IB Biology DP

YOUR NOTES

6. Human Physiology

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6.1 Digestion & Absorption

6.1.1 Digestion

Introduction to Digestion

- The digestive system is an example of an **organ system** in which several organs work together to digest and absorb food
- Digestion is a process in which relatively **large, insoluble molecules** in food (such as **starch** and **proteins**) are broken down into **smaller, soluble molecules** that can be absorbed into the bloodstream and delivered to cells in the body
- These small, soluble molecules (such as **glucose** and **amino acids**) are used either to release **energy** (via respiration) to the cells, or to provide cells with materials with which they can **build other molecules** to **grow, repair and function**
- The human digestive system is made up of the organs that form the alimentary canal, and accessory organs
    - The alimentary canal is the channel or passage through which food flows through the body, starting at the **mouth** and ending at the **anus**
    - Digestion occurs within the alimentary canal
    - Accessory organs produce substances that are needed for digestion to occur (such as **enzymes** and **bile**) but food does not pass directly through these organs

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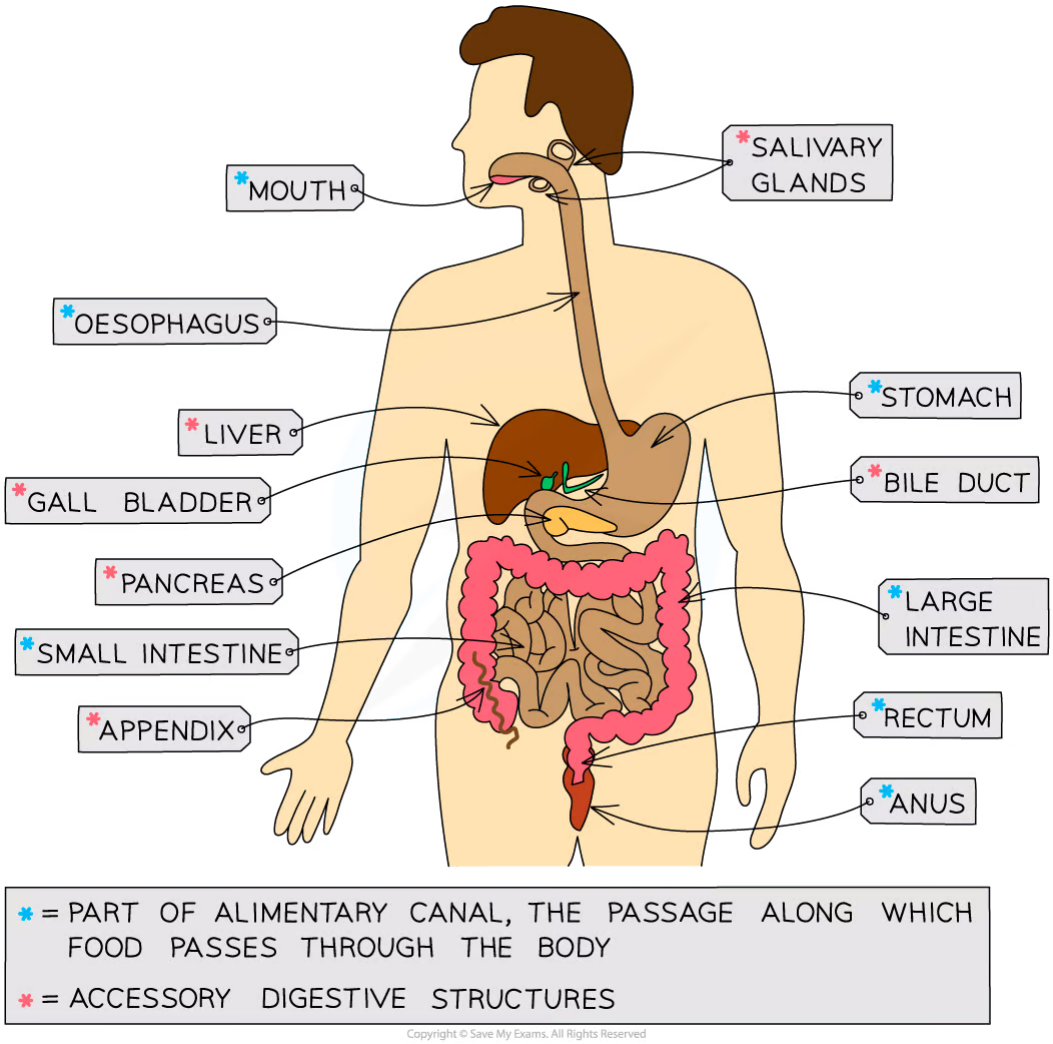

The human digestive system includes the organs of the alimentary canal and accessory organs that work together to break large insoluble molecules into small soluble molecules

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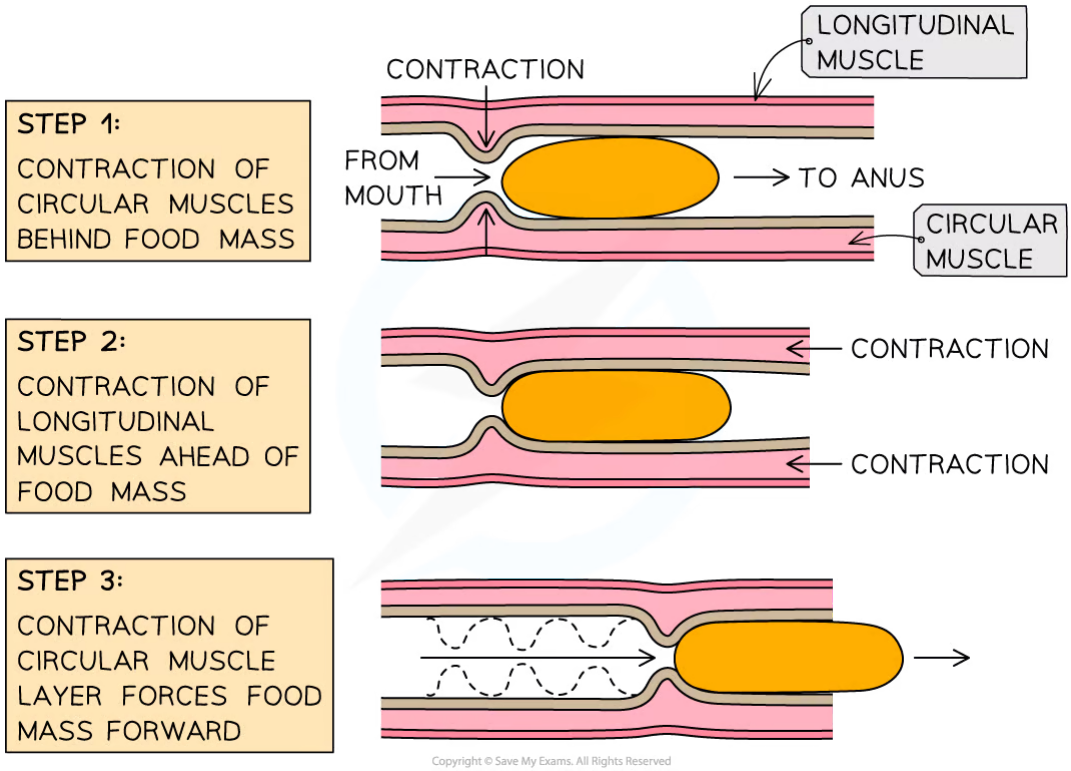
Peristalsis

- Peristalsis is **series of muscle contractions** in the **walls of the oesophagus** or **small intestine** that pass like a **wave** along the alimentary canal
  - This wave forces the bolus of food along the alimentary canal
  - These contractions are controlled unconsciously by the autonomic nervous system
- Peristalsis is controlled by **circular** and **longitudinal** muscles
- These muscles are smooth muscle (not striated)
  - **Circular muscles** contract to reduce the **diameter** of the lumen of the oesophagus or small intestine
    - This **prevents the food moving backwards** towards the mouth
  - **Longitudinal muscles** contract to reduce the **length** of that section the oesophagus or the small intestine
    - This **forces the food forwards** through the alimentary canal
- Once the bolus has reached the stomach, it is churned into a less solid form, called chyme, which continues on to the **small intestine**
- **Mucus** is produced to continually **lubricate** the food mass and reduce friction
- In the **small intestine** peristalsis is **slow** compared to the peristalsis that occurs in the oesophagus. It also aids digestion by **churning** up the food with enzymes as it pushes it along the gut



Circular and longitudinal muscles in the alimentary canal contract rhythmically to move the bolus along in a wave-like action

Pancreatic Juices

YOUR NOTES

- The pancreas is a gland made up of two types of tissue
  - The first type of tissue secretes the hormones insulin and glucagon into the **blood**
  - The second type of tissue **synthesises** and **secretes digestive enzymes** into the lumen of the small intestine
    - Enzymes are synthesised on the **ribosomes** of the rough endoplasmic reticulum. They are then processed within the Golgi apparatus before being secreted by exocytosis into the lumen of the **small intestine**
- Secretion of pancreatic enzymes is stimulated by the release of **hormones** into the stomach and intestines in response to ingestion of food
  - This is an automatic response of the **autonomic nervous system**
- The **enzymes found in pancreatic juice** include amylase, lipase, phospholipase, and protease enzymes.

The structure of the pancreas

- Digestive enzymes are produced in specialised gland cells which are known as **acinar** cells
- These cells are located in clusters around the ends of tubes called **ducts**
- Ducts join together to form larger ducts and eventually, one **pancreatic duct**
  - This is where the pancreatic juices, containing enzymes, are secreted into the duodenum of the small intestine

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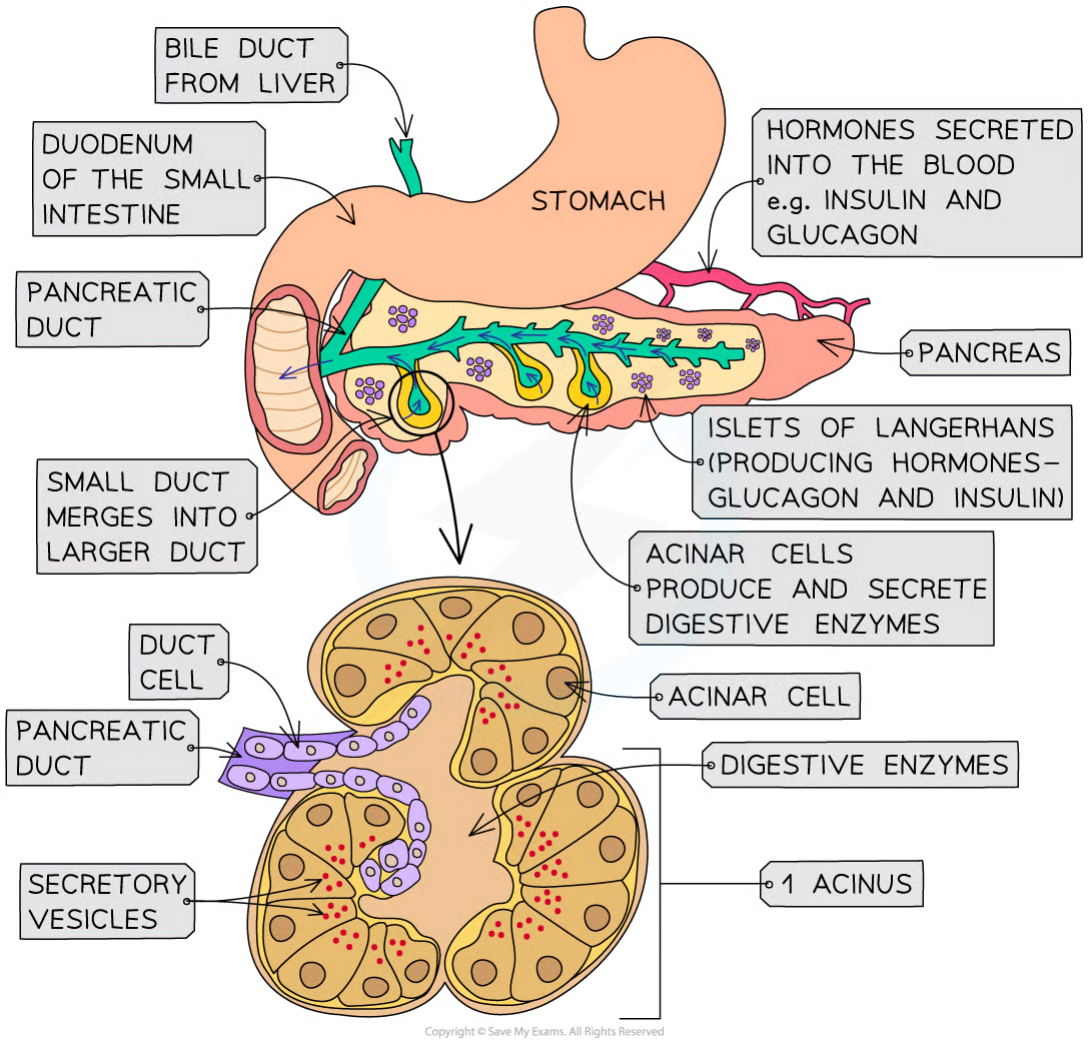

Acinar cells synthesise and secrete pancreatic enzymes into the ducts and the pancreatic duct secretes the pancreatic juice into the small intestine

Enzymes in Small Intestine Digestion

YOUR NOTES

- Enzymes are required to carry out the **hydrolysis** reactions required to digest large insoluble macromolecules into small, soluble, monomers
- The **enzymes found in pancreatic juice** include:
  - **Amylase** - for the partial digestion of starch into maltose
  - **Lipase** - for digestion of triglycerides into fatty acids and glycerol/monoglycerides
  - **Phospholipase** - for digestion of phospholipids into fatty acids, glycerol and phosphate
  - **Protease** - for the partial digestion of proteins and polypeptides into shorter peptides
- As well as those enzymes found in **pancreatic juices**, enzymes are also produced in the walls of the **small intestine**
  - These enzymes break the products of pancreatic enzyme digestion down into **monomers,** e.g.
    - Nucleases break down nucleic acids
    - Lactase digests lactose
    - Sucrase digests sucrose
    - Maltase digests maltose
    - Dipeptidase digests dipeptides
  - Some enzymes are **secreted** from the **epithelial cells** into the intestinal lumen with partially digested food
  - Other enzymes e.g. maltase, are **immobilised and are attached to the membrane** of the epithelial cells where they digest substrate molecules as the food is forced through the small intestine
    - These enzymes are examples of **integral proteins**
- Some substances that we consume, such as **cellulose**, may remain **undigested** as humans are unable to produce the enzymes required

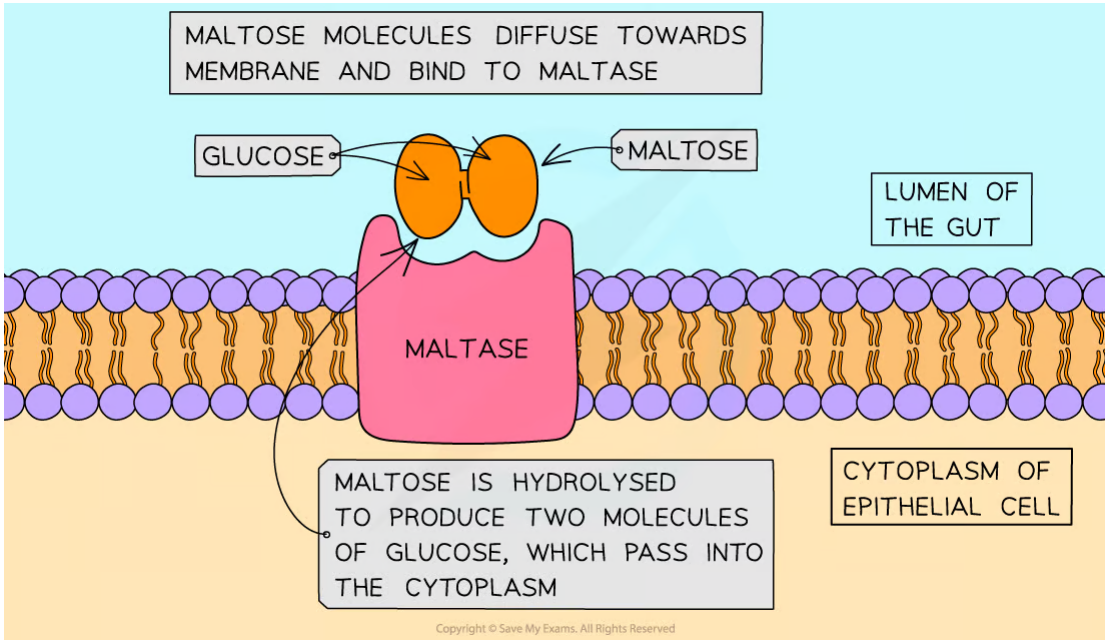

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Image showing maltase enzyme attached to the cell-surface membrane of an epithelial cell

Enzymes of the Digestive System Table

Substrate	Product	Enzymes involved
Starch	Maltose	Amylase
Triglycerides	Fatty acids & glycerol Or Fatty acids & monoglycerides	Lipase
Phospholipids	Fatty acids, glycerol & phosphate	Phospholipase
Proteins	Shorter polypeptides	Protease
DNA and RNA	Nucleotides	Nucleases
Maltose	Glucose	Maltase
Lactose	Glucose & galactose	Lactase
Sucrose	Glucose & fructose	Sucrase
Peptides	Dipeptide	Exopeptidases
Dipeptides	Amino acids	Endopeptidases

Small Intestine Digestion

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Digestion of proteins

- **Pancreatic juice** contains endopeptidases and exopeptidases
  - **Endo**peptidases hydrolyse peptide bonds **within** polypeptide chains to produce dipeptides
  - **Exo**peptidases hydrolyse peptide bonds at the **ends** of polypeptide chains to produce dipeptides
- Lastly, there are **dipeptidase** enzymes found within the cell surface membrane of the epithelial cells in the small intestine. These enzymes hydrolyse dipeptides into **amino acids** which are released into the cytoplasm of the cell

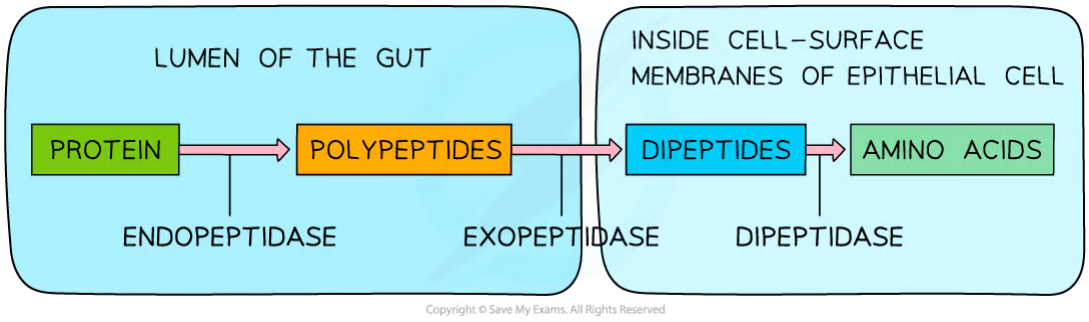

Image showing the digestion of protein by several enzymes

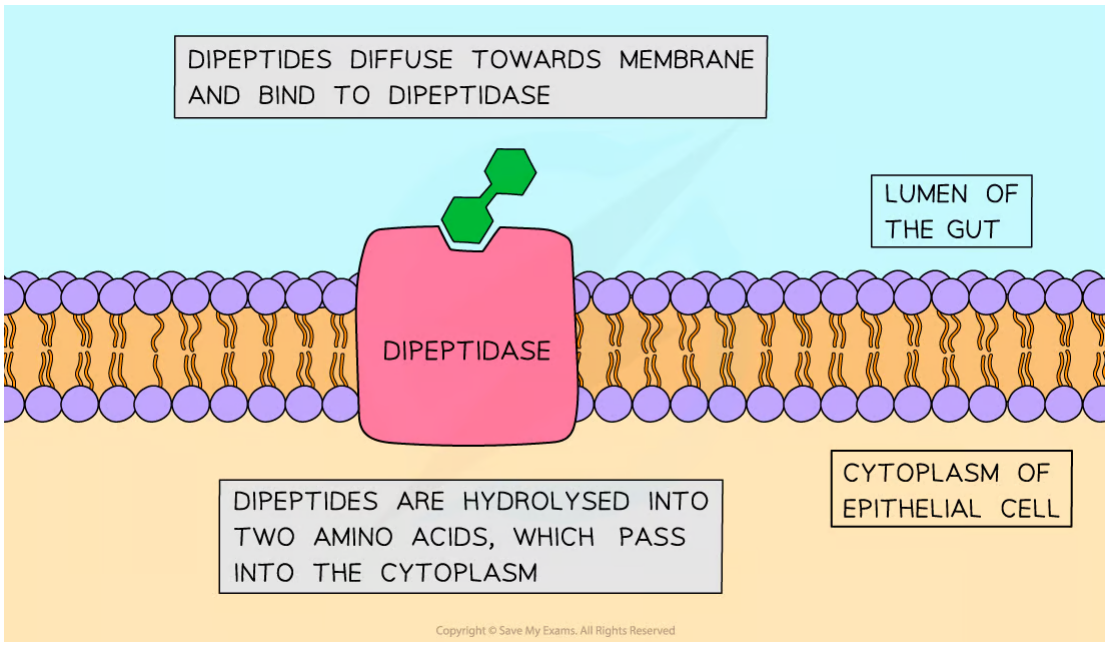

Image showing dipeptidase inside the cell-surface membrane of an epithelial cell

Emulsification of lipids

- When fatty liquid arrives in the small intestine **bile** (containing bile salts), which has been made in the liver and stored in the gallbladder, **is secreted**

YOUR NOTES

- The bile salts bind to the fatty liquid and break the fatty droplets into smaller ones via **emulsification**
  - Emulsification helps to **increase the surface area** of the fatty droplets for action of digestive enzymes

Digestion of lipids

- The digestion of lipids takes place solely in the **lumen of the small intestine**
- Lipase enzymes break down lipids to **glycerol and fatty acids**
  - Lipids can also be broken down into **monoglycerides and fatty acids**
- Lipase enzymes are produced in the **pancreas** and secreted into the **small intestine**

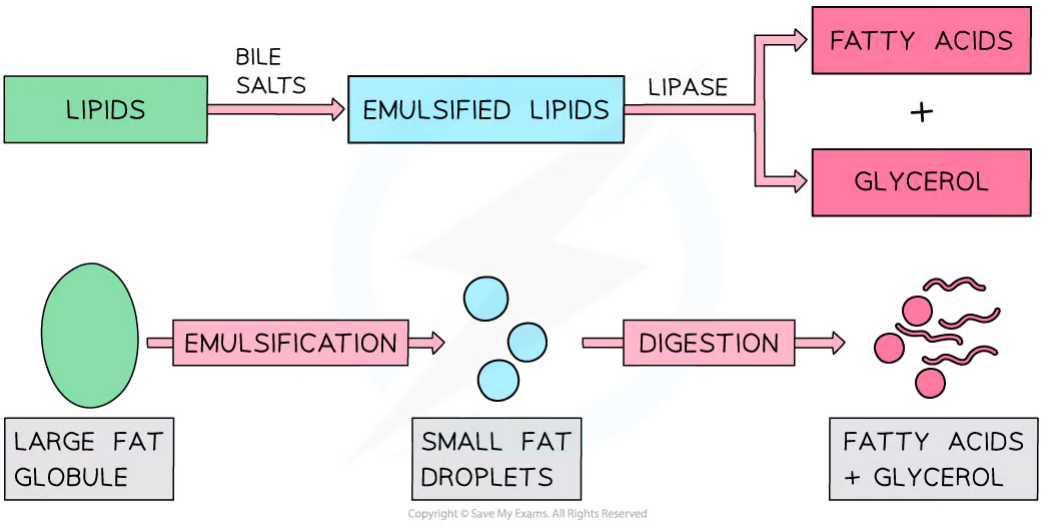

Image showing the digestion of lipids by lipase enzymes in the lumen of the gut.

Digestion of starch

- Starch is a macromolecule made up of many **α-glucose** molecules bonded together in **condensation** reactions
- There are two main types of starch
  - **Amylose** - an unbranched molecule containing [popover id="tpMGiuKDIISd8vkG" label="1,4 glycosidic bonds" only]
  - **Amylopectin** - a branched molecule with 1,4 and 1,6 glycosidic bonds
- The digestion of starch begins in the **mouth** and the **small intestine** with the enzyme **amylase**
  - **Amylase** is a carbohydrase that is made in the salivary glands, the pancreas and the small intestine
  - It **hydrolyses** the **1,4 glycosidic bonds** found in both amylose and amylopectin
  - Amylase action breaks starch down into **maltose**
  - Amylase is **unable** to digest the **1,6 bonds** found in amylopectin; as a result, short strands of amylopectin (containing these bonds) are produced. These short strands are called **dextrins**.
- The next stage of starch digestion involves enzymes **immobilised** in the **membranes of the microvilli** e.g.

YOUR NOTES

- **Maltase** - a disaccharidase which hydrolyses maltose into **glucose**
- **Dextrinase** - digests the 1,6 glycosidic bonds found in dextrins

- After digestion, the monosaccharides can be absorbed into epithelial cells of the small intestine which pass them into the blood stream
  - Glucose is absorbed by **co-transport** with **sodium ions** into the **epithelium cells**
  - It then moves by **facilitated diffusion** into the spaces between villus cells, before entering the villus **capillaries**

- Note that the lining of the small intestine is folded and there are **microvilli** present. This increases the surface area for proteins such as membrane-bound disaccharidases and co-transporters

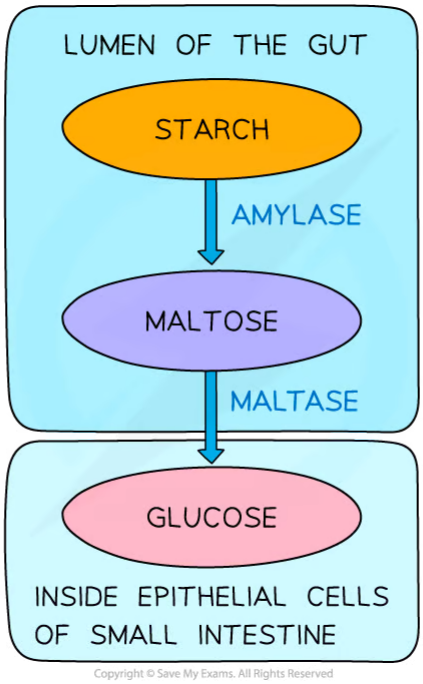

Image showing the digestion of starch by enzymes. Amylase is a carbohydrase enzyme and maltase is a disaccharidase enzyme.

Digestion of nucleic acids

- **Nucleases** are enzymes which break down **DNA and RNA** into **nucleotides**
- They break the **phosphodiester bonds** between the nucleotide bases
- These can then be **absorbed** into the blood

The products of digestion

- The products of digestion travel via the **hepatic portal vein** into the **liver**
- The liver absorbs **excess glucose** and stores it as **glycogen**
  - Glycogen has a similar branched structure to amylopectin but is **more branched** due to having a higher proportion of 1,6 glycosidic bonds

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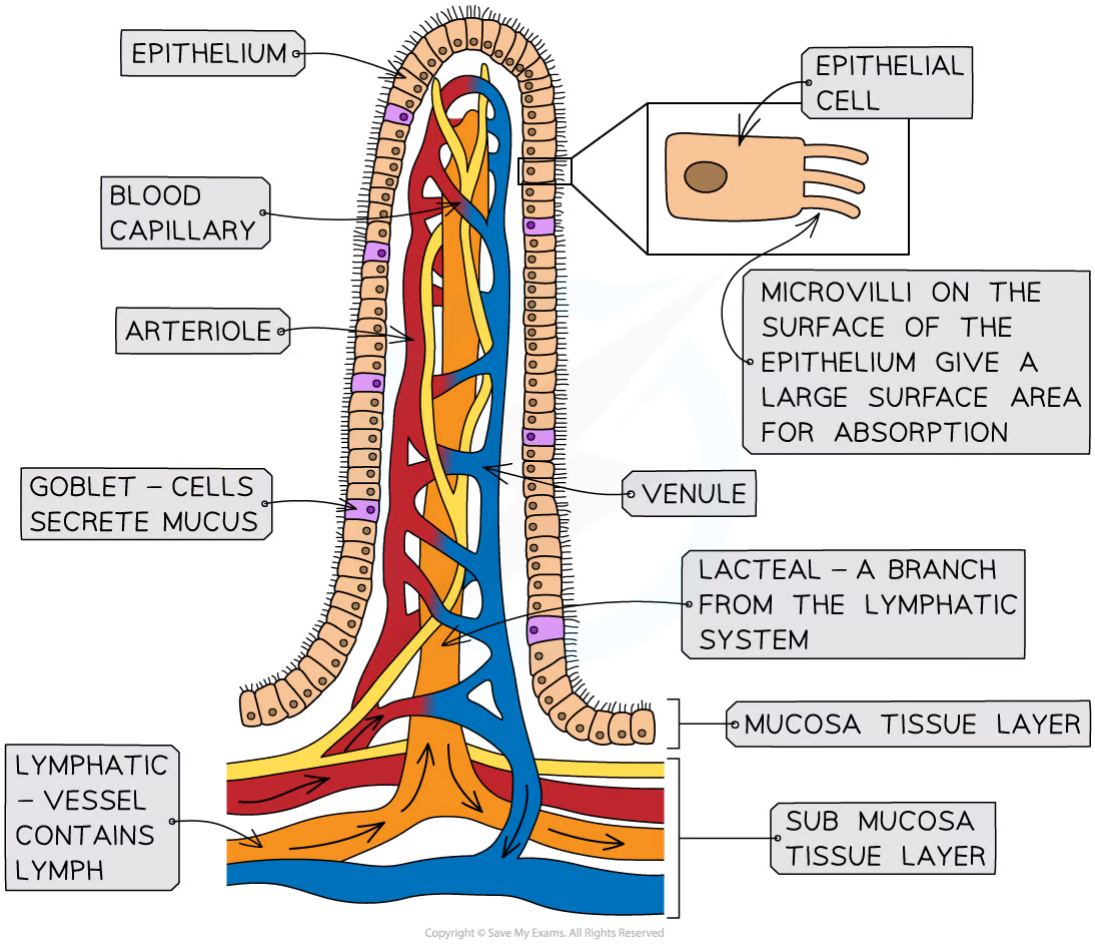
Villi: Increasing the Surface Area

- The **ileum** (the second section of the small intestine) is adapted for **absorption**
  - It is **very long**
  - It has a **highly folded surface**
  - It has **millions of villi** (singular villus)
    - Finger like projections on the internal intestinal walls
  - The epithelium of each villus is covered in **microvilli**
    - Foldings of the cell surface membrane of the epithelial cells
- All of these features significantly **increase the surface area** of the ileum, allowing absorption to take place faster



A villus is covered in microvilli which provide a huge surface area to maximise absorption in the small intestine

Villi: Absorption

YOUR NOTES

- **Absorption** takes place in the **ileum**
- Absorption is the **movement of digested food molecules, vitamins and mineral ions from the digestive system into the blood and lymph**
- This includes the following **products of digestion:**
  - **Simple monosaccharides** e.g. glucose, fructose, galactose
  - **Amino acids**
  - **Fatty acids, monoglycerides and glycerol**
  - **Nucleotide bases**
- And the following **additional substances**:
  - **Mineral ions** e.g. calcium, potassium, sodium
  - **Vitamins** e.g. vitamin C
- **Water** is absorbed in both the **small intestine** and the **colon**, but **most absorption of water** occurs in the **small intestine**

Absorption of unwanted substances

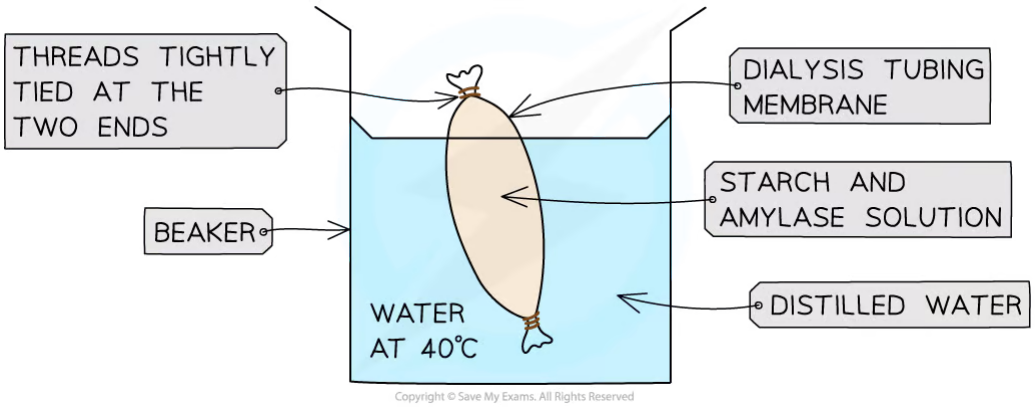
- The epithelium provides a **barrier** to prevent absorption of some harmful substances
- However, some **unwanted substances** can still pass into the blood. This includes:
  - Some **harmless chemicals** found in food colourings and flavours; these are removed by the **kidney** and lost in the urine
  - Small numbers of **bacteria –** these are **engulfed** and digested by **phagocytes** in the blood
  - Some other **harmful substances –** these are removed from the blood and broken down by the **liver**

YOUR NOTES

Dialysis Tubing Experiment

Investigating the absorption of the products of digestion using dialysis tubing

- **Dialysis tubing** (sometimes referred to as Visking tubing) is a non-living, **partially permeable** membrane made from cellulose
- It is sometimes used to model the process of **digestion** and **absorption** that occurs in the small intestine
- Pores in the membrane are small enough to **prevent the passage of large molecules** (such as **starch** and **sucrose**) but allow **smaller molecules** (such as **glucose**) to pass through by **diffusion**



Dialysis tubing can be used to model the epithelium of the small intestine

Method

- Fill a section of **dialysis tubing** (tube 1) with a mixture of:
  - 1 ml 1% amylase solution
  - 10 ml 1% starch solution
- Tie up the tubing tightly with a piece of thread
- Suspend the tubing in a beaker of water for a set period of time at 40°C
- Take samples from the liquid outside the dialysis tubing at regular intervals and **test for the presence of starch** and **glucose**
  - **Iodine** is used to test for the presence of starch. A **blue-black colour** is produced in the presence of starch
  - **Benedict's reagent** is used to test for the presence of glucose. An **orange-red precipitate** is formed in the presence of glucose when Benedict's solution is added and the solution is heated to 90°C or above
- **Repeat** the same method in a second dialysis tube (tube 2) with a mixture of:
  - 1 ml distilled water
  - 10 ml 1% starch solution

Results

- **Tube 1**:
  - The **amylase** present inside the dialysis tube **breaks down** starch into **glucose**

YOUR NOTES

- Over time the **concentration of glucose** in the liquid outside the dialysis tube should **increase** as more starch is digested
  - Glucose is **small enough to diffuse across** the partially permeable membrane
  - The amount of precipitate produced from the Benedict's reagent test will **increase over time**
- **No starch** should be found in the liquid outside the dialysis tubing
  - Starch molecules are **too large to diffuse across** the partially permeable membrane
  - The iodine test will be negative

- **Tube 2:**
  - Without amylase present, the starch is **not broken down** into glucose
  - The glucose tests done on the water outside the dialysis tube show no glucose is present as **no precipitate** is formed
  - Starch molecules are **too large to diffuse across** the partially permeable membrane, so the iodine test will be negative

Limitations

- This test is **qualitative**, so does not show the rate of enzyme activity
  - The rate of digestion can be investigated **quantitatively** by using the semi-quantitative Benedict's test
    - Comparisons can be made at time intervals using a set of colour standards (known glucose concentrations) or a **colorimeter** to give a quantitative set of results
    - A graph could be drawn showing how the rate of diffusion changes with the concentration gradient between the inside and outside of the tubing

Other investigations using dialysis tubing

- Dialysis tubing can also be used to investigate other features of digestion such as
  - The effects of different **factors** on the rate of digestive enzyme activity
    - Investigating the effect of **pH**
      - Eg. multiple dialysis tubings are set up containing solutions of starch and amylase kept at different pH levels using buffer solutions
    - Investigating the effect of **temperature**
      - Eg. multiple dialysis tubings are set up in water baths of different temperatures
  - The effect of **membrane permeability** on absorption
    - E.g. using cola to show how some smaller particles (glucose) can diffuse through the partially permeable membrane whilst larger molecules (food colouring) cannot

Using Models to Represent Real Life

YOUR NOTES

NOS: Use models as representations of the real world; dialysis tubing can be used to model absorption in the intestine

- Models are often used to study **living systems** which may be **too complicated** to observe in reality and achieve meaningful results
  - There may be too many factors influencing a system at any one time
- Scientists may have access to specialist equipment that enables them to carry out **computer based models** e.g. the Dynamic Gastric Model, used to analyse factors influencing digestion
- It is also possible to model some systems using much **simpler equipment**, such as the **dialysis tubing model** from the experiment above
  - The **dialysis tubing membrane** is used to represent the membrane of the small intestine:
    - It is an accurate model because both are **partially permeable** so smaller particles can pass through the membrane whilst larger particles cannot; the membrane therefore allows the passive movement of solutes in **diffusion,** and water molecules in **osmosis**
    - However, the small intestine has a **much larger surface area** due to the presence of villi
    - Additionally, dialysis tubing is limited in the processes it can mirror and cannot show **active transport**
  - **Distilled water** is used to represent **blood**:
    - This is a good model because both have an initially **low solute concentration**
    - However, the distilled water does not **flow** in the same way as blood and so does not maintain the **concentration gradient** as blood does

YOUR NOTES

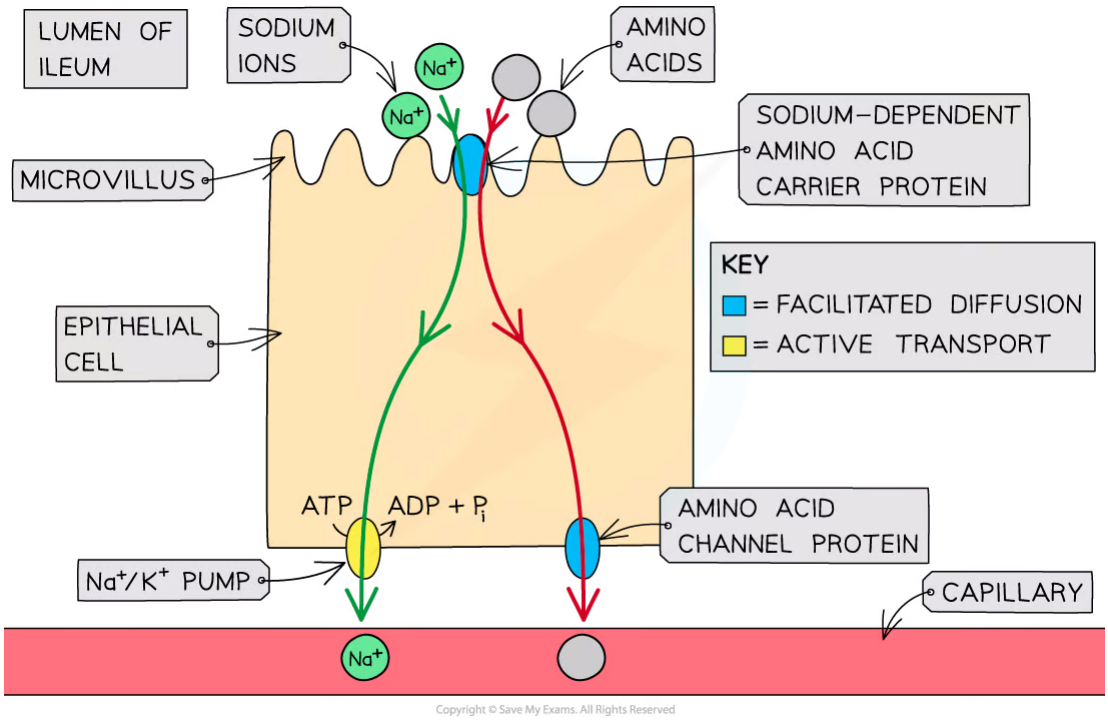
Methods of Absorption

- Digestion breaks down food into **smaller, soluble molecules**
- These products of digestion then pass from the **lumen** of the intestine into the **blood**
  - They pass through the microvilli of the cell surface membrane and into the **epithelium cells**
  - Then they move through the cell surface membrane that separates the epithelium cells from the blood; into the **blood capillaries** and **lacteal** (lymph vessels within the villus)
- Different mechanisms are required in the process of absorption including **diffusion, active transport, exocytosis**, and **facilitated diffusion**
  - **Amino acids** and **monosaccharides** both use facilitated diffusion, active transport and **co-transport proteins** in order to move across the epithelial membrane
  - **Lipids** are absorbed in a different way using simple diffusion, facilitated diffusion and exocytosis

Absorption of amino acids

- Specific **amino acid co-transport proteins** (a type of carrier protein) are found within the cell-surface membrane of the **epithelial cells** lining the ileum
- They transport amino acids only when there are **sodium ions** present
- For every sodium ion that is transported into the cell, an **amino acid is also transported in**
  - This occurs via **facilitated diffusion**, which requires the movement of molecules **down their** concentration gradient
- Amino acids diffuse across the epithelial cell and then pass into the capillaries via **facilitated diffusion**
- The concentration gradient of sodium ions from the lumen of the ileum into the epithelial cell is maintained by the **active transport of sodium ions** out of the cell and into the blood via a **sodium-potassium pump** at the capillary end of the cell

YOUR NOTES

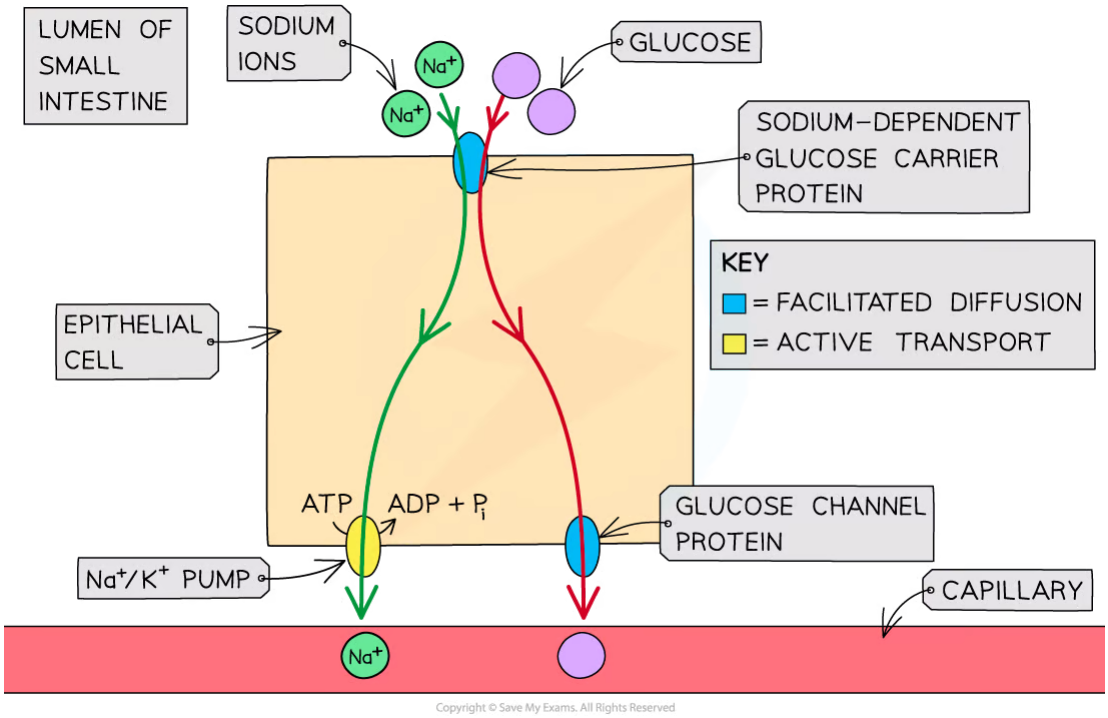


The co-transport of sodium ions and amino acids in the ileum. Both facilitated diffusion and active transport are involved in the process.

Absorption of monosaccharides

- Glucose is polar so cannot pass into the blood by diffusion
- The **glucose carrier proteins** in the cell-surface membrane of the small intestine work in a similar way to the amino acid carrier proteins
  - **Sodium ions and glucose molecules are co-transported** into the epithelial cells via **facilitated diffusion**
    - This is a **passive process** but depends on the **concentration gradient** of sodium ions from the lumen of the ileum into the epithelial cell
    - The gradient is maintained by the **active transport of sodium ions** out of the cell and into the blood via a **sodium-potassium pump** at the capillary end of the cell
  - The glucose molecules diffuse across the epithelial cell and enter the capillary by **facilitated diffusion** through a glucose channel protein

YOUR NOTES

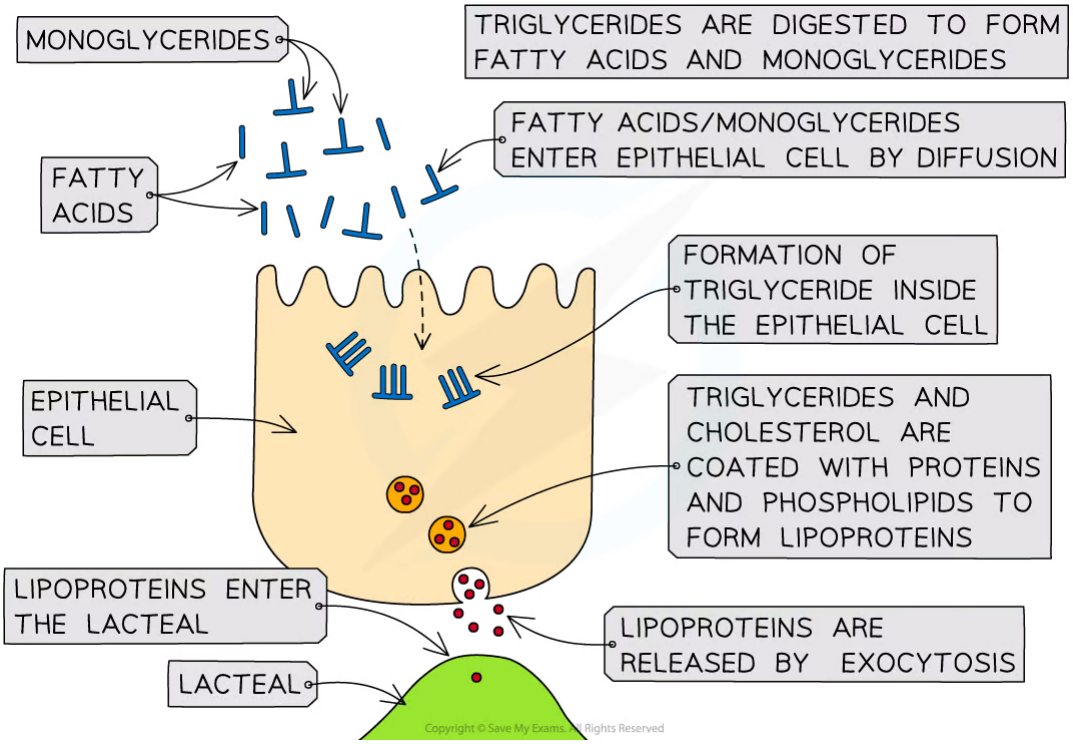


The co-transport of sodium ions and glucose in the small intestine. Both facilitated diffusion and active transport are involved in the process.

Absorption of lipids

- The products of lipid digestion are **fatty acids, monoglycerides,** and **glycerol**
- Absorption of these products is **different** from the absorption of monosaccharides and amino acids
- **Fatty acids** and **monoglycerides** can enter the epithelial cell by **simple diffusion**
  - They are non-polar molecules so they can diffuse through the phospholipid bilayer of the cell surface membrane
- Fatty acids also move by **facilitated diffusion** through fatty acid transport proteins
- Inside the epithelial cell, **fatty acid chains** recombine with **monoglycerides** or **glycerol** to form **triglycerides,** which are unable to diffuse back into the lumen
- The **triglycerides** are packaged up with **cholesterol** and encased in phospholipids and proteins to form **lipoproteins**
- These droplets then enter the **lacteal** or **capillaries** via exocytosis

YOUR NOTES



Lipids are absorbed in the small intestine through a combination of simple diffusion, facilitated diffusion and exocytosis

YOUR NOTES

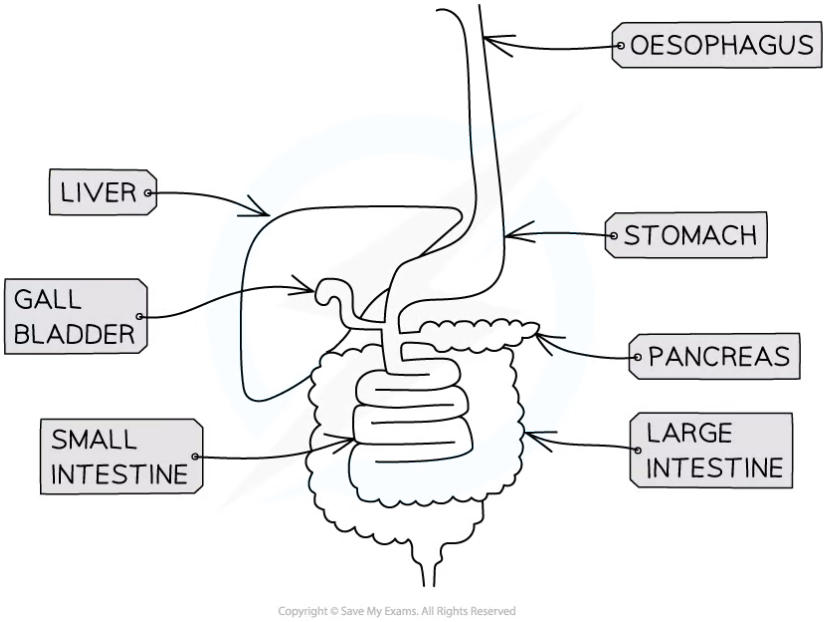
Digestive System Diagram

Human Digestive System

- The human digestive system includes the following:
  - **Glands** - the salivary glands, and glands in the pancreas that produce digestive juices
  - The **stomach** and **small intestine** - the sites of digestion
  - The **liver** - produces bile
  - **Small intestine** - the site of absorption of the products of digestion
  - **Large intestine** - the site of water absorption

Tips for drawing an annotated digestive system diagram

- A simple annotated diagram should include some clear features:
  - The junctions between each section should be **obvious and unobstructed** or covered by other parts of your drawing, this includes the following junctions:
    - Between the stomach and oesophagus
    - Between the stomach and small intestine
    - Between the pancreas, small intestine and gall bladder
  - The shapes of organs should be approximately **true to form** e.g. the stomach should be a j-shaped sac
  - The liver should be the **largest organ** represented and located to the **left of the stomach**
  - The **diameter of the small intestine** needs to be obviously **smaller** than the **diameter of the large intestine**



A diagram of the key components of the human digestive system

Exam Tip

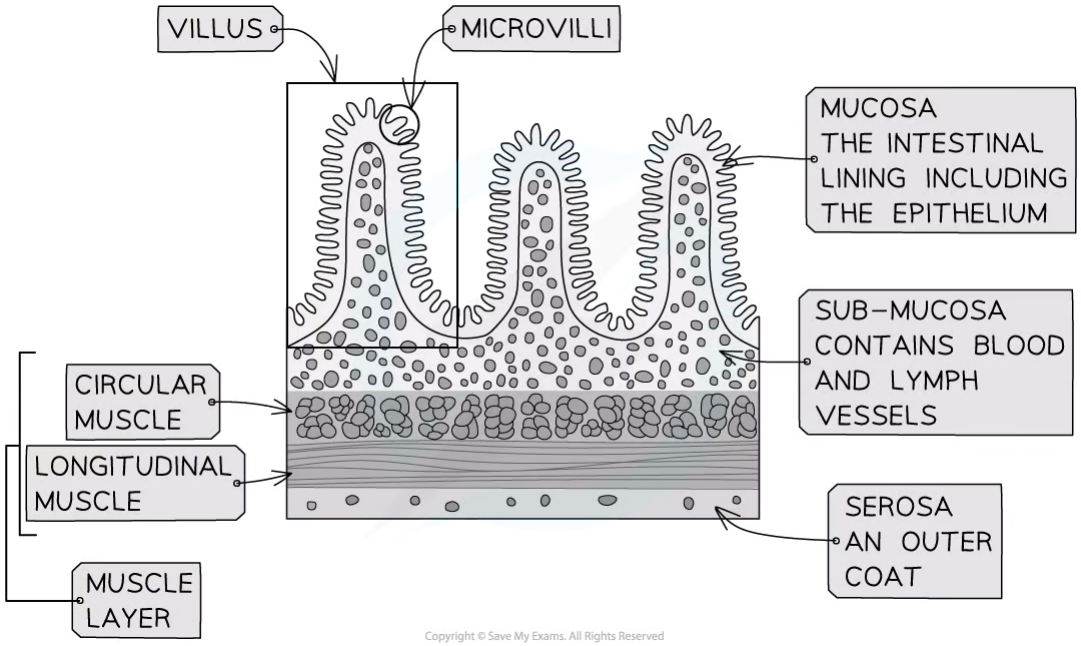
Draw your diagrams using a dark pen or pencil to ensure that all components are clear (remember that your paper will be scanned for marking, so your drawing will need to show up clearly after scanning).

YOUR NOTES

Small Intestine: Identifying Tissue Layers

YOUR NOTES

- The wall of the small intestine is made up of several layers including the following:
  - **Serosa** - an outer coat which includes a membrane and connective tissue
  - **Muscle layer** - including longitudinal muscle tissue in the outermost layer with a layer of circular muscle tissue on the inside
  - **Sub-mucosa** - connective tissue containing blood and lymph vessels
  - **Mucosa** - the lining of the small intestine, composed of epithelium which is folded to form the villi



The layers of tissue in the wall of the small intestine

YOUR NOTES

The layers of tissue in the wall of the small intestine as viewed under a microscope. Seen in both longitudinal section and cross section

YOUR NOTES

6.2 The Blood System

6.2.1 The Blood System: History

Discovery of the Circulation of Blood

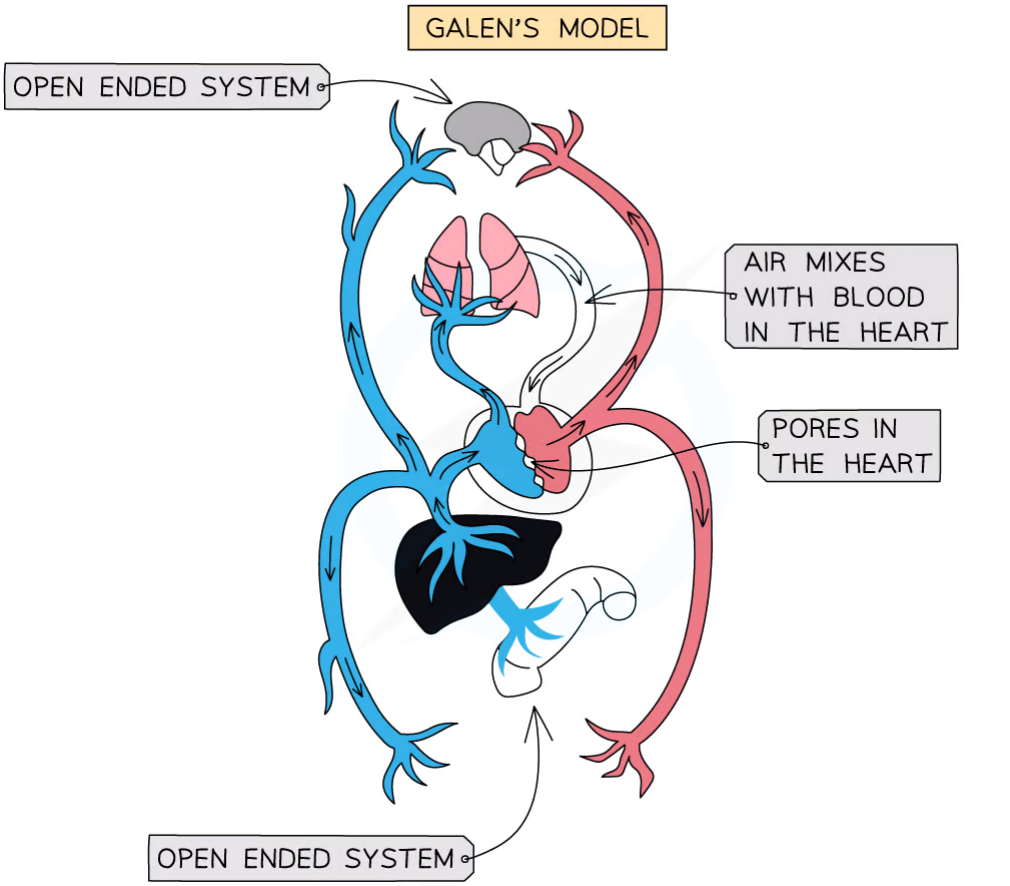
NOS: Theories are regarded as uncertain; William Harvey overturned theories developed by the ancient Greek philosopher Galen on movement of blood in the body

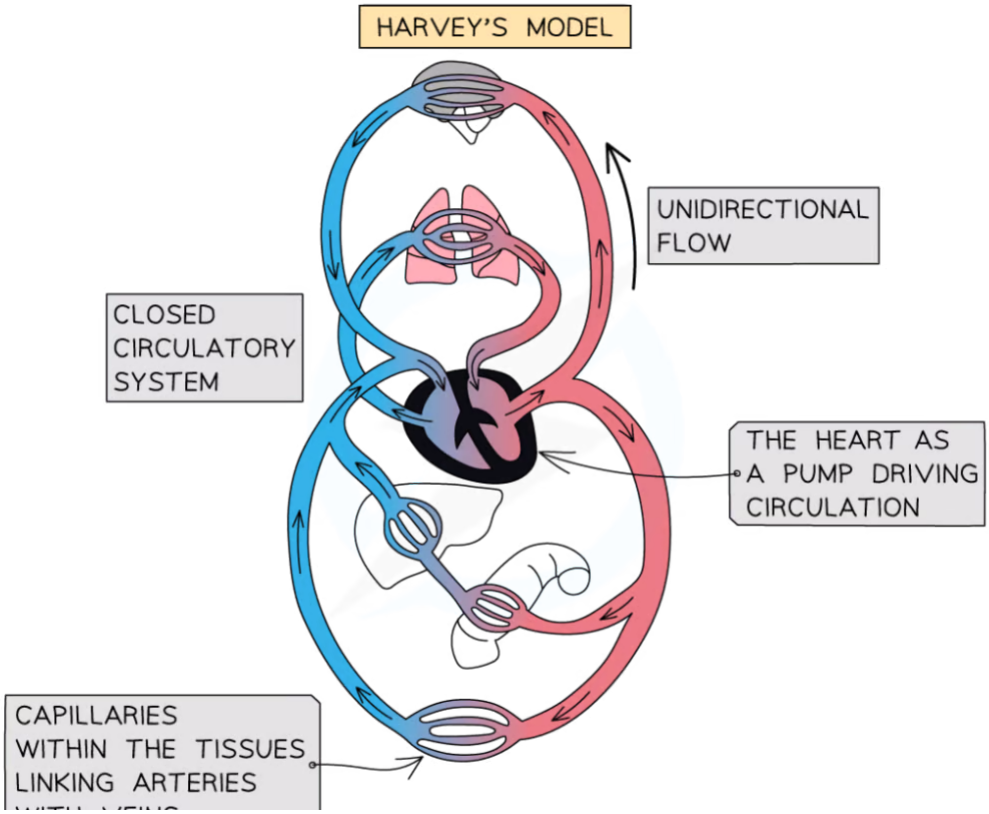
- A theory can be defined as:
  - **A carefully thought-out idea, with accompanying evidence, that explains observations of the natural world**
- Theories are often **constructed using the scientific method** which involves bringing together many facts and hypotheses
  - There is always a level of **uncertainty** when using scientific methods
  - Uncertainty can be due to
    - Natural **variability of individual organisms**
    - **Accuracy** of measurements taken
- Theories can therefore be regarded as **uncertain** due to the **uncertainties in the methods used**
- New technology or the discovery of new evidence often results in theories being falsified or overturned
- An example of the **falsification of a set of theories** is that of Galen's theories about the blood and circulation
  - **Galen** was an **ancient Greek philosopher** and surgeon who developed the following theories
    - Blood is formed in the **liver from ingested food**
    - Blood is pumped backwards and forwards between the **liver** and the **right ventricle** in the heart
    - Some blood moves into the **left ventricle** through invisible **pores** and mixes with **air from the lungs**
    - This mixing of air with blood produces **spirits** which are distributed to the body via the **brain**
    - Blood is **consumed by the tissues** so that new blood must be continuously made
  - Galen **failed to present any evidence** for his theories
- Galen's theories were **overturned** by English physician **William Harvey** through a series of **experiments and observations**
  - Harvey developed the following theories, which were ridiculed at the time
    - Blood is pumped to the **brain and body by the heart**
    - Blood circulates through the **pulmonary** and **systemic circulation systems**
    - **Capillaries exist** which link arteries to veins
    - Blood flow is too fast for blood to be consumed by the tissues; it would run out too quickly to be replaced. Instead, blood **returns to the heart** and **re-circulates**

- Harvey refused to accept Galen's theories without **direct evidence** and he toured Europe to **demonstrate evidence** for his own theories to others, eventually leading to acceptance of his new theories

YOUR NOTES

YOUR NOTES





WITH VEINS

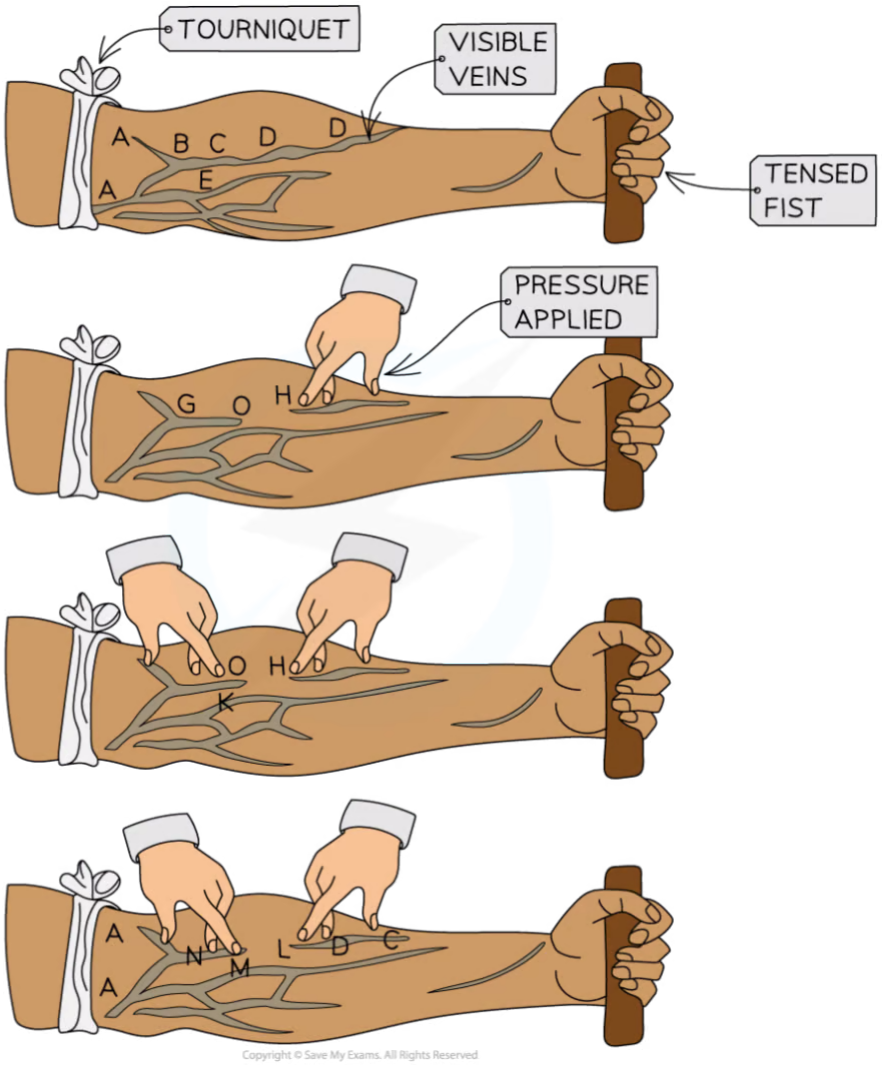
YOUR NOTES

Galen proposed a model which was later disproved by William Harvey

Discovery of the Heart as a Pump

YOUR NOTES

- Harvey used a **series of experiments** to show that blood flow is **unidirectional** and that the presence of **valves prevents backflow** in veins
  - Harvey attached a tourniquet to a person's upper arm and instructed them to grip tightly onto a pole
    - A tourniquet is a band applied to a limb to limit blood flow to the lower part of that limb
  - Once the veins became visible, Harvey proceeded to **apply pressure to the veins systematically** to show how blood flow was affected
  - He used this method to demonstrate how **blood moves unidirectionally** through the veins in the arm



William Harvey showed the movement of blood into the veins of the arms in this simple experiment

- He then demonstrated how the **heart acts as a pump** which forces blood out through the arteries; it then **circulates** around the body before it **returns to the heart** through the veins
- He also showed that the blood being pumped out of the heart was **travelling too quickly** to be constantly used up by the tissues, as described by Galen
- Despite not having powerful enough microscopes to see the capillaries, Harvey **predicted** their presence as small vessels which link the arteries to the veins

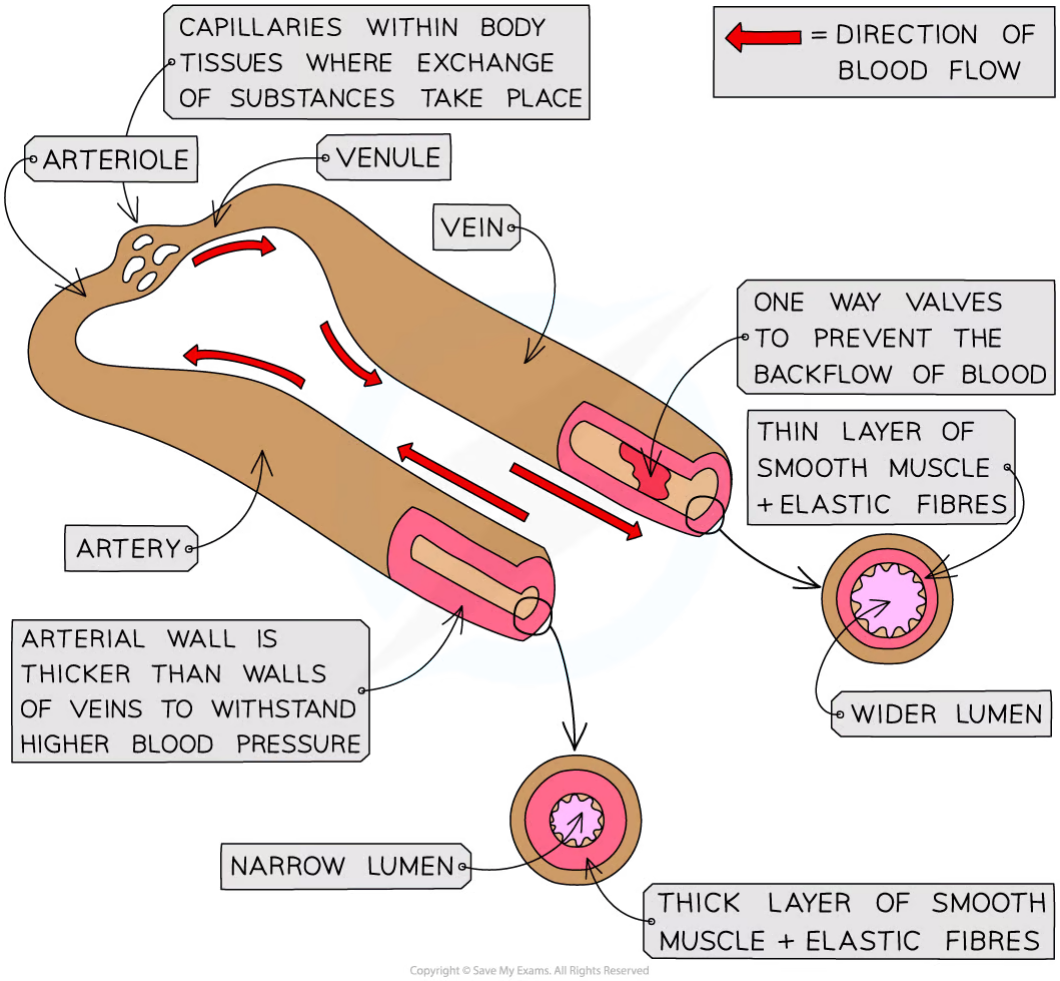
YOUR NOTES

YOUR NOTES

Arteries

Introduction to blood vessels

- The **circulatory system** of the human body contains several different types of **blood vessel**:
  - Arteries
  - Arterioles
  - Capillaries
  - Venules
  - Veins
- Each type of blood vessel has a **specialised structure** that relates to the function of that vessel



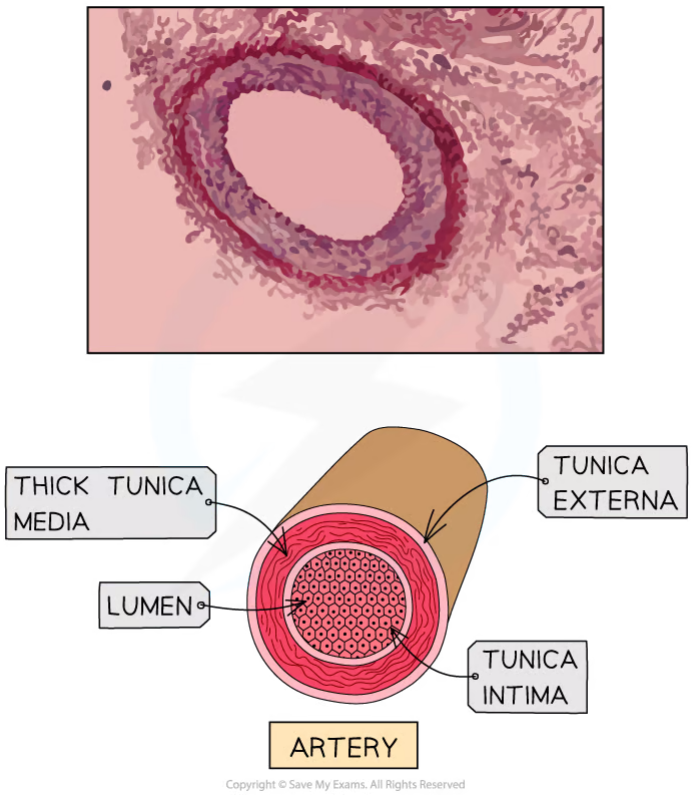
The circulatory system includes several blood vessels, each specialised to carry out its function

Structure and function of arteries

YOUR NOTES ⬇

- **Arteries** transport blood away from the heart at high pressure
  - Blood travels from the ventricles to the tissues of the body
  - Remember; **a**rteries carry blood **a**way from the heart
- Artery walls consist of **three layers**:
  - The **tunica intima** is the innermost layer and is made up of **an endothelial layer, a layer of connective tissue** and **a layer of elastic fibres**
    - The endothelium is one cell thick and lines the lumen of all blood vessels. It is very smooth and reduces friction for free blood flow
  - The **tunica media** is made up of **smooth muscle cells** and a **thick layer of elastic tissue**
    - Arteries have a **thick** tunica media
    - The layer of muscle cells strengthen the arteries so they can **withstand high pressure**
      - Blood leaves the heart under high pressure
    - Muscles cells can also **contract or relax** to control the diameter of the lumen and **regulate blood pressure**
    - The elastic tissue helps to **maintain blood pressure** in the arteries. It **stretches** and **recoils** to even out fluctuations in pressure
  - The **tunica externa** covers the exterior of the artery and is mostly made up of **collagen**
    - Collagen is a strong protein and protects blood vessels from damage by over-stretching
- Arteries have a **narrow lumen** which helps to maintain a high blood pressure
- A **pulse** is present in arteries due to blood leaving the heart under high pressure

YOUR NOTES



Arteries have thick muscular walls made up of three layers of tissue and a narrow lumen

Structure and function of arterioles

- **Arterioles** branch off from arteries forming narrower blood vessels which transport blood into capillaries
- Arterioles are similar in structure to arteries, but they have a **lower proportion of elastic fibres** and a **large number of muscle cells**
- The presence of muscle cells allows them to **contract** and close their lumen to **regulate blood flow** to specific organs
    - Eg. during exercise blood flow to the stomach and intestine is reduced while blood flow to the muscles increases

Arterial blood pressure

- Arteries, and to a slightly lesser extent arterioles, must be able to **withstand high pressure** generated by the contracting heart, and both must **maintain this pressure** when the heart is relaxed
- **Muscle** and **elastic fibres** in the arteries help to maintain the **blood pressure** as the heart contracts and relaxes
    - **Systolic pressure** is the peak pressure point reached in the arteries as the blood is forced out of the ventricles at high pressure
        - At this point, the walls of the arteries are forced outwards, enabled by the **stretching** of elastic fibres
    - **Diastolic pressure** is the lowest pressure point reached within the artery as the heart relaxes

YOUR NOTES

- At this point, the stretched elastic fibres **recoil** and force the blood onward through the lumen of the arteries
  - This maintains high pressure throughout the heart beat cycle

- Vasoconstriction of the circular muscles of the arteries can increase blood pressure by **decreasing the diameter of the lumen**
- Vasodilation of the circular muscles causes blood pressure to decrease by **increasing the diameter of the lumen**

Exam Tip

Be careful with the language you use to describe the roles of muscle and elastic tissue; muscle can **contract** and **relax**, while elastic tissue can **stretch** and **recoil**.

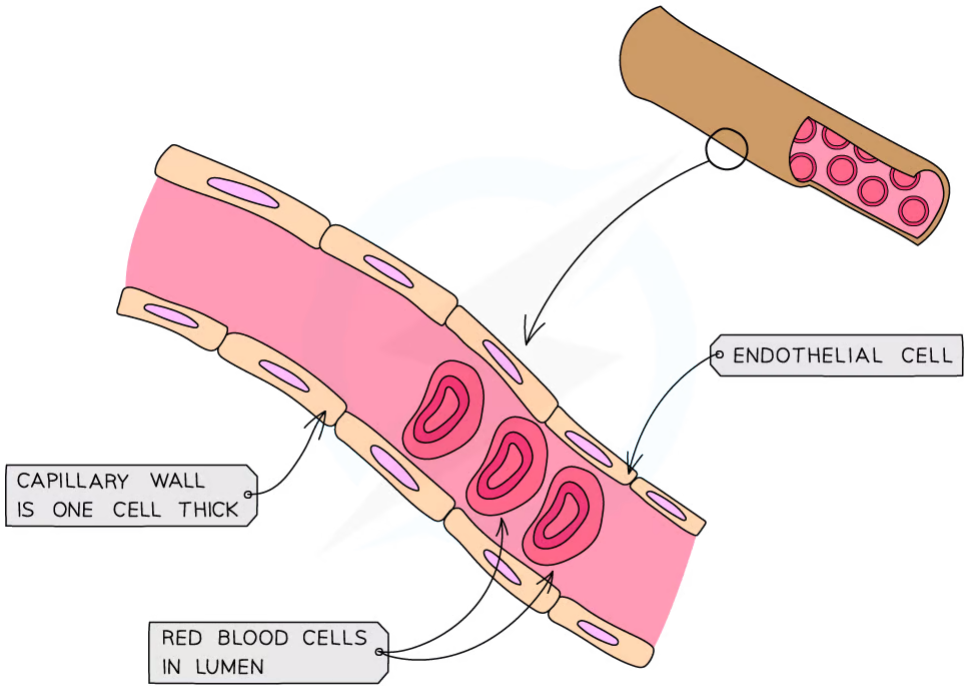
Capillaries

YOUR NOTES

Structure and function of capillaries

- **Capillaries** provide the **exchange surface** in the tissues of the body through a network of vessels called capillary beds
  - The wall of a capillary is made from a **single layer of endothelial cells** (this layer is also found lining the lumen in arteries and veins)
    - Being just **one cell thick** reduces the **diffusion distance** for **oxygen** and **carbon dioxide** between the blood and the tissues of the body
  - The thin endothelium cells also have gaps between them called **pores** which allow blood plasma to leak out and form **tissue fluid**
    - Tissue fluid contains **oxygen, glucose** and other small molecules from the blood plasma
    - Large molecules such as proteins usually can't fit through the pores into the tissue fluid
    - Tissue fluid surrounds the cells, enabling **exchange** of substances such as oxygen, glucose, and carbon dioxide
    - The **permeability** of capillaries can vary depending on the requirements of a tissue
  - Capillaries have a lumen with a **small diameter**
    - Red blood cells squeeze through capillaries in single-file
    - This forces the blood to travel slowly which provides more opportunity for diffusion to occur
  - Capillaries form **branches in between the cells;** this is the capillary bed
    - These branches increase the **surface area** for diffusion of substances to and from the cells
    - Being so close to the cells also reduces the **diffusion distance**

YOUR NOTES



Capillaries have a narrow lumen and walls that are one cell thick

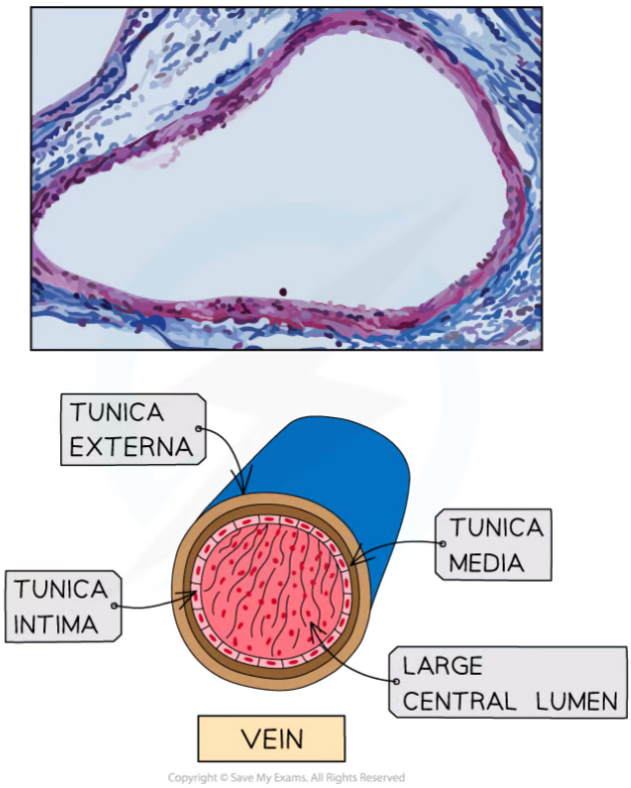
Veins

YOUR NOTES

Structure and function of veins

- **Veins** transport blood to the heart at **low pressure**
  - Remember; ve**in**s carry blood **in**to the heart
- They receive blood that has passed through capillary networks, across which **pressure has dropped** due to the slow flow of blood
- The structure of veins differs from arteries:
  - The **tunica media** is much **thinner** in veins
    - There is no need for a thick muscular and elastic layer as veins don't have to maintain or withstand high pressure
  - The **lumen** of veins is much **wider in diameter** than that of arteries
    - A larger lumen helps to ensure that blood returns to the heart at an adequate **speed**
    - A large lumen **reduces friction** between the blood and the endothelial layer of the vein
    - The rate of blood flow is slower in veins but a larger lumen means the volume of blood delivered per unit of time is equal
  - Veins contain **valves**
    - These **prevent the back flow** of blood that can result under low pressure, helping return blood to the heart
    - Movement of the skeletal muscles pushes the blood through the veins, and any blood that gets pushed backwards gets caught in the valves; this blood can then be moved forwards by the next skeletal muscle movement
- A pulse is **absent** in veins; the pressure changes taking place due to the beating of the heart are no longer present

YOUR NOTES



Veins have a structure similar to arteries with three layers of tissue and a large lumen

Structure and function of venules

- Venules connect the **capillaries to the veins**
- They have **few** or **no elastic fibres** and a **large lumen**
  - As the blood is at low pressure after passing through the capillaries there is no need for a muscular layer to maintain pressure
  - The large lumen enables a large volume of blood to be transported

Exam Tip

For "Explain" questions, remember to pair a description of a structural feature to an explanation of how it helps the blood vessel to function. For example, "Capillaries have walls that are one-cell thick, enabling quick and efficient diffusion of substances due to a short diffusion distance."

YOUR NOTES

Double Circulation

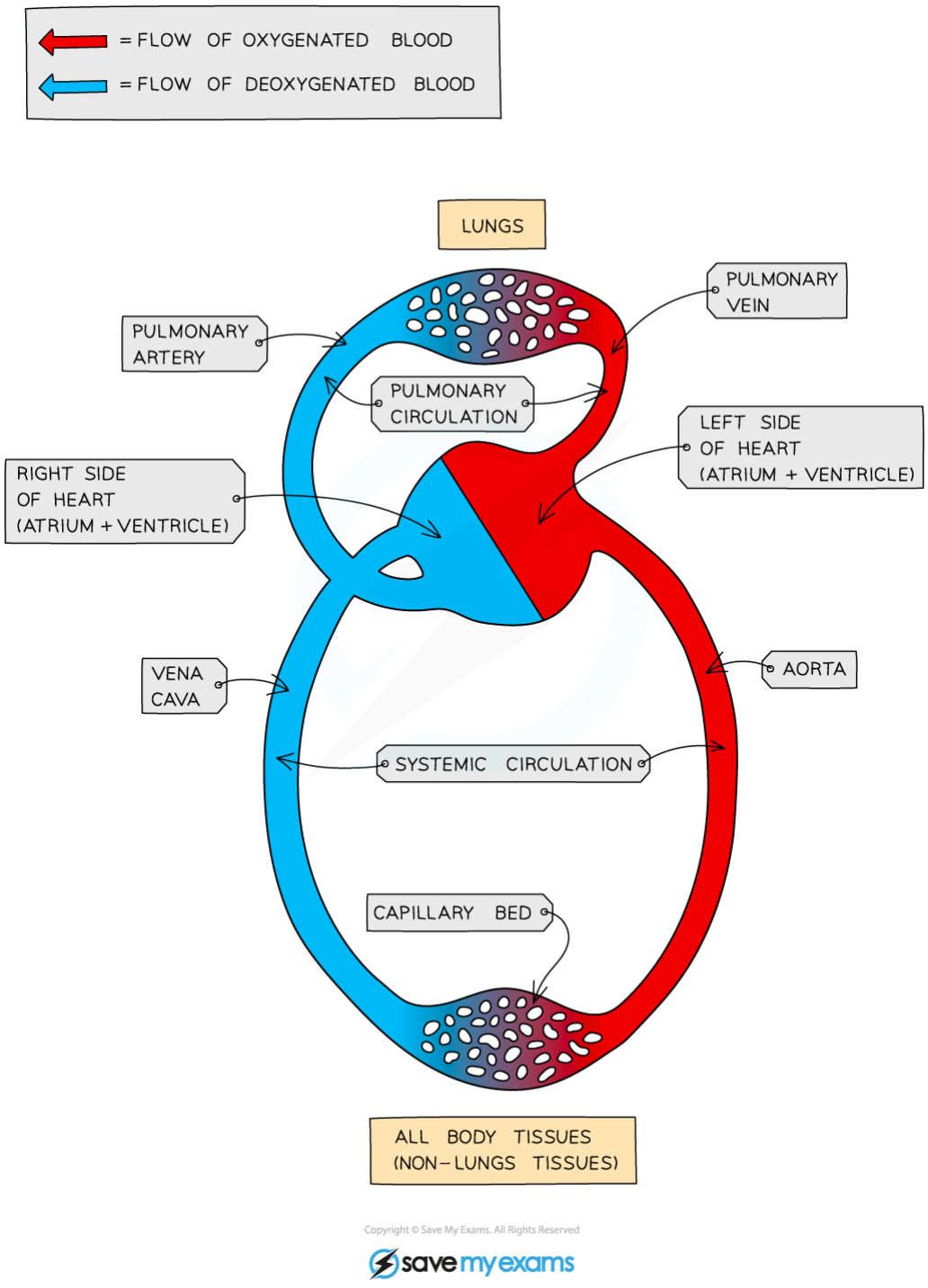
The need for a circulatory system

- All organisms need to **transport** materials to where they are needed inside their tissues
  - **Small organisms** (or relatively inactive animals like jellyfish) can rely on **diffusion** alone to transport oxygen, carbon dioxide and nutrients around their bodies
  - **Larger organisms** have more layers of cells, so diffusion alone is insufficient for transport of materials between cells further from the exchange surface of the organism
- **Circulatory systems** are systems which **transport fluids** containing materials needed by the organism, as well as waste materials that need to be removed
  - Circulatory systems ensure that fluids containing these substances reach all of the cells in an organism **quickly enough** to supply their needs and remove waste

Humans have a closed, double circulatory system

- A **closed** circulatory system is one in which blood is **contained within a network of blood vessels**
  - As opposed to an open circulatory system in which the fluid fills the body cavity e.g. as in insects
- A **double** circulatory system passes through the heart **twice** for every **one** complete circuit of the body, with blood passing through **two separate circuits** known as **pulmonary** and **systemic** circulation
  - In the **pulmonary circulatory system**
    - The right side of the heart pumps **deoxygenated** blood to the **lungs** for gas exchange
    - **Blood pressure is lower** in the pulmonary system; this prevents damage to the lungs
  - In the **systemic circulatory system**
    - **Oxygenated** blood returns to the left side of the heart from the lungs
    - The left ventricle then pumps the oxygenated blood at **high pressure** around the **body**

YOUR NOTES



The double circulatory system in mammals

YOUR NOTES

Main Circulatory System Structures Table

Structure	Function
Heart	A hollow, muscular organ located in the chest cavity which pumps blood. Cardiac muscle tissue is specialised for repeated involuntary contraction without rest.
Arteries	Blood vessels which carry blood away from the heart. The walls of the arteries contain lots of muscle and elastic tissue and a narrow lumen, to maintain high blood pressure. Arteries range from 0.4 – 2.5cm in diameter.
Arterioles	Small arteries which branch from larger arteries and connect to capillaries. These are around 30 μm in diameter.
Capillaries	Tiny blood vessels (5–10 μm in diameter) which connect arterioles and venules. Their size means they pass directly past cells and tissues and perform gas exchange and exchange of substances such as glucose.
Venules	Small veins which join capillaries to larger veins. They have a diameter of 7 μm – 1mm.
Veins	Blood vessels which carry blood back towards the heart. The walls of veins are thin in comparison to arteries, having less muscle and elastic tissue but a wider lumen. Valves help maintain blood flow back towards the heart.

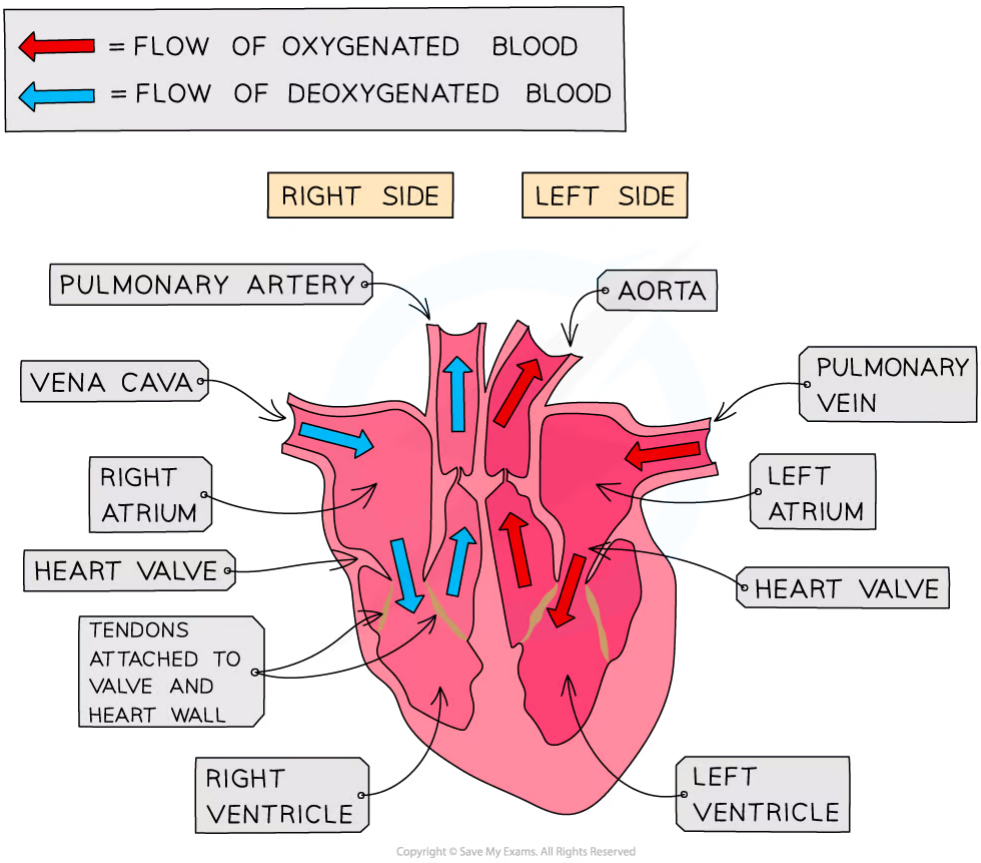
YOUR NOTES

Introduction to the Heart

Mammalian heart structure

- The heart is a hollow, **muscular organ** located in the chest cavity
- The heart is divided into **four chambers**
  - The two top chambers are **atria**
  - The bottom two chambers are **ventricles**
- The left and right sides of the heart are separated by a wall of muscular tissue called the **septum**.
  - The septum is very important for ensuring blood doesn't mix between the left and right sides of the heart
- **Valves** are important for keeping blood flowing **forward** in the right direction and stopping it flowing backwards. They are also important for maintaining the correct pressure in the chambers of the heart
  - The atria and ventricles are separated by the **atrioventricular valves**
  - The ventricles and the arteries that leave the heart are separated by **semi-lunar valves**
    - The right ventricle and the pulmonary artery are separated by the **pulmonary valve**
    - The left ventricle and aorta are separated by the **aortic valve**
- There are two blood vessels bringing blood to the heart; the **vena cava** and **pulmonary vein**
- There are two blood vessels taking blood away from the heart; the **pulmonary artery** and **aorta**

YOUR NOTES



The human heart has four chambers and is separated into two halves by the septum

Sinoatrial Node

YOUR NOTES

Contraction of the heart muscle

- The contraction of the heart is called **systole**, while the relaxation of the heart is called **diastole**
- **Atrial systole** is the period when the atria are contracting and **ventricular systole** is when the ventricles are contracting
- Atrial systole happens around 0.13 seconds after ventricular systole
- Atrial systole forces blood **from the atria into the ventricles**
- During ventricular systole, blood is forced **from the ventricles into the pulmonary artery** and **aorta**
- One systole and diastole makes a heartbeat and lasts around 0.8 seconds in humans.
- This is the **cardiac cycle**

Initiation of the heartbeat by the sinoatrial node

- The heart muscle is **myogenic**, meaning that the heart will beat without any external stimulus from other organs or the nervous system
  - This intrinsic control causes the heart to beat at around 60 beats per minute
- The heart beat is initiated by a **group of cells** in the wall of the **right atrium** called the **sinoatrial node** (**SAN**)
- The cells of the sinoatrial node **depolarise**, reversing the charge across their membranes
  - This triggers a **wave of depolarisation** that spreads across the rest of the heart
- The sinoatrial node is considered to be the **pacemaker** of the heart because it **initiates** the heart beat and so controls the **speed at which the heart beats**
  - Note that **artificial pacemakers** are electronic devices implanted just underneath the skin. They can be used to replace or regulate the sinoatrial node if it becomes defective

Cardiac Cycle

YOUR NOTES

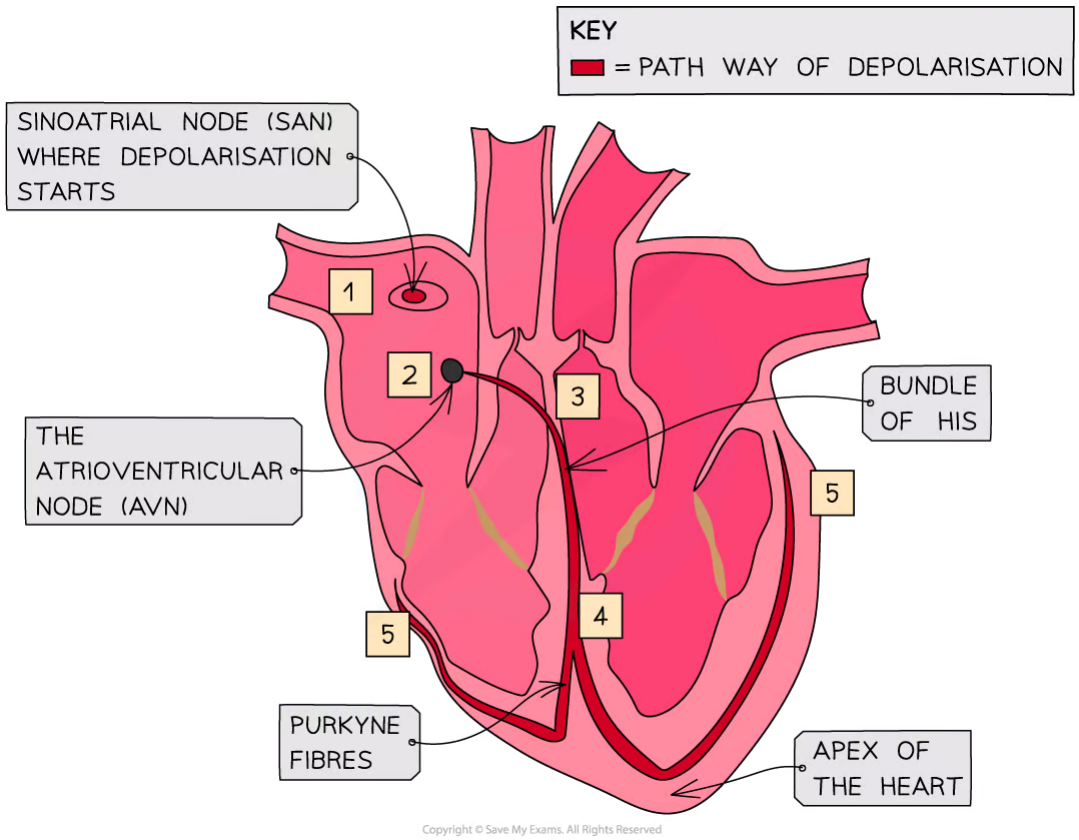
Electrical control of the cardiac cycle

- The **cardiac cycle** is the series of events that take place in **one heart beat**, including **atrial** and **ventricular systole**
- The cardiac cycle is controlled by **electrical signals** that are initiated in the **sinoatrial node**
  - Depolarisation of the cells in the **sinoatrial node** sends an electrical signal over the **atria**, causing them to contract in **atrial systole**
  - The electrical signal then reaches a region of **non-conducting** tissue which prevents it from spreading straight to the ventricles; this causes the signal to pause for around 0.1 s
    - This delay means that the atria can **complete their contraction** before the ventricles begin to contract
  - The electrical signal is carried to the ventricles via the **atrioventricular node** (**AVN**)
    - This is a region of conducting tissue between atria and ventricles
  - The signal then travels to the base of the heart via **conductive fibres** in the septum known as the bundle of His
  - The electrical signal is then carried through another set of conductive fibres called Purkyne fibres which spread around the sides of the ventricles, causing **contraction of the ventricles** from the apex, or base, of the heart upwards
    - This is called **ventricular systole**
    - Blood is forced out of the heart into the **pulmonary artery** and **aorta**

Electrical Control of the Cardiac Cycle Table

Stage in sequence	Event
1	Sinoatrial node sends out a wave of excitation
2	Atria contract
3	Atrioventricular node sends out a wave of excitation
4	Purkyne tissue conducts the wave of excitation
5	Ventricles contract

YOUR NOTES



The wave of depolarisation spreads across the heart in a coordinated manner

Worked Example

Explain the roles of the sinoatrial node, the atrioventricular node and the conductive fibres in a heartbeat.

The cells of the sinoatrial node depolarise and send out an electrical signal which spreads across both atria, causing atrial systole. Non-conducting tissue between the atria and ventricles prevents depolarisation from spreading to the ventricles, ensuring that the atria finish contracting before the ventricles begin. The atrioventricular node then sends the electrical signal to the apex of the ventricles via conductive fibres in the septum known as the bundle of His. The electrical signal is then carried upwards around the walls of the ventricles by conductive tissues called Purkyne fibres. This means that during ventricular systole, the blood contracts from its base and blood is pushed upwards and outwards.

Cardiac Cycle Pressure Changes

YOUR NOTES

- **Contraction** of the heart muscle causes an **increase in pressure** in the corresponding chamber if the heart, which then **decreases** again when the muscle **relaxes**
- Throughout the cardiac cycle, **heart valves open and close** as a result of **pressure changes** in different regions of the heart:
  - Valves **open** when the pressure of blood **behind them is greater than the pressure in front of them**
  - They **close** when the pressure of blood **in front of them is greater than the pressure behind them**
- Valves are an important mechanism **to stop blood flowing backwards**
- The pressure changes of the cardiac cycle can be represented in a graph

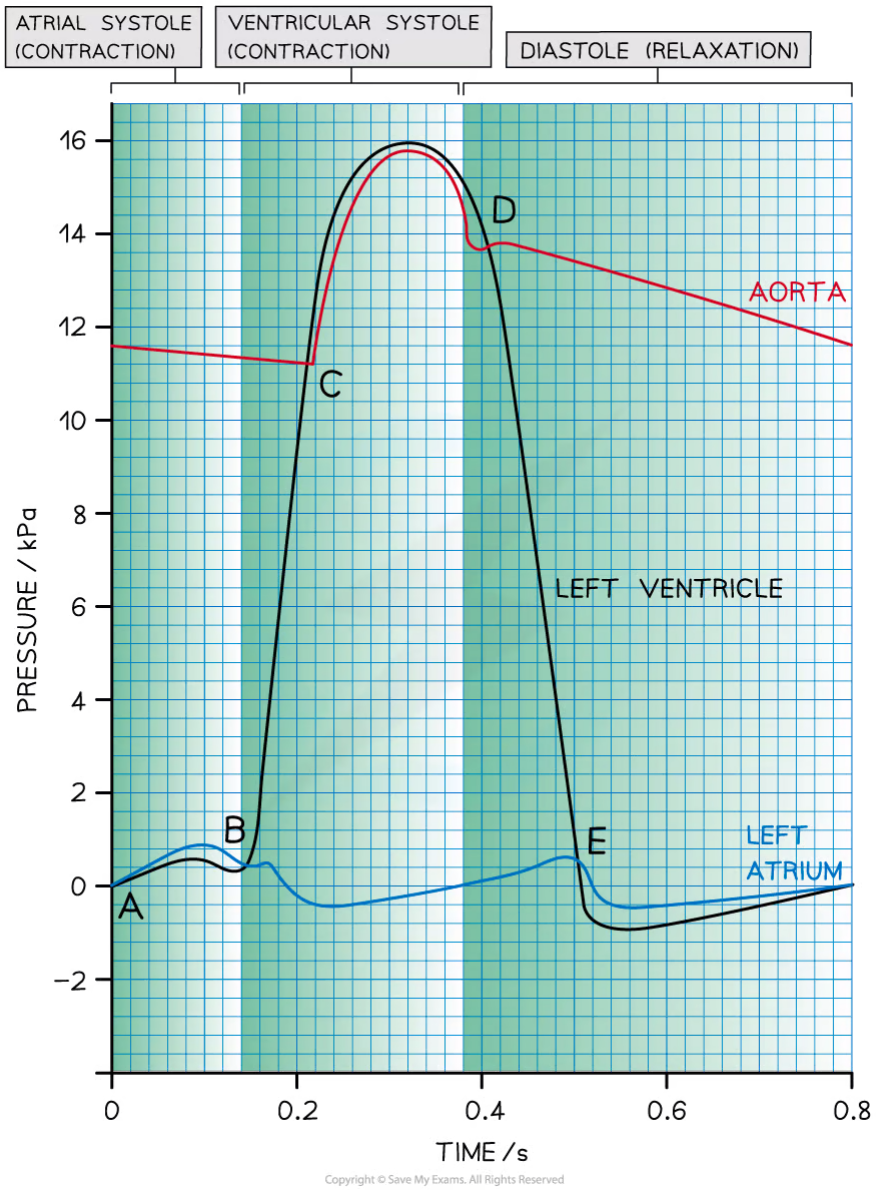
Pressure changes during diastole

- During **diastole**, the heart muscle is **relaxing**
  - During this period, blood begins to flow into the atria from the veins, **increasing the atrial pressure**
- Relaxed muscle in the heart walls **recoils**, **increasing the volume** of the chambers of the heart:
  - The **atrioventricular valves open** as the pressure in the atria is higher than the pressure in the ventricles
  - The **semilunar valves close** as the pressure in the pulmonary artery and aorta is higher than the pressure in the ventricles

Pressure changes during systole

- During **systole**, the heart **contracts** and pushes blood out of the heart
- The **contraction of the muscles** in the wall of the heart **reduces the volume** of the heart chambers and **increases the pressure** within that chamber
- In **atrial systole**, the atria contract
  - The **atrioventricular valves are open** as the pressure in the atria exceeds the pressure in the ventricles
  - The **semilunar valves are closed** as the pressure in the ventricles is less than the pressure in the aorta and pulmonary artery
- In **ventricular systole**, the ventricles contract
    - The **atrioventricular valves are closed** as the pressure in the ventricles exceeds the pressure in the atria
    - The **semilunar valves are open** as the pressure in the ventricles exceeds the pressure in the aorta and pulmonary artery

YOUR NOTES



Graph showing the pressure changes within the aorta, left atrium and left ventricle during the cardiac cycle. The atrioventricular valves open at E and close at B, while the semilunar valves open at C and close at D.

Analysing the cardiac cycle

- The lines on the graph represent the **pressure** of the left atrium, aorta, and the left ventricle
- The points at which the **lines cross each other** are important because they indicate when **valves open and close**

Point A - the end of diastole

- The atrium has filled with blood during the preceding diastole
- Pressure is higher in the atrium than in the ventricle, so the **AV valve is open**

Between points A and B - atrial systole

YOUR NOTES

- **Left atrium contracts,** causing an increase in atrial pressure and forcing blood into the left ventricle
- Ventricular pressure increases slightly as it fills with blood
- Pressure is higher in the atrium than in the ventricle, so the **AV valve is open**

Point B - beginning of ventricular systole

- **Left ventricle contracts** causing the ventricular pressure to increase
- Pressure in the left atrium drops as the muscle relaxes
- Pressure in the ventricle exceeds pressure in the atrium, so the **AV valve shuts**

Point C - ventricular systole

- The ventricle continues to contract
- Pressure in the left ventricle exceeds that in the aorta
- **Aortic valve opens** and blood is forced into the aorta

Point D - beginning of diastole

- Left ventricle has been emptied of blood
- Muscles in the walls of the left ventricle relax and pressure falls below that in the newly filled aorta
- **Aortic valve closes**

Between points D and E - early diastole

- The ventricle **remains relaxed** and ventricular pressure continues to decrease
- In the meantime, blood is **flowing into the relaxed atrium** from the pulmonary vein, causing an increase in pressure

Point E - diastole

- The relaxed left atrium fills with blood, causing the pressure in the atrium to exceed that in the newly emptied ventricle
- **AV valve opens**

After point E - late diastole

- There is a short period of time during which the **left ventricle expands** due to relaxing muscles
- This increases the internal volume of the left ventricle and **decreases the ventricular pressure**
- At the same time, blood is flowing slowly through the newly opened AV valve into the left ventricle, causing a **brief decrease in pressure** in the left atrium
- The pressure in both the atrium and ventricle then **increases slowly** as they continue to fill with blood

Exam Tip

When looking at the heart, remember the right side of the heart will appear on the page as being on the left. This is because the heart is labelled as if it were in your body and flipped around. Remember that the heart muscle is **myogenic**, which means that the heart will generate a heartbeat by itself and without any other stimulation. Instead, the electrical activity of the heart regulates the heart rate.The maximum pressure in the ventricles is substantially higher than in the atria. This is because there is much **more muscle** in the thick walls of the ventricles which can **exert more force** when they contract.

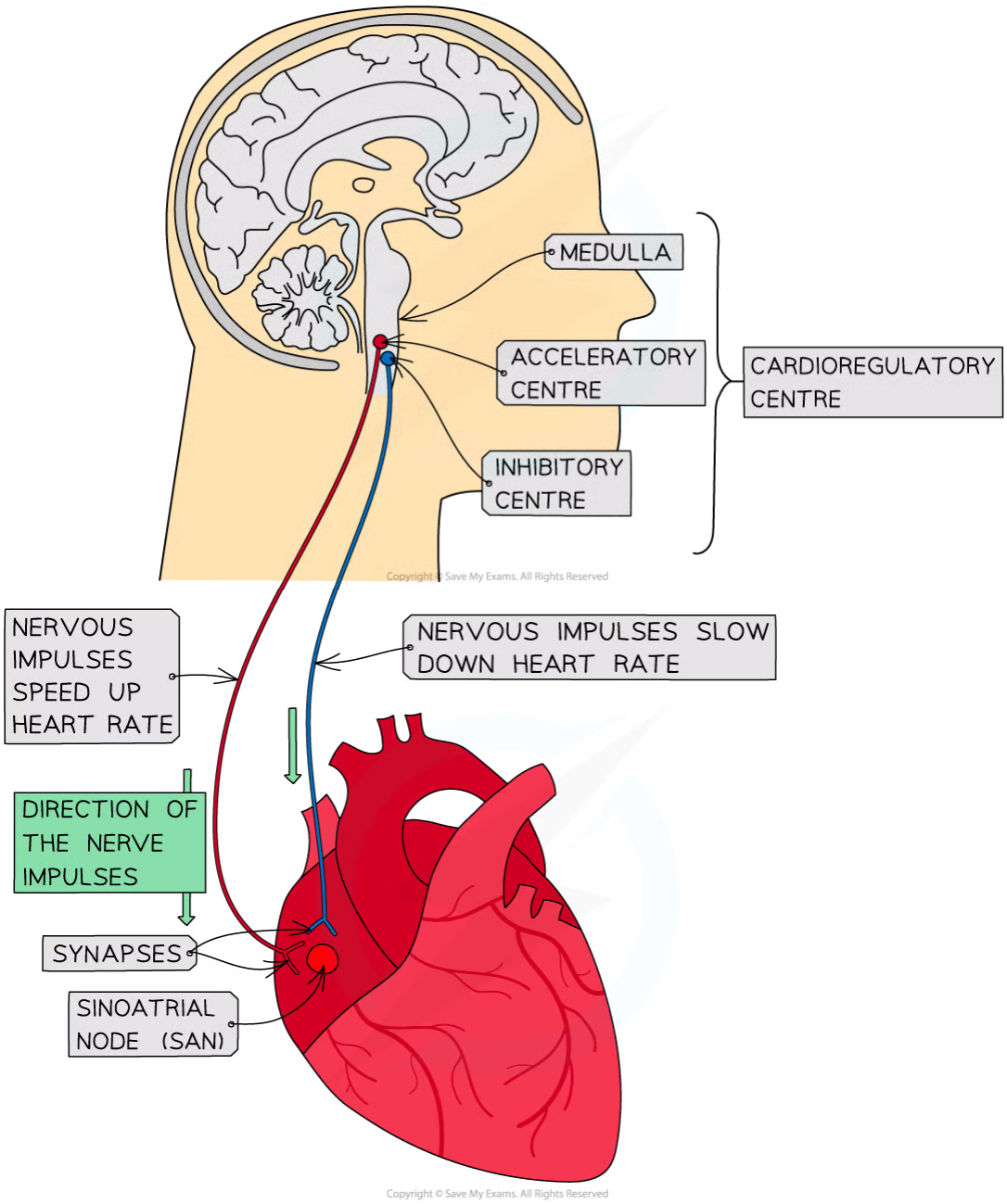
YOUR NOTES

YOUR NOTES

Heart Rate: Alteration by Nervous System

- Although the heart muscle maintains a base heart rate via myogenic stimulation, there are several circumstances that can cause an individual's heart rate to change, e.g.
  - Exercise
  - Stress
  - Relaxation
- The **brain** is involved in the regulation of heart rate, though it does not require conscious thought
  - The branch of the nervous system that does not require conscious thought is known as the **autonomic nervous system**
- The area of the brain that controls heart rate is the **cardiovascular centre,** located in a region of the brain called the **medulla**
- The medulla is found at the base of the brain near the top of the **spinal cord**
- Two nerves connect the medulla with **the sinoatrial node** (SAN):
  - One nerve connects to the **acceleratory centre**, which causes the heart to **speed up**
    - This happens in response to **low blood pressure, low oxygen concentrations** and **low pH**
    - These changes might occur during **exercise**
    - The blood vessels dilate, causing a decrease in blood pressure
    - The muscle cells are using up oxygen at a faster rate, causing blood oxygen levels to drop
    - The production of carbon dioxide by respiring cells causes blood pH to decrease
  - The other nerve connects to the **inhibitory centre**, which causes the heart to **slow down**
    - This happens in response to **high blood pressure, high oxygen concentrations and high pH**
    - These changes are likely to occur when the body is at rest

YOUR NOTES



The heart rate is controlled by the cardiovascular centre in the medulla

Heart Rate: Alteration by Hormonal System

- **Epinephrine,** also called **adrenaline,** is produced by the **adrenal glands**, located above the kidneys, in times of fear, stress, or excitement
- The **brain** controls the release of epinephrine from the adrenal glands
- Epinephrine **increases** the **heart rate** and **boosts** the delivery of **oxygen** and **glucose** to the **brain** and **muscles**, preparing the body for 'flight or fight'
    - Increased glucose and oxygen are needed by the cells for **aerobic respiration** to **release** energy, e.g. to fuel the muscles to move/run away!

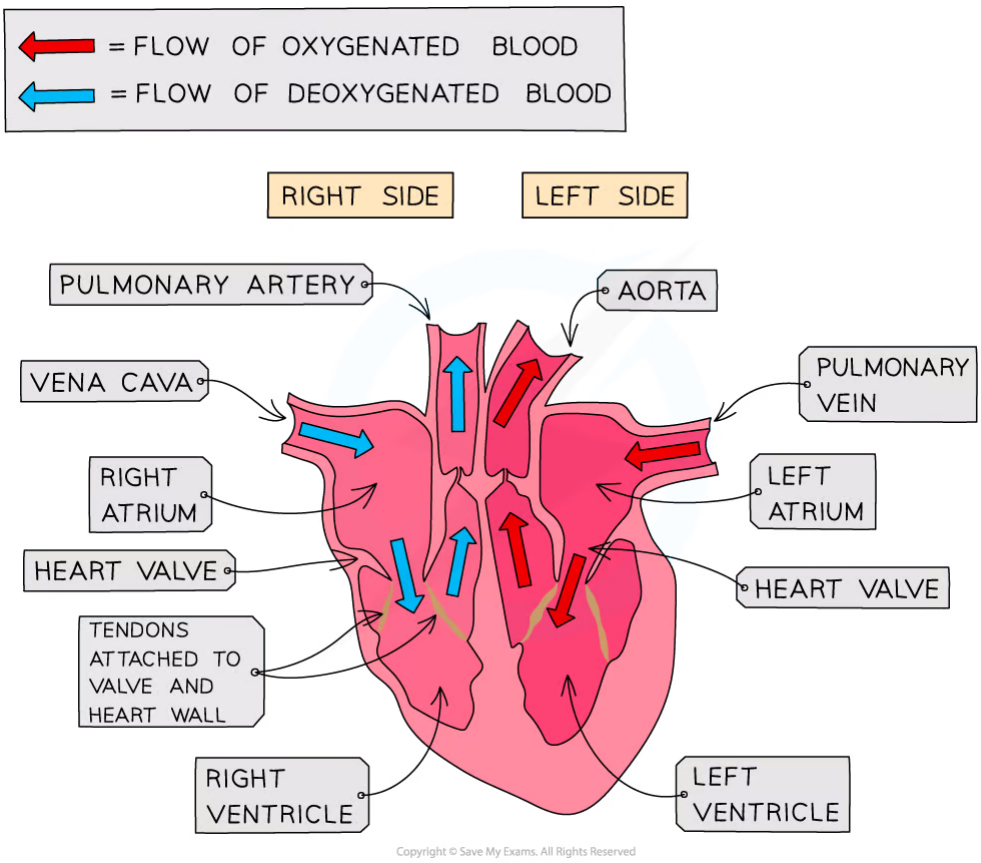
YOUR NOTES

The Structure of the Heart

Heart structure

- The heart has **two sides**:
  - The **left** side pumps **oxygenated** blood around the body in the **systemic circulation**
  - The **right** side pumps **deoxygenated** blood to the lungs in the **pulmonary circulation**
- The left and right sides of the heart are separated by a wall of muscular tissue called the **septum**.
  - The septum is very important for ensuring blood doesn't mix between the left and right sides of the heart
- The heart is divided into **four chambers**
  - The two top chambers are **atria** (singular atrium) - they receive blood from the veins and pump it through to the ventricles
  - The bottom two chambers are **ventricles –** they receive blood from the atria and pump it out into the arteries
- **Valves** are important for keeping blood flowing forward in the right direction and stopping it flowing backwards. They are also important for maintaining the **correct pressure** in the chambers of the heart
  - The atria and ventricles are separated by the **atrioventricular valves**
    - The right atrium and ventricle are separated by the tricuspid valve
    - The left atrium and ventricle are separated by the bicuspid valve
  - The ventricles and the arteries that leave the heart are separated by **semi-lunar valves**
    - The right ventricle and the pulmonary artery are separated by the **pulmonary valve**
    - The left ventricle and aorta are separated by the **aortic valve**
- There are two blood vessels bringing blood into the heart; the **vena cava** and **pulmonary vein**
- There are two blood vessels taking blood out of the heart; the **pulmonary artery** and **aorta**

YOUR NOTES



The human heart has four chambers and is separated into two halves by the septum

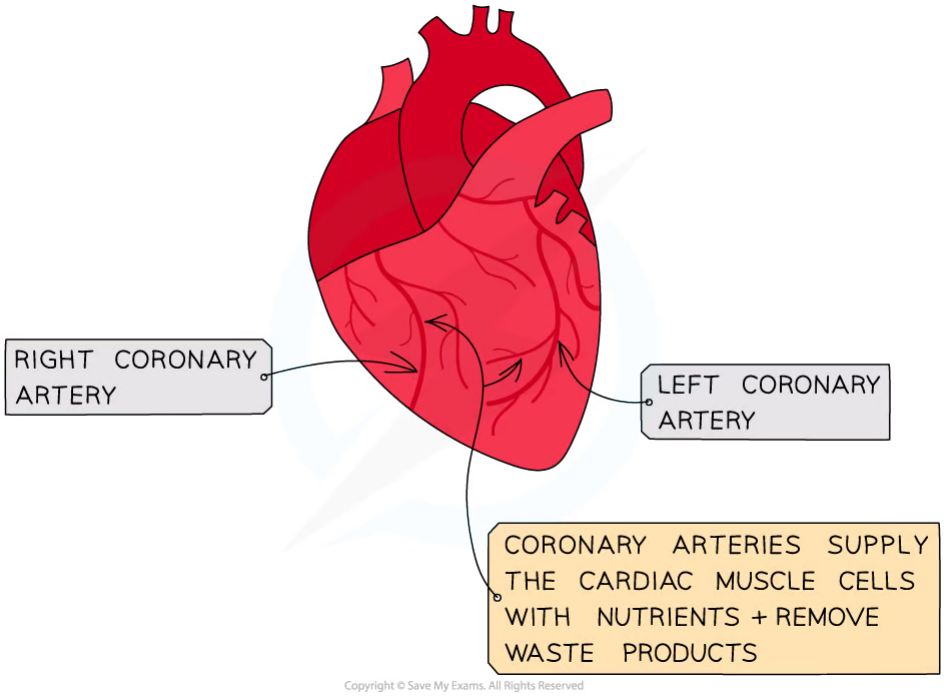
The pathway of blood through the heart

- **Deoxygenated blood** coming from the body flows through the **vena cava** and into the **right atrium**
- The **atrium contracts** and the blood is forced through the **atrioventricular** (tricuspid) **valve** into the **right ventricle**
- The ventricle **contracts** and the blood is pushed through the **semilunar valve** into the **pulmonary artery**
- The blood travels to the **lungs** and moves through the capillaries past the alveoli where **gas exchange** takes place
  - **Low pressure** blood flow on this side of the heart prevents damage to the capillaries in the lungs
- **Oxygenated blood** returns via the **pulmonary vein** to the **left atrium**
- The **atrium contracts** and forces the blood through the **atrioventricular** (bicuspid) **valve** into the **left ventricle**
- The ventricle **contracts** and the blood is forced through the **semilunar valve** and out through the **aorta**
  - Thicker muscle walls of the left ventricle produce a **high enough pressure** for the blood to travel around the whole body

Coronary arteries

YOUR NOTES

- The heart is a muscle and so requires its own blood supply to enable its cells to carry out **aerobic respiration**
- The heart receives blood through arteries on its surface called **coronary arteries**
- It's important that these arteries remain clear of blockages called plaques, as this could lead to angina or a heart attack (myocardial infarction)



The coronary arteries cover the outside of the heart, supplying it with oxygenated blood

Dissection of a mammalian heart

- Dissections are a vital part of scientific research
- They allow for the internal structures of organs to be examined so that theories can be made about how they function

Apparatus

- Scissors
- Scalpel
- Tweezers / Forceps
- Dissection board
- Paper towels
- Biological specimen
- Pins
- Gloves
- Goggles

Method

- A lab coat, gloves and eye protection should be worn
  - This is done to avoid contamination with biological material which could cause an allergic reaction or contain harmful microorganisms

YOUR NOTES ⬇

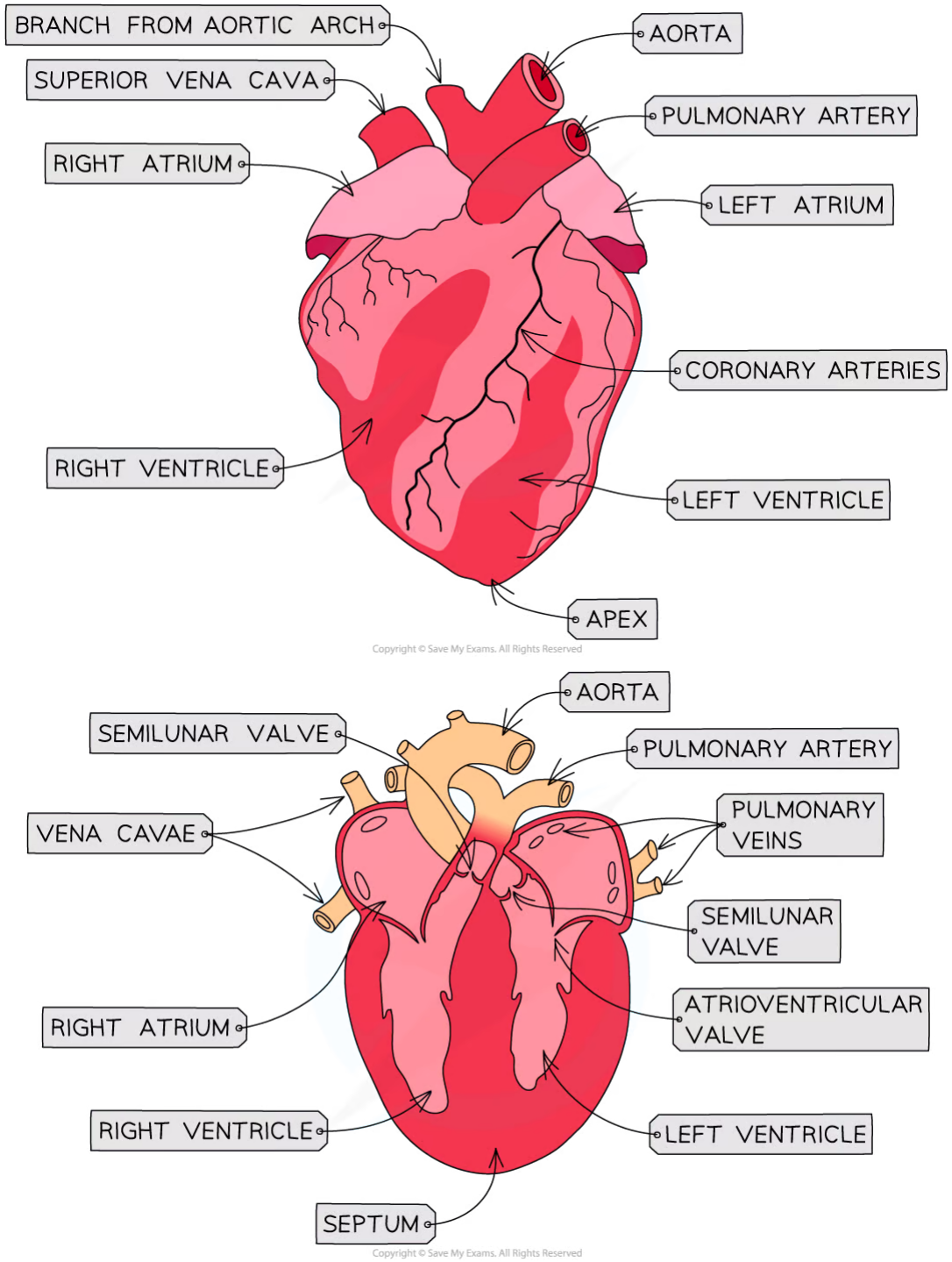
- Place the specimen on the dissecting board
- Use the tools to access the desired structure
  - When using the scalpel cut **away** from your body and keep your fingers **far from the blade** to reduce the chance of cutting yourself
  - Scissors can be used for cutting large sections of tissue (cuts do not need to be precise)
  - Scalpel enables finer, more precise cutting and needs to be sharp to ensure this
- Use pins to move the other sections of the specimen aside to leave the desired structure exposed

Identifying structures during the dissection

- Observe the outside of the heart to identify the **coronary arteries** supplying the cardiac muscle with a oxygenated blood and nutrients
  - The coronary arteries branch off the **aorta** near to the **semilunar valves**
  - The coronary arteries are often surrounded by white, fatty tissue
- Position the heart and study it from the top, you should be able to identify
  - **Arteries** leaving the heart - these can be identified by the thicker walls
    - Poke a glass rod through the **aorta** to feel the thicker walls of the left ventricle and through the **pulmonary artery** to feel the thinner walls of the right ventricle
  - **Veins** entering the heart - these can be identified by their thinner walls
    - Poking a glass rod through the **pulmonary vein** will lead to the left atrium and poking a glass rod through the superior or inferior **vena cava** will lead to the right atrium.
- Lay the heart down on its flatter side, this is the **dorsal side**.
  - Dorsal refers to the back of an organism
- The **ventral side** is now closest to you with the pulmonary artery facing outwards and in front of the aorta
  - Ventral refers to the front of an organism
- Make an incision from the Aorta, underneath the pulmonary artery and around the **apex** of the heart to cut the heart into halves
- This should open up the heart to show the **ventricles** so that you can compare the thickness of the walls
- The **atrioventricular valves** should also be visible as a white flap of connective tissue attached by tendinous cords which prevent inversion of the valve
  - The tendinous cords are stringy in appearance and are sometimes referred to as the heartstrings
- The **atria** are wrinkled in appearance and can be tricky to see compared with the ventricles.
  - They sit just above the atrioventricular valves and are the entry point for the veins (the pulmonary vein and the vena cava)
  - They are significantly smaller than the ventricles
  - It is possible that the atria and blood vessels may be sliced off some specimens
- Observe the **septum** of the heart which separates the left and right-hand sides. The septum contains the **conductive fibres** which stimulate contraction, however, these are

not visible to the eye

YOUR NOTES



Following a careful method during a heart dissection will allow you to identify the different structures

YOUR NOTES

Exam Tip

Remember:

- **A**rteries carry blood **a**way from the heart
- Ve**in**s carry blood **in**to the heart

When explaining the route through the heart we usually describe it as one continuous pathway with only one atrium or ventricle being discussed at a time, but remember that in reality, both atria contract at the same time and both ventricles contract at the same time

Also, the heart is **labelled as if it was in the chest** so the left side of a diagram is actually the right hand side and vice versa

Atherosclerosis

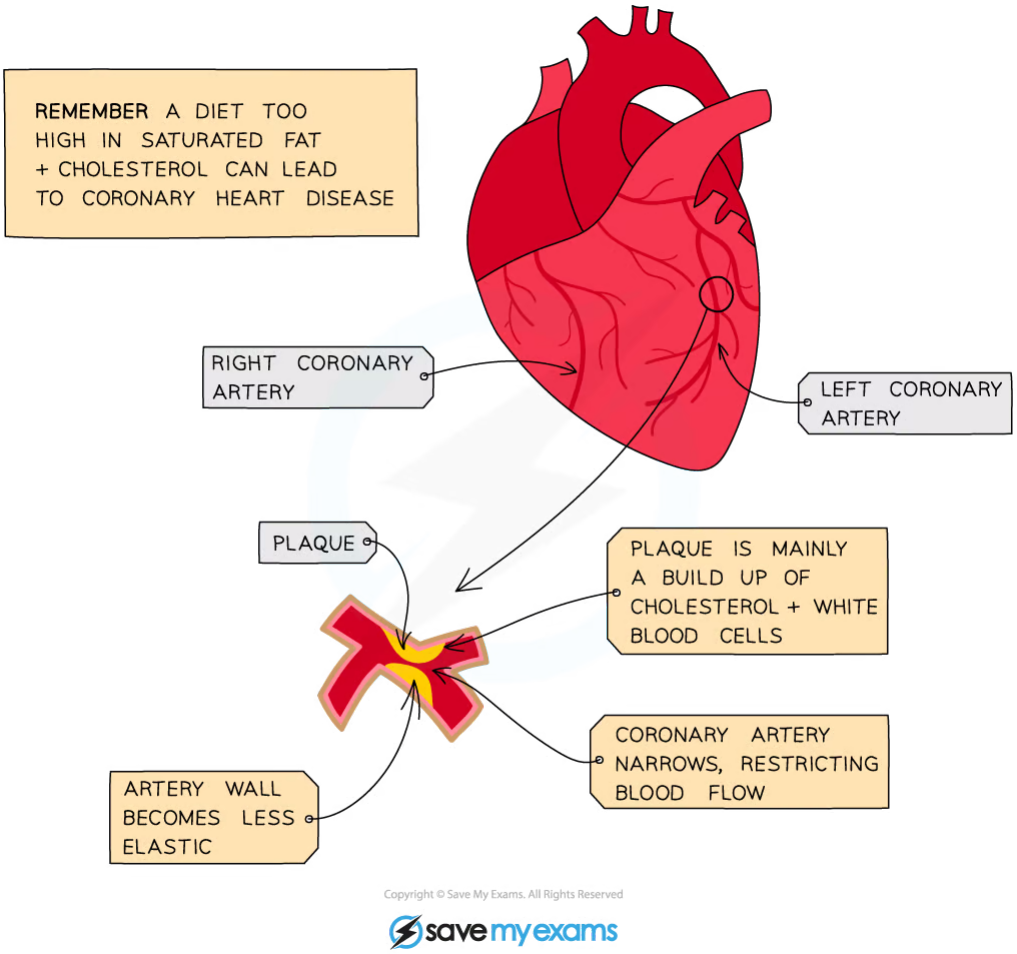
YOUR NOTES

- **Occlusion** can be defined as
  - **The narrowing of the arteries due to a blockage**
- The arteries can be blocked by the process of **atherosclerosis**
- **Atherosclerosis** results in a build-up of layers of fatty material known as plaque inside **arteries**
- The main cause of atheroma development is the presence of low-density **lipoprotein** (**LDL**) which forms from saturated fats and cholesterol
- LDL builds up in regions of the arteries and **phagocytes** move to these areas, engulfing the LDL by **endocytosis**
- The enlarged phagocyte cells are then covered by **smooth muscle cells** which cause a bulging of the **endothelium** in the artery
- Deposition of **calcium ions** can worsen the situation by hardening the endothelium
- This **narrows the lumen** of the artery, reducing the space for blood flow

Consequences of occlusion of the arteries

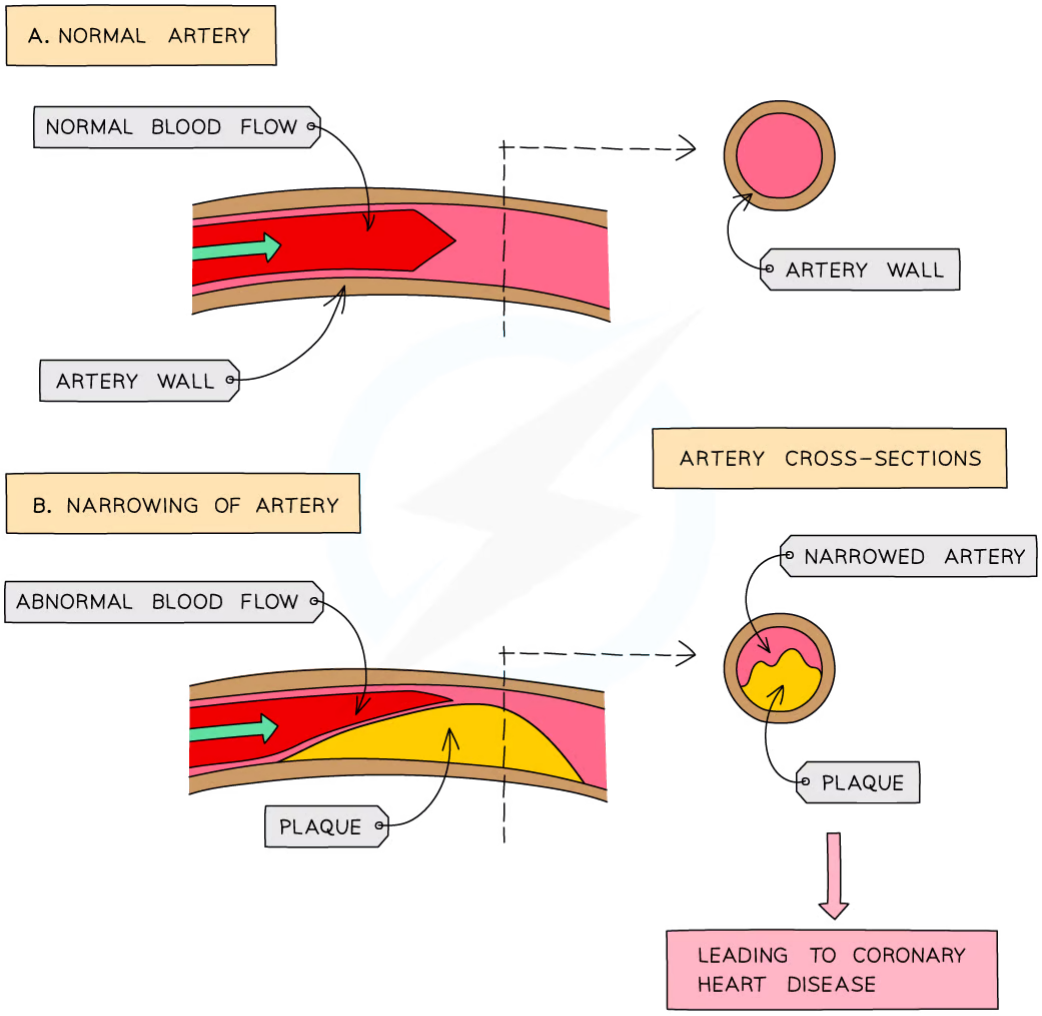
- When an atheroma builds up enough to cause impeded blood flow, tissues do not receive the required level of **oxygen** and **nutrients**
  - This can **inhibit cell functions**
- **Occlusion** of the **coronary arteries** in particular can lead to significant health issues such as **coronary heart disease**
  - The flow of blood through the coronary arteries is reduced, resulting in a lack of oxygen and nutrients for the heart muscle
  - **Partial blockage** of the coronary arteries creates a restricted blood flow to the cardiac muscle cells and results in severe chest pains called **angina** as the heart muscle beats faster to try to increase blood supply
  - **Complete blockage** means cells in the area of the heart not receiving blood will not be able to respire aerobically; these cells will be unable to contract, leading to a heart attack
  - Atheromas can sometimes rupture, leading to the development of a **blood clot**
    - Blood clots can worsen existing blockages, or break off and travel into smaller blood vessels
      - Blood clots that travel to the coronary arteries can cause a heart attack
      - Blood clots that travel to the brain can lead to a stroke

YOUR NOTES



Buildup of plaque in the coronary arteries narrows the lumen

YOUR NOTES



The effect of a narrowed lumen in a coronary artery is reduced blood flow to the heart

Risk factors for atherosclerosis

- There are several **risk factors** which will increase the chances of coronary heart disease:
  - **Consumption of *trans*-fats**
    - These damage the endothelium of the artery initiating formation of an atheroma
  - **Constant high blood sugar**
    - This is usually the result of consumption of foods high in carbohydrate
  - **High blood pressure**
    - This increases the force of the blood against the artery walls and consequently leads to damage of the vessels
    - Blood pressure can increase due to smoking or stress
  - **High blood concentrations of LDL**

- Speeds up the build up of fatty plaques in the arteries, leading to blockages

YOUR NOTES

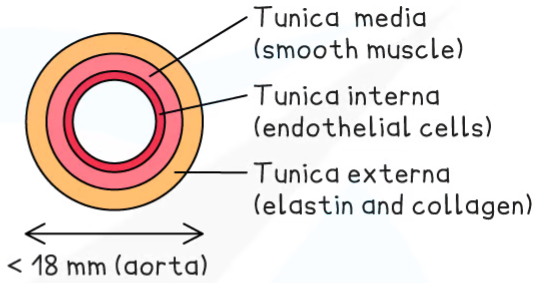
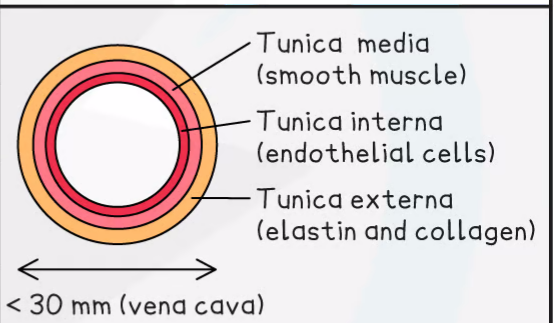
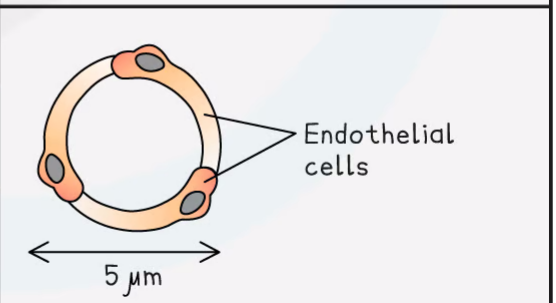
- **Smoking**
  - Chemicals in smoke cause an increase in plaque build up and an **increase in blood pressure**
  - Carbon monoxide also reduces the oxygen carrying capacity of the red blood cells
- **Infection by certain microbes**
  - *Chlamydia pneumoniae* can infect the arterial wall and trigger **inflammation** which promotes atherosclerosis
  - Microbes of the small intestine produce the **chemical** trimethylamine N-oxide which promotes atherosclerosis

Structure of the Blood Vessels

YOUR NOTES

- The body contains several different types of blood vessel
- The walls of each type of blood vessel have a structure that relates to the function of the vessel
  - **Arteries** transport blood **a**way from the heart (usually at high pressure). They are structured as follows:
    - Three thick layers in their walls
    - A high proportion of muscle and elastic fibres
    - Narrow lumen
    - No valves
  - **Capillaries** transport blood from arteries to veins, and are located between the cells in the tissues. They are structured as follows:
    - Walls are only one cell thick (endothelial layer only)
    - No muscle or elastic fibres
    - No valves
  - **Veins** transport blood **in**to the heart (usually at low pressure). They are structured as follows:
    - Thin walls with three layers
    - Low proportion of muscle and elastic fibres compared to arteries
    - Large lumen
    - Valves (usually) present

YOUR NOTES

Artery	Thicker tunica externa with a high proportion of elastin and collagen	
	Thicker tunica media with a high proportion of muscle fibres	
	Narrow lumen	
Vein	One-way valves	
	Wide lumen	
	Less smooth muscle and elastin	
	Lots of collagen	
Capillary	Very small diameter	
	Capillaries branch between cells	
	Thin walls, no elstic, smooth muscle or collagen	

The three main categories of blood vessel can be identified by comparing their structures

Exam Tip

For "explain" questions relating to blood vessel structure, remember to pair a description of a structural feature to an explanation of exactly how it helps the blood vessel to function. For example "capillary walls are one-cell thick, which enables quick and efficient diffusion of substances such as oxygen and glucose to the cells"

YOUR NOTES

6.3 Defence Against Infectious Disease

6.3.1 Skin

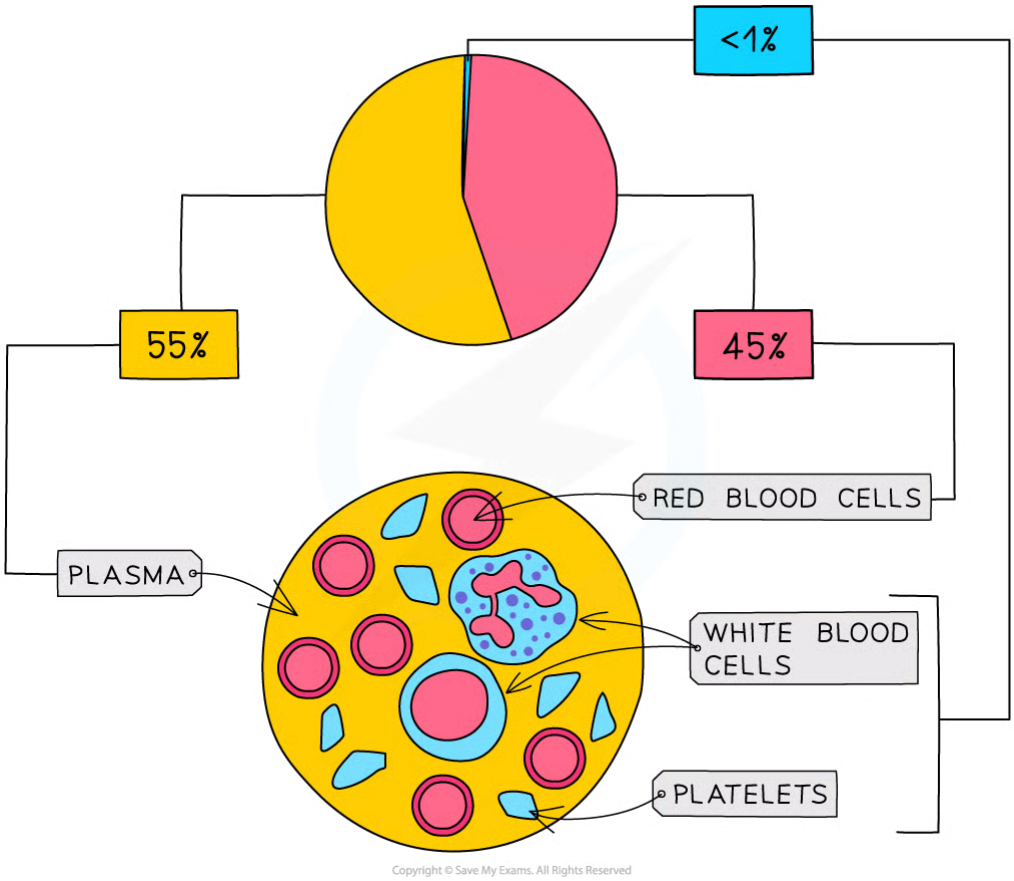
Skin

- The **skin and mucous** membranes form a **primary defence** against pathogens that cause infectious disease
- **Skin** is the largest organ of the body and is covered in **microorganisms** that usually cause no issues, as they can't enter the body. Skin provides:
  - A **tough physical barrier** that prevents entry of pathogens into our bodies
  - Cuts in the skin are sealed by formation of **blood clots** to prevent entry of pathogens
  - **Chemical protection** through the production of **sebum** from the sebaceous glands of the hair follicles
    - Sebum is a chemical responsible for maintaining a **low skin pH** which inhibits the growth of microorganisms
- **Mucous membranes** are found lining vulnerable areas which may be a route for pathogens into the body
  - This includes the **airways**, areas around the **reproductive organs** (foreskin and vagina) and the **digestive system**
- The membranes contain goblet cells which produce mucus containing **glycoproteins**
  - Microorganisms and particles become **trapped** by the mucus and are then either **swallowed** (into the stomach) or **expelled**, therefore preventing infection
  - Mucus also contains **lysozyme enzymes** which have **antibacterial** properties, providing more protection from invading microorganisms

YOUR NOTES

Platelets

- When the skin is cut, microorganisms have an entry point to get into the body
  - The first line of defence is compromised
- In order to minimise the risk of substantial **blood loss** and entry of **unwanted microorganisms**, the blood starts to clot to **seal the wound**
- In response to **blood vessel damage**, platelets form a temporary **plug** to stem bleeding
  - Platelets are **cellular fragments** that make up one component of the blood
- They release chemicals called **clotting factors** that trigger a **chemical cascade** which results in blood clotting



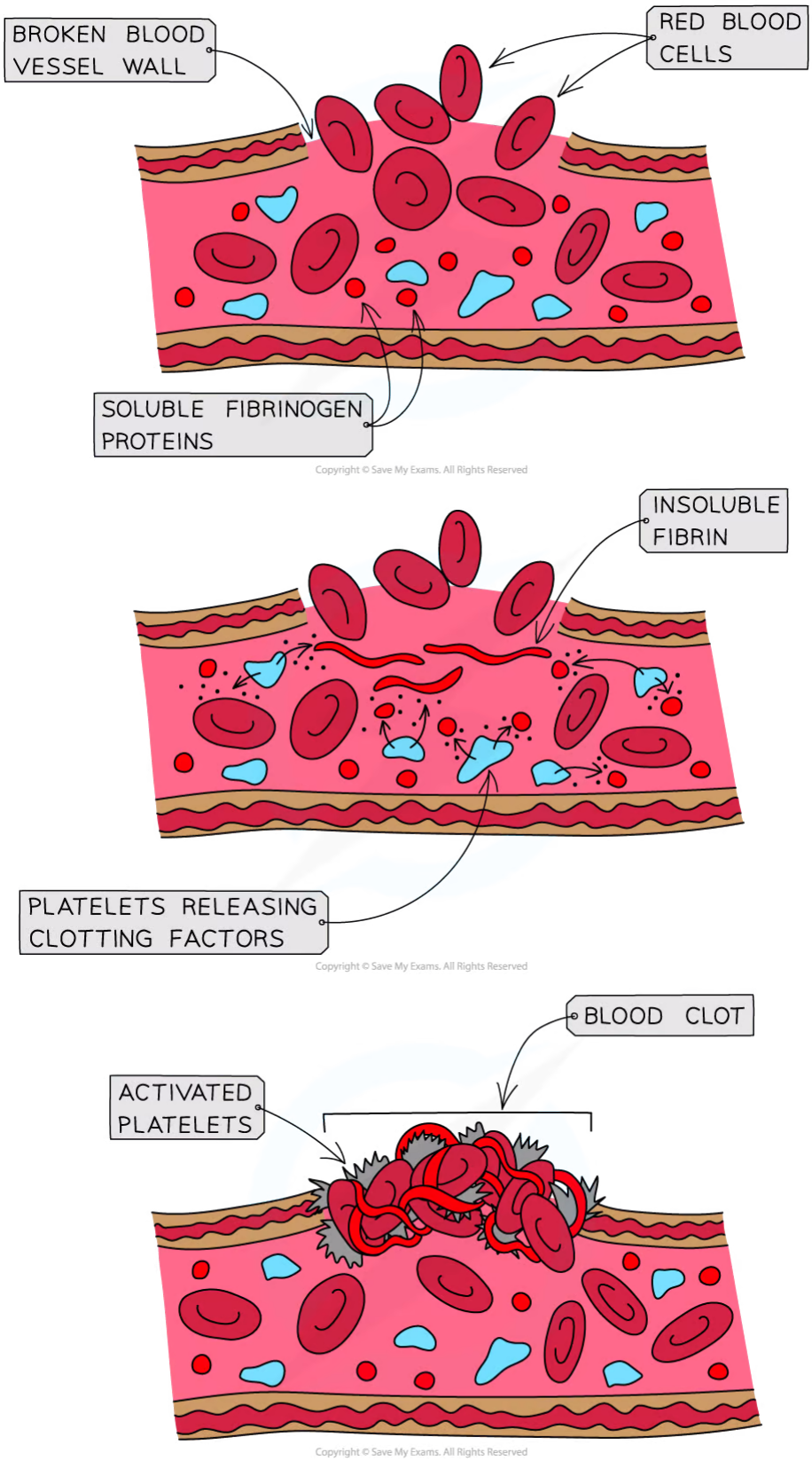
The blood is made up of 4 key components including plasma, red blood cells, white blood cells and platelets

Blood Clotting Proteins

YOUR NOTES

- The chemical cascade, triggered by the clotting factors, involves a large number of steps and several plasma proteins
  - First of all, the **clotting factors** stimulate the release of the enzyme **thrombin**
  - Thrombin catalyses the conversion of the soluble protein **fibrinogen** into **fibrin**, which is insoluble
  - Fibrin forms a **mesh** that traps more platelets and blood cells to prevent entry through the wound
    - A small initial stimulus is **amplified** to produce a large amount of fibrin so that the wound is quickly sealed
  - Exposure to air results in the hardening of the mesh to create a **scab**

YOUR NOTES



Blood clot formation

Clotting in Coronary Arteries

YOUR NOTES

Causes of blood clots in the coronary arteries

- A blood clot in the coronary arteries is called **coronary thrombosis**
- Several factors may **increase the risk** of coronary thrombosis developing:
  - **Atherosclerosis in the coronary arteries** results in a build-up of layers of fatty material (plaque) causing **damage to the endothelium wall**
    - Bulging of **the lumen** of the artery causes a blockage which reduces the space for blood flow
    - Deposition of **calcium ions** can worsen the situation by hardening the endothelium
    - **Lesions** can also sometimes form due to **ruptures** in the atheroma

Consequences of blood clot formation in the coronary arteries

- **Occlusion** of the **coronary arteries** is a common problem that can lead to significant health issues such as **coronary heart disease**
- The coronary arteries deliver **oxygen** and **nutrients** to the cardiac muscle tissue
- If a blood clot forms in the coronary arteries, it can cause **blockages**
- A blockage means that the tissue beyond that point is deprived of oxygen and nutrients, so it is unable to **respire aerobically**
- As a result, cells are unable to produce a **sufficient amount of ATP** which inhibits normal cardiac muscle contraction resulting in **irregular** and **uncoordinated** movement called **fibrillation**
  - If not rectified, either naturally or through medical intervention, fibrillation could lead to **death**
- A **heart attack** (myocardial infarction) may also occur in situations where the blood supply is completely inhibited so that the cardiac muscle tissue starts to die
  - This can be fatal

Risk factors for coronary thrombosis

- There are several factors which have shown a clear **correlation** with increased chances of coronary thrombosis or heart attacks
- The main risk factors for include:
  - **Genetic factors**
  - **Age and sex**
  - **High blood pressure**
  - **Smoking**
  - **High concentrations of low-density lipoproteins (LDLs)**
  - **Diabetes**
  - **Obesity**
  - **Lack of exercise**

Exam Tip

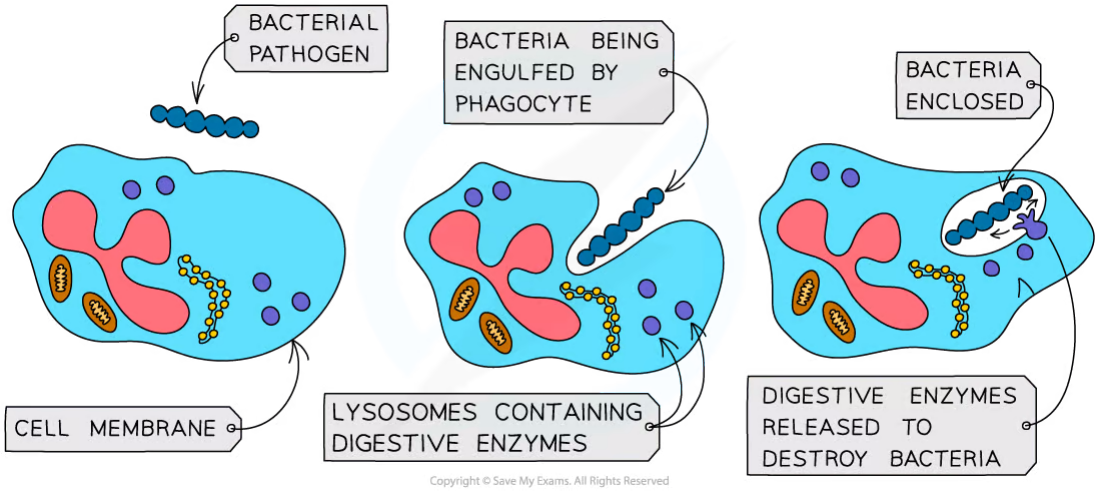
Remember, **correlation does not prove causation**: There are many contributing factors which will affect the likelihood of developing a coronary thrombosis, as a result, we cannot say that any single factor is **causative**. We can say that there is a **correlation** between that factor and the incidence of coronary thrombosis

YOUR NOTES

YOUR NOTES

White Blood Cells

- **Phagocytes** are white blood cells that are produced continuously in the **bone marrow**
- They are responsible for **removing dead cells and invasive microorganisms**; a **non-specific immune response**
- Phagocytes move to the site of infection and attach to pathogens
- The **cell surface membrane** of the phagocyte extends out and around the pathogen, **engulfing it** by **endocytosis**
- They then digest the pathogen using **enzymes** which are stored within **lysosomes** (in their cytoplasm)

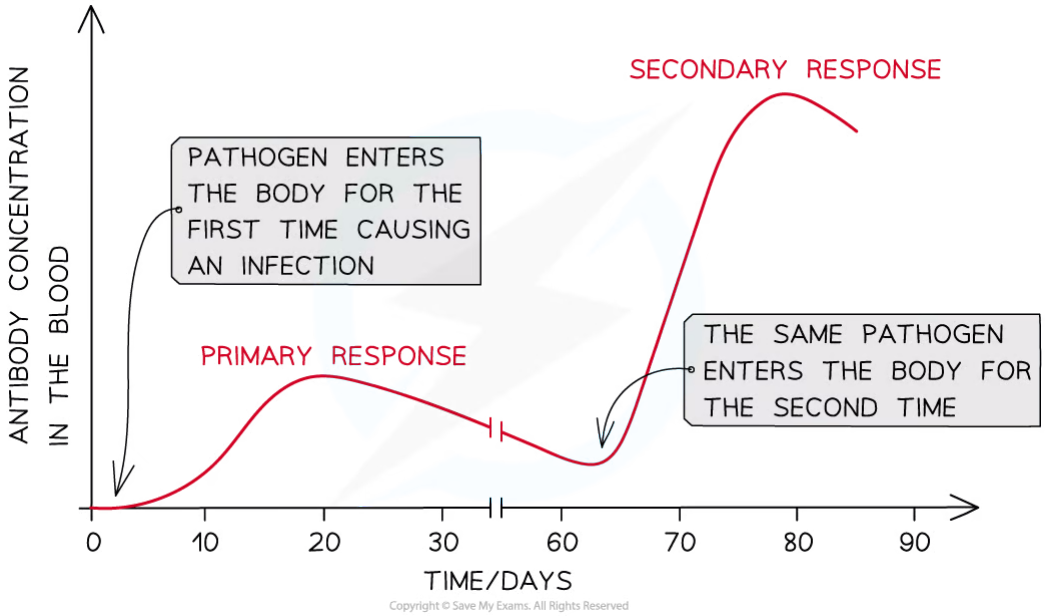


Phagocytic cells ingest pathogens and digest them using enzymes

YOUR NOTES

Antibody Production

- Pathogens possess protein molecules on their cell membranes called **antigens**
- When a **lymphocyte** is exposed to a specific foreign antigen, it will produce specific **antibodies**
  - It is known as a **specific immune response** because one lymphocyte will respond to just **one type of antigen**
- Antibodies have two functional regions:
  - A hypervariable functional region that binds to antigens on pathogens
  - A functional region which aids the body in fighting the pathogen by **labelling the pathogen** (making it easier for phagocytes to find and engulf) and by **preventing virus cells from binding** to receptors on host cells (meaning they cannot enter the cell)
- When activated by a pathogen, lymphocytes clone themselves to produce **plasma cells** which are capable of mass **antibody production**
- Antibodies are only short-lived, degrading within weeks or months and the plasma cells that produced them are lost soon after
- However, **inactive long-living memory cells** are produced which remain in the blood for a long period of time to give **immunity**
- Memory cells allow for the **rapid production of antibodies** after secondary infection
  - If the same pathogen infects for a second time, the inactive **memory cells** will become active and divide to produce **plasma cells** at a rapid rate
  - These plasma cells are able to supply a **large number of antibodies at a rapid rate** to fight the pathogen before symptoms appear



Memory cells allow for the rapid production of antibodies

Effects of HIV on Antibody Production

YOUR NOTES

- **Human Immunodeficiency Virus** is a retrovirus made up of several key components including **RNA** and the enzyme, **reverse transcriptase,** which is used to produce DNA in the host cell
- HIV infects the body and attacks a type of lymphocyte cell called a **T-helper cell**
- T-helper cells are a key component in the production of antibodies, so HIV **inhibits the bodies capacity to produce antibodies**
- In the **early stages of infection**, antibodies are produced to fight HIV, these can be **detected in blood tests**
    - The individual is said to be **HIV positive**

The development of AIDS

- As the **infection progresses**, the ability to produce antibodies significantly reduces
- This renders the immune system unable to fight off other pathogens and so the individual becomes **prone to infection** from other **opportunistic pathogens**
- When the individual is suffering from **several diseases** or conditions at the same time, they are said to have **acquired immune deficiency syndrome** (AIDS)
- **Progression of HIV,** from the initial infection to the development of AIDS, can be slowed down using **anti-retroviral drugs**
    - Due to highly successful drugs, many HIV positive individuals are able to live full-quality lives with normal life expectancies

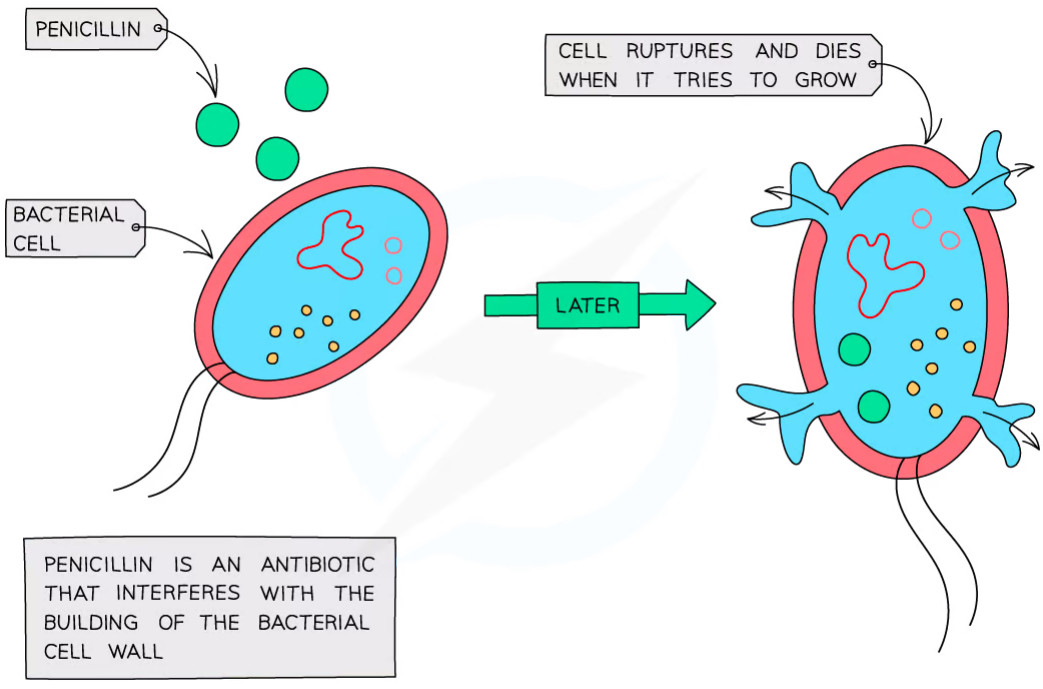
Transmission of HIV

- HIV is unable to survive outside of the human body and so is mainly **transmitted by the direct exchange of body fluids**
    - Viruses need host cells in order to replicate
- This means HIV can be transmitted in the following ways:
    - **Sexual intercourse**
    - **Blood donation**
    - **Sharing of needles** used by intravenous drug users
    - From mother to child **across the placenta**
    - Mixing of blood between mother and child **during birth**
    - From mother to child **through breast milk**

YOUR NOTES

Antibiotics

- **Antibiotics** are **drugs** that **inhibit the growth** of microorganisms
  - Most antibiotics **kill or stop the growth of bacteria** (prokaryotes) but do not harm the cells of the infected organism
  - This is because they block specific processes that occur in **prokaryotic cells** but **do not have the same effect on eukaryotic cells**
- Processes that might be targeted include:
  - Transcription
  - Translation
  - DNA replication
  - Ribosome function
  - Cell wall formation
- Some antibiotics are derived from living organisms such as saprotrophic fungi
  - **Penicillin** is produced by certain fungi in the genus *Penicillium*
  - When growing in the wild the antimicrobial secretions of the fungus helps it to **compete** by killing nearby saprotrophic bacteria
- Antibiotics can also be made synthetically (in a laboratory)



How penicillin works

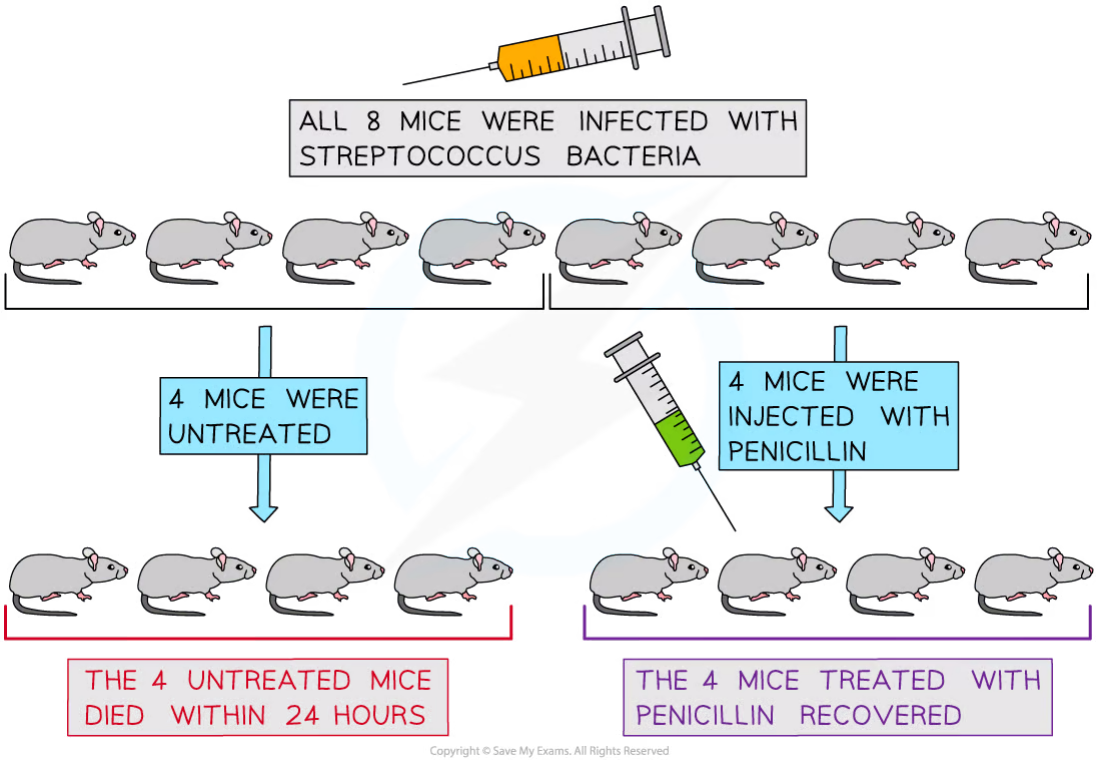
- Penicillin is not effective against **all bacteria** (eg. *tuberculosis*) because the bacteria may have:
  - **Thicker cell walls** which reduce permeability
  - **Enzymes which breakdown penicillin**
- There are many different examples of antibiotics which are effective against a range of bacterial diseases

YOUR NOTES

Florey & Chain's Experiments

YOUR NOTES

- **Howard Florey and Ernst Chain** carried out experiments to test penicillin on bacterial infections in mice in the 1930s
- First of all, they developed a technique for **purifying and concentrating** penicillin from liquid cultures of *Penicillium*
  - The method they used was very **inefficient** and only produced small quantities of the antibiotic
- Secondly, they showed that Penicillin was effective in preventing bacterial growth on agar plates
- After they had collected this evidence, Florey and Chain used mice to show the effect of penicillin at the level of an organism
  - In order to carry out these tests on mice, the mice first needed to be **infected** with a known bacterial pathogen. A deadly ***Streptococcus* bacteria** was used to develop pneumonia in 8 mice
  - Of these 8 mice, 4 were **injected with penicillin** and 4 were left **untreated**
  - In less than 24 hours, the 4 untreated mice had **all died** whereas those that were treated with penicillin **survived**



Florey and Chain showed that penicillin could aid the recovery of mice infected with Streptococcus bacteria

Human tests

- After successful trials using penicillin to treat mice, Florey and Chain were ready to begin testing **human patients**

- It took some time to build up a **large enough supply of penicillin** using their purification techniques
- They then started treatment on their first patient, a policeman who was suffering from a life-threatening bacterial infection resulting from a scratch on his face
- The patient showed improvement but unfortunately, the supply of penicillin was **not enough to complete the treatment** and so the man died of his infection
- Following this, a series of other patients were treated with varying success and Florey and Chain realised that they needed to produce much larger quantities of penicillin than their current capacity
- Larger scale testing and treatment (using penicillin) became possible after an **American pharmaceutical company started mass production**
- It was after this that the true level of efficacy for penicillin was established

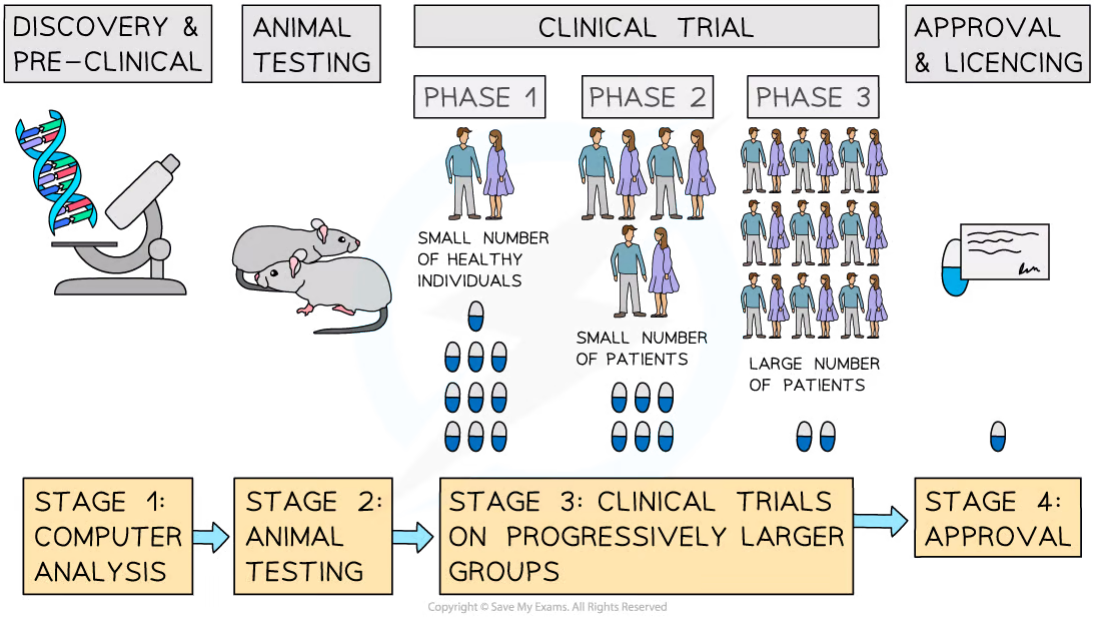
YOUR NOTES

Florey & Chain's Experimental Technique

YOUR NOTES

NOS: Risks associated with scientific research; Florey and Chain's tests on the safety of penicillin would not be compliant with current protocols on testing

- New drugs carry new risks as scientists can not always predict how the body may **respond** to the drug, whether the drug will be **effective** or how significant any **side effects** might be
- Before drugs become licenced and available for use, they must go through a rigorous series of tests and trials to **minimise the risks**
- A summary of the procedure is as follows:
  - Initially, after a computer analysis has been carried out on the structure of the drug, trials are carried out with **animals** to see the effect on a whole organism level
  - Next, a **small number of healthy humans** will trial the drug to measure the **toxicity**
  - If these first 2 stages are successful, testing will be carried out on a progressively larger number of **patients** suffering from the target disease
    - In this final stage, the aim is to establish how **effective** the drug is and collect as much information as possible about **side effects**
  - Once the clinical trials are complete, the new drug can be **approved and licenced** for medical use
  - The process usually takes **years** to reach the approval stage
- When Florey and Chain carried out their trials with penicillin, these protocols for safe testing were not in place and their work was only carried out over a matter of **months**
  - This meant that some patients received **treatment very rapidly** for infections that were previously incurable, however, there was a **huge risk** that the new drug, penicillin, could have caused **significant side effects**



New drugs go through a series of tests and trials in order to be approved for medical use

Previous drugs trials

YOUR NOTES

- Carefully designed drugs testing protocols do now exist, but serious problems can still arise
  - **Thalidomide** was a drug that was used in the 1950s to treat a variety of conditions including some cancers and leprosy
    - It was found that thalidomide provided an effective cure for **morning sickness** and so pregnant women were prescribed thalidomide as a treatment
    - The effects of the drug **on a foetus** had **not been tested** and in subsequent years, babies were born with a **range of disabilities** including the absence of limbs, sensory impairment and disfigurement, amongst others
    - It took several years for the link to be made between Thalidomide and the disabilities of the thousands of children who were born
    - Thalidomide was **withdrawn** from use in the early 1960's
  - A drugs trial was carried out in 2006 to test an experimental **leukaemia drug, TGN1412**
    - The drug had **successfully passed the animals trials** where it was given to monkeys, so it moved to the next stage of testing
    - Eight healthy volunteers took part in the trial and after an hour of receiving the drug, six of them were rushed to **intensive care with multiple organ failure**
    - Although they all recovered, the **long term effects** on their immune systems are unknown
    - This is one of the most infamous clinical trial emergencies of modern day

Viruses

Antibiotics and viruses

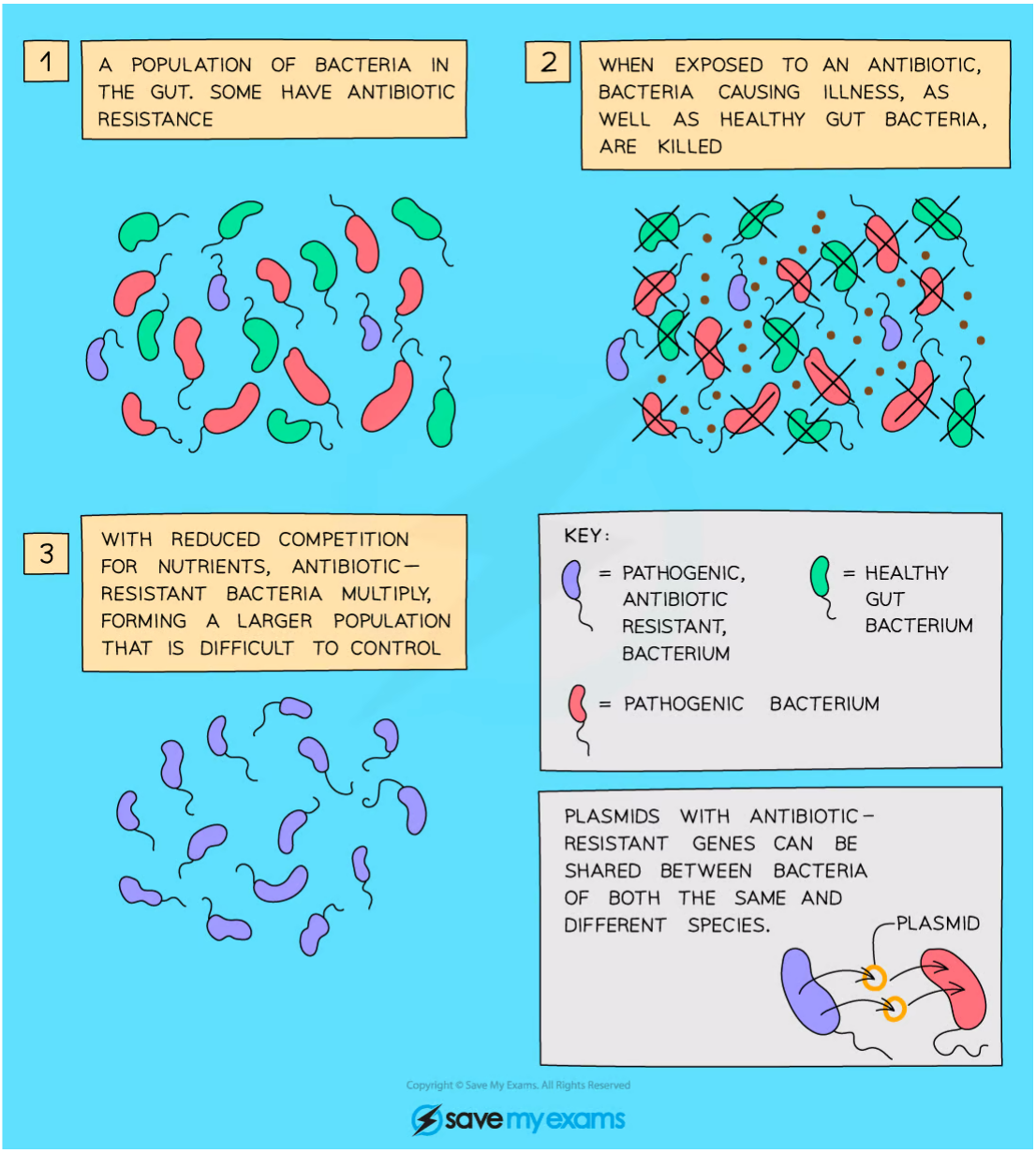
- Antibiotics are ineffective against **viruses** as they are **non-living**
- Viruses are **particles** and not cells
  - They have **no metabolism** or cell structure and therefore cannot be targeted in any of the ways that antibiotics target a bacterial cell
- When a virus **replicates**, it uses the **host cell's mechanisms** for transcription, translation and other metabolic pathways, so not even these processes can be targeted as antibiotics do not bind to the proteins that host cells use in these processes
  - Drugs that would target these processes would **damage the host cells** and cause even more harm
- **Antivirals** are drugs that target viral **enzymes** without harming the host cell

YOUR NOTES

Antibiotic Resistance

- Within a bacterial population, there is **variation** caused by **mutations** (as occurs in populations of all species)
- A chance mutation might cause some bacteria to become **resistant** to an antibiotic (eg. penicillin)
- When the population is treated with this antibiotic, **the resistant bacteria do not die**
- This means the resistant bacteria can continue to reproduce with **less competition from the non-resistant bacteria**, which are now dead
- Therefore the **genes for antibiotic resistance are passed on** with a much greater frequency to the next generation
    - As bacteria only have one copy of each gene, a mutant gene will have an immediate effect on any bacterium possessing it
- Over time, the whole population of bacteria becomes **antibiotic-resistant** because the antibiotic-resistant bacteria are best suited to their environment
- This is an example of **evolution by natural selection**
- Some pathogenic bacteria have become **resistant to penicillin** as they have acquired **genes that code for the production of the enzyme β-lactamase** (also known as penicillinase), which breaks down penicillin

YOUR NOTES



Bacteria evolve rapidly as they reproduce quickly and acquire random mutations – some of which confer resistance

The future of antibiotic resistance

- Antibiotic-resistant strains are a major problem in human medicine
- New resistant strains are constantly emerging due to the **overuse of antibiotics**
  - By using antibiotics frequently, humans exert a **selective pressure** on the bacteria, which supports the evolution of antibiotic resistance
- Scientists are trying hard to find **new antibiotics** that bacteria have not yet been exposed to, but this process is expensive and time-consuming
- Some strains of bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), can be **resistant to multiple antibiotics** and they create infections and diseases which are very

difficult to treat
- When antibiotics were discovered, scientists thought they would be able to **eradicate** bacterial infections, but less than a century later a future is being imagined where many bacterial infections cannot be treated with current medicines

YOUR NOTES

Measures to avoid antibiotic resistance

- Antibiotic resistance in bacteria is an example of natural selection that humans have helped to develop through **incorrect use or overuse** of antibiotics
- Implementation of certain measures can help to avoid antibiotic resistance. These measures may include:
  - Avoiding prescription of antibiotics for **non-serious or non-bacterial infections**
  - **Completing the full prescribed course** of antibiotics to ensure the infection is completely cleared
  - Maintaining **high standards of hygiene** in the hospital environment
  - Minimising use of antibiotics for routine treatment to animals in **agriculture**
  - Development of **new types of antibiotic**

YOUR NOTES

6.4 Gas Exchange

6.4.1 Ventilation: Function & Structures

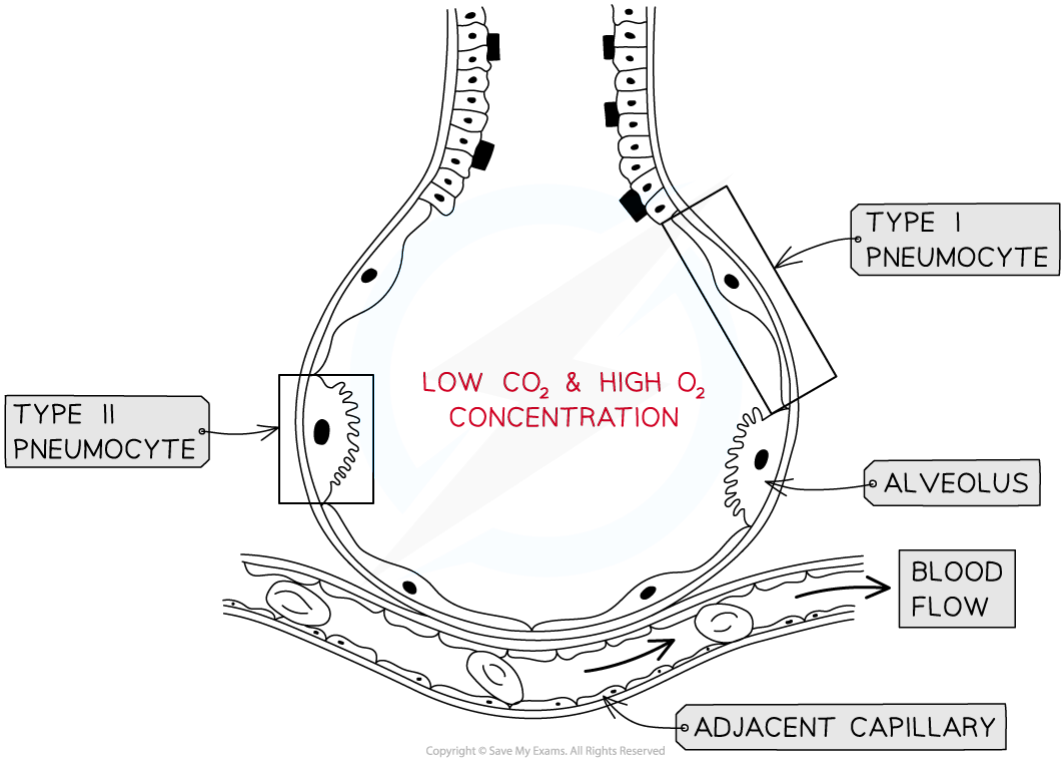
Ventilation

- **Ventilation** can be defined as
  - **The replacement of older air in the lungs with fresh air from the body's external environment**
- Ventilation is essential for the effective **exchange of gases** in the lungs
- The **exchange** of oxygen and carbon dioxide occurs between the alveoli and the capillaries in the lungs
- Gases are exchanged by **simple** diffusion which requires a concentration gradient
- This gradient is maintained by
  - **Ventilation**
  - The **continuous flow of blood** in the capillaries

The impact of ventilation

- Ventilation maintains **concentration gradients** of oxygen and carbon dioxide between air in the alveoli and blood flowing in adjacent capillaries
  - **Breathing in** fresh air from the surrounding environment increases the concentration of oxygen in the air inside the alveoli
  - **Breathing out** removes carbon dioxide
- This means that after ventilation, compared to the blood found in adjacent capillaries, the alveoli have
  - **Higher oxygen levels**
  - **Lower carbon dioxide levels**
- This ensures that oxygen continues to **diffuse** from the alveoli into the capillaries, while carbon dioxide continues to diffuse from the capillaries into the alveoli
  - Both gases move down their **concentration gradient**

YOUR NOTES

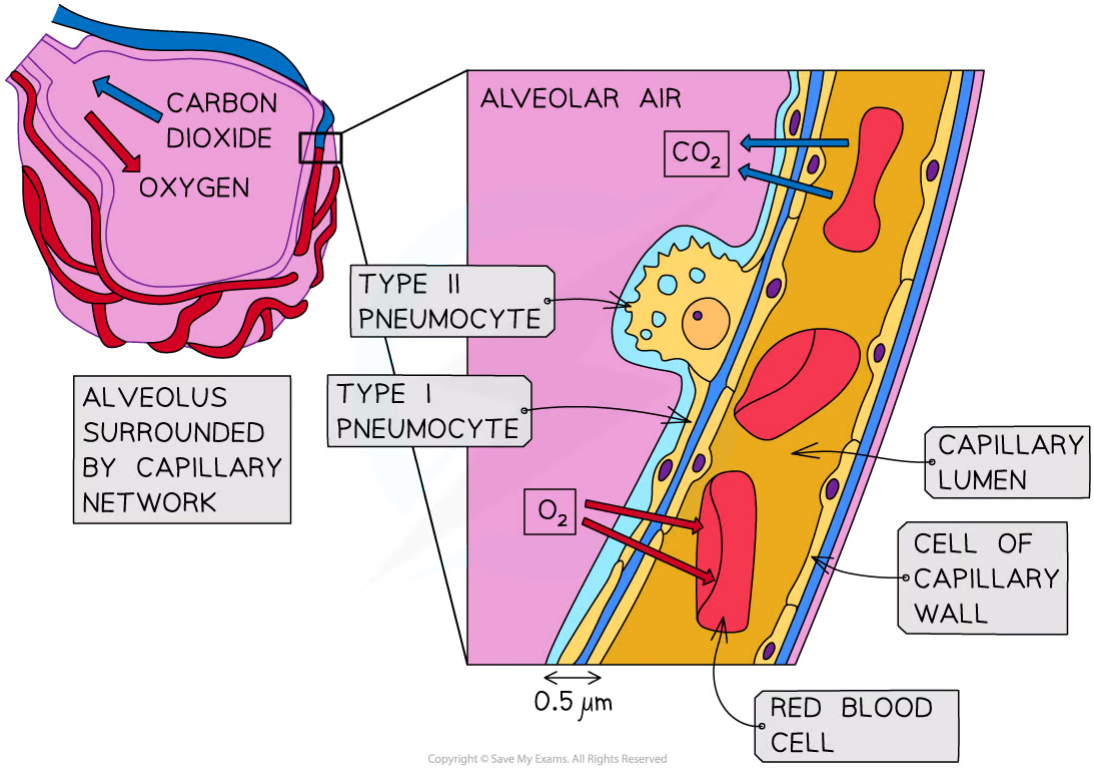


Ventilation maintains a concentration gradient between the air in the alveolus and the blood in the adjacent capillary

YOUR NOTES

Type I Pneumocytes

- The alveoli are specifically adapted for gas exchange as they collectively have a **very large surface area** and the alveolar walls are only one cell thick which provides a **short diffusion distance**
  - The alveolar walls are also known as the alveolar epithelium
- **Type I pneumocytes** are extremely **thin alveolar cells** which make up the majority of the alveolar epithelium
  - They are adapted to maximise the rate of gas exchange by providing a **short diffusion distance**
- The capillary walls are also only **one cell thick** which means there is usually less than **0.5µm** between the air in the alveoli and the blood, this **maximises the rate of diffusion**

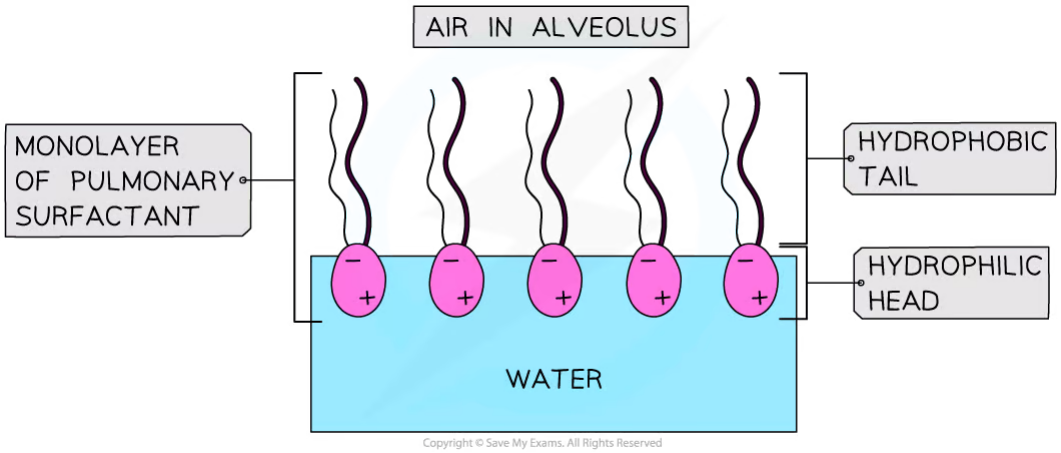


The thin type I pneumocyte cells and the thin capillary walls provide a short diffusion distance to maximise gas exchange

YOUR NOTES

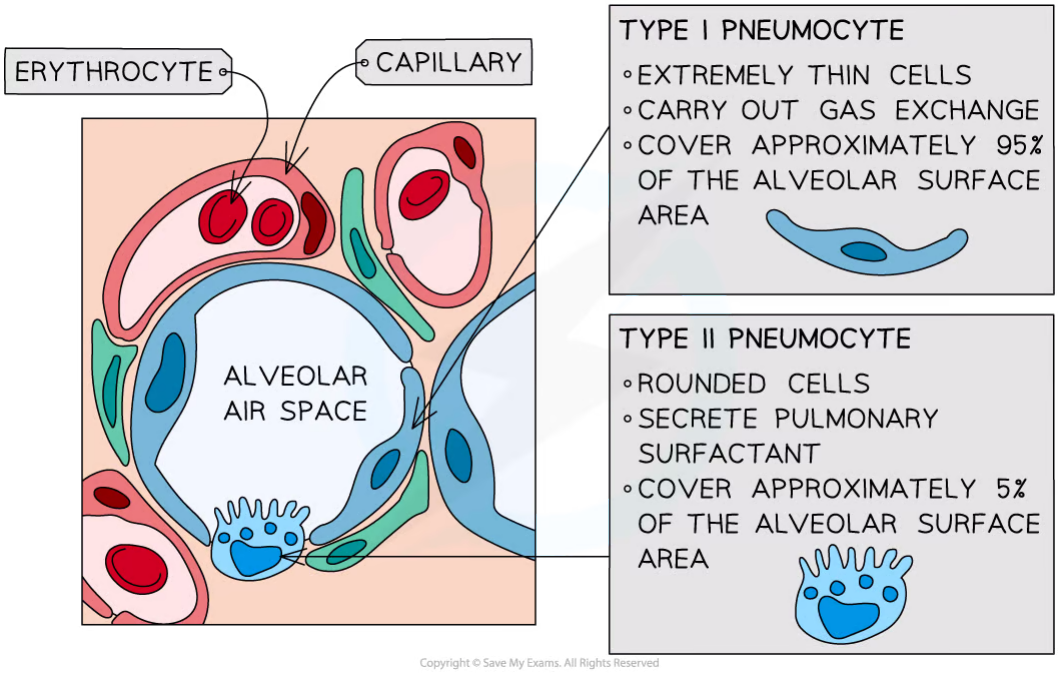
Type II Pneumocytes

- Type II pneumocytes are **rounded cells** which secrete a solution that coats the epithelium of the alveoli
- They occupy a much smaller proportion of the alveolar epithelium than the type I pneumocytes; around 5%
- The solution released by type II pneumocytes contains **pulmonary surfactant**
  - Pulmonary surfactant has hydrophobic **tails and** hydrophilic **heads**
  - The molecules form a monolayer with the hydrophobic tails facing the alveolar air
- Pulmonary surfactant **reduces** surface tension, maintaining alveolar **shape** and **preventing the sacs sticking** together
  - This prevents the alveoli, and therefore the lungs, from **collapsing**
- The solution also aids gas exchange
  - The layer of moisture provided by the solution allows **oxygen to dissolve** before it diffuses into the blood
  - **Carbon dioxide** diffuses from the moist surface before it is removed in exhalation



The type II pneumocyte cells in the alveoli produce a solution containing pulmonary surfactant which reduces surface tension

YOUR NOTES



The alveolar epithelium is made up of type I and type II pneumocyte cells

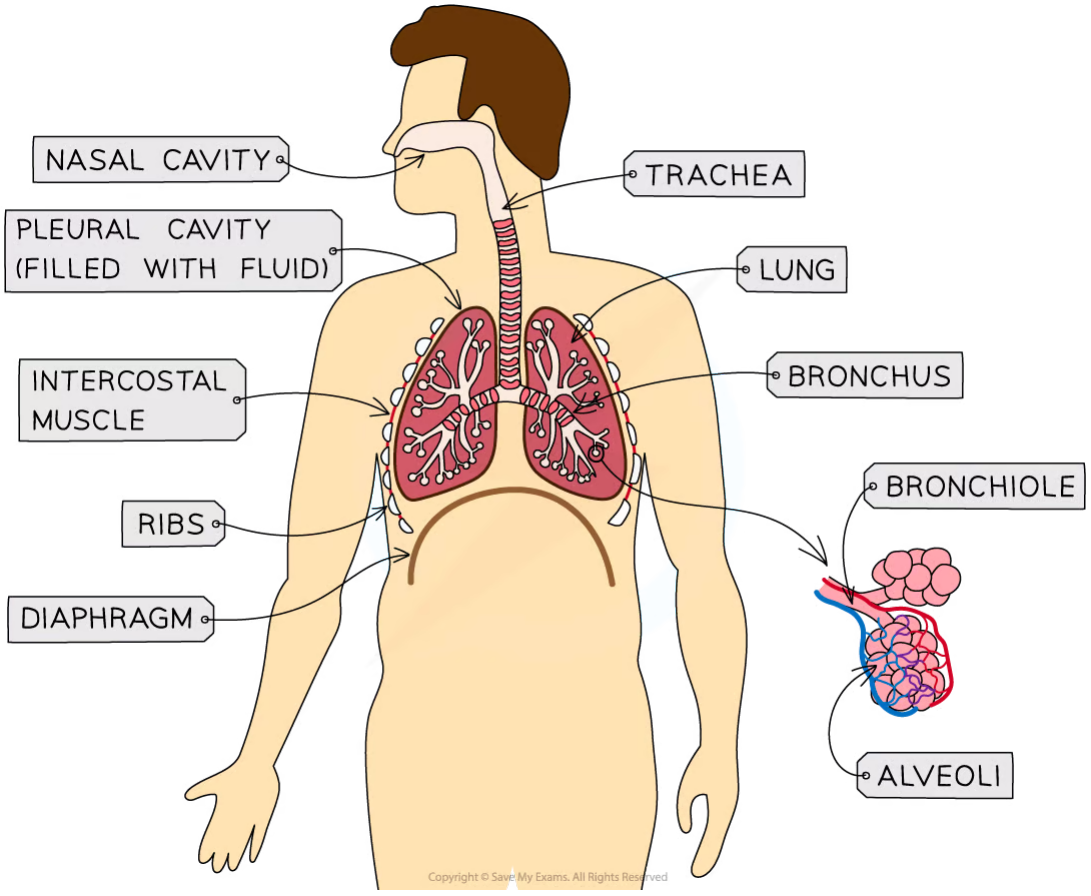
Air Pathway

YOUR NOTES

- Air moves in through the nose and mouth before it is carried to the lungs through the **trachea**
- The **trachea** is a tube supported by **rings of cartilage** which help to support its shape and ensure it stays open, while allowing it to move and flex with the body
- The **trachea** divides to form the two **bronchi** (singular bronchus) with walls also strengthened with cartilage and has a layer of smooth muscle which can **contract** or **relax** to change the diameter of the airways.
-
  - One bronchus leads to each lung

- **Bronchioles** branch off the two bronchi to form a network of narrow tubes
  - The walls of the bronchioles are lined with a layer of **smooth muscle** to alter the diameter of the bronchiole tubes
  - This helps to regulate the flow of air into the lungs by dilating when more air is needed and constricting when e.g. an allergen is present

- Groups of **alveoli** are found at the end of the bronchioles
- Each alveolus is surrounded by an extensive network of **capillaries** to provide a **good blood supply** for maximum gas exchange



The main structures of the human gas exchange system

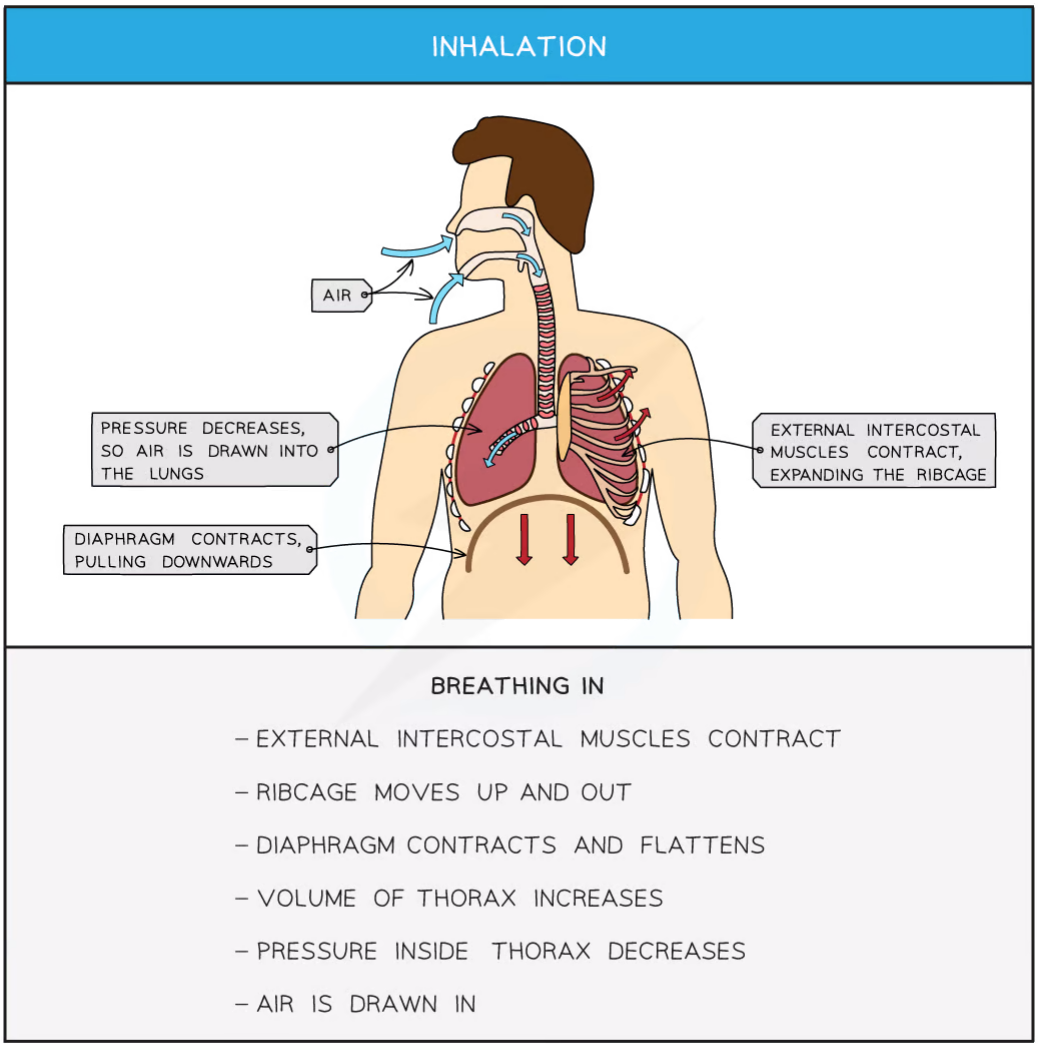
YOUR NOTES

Inspiration & Expiration

Breathing in

- The breathing-in, or **inspiration**, process causes the **volume of the chest to increase** and the **air pressure to decrease** until it is **lower than the atmospheric pressure**
  - When gas is in a large-volume container that allows the gas particles to spread out, the pressure exerted by the gas on the walls of the container is low
- As a result, air moves **down the pressure gradient** and rushes into the lungs
  - A gas will always move down a pressure gradient from an area of high pressure to an area of low pressure
- The inspiration process
  - The diaphragm **contracts** and **flattens**, increasing chest volume
  - In addition to the flattening of the diaphragm the **external** intercostal muscles **contract**, causing the ribcage to move **upwards** and **outwards**; this also increases chest volume

YOUR NOTES



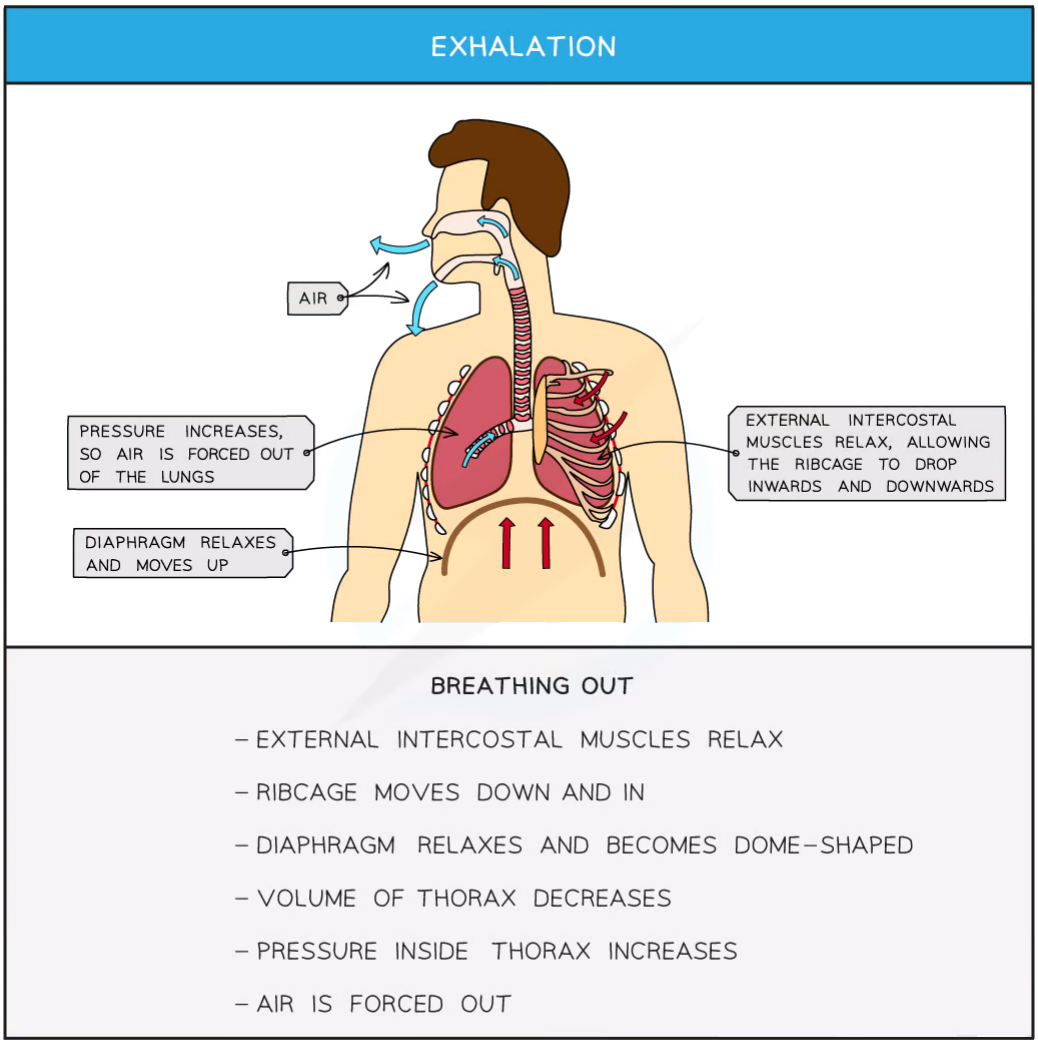
The process of inspiration

Breathing out

- Breathing out, or **expiration**, occurs mostly due to the recoil of the lungs after they have been stretched by the inspiration process, and is therefore a mainly passive process
- **Volume of the chest decreases** and **pressure increases**, causing air to be forced out down its **pressure gradient**
  - When gas is in a low-volume container it is compressed, causing the gas particles to exert more pressure on the walls of the container
- The passive expiration process
  - External intercostal muscles **relax,** allowing the ribcage to move **down** and **in**
  - Diaphragm **relaxes** and becomes **dome-shaped**
  - The **recoil** of **elastic fibres** in the alveoli walls reduces the volume of the lungs

YOUR NOTES

- The expiration process can be active when there is a need to expel excess air from the lungs e.g. when blowing out a candle
- The active expiration process
  - **Internal** intercostal muscles **contract** to pull the ribs **down** and **in**
  - **Abdominal muscles contract** to push organs upwards against the diaphragm, decreasing the volume of the chest cavity
  - This causes **forced exhalation**



The process of passive expiration

Antagonistic Muscle Action

YOUR NOTES

- Muscles only carry out the work of moving the body when they are **contracting**, or **pulling;** they cannot push
- As a result of this limitation muscles often operate in **pairs** when movement in two directions in required
- One muscle of the pair pulls in one direction and the other muscle **pulls in the opposite direction**
  - This is described as **antagonistic** muscle action
- Examples of antagonistic muscle action in ventilation are
  - **Internal** and **external intercostal muscles**
    - When the internal intercostal muscles contract, the rib cage moves down and in
    - When the external intercostal muscles contract, the rib cage moves up and out
  - The **diaphragm** and **abdominal muscles**
    - When the diaphragm contracts, it flattens and moves downwards
    - When the abdominal muscles contract, the internal organs of the abdomen are compressed and pushed upwards, exerting upward pressure on the diaphragm

Exam Tip

The intercostal muscles work in an **antagonistic** manner; as one contracts the other relaxes!Note that the internal intercostal muscles only contract to cause **forced expiration**; expiration is **passive** the majority of the timeRemember, if you learn one of either inspiration or expiration, the other is almost exactly the opposite.

YOUR NOTES

Cancer

NOS: Obtain evidence for theories: epidemiological studies have contributed to our understanding of the causes of lung cancer

- **Theories** are developed based on **evidence** collected through observation and where possible, scientific investigations
- Obtaining **valid** and **reliable** evidence for theories on causes and consequences of different diseases can be difficult for several reasons.
  - The sensitive nature of the data required
  - Difficulty finding volunteers with the correct specific diagnoses
  - The effect of confounding factors
- **Epidemiology** is the study of disease which includes monitoring the numbers and distribution of cases that arise, as well as building a bigger picture of the potential causes of the disease
- **Epidemiological studies** are carried out on **large numbers** of patient volunteers to give an unbiased and reliable collection of data which make it possible to draw links between certain factors and the development of a disease

Causation and correlation

- It is very tricky to show that one particular factor is responsible for **causing** a disease, such as lung cancer, instead, data is usually used to show a **correlation** between a certain risk factor and the incidence of a disease
- **Confounding factors** which share a similar correlation and also imply causation of the disease can make it difficult to establish the actual determinant
  - Therefore it is necessary to study **several factors** simultaneously to collect enough data to carry out **statistical analysis** and develop the overall picture
- **Risk factors** contribute towards the likelihood of developing a disease
  - Therefore risk factors that are more easily controlled and measured in isolation are more likely to have a proven causal relationship, as they can be investigated in a more scientific manner
  - For example, an individual's exposure to smoking is much easier to quantify than their exposure to air pollution
- When analysing data and studies it is always important to remember that **risk factors interact with each other**
  - For example, a smoker with asthma is likely to suffer the associated negative health side effects more quickly than a smoker without asthma
- It is always important to remember that even though there is a correlation, this **does not mean** that there is a direct causal link
  - For example, in places with higher pollution, there may be more asthmatic individuals but this does not mean that pollution caused asthma as there are many other variables at play

Causes of lung cancer

YOUR NOTES

- Of all the cancers, lung cancer is the most commonly diagnosed and results in the most deaths globally
- Cancer occurs if **mutations** affect the regulation of mitosis in cells
- This causes uncontrolled mitosis which develops into **a mass of cells** in the **lumen** of the airways
- The tumour becomes larger because it has no method of programmed cell death and survives because it develops its own blood supply (vascularisation)
- The tumour then starts to interfere with the normal working of the lungs, such as by squeezing against blood vessels or cancer cells entering into the **lymphatic system**, where they may develop another tumour
- A **causal** relationship has been **proven** for some risk factors relating to lung cancer
  - **Smoking** is a key contributor
    - **Tobacco** in cigarette smoke has been shown to have mutagenic effects on body cells due to chemicals found in the smoke
    - The effects of these **mutagenic chemicals** can lead to cancer in smokers as well as the passive smokers inhaling their second hand smoke
  - Inhalation of **air pollution** similarly, can result in lung cancer
    - In cities, average rates of lung cancer diagnoses are much higher due to high levels of vehicle exhaust fumes and smoke from burning organic matter
  - **Radon gas** is a radioactive gas which can contribute to the numbers of lung cancer in some areas more than others
    - Radon is released from rocks and buildings made from rocks containing high levels of radon gas
  - Various building materials, such as **asbestos** and **silica**, produce small dust particles which can cause lung cancer if they are inhaled
    - There are strict rules about using or working with materials, such as asbestos and silica, to minimise exposure and therefore the associated risks

Consequences of lung cancer

- There are many symptoms associated with a lung cancer diagnosis, including:
  - Breathing difficulties
  - Coughing, sometimes coughing up blood
  - Chest pains
  - Loss of appetite and weight loss
  - Persistent fatigue
  - Tumours can form in the lungs
  - In severe cases, the **primary tumours metastasise** and lead to the formation of **secondary tumours** elsewhere in the body
- Survival rates from lung cancer are very low compared to other cancer types
  - Only 15% of patients will survive more than 5 years
- Patients that do survive may suffer from **long term symptoms** such as:
  - Pain
  - Breathing difficulties
  - Fatigue

YOUR NOTES

- Anxieties associated with a cancer diagnosis and future prognosis

- **Treatments** for lung cancer include:
  - Chemotherapy
  - Radiotherapy
  - Lung removal

Exam Tip

Scatter diagrams are used to identify **correlations** between two variables to determine the relationships between two factors. For example, between risk factors and certain disease.Correlation can be **positive or negative**

- Positive correlation: as variable A increases, variable B increases
- Negative correlation: as variable A increases, variable B decreases
- If there is **no correlation** between variables the **correlation coefficient will be 0**

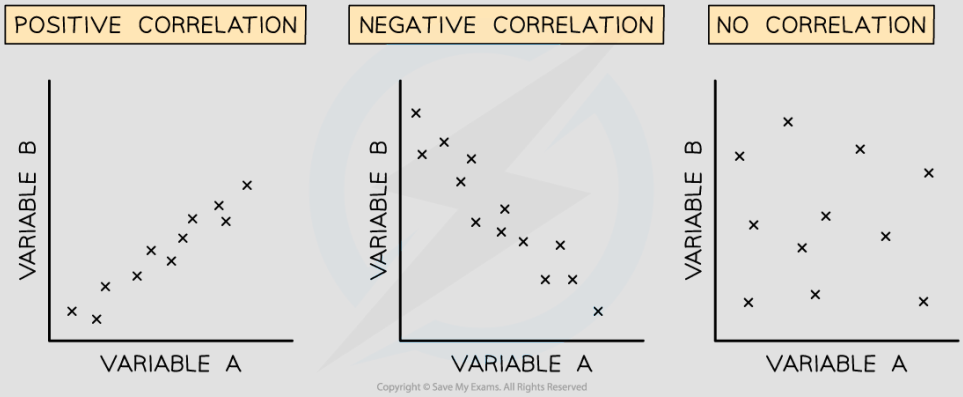


Image showing different types of correlation in scatter graphs

- There is a clear distinction between correlation and causation: **a correlation does not necessarily imply a causative relationship**
- **Correlation** is an association or relationship between variables
- **Causation** occurs when one variable has an influence or is influenced by another

Emphysema

YOUR NOTES

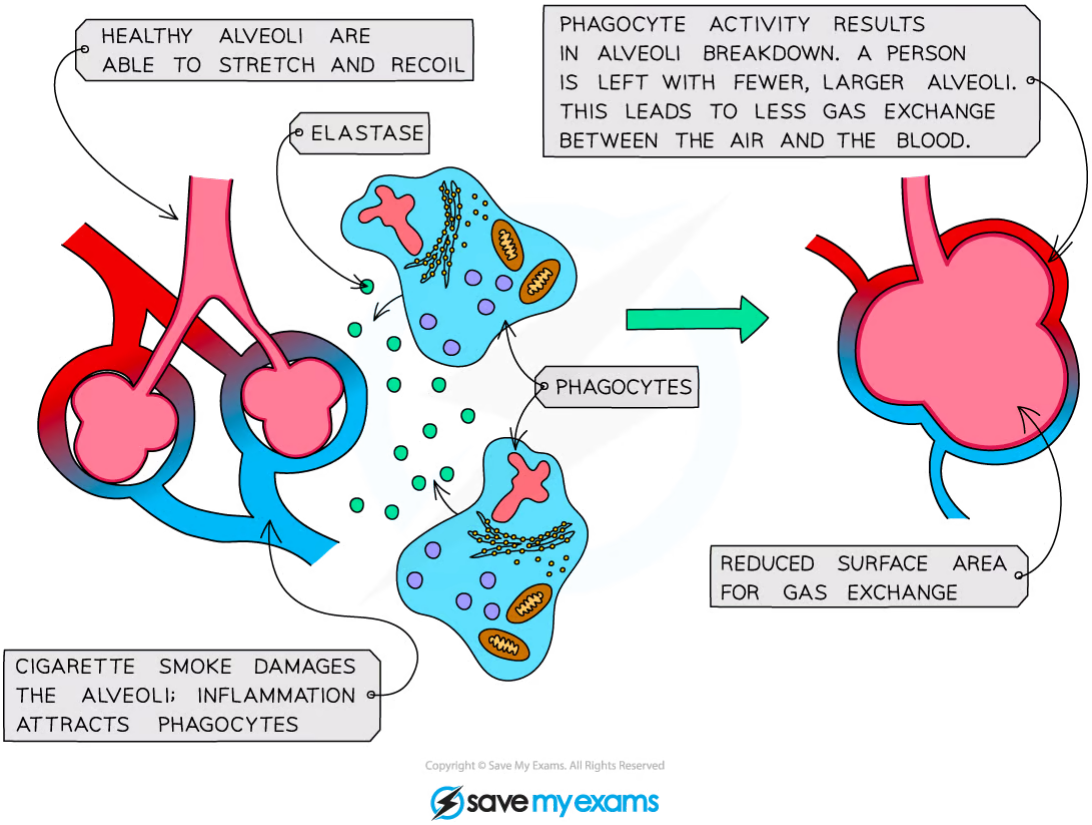
Causes of emphysema

- **Emphysema** is an example of a **Chronic obstructive pulmonary disease** (COPD) which also includes lung diseases such as asthma and chronic bronchitis
- In a healthy lung, **some phagocytes** are present as part of the **non-specific** immune response to protect against bacteria found in the lungs
  - Phagocytes produce the protein digesting enzyme, **elastase** to destroy **bacteria**
  - Elastase also breaks down proteins in the cells of the lungs, including **elastin**
  - An enzyme inhibitor, **alpha 1-antitrypsin (A1AT)**, is produced by lung cells to prevent damage caused by elastase
- In **smokers**, goblet cells in the ciliated epithelium become enlarged and produce more mucus which destroys the **cilia** in the trachea and
- This prevents cilia from sweeping mucus, containing **bacteria, dust and other microorganisms** away from the lungs, this leads to infections in the lungs
- Infections attract more **phagocytes** to the lungs and the phagocytes release **elastase**
- A1AT is not effective against the increased levels of elastase and so the enzyme damages the elasticity of the **alveolar walls**
- Without enough elastin, the alveoli **break down** and may burst, creating large air spaces in the alveoli with an insufficient **surface area to volume ratio**
- **Thickening** of the alveolar walls increases the **diffusion distance** for gas exchange
- This reduces the efficiency of gas exchange, causing **emphysema** where less oxygen is carried in blood (making exercise difficult)
- Once the disease progresses, people often need a constant supply of oxygen to stay alive

Consequences of emphysema

- Damage to the alveoli which result in emphysema, is **irreversible**
- It leads to **low blood oxygen** levels and **high carbon dioxide** levels in patients
- The resultant **symptoms** include
  - Shortness of breath or laboured ventilation
  - A chronic or persistent cough
  - Chest tightness
  - Wheezing and difficulty breathing when exercising or during any physical activity
  - Lack of energy

YOUR NOTES



Emphysema can lead to a reduced number of alveolar air sacs with thicker walls

YOUR NOTES

Practical 6: Monitoring Ventilation

- The volume of air within the lungs of an individual will change depending on their level of activity
  - When at rest, breathing is shallow and slow
  - When exercising, breathing is deeper and more frequent
- The volume of air breathed in and out during normal breathing is the **tidal volume**
  - Normal breathing here refers to a breath that does not involve forced expiration
- The **ventilation rate** is the number of breaths taken per minute
- A piece of equipment called a **spirometer** can be used to create a trace to show the volume changes in the lungs

Practical 6: Monitoring of ventilation in humans at rest and after mild and vigorous exercise

- It is possible to investigate the effect of exercise on ventilation using the following variables
- Dependent variable: The ventilation parameter that is measured
  - This could be the ventilation rate, the tidal volume, or a combination of both
  - These measurements can be taken using a variety of methods, e.g. Basic observations such as counting breaths to measure ventilation rate
  - A data logger such as an inflatable chest belt and pressure sensor to measure ventilation rate
  - A spirometer can measure both ventilation rate and tidal volume
- Independent variable: The type or intensity of exercise
  - The type of exercise could include a range from inactive e.g. lying down, to very active e.g. sprinting, and everything in between
  - E.g. the intensity of the exercise could be measured by increasing speed on a treadmill

Apparatus

- Stop watch
- Inflatable chest belt and pressure sensor OR spirometer

Method: Using an inflatable chest belt

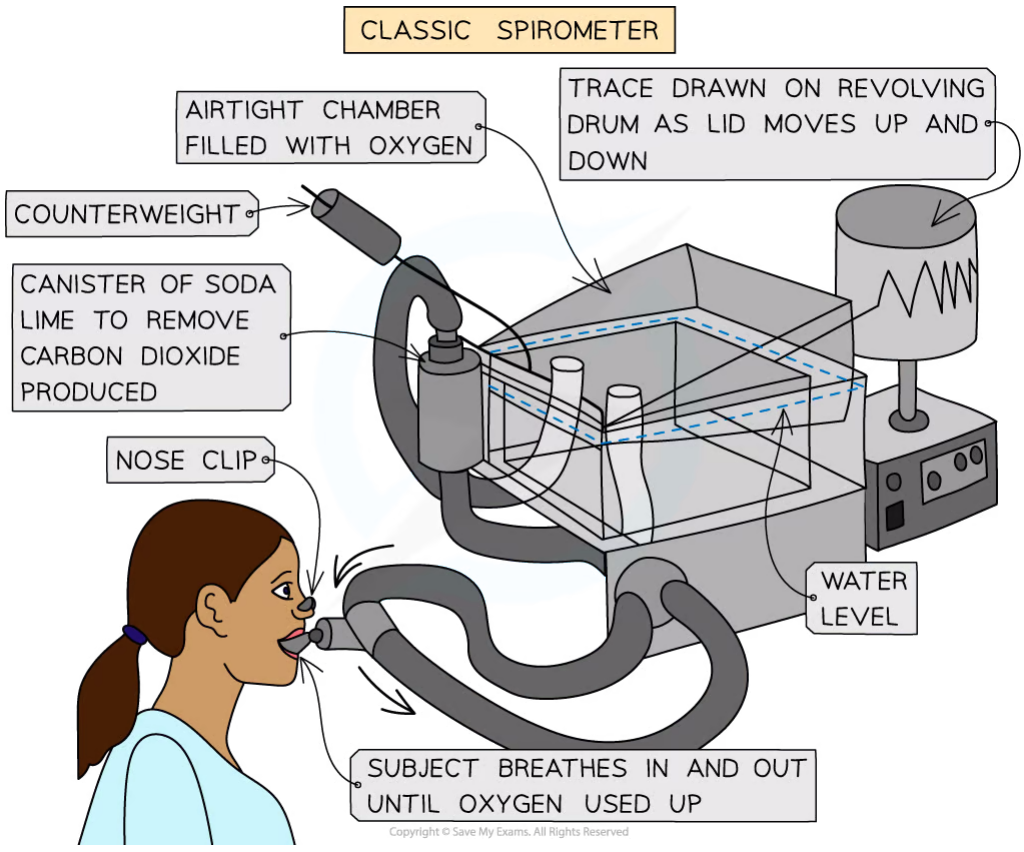
1. Taking breathing measurements using an inflatable chest belt and pressure sensor
2. The person (subject) being examined breathes in and out with a **chest belt** placed around the thorax, that has had air pumped into it
3. As the subject breathes the pressure sensor logs the changes in pressure due to ventilation; the data logged can be viewed on a computer
4. From the data collected, the rate of ventilation can be deduced
5. The subject then repeats steps 1–4 after a period of exercise
   - The **type or intensity** of exercise should be specified
6. The subject then repeats step 5 several more times after exercise of different specified type or intensity e.g., gradually increasing in intensity

YOUR NOTES

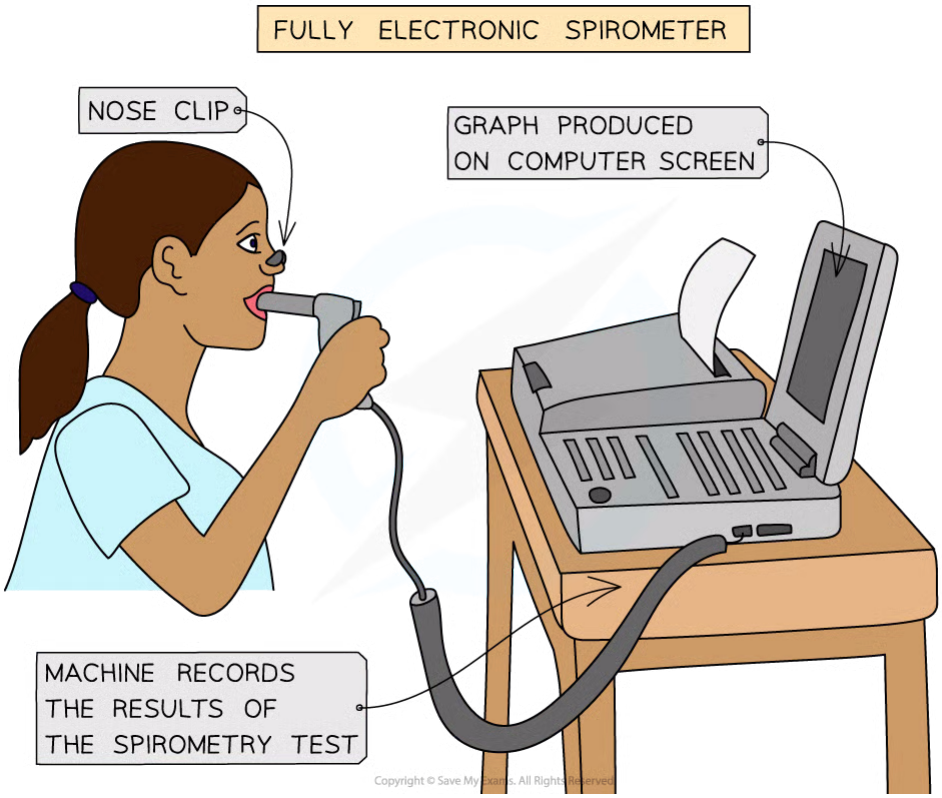
7. A **repeat** of all measurements should be taken and several subjects should be tested in order to collect **reliable results**

Method: Using a spirometer

1. Taking breathing measurements using a **spirometer**
2. The subject being examined breathes in and out **through** the spirometer after a period of rest
3. As the subject breathes through the spirometer, a **trace** is drawn on a rotating drum of paper, or a **graph** is formed digitally which can be viewed on a computer
4. From this trace, the subject's **tidal volume** and **breathing rate** can all be **calculated**
5. The person then completes steps 1–4 after a period of exercise
    - The **type or intensity** of exercise should be specified
6. The subject then repeats step 5 several more times after exercise of different specified type or intensity e.g., gradually increasing in intensity
7. A **repeat** of all measurements should be taken and several subjects should be tested in order to collect **reliable results**



YOUR NOTES



Using a spirometer to monitor ventilation

Analysis

- The effect of exercise on ventilation can be seen in the spirometer trace below
  - Exercise can be seen to increase the rate of ventilation resulting in **more breaths taken per minute**
  - It is also evident that after exercise the tidal volume of the person has increased, which means **more air** is breathed in and out in each breath
  - After exercise, both tidal volume and ventilation rate eventually return to **resting values**

YOUR NOTES

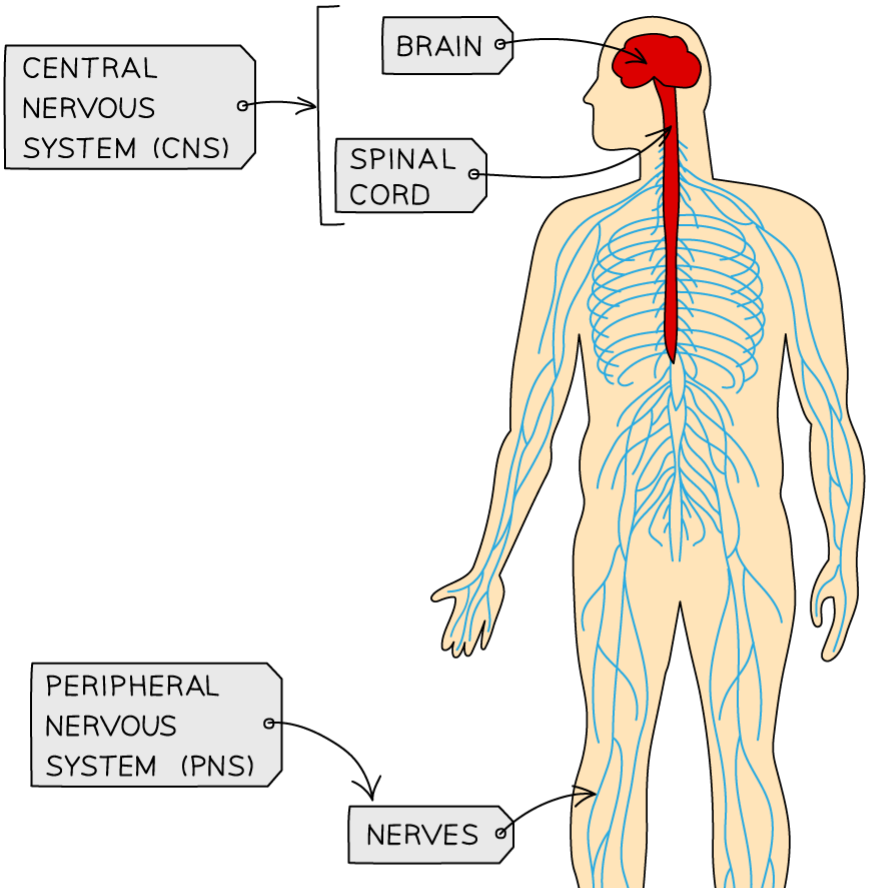
6.5 Neurones & Synapses

6.5.1 Neurones: Function & Structure

Function & Structure of Neurones

The nervous system

- The human nervous system consists of:
  - **Central nervous system** (CNS) – the **brain** and **spinal cord**
  - **Peripheral nervous system** (PNS) – all of the **nerves** in the body
- It allows us to make sense of our surroundings and respond to them, and to **coordinate and regulate body functions**
- Information is sent through the nervous system in the form of **electrical impulses** – these are electrical signals that pass along **nerve cells** known as **neurones**
  - A **bundle of neurones** is known as a **nerve**
- The nerves spread out from the central nervous system to **all other regions of the body** and importantly, to all of the **sense organs**
  - The **CNS** acts as a **central coordinating centre** for the impulses that come in from, and are sent out to, any part of the body



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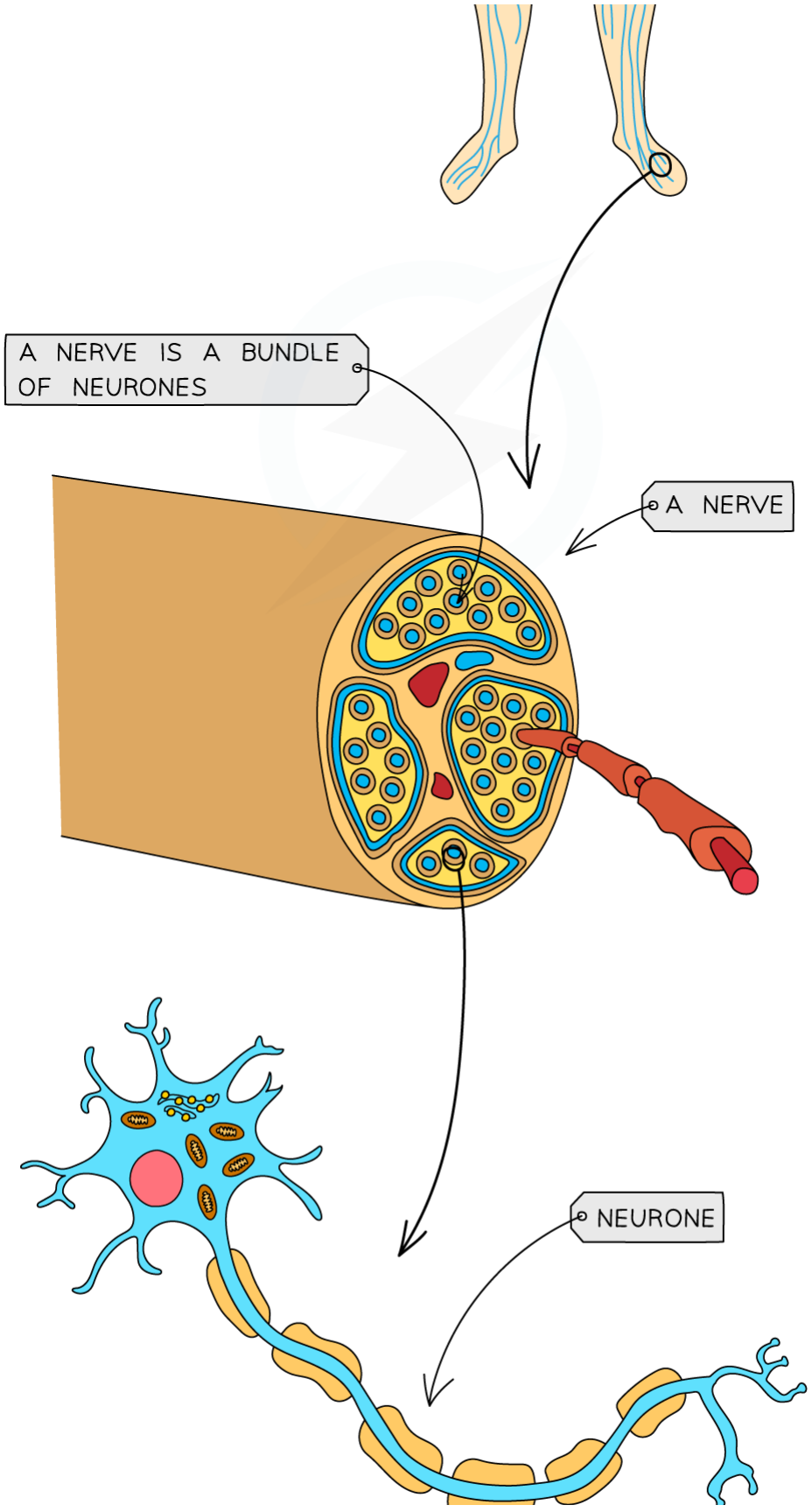
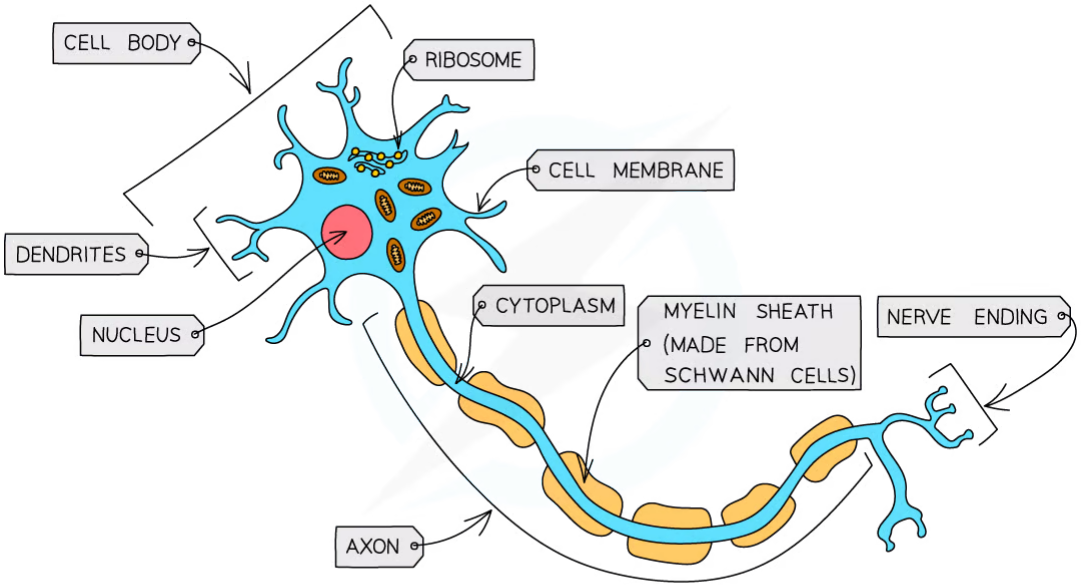


YOUR NOTES

The human nervous system is comprised of the CNS and the PNS

Neurones

- The following features are found in neurones:
  - Neurones have a **main, long, fibre** known as an **axon**
  - They have a **cell body** that contains the **nucleus** and other cellular structures
  - Their **cell bodies** and **axon terminals** contain many extensions called **dendrites**
  - These **dendrites** allow them to **connect** to **many other neurones** and receive **impulses** from them, forming a **network** for easy **communication**



Neurones have a characteristically elongated structure which allows them to transfer information between the central nervous system and the rest of the body

Research

YOUR NOTES

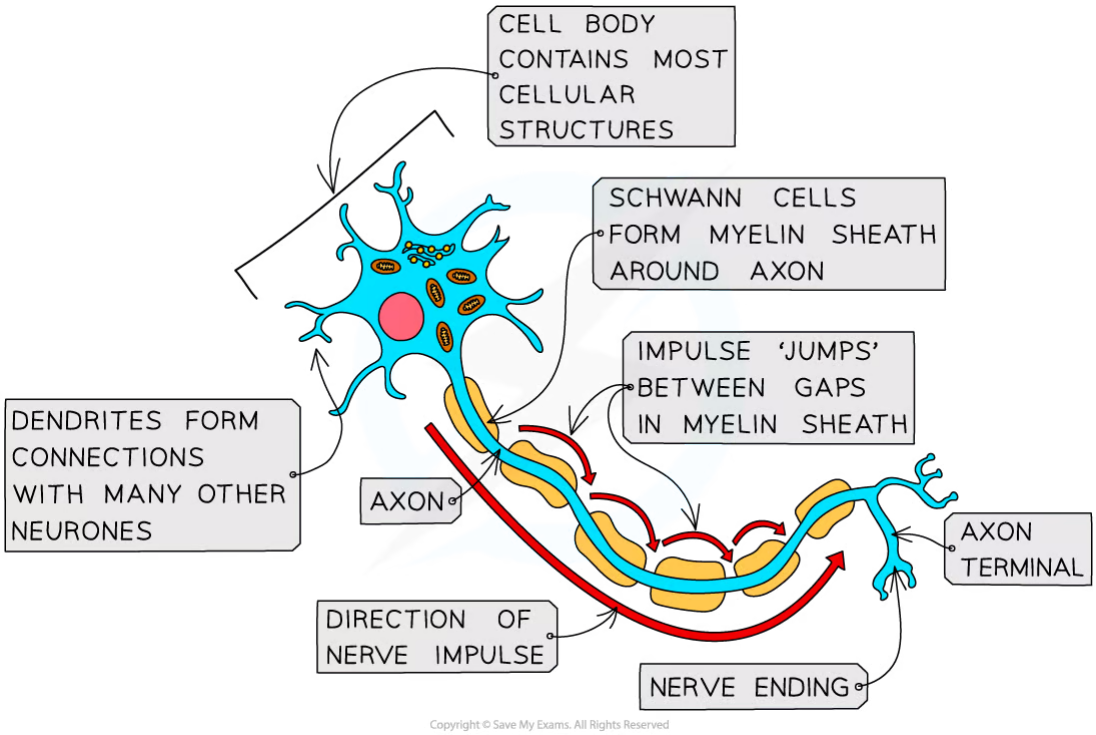
NOS: Cooperation and collaboration between groups of scientists; biologists are contributing to research into memory and learning

- Some of the so-called **'higher' functions of the brain** e.g., memory and learning, are still not fully understood and are the focus of much **current research**
- **Biologists are becoming increasingly involved** in this research, which uses techniques from the fields of **neurobiology**, **molecular biology,** and **biochemistry** to understand the mechanisms behind these brain functions
- The Centre for Neural Circuits and Behaviour (CNCB) at the University of Oxford is a good example of an institution in which scientists with different areas of expertise **collaborate**, or work together, with a **common research goal**
    - The research team at the CNCB contains experts in various fields of biological science, including medicine, physiology, genetics, molecular biology, neurobiology, and neurogenetics
- Research into functions of the brain such as memory and learning not only involves **collaboration** between scientists from **different specialities,** but also from **different countries**

YOUR NOTES

Myelination

- Neurones have a **main, long, fibre** known as an **axon**
- The axons of neurones are **surrounded** by specialised cells called **Schwann cells**
- Schwann cells **wrap themselves around the axon**, forming a structure known as a **myelin sheath**
  - **Myelin** contains the **phospholipids** of the **Schwann cell membranes**; it is built up in layers as the Schwann cells grow around the axon
  - The **lipid** content of the myelin sheath gives it a **high electrical resistance**
- The myelin sheath acts as an **electrical insulator;** impulses cannot pass through the myelin sheath
- The myelin sheath has **small, uninsulated sections** in the gaps between the individual Schwann cells
  - These gaps are called **nodes of Ranvier**
- Electrical impulses effectively **jump** from one node of Ranvier to the next
  - This process is known as **saltatory conduction**
  - It greatly **speeds up the rate of transmission of impulses** along myelinated neurones
  - In non-myelinated neurones the axon is not insulated by myelin, so the impulse travels **more slowly**



An impulse travels down a neurone via saltatory conduction

YOUR NOTES

Resting Potential

- **Neurones** transmit information in the form of **impulses**, which travel extremely quickly along the neurone from one end to the other
  - Note that an impulse is **not** an electrical current that flows along neurones as if they were wires
  - Instead, an impulse is a **momentary reversal in the electrical potential difference** across the **neurone cell surface membrane**
    - The electrical potential difference across a membrane can also be described as the **voltage** across a membrane, the **difference in charge** across a membrane, or the **membrane potential**
- In an axon that is **not transmitting an impulse** the **inside** of the axon always has a **negative electrical potential**, or charge, compared to **outside** the axon, which has a **positive electrical potential**
  - This membrane potential in a resting neurone is known as **resting potential**
- The **resting potential** is usually about **–70 millivolts (mV)**
  - This means that the **inside** of the resting axon has a **more negative** electrical charge than the **outside** by about 70 mV
- Two main processes contribute to establishing and maintaining resting potential:
  - **The active transport of sodium ions and potassium ions**
  - **A difference in rates of diffusion of sodium ions and potassium ions**
- In addition to these two main processes, **negatively charged proteins** inside the axon also contribute to the negative resting potential

The **active transport of sodium ions and potassium ions**

- Carrier proteins called sodium-potassium pumps are present in the cell surface membranes of neurones
- These pumps use **ATP** to actively transport **sodium ions** (Na^+) **out** of the axon and **potassium ions** (K^+) **into** the axon
- The two types of ion are pumped at an unequal rate; for every **3 sodium ions that are pumped out** of the axon, only **2 potassium ions are pumped in**
- This creates a concentration gradient across the membrane for both sodium ions and potassium ions

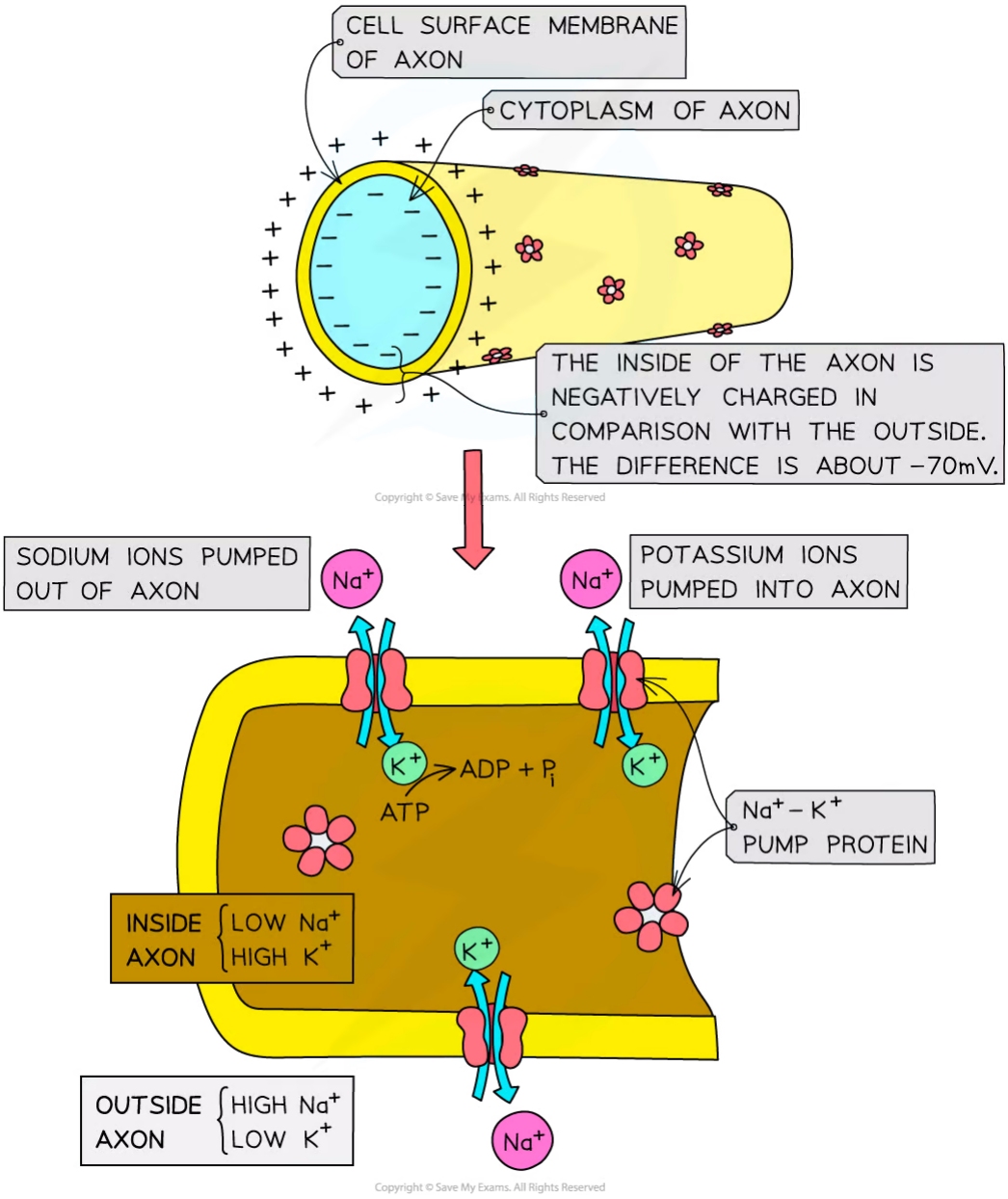
Difference in rates of diffusion of sodium ions and potassium ions

- Because of the concentration gradient generated by the **sodium–potassium pumps**, both sodium and potassium ions will diffuse back across the membrane
  - The neurone cell surface membrane has **sodium ion channels** and **potassium ion channels** that allow sodium and potassium ions to move across the membrane by **facilitated diffusion**
- The neurone membrane is much **less permeable** to sodium ions than potassium ions, so potassium ions inside the neurone can diffuse **out** at a **faster rate** than **sodium ions** can

YOUR NOTES

diffuse **back in**

- This results in **far more positive ions** on the **outside** of the neurone than on the inside, generating a **negative charge inside** the neurone in relation to the outside
- The result of this is that the neurone has a **resting membrane potential** of around **-70 millivolts (mV)**



Sodium-potassium pumps in the membrane of a resting neurone generate a concentration gradient for both sodium ions and potassium ions. This process, together with the facilitated diffusion of potassium ions back out of the cell at a faster rate than sodium ions diffuse back into the cell, generates a negative resting potential across the membrane.

Action Potential

YOUR NOTES

- Once resting potential is reached, the neurone membrane is said to be **polarised**
- To initiate a nerve impulse in a neurone, the neurone membrane needs to be **depolarised**
  - Depolarisation is the **reversal of the electrical potential difference** across the membrane
- The depolarisation of the membrane occurs when an **action potential** is generated
  - Action potentials lead to the reversal of resting potential from around **-70 mV** to around **+40 mV**
- Action potentials involve the **rapid movement** of **sodium ions** and **potassium ions** across the **membrane** of the **axon**
- An action potential is the **potential electrical difference** produced across the axon membrane when a neurone is **stimulated** e.g. when an environmental stimulus is detected by a receptor cell

How an action potential is produced

- Some of the ion channels in the membrane of a neurone are **voltage gated**, meaning that they open and close in response to changes in the **electrical potential** across the membrane
  - Voltage gated ion channels are **closed** when the membrane is at rest, but they are involved in the generation and transmission of action potentials
  - Note that not all of the channels in a neurone membrane are voltage gated e.g. some types of potassium ion channel are open when a neurone is at rest to enable potassium ions to diffuse out of the axon and generate resting potential
- When a neurone is stimulated, the following steps occur:
  - A small number of **sodium ion channels** in the axon membrane **open**
  - **Sodium ions** begin to move **into the axon** down their **concentration gradient**
    - There is a greater concentration of sodium ions outside the axon than inside due to the action of sodium-potassium pumps
  - This **reduces** the **potential difference** across the axon membrane as the **inside** of the axon becomes **less negative**
  - If enough sodium ions enter the axon and the potential difference is reduced enough, **voltage gated sodium ion channels** open, leading to a further, large influx of sodium ions
  - Once the charge has been reversed from -70 mV to around +40 mV, **an action potential** is said to have been **generated**

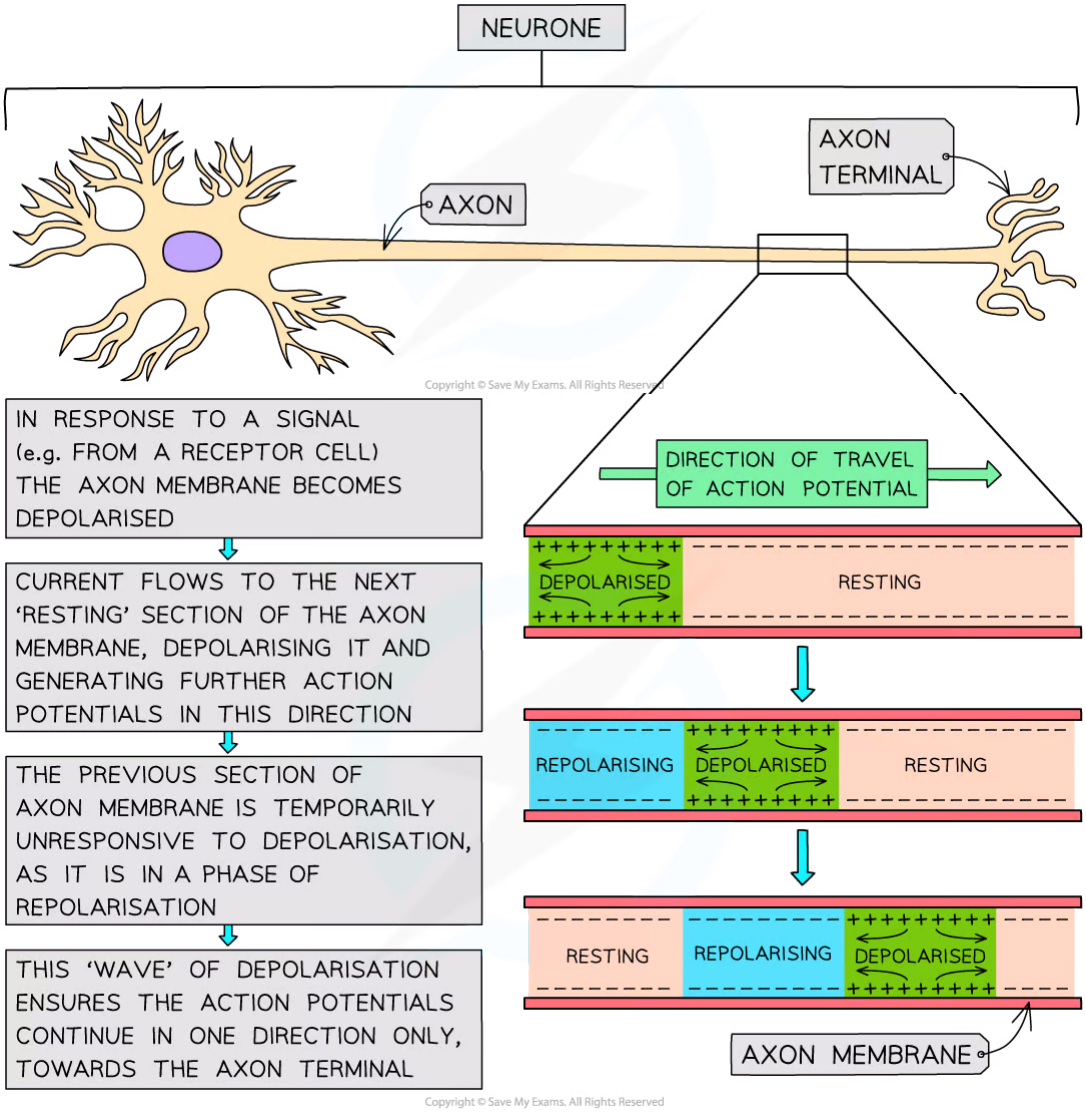
How an action potential is propagated

- Once an action potential has been generated, it can be **propagated**, or transmitted, along the length of the axon
  - The depolarisation of the membrane at the site of the first action potential causes **sodium ions** to diffuse along the cytoplasm into the next section of the axon, **depolarising** the membrane in this new section, and causing voltage gated sodium channels to open
  - This triggers **another action potential** in this section of the axon membrane

YOUR NOTES

- This process then repeats along the length of the axon

- In the body, this allows action potentials to begin at one end of an axon and then pass along the entire length of the axon membrane



How an impulse is propagated in one direction along the axon of a neurone

Repolarisation

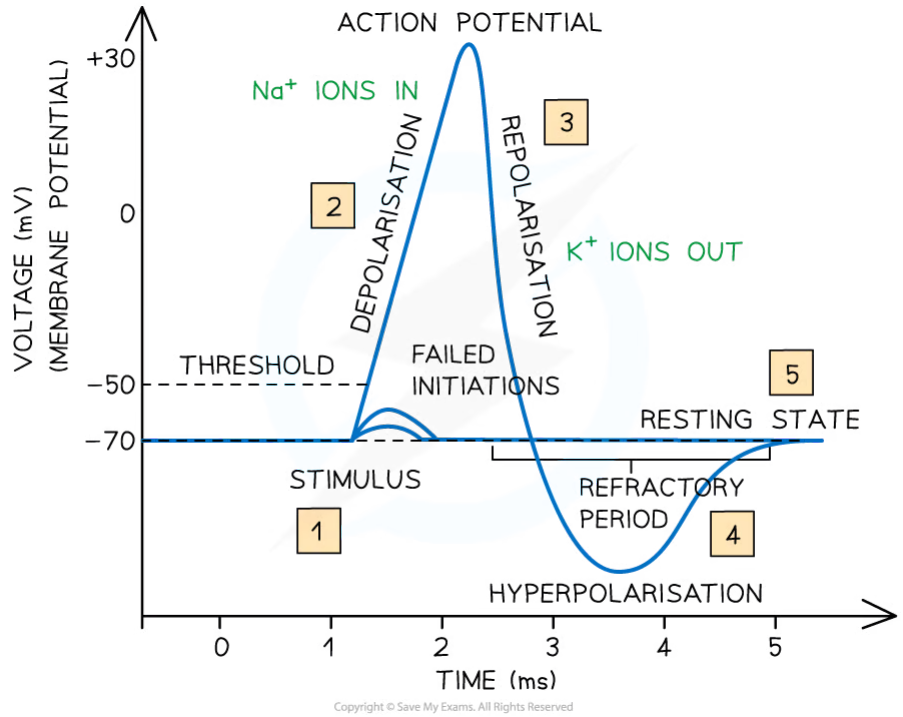
- About 1 ms after an action potential is generated, all the **voltage gated sodium channels** in this section of membrane **close**
- **Voltage gated potassium channels** in this section of axon membrane now **open**, allowing the diffusion of potassium ions **out of the axon**, down their concentration gradient
  - Remember that the sodium-potassium pumps have not stopped working during the action potential; hence the potassium ion gradient is still present

- This movement of potassium ions causes the inside of the axon to become negatively charged again, a process known as **repolarisation**

YOUR NOTES

- There is a short period during which the membrane potential is more negative than resting potential; this is known as **hyperpolarisation**
- The period during which the membrane is hyperpolarised is known as the **refractory period**
  - The membrane is unresponsive to stimulation during the refractory period, so a new action potential cannot be generated at this time
  - This makes the action potentials **discrete** events and means the impulse can **only travel in one direction**
  - This is essential for the successful and efficient transmission of nerve impulses along neurones

- The voltage gated potassium channels then **close,** and the **sodium-potassium pumps** work to restore **resting potential**
  - Only once resting potential is restored can the membrane be stimulated again



The depolarisation and repolarisation of an action potential can be clearly seen in a graph of membrane potential against time

Threshold Potential

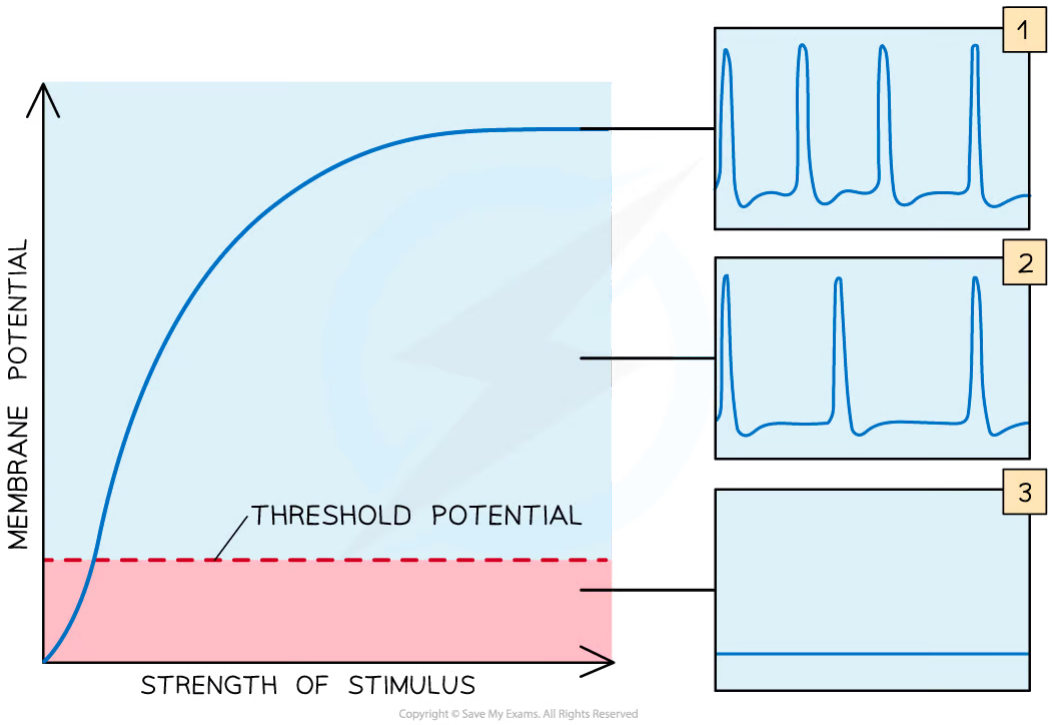
YOUR NOTES

- An **action potential** is only **initiated** if the **threshold potential** is reached
- When a neurone is stimulated, sodium ion channels in the axon membrane open and sodium ions pass into the axon down their concentration gradient
- This causes the inside of the axon to become **less negative,** but exactly how much less negative it becomes is dependent on the number of sodium ion channels that open
  - A large stimulus will cause more channels to open than a small stimulus
  - If more channels open, then more sodium ions will enter the axon, causing it to become less negative
- If the potential difference reaches around **-50 mV,** known as the **threshold potential**, voltage gated sodium ion channels open and **many more** sodium ions enter the axon
  - This causes the membrane potential to reach around +40 mV
- Once the charge has been reversed from -70 mV to +40 mV, an action potential is generated

The all-or-nothing principle

- Action potentials are either generated or not generated depending on whether the threshold potential is reached; there is **no such thing as a small or large action potential**
  - If a stimulus is **weak,** only a few sodium ion channels will open and the membrane won't be sufficiently depolarised to reach the **threshold potential;** an action potential will not be generated
  - If a stimulus is **strong enough** to raise the membrane potential above the **threshold potential** then an action potential will be generated
- This is the **all-or-nothing principle**
  - An impulse is **only transmitted** if the **initial stimulus is sufficient** to increase the membrane potential above a **threshold potential**
- Stimulus size can be detected by the brain because as the **intensity of a stimulus increases**, the **frequency** of action potentials transmitted along the neurone **increases**
  - This means that a small stimulus may only lead to one action potential, while a large stimulus may lead to several action potentials in a row

YOUR NOTES



1 THE MEMBRANE IS GIVEN A STRONG STIMULUS WHICH GENERATES A HIGH FREQUENCY OF ACTION POTENTIALS

2 THE MEMBRANE IS GIVEN A WEAK STIMULUS WHICH GENERATE A LOW FREQUENCY OF ACTION POTENTIALS

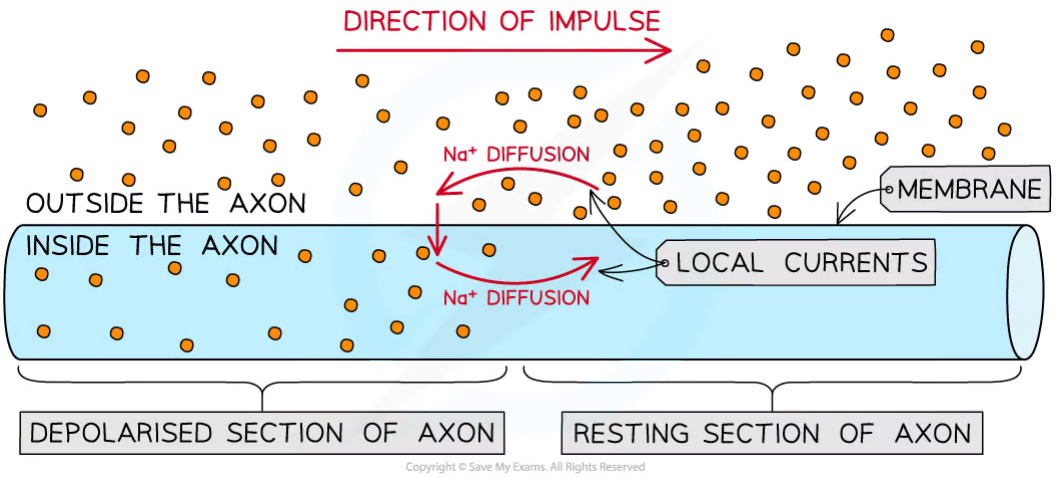
3 THE MEMBRANE IS GIVEN A VERY WEAK STIMULUS WHICH FAILS TO GENERATE AN ACTION POTENTIAL

As the strength of a stimulus increases beyond the threshold potential, the frequency of action potentials increases

Local Currents

YOUR NOTES

- The propagation of nerve impulses along axons occurs due to **local currents** that cause each successive section of the axon to reach the **threshold potential**
- **Inside** the **depolarised** section of the axon
  - There is a **high concentration** of sodium ions due to their recent **influx**
  - This creates a **concentration gradient** between the section of the axon that has depolarised and the section next to it
  - Sodium ions diffuse along **inside** the axon to the neighbouring section of axon that has not yet become depolarised
  - This reduces the negative membrane potential in the new section of axon and, if a threshold is reached, begins the initiation of an action potential
    - This enables the original action potential to be propagated
- On the **outside** of the axon
  - There is a higher concentration of sodium ions outside the section of axon that has **not yet become depolarised** due to the diffusion of sodium ions into the depolarised section
  - Sodium ions diffuse from here along the outside of the axon to the section of axon that has just become depolarised
- These movements of sodium ions are known as **local currents**
- These local currents cause a **wave of depolarisation** and **repolarisation** to travel along the axon, resulting in the **propagation of a nerve impulse**

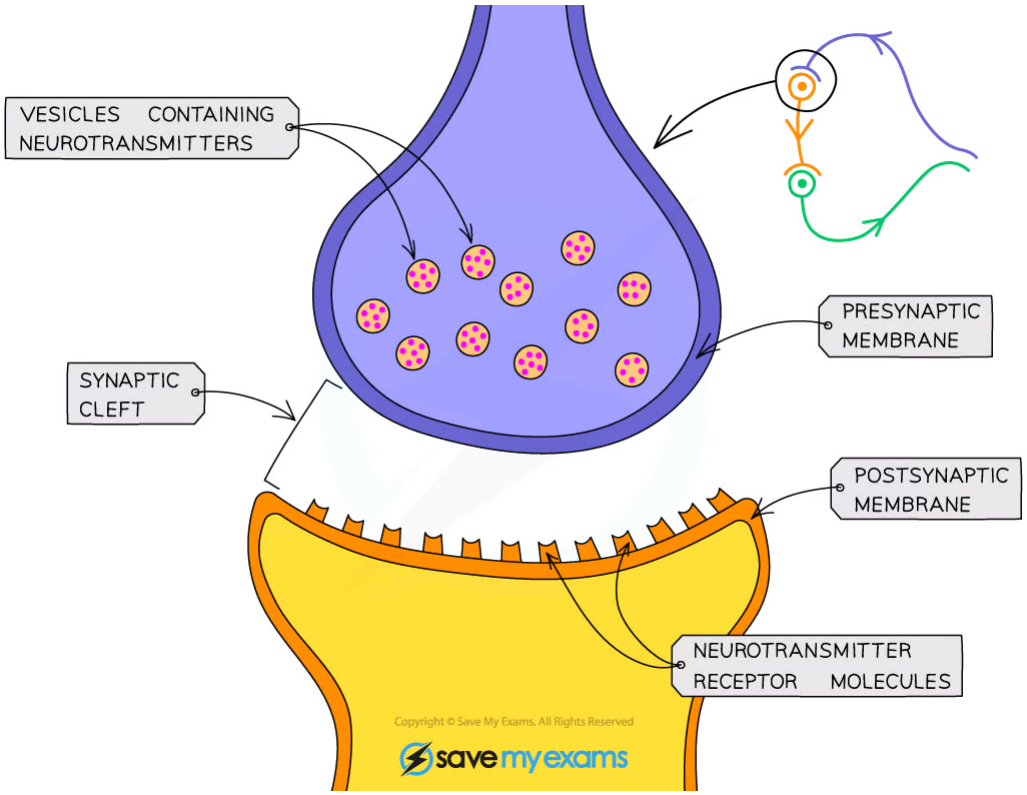


The propagation of nerve impulses along axons occurs due to local currents created by the diffusion of sodium ions

YOUR NOTES

Synapses

- Where two neurones meet, they do not actually come into **physical contact** with each other
- Instead, a very small gap, known as the **synaptic cleft**, separates them
- The ends of the two neurones, along with the synaptic cleft, form a structure known as a **synapse**
- Synapses act as the junctions **between any cells in the nervous system**, e.g.
  - In the sense organs, there are synapses between **sensory receptor cells** and **sensory neurones**
  - In muscles, there are synapses between **motor neurones** and **muscle fibres**



A synapse

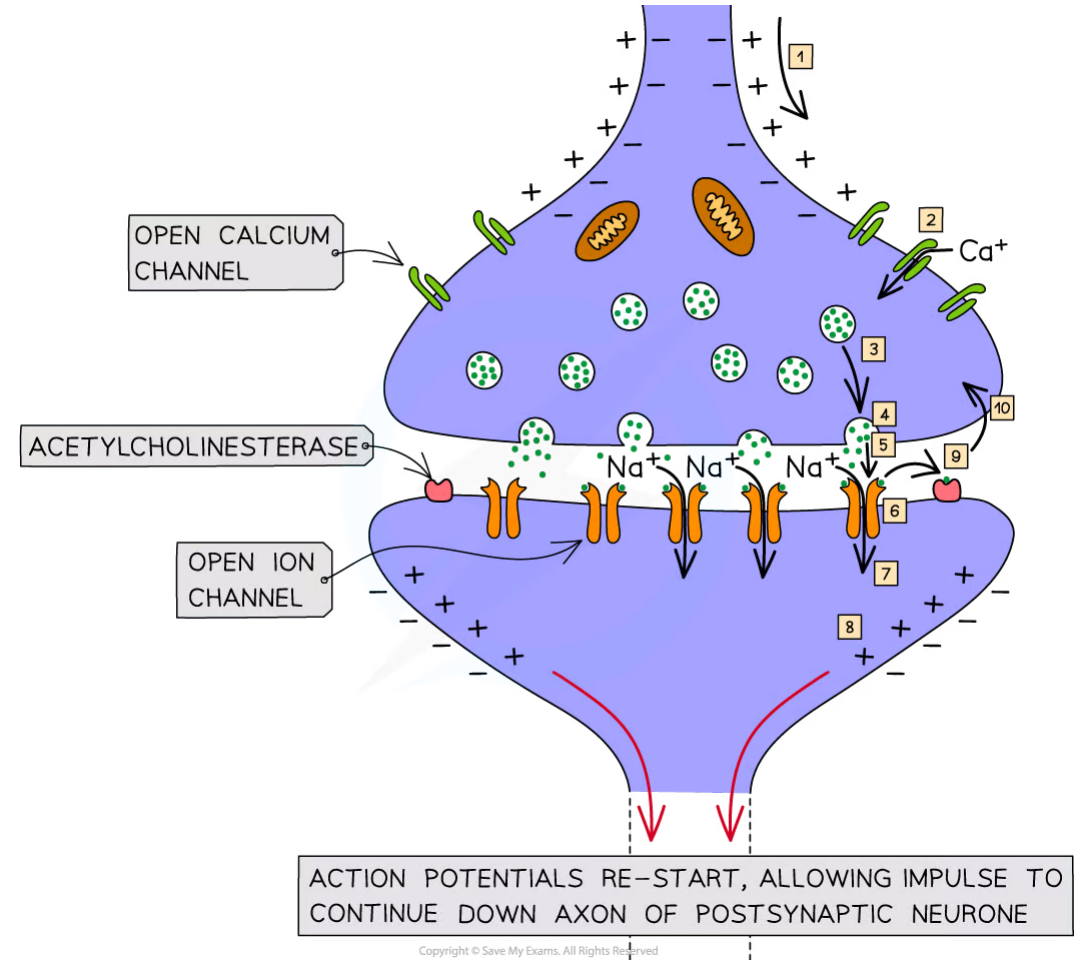
Synaptic transmission

- Electrical impulses cannot 'jump' across the synaptic cleft
- When an electrical impulse arrives at the end of the axon on the **presynaptic neurone**, the **membrane** of the presynaptic neurone becomes depolarised, triggering an influx of **calcium ions** into the presynaptic cell via **calcium ion channels** in the membrane
- The calcium ions cause vesicles in the presynaptic neurone to move towards the presynaptic membrane where they fuse with it and **release chemical messengers** called **neurotransmitters** into the synaptic cleft
  - A common neurotransmitter is **acetylcholine**, or **ACh**

YOUR NOTES

- The neurotransmitters **diffuse** across the **synaptic cleft** and **bind with receptor molecules** on the **postsynaptic membrane**; this causes associated **sodium ion channels** on the postsynaptic membrane to open, allowing **sodium ions** to diffuse into the postsynaptic cell
- If enough neurotransmitter molecules bind with receptors on the postsynaptic membrane then an **action potential** is generated, which then travels down the **axon** of the **postsynaptic neurone**
- The neurotransmitters are then **broken down** to prevent continued stimulation of the postsynaptic neurone
    - The enzyme that breaks down acetylcholine is **acetylcholinesterase**

YOUR NOTES



Synaptic transmission using the neurotransmitter acetylcholine

Unidirectionality

YOUR NOTES

- Synapses ensure the **one-way transmission** of impulses
- Impulses can only pass in **one direction** at synapses because **neurotransmitter is released on one side** and its **receptors are on the other** – chemical transmission cannot occur in the opposite direction
- This prevents impulses from travelling the wrong way

Acetylcholine

- There are over 40 different known **neurotransmitters**
  - Examples include dopamine and noradrenaline
- One of the key neurotransmitters used throughout the nervous system is **acetylcholine (ACh)**
  - ACh is produced in the **presynaptic neurone** by combing **choline** with an **acetyl group**
  - Synapses that use the neurotransmitter ACh are known as **cholinergic synapses**
- Acetylcholine is released into the **synaptic cleft** when **ACh-containing vesicles** fuse with the **presynaptic membrane**, releasing ACh molecules into the **synaptic cleft**
- ACh **binds to specific receptors** on the postsynaptic membrane, where it can **generate an action potential** in the postsynaptic cell by opening **associated sodium ion channels**
- To prevent the sodium ion channels staying permanently open and to stop permanent depolarisation of the postsynaptic membrane, the **ACh molecules are broken down** and **recycled**
  - The enzyme **acetylcholinesterase** catalyses the **hydrolysis** of ACh molecules into **acetate** and **choline**
  - The products of hydrolysis are then **absorbed back into the presynaptic neurone**, and the **active neurotransmitter** ACh is reformed

Inhibition of Acetylcholine Receptors

- **Neonicotinoids** are synthetic compounds similar to nicotine that are commonly found in **pesticides**
- Neonicotinoids can **block** synaptic transmission at **cholinergic synapses** in **insects** by binding to **acetylcholine receptors**
  - This binding is **irreversible**, as **acetylcholinesterase** cannot break down neonicotinoids
  - As the acetylcholine receptors are blocked, **acetylcholine is unable to bind**, which **stops impulses** from being transmitted across synapses
  - This leads to **paralysis** and **death** in insects
- Neonicotinoids are considered to be especially suitable as pesticides because they're **not toxic to humans and other mammals**
  - A much larger proportion of synapses in insects are cholinergic compared to mammals
  - Neonicotinoids bind much more strongly to acetylcholine receptors in insects
- There is a great deal of controversy over the use of neonicotinoid pesticides because of the impact that they are thought to have on essential pollinators such as bees

YOUR NOTES

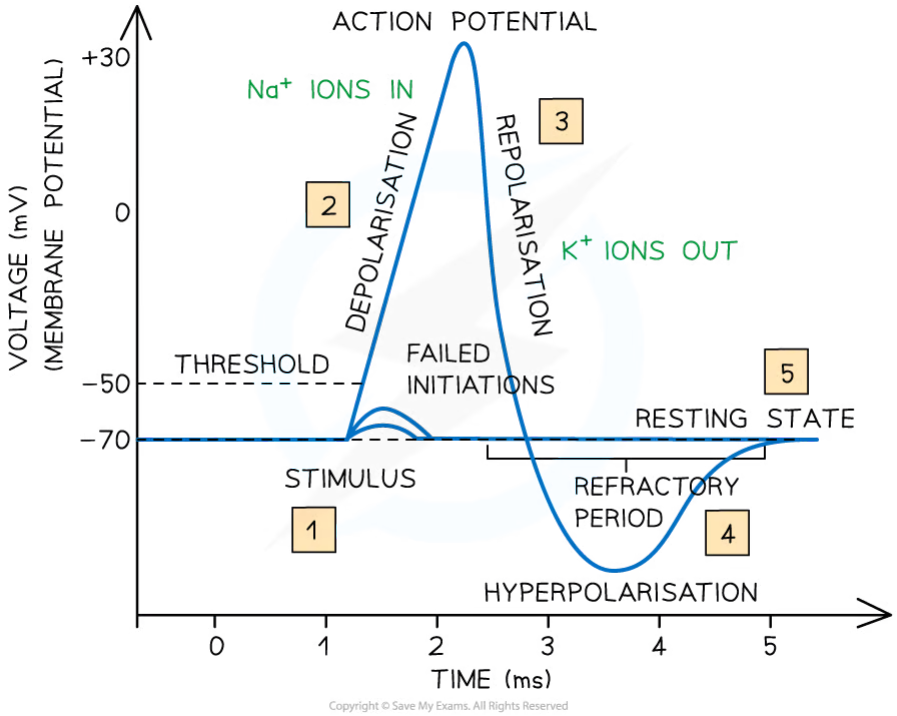
Analysis of Oscilloscope Traces

- It is possible to **measure membrane potentials** in neurones by placing electrodes on each side of the membrane
  - A membrane potential is the **difference in charge** between one side of a membrane and the other, sometimes described as the potential difference, or the voltage
- The membrane potential can then be **visually represented** and **displayed** using an **oscilloscope**
- An oscilloscope is a type of **electronic test instrument** that **graphically displays varying signal voltages**
- The display produced is **like a graph** with **time** in milliseconds on the **x-axis** and the membrane **potential** in millivolts on the **y-axis**

How to analyse oscilloscope traces showing resting potentials and action potentials

- If there is a **resting potential**, a **straight, horizontal line** should be shown on the display screen of the oscilloscope at a level of **-70 mV**
- If an **action potential** occurs a **spike,** rising up to a maximum voltage of **between +30 and +40 mV,** should be shown on the display
  - The **rising phase** of the spike shows depolarisation
  - The **falling phase** of the spike shows repolarisation
- Often not shown on an action potential graph is the gradual rise in membrane potential just before the membrane rapidly depolarises
  - Before threshold potential is reached, only a small number of sodium channels in the membrane are open, so the membrane depolarises slowly, but when the threshold is reached many more sodium channels open
- Instead of repolarisation causing the membrane potential to return **immediately** to the normal resting potential of -70 mv, the trace often shows a **short period** of **hyperpolarisation**
  - This is when the membrane potential briefly becomes **more negative** than resting potential

YOUR NOTES



An example of an oscilloscope trace showing resting potential and an action potential

YOUR NOTES

6.6 Hormones, Homeostasis & Reproduction

6.6.1 Hormones

Insulin & Glucagon

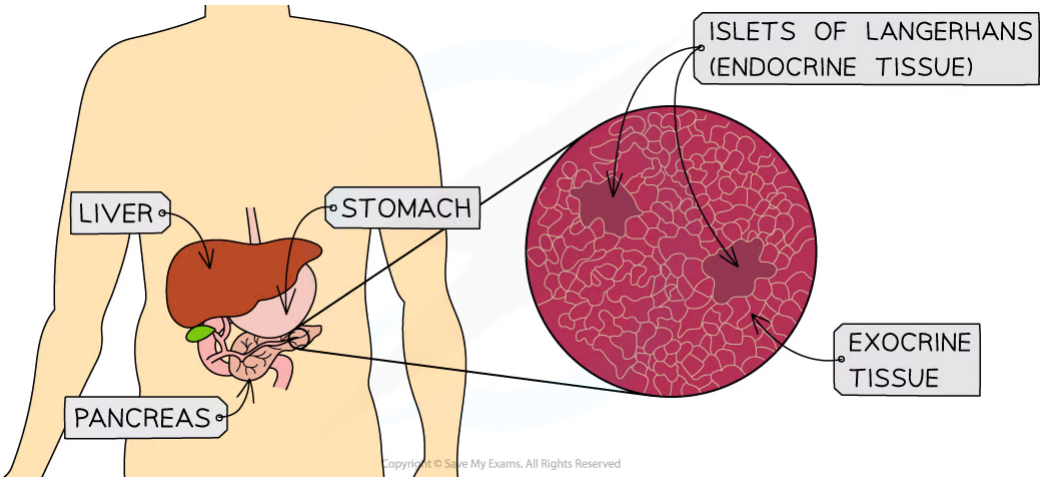
Introduction to Hormones

- A **hormone** is a chemical substance produced by an **endocrine gland** and **carried by the blood**
  - The endocrine glands that produce hormones in animals are known collectively as the **endocrine system**
  - A **gland** is a group of cells that produces and releases one or more substances (a process known as secretion)
- Hormones are **chemicals** which transmit information from one part of the organism to another and that bring about a **change**
- They alter the activity of one or more **specific target organs**
  - Hormones only affect cells with **receptors** that the hormone can bind to
  - These are either found on the cell surface membrane, or inside cells
  - Receptors have to be **complementary** to hormones for there to be an effect
- Hormones are used to control functions that **do not need instant responses**

Insulin and Glucagon

- The pancreas is an organ found in the abdomen of mammals
- It functions as both an **endocrine gland** and an **exocrine gland**
  - Endocrine glands secrete hormones **directly** into the blood, whereas exocrine glands secrete substance **via a duct**
  - The **exocrine** function of the pancreas is to **produce digestive enzymes** to be delivered to the small intestine
  - The **endocrine** function of the pancreas is to **produce the hormones glucagon and insulin**
- Within the pancreas, these two functions are performed by **different tissues**
  - Most of the cells of the pancreas secrete digestive enzymes, but throughout the organ, there are small sections of cells known as the **islets of Langerhans** that produce hormones
  - The islets of Langerhans contain **two** cell types: **alpha cells** (α cells), which secrete **glucagon**, and **beta cells** (β cells), which secrete **insulin**

YOUR NOTES

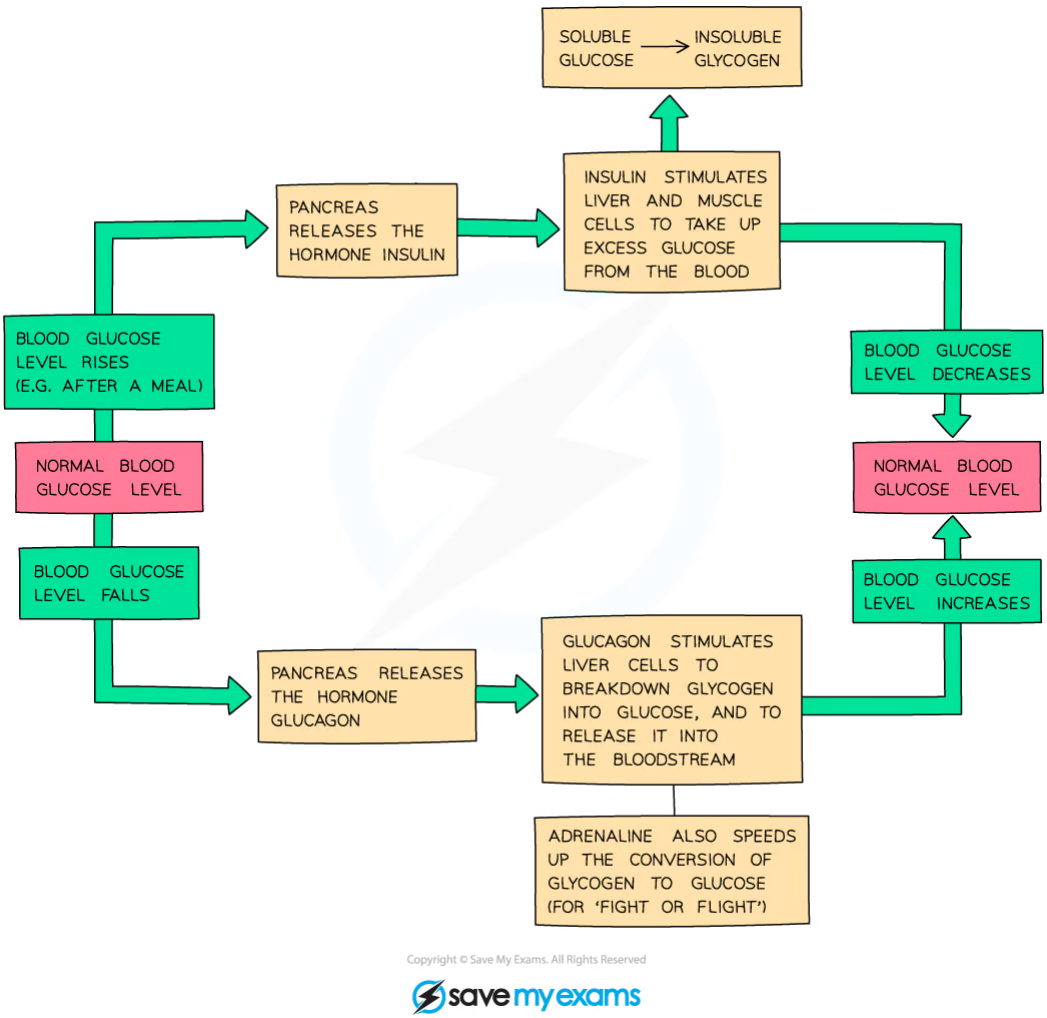


The location and structure of the pancreas

The control of blood glucose by glucagon and insulin

- If the concentration of glucose in the blood **decreases** below a certain level, cells may not have enough glucose for **respiration** and so may not be able to function normally
- If the concentration of glucose in the blood **increases** above a certain level, this can also **disrupt the normal function of cells**, potentially causing major problems
- The control of blood glucose concentration is a key part of **homeostasis**
- Blood glucose concentration is controlled by **glucagon** and **insulin**:
  - **Glucagon** is synthesised and secreted by **α cells** when **blood glucose falls** and stimulates liver and muscle cells to **convert stored glycogen** into **glucose** to be released into the blood, **increasing blood glucose concentration**
  - **Insulin** is synthesised and secreted by **β cells** when **blood glucose rises** and stimulates liver and muscle cells to **convert excess glucose into glycogen** to be stored, **decreasing blood glucose concentration**

YOUR NOTES



Control of blood glucose levels

Exam Tip

The terms glucagon and glycogen are very often mixed up by students as they sound similar. Remember:

- Glucagon is the **hormone**
- Glycogen is the **polysaccharide** that **glucose is stored as**

Learn the differences between the spellings and what each one does so you do not get confused in the exam!

Diabetes

YOUR NOTES

- There are over 3 million people suffering from diabetes in the UK
- Diabetes is a condition in which the homeostatic control of blood glucose has failed or deteriorated
- In individuals with diabetes their **insulin function is disrupted** which allows the **glucose concentration in the blood to rise**
- An elevated blood glucose level can lead to noticeable symptoms, some of which are harmful, e.g.
  - The kidneys are unable to filter out this excess glucose in the blood and so it is often present in the **urine**
  - The increased glucose concentration also causes the kidneys to produce large quantities of urine, making the individual feel thirsty due to **dehydration**
  - Continuously elevated blood glucose levels can also damage tissues, in particular their proteins
- There are two different types of diabetes: **type I** and **type II**

Type I diabetes

- **Type 1 diabetes** is a condition in which the pancreas fails to produce sufficient insulin to control blood glucose levels
- It normally begins in childhood due to an **autoimmune response** whereby the body's immune system **attacks the β cells** of the islets of Langerhans in the pancreas
  - The β cells **produce** and **release insulin**
- Insulin causes the cells to take up glucose from the blood for **respiration** and for storage as **glycogen**; without insulin the glucose remains in the blood, resulting in an individual feeling **fatigued**
- If the blood glucose concentration reaches a dangerously high level after a meal then **organ damage** can occur
- Type 1 diabetes is normally treated with regular blood tests to check glucose levels, **insulin injections** and a diabetes appropriate **diet**
  - Health authorities encourage type I diabetics to eat a similar diet to the general public. They suggest five portions of fruit and veg a day, minimally processed food and consuming more polysaccharides than monosaccharides or disaccharides
- The insulin used by diabetics can be **fast-acting** or **slow-acting**; each allowing for a different level of control

Type II diabetes

- Type II diabetes is more common than type I
- It usually develops in those **aged 40 and over,** however more and more young people are developing the condition
- In type II diabetes the pancreas still produces insulin but the receptors have reduced in number or no longer respond to it
- The lack of response to insulin means there is a **reduced glucose uptake** by the cells, which leads to a **high blood glucose concentration**
  - This can cause the **β cells** to produce more and more insulin in the attempt to lower blood glucose levels

YOUR NOTES

- Eventually the β cells can no longer produce enough insulin and blood sugar becomes uncontrollable

- For type II diabetes treatment involves a **sugar and fat controlled diet** and an **exercise regime**
  - Any food that is rapidly digested into sugar will cause a sudden, dangerous spike in blood sugar

- **Obesity** is a major risk factor for type II diabetes

Type I Diabetes and Type II Diabetes Table

	Type 1	Type 2
Cause	Inability of pancreas to produce insulin	Cells of the body become resistant to insulin or insufficient insulin produced by the pancreas
Treatment	Monitoring blood glucose levels and injecting human insulin throughout the day (particularly after meals consumed)	Maintain a low-carbohydrate diet and regular exercise to reduce need for insulin

Thyroxin

YOUR NOTES

- **Thyroxin** is a **hormone** that is released from the **thyroid gland,** located in the neck
- Thyroxin's main role is to **regulate** the **basal metabolic rate** (BMR); this is the speed at which **metabolic reactions occur** in the body when it is at rest
  - Thyroxin therefore **targets almost all cells in the body,** as all cells metabolise
  - However, the most metabolically active cells, such as those of the **liver**, **muscle** and **brain**, are most affected
- Thyroxin plays a role in regulating body temperature
  - If the body becomes **cooler**, this triggers **increased thyroxin secretion** by the thyroid gland
  - The increase in thyroxin **increases the metabolic rate**, which **increases the generation of body heat**
  - This causes **body temperature** to **rise**
- Thyroxin **deficiency,** caused by a condition known as **hypothyroidism,** has the following effects on the body:
  - Lack of energy
  - Low mood
  - Forgetfulness
  - Weight gain
    - Less glucose and fat is broken down by cellular respiration to release energy
  - Constantly feeling cold
    - Less heat is generated by respiration
  - Constipation
    - Muscular contractions in the gut wall slow down due to reduced energy from respiration
  - Impaired brain development in children

YOUR NOTES

Leptin

- **Leptin** is a **hormone** that is secreted by fat storage cells known as **adipose cells**
- The concentration of leptin in the blood is controlled by the **amount of adipose tissue** in the body
- As we eat food over a period of time, adipose cells store fats in the form of **lipids**
  - As adipose cells fill up, they secrete **more leptin**
  - This leptin circulates in the blood and targets groups of cells in the **hypothalamus** that are responsible for **controlling appetite**
  - It does this by **binding to receptors** in the membranes of these cells
  - This **inhibits appetite** and causes the **sensation of hunger to be suppressed,** or stopped
- If food intake is **low** over a period of time, the lipid reserves in adipose cells are **used up** and the adipose cells become empty again
  - As adipose cells empty and shrink, they secrete **less leptin**
  - The suppression of **appetite** stops, and the **sensation of hunger returns**

Testing Leptin

YOUR NOTES

- As leptin **inhibits appetite** and causes the sensation of hunger to be suppressed, it was once thought that **clinical obesity** could be **controlled** by **injecting patients with leptin**
- Early trials in mice showed promise
  - Mice with a genetic leptin deficiency were shown to be less active and to gain weight faster than mice without this deficiency
  - Individuals with leptin deficiency lost 30% of their body mass when injected with leptin
- However, clinical trials to test whether this could be an effective treatment for obesity in humans found it to be **ineffective**

Reasons for the failure to control obesity with leptin injections

- Unlike in mice, most obese humans have **very high concentrations of leptin in their blood**
  - There are some human individuals who have problems with leptin production, but these are the exception rather than the rule
- It seems as though their bodies have become **resistant to the effects of the hormone**
  - The **target cells** in the **hypothalamus** become **resistant to leptin** and therefore **fail to respond to it**
  - This leads to a **lack of appetite suppression**, causing a **continuous sensation of hunger** and **excessive food intake**
- This means that **injections of extra leptin fail to control obesity** in the majority of obese patients
- Other problems with the clinical trials included
  - The need to inject leptin **several times a day**
  - **Irritation** at the injection site
  - **Regain of any weight lost** after the end of the trial
- It is always important to remember that while other mammalian research models such as mice are important, they are **not always perfect**

Melatonin

YOUR NOTES

- Many **physiological processes** and **behavioural patterns** occur in **regular, daily rhythms** in organisms throughout the plant and animal kingdoms
  - Many animal species are only active for a **specific part of the 24-hour cycle** e.g. nocturnal animals are only active at night
- Humans are **adapted** to live in a 24-hour cycle and many aspects of our physiology and behaviour, including **physical activity**, **sleep**, **body temperature,** and **secretion of hormones,** follow specific and regular cycles throughout the 24-hour period
  - These daily cycles are known as **circadian rhythms**
- In humans, many circadian rhythms are influenced by the hormone **melatonin**
  - Melatonin is **secreted** by the **pineal gland**, which is located in the **brain**
  - Melatonin secretion **increases in the evening** in response to **darkness** and **decreases at dawn** in response to **light**
- Although melatonin affects **many aspects of human physiology and behaviour**, one of the main circadian rhythms it controls is our **sleep-wake cycle**
  - **Increasing melatonin** levels lead to feelings of **tiredness** and **promote sleep**
  - **Decreasing melatonin** levels lead to the body's preparation for **waking up** and **staying awake during the day**
- Experiments have also suggested that
  - Increased melatonin at night contributes to the **night-time drop in core body temperature** in humans
  - Melatonin receptors in the kidney enable melatonin produced at night to cause the **night-time decrease in urine production** in humans
  - Melatonin is **still released in the absence of light and dark signals**, but on a slightly longer cycle than the usual 24 hours
    - Subjects living in the dark with no access to natural daylight still release melatonin on a roughly 24 hour cycle
    - This suggests that the role of light is to **reset the melatonin system** every day to keep the circadian rhythm in line with daylight hours

Uses of Melatonin

YOUR NOTES

- **Jet lag** is the term used to describe the **various symptoms** a person can experience after **crossing multiple time zones** during a long **flight**
- The symptoms can include:
  - Difficulty in remaining awake during the day
  - Difficulty in sleeping during the night
  - General fatigue
  - Irritability
  - Headaches
  - Indigestion
- Jet lag occurs because the body's **circadian rhythms** are **still set to the timing of day and night** in the **time zone** from which the person has just **departed**, rather than the time zone they have just arrived in
- Jet lag usually only last for a **few days** as the body adjusts to the new day and night regime
- **Melatonin tablets** are sometimes taken to **prevent** or **reduce** jet-lag symptoms
  - The tablets are normally taken **just before going to sleep**
  - Some clinical trials have shown this use of melatonin to be **effective** in **promoting sleep** and reducing other jet lag symptoms
  - However, the **safe** and **appropriate** use of this medication **still needs more testing**

YOUR NOTES

William Harvey & Sexual Reproduction in Deer

- William Harvey (1578 - 1657) was an English **physician** who contributed greatly to our understanding of anatomy and physiology
- He is mainly remembered for his work on the **circulation of the blood,** however, he also spent a lot of time studying **how life passes from one generation to the next** and conducted much research into **sexual reproduction**
- At the start of the 17th century there was **very little understanding** of how each sex; males and females, contributed to **producing offspring**
    - The main hypothesis at the time was that the **semen** produced by males **combined with the menstrual blood** of females to form an '**egg**', which would then develop into a **foetus** inside the mother

- William Harvey's work on understanding sexual reproduction involved **testing this old hypothesis** using animals, mainly **deer**
- His work included:
    - Dissecting the **uteruses,** or **wombs,** of female deer at all stages of pregnancy
        - Harvey found that the uterus was always empty at the time of conception i.e. just after successful mating, **disproving the hypothesis** that semen and menstrual blood combined in the uterus to form a foetus
        - Harvey expected to find 'eggs' developing in the uterus immediately after mating; instead, he only found something developing there **two or more months after mating**
    - Dissecting the **ovaries** of female deer throughout the mating season
        - He found **no sign** of an '**egg**'
        - Note that **he did not have access to a microscope** during his work

William Harvey's Experimental Technique

YOUR NOTES

NOS: Developments in scientific research follow improvements in apparatus; William Harvey was hampered in his observational research into reproduction by lack of equipment. The microscope was invented 17 years after his death

- In scientific research, **critical developments often follow improvements in scientific apparatus**
  - For example, distant objects in Space often remain undiscovered until a telescope, or some other piece of equipment, powerful enough to detect them is developed
- William Harvey was greatly held back in his observational research into reproduction by a **lack of suitable equipment**
  - The **microscope** was invented 17 years after his death
  - Harvey failed to solve the mystery of sexual reproduction because **effective microscopes were not available** when he was working
  - This meant he could not find and observe male and female gametes, so the fusion of gametes and subsequent embryo development remained undiscovered
    - In addition, Harvey's decision to use deer as a study species was unlucky, as deer embryos remain microscopically small i.e. small enough that they can only be viewed using a microscope, for an unusually long period of time
- Although the presence of sperm cells in semen was first reported in 1677, it wasn't until the 19th century that the fertilisation of an egg cell by a sperm cell was finally observed
  - This showed that something contained within the egg **and** the sperm was being **inherited by offspring**, which lead to a much **greater understanding of sexual reproduction**
- The fact that scientific research is often held back by a lack of **sufficiently powerful** or **precise apparatus** is a problem that will continue into the future
- In some ways this is very exciting, as it suggests that our scientific knowledge and understanding of the universe will **continue to expand** as new **scientific techniques** and **technologies** are developed

YOUR NOTES

SRY Gene

- In **sexual reproduction** in **humans**, a sperm from a male fuses with, or fertilises, an egg from a female to form a zygote, which then develops into an **embryo**
- To begin with the embryo develops **in the same way regardless of its sex,** and **embryonic** gonads develop that will either become **ovaries** in females or **testes** in males
- The factor that determines whether the embryonic gonads will develop into ovaries or testes is the **presence or absence** of a **single gene** known as the **SRY gene**
  - The SRY gene is located on the **Y chromosome**, meaning that is only present in roughly 50% of embryos
  - The SRY gene codes for a DNA-binding protein known as TDF, or testis determining factor, which stimulates the expression of further genes responsible for the **development of testes**
- If the SRY gene is present in the embryo's DNA, the **embryonic gonads** will develop into **testes**
- If the embryo has **two X chromosomes,** and therefore the SRY gene is **not present** in its DNA, the **embryonic gonads** will develop into **ovaries**

Testosterone

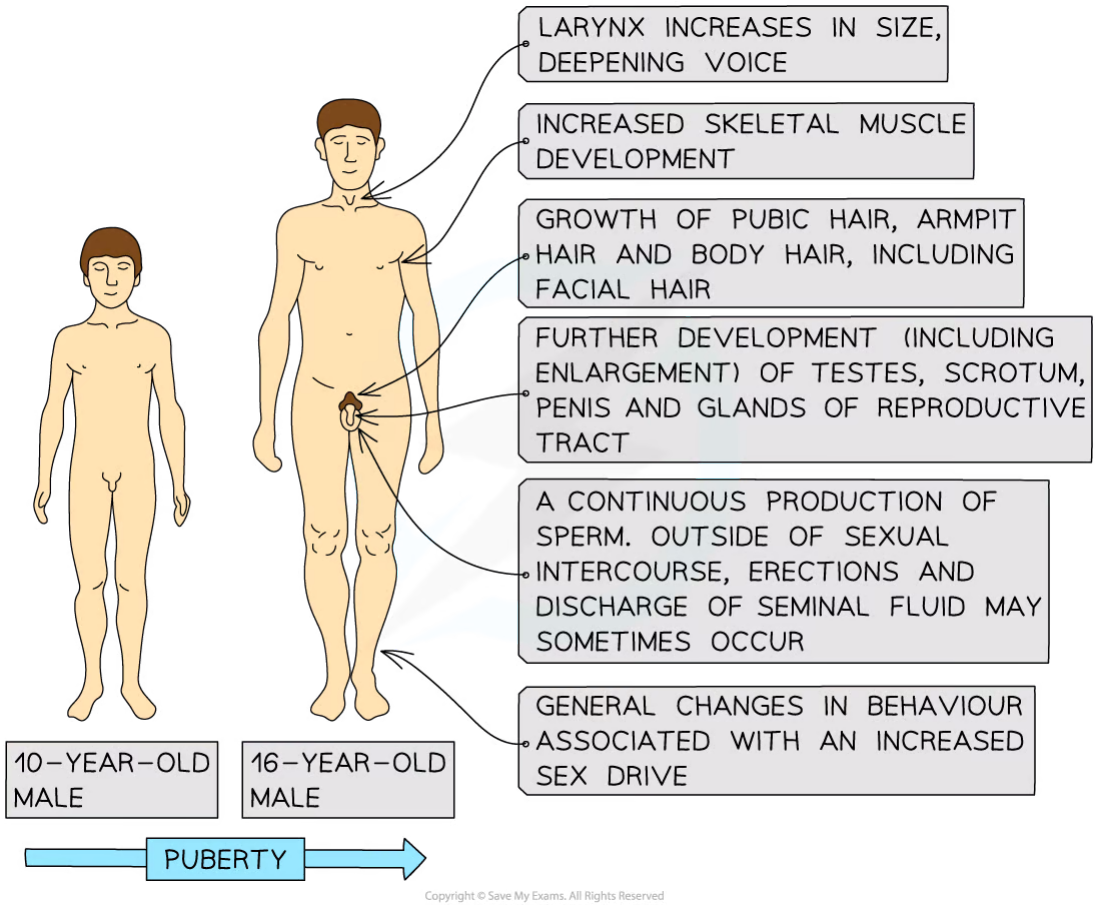
YOUR NOTES

- During embryonic development, at the time when the embryo is developing into a foetus, the testes develop **testosterone-secreting cells** which produce and secrete **testosterone**
- This testosterone causes **pre-natal development of male genitalia**
  - This testosterone secretion declines in the latter stages of pregnancy so that, at birth, the testes are **inactive**
- During **puberty** in males, **testosterone secretions increase** once again
- This leads to:
  - The stimulation of **sperm production in the testes;** a primary sexual characteristic of males
  - The development of male **secondary sexual characteristics** e.g.
    - The penis gets larger
    - Growth of facial hair
    - Deepening of the voice

Secondary sexual characteristics

- **Primary sexual characteristics** are the features of reproductive organs that differ between males and females
  - They are **present during development** in the uterus
- **Secondary sexual characteristics** are the changes that occur **during puberty** as children grow into adults
- They are controlled by the release of **hormones**
  - **Oestrogen and progesterone** in females
  - **Testosterone** in males
- Some changes occur in both males and females, including:
  - The **further development of sexual organs**
  - The **growth of body hair**
- **Emotional changes** also occur at this time due to the increased levels of hormones in the body

YOUR NOTES

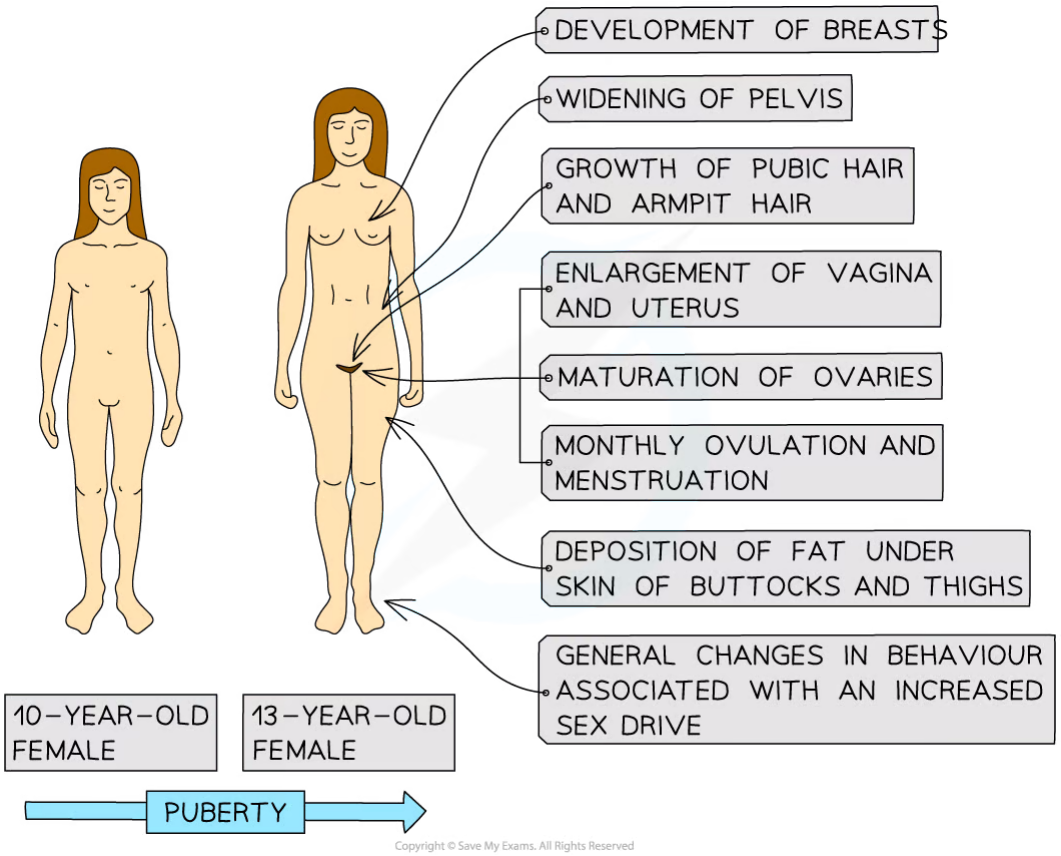


Secondary sexual characteristics of a human male

YOUR NOTES

Oestrogen & Progesterone

- During early development an embryo develops **embryonic** gonads that will either become **ovaries** in females or **testes** in males
- The factor that determines whether the embryonic gonads will develop into ovaries or testes is the **presence or absence** of a **single gene** known as the **SRY gene**
- The SRY gene is on the **Y chromosome,** so if the embryo has **two X chromosomes** the embryonic gonads will develop into **ovaries**
- This means **testosterone** will not be secreted by the developing embryo
- The two female hormones **oestrogen** and **progesterone** are **present throughout pregnancy**
    - These hormones are secreted by the **mother's ovaries** and the **placenta**
- The absence of foetal testosterone and presence of maternal oestrogen and progesterone causes female reproductive organs to develop
- During female **puberty, oestrogen and progesterone secretions increase**.
- This leads to:
    - The start of the **menstrual cycle**
    - The development of female **secondary sexual characteristics** e.g. breast development

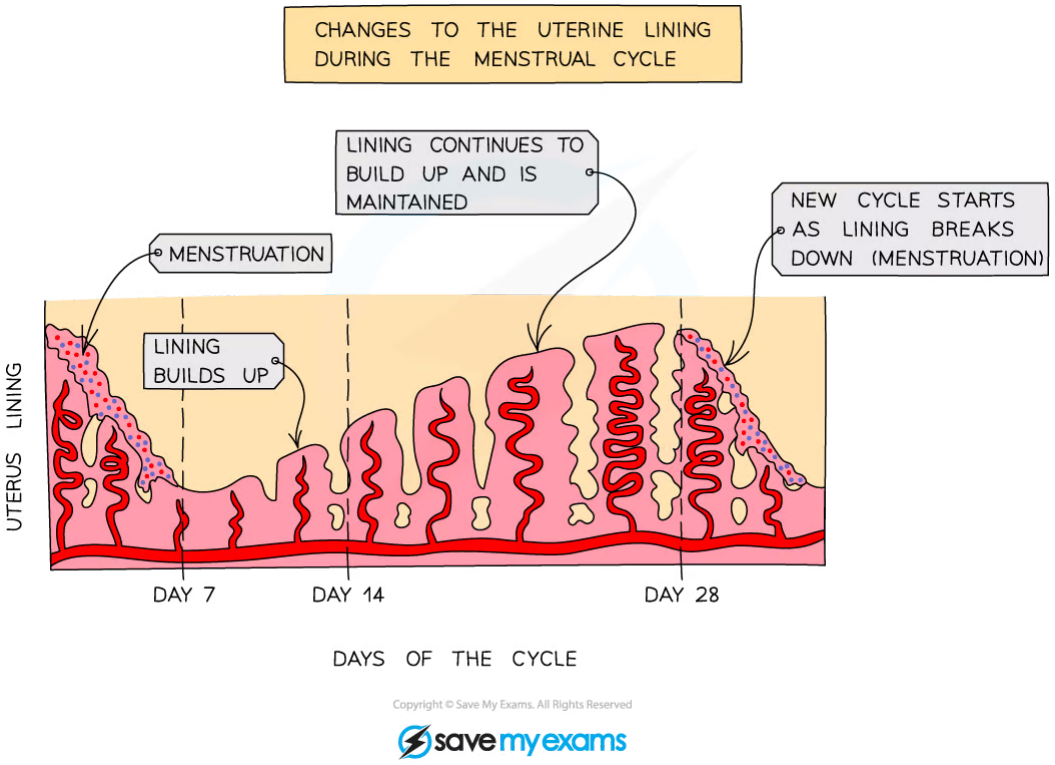


Secondary sexual characteristics of a human female

Menstrual Cycle

YOUR NOTES

- The **menstrual cycle** is the series of changes that take place in the female body leading up to and following the release of an egg from the ovaries
  - It starts in early adolescence in girls and is controlled by **hormones**
  - The average menstrual cycle is **28 days** long
- The **uterus lining**, or **endometrium**, thickens from **day 7** through to **day 28** of the cycle in preparation for receiving a fertilised egg
- The release of an egg, or **ovulation**, occurs about **halfway** through the cycle on **day 14,** and the egg then travels down the oviduct to the uterus
  - Eggs develop inside fluid-filled sacs known as **egg follicles** inside the ovary
  - The follicle releases the egg at ovulation and becomes an empty follicle known as a **corpus luteum**
- Failure to fertilise the egg leads to **menstruation,** commonly known as a period
  - Menstruation involves the loss of menstrual blood via the vagina
  - This is caused by the **breakdown of the endometrium**
- Menstruation takes place roughly between **days 1–7** of the cycle
  - The number of days during which menstruation occurs can vary
- After menstruation finishes, the endometrium starts to **thicken again** in preparation for the **possible implantation** of a fertilised egg in the next cycle



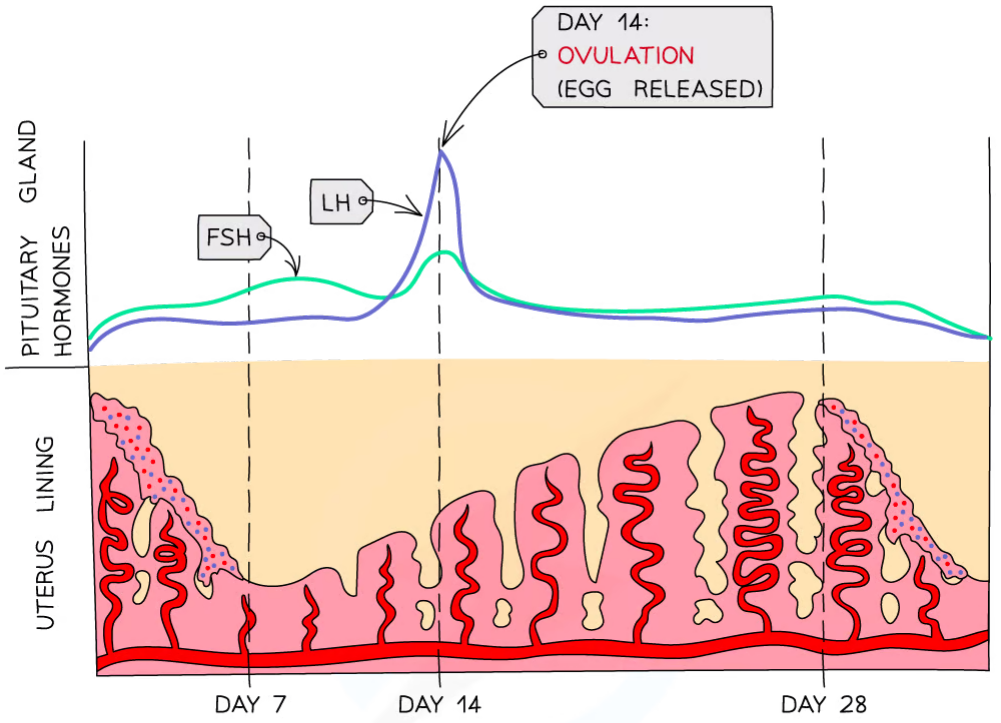
Changes in the endometrium during the menstrual cycle

How ovarian and pituitary hormones control the menstrual cycle

YOUR NOTES

- **Four hormones** control the events that occur during the menstrual cycle:
  - Two of these hormones are produced by the **pituitary gland** in the brain
    - **F**ollicle-**s**timulating **h**ormone (**FSH**)
    - **L**uteinising **h**ormone (**LH**)
  - The other two hormones are produced in the **ovaries**
    - **Oestrogen;** produced by the **egg follicle,** and by the **corpus luteum** after ovulation
    - **Progesterone;** produced by the corpus luteum
- The roles of FSH and LH:
  - FSH is secreted by the **pituitary gland** and stimulates the **development** of several immature **egg cells** in **follicles** in the **ovary**
  - FSH also stimulates the **secretion of oestrogen** by the **follicle wall**
  - The **pituitary gland** is stimulated to release LH when **oestrogen** levels have reached their **peak**
  - LH causes **ovulation to occur;** the shedding of the mature egg cell from the follicle and its release from the ovary
    - The shedding of the mature egg cell leaves behind an empty egg follicle called the corpus luteum
  - LH also **stimulates** the production of **progesterone** from the corpus luteum

YOUR NOTES



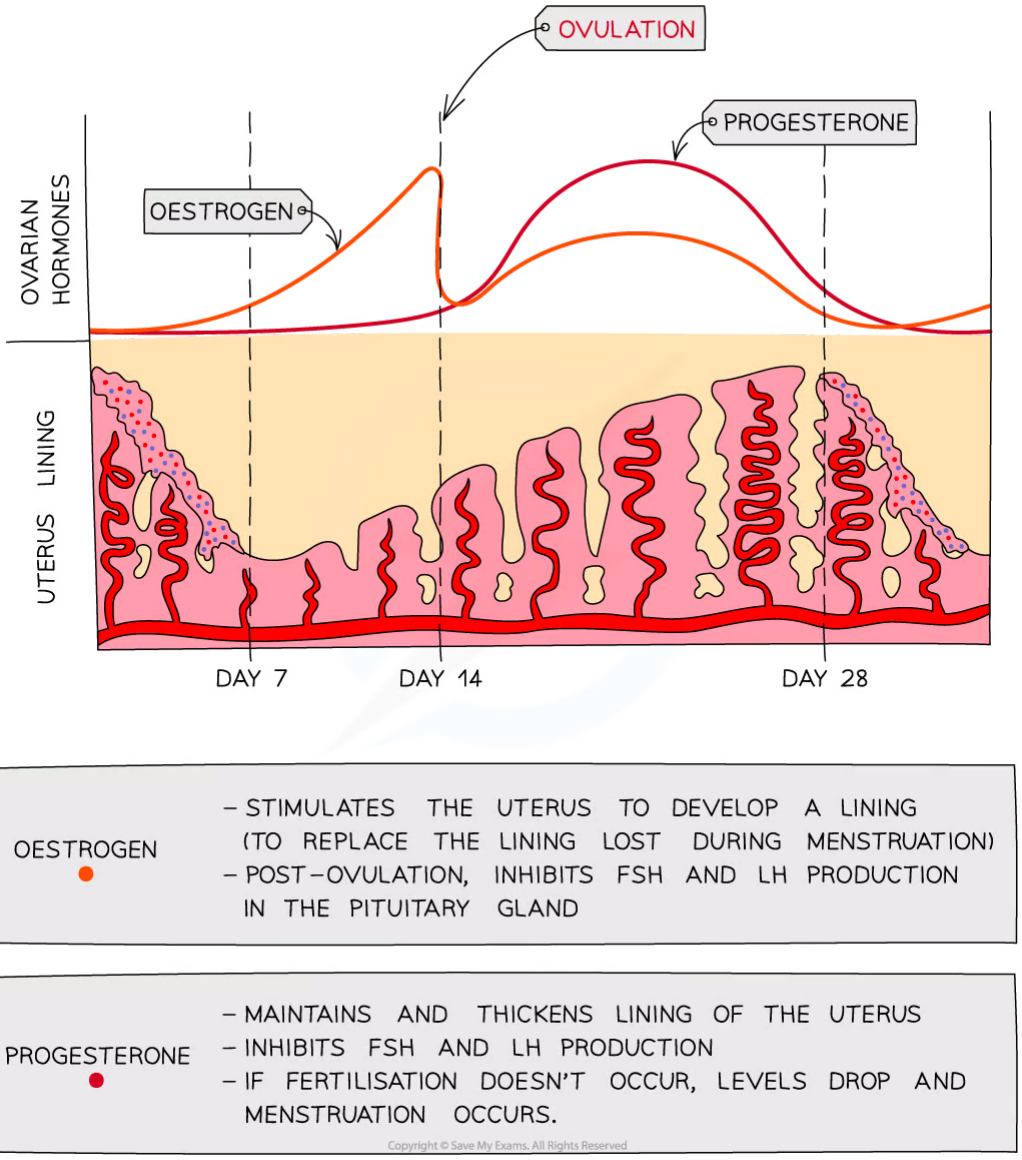
FSH	– STIMULATES EGG MATURATION IN THE FOLLICLES OF THE OVARY – STIMULATES FOLLICLES IN THE OVARIES TO SECRETE OESTROGEN
LH	– AT ITS PEAK STIMULATES OVULATION (RELEASE OF EGG INTO OVIDUCT) – RESULTS IN THE FORMATION OF A CORPUS LUTEUM

Changes in the levels of the pituitary hormones FSH and LH in the blood during the menstrual cycle

- The roles of oestrogen and progesterone:
  - **Oestrogen** levels rise from **day 1** to **peak** just before **day 14**
  - This causes the **endometrium** to start **thickening** and the egg cell to **mature**
  - The peak in oestrogen occurs just before the egg is released
  - **Progesterone** stays low from day 1–14 and starts to rise once ovulation has occurred
    - Progesterone is produced by the corpus luteum
  - The increasing levels of progesterone cause the endometrium to continue to thicken

YOUR NOTES

- A fall in progesterone levels as the corpus luteum deteriorates causes the endometrium to **break down**, resulting in **menstruation**



Changes in the levels of oestrogen and progesterone in the blood during the menstrual cycle

Negative and positive feedback mechanisms controlling the menstrual cycle

- The four hormones all **interact** to control the menstrual cycle via both negative and positive feedback
  - FSH and oestrogen
    - FSH stimulates the development of a follicle, and the follicle wall produces the hormone oestrogen; it can be said that **FSH stimulates the production of**

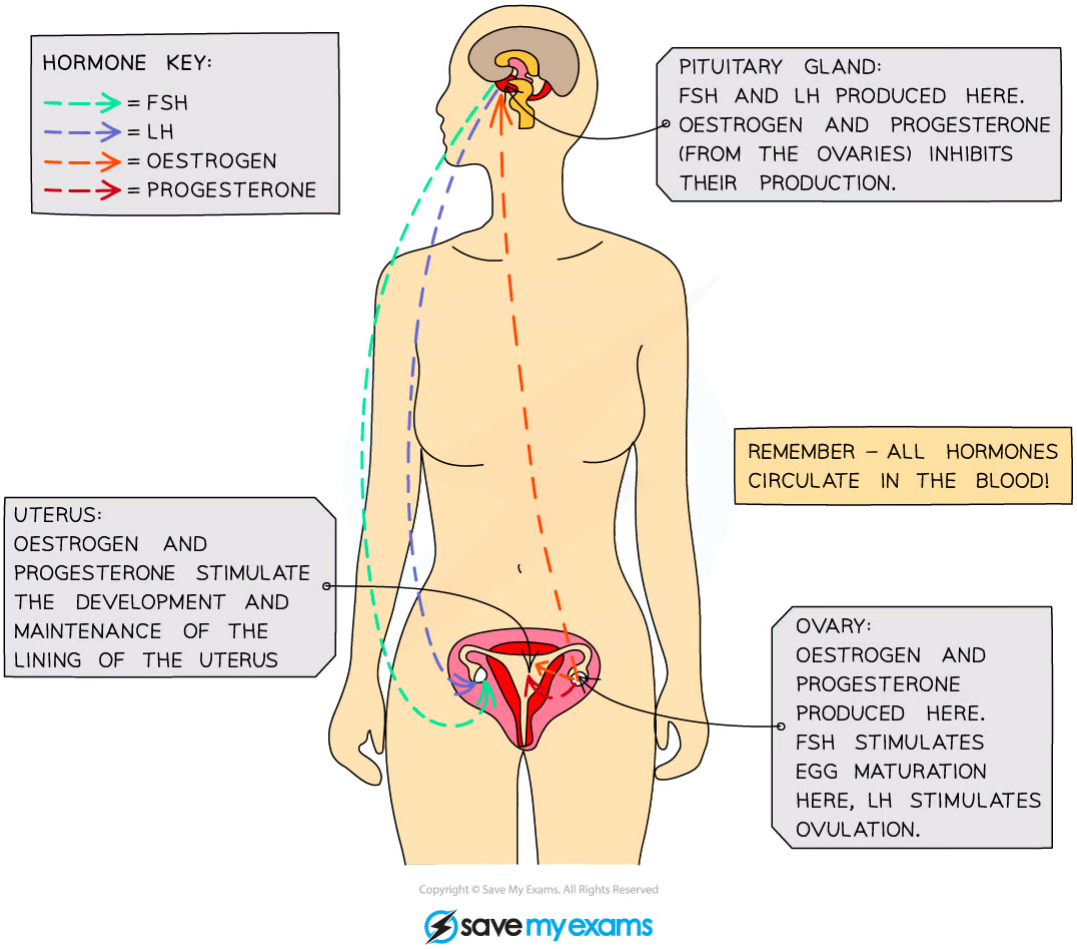
YOUR NOTES

oestrogen

- As well as causing growth and repair of the endometrium, oestrogen also causes an **increase in FSH receptors;** this makes the follicles **more receptive to FSH** which, in turn, **stimulates more oestrogen production**
  - This is **positive feedback**
- When oestrogen levels are high enough, it **inhibits the secretion of FSH**
  - This is **negative feedback**

- LH and oestrogen
  - When oestrogen rises to a high enough level, it **stimulates the release of LH** from the pituitary gland, causing ovulation on around day 14 of the cycle
  - After ovulation, **LH causes the wall of the follicle to develop into the corpus luteum,** which **secretes more oestrogen**
    - This is **positive feedback**
- LH and progesterone
  - **LH** stimulates the wall of the follicle to develop into the **corpus luteum,** which **secretes progesterone**
  - Progesterone thickens and maintains the endometrium but also **inhibits the secretion of FSH and LH** from the pituitary gland
    - This is **negative feedback**

YOUR NOTES



Where hormones involved in the menstrual cycle are made and act – remember that hormones travel around the body in the bloodstream but only have an effect on a target organ

Hormones & IVF

YOUR NOTES

- A couple may find it difficult to conceive a baby **naturally**
- This can be due to **insufficient levels of reproductive hormones** affecting the development of egg and sperm cells, or as a result of **issues with the reproductive system of the male or female**
- One possible treatment is for eggs to be fertilised by sperm **outside the body** in carefully controlled laboratory conditions
  - This is known as ***i**n **v**itro **f***ertilisation, or **IVF**

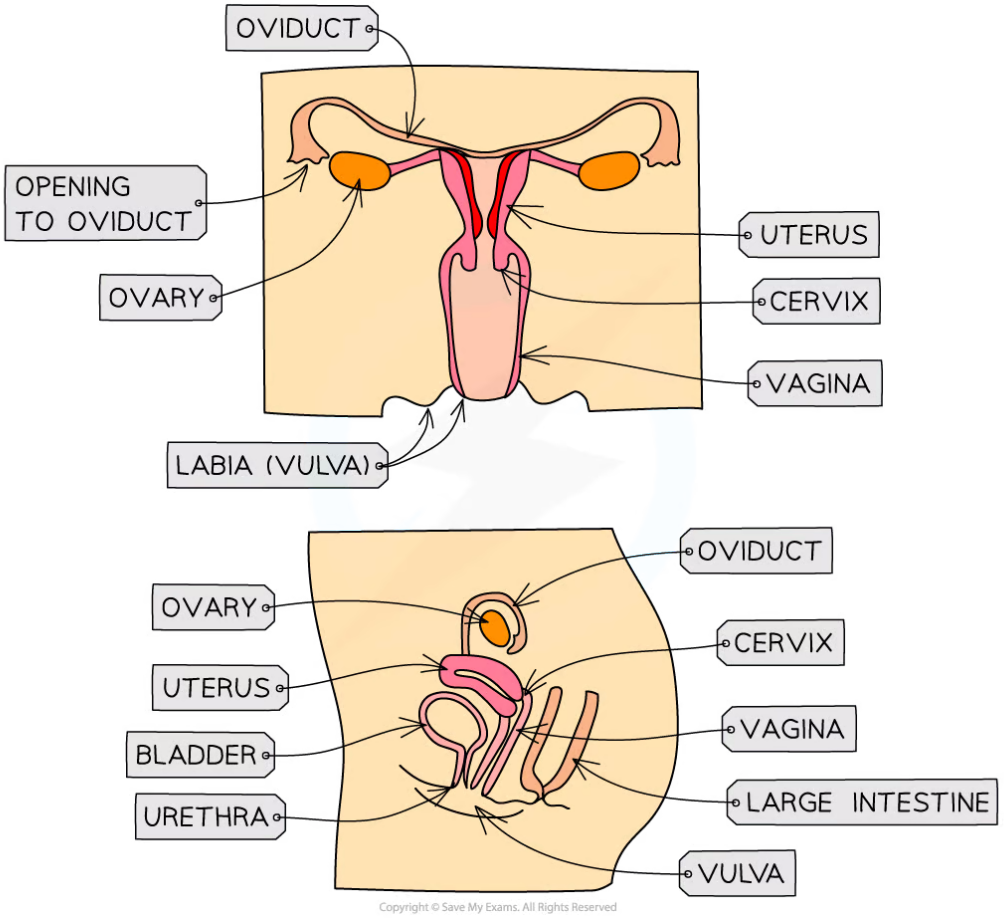
- Although the process can vary, it normally follows the same main steps:
  - The first step involves stopping the normal secretion of hormones; the woman takes a drug to **inhibit the secretion of FSH and LH** from the pituitary gland
    - This also causes oestrogen and progesterone secretions to stop
  - This **temporarily halts the menstrual cycle**, allowing doctors to control the **timing** and **quantity** of **egg production** in the woman's ovaries
  - The woman is then given **injections of FSH and LH to stimulate the development of follicles;** as the injection gives a much higher FSH concentration than is present during a normal menstrual cycle, '**superovulation**' occurs
    - Many more follicles than normal begin to mature
  - The eggs are then collected from the woman and fertilised by sperm from the man in **sterile conditions in the laboratory**
  - The fertilised eggs develop into **embryos**
  - At the stage when they are tiny balls of cells, about **48 hours after fertilisation**, one or more embryos are inserted into the mother's uterus
  - Finally, **extra progesterone** is normally given to the woman to ensure the **endometrium** is **maintained**

- The success rate of IVF is low (~30%) but there have been many improvements and advancements in medical technologies which are helping to increase the success rate

YOUR NOTES

Male & Female Diagrams

- You should be able to **annotate diagrams** of the female and male **reproductive systems** to show the names of the different **structures**
- You should also be able to recall the **function** of each of these structures



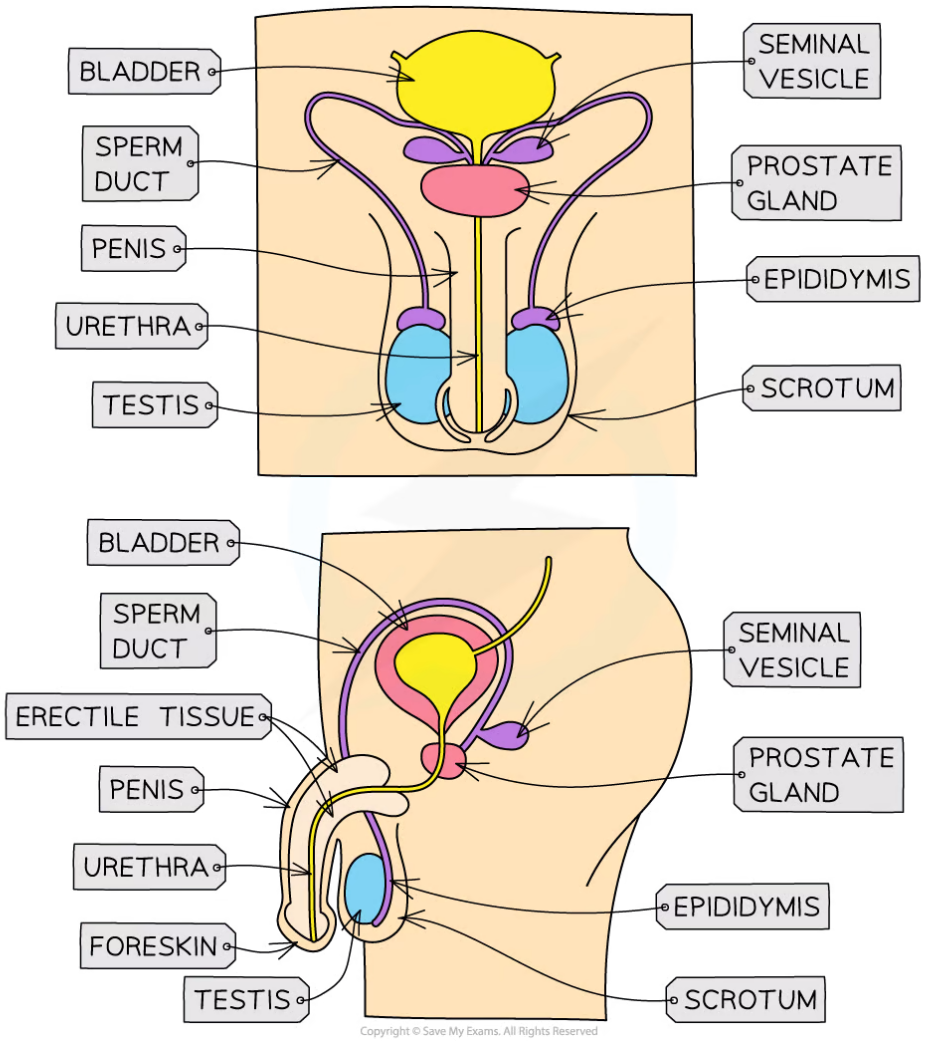
Front and side view of the female reproductive system

Female Reproductive System Table

Structure	Function
Oviduct	Connects the ovary to the uterus and is lined with ciliated cells to push the released ovum down it. Fertilisation occurs here
Ovary	Contains ova (female gametes) which will mature and develop when hormones are released
Uterus	Muscular bag with a soft lining where the fertilised egg (zygote) willbe implanted to develop into a foetus
Cervix	Ring of muscle at the lower end of the uterus to keep the developing foetus in place during pregnancy
Vagina	Muscular tube that leads to the inside of the woman's body, where the male's penis will enter during sexual intercourse and sperm are deposited
Vulva	A collection of structures (including the pubic mound, labia, clitoris and hymen), one function of which is to protect the more internal parts of the female reproductive system

YOUR NOTES

YOUR NOTES



Front and side view of the male reproductive system

Male Reproductive System Table

Structure	Function
Prostate gland and seminal vesicle	Produces fluid called semen that provide sperm cells with nutrients
Sperm duct	Sperm passes through the sperm duct to be mixed with fluids produced by the glands before being passed into the urethra for ejaculation
Urethra	Tube running down the centre of the penis that can carryout urine or semen, a ring of muscle in the urethra prevents the urine and semen from mixing
Testis	Contained in a bag of skin (scrotum) and produces sperm (male gamete) and testosterone (hormone)
Scrotum	Sac supporting the testes outside the body to ensure sperm are kept at temperature slightly lower than body temperature
Penis	Passes urine out of the body from the bladder and allows semen to pass into the vagina of a woman during sexual intercourse
Epididymis	Coiled tubes that store sperm until ejaculation

YOUR NOTES