken to reduce immune function and prevent inflammation Immunotherapy against the antibodies produced can also be given in severe cases

Anaphylaxis	A severe allergic reaction that occurs rapidly and if not treated can cause death	Food including nuts, milk, eggs and shellfish Medications including antibiotics and aspirin Bee and wasp stings Latex found in some rubber gloves and condoms	Feeling lightheaded or faint Breathing difficulties Wheezing Fast heart rate Confusion Losing consciousness	People who have awareness of a severe allergy must avoid the allergen. They may also carry an adrenaline pen (epi-pen) which can be used to inject adrenaline in the case of an anaphylactic reaction. If anaphylaxis is suspected, you should call 999. Oxygen therapy, anti-histamine medication and adrenaline may then be given by a health professional.
Dermatitis	A type of eczema that is triggered by skin contact with an allergen	An irritant, such as soap or detergent. that damages the outer layer of skin. An allergen that causes an immune response such as cosmetics, metals in jewellery, latex and clothing	Skin becomes itchy, blistered, dry and cracked.	The best way to treat dermatitis is to avoid the trigger that is known to cause it. Skin emollients (skin oils or creams) for dry skin can also help Topical corticosteroid creams or steroid tablets can also be prescribed by a doctor

Key points

Immunosuppressant – medication which reduces the activity of the immune system.

Allergy – an abnormal reaction to a substance which does not typically cause an immune response.

Allergen – the substance that causes an allergy, e.g., pollen.

Assessment activity 1.11

1. Describe the body's innate defences against disease.
2. Explain why these defences are known as non-specific defences.
3. Describe the adaptive primary immune response.
4. Describe the adaptive secondary immune response.
5. Explain why these responses are known as the specific defences.
6. Describe the different ways that immunodeficiency can occur and explain the impact on health.

C Genetics and health

C1 Genetic expression

Scientists use genetics to understand inheritance of characteristics, diseases and genetic conditions in order to understand the processes in involved you need to know about the structure of nucleic acids (DNA and RNA), and how these are involved in protein synthesis and gene expression.

Nucleic acids

Nucleic acids are universal. They occur in all living organisms on earth, they are large molecules that are found inside the nucleus of a cell. Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA) are both **polymers**. The monomers are **nucleotides**. They are responsible for storing genetic information and for the synthesis of proteins. It is this code that is stored in DNA and which provides instructions for cells to build the polypeptides which make the structure and carry out most of the functions of the bodv.

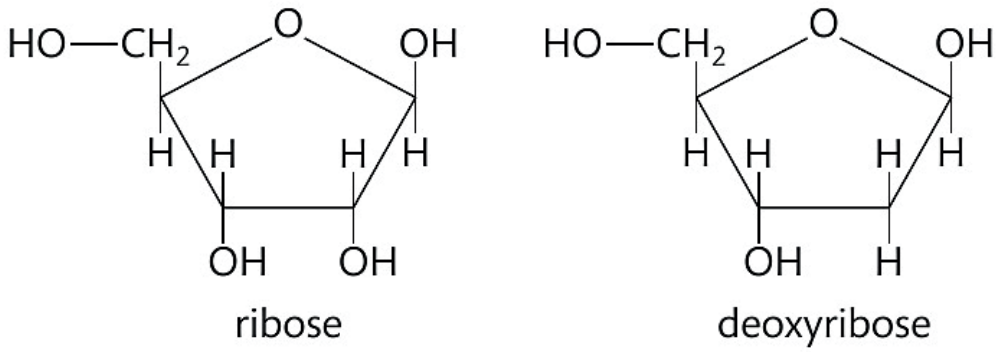


Figure 1.72: Ribose and deoxyribose sugars

Nucleotides

A **nucleotide** consists of three components:

- Pentose monosaccharide (5 carbon sugar)
- A phosphate group
- A nitrogenous base.

A **condensation reaction** occurs between the hydroxyl functional group (-OH) of the sugar and the hydrogen atom of an –OH from the phosphate, so water is expelled. The nitrogenous base also undergoes a condensation reaction with the hydroxyl functional group of carbon 1 on the sugar reacting with a hydrogen atom on the base.

Key points

Nucleotide – a nucleotide consists of a pentose (5-carbon) sugar, a phosphate and a nitrogenous base (adenine, thymine, cytosine, guanine or uracil). Nucleotides are the monomers of nucleic acids.

Polymers – large molecules consisting of repeating smaller subunits called monomers.

Condensation reaction – chemical reaction where two molecules are joined, with the elimination of water.

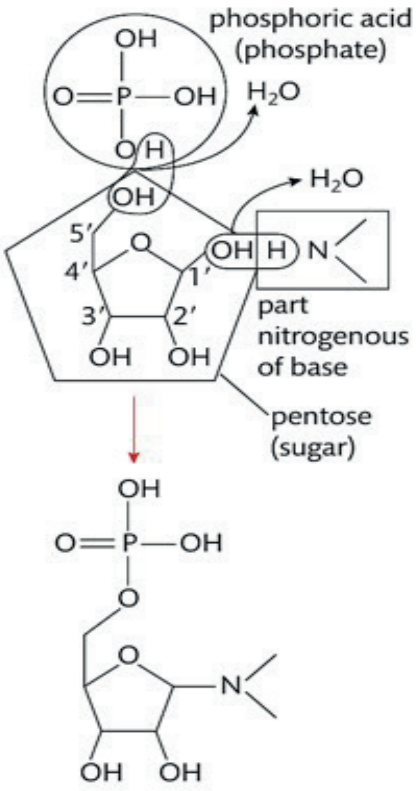


Figure 1.73: Formation of a nucleotide

The five organic nitrogenous bases (Figure 1.74) that make up the structure of nucleotides all contain carbon, hydrogen, oxygen and nitrogen. They are:

- adenine (A),
- thymine (T),
- guanine (G),
- cytosine (C)
- uracil (U).

Thymine is found only in DNA and uracil is found only in RNA. Adenine and Guanine nitrogenous bases are called purines, they consist of a double ring structure. Thymine, Cytosine and Uracil nitrogenous bases are pyrimidines, they consist of a simple ring structure.

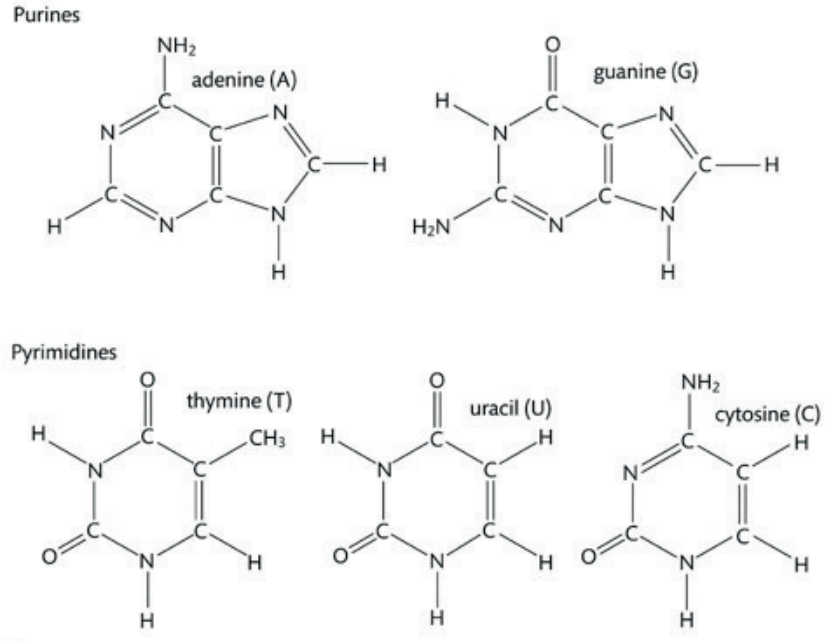


Figure 1.74: The five organic nitrogenous bases: adenine, guanine, thymine, cytosine and uracil

Many nucleotides joined together make a polynucleotide. The phosphate group from one nucleotide forms a covalent bond with the hydroxyl (OH) group attached to the carbon 3 of the next nucleotide. The bonds formed are called phosphodiester bonds. They produce a very strong sugar-phosphate backbone. Note that the nitrogenous bases do not take part in polymerisation and they extend out from the polynucleotide structure.

Key points

Polymerisation – the chemical process that combines many monomers to form a polymer.

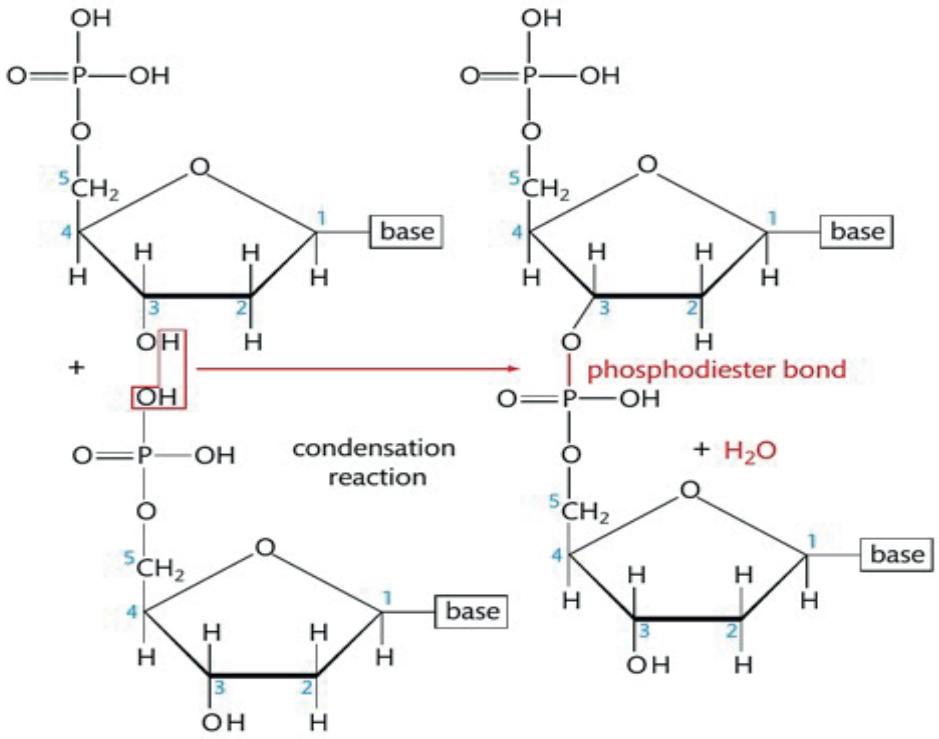


Figure 1.75: Nucleotide polymerisation

DNA is a double helix

DNA is a double stranded polynucleotide. Its individual nucleotides contain deoxyribsose sugar and nitrogenous bases A, T, C and G. Specific types of viruses contain either DNA or RNA, surrounded by a protein coat.

In prokaryotic cells (bacteria), their DNA is found as one circular chromosome lying freely in cytoplasm. They also have some smaller loops of DNA, called **plasmids**. In eukaryotic cells, DNA is mostly organised into chromosomes which also have **histone proteins** associated with that DNA.

Each DNA molecule consists of the following:

- two polynucleotides chains alongside each other. The sugars in the polynucleotide chains run in opposite directions so the two chains are described as antiparallel. The two strands are joined together because hydrogen bonds form between the nitrogenous bases. The bases form base pairs, two hydrogen bonds form between the bases A and T and three hydrogen bonds form between the bases C and G. This is known as complimentary base pairing. The two strands form a double helix (see Figure 1.76) as they twist around each other. It is within this double-stranded polynucleotide chain that genetic information is stored. DNA stores the genetic code that is used to build organisms and to produce essential proteins.
- The hydrogen bonds make each molecule of DNA very strong and stable, whilst enabling it to unzip in order to copy itself before cell division, or allowing part of it (a gene) to unzip before being used as a template to make messenger RNA before the assembly of a new protein.
- The sequence of base pairs forms the coded information, and this is protected from corruption by these base pairs being inside the sugar-phosphate backbones.

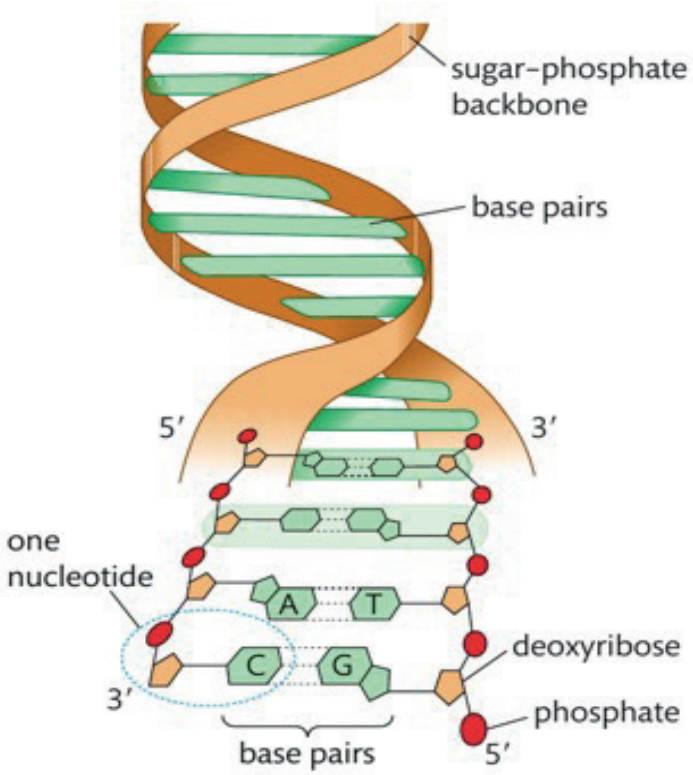


Figure 1.76: DNA Double Helix. The antiparallel chains, with base pairs, are twisted into a helix. The directions 3′ ND 5′ relate to the position of the carbon atoms on the sugars

Key points

Plasmids – small circular piece of DNA found in prokaryotic cells.

Histone proteins – proteins in the nucleus of eukaryotic cells, around which the DNA is wound.

Differences between RNA and DNA

RNA is structurally different from DNA. In RNA:

- the pentose sugar is ribose
- the nitrogenous bases present are A, U, C and G (there is no thymine) the polynucleotide chain is usually single-stranded, not double-stranded.

In DNA:

- the pentose sugar is deoxyribose
- the nitrogenous bases present are A, T, C and G
- the polynucleotide chain is almost always double-stranded.

In eukaryotic cells:

- RNA occurs in the nucleus (including the nucleolus) and cytoplasm, as well as in ribosomes
- DNA occurs in the nucleus, chloroplasts and mitochondria.

There is more than one type of RNA.

- Messenger RNA (mRNA) is a short, single stranded molecule containing A, U, C and G held together by a sugar-phosphate backbone. It carries the genetic code of a gene from the nucleus to ribosomes where the code is read and used as instructions to assemble amino acids to synthesise proteins.
- Transfer RNAs (tRNA) is also single stranded and is only about 80 nucleotides long. tRNA (see Figure 1.74) has two very important regions called the anticodon and a region where a specific amino acid attaches. Each tRNA contains three unpaired nucleotide bases at one end where the amino acid joins, this is 'anticodon.' Anticodons allow tRNA to bring the correct amino acid in line with an mRNA during protein production. The sequence of these three bases determines which amino acid joins the tRNA molecule.

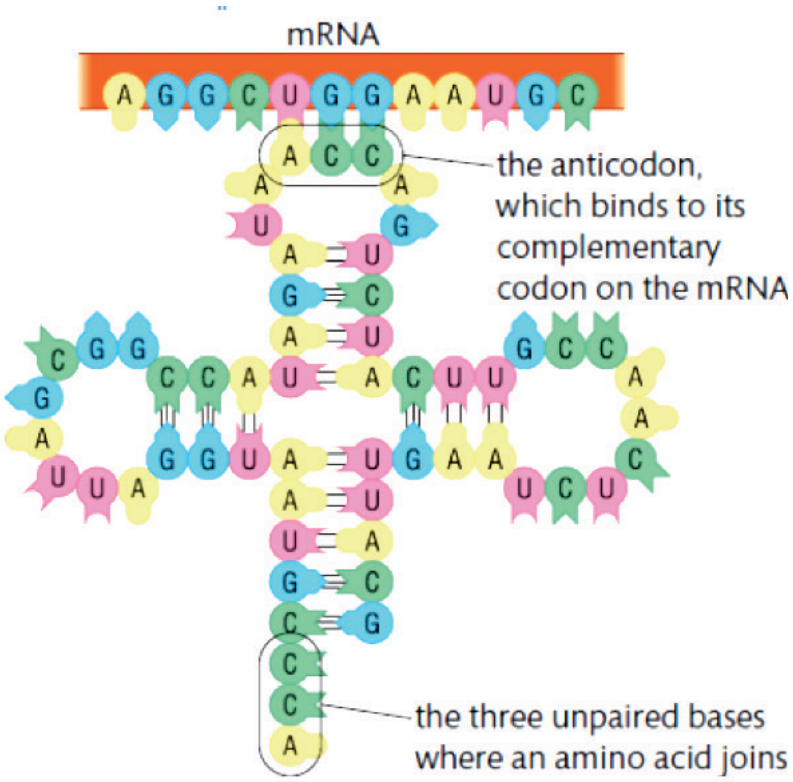


Figure 1.77: A tRNA molecule bonding temporarily to a codon on a section of an mRNA

Pause point

Can you describe the structure of mononucleotides and polynucleotides?

Hint

Draw and label the structure of both mononucleotides and polynucleotides.

Extend

Compare RNA and DNA, produce a table of comparison.

DNA replication

Before a cell divides each DNA, molecule replicates, during a part of the cell cycle known as the S phase of **interphase.**

- The DNA double helix unwinds and the hydrogen bonds between complementary base pairs break. This is catalysed by the enzyme helicase.
- This exposes the nucleotide bases.
- Free DNA nucleotides within the nucleoplasm of the nucleus, bind onto the exposed nucleotide bases, following complementary base-pairing rules, A bonds with T and C bonds with G. This is catalysed by the enzyme DNA polymerase.
- Covalent bonds form between the sugar of one nucleotide and the phosphate group of the adjacent nucleotide, forming the new backbones. This is catalysed by the enzyme ligase.

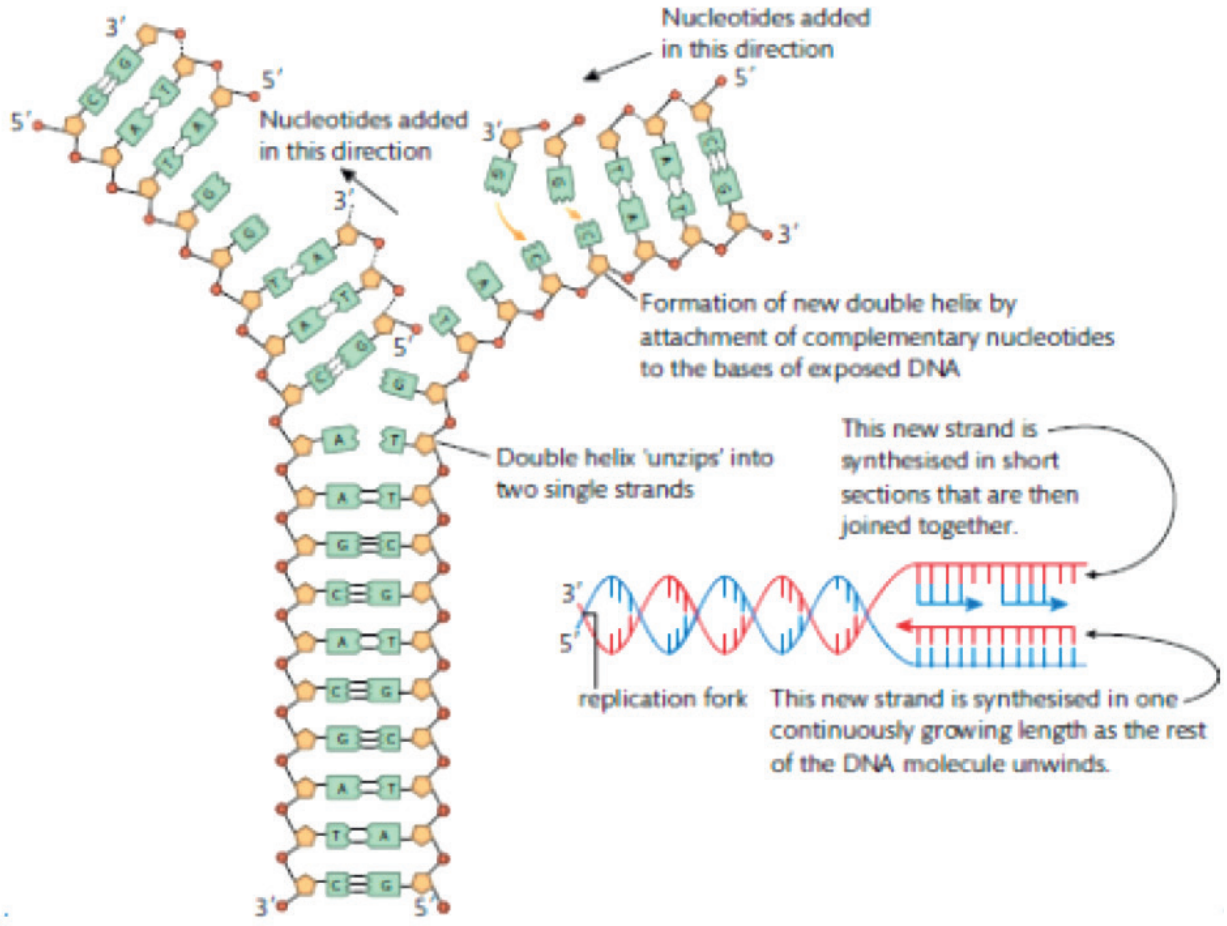


Figure 1.78: How DNA replicates. The addition of the new DNA nucleotides is catalysed by the enzyme DNA polymerase.

At the end of replication, two new molecules of DNA, both identical to each other and to the parent molecule, are made. Each new molecule contains one old strand and one new strand, so this type of replication is called **semi-conservative replication**.

Key points

Interphase – the phase of the cell cycle in which most cells spend most of their time. They synthe-sise molecules, grow and the organelles and DNA replicate prior to mitosis.

Semi conservative replication – mode of replication where two new molecules are formed, each identical to the other and to the parent molecules and each consisting of one old strand and one new strand of DNA.

Pause point

Explain why the replication of DNA is described as 'semi-conservative'.

Hint
Think about how DNA replicates.

Extend
A mutation is a change to the base sequence of DNA. When during the cell cycle is it likely to hap-pen?

The genetic code

Genes exist on chromosomes; they are specific lengths of DNA. Genes carry the code for making proteins needed in the body, some of which are **transcription factors** that activate or suppress the expression of other genes.

You were introduced to the proteins structure earlier in this unit, proteins are polymers of amino acids. Their **primary structure** determines their **secondary structure** and finally folds into its tertiary structure. The **tertiary structure** (3D shape) is crucial for a protein to carry out its task. If the primary structure of the protein is wrong, then the tertiary structure will be wrong, and the protein will not function well or may not function at all.

Key points

Gene – length of DNA that codes for one (or more) proteins/polypeptides or codes for one (or more) length(s) of RNA that may regulate the expression of another gene/other genes.

Transcription factors – proteins that activate or suppress the expression of genes.

Primary structure of a protein – the sequence of amino acids within the protein chain.

Tertiary structures of a protein – the 3D shape of a protein, caused by its folding.

Triplet codes

The sequence of nucleotide bases on the DNA strand provides the instructions for the sequence of amino acids in the protein chain. In fact, each three-base section corresponds to one specific amino acid. This is called the triplet code.

First position	Second position T	Second position C	Second position A	Second position G	Third position
T	Phe	Ser	Tyr	Cys	T
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	T
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	T
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	T
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Key:

- Asp Aspartic acid
- Glu Glutamic acid
- His Histidine
- Ile Isoleucine
- Arg Arginine
- Thr Threonine
- Ser Serine
- Lys Lysine
- Gly Glycine
- Asn Asparagine
- Gln Glutamine
- Trp Tryptophan
- Tyr Tyrosine
- Ala Alanine
- Cys Cysteine
- Phe Phenylalanine
- Leu Leucine
- Met Methionine
- Pro Proline
- Val Valine

Figure 1.79: The DNA triplet codes and corresponding amino acids. Three base triplets do not act for an amino acid but act as stop codes.

Degenerate code

There are 20 amino acids involved in protein synthesis. So at least 20 different base triplets are needed to code for these amino acids. However, there must also be one or more triplets that signal 'stop' and cause termination of the building of the protein or length of RNA. Because the four DNA bases are read in triplets, there are 43 = 64 different combinations which is more than enough to code for the 20 amino acids and for the other instructions. In fact, most amino acids have more than one base triplet code. The genetic code is said to be degenerate because for all amino acids except methionine and tryptophan, there is more than one base triplet. This may reduce the effect of **point mutations**, because a change of one base triplet could produce another base triplet that still codes for the same amino acid.

The genetic code is also non-overlapping, which means it is read from a fixed point in groups of three bases (triplets) that occur one after another, they do not overlap. If a base mutation was to occur in which a base was added or deleted (rather than just substituted) it would cause a frame shift of every base triplet after the mutation. This would mean that every amino acid coded for by parts of the DNA after the mutation would change.

Key points

Point mutation – change in base sequence of DNA cause by a substitution of one base for another, e.g., CGA becomes CCA.

Codons

DNA is in the cell nucleus but proteins are assembled at ribosomes in the cell cytoplasm. The genetic code therefore has to be copied and carried out of the nucleus to the ribosomes. This process is called transcription and a length of messenger RNA (mRNA) is produced that corresponds to the coding strand of the gene (length of DNA). The base triplets on the mRNA are called codons. Each is a copy of the base triplet on the DNA coding strand but in place of the base thymine there is the base uracil.

Anticodons

When the mRNA has passed out through a pore in the nuclear envelope and arrived at a ribosome, amino acids are brought by tRNA molecules. Each of these tRNA molecules is specific to a particular amino acid and also has a triplet of bases, called an anticodon, complementary to the mRNA codon (see Figure 1.14 on page 118).

Protein synthesis

The assembly of amino acids into proteins is known as Protein synthesis. There are two main stages:

- transcription
- translation.

Transcription of DNA and RNA

During this process the instructions on the coding strand of the length of DNA are copied on to a messenger molecule – a length of mRNA. Transcription occurs in the cell nucleus in eukaryotes.

1. The gene (length of DNA) unwinds and unzips as the hydrogen bonds between the nitrogenous bases break due to the action of the enzyme RNA polymerase.
2. This exposes the bases of the DNA nucleotides that make up the gene. This is now a template strand
3. Free RNA nucleotides line up along the template strand of the DNA and make temporary hydrogen bonds with their complementary bases. Adenine, from an RNA nucleotide, pairs with thymine on the DNA template strand. Uracil from an RNA nucleotide pairs with the base adenine on the DNA template strand. The enzyme RNA polymerase catalyses these reactions.
4. Sugars and phosphate groups of adjacent RNA nucleotides bond together.
5. This forms a single polynucleotide chain of RNA that is complementary to the DNA template strand of the gene. It is therefore a copy of the coding strand of the gene.
6. Each codon on the mRNA codes for a specific amino acid.
7. The mRNA can now break away from the gene, and the original DNA strands winds up to form double-stranded DNA again.

Before this can act as mRNA during the next stage of protein synthesis (translation), it has to be edited. Therefore, the mRNA is known as pre-mRNA at this stage.

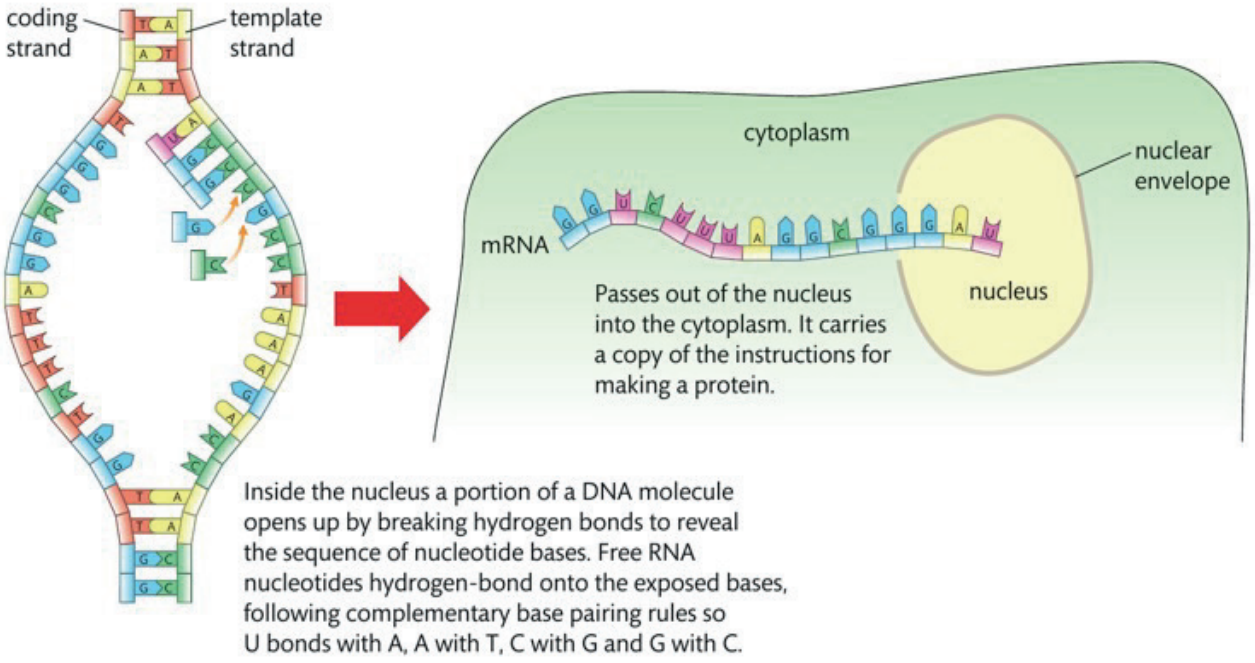


Figure 1.80: Transcription of a gene

Introns, exons and splicing

Within genes there are non-coding regions of DNA called introns. Introns are portions of a gene that do not code for amino acids – they are not expressed. The coding or expressed regions of the gene, which are called exons are separated from the introns.

1. All the DNA of a gene, both introns and exons are transcribed, and the resulting mRNA is called pre-mRNA.
2. This pre-mRNA is then edited. The RNA introns (lengths corresponding to the DNA introns) are removed and the remaining mRNA exons are joined together. The process of joining is known as splicing.
3. Endonuclease enzymes may be involved in the editing and splicing processes.
4. Some introns may become short, g+
5. non-coding lengths of RNA involved in gene regulation.
6. Genes can be spliced in different ways so that a length of DNA with its introns and exons can encode more than one protein.

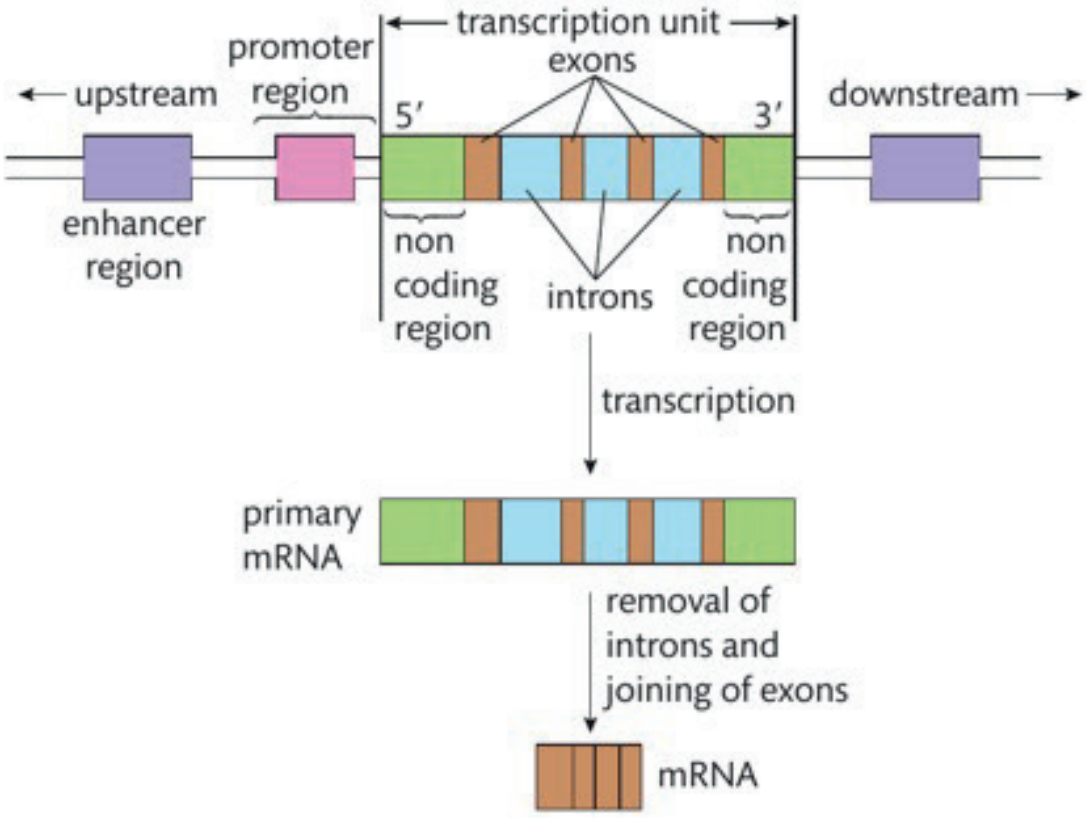


Figure 1.81: Removal of introns and joining exons during splicing and pre-mRNA to produce mRNA that will be translated into a protein

Translation of RNA

Transfer RNA molecules

Transfer RNA molecules (tRNAs) made in the nucleolus pass out of the nucleus into the cytoplasm. Each is a single stranded polynucleotide but can twist into hairpin shapes. At one end is a triplet of nucleotide bases that recognises and attaches to a specific amino acid. At the loop of the hairpin is another triplet of bases called an anticodon that is complementary to a specific codon on the mRNA.

Translation at the ribosome

Ribosomes catalyse the synthesis of polypeptides (proteins). Ribosomes are made of two subunits (a larger and a smaller) that are made within the nucleus and pass out into the cytoplasm where they join together.

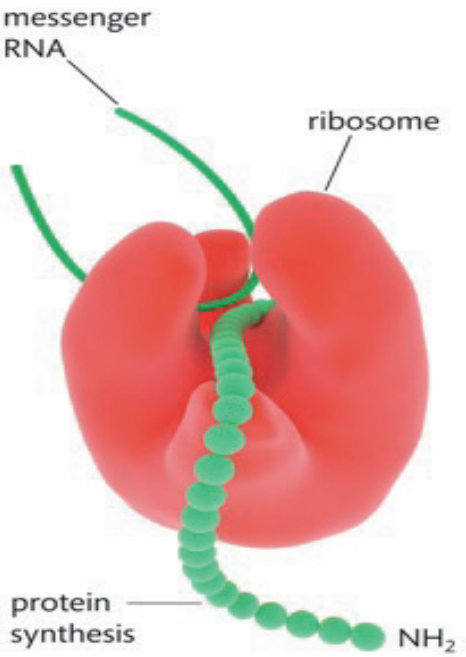


Figure 1.82: Translation at the ribosome

Stages of translation at a ribosome

1. The mRNA molecule binds to a ribosome so that two of its codons are attached to the small ribosomal subunit.
2. AUG is always the first exposed codon. A tRNA molecule with the corresponding anticodon, UAC, with the amino acid methionine attached, forms hydrogen bonds with this AUG codon. ATP is needed for this reaction to happen.
3. A second tRNA molecule, complementary to the second codon, brings the next amino acid coded for and binds to the second codon.
4. Now two amino acids are side by side so a peptide bond forms between them.
5. The ribosome moves along the mRNA exposing the codons to the sub-unit.
6. tRNA continues to bind to the codons, bringing corresponding amino acids. The first tRNA molecule leaves and is free to collect and bring another amino acid of the same type to the ribosome.
7. This continues until an mRNA codon that does not code for an amino acid is reached. This codon is effectively a stop codon.
8. The chain of amino acids leaves the ribosome and can be modified into its functioning form.

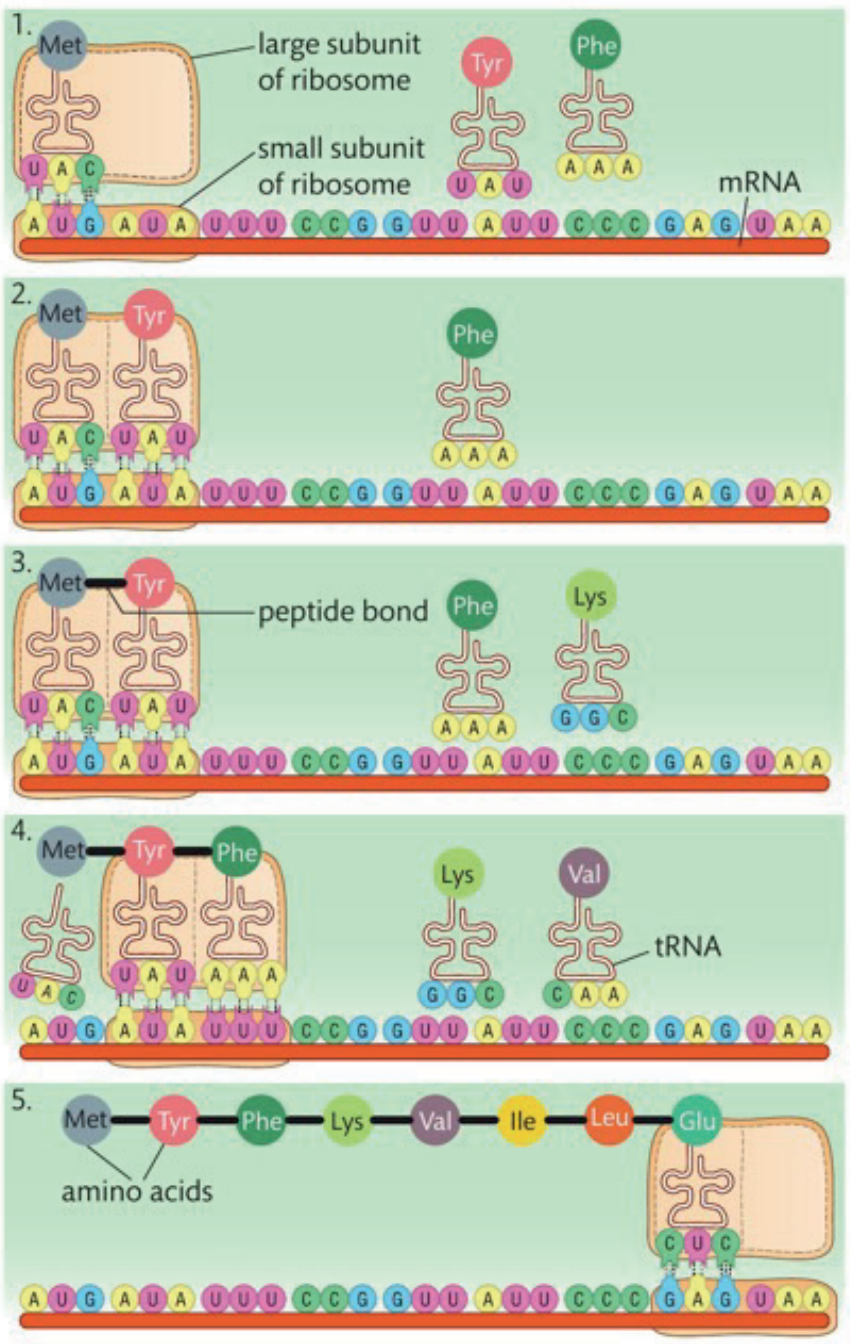


Figure 1.83: Translation – stages of assembly of a protein at a ribosome

Pause point

Make a table to compare transcription with DNA replication.

Hint

Remember to look at ways in which the two are similar and also how they differ.

Extend

Explain the difference between transcription and translation.

Genetic mutations

Errors may occur during the replication of a DNA molecule, despite the structure of the DNA molecule making it stable.

- Mutations associated with DNA replication prior to mitotic division are somatic mutations and are not passed to offspring. However, they may be associated with the development of cancerous tumours.
- Mutations associated with DNA replication prior to meiosis and gamete formation may be inherited by offspring.

There are three main classes of DNA mutations.

- Point mutations, in which one base pair replaces (is substituted for) another.
- Insertion or deletion (indel) mutations, where one or more nucleotide pairs are inserted or deleted from a length of DNA. These may cause a frameshift where every base triplet after the insertion or deletion is altered.
- Expanding triple nucleotide repeats, where a base triplet is repeated many more times.

Point mutations

The table below lists the three types of point mutation.

Table 1:23: Point mutations

Point mutation	Effect on structure of protein
Silent	Most amino acids have more than one triplet of bases coding for it. When one base is substituted for another but the base triplet still codes for the same amino acids, it is a silent mutation. This will not alter the structure for the protein.
Missense	A point mutation that changes the base triplet so it now codes for a different amino acid is a missense mutation.
Nonsense.	If a point mutation alters a base triplet so it becomes a stop triplet, then the assembly of the protein will stop too soon, resulting in a truncated (very short protein) that is unable to function.

Indel mutations

The genetic code is non-overlapping so if nucleotide base pairs, not in triplets, are inserted into the gene or deleted from the gene, all subsequent base triplets will be altered resulting in frameshift. The protein will be very abnormal and unable to function.

Expanding triple nucleotide repeats

Some genes contain a repeating triplet such as - CAG CAG CAG -. Huntington disease results from an expanding triple nucleotide repeat – the number of CAG triplets increasing at DNA replication prior to meiosis and increasing from generation to generation. If the number of repeating CAG sequences goes above a certain critical number, then the person with that **genotype** will develop the symptoms of Huntington disease later in life.

Key points

Genotype – genes/alleles present in an individual/cell; may refer to just one characteristic.

C2 Genetic disorders and diagnosis

In order to understand the causes, progression and diagnosis of genetic and chromosomal disorders you need to understand the terms in the table below.

Table 1.24: Key genetic terminology

Term	Definition
Allele	Different versions of the same gene
Dominant Allele	Dominant alleles will show their affect even if the individual only has one copy of this allele
Recessive Allele	Recessive alleles will only show their effect if the individual inherits two copies of the allele, one from the mother and one from the father
Genotype	The set of genes in DNA responsible for a particular trait
Phenotype	The physical expression of those genes, e.g., eye colour
Heterozygous	Possessing two different alleles for a particular gene (e.g.,one dominant and one recessive)
Homozygous	Possessing the same alleles for a particular gene (e.g., two recessive)
Sex Linkage	Applies to genes that are located on the sex chromosomes. They are considered sex linked because their inheritance and expression differ between females and males
Carrier	An individual that carries a recessive gene for a disease and is capable of passing it on, however they do not display the symptoms of the disease
Affected/Sufferer	An individual that has inherited mutated genes and displays symptom of the disease
Non-affected/ non sufferer	An individual who has not inherited faulty genes and is not affected by a genetic disease

Genetic diagrams

All individuals physically look unique but share many similar characteristics. Within the populations there is variation, some variation is due to genetics, some is environmental, and some is down to both. Genetic and familial pedigree diagrams are used to predict and analyse the pattern of inheritance from parent to offspring and throughout families. Pedigrees show the presence or absence of genetic traits through family lines from parents to offspring.

Genetic and chromosomal disorders

There are several thousand genetic disorders known to occur in humans. Some are extremely rare and some are more common, such as cystic fibrosis and sickle cell anaemia. Some are caused by single gene defects (mutations) and some are the result of chromosome abnormalities. Some gene defects have dominant inheritance patterns and some have recessive.

Cystic fibrosis

In the UK about 1 in 1600 people born are affected by Cystic Fibrosis (CF) and about 1 in 20 people are symptomless carriers.

- The gene, CFTR, codes for a chloride ion channel protein (CFTR – cystic fibrosis transmembrane regulatory protein) in the cell surface membranes of epithelial cells lining the lungs, gut and reproductive tracts.
- 70% of CF cases are caused by a mutation involving the deletion of a codon, leading to the loss of the amino acid phenylalanine at position 508 in the polypeptide chain of the protein which makes the ion channel.
- Symptomless carriers have one mutated allele and one normal allele of the CFTR gene.

- Sufferers have two mutated alleles of this gene, which is on chromosome 7. Sufferers inherit one faulty allele form each parent.
- This disorder has an autosomal recessive inheritance pattern.
- Genotypes are represented by symbols. The symbol C or F can be used to represent the normal, dominant allele for CF and the symbol c or f represents the abnormal, recessive allele.

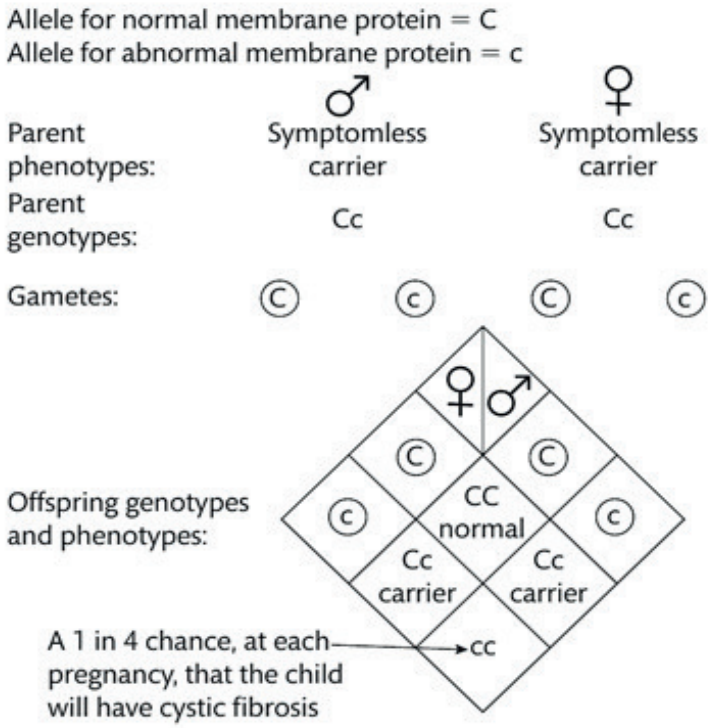


Figure 1.84: Genetic diagram illustrating the inheritance pattern for cystic fibrosis

Huntington's disease

Huntington's disease is a progressive brain disorder that usually shows symptoms, in those affected, after the age of 35 years.

- It is caused by a mutation in a gene called HTT that codes for a protein important for normal function of brain neurones named huntingtin.
- The mutation is an expanding triple nucleotide repeat and is sometimes called a 'stutter'. In part of the HTT gene there is a base triplet CAG that is normally repeated between 10 and 35 times. However, if this trinucleotide sequence repeats more than 40 times then the abnormally long, altered protein is cut by enzymes in brain neurones into shorter, but toxic, fragments. These fragments bind together and interfere with brain neurone function leading to death of brain neurones, producing symptoms of Huntington's disease.
- Early symptoms include low mood, poor coordination, jerky, involuntary twitching movements, known also as chorea.
- As the disease progresses these involuntary movements become more pronounced and sufferers have difficulty with walking, swallowing and talking. They also experience changes in personality, and dementia.
- People with 27–35 CAG repeats do not develop the disease, but they are at risk of producing children with the disease since, at meiosis, the repeat sequence can expand.
- People who have 36–40 or more CAG repeats may develop the disease later in life. By this time, they have probably had children who may have inherited the mutated allele of the gene.

- Huntington's disease has an autosomal dominant inheritance pattern. Sufferers only need to inherit one mutated allele for the disease to develop. Only one parent needs to be affected and at each pregnancy there is a 50% (1 in 2) chance of the child inheriting the disorder.
- The symbol h is used to represent the normal, functioning allele for Huntington's disease and the symbol H represents the abnormal, dominant allele.

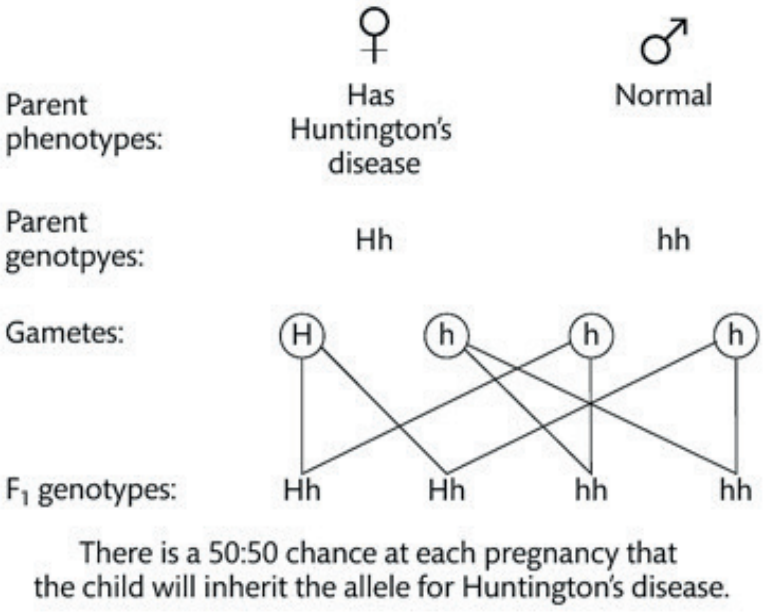


Figure 1.85: Genetic diagram illustrating the inheritance pattern for Huntington's disease

Sex linkage

In humans the XY chromosomes determine our sex. These are the sex chromosomes.

- The human X chromosome contains over 1000 genes that are involved in determining many characteristics or metabolic functions, not concerned with sex-determination, and most of these have no partner alleles on the Y chromosome.
- If a female has one abnormal allele on one of her X chromosomes, she will probably have a functioning allele of the same gene on her other X-chromosome.
- Males inherit their X chromosome from their mother, if this X chromosome has an abnormal allele for a particular gene, he will suffer from a genetic disease, because he will not have a functioning allele for that gene. Males are functionally haploid, or hemizygous, for X-linked genes. They cannot be heterozygous or homozygous for X-linked genes.

Haemophilia A

One of the genes on the non-homologous (being of unlike genetic constitution) region of the X chromosome codes for a blood clotting protein called factor 8. If this allele is faulty then it will produce a non-functioning factor 8. A female with one abnormal allele and one functioning allele will produce enough factor 8 to enable her blood to clot normally when required.

If a female passes the X chromosome with the faulty allele to her son, he will suffer from haemophilia A., because he has no functioning allele for factor 8 on his Y chromosome. This results in the inability for blood to clot fast enough. A significant issue associated with this condition is that internal haemorrhage following injuries sustained by falling over or receiving a knock may not be immediately apparent whereas injuries that involve external wounds cuts are obvious and first aid can be given immediately.

Genotypes representing sex-linked genes are represented by symbols that show they are situated on the X chromosome. The symbol H is used to represent the normal functioning allele for factor 8 and the symbol h represents the abnormal allele. Figure 1.81 shows the inheritance pattern for haemophilia A where the father does not have haemophilia A and the mother is a symptomless carrier.

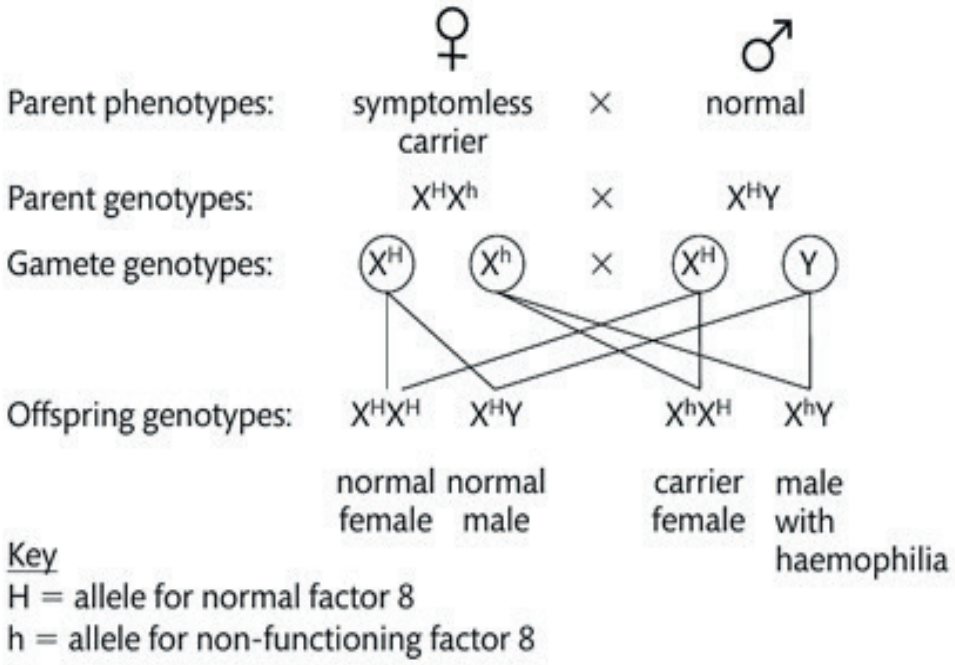


Figure 1.86: Inheritance of haemophilia A

Chromosome mutations

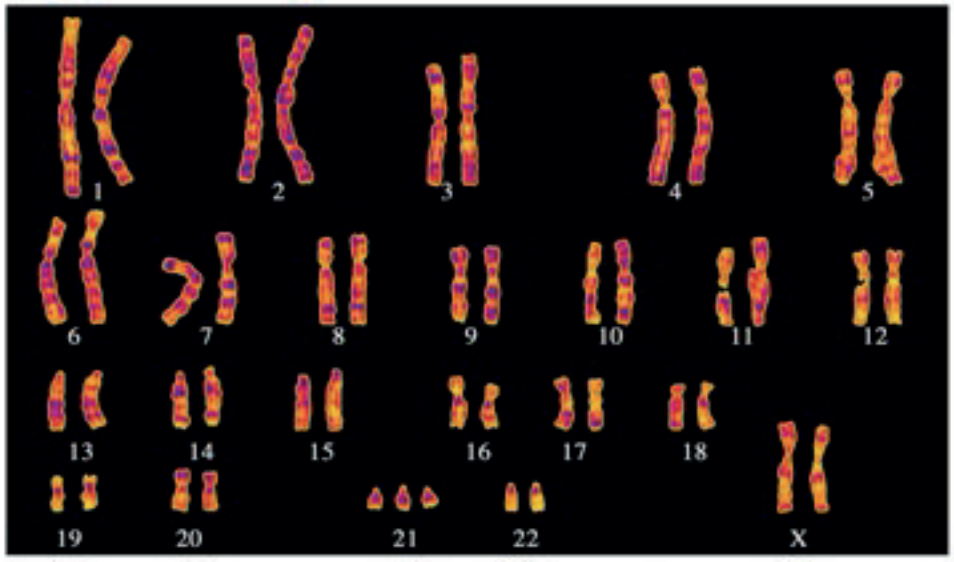
Aneuploidy refers to a condition where the number of chromosomes in the cells of an individual is abnormal.

Sometimes, during meiosis, a pair of homologous chromosomes fails to separate, resulting in an extra chromosome in one gamete or a gamete lacking a chromosome. If the gamete with an extra chromosome is fertilised by a viable haploid gamete, then the embryo will have three copies of a particular chromosome.

Down syndrome

Individuals with Down syndrome have an extra copy of chromosome 21. This leads to over expression of the genes on that chromosome and all the symptoms of Down syndrome.

- This is a genetic condition but is not inherited.
- Neither parent usually has Down syndrome and there are no symptomless carriers, since if you have an extra chromosome 21, you will have Down syndrome.
- The condition arises spontaneously when either an egg or a sperm are produced.



igure 1.87: DNA with an extra chromosome 21

When regulation goes wrong

Earlier in the unit you learned about the cell cycle and cell division. There are proto-oncogenes, which help regulate cell division. They code for proteins that help regulate cell growth and differentiation. If mutations occur in the proto-oncogenes, they become oncogenes, Oncogenes can cause cells that should undergo apoptosis to keep dividing.

If a mutation occurs in the **p53 gene**, it may not be able to regulate cell division. This can lead to uncontrolled cell division and the formation of tumour. Cells should normally only undergo a certain number of cycles or divisions. This is about 50 and is known as the Hayflick constant. If cell division becomes uncontrolled and cells divide more than 50 times, a tumour can form which may become cancerous.

Tumours can be benign or malignant. Benign tumours are not cancerous. They are a mass of cells that do not have the ability to spread into neighbouring tissues (called metastasizing), they grow at a slower rate than malignant tumours, they also have more normal features. Whereas malignant tumours grow uncontrollably and rapidly. They are cancerous and can spread to other parts of the body.

Key points

p53 gene – also known as the tumour-suppressor gene.

Methods and limitations of obtaining DNA samples

There are many reasons why it is necessary to obtain DNA samples for example after a serious crime, paternity tests or screening for genetic diseases. There are several ways to collect DNA samples most are painless and non-invasive.

Swabbing is a very common techniques used to obtain DNA samples. It involves buccal (cheek) swabs. The inside of the inner cheek should be scraped with the moist swab for up to 1 min. Once complete, it should be allowed to dry and then placed inside a sterile container. A further swab can be done on the other side of the mouth hours apart for better results. It is best to try to ensure the following have not been done in the hour leading up to the swab; eating, drinking, smoking, brushing teeth, chewing gum or using mouth wash. Limitations include over saturating the swabs with water, not scraping for long enough or hard enough and because cheek cells are not visible it is hard to tell if there is enough. Contamination can be an issue if from bacteria in the mouth and if sterile containers are not used to store the swab.

Blood samples for DNA testing is more invasive as it requires a needle to be inserted and blood taken. The blood is collected in sterile medical tubes which reduces the chance of contamination. The sample is visible which is an advantage. However, limitations are some people will feel pain because of this, children tend not to like giving these samples. More than 1 attempt may be needed is the patient has small veins. This method of collection should be carried out by a trained medical specialist. Whereas the buccal swab can be carried out by anybody.

Both methods of DNA collection give highly reliable DNA test results.

Diagnostic test for genetic and chromosomal disorders

There are antenatal tests offered to pregnant woman to test for genetic or chromosomal conditions, for example Down's Syndrome.

Chronic villus sampling (CVS)

This test is carried out between the 11th and 14th weeks of pregnancy. A small sample of cells are removed from the placenta by one of two methods:

- Transabdominal CVS- involves inserting a needle through the patient's abdomen, into the uterus and placenta guided by ultrasound scanning.
- Transcervical CVS- a small tube or forceps are inserted through the vagina and cervix and guided to the placenta using ultrasound scanning

The number of chromosomes in the cells can be counted and chromosomes structure can be checked. It cannot test for every condition and sometime results can be inconclusive. Perhaps too few cells were collected. If this is the case it may be necessary to have an alternative test a few weeks later.

Amniocentesis

This test is carried out between the 15th and 20th weeks of pregnancy and can also be carried out later if necessary.

A long, thin needle is inserted through the abdomen wall using an ultrasound image to guide it. The needle is passed into the amniotic sac surrounding the foetus and a small sample of amniotic fluid is collected for analysis. Many women will get a 'normal result' where none of the conditions tested for were found but this does not guarantee that the baby will be completely healthy. If the test results are positive then the baby has of the conditions that were tested for, the implications will be discussed in counselling sessions and couples will have to decide what to do next.

Think future skills

Felicity Metcalfe: Medical Microbiologist

I started work at 22 after I finished at university. I studied Microbiology at university where I gained many scientific practical skills such as aseptic techniques, using pipettes and microscopes. My first job was working as a pharmacy technician making chemotherapy drugs. When I first started, I used lots of scientific techniques and equipment that I had previously used at university, I worked there for two years. I then moved jobs to work in a Medical Microbiology laboratory in a local hospital analysing patients' samples for example urine and blood for infectious diseases. I spend most of my time carrying out specific microbial techniques, such as Gram staining and antibiotic sensitivity tests. These take place in highly specialist sterile laboratories.

I have excellent practical techniques and good health and safety awareness, which is extremely important when working in the science industry. I have good communication and computer skills as I need to work with others in the team and feedback results verbally and electronically. I have good maths skills as I am required to carry out serial dilutions, viable counts and to take measurements. I have to use electronic laboratory information management systems to ensure the patient samples are tracked from start to finish, to maintain accurate records.

No two days are the same for me which I really like. I get to use a variety of skills and work in a science laboratory. I work from 8am to 6pm in the week and also do a night shift pattern on a rota basis. Sometimes I am involved in talking about my work to schools and colleges. I enjoy this part of my job.

Focusing your skills

Think about the role of a microbiologist

Consider the following:

- What types of people will you work with?
- How working within a team will ensure that accurate results are obtained.
- How IT skills can help a microbiologist ensure that they accurately document and report all of the techniques they carry out and the results they find.

Getting ready for assessment

This section has been written to help you to do your best when you take the assessment test. Read through it carefully and ask your tutor if there is anything you are still not sure about.

About the external assessment

The external assessment will last 1 hours and 30 minutes and there are a maximum of 80 marks available. It has one section and there are a series of short answer questions, some of which are multiple choice questions and there are also longer question worth up to 9 marks. There are three types of question in the paper:

- Multiple choice questions
- Short answer questions worth 2-4 marks
- A longer answer question worth up 6-9 marks.

Remember you should attempt to answer all of the questions.

Sitting the external assessment

Listen to and read carefully, any instructions you are given. Lots of marks are often lost through not reading questions properly and misunderstanding what the question is asking.

Most questions contain command words. Understanding what these words mean will help you understand what the question is asking you to do.

Command word	Definition – what it is asking you to do
Analyse	Identify several relevant facts of a topic, demonstrate how they are linked and then explain the importance of each, often in relation to the other facts.
Assess	Evaluate or estimate the nature, ability, or quality of something.
Consider	Think carefully about (something). The question will often require you to make a decision on the issue as part of your answer.
Define	State the meaning of something, using clear and relevant facts.
Describe	Give a full account of all the information, including all the relevant details of any features, of a topic.
Discuss	Write about the topic in detail, taking into account different ideas and opinions.
Evaluate	Bring all the relevant information you have on a topic together and make a judgment on it (for example on its success or importance). Your judgment should be clearly supported by the information you have gathered.
Justify	Give reasons for the point your answer is making, so that your reader can tell what you are thinking. These reasons should clearly support the argument you are making.

Work out what question you need to answer and then organise your time, based on the marks available for each question. Set yourself a timetable for working through the test and then stick to it – don't spend ages on a short 1-2-mark question and then find you only have a few minutes for a longer 6-9 mark question.

If you are writing a longer answer, try and plan before you start writing. Have a clear idea of the point your answer is making, and make sure this comes across in everything you write, so it is all focused on answering the question.

Exam tip

- Arrive in good time so you are not in a panic.
- Remember you can't lose marks for a wrong answer, but you can't gain any marks for a blank space!
- Try answering all the simpler questions first then come back to the harder questions. This should give you more time for the harder questions.

Answering multiple choice questions

You need to be careful when choosing answers. Some may look sensible but aren't suitable for the CONTEXT of the question. Always read the question carefully and choose the MOST APPROPRIATE answer.

Worked example

Examples:

What organelle is responsible for protein synthesis?

A Mitochondria

B Rough ER

C Ribosomes

D Golgi Apparatus

Read the question very carefully. Sometimes more than one answer is required.

Answering short-answer questions

- Read the question carefully.
- Highlight or underline key words.
- Note the number of marks available.

Make sure you make the same number of statements as there are marks available. For example, a two-mark question needs two statements.

Worked example

Exam tip

Look carefully at how the question is set out to see how many points need to be included in your answer.

Define the term 'vital capacity' and give an example. **[2]**

Answer:

Vital capacity is the maximum volume of air that can be exhaled after a maximum inspiration

Exam tip

This answer gives a brief definition – a description of what the term means, marks would be awarded for maximum volume of air exhaled (1) after maximum inspiration (1).

Answering extended answer questions

Example:
Water is reabsorbed into the blood in the kidneys. If more water is reabsorbed than the body needs, a person can develop hypertension. One effect of hypertension is that it can affect the tissues of the body by increasing the amount of tissue fluid formed at the arterial end of the capillaries and decreases the amount reabsorbed at the venous end.

Discuss the impact of hypertension on tissue fluid formation [9].

Exam tip

For a question using the word 'discuss', you must do more than just explain. You might need to talk about the issues or the advantages and disadvantages of an approach.

Answer: Hypertension is high blood pressure. Blood pressure is a measure of the pressure created when the heart contracts. It has two numbers. The top number represents the systolic pressure and the bottom number represents the diastolic pressure. Normal blood pressure is 120 / 80. Hypertension is diagnosed when blood pressure is over 140 / 90. In the body tissue fluid is formed at the capillaries. Fluid leaves the blood and forms tissue fluid. Some of it is reabsorbed back into the blood. If too much fluid goes into the tissue fluid it can cause it to build up and can cause swelling.

Exam tip

This answer does describe what hypertension is and briefly describes the formation of tissue fluid.

The answer also links hypertension to tissue fluid and goes on to say that it can cause swelling. There is not enough scientific detail in this answer to be awarded 9 marks. There needs to be more detail about the formation of tissue fluid and discussion of how it is affected by hypertension.

This is an introduction to the answer giving some detail about hypertension without going off topic. Any more detail than this may lead you to not answer the question given.

Hypertension is high blood pressure. Normal blood pressure is 120/80 mmHg but a person with hypertension will have blood pressure in excess of 140/90 mmHg. This can cause swelling due to increased production of tissue fluid.

Tissue fluid is formed at the capillary bed. When blood enters the capillary bed at the arterial end, it is under high pressure. This forces fluid out of the blood through the small gaps in the walls of the capillary to form tissue fluid. Fluid moves because the hydrostatic pressure of the blood is greater than the osmotic pressure. Plasma proteins and red blood cells remain in the blood which maintains the blood's osmotic potential. As blood moves along the capillary bed, the pressure is decreased. This causes tissue fluid to drain back into the blood at the venous end of the capillary bed. Here the osmotic pressure is greater than the hydrostatic pressure.

This is a discussion of the normal process of tissue fluid formation including detailed scientific knowledge and correct terminology.

Hypertension is linked to tissue fluid formation. This discusses how tissue fluid formation is affected by hypertension using correct scientific terminology.

Hypertension causes the blood to contain excess water. This increases the water potential of the blood. At the venous end of the capillary bed there is a smaller water potential gradient between the tissue fluid and the blood. This reduces the volume of water that is reabsorbed back into the capillary. The result of this is formation of excess tissue fluid which can cause swelling.