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Updated to 2019-21 Syllabus

CIE AS-LEVEL BIOLOGY 9700

SUMMARIZED NOTES ON THE SYLLABUS

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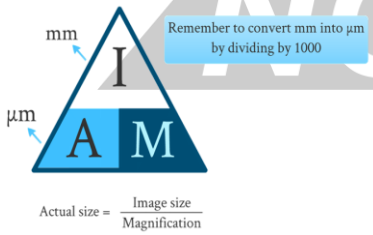
1. Cell Structure

1.1 Microscopy in the Cell

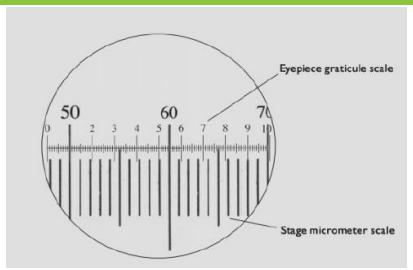
- **Types of microscopes:**

FEATURE	LIGHT	ELECTRON
SOURCE OF RADIATION	• Light	• Electrons
WAVELENGTH OF RADIATION	• 400-700nm	• ±0.005nm
MAX RESOLUTION	• 200nm	• 0.1-0.5nm
LENS	• Glass	• Electromagnet
SPECIMEN	• Alive	• Dead
STAINS	• Coloured dyes (so easier to use)	• Heavy metal
IMAGE	• Coloured photomicrograph	• Black and white electron micrograph
VIEW	• Eye piece	• Fluorescent screen

  - Vacuum present in EM to prevent electrons from colliding with air particles to gain a sharp image.
  - Water boils in RT in a vacuum, so specimen should be dead.
- **Magnification**: number of times larger an image is compared to the real size of the object.
  - Depends on the power of the objective and eyepiece lens used.
- **Calculating magnification:**

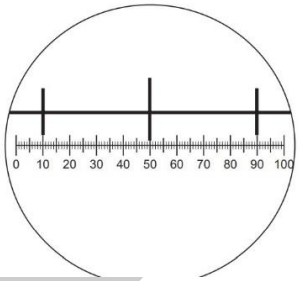


- **Eyepiece graticule**: fitted into the eyepiece of the microscope and is used to measure objects.
  - Has no units and is calibrated by the stage micrometer which has an accurate scale (in mm) and provides refrence dimentions.
  - 1mm= 1000 μm
  - 1μm= 1000 nm

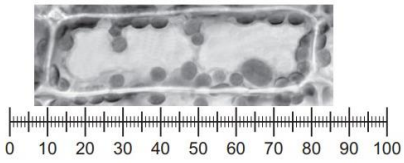


- **Calculation example:**

3 The diagram shows a stage micrometer scale on which the small divisions are 0.1 mm. It is viewed through an eyepiece containing a graticule.



The stage micrometer scale is replaced by a slide of a plant cell.



What is the width of a chloroplast?

A 0.5 mm B 10 μm C 50 μm D 100 μm

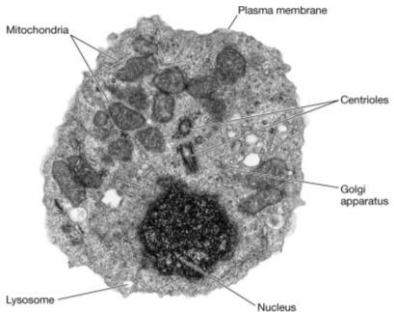
  - 0.1mm of SM = 40 div of EG
  - 1 div of EG= 0.1/40
  - 0.0025mm*1000= 2.5μm
  - 2.5μm*4 egu of chloroplast width= 10μm
- **Resolution:** ability to distinguish between two separate points. The amount of detail that can be seen- higher resolution, higher detail.
  - **Limit of resolution:** half the wavelength of radiation used to view specimen.
    - Electrons have extremely short wavelength.
    - They're negatively charged, thus easily focused using electromagnets.

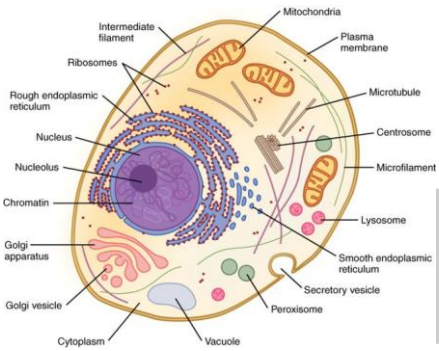
1.2 Cells as the Basic Unit of Living Organism

- **In an electron micrograph:**
  - Very small particles can be observed as the electrons are easily absorbed.
  - The parts of the specimen that appear darker in the final image are denser and absorb more electrons.
  - Due to higher resolution, the electron micrographs of plant and animal cells show most organelles.

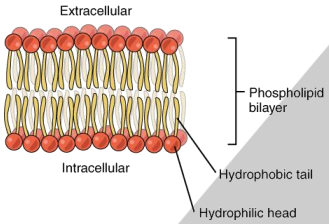
- **Ultrastructure:** the structure revealed by the electron micrograph.

- **Organelles:** functionally and structurally distinct part of a cell, usually membrane bound.
  - **A generalised animal cell (20µm):**



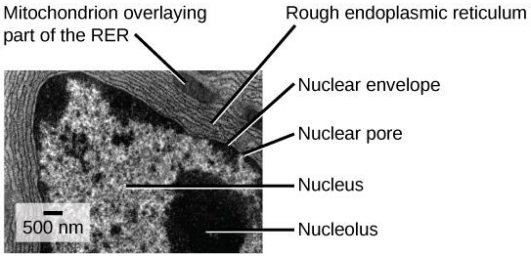


- **Cell surface membrane (7nm)**: a selectively permeable membrane in plant and animal cells that allows for the exchange of certain biological molecules and ions.

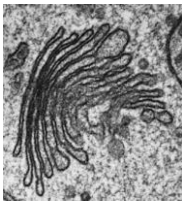


  - Extremely thin with trilaminar appearance
  - It is comprised of phospholipid bilayers which are assembled with the hydrophilic phosphate heads facing the aqueous environment (inside and outside the cell) and the hydrophobic tails facing each other.
  - **Function**:
    - Barrier between cytoplasm and external environment
    - Cell signalling
    - Cell recognition (surface antigens)
    - Cell-to-cell adhesion
    - Site for enzyme catalysed reactions
    - Anchoring the cytoskeleton
    - Selection of substances that enter/leave the cell
    - Formation of Hydrogen bonds with water for stability

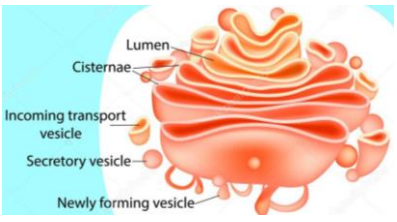
- **Nucleus (10µm):** the largest organelle surrounded by the double membraned nuclear envelope and is continuous with rough endoplasmic reticulum.
  - **Nuclear pore:** gaps in the nuclear envelope that allow exchange between the nucleus and cytoplasm.
    - **Substances leaving:** mRNA and ribosomes for protein synthesis.
    - **Substances entering:** protein to help make ribosome, nucleotide, ATP, & some hormones.
  - **Chromosome:** contains the hereditary material DNA that is organised into genes which controls the activities of the cell and inheritance.
  - **Nucleolus (0.2-0.5µm)** one or more found (nucleoli) containing DNA and RNA, functioning to make ribosomes.



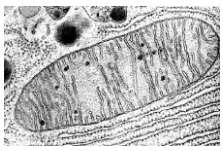
- **Rough endoplasmic reticulum**: 80S ribosomes of the rough endoplasmic reticulum are sites for protein synthesis and produce the rough appearance. The R.E.R provides a pathway for transport of materials through cell.
  - Made of two-dimensional flattened sacs, which are membrane-enclosed structures.
  - Proteins made by ribosomes on RER enter sacs and move through them. Transport vesicles bud off from the RER and join forming the Golgi body.
- **Smooth Endoplasmic reticulum:** site for lipid synthesis and steroids eg cholesterol and reproductive hormones.
  - Meshwork of tubular membrane vesicles with fluid filled sacs that have no ribosome on its surface
- **Golgi body/complex/apparatus:** stack of flattened sacs formed by transport vesicles which bud off of the RER, and broken down to form Golgi vesicles.



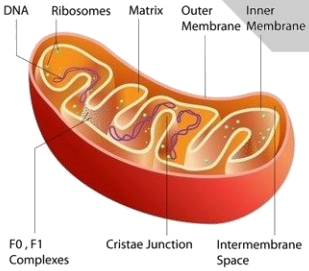
  - Collects, processes, modifies and sorts molecules that are ready for transport in Golgi vesicles to other parts of the cell or out of the cell by:
    - **Secretion/exocytosis:** fusion of vesicle with plasma membrane to release content.
  - Makes lysosomes, glycoproteins and functioning proteins.



- **Mitochondria (1µm):** surrounded by mitochondrial envelope; provides energy for aerobic respiration, synthesizes lipids and is more in areas that require maximal energy.

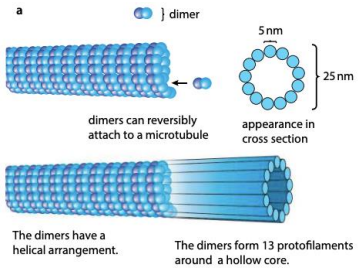


  - Has a matrix that contains 70S ribosomes and circular DNA which is used to make some of the mitochondrion's own proteins.
  - **Cristae:** folding of inner membrane that projects into interior solution, matrix.
  - **Intermembrane space:** space between the two membranes.
  - **Porin:** transport protein in outer membrane, forms wide aqueous channel allowing water-soluble molecules from cytoplasm to intermembrane space.
  - **Inner membrane:** selective barrier controlling entrance of ions and molecules into the matrix.

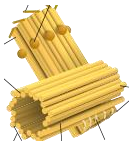


- **Role of adenosine triphosphate (ATP):**
  - Made up of 3 phosphate groups, a nitrogenous base and a ribose sugar.
  - The energy carrying molecule produced in mitochondria that spreads to parts where needed.
  - Energy is released by breaking ATP to ADP, a reversible hydrolysis reaction.
- **Endosymbiont theory:** mitochondrion and chloroplast were bacteria that now live inside larger cells of animals and plants, which is why chloroplast and mitochondrion have circular DNA.
- **Ribosomes:** the site at which mRNA (transcribed from the nucleus) is translated into polypeptides with the help of tRNA, therefore help with protein synthesis.
  - **80S ribosomes:** in the cytoplasm and R.E.R
  - **70S ribosomes:** in chloroplast and mitochondria.
- **Lysosomes (0.1-0.5µm):** a single membrane with no internal structure in animal cells. They contain digestive (hydrolytic) enzymes that's kept separate from rest of cell to prevent damage.
  - Responsible for breakdown of unwanted structures eg old organelles or whole cells, in WBC to digest bacteria.

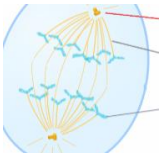
- **Microtubules:** long hollow tubes that make up the cytoskeleton which helps determine cell shape.

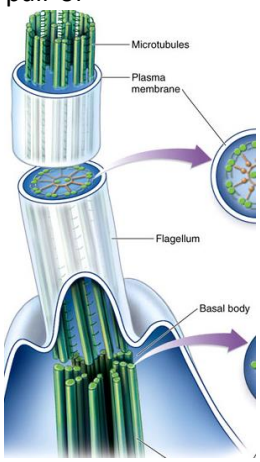


  - Made up of alpha and beta tubulin that combine to form dimers.
  - Dimers join end to end to form protofilaments (polymerisation).
  - 13 protofilaments line up alongside each other in a ring to form a cylinder with a hollow center ie microtubule.
  - Forms an intracellular transport system by moving along secretary vesicles, organelles and cell components on its outer surface.

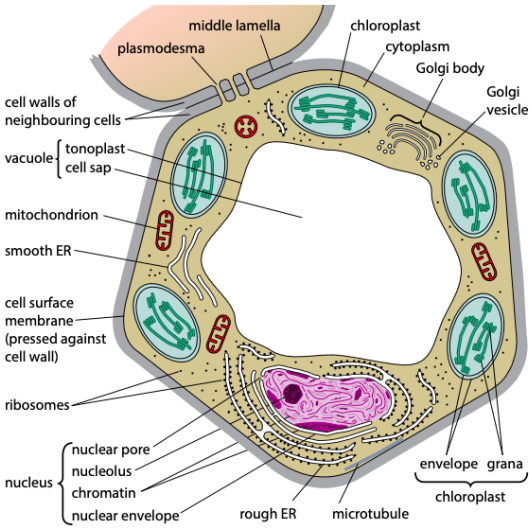


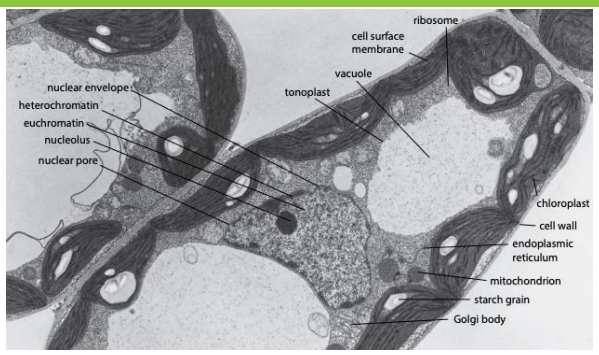
- **Centrosome:** pair of centrioles at right angles that's involved in nuclear division and act as MTOCs.
- **Centriole:** formed by 9 triplets of microtubules. Microtubules extend from centriole and attach themselves to kinetochore of chromosomes, forming spindle fibres. Centrioles duplicate, and a pair of centrioles then move to opposite poles of the cell (2 centrosome regions), thus separating sister chromatids during nuclear division.



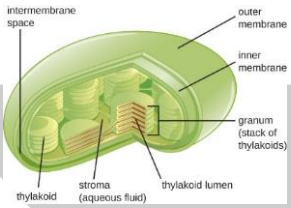


  - Centrioles at bases of cilia and flagella (basal bodies) act as MTOCs. Microtubules extending from basal bodies into cilia and flagella help with their beating movements.
- **A generalised plant cell (40 µm):**

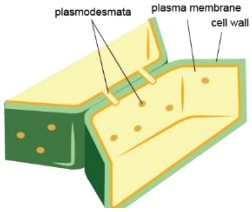




- **Chloroplasts (5-10µm):** This cell structure is only found in plant cells in the palisade mesophyll, spongy mesophyll and surface of stem and carries out photosynthesis.
  - It has a double membrane and contains flattened sacs known as thylakoids.
  - Chlorophyll is embedded in thylakoid membranes.
  - Thylakoids stacked on top of each other to form grana.
  - Grana are linked by lamella. These structures are present in a matrix called the stroma.
  - Contains starch grains, circular DNA and 70S ribosomes.

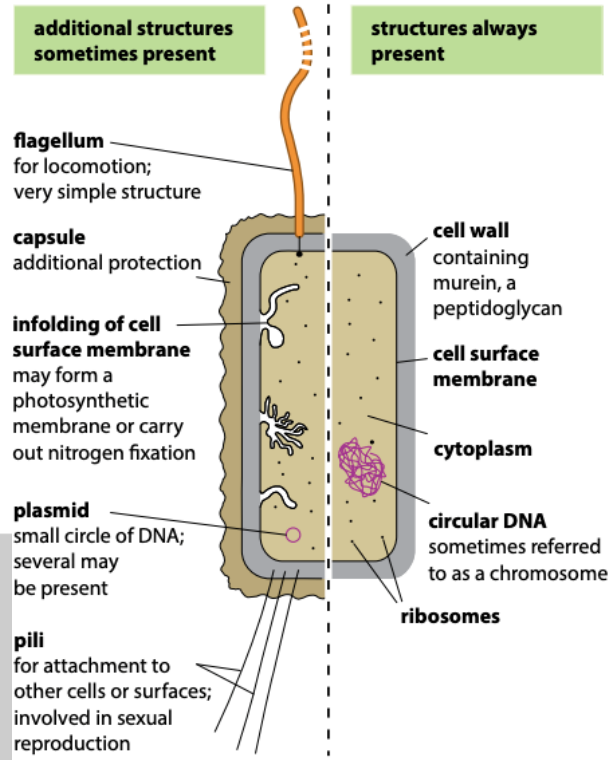


- **Cell wall (10 nm):** rigid as it contains fibres of cellulose (polysaccharide).
  - Gives the cell its definite shape and prevents it from bursting (by osmosis), allowing turgidity.
  - May be reinforced by lignin for extra strength.
  - Freely permeable.
- **Plasmodesmata:** pore-like structures found in cell walls that allow a link between neighbouring cells by fine threads of cytoplasm.
- **Large vacuole and tonoplast:** surrounded by partially permeable tonoplast, has cell sap (fluid) that consists of enzymes, sugars, waste products, pigments, mineral salts, oxygen, C02 and regulates osmotic properties.

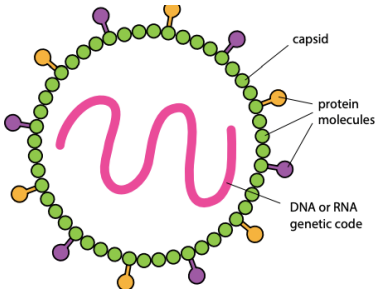


- **Eukaryote:** organisms with a true nucleus and have membrane bound organelles eg animals, plants, fungi, protoctist.
- **Prokaryote:** organisms that lack a nucleus and have simpler structure eg bacteria.

- **Generalised bacterium:**



- **Viruses (20-300nm):** non-cellular and are parasitic as they reproduce by infecting and taking over living cells. The virus DNA/ RNA hijacks the protein synthesising machinery of the host cell, which then helps to make new viral proteins to make capsid.



- **Comparing eukaryotes with prokaryotes:**

FEATURE	PROKARYOTE	EUKARYOTE
AVARAGE DIAMETER OF CELL	• 0.5-5µm	• 40µm • 10k-100k times volume of prokaryote
DNA	• Circular • Lies free in the cytoplasm • Is naked	• Linear • Surrounded by nucleus • Associated with histone, forming chromosome
RIBOSOME ER	• 70S (20nm) • Absent	• 80S (25nm) • Present, to which ribosome may be attached

ORGANELLES	• Very few • No membrane bound organelles unless formed by infoldings of plasma membrane	• Many • Single, double and no membrane bound organelles
CELL WALL	• Murein, a peptidoglycan (polysaccharide with amino acid)	• Cellulose and lignin in plants • Chitin (nitrogen containing polysaccharide) in fungi

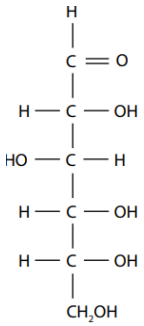
2. Biological Molecules

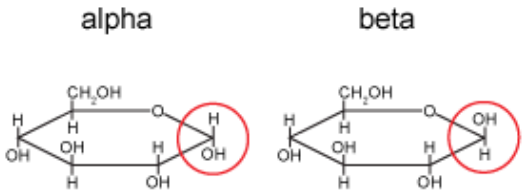
2.1 Testing for Biological Molecules

- **Benedict's test for reducing sugars**: Equal volume of sample being tested and Benedict's solution are mixed and heated in a water bath up to 95C, giving brick red.
- **Acid or enzyme hydrolyis followed by benedict's test for non-reducing sugars**: Hydrochloric acid is added to a the sample being tested in the ratio of 1:2 respectively and heated in a water bath for approximetly 2 minutes. A pinch of sodium hydroxide is added to make the solution alkaline. After this, benedicts test is carried out.
- **Buiret's test used to detect the presence of protiens**: Equal amounts of the sample and buirets solution are added together, giving purple colour over several minutes.
- **Emulsion test for lipids**: The sample is added to 2cm3 of ethanol and mixed well until it dissolves (lipids are soluble in ethanol). This mixture is then placed into a test tube containing the same amount of water. A milky white emulsion will appear if lipids are present and remain clear if not.
- **Iodine test for the presence of starch**: Iodine solution is orange-brown. Add a drop of iodine solution to the solid or liquid substance to be tested. A blue-black colour is quickly produced if starch is present.

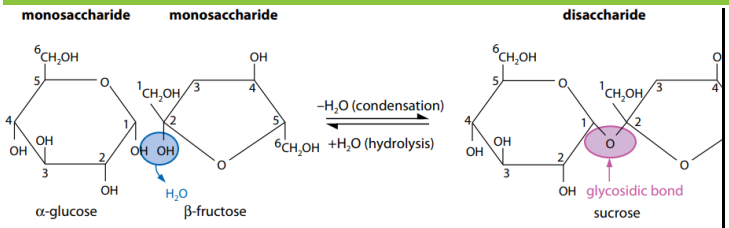
2.2 Carbohydrates and Lipids

- Glucose has the molecular formula C6H12O6. It is an energy source which is broken down during respiration. It is also the monomer from which Starch and Cellulose are made. There are two different kinds of glucose monomers known as α-glucose and β - glucose and their difference lies between the position of an –OH group in their ring structures.

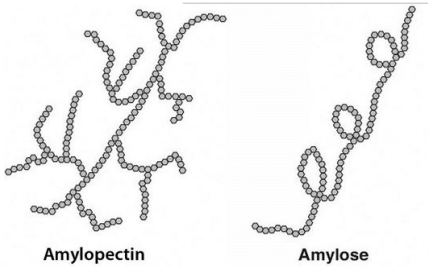




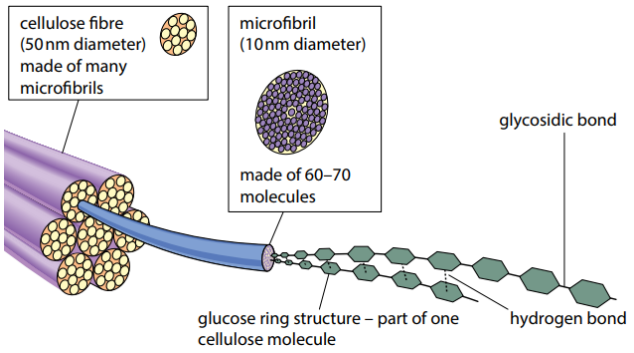
- **Monomer**: simple molecule which is used as a basic building block for the synthesis of a polymer; many monomers are joined together to make the polymer, usually by condensation reactions eg monosaccharides, amino acids, nucleic acids
- **Polymer**: is a giant molecule made from monomers eg polysaccharides, proteins, nucleic acids
- **Macromolecule**: These are large and complex molecules that are formed due to polymerisation of smaller monomers eg polysaccharides, nucleic acids
- **Monosaccharide**:This is a molecule consisting a single sugar unit, the simplest form of carbohydrate and cannot be hydrolised further. It has a general formuala of $(CH_2O)_n$.
- **Disaccharide**: a sugar molecule consisting of two monosaccharides joined together by a glycosidic bond.
- **Polysaccharide**: a polymer whose subunits are monosaccharides joined together by glycosidic bonds.
- **Glycosidic bonds:** covalant bonds that occur between constituent monomers and are formed due to a condesation reaction which involves the removal of a water molecule in order to form polysaccharides and disaccharides such as sucrose.
  - These constituent molecules can also be sepreated by hydrolysis which breaks the glycosodic bond between monomers eg: Acid hydrolysis of non-reducing sugars (sucrose) breaks glycosidic bond in order to retrieve contituent monomers.



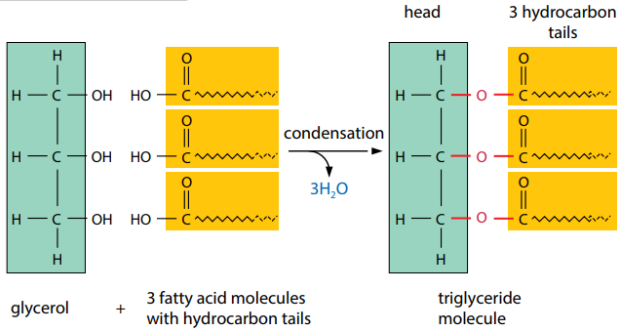
- **Starch** is a macromolecule that is found in plant cells and is made up of two components known as amylose and amylopectin. These components are polysaccharides that are made from a glucose molecules and contain a 1,4 glycosidic bonds. **Amylopectin** is branched in structure and therefore also contains α 1,6 glycosidic bonds. **Amylose** is helical in shape and more compact while amylopectin in branched. Starch is higly compact and stores energy.



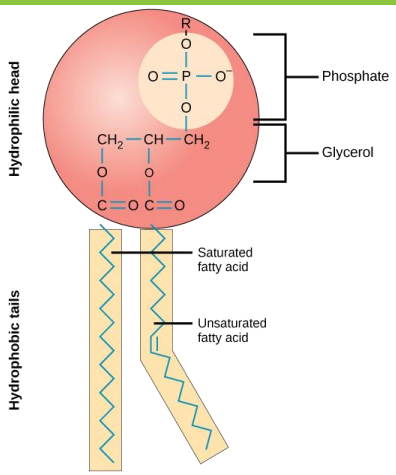
- **Glycogen**: a macromolecule that is used for the storage of energy is animal cells and is also made from α glucose molecules. The structure of glycogen is very similar to that of amylopictin, however, it is more branched and therefore contains more α 1,6 glycosidic bonds.
- **Cellulose**: found in the cell wall of plant cells and is made from βglucose units that form β-1,4 glycosidic bonds. Alternate β- glucose molecules are rotated 180 degrees in order to form these bonds.
  - Hydrogen bonds are also formed between parrallel cellulose molecules. 60 and 70 cellulose molecules become tightly cross-linked to form bundles called microfibrils. Microfibrils are in turn held together in bundles called fibres by hydrogen bonding.
  - Fibres increase tensile strength to withstand osmotic pressure, making the plant rigid and determine cell shape. They're also freely permeable..



- **Triglyceride:** forms by the condensation of 3 fatty acid chains and a glycerol molecule, forming an ester bond. Fatty acid chains are long hydrocarbon chains with a carboxylic head. Glycerol is an alcohol containing 3 OH groups.
  - **Unsaturated fatty acids:** contain c=c bonds that are easier to break and melt easily. More than one c=c is a polyunsatured fatty acid.
  - **Saturated fatty acids:** contain c-c bonds that are solids at room temperature.

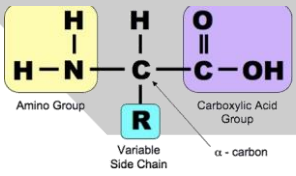


- **Role of triglyceride:**
  - Better energy reserves than carbohydrates as more CH bonds
  - Acts as an insulator and provides buoyancy
  - A metabolic source of water as gives CO2 and H20 on oxidation in respiration
- **Phospholipid:** The hydrophilic <u>head</u> contains a phosphate group and glycerol while the hydrophobic <u>tail</u> contains 2 fatty acid chains. This is due to the partial negative charge on the phosphate group that gets attracted to the partial positive charge on the hydrogen atom of the water molecule.



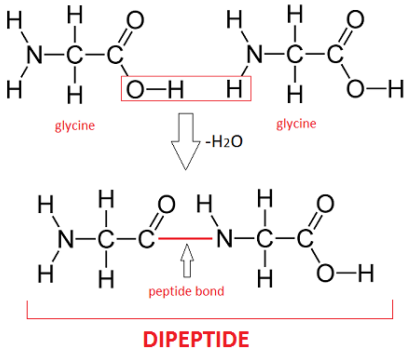
- **Role of phospholipids:** ref 4.1 phospholipids

2.3 Proteins



Proteins are made of amino acids which only differ in the R- groups/ variable side chains and will always contain an amine group (basic), carboxyl group (acidic) and a hydrogen atom attached to the central carbon atom.

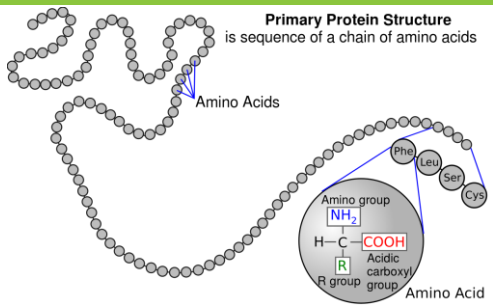
- A peptide bond is formed by condensation betwee 2 amino acids, forming a dipeptide. Many amino acids that join together by peptide bonds form a polypeptide.



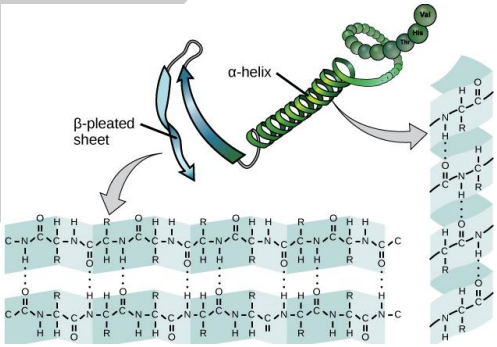
- Peptide bonds are broken when hydrolysed into amino acids, often occuring in the small intestine and stomach.

2.4 Protein Structure

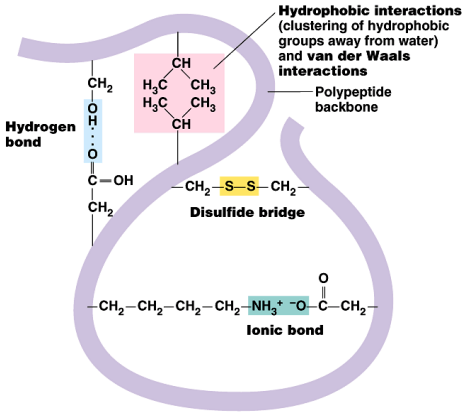
- **Primary structure:** sequence of amino acids in a polypeptide/protein. A slight change in the sequence of amino acids can affect the protein's structure and function.



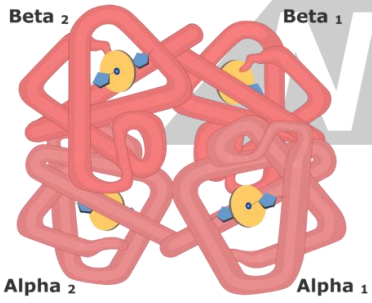
- **Secondary structure:** the structure of a protein molecule resulting from the regular coiling or folding of the chain of amino acids.
  - **α- helix**: the polypeptide chain twists into a regular spiral and is maintained by hydrogen bonds between the (-NH) group of one amino acid and the (CO-) group of another amino acid 4 spaces later in the polypeptide chain.
  - **β- pleated sheet:** the chain is not tightly coiled and lies in a looser, straighter shape.



- **Tertiary structure:** the compact structure of a protein molecule resulting from the three-dimensional coiling of the already-folded chain of amino acids.
  - Hydrogen bonds between wide varieties of R- groups (can be broken by PH and temperature changes)
  - Disulphide bridges between two cysteine molecules (can be broken by reducing agents)
  - Ionic bonds between R groups containing amine and carboxyl groups. (Can be broken by PH changes.)
  - Hydrophobic interactions between non polar R groups.

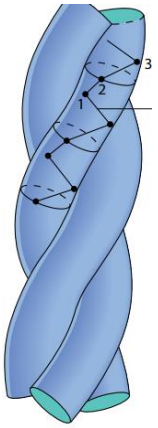


- **Quaternary structure:** the three-dimensional arrangement of two or more polypeptides, or of a polypeptide and a non-protein component such as haem, in a protein molecule. The polypeptide chains are held together by bonds in the tertiary structure.
- **Globular proteins:** curl up into a spherical shape with their hydrophobic regions pointing into the centre of the molecule and hydrophilic regions pointing outwards. They are soluble in water eg enzymes and haemoglobin.
- **Fibrous proteins:** form long strands, are insoluble in water, and have structural roles eg collagen, hair, nails.
- **Haemoglobin:** a globular protein that has a quaternary structure with 4 polypeptide chains, 2 α-globin and 2 β-globin chains. Each chain has one prosthetic haem group containing an iron atom that reversibly binds to an oxygen molecule. Oxyhaemoglobin is bright red, when the haem group is combined with oxygen, otherwise it's purplish.

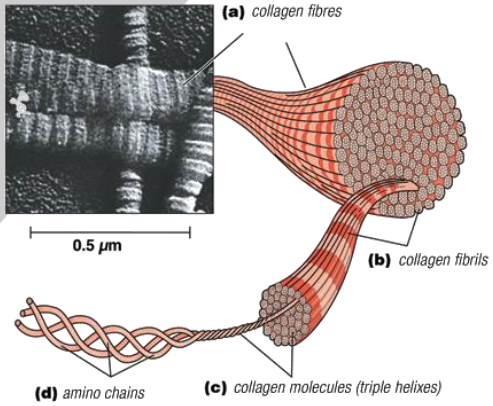


  - **Sickle cell anemia:** is a genetic condition in which a polar amino acid, glutamic acid is substituted by non polar valine on the surface of the β chain in haemoglobin, making it insoluble.

- **Collagen**: a fibrous protein that is present in the skin, bones, teeth, cartilage and walls of blood vessels. It is an important structural protein.



  - A collagen molecule has 3 polypeptide chains that are coiled in the shape of a stretched-out helix. The molecule has a compact structure and almost every 3rd amino acid is glycine, the smallest amino acid. Glycine is found on the insides of the strands and its small size allows the three strands to lie close together and form a tight coil. The 3 polypeptide strands are held together by hydrogen and covalent bonds.
  - Many of these collagen molecules lie side by side, linked to each other by covalent cross-links between the side chains of amino acids, forming fibrils, and many fibrils make up a fibre.



- **Hydrogen bonding:** A water molecule contains two hydrogen atoms and one oxygen atom held together by hydrogen bonds.
- **Solvent:** Water is an effective solvent because of its polarity and so can form electrostatic interactions with other polar molecules and ions. Thus it's a transport medium and reagent for metabolic and other reactions in the cells of plants and animals.
- **High surface tension and cohesion:** cohesion refers to the attraction of one water molecule to the other. Water molecules have strong cohesive forces due to hydrogen bonds, thus having high surface tension.
- **High specific heat capacity:** the amount of heat energy required to raise the temperature of 1 kg of water by 1 °C. Water has high SPC due to its hydrogen bonds. Temperature within organisms remains constant compared to external temperature, and water bodies

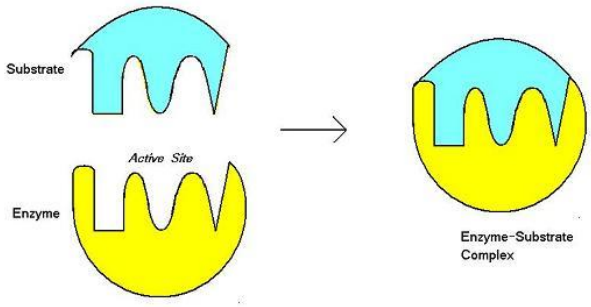
also have a slow change in temperature, providing stable aquatic habitats.

- **High latent heat of vaporization:** measure of the heat energy needed to vaporise a liquid. Water has a high LHV due to its high SPC as H bonds need to be broken before water can be vapourised, cooling the surrounding environment. Sweating is a good cooling mechanism. However, a large amount of energy can be lost for little amount of water, thus dehydration is prevented eg in transpiration.
- **Density and freezing properties:** ice is less dense than water and floats on it, insulating water and preventing it from freezing, preserving aquatic life underneath it. Changes in the density of water with temperature cause currents, which help to maintain the circulation of nutrients in the oceans.

3. ENZYMES

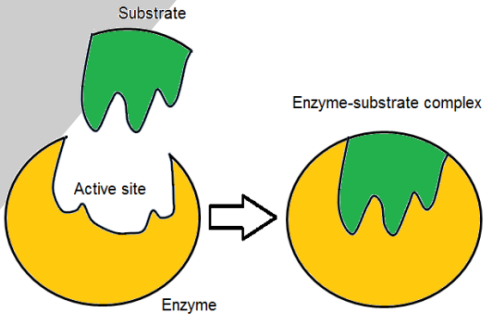
3.1 Mode of Action of Enzymes

- An enzyme is a biological catalyst that accelerates metabolic reactions. Enzymes are globular proteins as they have a roughly spherical shape and are water soluble. Enzymes functioning inside a cell are intracellular, but those that are secreted by cells and catalyse reactions outside cells are described as extracellular.
- Enzymes have specific active sites that are complementary to the shape of the substrate. The substrate is held in place at the active site by weak hydrogen and ionic bonds. The combined structure is called the enzyme-substrate complex.
- Activation energy is the energy required in any chemical reaction to break the bonds in reactant molecules so that new bonds are formed to make the product. An enzyme lowers the activation energy required for the reaction. However, overall energy released during reaction is maintained.
- **Lock-and-key theory**: the shape of the active site is very precise and substrates that are not complementary to the shape of the active site cannot bind. The enzyme-substrate complexes formed enable the reaction to take place more easily.

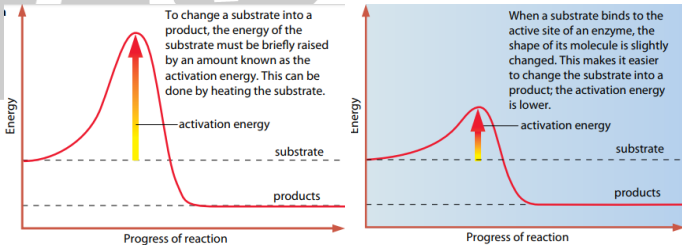


Lock-and-key Model.- The substrate and enzyme active site have complementary shapes

- **Induced fit theory**: the enzyme's active site is not initially an exact fit to the substrate molecule. However, the enzyme molecules are more flexible and can change shape slightly as the substrate enters the enzyme. This means that the enzyme molecule will undergo conformational changes as the substrate combines with enzyme's active site, forming the enzyme-substrate complex.



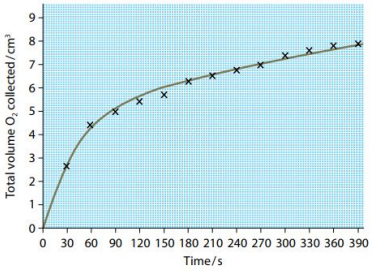
- Enzymes speed up the rate of a reaction by lowering the **activation energy** of a reaction, They do this by holding the substrate or substrates in such a way that their molecules can react more easily.



- **The effect that enzymes have on the rate of reactions can be measured in two ways:**
  - By measuring the amount of product accumulated over a period of time. Rate of reaction = volume of product produced/ time eg enzyme catalase breaking hydrogen peroxide to H2O + o2
  - By measuring the rate at which the reactants disappear from the reaction mixture, the effect of the enzyme on the rate of reaction can be determined. Eg:

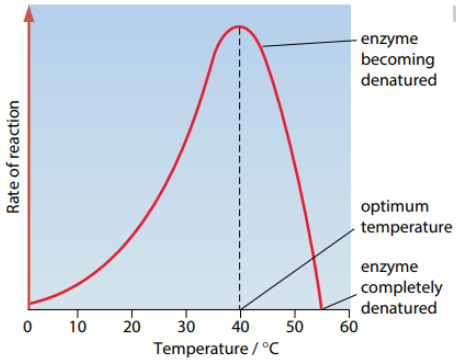
measuring the rate at which starch disappears when the enzyme amylase is added.

- **Course of a reaction:** Initially, there's a large number of substrates and every enzyme has a substrate in its active site. The rate at which the reaction occurs depends only on how many enzymes there are and the speed at which the enzyme can convert the substrate into product, release it, and then bind with another substrate. However, overtime, there are fewer substrates to bind with enzymes; the reaction gets slower, until it eventually stops. The rate of an enzyme-controlled reaction is always fastest at the beginning.

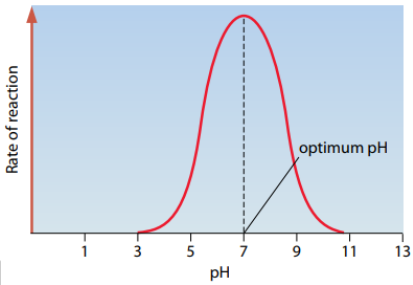


3.2 Factors that affect Enzyme Action

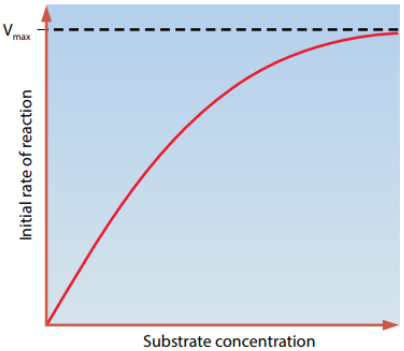
- **Temperature**: As the temperature increases, the kinetic energy and the enzyme activity increases as there's more collisions until optimal temperature is reached (usually 40C). At optimal temperature, maximum rate of reaction is achieved. If the temperature continues to increase beyond optimal temperature, the rate of the reaction begins to decrease as more kinetic energy breaks the hydrogen bonds in the secondary and tertiary structure of enzyme. This changes the shape of the enzyme and its active site and causes the substrate to no longer fit. The enzyme is denatured.



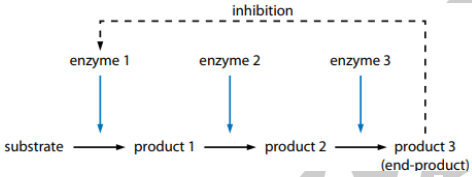
- **pH:** Any change in the pH value of the medium around the enzyme will cause ionic and hydrogen bonds to be damaged, this will change the 3-D shape of the enzyme and deform the active site. The substrate will therefore not be able to fit into active site so the reaction slows down or stops. The effects of pH is reversible within certain limits but if the pH is far from optimal value, the enzyme gets denatured.



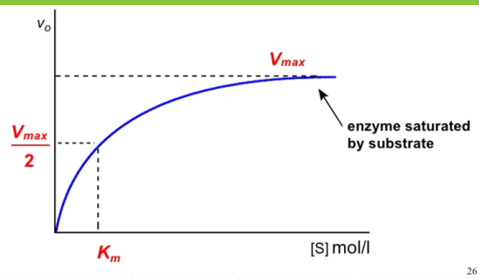
- **Enzyme concentration:** As the concentration of enzymes is increased, there are more available active sites for substrates to fit into. More enzyme-substrate complexes are formed, more products are formed and the rate of reaction is increased. The limiting factor is the enzyme concentration. Once all substrates have formed enzyme-substrate complexes, a further increase in concentration will have no effect on the rate of reaction. At this point, the limiting factor is the substrate concentration. During comparison, look at initial rate to ensure differences in reaction rate are caused only by differences in enzyme concentration.
- **Substrate concentration:** As the concentration of the substrates increases, there are greater chances of collision with enzyme. More enzyme-substrate complexes are formed, more products are formed and the rate of reaction is increased. The limiting factor is the substrate concentration. Once all enzymes are occupied and working at maximum rate (vmax), a further increase in substrate concentration will have no effect on the rate of reaction. At this point, the limiting factor is the enzyme concentration.



- **Inhibitor concentration**: Inhibitors interfere with enzyme activity and reduce the rate of an enzyme catalysed reaction. Therefore, as the concentration of inhibitors increases, the rate of reaction decreases.
  - **Reversible competitive inhibitor**: has a similar shape to the substrate and fits into the active site. This reduces the number of enzyme-substrate complexes formed and the rate of reaction decreases. It is said to be reversible because it can be reversed by increasing the concentration of the substrate.
  - **The reversible non-competitive inhibitor:** has a different shape to the substrate and fits into a site other than the active site. While the non-competitive inhibitor is bound, the tertiary structure of the entire enzyme is distorted, preventing the formation of enzyme-substrate complexes and decreasing the rate of reaction regardless of substrate concentration.
  - **End-product inhibition:** used to control metabolic reactions via non-competitive reversible inhibitors. As the enzyme converts substrate to product, it is slowed down because the end product binds to another part of the enzyme and prevents more substrate binding. However, the end-product can lose its attachment to the enzyme and go on to be used elsewhere, allowing the enzyme to reform into its active state.

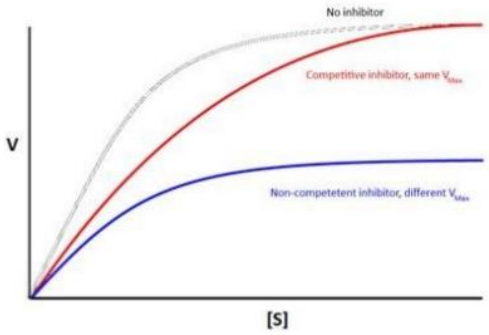


- **Theoretical maximum rate velocity (Vmax):** the reaction rate is measured at different substrate concentrations while keeping the enzyme concentration constant. As substrate concentration is increased, reaction rate rises until the reaction reaches its maximum rate.
- **Michaelis–Menten constant (Km):** The substrate concentration that corresponds to half of Vmax is Km. Km measures the affinity of the enzyme for the substrate. The higher the affinity, the more likely the product will be formed when a substrate molecule enters the active site. The higher the affinity of the enzyme for the substrate, the lower the substrate concentration needed for this to happen. The higher the affinity, the lower the Km and the quicker the reaction will proceed to Vmax.

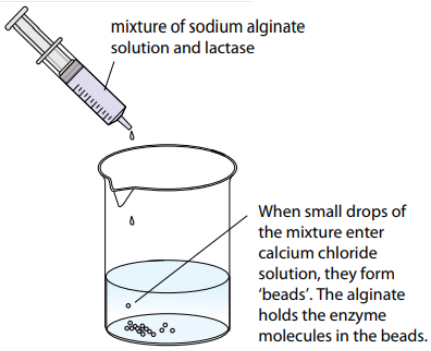


Competitive inhibitor: Vmax stays the same, but Km increases

Non-competitive inhibitor decreases the turnover number of the enzyme rather than preventing substrate binding- Vmax decreases but Km stays the same. This cannot be overcome with an increase in substrate concentration.



- **Enzyme immobilization:**
  - The enzyme is mixed with a solution of sodium alginate.
  - Little droplets of this mixture are then added to a solution of calcium chloride.
  - The sodium alginate and calcium chloride instantly react to form jelly, which turns each droplet into a little bead. The jelly bead contains the enzyme.



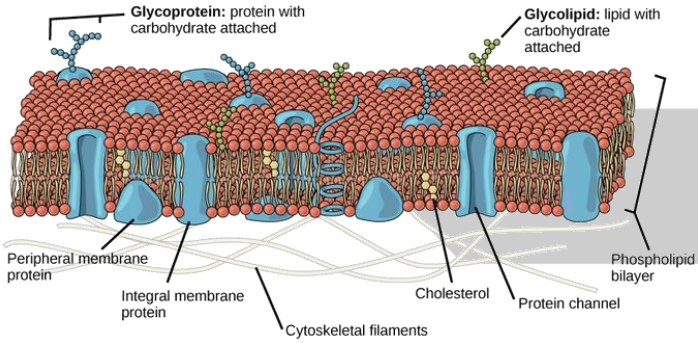
  - Can reuse the enzyme as it is not mixed with the solution, and can keep the product enzyme free, thus preventing contamination.
  - More tolerant to PH changes as the enzyme molecules are held firmly in shape by the alginate beads, thus don't denature easily.
  - More tolerant to temperature changes as parts of the molecules embedded in the beads are not fully exposed to temperature or pH changes.

- Active site may be distorted by immobilizing
- Substrate passes through matrix when immobilized
- Some product is retained within matrix

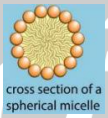
4. Cell Membrane and Transport

4.1 Fluid Mosaic Membranes

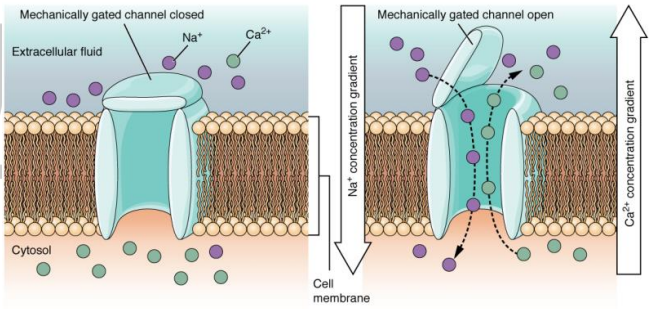
- **Fluid mosaic model:** individual phospholipid and protein molecules move around within their own monolayer. The word 'mosaic' describes the pattern produced by scattered protein molecule when the surface of the membrane is viewed from above.



- **Phospholipid bilayer:** This provides the basic structure of membranes, it is selectively permeable and acts as a barrier to most water-soluble substances.
  - The more unsaturated the tails, the more fluid the membrane as unsaturated fatty acid tails are bent and therefore fit together more loosely.
  - The longer the tail, the less fluid the membrane.
- **Micelle:** phospholipid molecules that arrange themselves in a spherical form in aqueous solutions.

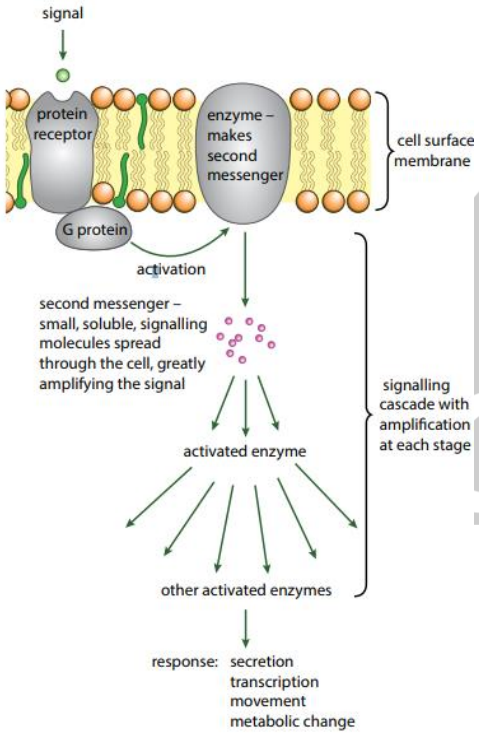


- **Cholesterol:** regulates the fluidity of a membranes. Its hydrophobic region prevents polar molecules from passing through the membrane eg in myelin sheath
  - **At low temperatures:** cholesterol increases the fluidity of the membrane, preventing it from becoming too rigid.
  - **At higher temperatures:** helps stabilize cells when the membrane could otherwise become too fluid.
  - Helps with mechanical stability
- **Glycolipids and glycoproteins**: Carbohydrate chains that are attached to membrane protein (glycoprotein) and phospholipids (glycolipid) project out into the watery fluids surrounding the cell where they form hydrogen bonds to stabilize the membrane structure.
  - **Carbohydrate chains act as receptors, mainly:**
    - **Signalling receptors:** The receptors recognise messenger molecules like hormones and neurotransmitters. When the messenger molecule binds to the receptor, a series of chemical reactions is triggered inside the cell.
    - **Endocytosis:** These group of receptors bind to molecules that are to be engulfed by the cell surface membrane.
    - **Cell adhesion:** binding cells to other cells in tissues and organs. Some glycolipids and glycoproteins act as antigens, allowing cell–cell recognition.
- **Proteins**: Transport proteins provide hydrophilic channels for ions and polar molecules. Enzymes catalyse the hydrolysis of molecules. Cytoskeleton made of protein filaments help maintain the shape of the cell.
  - **Intrinsic/integral proteins**: Proteins that are found embedded within the membrane. They may be found in the inner layer, the outer layer or, most commonly, spanning the whole membrane, known as transmembrane proteins.
  - **Extrinsic/peripheral proteins**: found on the inner or outer surface of the membrane. Many are bound to intrinsic proteins or to phospholipids.
  - **Channel proteins:** water-filled pores that allow charged substances, usually ions, to diffuse through the membrane. They have a fixed shape and can be gated to control ion exchange. This does not use ATP and is in facilitated diffusion.



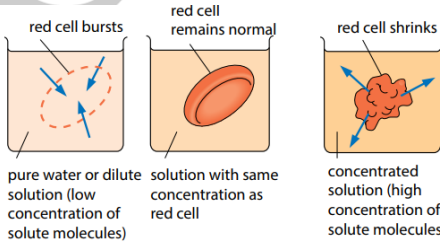
  - **Carrier proteins:** can flip between two shapes, and is mainly in active transport where it uses ATP to change shape and carry ions/molecules up the concentration gradient. It is also involved in passive transport (facilitated diffusion) down the concentration gradient without the use of energy.
- **Cell surface receptors:** These are present in membranes and bind with particular substances, eg: hormones which are chemical messengers which circulate in the blood but only bind to specific target cells.

- **Cell surface antigen:** These act as cell identity markers. Each type of cell has its own antigen. This enables cells to recognise other cells and behave in an organised way.
- **Cell signalling:** Cells communicate by sending and receiving signals.
  - A signal arrives at a specific protein receptor in a cell surface membrane that recognises the signal.
  - The signal brings about a conformational change in the shape of the receptor, spanning the membrane, and the message is passed to the inside of the cell (signal transduction).
  - Changing the shape of the receptor allows it to interact with the G protein, which brings about the release of a 'second messenger' (a small molecule which diffuses through the cell relaying the message).
  - The second messenger activates a cascade of enzyme catalysed reactions which brings about the required change.
  - This is an active process involving ATP use.



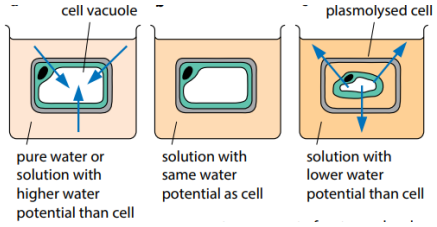
4.2 Movement of Substances into & out of Cells

- **Diffusion**: the net movement of molecules or ions from a region of high concentration to a region of low concentration. It is a passive process (molecules have natural kinetic energy). As a result of diffusion, molecules reach equilibrium.
  - Steeper concentration gradient, higher temperature and increased surface areas all increase rate of diffusion.
  - Non polar molecules can pass directly through the membrane eg steroid hormones
  - Gases can diffuse through the membrane directly
  - Water can diffuse through directly as it is a small molecule despite being polar.
- **Facilitated diffusion**: Movement of molecules from a region of high concentration to a region of low concentration down a concentration gradient. The movement is passive, however, molecules go through transport proteins instead of passing through phospholipids. This allows for the passage of large polar ions and molecules eg glucose, amino acids, Na+, Cl-
- **Osmosis**: the diffusion of water molecules from a region of higher water potential (ψ) (less negative) to a region of lower ψ (more negative) through a selectively permeable membrane.
  - ψ is the tendency of water to move out of a solution; pressure potential (ψp) on liquid increases ψ
  - Pure water has 0 ψ
  - Negative ψ means that solution has more solute than solvent, therefore solute potential (ψs) reduces ψ.
  - **In red blood cells:**

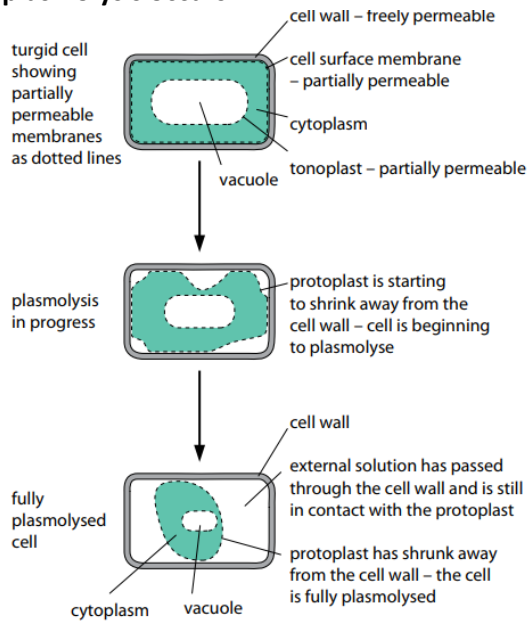


  - **In plant cells:** ψ = ψs + ψp
    - **Protoplast:** the living part of the cell inside the cell wall
    - **In pure water:** water enters the cell by osmosis, and the cell wall pushes back against the expanding protoplast, building up pressure rapidly, becoming turgid. This is the ψp, and it increases the ψ of the cell until equilibrium is reached.

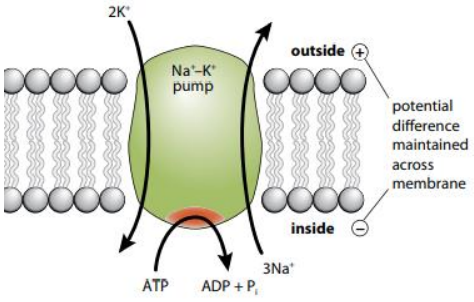
- **In concentrated solution:** water will leave the cell by osmosis. The protoplast gradually shrinks until it is exerting no pressure on the cell wall. The ψp = 0, so ψ = ψs. The protoplast continues to shrink and pulls away from the cell wall, so the cell is plasmolyzed. The point at which ψp has just reached 0 and plasmolysis is about to occur is referred to as incipient plasmolysis.



- **How plasmolysis occurs:**



- **Active transport**: Movement of substances from a region of low concentration to a region of high concentration against a concentration gradient. This occurs via specific carrier proteins for specific ions/molecules that use energy from ATP.
  - **Na+ – K+ pump:**



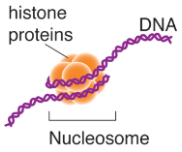
- **Exocytosis**: This is the movement of substances out of the cell. A secretory vesicle from golgi body moves towards the plasma membrane with the help of cytoskeleton, using energy from ATP. The vesicles fuse with the cell surface membrane releasing the contents outside.
- **Endocytosis**: involves the engulfing of the material by fusing with the plasma membrane to form an endocytic vacuole in the form of phagocytosis (bulk uptake of solids) or pinocytosis (bulk uptake of liquids) using ATP.

5. The Mitotic Cell Cycle

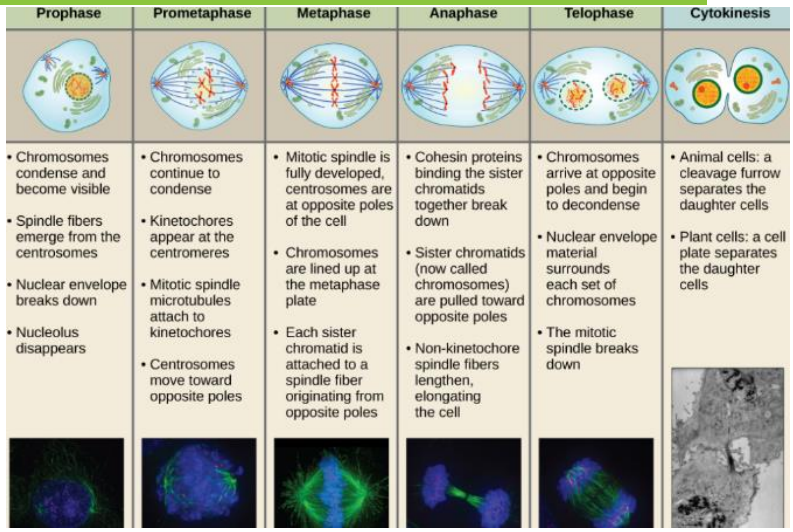
5.1 Replication & Division of Nuclei & Cells

- **Chromosome**: threadlike structure containing DNA and genes.
- **Chromatin**: combination of DNA (acidic) wound around histones proteins (basic).
  - **Heterochromatin**: tightly coiled (condensed);
    - Most condensed at metaphase;
    - Densely stained.
  - **Euchromatin**: loosely coiled;
    - At interphase (between divisions);
    - Not as densely stained.
  - **Main functions of chromosome in nuclear division:**
  - Chromosome condensed, so DNA is tightly packed ∴ easier to separate chromatids at centromere into daughter cells.
  - **Telomeres**: repeated short base sequence at end of chromosome (by telomerase).
    - Ensures ends of DNA are included during DNA replication.
    - Copying enzyme can't copy the end of DNA so pieces of info are lost; eventually including loss of vital genes.
    - **Ageing**: specialised cells don't top up their telomeres after DNA replication, therefore causing loss of genes, DNA and cell death.
  - **Centromere:** region where chromatids are held together.

- **Nucleosome:** DNA wrapped around histones making 1⅔ turns (147 base pairs)

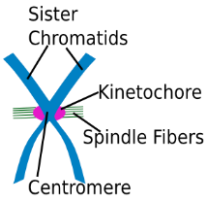


  - 11nm wide, 6nm long;
  - Made of 8 histone molecules;
  - Linker DNA is also held by a histone;
  - Nucleosomes line up to form a fibre 10nm wide which is further coiled to a supercoil, involving non-histone molecules thus the DNA (1.8m long, 2nm wide) is packed in nucleus (6um diameter)
- **Mitosis:** nuclear division producing two genetically identical daughter nuclei, each containing the same no. of chromosomes as the parent. Sister chromatids contain DNA with identical genes which is key to precise nuclear division (when each chromatid goes into each daughter cell, it makes them genetically identical).
- **The cell cycle:** 3 phases; interphase, nuclear division and cell division.
- **Interphase**: cell grows to its normal size after cell division, and synthesises important substances eg proteins.
  - **Growth 1 phase:** gap after cell division and before S phase.
    - Prepares for growth and DNA synthesis (S phase) by producing RNA, proteins and enzymes.
    - If there are insufficient growth factors, or when cell has reached its maximum size, cell will not divide and remain in G zero.
  - **S phase**: synthesis of DNA (in euchromatin form) so each chromosome consists of two identical chromatids (short phase).
    - Chromatin also replicates along with DNA so histones are replicated (for M phase)
  - **Growth 2 phase:** gap after S phase and before nuclear division (prepares for mitosis)
    - New DNA checked, and errors are repaired.
    - Sharp increase in the production of tubulin to make microtubules for the formation of mitotic spindle.
    - Nuclear envelope envelopes nucleus.
- **Cell division:**
  - **Nuclear division:** division of nuclei at M phase.
    - Growth stops temporarily during mitosis.
  - **Cytokinesis:** division of cytoplasm between daughter cells, last stage of cell division.



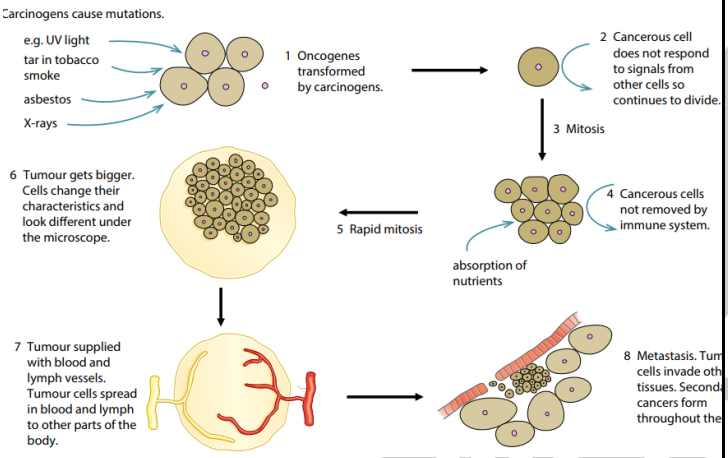
  - **Note:** nuclear envelope breaks down into vesicles during prophase and reassembles when the vesicles fuse to form the envelope back at telophase

- **Kinetochore:** two kinetochore at centromere on each chromatid during metaphase.



  - Made of proteins that bind to DNA in centromere and also to microtubules.
  - Microtubules extend from kinetochore to the poles of spindle.
- **Centrosome:** poles of spindle and act as MTOC with a pair of centriole that are surrounded by proteins which make microtubules.
- **Significance of mitosis:**
  - **Growth:** clones produced allow growth of multicellular organism from unicellular zygote.
  - **Replacement of cells and repair of tissues:** cells die and are replaced by GI cells; rapid in skin, lining of gut, and to regenerate whole parts of body.
  - **Asexual reproduction:** production new individual by a single parent.
    - In unicellular organisms, cell division results in reproduction.
    - In multicellular organisms, new individual produced bud off from parent.

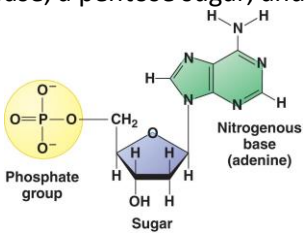
- **Stem cells:** cells that divide repeatedly by mitosis, and differentiate into specialized cells or remain as stem cells. **There are three different kinds:**
  - **Totipotent:** cells that can divide repeatedly to form any other cell in the body, eg: zygote
  - **Pluripotent:** embryotic stem cells that lead to development of the embryo and later the adult. They are not specialized into placenta.
  - **Multipotent:** Adult stem cells that are only able to produce a few types of cells eg stem cells in bone marrow.
- **Cancer:** mutation occurs in genes that control cell division, an oncogene, that results in uncontrolled mitosis. Cancerous cells divide repeatedly and form a tumour, which is an irregular mass of cells.
  - **Malignant tumour:** tumours that spread through the body, invade other tissues and destroy them. These cells break off from the tumour and form secondary growth, known as metastasis.



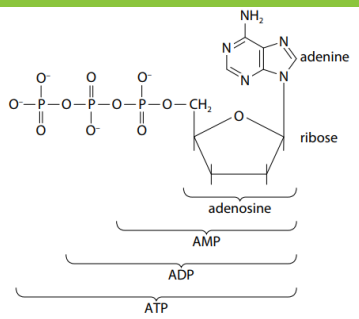
6. Nucleic Acid & Protein Synthesis

6.1 Structure & Replication of DNA

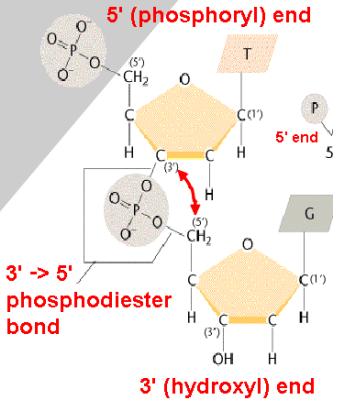
- **Nucleotides**: basic building block of nucleic acids, such as DNA and RNA. It is an organic compound made up of nitrogenous base, a pentose sugar, and a phosphate group.



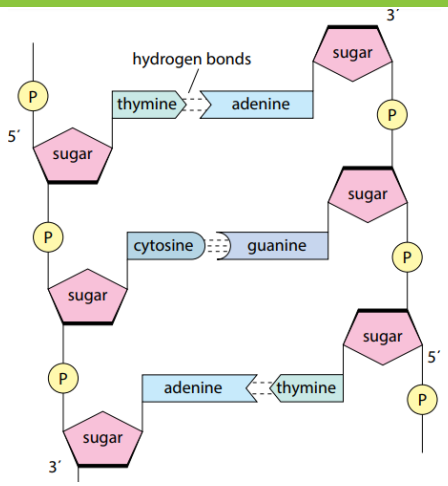
- **Structure of ATP:**



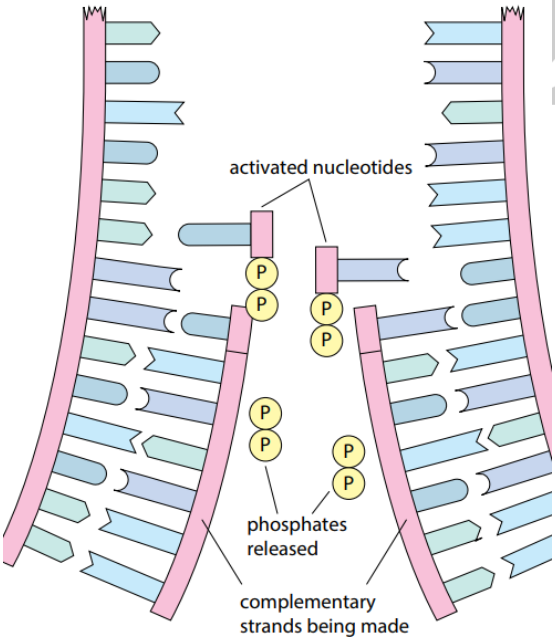
- **Polynucleotide:** many nucleotides are linked together into a long chain forming polynucleotides DNA/RNA. This happens in the nucleus during interphase.
  - The covalent sugar–phosphate bonds (phosphodiester bonds) link the 5-carbon of one sugar molecule and the 3-carbon of the next. The polynucleotide strand is said to have 3′ and 5′ ends



- **DNA** is made up of two antiparallel polynucleotide strands lying side by side, held together by hydrogen bonds. The H bonds ensure stability, 3d structure and makes DNA replication easier. These strands are arranged into a ladder-like structure called a double helix. The phosphate and the sugar form the back bone of the DNA molecule while the base pairs form the rings. **It has 4 nitrogenous bases:** Adenine, thymine, guanine and cytosine.
  - **Complementary base pairing: between** adenine and thymine (or adenine and uracil in RNA) and between guanine and cytosine. Because of complementary base pairing, the order of the bases in one strand determines the order of the bases in the other strand and therefore the strands are complementary to each other as well.
    - **Purines** are nitrogenous bases with double ring structures (Guanine and adenine).
    - **Pyrimidines** are nitrogenous bases with single ring structures (Adenine, uracil and cytosine).



- **Semi-conservative replication of DNA**: occurs during interphase. The DNA separates into two strands and each strand acts as a template. Each new DNA molecule consists of one old strand and a complementary new strand.
  - The DNA double helix unwinds and 'unzips' as the hydrogen bonds between the bases break by helicase.
  - In the nucleus, there are nucleotides to which two extra phosphates have been added to activate the nucleotides, enabling them to take part in the reaction.
  - Each of the bases of the activated nucleotides pairs up with its complementary base on each of the old DNA strands, DNA polymerase ensures this and links adjacent nucleotides to each other by catalyzing phosphodiester bonds. The two extra phosphates are broken off and released into the nucleus.

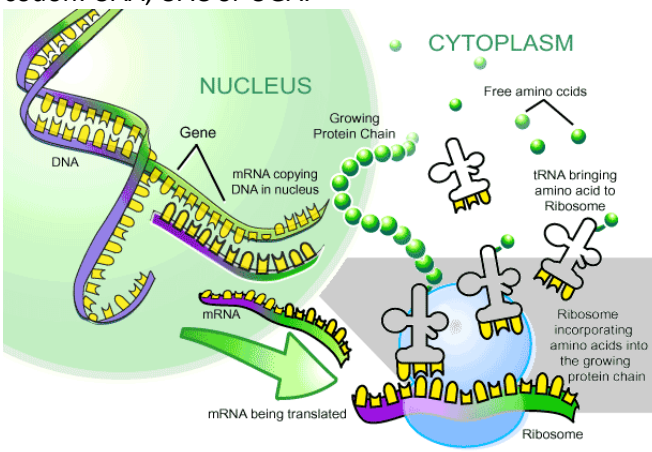


  - **Note:** on the lagging strand, the replication occurs in fragments known as Okazaki fragments. All these fragments are joined together by DNA ligase.
- **RNA:** a single stranded polynucleotide chain present in the nucleus, cytoplasm and ribosome. It contains a pentose sugar (ribose) and has 4 nitrogenous bases: Adenine, uracil, guanine and cytosine. **There are different types of RNA which include:**
  - **mRNA (messenger RNA):** carries the genetic information in the form of a template from the nucleus to the ribosome for translation.
  - **tRNA (transfer RNA)**: has a specific amino acid at one end and an anticodon at the other end. It fits onto the mRNA at ribosomes at complementary mRNA codon for protein synthesis.

6.2 Protein Synthesis

- **Gene:** a sequence of nucleotides that forms part of a DNA molecule and codes for a polypeptide.
- **Mutation:** a change in the nucleotide sequence of a gene, which may then result in an altered polypeptide. Most genes have several different variants called alleles.
- **Sickle cell anemia:** ref 2.4
- **Transcription:** in the nucleus the following happens:
  - DNA unwinds to form two strands and the antisense strand acts as a template.
  - Free activated RNA nucleotides line up with their complimentary base.
  - Phosphodiester bonds formed between sugar phosphate groups with the help of RNA polymerase
  - Starts at Promoter (initiates transcription)
  - Ends at terminator (the enzyme stops adding nucleotides to the growing mRNA)
  - Hydrogen bonds between the DNA and mRNA strand are then broken
  - DNA is reformed
  - mRNA strand then leaves the nucleus through the nuclear pores
- **Translation:**
  - Small ribosomal subunit attaches to mRNA
  - tRNA enters the ribosome and attaches to the mRNA
  - A codon on the mRNA attaches to a specific anticodon on the tRNA
    - AUG is start codon, complementary anticodon is UAC that brings amino acid methionine
  - Only 2 tRNA molecules can fit in the ribsosme at the same time
  - Each tRNA carries a specific amino acid

- A peptide bond is formed between the amino acids of 2 adjacent tRNA molecules with the help of peptidyl transferase
- Ribosome moves along the mRNA, reading the next codon. A third tRNA molecule brings a third amino acid, which joins to the second one. The first tRNA leaves and is reused.
- The polypeptide chain continues to grow until a 'stop' codon: UAA, UAC or UGA.



7. Transport in Plants

7.1 Structure of Transport Tissue

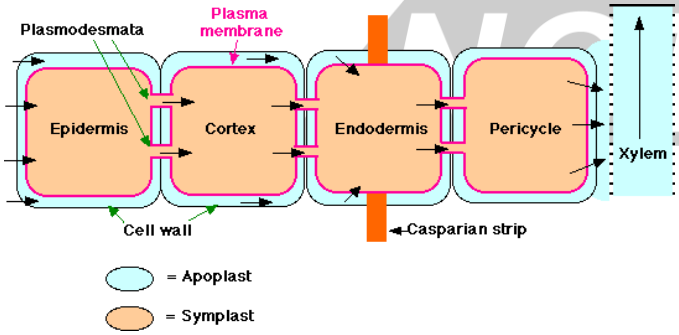
- **Xylem vessels:** These are dead cells which from a long, narrow and hollow tube to increase capillarity.
  - **Hollow / no cell contents and no end walls:** little resistance to flow of water
  - **Wide lumen:** large amounts of water can be transported
  - **Lignified cell walls:** prevents collapse of vessels - mechanical support, impermeable to water
  - **Cellulose cell wall:** allows adhesion of water molecules to xylem walls as walls are hydrophilic
  - **Pits:** allow lateral movement of water and connect to all parts of plant
  - **Narrow diameter:** for adhesion and prevent air locks
- **Phloem** tissue - contains 2 types of cells
  - **Sieve tube elements:** It does not contain many organelles (no vacuole and nucleus) to decrease resistance to flow of phloem sap.
  - **Companion cells:** contains higher numbers of mitochondria and ribosomes as they are metabolically active cells.
  - **Adaptations:**
    - **Sieve pores:** allow easy flow from one sieve tube element to the next.
    - **Sieve plates:** prevents sieve tube from bursting
    - **Little cell contents:** little resistance to flow of sap
    - **Plasmodesmata:** Allows flow to/from companion cells for loading and unloading of sucrose
    - **Thin walls:** Rapid entry of water at source to build up hydrostatic pressure

7.2 Transport Mechanisms

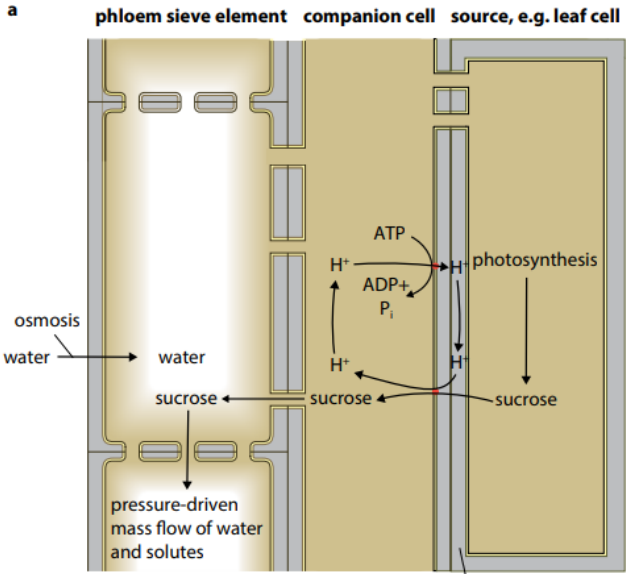
- **Transpiration** is a process involving the loss of water in the form of water vapour from the aerial parts of the plant. It is an inevitable consequence of gaseous exchange and thus photosynthesis, as stomata open and this allows water vapour to diffuse.
  - Water vapour in air spaces diffuses out of the leaf through stomata down the water potential gradient.
  - Water evaporates from cell walls of spongy mesophyll cells into the intercellular air spaces. This causes water to move from the cell's cytoplasm into the cell wall.
  - Water from neighboring xylem vessels (through pits) move into mesophyll cells by osmosis, down a water potential gradient.
  - A cohesion-tension and transpiration pull is created at the top of the plant due to the evaporation of water, as the hydrostatic pressure at the top of the xylem is reduced. This causes water to move up the xylem from roots to leaves.

- **Hydrogen bonding in water causes:**
  - **Cohesion**: Hydrogen bonds are formed between individual water molecules. Therefore, as one water molecule moves up the xylem, it pulls the other molecule along with it. This allows for water molecules to move up as a continuous stream.
  - **Adhesion**: Hydrogen bonds are formed between a water molecule and cellulose cell walls of xylem temporarily. This allows water molecules to continue moving upwards against gravity.
  - Water then moves from root hairs to xylem in the roots by passing through cortical parenchyma cells.

  There are 2 pathways for water transport:
  - **Apoplastic pathway**: involves the movement of water through cell walls and intercellular spaces/ dead material by mass flow. Water can pass via apopolast pathway until it reaches the Casparian strip, as it is impermeable to water due to a suberin deposition in the cell wall. The apoplastic pathway has little resistance to water, allowing water to flow faster. Water moving through the xylem takes the apoplastic route as xylem vessels are dead and contain no cytoplasm.
  - **Symplastic pathway**: This pathway involves the movement of water through the cytoplasm/ living material. Firstly, water passes through the partially permeable membrane. Then, the water passes through cytoplasm and vacuole before moving from one cell to another through the plasmodesmata.



- **Soil to root hair:**
  - Water is taken up by the root hairs from the soil. The soil has a relatively high water potential while the cytoplasm of the root hair cell has a relatively low water potential, as it contains many more inorganic and organic substances. Therefore, water moves into the root hair cells by osmosis. The large number of root hairs increases the surface area, allowing more water and ions to be taken up by the cells.
  - Ions may be taken up along with water by osmosis, or separately through facilitated diffusion or active transport.
- **Translocation** is transport of soluble organic substances within a plant. These are called assimilates and they include sucrose and amino acids. Sugars are transported as sucrose instead of glucose as glucose interferes with the water potential of cells.
- Sucrose is loaded into the phloem tubes by companion cells at the source (leaves). This is made possible due to the transport proteins present in the cell surface membrane of companion cells. **The two transport proteins are:**
  - The proton pump driven by ATP, pumps H^+ ions (protons) out of the companion cell into the cell wall (apoplast pathway), creating a high concentration of H+ ions in the cell wall.
  - The H^+ ion-sucrose co-transporter then drives the movement of H^+ ions from a region of high concentration (cell wall of companion cells) to a region of low concentration (cytoplasm of companion cell) along with sucrose.



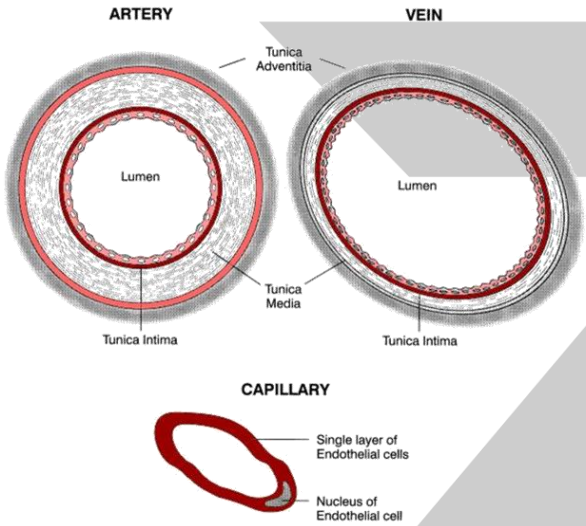
- After sucrose is in the cytoplasm of the companion cell, it diffuses into the phloem sieve tubes through plasmodesmata, down a concentration gradient.
- When sucrose enters phloem sieve tubes, the water potential of the cells decreases, due to an increase in solute. This causes water to move in from xylem vessels, causing an increase in hydrostatic pressure.
- Unloading occurs at the sink (roots, tubers), where sucrose is used for metabolism or storage.
- Assimilates are transported in large quantities by mass flow and from a region of high hydrostatic pressure to a region of low hydrostatic pressure from the source to the sink.
- **Adaptations of xerophytes:**
  - **Rolled leaf:** Increases humidity around stomata, reducing the water potential gradient
  - **Thick waxy cuticle:** Increases distance for diffusion, acting as a barrier for transpiration. Shiny surface reflects heat, lowering temperature.
  - **Hairs / trichomes on surface:** trap moisture to reduce water potential gradient
  - **Sunken stomata/ stomata in pits:** Moist air trapped in pits reduces
  - **No stomata on upper surface:** Not exposed to sunlight, reducing evaporation rate
  - **Small leaves, reduced to spines:** reduce surface area for transpiration
- **Factors affecting rate of transpiration:**
  - Surface area of leaf
  - Humidity
  - Wind speed
  - Number of stomata
  - Temperature
  - Light intensity
  - Thickness of cuticle
  - Water potential gradient between leaf and surrounding air
- **Root pressure:** increasing the pressure difference between the top and bottom by raising the water pressure at the base of the vessels.
  - Pressure is raised by active secretion of solutes into the xylem vessels in the roots, lowering the water potential and thus drawing water from surrounding root cells by osmosis.

8. Transport in Mammals

8.1 The Circulatory System

- The mammalian circulatory system is a closed double circulation. This is because blood passes through the heart twice in one circulation of the body (pulmonary circuit and systemic circuit), contained inside blood vessels.
- The circulatory system also includes a heart and blood vessels (arteries, capillaries and veins).
- Arteries and veins contain three layers of tissues known as the tunica intima, tunica media, and tunica externa.
  - **Tunica interna:** endothelium, containing squamous epithelial cells
  - **Tunica media:** containing smooth muscle, elastic fibres, and collagen fibres
  - **Tunica externa:** containing elastic and collagen fibres
- **Arteries:** These blood vessels transport oxygenated blood swiftly to the tissues at high pressures. They have thick walls to withstand this high pressure. The exception to this is the pulmonary artery, carrying dexoygenated blood to the lungs. As arteries reach tissues they branch into smaller vessels called arterioles.
  - The tunica media and externa contain elastic fibres that recoil and contract, squeezing the blood and so moving it along in a continuous flow. They allow the walls to stretch, as pulses of blood surge through.
  - The tunica media also contains smooth muscles which contracts, reducing blood flow in arterioles. This controls volume of blood flowing into a tissue.
  - The increased collagen in the tunica media and externa give arteries strength, structure and flexibility.
- **Capillaries**: Arterioles continue to branch into capillaries. These are the smallest blood vessels and they take the blood as close as possible to the cells. This allows for rapid transfer of substances between cells and the blood. Due to the very small diameter of these blood vessels, blood travels very slowly. This increases the opportunity for diffusion to occur.
  - Walls of capillaries are made of a single layer of endothelial cells with pores between individual cells present to allow some components of blood to pass through into the cells and tissues of the body.

- **Veins**: Many capillaries join to form venules which then join to form veins. These blood vessels carry deoxygenated blood back to the heart. The exception is pulmonary vein, carrying oxygenated blood from the lungs to the heart.
  - There are fewer elastic and collagen fibres and smooth muscles in veins when compared to arteries, as the blood in veins is at a lower pressure.
  - Valves are also present to prevent backflow of blood.
  - To keep blood flowing upwards from legs, veins are usually near muscles, so pressure is increased when muscles contract.
  - Veins also have a much larger lumen than arteries.
- **Comparison of Blood Vessels:**



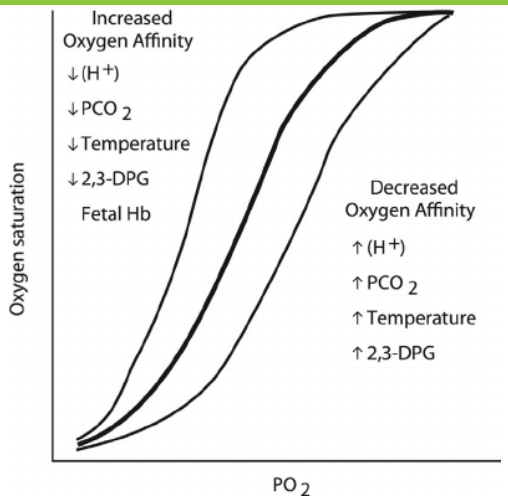
- **Blood** is composed of 4 components:
  - **Plasma**: This is the liquid part of the blood. It is a dilute solution of salts, glucose, amino acids, vitamins, urea, protein and fats.
  - **Leukocytes (white blood cells):** Involved in the immune system.
  - **Platelets**: Involved in blood clotting.
  - **Erythrocytes (red blood cells**): Involved in carrying oxygen.
- **Tissue fluid:** This fluid surrounds all the cells. Substances move from the blood to the tissue fluid and from the tissue fluid they diffuse into the cells. Tissue fluid has almost the same components as plasma, but lacks large plasma proteins which are too large to diffuse through pores in capillaries. Osmotic pressure causes tissue fluid to move into and out of capillaries.
- **Lymph:** About 90% of fluid that leaks from capillaries at the arterial end into tissue spaces eventually returns to the capillaries at the venous end. The remaining 10% is returned back to the lymphatic system. Fluid inside the lymphatic vessels is called lymph. Lymph is very similar to tissue fluid but has a different name as it is in a different place. Lymph contains more large proteins and white blood cells than tissue fluid.
- **Haemoglobin (Hb) transports oxygen and carbon dioxide:**
  - **In respiring tissues:** The pCO_2 is high and the pO_2 is low.
    - CO2 from the cells diffuses into the plasma.
    - CO2 combines with -NH2 terminal of Hb to form carbaminohaemoglobin. (10% carried this way)
    - Most CO2 combines with water (catalysed by carbonic anhydrase) to form carbonic acid which then dissociates into H+ and HCO3- ions.

$$\underset{\text{carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \overset{\text{carbonic anhydrase}}{\rightleftharpoons} \underset{\text{carbonic acid}}{H_2CO_3}$$

The carbonic acid dissociates:

$$\underset{\text{carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{hydrogen ion}}{H^+} + \underset{\text{hydrogencarbonate ion}}{HCO_3^-}$$

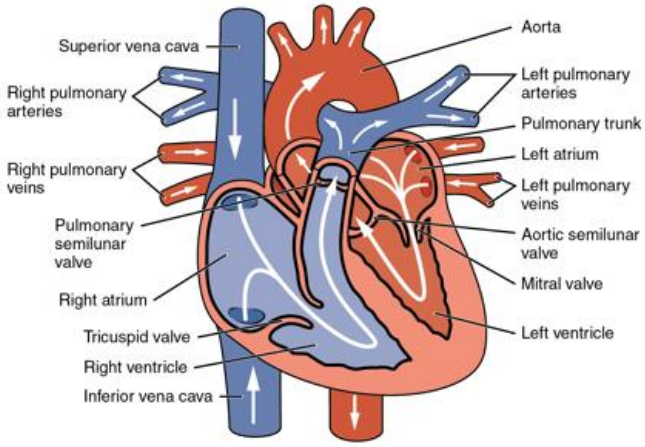
    - H+ ions combine with Hb to form Haemoglobinic acid (HHb).
  - **In the lungs:** The pO2 is high and the pCO2 low.
    - CO2 in plasma diffuses from the blood into the alveoli and oxygen diffuses into the blood from the alveoli.
    - Carbaminohaemoglobin dissociates to form CO2 and Hb
    - Hb then picks up O2, and HHb (haemoglobinic acid) dissociates to form H+ and Hb.
    - The H+ ions combine with HCO3- to form carbonic acid, which dissociates to form CO2 and water (catalysed by carbonic anhydrase).
    - CO2 diffuses into alveoli.
- The presence of a high pCO_2 causes Hb to release oxygen. This is called the **Bohr Effect**. High pCO_2 are found in actively respiring tissues which need oxygen. This causes Hb to release oxygen even more readily than it would otherwise.



- **In high altitudes:** the pO_2 is low, causing altitude sickness. In order to increase oxygen intake, populations that live in high altitude areas have adapted by developing higher haemoglobin count, larger lung capacity, increased red blood cell count and greater number of mitochondria to increase the efficiency of oxygen transport from lung to tissue. The muscular wall of the right ventricle also thickens (∴ larger heart), so more blood can be oxygenated.
- **Adaptations of Red Blood Cells:**
  - **Biconcave shape** increases surface area: volume ratio, for more efficient diffusion of oxygen
  - Contain **haemoglobin** to transport oxygen
  - **Nucleus, mitochondrion, ER absent**: more room for Hb, thus more o2 carrying capacity.
  - **Thin outer membrane** to allow oxygen to diffuse easily
  - **Very small (7µm):** no haemoglobin molecule within the cell is very far from the cell surface membrane, thus oxygen is exchanged quickly with outer fluid. Capillaries are 7µm allowing RBC to squeeze through.
  - **Flexible:** capillaries narrow than 7µm cause RBC to deform (as they have a specialized cytoskeleton) and return back to shape in venules.

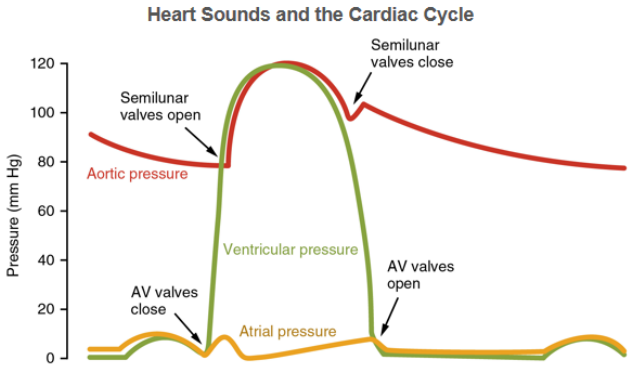
8.2 The Heart

- **External structure of the heart:** Blood vessels that leave the heart are the Aortic arch and pulmonary artery. Blood vessels that enter the heart are the superior vena cava, the inferior vena cava and the pulmonary vein. The left and right side of the heart are separated by the septum.
- **Internal structure of the heart-** The human heart has four chambers:
  - **Atria**: 2 upper chamber are known as atria. They are thin walled and receive blood at low pressure.
  - **Ventricles**: 2 lower chambers are known as ventricles. They are thick walled, receive blood from atria and pump it out through arteries.
    - The left ventricle has a thicker muscular wall, as it has to pump blood into the systemic circuit which has a higher resistance to blood flow than the pulmonary circuit. The systemic circuit is also longer and requires more pressure.

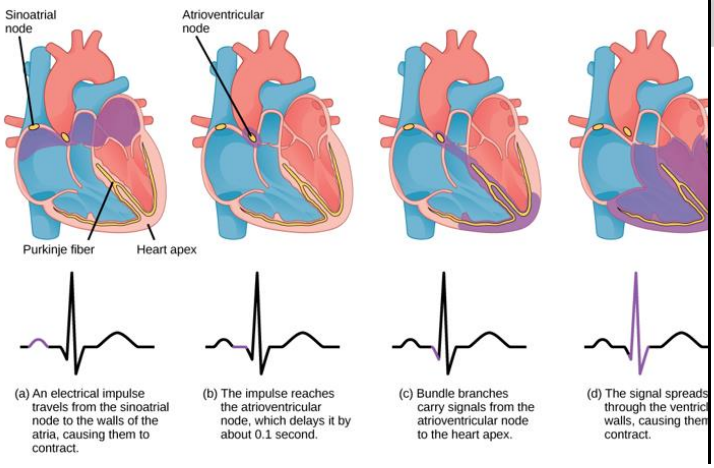


- **The cardiac cycle is divided into 2 stages, systole and diastole:**
  - **Atrial systole:** This occurs when muscles in the atrial walls contract and blood passes on to the ventricles. 70% of the blood flows passively down to the ventricles. The bicuspid and tricuspid valves open while the semilunar valves are closed.
  - **Ventricular systole**: 0.1 seconds after the atria contracts, the ventricle walls contract as well increasing the blood pressure and pushing it out of the heart. The blood passes through the aorta and pulmonary arteries. The semilunar valves open and the bicuspid and tricuspid valves are closed.
  - **Ventricular diastole:** This lasts for about 0.3 seconds, the ventricles relax and the pressure falls below that in the arteries. The higher pressure in the arteries pushes against the semilunar valves, shutting them.
  - **Diastole**: All muscles of the heart relax and the pressure inside ventricles gets lower than in the atria. When this happens most of the blood starts to flow from the atria to the ventricles even though the atria is not contracting. However, the atria contracts towards the end to push out the last bit of blood into the ventricles and the cycle begins all over again.

- **Control of the heart beat:** The cardiac cycle begins in the right atrium. There is a specialised patch of muscles in the wall of the right atrium known as the Sino-Atrial node. Cells at the SAN set the rhythm for all of the cardiac muscle cells to beat as they send out electrical impulses to the rest of the atria. This causes atrial contraction.
- The electrical impulses do not pass down to the ventricles. Instead, a second node (Atrio-ventricular node) picks up the electrical impulses from the atria.



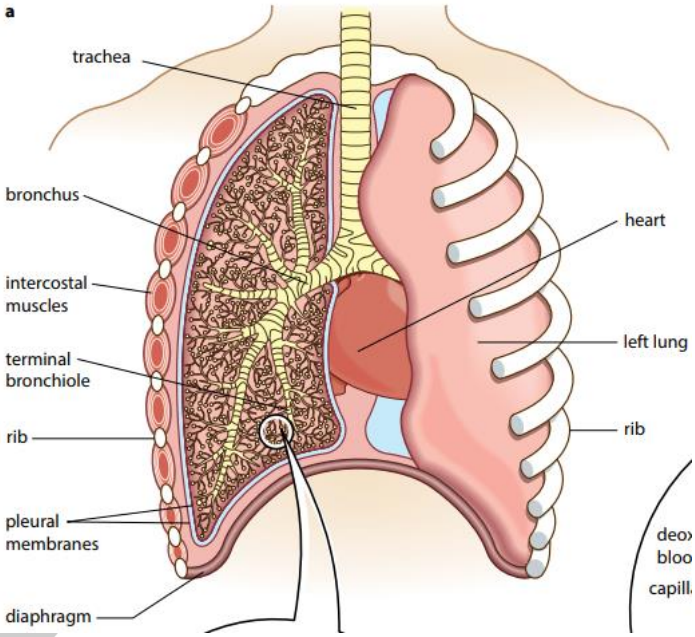
- The AV node causes the impulse to be delayed by 0.1 seconds, so the atria contract before the ventricles, giving the ventricles time to fill up with blood.
- The impulse swiftly moves down to the septum of the heart, along fibres called Purkyne tissue. Once the impulse arrive at the base of the ventricles, it moves outwards and upwards through ventricular walls. This causes the ventricle to contract. This is important as the ventricles must push blood upwards into the Aorta and the pulmonary artery.



9. Gas Exchange and Smoking

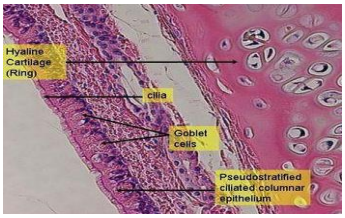
9.1 The Gas Exchange System

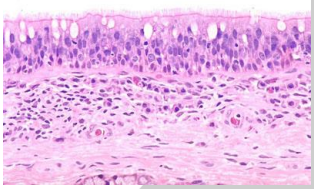
- **Gross structure of lungs:** lungs are in chest cavity surrounded by the pleural membranes, which enclose an airtight space. This space contains a small quantity of fluid to allow friction-free movement as the lungs are ventilated by the movement of the diaphragm and ribs.



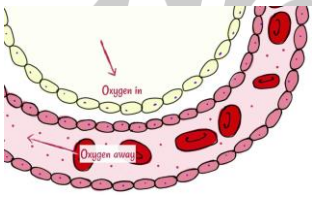
- **Bronchi:** branch to form smaller bronchioles.
  - Bronchioles are surrounded by **smooth muscle,** which can contract or relax to adjust the diameter of these tiny airways due to the absence of cartilage. During exercise, the muscles relax to allow a greater flow of air to the alveoli.
- **Cartilage:** It is a connective tissue. It keeps airways in trachea and bronchi open and air resistance low, and prevents them from collapsing or bursting as the air pressure changes during breathing.
  - Cartilage present in irregular plates and incomplete rings in bronchus, and as incomplete rings only in trachea

- **Epithelium:** Air flows down lungs through trachea and bronchi which are lined by cells adapted to remove particles from air before it reaches the lungs. These cells make up a tissue called epithelium. **There are two main kinds:**
  - **Ciliated cells:** lined with tiny cytoplasmic extensions known as cilia. They are responsible for the continual beating of mucus towards the larynx.
  - **Goblet cells:** found in between ciliated cells in large amounts. The upper part of a goblet cell is swollen with mucin droplets that are secreted by the cell. The mucous secreted by goblet cells traps pathogens which are then moved out with the help of the cilia.
    - **Mucus**: a slimy solution of mucin, which is composed of glycoproteins with many carbohydrate chains that make them sticky and able to trap inhaled particles. It is also made by mucous glands (multicellular) beneath the epithelium.
    - SO_2 and NO_2 can dissolve in mucus to form an acidic solution that irritates the lining of the airways.



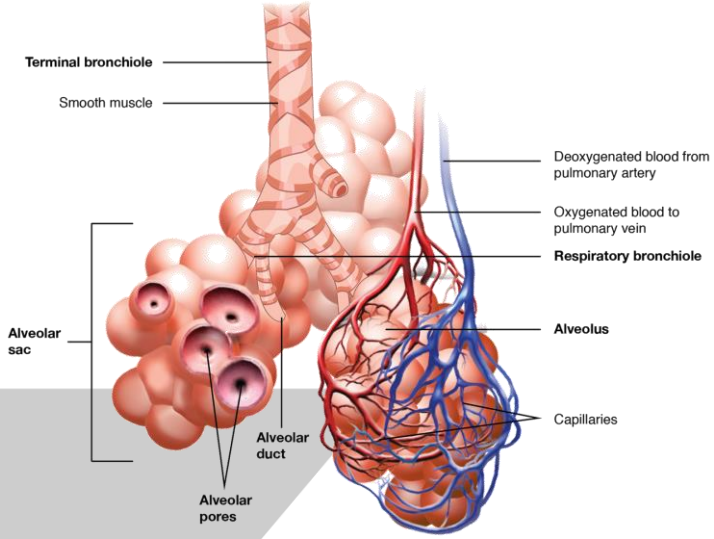


- **The lungs are the site for gas exchange between air and blood:**
  - Large number of alveoli are present to increase surface area.
  - The wall of alveolus is very thin (single layer of squamous epithelium) to decrease the diffusion distance for efficient gas exchange.



  - Outside the alveolus are capillaries also one cell thick. The steep concentration gradient of CO_2 and O_2 is maintained by blood circulation and breathing
  - **Elastic fibres** allow the alveoli to stretch during inhalation and recoil during expiration. During maximum expansion, surface area for diffusion increases and the air is expelled efficiently during recoil.

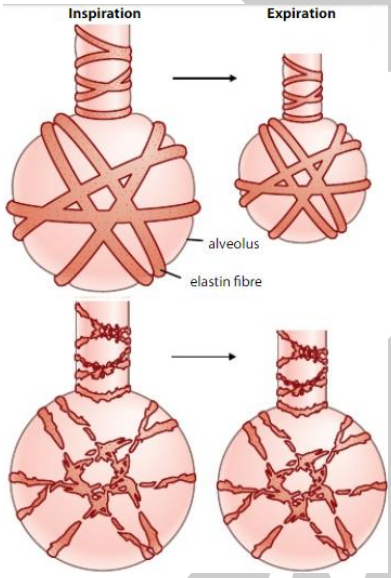
Airway	Number	Approximate diameter	Cartilage	Goblet cells	Smooth muscle	Cilia	Site of gas exchange
trachea	1	1.8 cm	yes	yes	yes	yes	no
bronchus	2	1.2 cm	yes	yes	yes	yes	no
terminal bronchiole	48 000	1.0 mm	no	no	yes	yes	no
respiratory bronchiole	300 000	0.5 mm	no	no	no	a few	no
alveolar duct	9×10^6	400 µm	no	no	no	no	yes
alveoli	3×10^9	250 µm	no	no	no	no	yes



9.2 Smoking

- **Passive smoking:** breathing in someone else's cigarette.
- **Mainstream smoking:** smoke from filter/mouth end.
- **Sidestream smoking:** the burning tip containing 85% of smoke released. Many toxic substances are in higher concentration here, and are exposed to others nearby.
- **Chronic bronchitis**: damage and obstruction of the airways.
  - **Tar**: stimulates goblet cells and mucus glands to enlarge and secrete more mucus.
    - Inhibits the cleaning action of the ciliated epithelium that lines the airways.
    - Destroys many cilia and weakens the sweeping action of those that remain.
  - Mucus, bacteria, viruses etc accumulate and obstruct the bronchioles.
  - Overtime, damaged epithelia are replaced by scar tissue.
  - Smooth muscle surrounding bronchiole becomes thicker, narrowing airways and causing difficulty breathing.
  - An infection in the lungs cause linings to become inflamed and further narrows the airways.
  - Sufferers cough out phlegm, a mixture of WBC, mucus and bacteria.

- **Emphysema:**
  - Lung inflammation causes phagocytes to leave the blood and line at the airways.
  - They release the protein-digesting enzyme elastase that destroys elastin of alveolar walls, making a pathway for the phagocytes to reach the lining and remove bacteria.
  - Thus, alveoli do not stretch and recoil during breathing.
  - Bronchioles collapse during expiration, trapping air in the alveoli, which often burst.
  - Large spaces appear where the alveoli have burst, and this reduces the surface area for gas exchange.
  - The number of capillaries also decreases, so less oxygen is absorbed into the blood.
  - Wheezing and breathlessness are common symptoms.



- **Chronic obstructive pulmonary diseases (COPD):** the complex disease when chronic bronchitis and emphysema occur with each other.
- **Lung cancer:** Tar also contains several carcinogens that cause mutation in epithelial DNA, leading to uncontrolled cell division and growth of tumours. Cancerous cells break away from primary tumours and begin to form secondary tumours in other parts of body (metastasis), known as malignant tumour.
  - Cancers often develop at the base of the trachea where it divides into the bronchi as this is where most of the tar is deposited.
- **Nicotine**:
  - Stimulates CNS to reduce diameter of arterioles due to build up of plaque, and also release adrenaline.
  - As a result, it increases blood pressure and heart rate, damaging endothelial lining and causing arthrosclerosis (narrowing of arteries).
  - Platelets become sticky, which increases chances of clot forming in blood vessels (thrombosis).
  - Blood flow is decreased in supply to extremities.
  - It stimulates nerve endings in the brain to release dopamine, which is associated with reinforcing pleasurable experiences and makes smoking addictive.
- **Carbon Monoxide:**
  - Binds to haemoglobin in RBCs to form carboxyhaemoglobin
  - This decreases a RBCs oxygen carrying capacity.
  - It also damages artery lining, leading to build up of fatty tissue and reduction of blood flow, causing stroke/CHD.

10. Infectious Diseases

10.1 Infectious Diseases

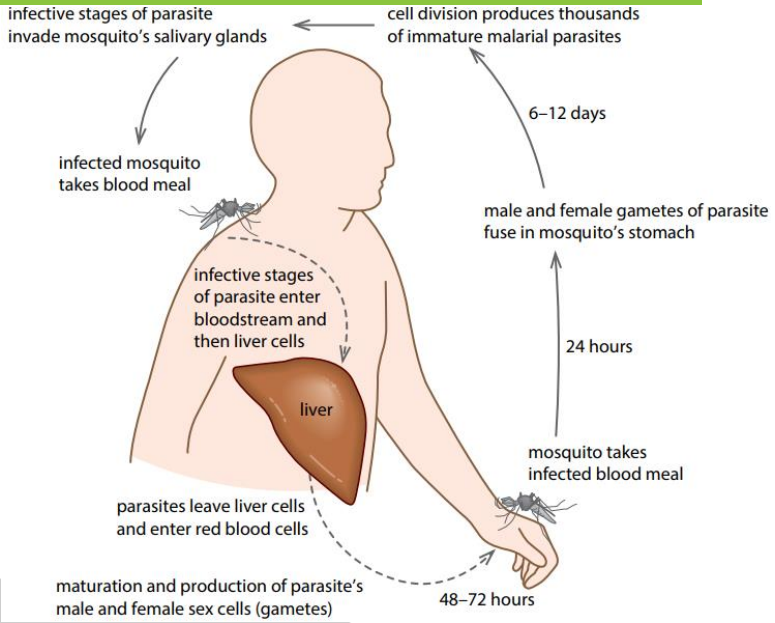
- **Disease**: an illness or disorder of the body or mind that leads to poor health; each disease is associated with a set of signs and symptoms.
- **Infectious diseases:** transmissible diseases caused by pathogens as they are passed from the infected to the uninfected, reducing effectiveness of funtions.
- **Non-infectious disease:** diseases that are not caused by pathogens. They can be cardiovascular eg lung cancer, or inherited/genetic eg sickle cell anemia, or deficiency diseases caused by malnutrition and mental diseases.

- **Cholera**: a water-borne disease that occurs where people do not have access to proper sanitation, a clean water supply or uncontaminated food.

PATHOGEN	*Vibrio cholerae*
ORGANISM	Bacterium
TRANSMISSION	Food borne, water borne, feacal-oral route
INCUBATION	2 hours – 5 days
SITE OF ACTION	Wall of small intestine
SYMPTOMS	Severe diarrhoea, loss of water and salts, dehydration.

  - **Treating cholera:**
    - **Oral rehydration therapy**: drinking a solution of glucose and salts to rehydrate the body.
  - **Preventing cholera:** sewage treatment, provision of clean water pipes that is chlorinated to kill bacteria.
- **Malaria**: Malaria is caused by Plasmodium parasites. The parasites are spread through the bites of infected female Anopheles mosquitoes.

PATHOGEN	*Plasmodium falciparum, P. vivax, P. ovale, P. malariae*
ORGANISM	Protoctist
TRANSMISSION	Female Anopheles mosquito (vector), blood transfusion, across the placenta, reuse of unsterile needles
INCUBATION	1 week – 1 year
SITE OF ACTION	liver, red blood cells, brain
SYMPTOMS	Fever, nausea, headaches, sweating, spleen enlargement, muscle pain



  - **Treatment of malaria:** use of anti-malarial drugs to treat the infected by inhibiting protein synthesis and sexual reproduction, thus preventing the parasite spreading within the body.
  - **Preventing malaria:**
    - Reduce number of mosquitoes by killing it, spreading oil in breeding grounds, draining marshes and clearing vegetation.
    - Avoid being bitten by mosquitoes by sleeping under mosquito nets.
    - Use drugs to prevent parasite infecting people.
    - **Biological control:** stocking bodies of water with fish which feed on mosquito larvae and spraying bacterium that kills larvae.
  - **Controlling malaria:**
    - Increase public knowledge about malaria.
    - Increase accessibility of healthcare in rural areas.
    - Diagnose infected people so treatments can be started earlier.
    - Use of modern techniques in gene sequencing and drug design.
    - Development of vaccines targeted against different stages of the parasite's life cycle (due to antigenic shift and different antigens per stage)
    - A renewed international will to remove the burden of disease from developing countries, allied to generous donations from wealthy individuals and foundations.

- **Factors affecting worldwide distribution**:
  - Almost 90% of cases of malaria are reported in Sub-Saharan Africa
  - Malaria is abundant in hot and humid places (tropical zone) as mosquitoes thrive in these conditions
  - Plasmodium parasites require temperatures higher than 20
  - No mosquito control programs
  - Increased use of DDT, causing DDT resistant Anopheles species
  - Stagnant water acts as a breeding ground for Anopheles mosquitoes
  - People who are heterozygous sickle cell (Hb^A Hb^S) are partial immune to malaria as the parasite is unable to reproduce inside the affected red blood cells

- **Acquired Immune Deficiency Syndrome**: HIV pathogens infect and destroy the T helper cells of the immune system, thus it does not respond adequately to infection. When T-Cell numbers are low, the body is particularly vulnerable to opportunistic infection eg TB. Thus, AIDS is not a disease, HIV is the virus that causes AIDS which is a syndrome.

PATHOGEN	Human immunodeficiency virus (retrovirus)
TRANSMISSION	Exchange of body fluids (during sexual intercourse, intravenous needle sharing, blood transfusions), pass through placenta and breast milk (mother to fetus)
INCUBATION	Initial incubation a few weeks, but up to ten years or more before symptoms of AIDS may develop
SITE OF ACTION	T helper lymphocytes, macrophages, brain cells
SYMPTOMS	HIV infection, susceptibility to disease- pneumonia, TB & cancers; weight loss, diarrhoea, fever, sweating, dementia

  - **Treating HIV:** There's no cure, however, drug therapy prevents replication of the virus, prolonging life. It binds to the viral enzyme reverse transcriptase and blocks its action. This stops the replication of the viral genetic material and leads to an increase in some of the body's lymphocytes.
  - **Preventing HIV:** Has antigenic shift, thus difficult to control to recognise and control.
    - Education about spread of infection.
    - Use of condoms and femidoms as they form barrier between body fluids.
    - **Contract tracing:** used to identify and isolate sources of infection by testing for HIV antibodies. This can be used to isolate and treat more people, and prevents further spread of infection.
    - Stop sharing needles or use sterile ones.
    - Blood should be HIV screened and heat treated to kill any viruses.
    - If tested HIV+, be given medical drugs and psychological support.
  - **Factors affecting worldwide distribution:**
    - The cases have been reported in all regions of the world, but largest part those existing with HIV (97%) reside in low and middle income countries, particularly in sub-Saharan Africa.
    - 70% of deaths due to HIV occur in Africa
    - People with multiple partners at risk of spreading/ contracting infection
    - Most people living with HIV or at risk for HIV do not have access to prevention, care, and treatment, and there is still no cure

- **Tubercolosis (TB):** an incredibly invasive disease. It often strikes HIV+ people and those suffering from malnutrition as their immune systems are weak and the bacteria activates. Particularly prevalent in overcrowded areas.

PATHOGEN	*Mycobacterium tuberculosis, Mycobacterium bovis*
PATHOGEN	Bacterium
TRANSMISSION	Airborne droplets (M. tuberculosis); via undercooked meat and unpasteurised milk (M. bovis)
INCUBATION	Few weeks – several years
SITE OF ACTION	primary infection in lungs; secondary infections in lymph nodes, bones and gut
SYMPTOMS	Coughing up blood, shortness of breath, fever, chest pain & sweating, weight loss

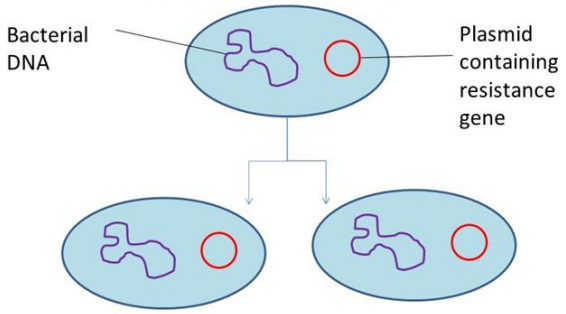
  - **Treating TB:** samples of sputum (mucus and pus) from their lungs are collected and TB bacteria is identified by microscopy. Infected patients are isolated and treated by drugs. Patients should take their full course of drugs otherwise they'll harbour drug-resistant bacteria.

- **Drug resistant TB:** stopping drug treatment allows the survival of bacteria that will multiply and perhaps undergo mutations, developing drug-resistant bacteria that further multiply. DOTS (direct observation treatment, short course) involves health workers or responsible family members making sure that patients complete their drug course to help reduce spread of MDR-TB and XDR-TB resistant bacteria,
- **Preventing TB:** contact tracing and screening for symptoms of TB. TB can be transmitted between cattle and humans. Thus, cattle should be routinely tested for TB and any found to be infected are destroyed. TB bacteria are killed when milk is pasteurized.
- **Factors affecting worldwide distribution:**
  - Prevalent in HIV+ positive areas
  - Areas where access to healthcare is low, or drugs are expensive can cause MDR and XDR strains to form
  - Distributed equally worldwide

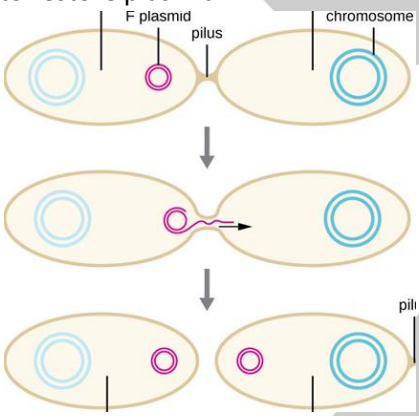
- **Smallpox**: an acute, highly infectious disease caused by the *variola* virus and transmitted by direct contact. Red spots containing a transparent fluid would appear all over the body, filled with thick pus. Symptoms are fever and a distinctive, progressive skin rash. Many smallpox survivors have permanent scars over large areas of their body, especially their faces. Some are left blind.
- **Measels**: caused by *Morbillivirus* virus that multiplies in the upper respiratory tract (trachea and nasal cavity). No symptoms after initial infection, followed by fever and rash with potentially fatal complications.
  - **Transmitted:** via airborne droplets.
  - **Babies under 8 months are immune:** due to passive immunity in the form of antibodies via the placenta.
  - Measles is no longer common most developed countries since most children are vaccinated. It commonly affects developing countries in places where conditions are overcrowded and insanitary. It can cause childhood blindness and severe brain damage.
- **More about measles, malaria and small pox in 11.2**
- These diseases are relevant because they are the ones of current concern as they are all in epidemic or pandemic status. Due to international travel, infectious diseases can be spread round the entire world very quickly.

10.2 Antibiotics

- **Antibiotics:** drug that kills or stops the growth of bacteria, without harming the cells of the infected organism.
- **How they work:** interfere with some aspect of growth or metabolism of the target bacterium **including:**
  - Synthesis of bacterial cell walls
  - Activity of proteins in the cell surface membrane
  - Enzyme action
  - DNA and protein synthesis
- **How penicillin works:**
  - Prevents synthesis of crosslinks between peptidoglycan polymers in bacterial cell walls by inhibiting enzymes that build these crosslinks.
  - When a newly formed bacterial cell is growing, it secretes enzymes called autolysins, which make little holes in its cell wall.
  - These little holes allow the wall to stretch so that new peptidoglycan chains can link together.
  - Penicillin prevents the peptidoglycan chains from linking up, but the autolysins keep making new holes.
  - The cell wall therefore becomes progressively weaker and it bursts due to osmotic pressure.
- Antibiotics are ineffective against viruses as they do not have any form of cell structure or metabolism. These viruses replicate only within living hosts.
- **Penicillin has no effect on M. tuberculosis because:**
  - Bacterium has thick impermeable cell wall;
  - Has a gene that codes for an enzyme (β-lactamase/penicillinase) which breaks down penicillin;
  - Proteins in the membranes of other species of bacteria can inactivate antibiotics so they have no effect;
  - Bacterial membranes have proteins that pump out antibiotics if they enter cytoplasm;
  - Sometimes, antibiotic simply can't bind to intended site of action.
- **DNA mutation:** an existing gene within the bacterial genome changes spontaneously to give rise to a nucleotide sequence that codes for a slightly different protein that is not affected by the antibiotic.
- **Vertical transmission:** Bacteria reproduce asexually by binary fission.
  - DNA in bacterial chromosome is replicated;
  - Cell divides into two;
  - Each daughter cell receives a copy of the chromosome.



- **Horizontal transmission:**
  - **Plasmid**: small loops of double stranded DNA often containing resistant gene.
  - **Conjugation:**
    - Conjugation tube is formed between two bacteria.
    - One strand of plasmid is transferred from donor to recipient bacterium.
    - Donor and recipient synthesise complementary strand to restore plasmid.

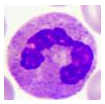


- **Selection pressure:** any phenomena which alters the behaviour and fitness of living organisms within a given environment. It is the driving force of evolution and natural selection eg- natural disaster, predators, diseases, etc.
  - Increasing misuse of antibiotics increases selection pressure exerted on bacteria to evolve resistance to them. (If no external disturbing factor, no selective pressure, so no need to evolve resistance)
  - Areas with widespread use of antibiotics (farms, hospitals), increases spread of resistance between bacteria.
  - Resistance may first appear in non-pathogenic bacterium (soil), then to pathogenic.
- **Multiple resistance**: multiple resistant genes in plasmid
  - **Eg**- methicillin-resistant Staphylococcus aureus (MRSA) was controlled by vancomycin.
  - Another bacteria common in hospitals, Enterococcus faecalis developed resistance to vancomycin and passed its resistance to MRSA.
- **Reducing bacterial resistance:**
  - Using antibiotics only when appropriate and necessary; not prescribing them for viral infections
  - Making sure that patients complete their course of medication
  - Medicines should only be given if prescribed
  - narrow spectrum drugs should be used rather than wide spectrum drugs
  - Reduce the use of antibiotics in drugs in agriculture
  - Use of many antibiotics to destroy the pathogen to make sure it doesn't mutate

11. IMMUNITY

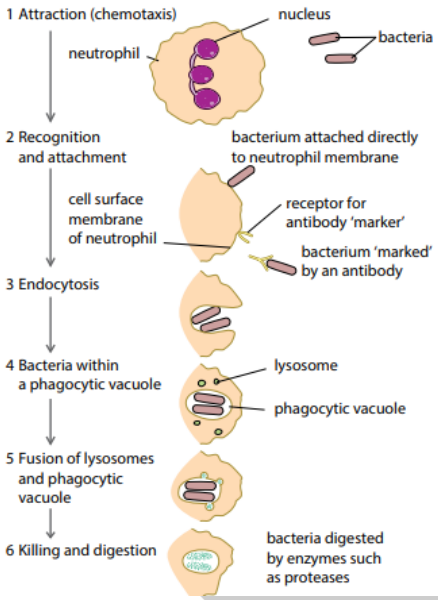
11.1 The Immune System

- **Immune response:** the body's immune system responding to non-self antigens by lymphocytes and phagocytes. It involves the production of antibodies and the killing of cells that have become infected by pathogens.
- **Phagocytes:** produced in and stored by the bone marrow throughout life before being distributed around the body by blood. They remove dead cells as well as invasive microorganisms.
  - **Neutrophils:** make up 60% of WBC. They circulate the blood and leave through capillary walls to enter tissues during an infection.

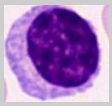


    - They are short lived and often die after ingesting and destroying bacteria, forming pus.
  - **Macrophages**: mature form of monocytes that have left the blood and settle in organs.

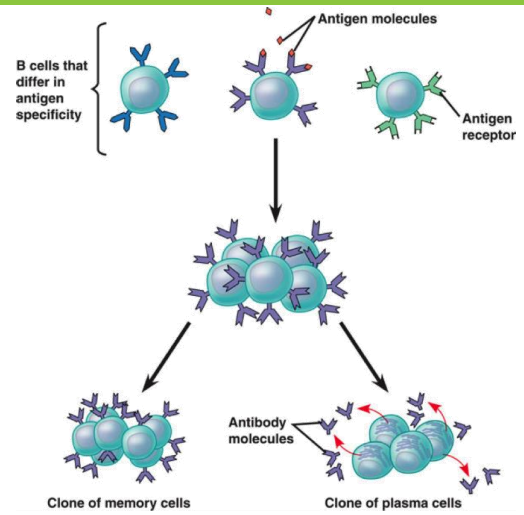
    - Are long lived and larger than neutrophils.
    - Found in lungs, liver, spleen, kidney & lymph nodes where they engulf foreign particles and microorganism.
    - Also known as antigen presenting cells (APCs) as they ingest antigens and display them on their surface, allowing T-lymphocytes to bind to the antigen and stimulate immune response.
- **Phagosytosis:** during an attack by pathogens, cells produce chemicals called histamin which attract neutrophils to site of infection (chemotaxis). **Then:**



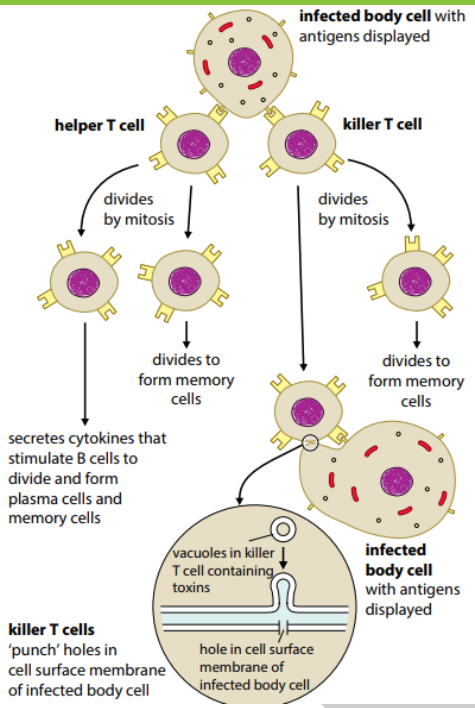
- **Lymphocytes:** WBC produced before birth in the bone marrow. They are smaller than phagocytes and have a nucleus that fills most of the cell.



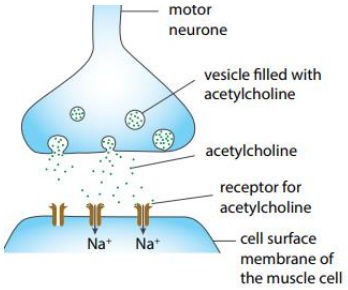
  - **B-lymphocytes:** produced and developed in the bone marrow, concentrating in lymph nodes and the spleen.
    - When mature, each B cell produces one type of antibody molecule.
    - Part of the antibody molecules form a glycoprotein receptor that combines specifically with one type of antigen.
    - Once combined, the B cell will undergo mitosis repeatedly to form clone cells.
    - As only the B cells with antibodies complementary to antigens divide like this, it is known as clonal selection followed by clonal expansion.
    - Some differentiate into short lived plasma cells (release antibodies into blood/lymph/linings of lungs and gut) and others become long term memory cells (have glycoprotein receptor on cell membrane)



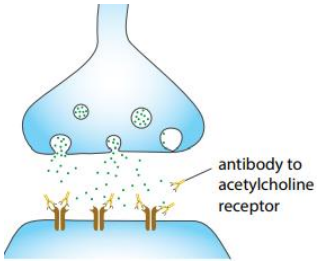
    - **Plasma cell:** there is an extensive network of RER in the cytoplasm for production of antibody molecules, which plasma cells secrete into blood or lymph by exocytosis. The mitochondria provide ATP for protein synthesis and the movement of secretory vesicles.
  - **T-lymphocytes:** these cells are produced at the bone marrow but collect in the thymus till maturity. Mature T cells have receptors that are complementary to antigens of pathogens. T cells only respond when they encounter this antigen on the cell surface membrane of a host cell such as a macrophage (APC). A particular T cell with complementary receptor will bind to antigen found on the surface of APC. Clonal selection and expansion also take place, and **differentiate into the following:**
    - **T helper cells:** secrete hormones called cytokines which stimulate B and T killer cells to divide, and macrophages to carry out phagocytosis more vigorously.
    - **T killer cells/ cytotoxic T cells:** destroy the cell to which they are bound. They search the body for cells that have become invaded by pathogens and are displaying the pathogen's antigen on their plasma membranes. When T-killer cells recognise the antigens, they attach themselves to the surface of infected cells and secrete toxic substances that kill the cells and pathogens within them.



- **The number of WBCs increase at time of infection:**
  - Neutrophils during bacterial infection and whenever tissues become inflamed and die.
  - Lymphocytes in the blood increases in viral infections and in TB.
  - Most of the lymphocytes that circulate in the blood are T cells. HIV invades helper T cells and causes their destruction, so blood tests for people who are HIV+ record the numbers of specific T cells.
- **Leukemias**: cancers of <u>immature</u> WBC, disrupting normal levels of RBC or platelets, causing anaemia and risk of excessive bleeding. Mature WBC decrease so that people become more susceptible to infections; they are said to be immunosuppressed.
  - **Myeloid leukaemias:** cancer of stem cells that give rise to neutrophils, RBC, platelet and monocytes.
  - **Lymphoblastic leukaemias**: the cancerous cells are those that give rise to lymphocytes.
  - **Acute leukaemias**: develop very quickly, have severe effects and need to be treated immediately after diagnosis.
  - **Chronic leukaemias**: develops over many years, changes in blood cell counts are monitored over time so that treatment is given.
- **Memory cells:** form the basis for immunological memory lasting many years, often a lifetime and are involved in long term immunity.
  - **Primary response:** there are very few B cells specific to the antigen thus production of antibodies is low.
  - **Secondary response:** there are many more antibodies produced as many memory cells divide quickly and differentiate into plasma cells.
- **Autoimune disease:** caused by the immune system producing antibodies against self antigens as it fails to distinguish between self and non self antigens.
  - **Myasthenia gravis (MG):** autoimmune disease that targets the neuromuscular junctions between motor neurones and skeletal muscle cells.
    - **Normally:** nerve endings of motor neurone release acetylcholine (ACh), a neurotransmitter, from synaptic vesicles into synapse between neuron and muscle (neuromuscular junction) by exocytosis.
    - ACh binds with receptor protein on plasma membrane of muscle fibres.
    - This interaction stimulates protein channels to open, allowing Na ions to move through the muscle, resulting in muscle contraction.



    - **In MG:** helper T cells that are specific for these cell surface receptors for ACh stimulate a clone of B cells to differentiate into plasma cells and secrete antibodies that bind to the receptor, blocking the transmission of impulses from motor neurones. Hence, muscle cells do not receive any stimulation, causing muscle weakness.

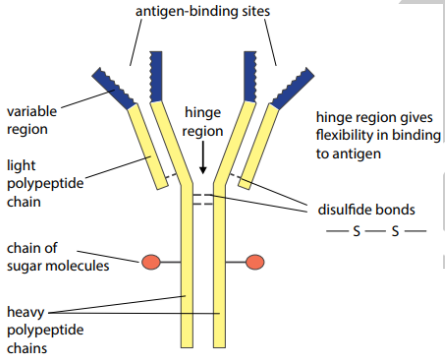


  - **Treatment for MG:**
    - Drug that inhibits acetylcholinerase, increasing the concentration of ACh in synapses so its action in stimulating muscle fibres to contract lasts for longer.
    - Surgical removal of the thymus gland as it is the site of maturation of the helper T cells that stimulate B cells to produce antibodies to the ACh receptors.

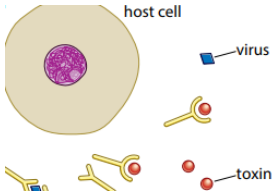
- **No cure because:**
  - Defective B cells are continuously produced
  - They continue to release antibodies against receptors
  - Even if all the B plasma cells are used up, memory cells of these defective B cells are still present

11.2 Antibodies & Vaccination

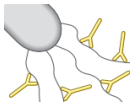
- **Antibodies:** globular glycoproteins with quaternary structure, forming plasma proteins called immunoglobulins.
  - 4 polypeptide chains, 2 heavy chains and 2 light chains which are held together by disulphide bridges and form a Y-shaped structure.
  - The lower part of the 'Y' is called the constant region as it has the same amino acid sequence in all antibodies. This region binds to receptors on phagocytes/macrophages/neutrophils and gives class of antibody (igM, igG, igA, igE).
  - The upper part of the 'Y' is called the variable region of the molecule and has a different amino acid sequence in different antibodies.
  - Antibodies have 2 identical binding sites formed by both light and heavy chains. The sequence of amino acids in this region make the specific 3-D shape which binds to just one type of antigen. R group interactions with the antigen gives it the specific shape.



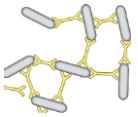
  - **Antibodies protect the body from pathogens in various ways such as:**
    - Combine with viruses and bacterial toxins preventing them entering or damaging cells.



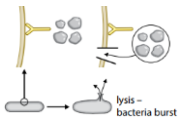
    - Antibodies that combine with toxins and neutralize them (antitoxins).
    - Attach to the flagellum of the bacterium making them less active and easier for phagocytes to engulf.



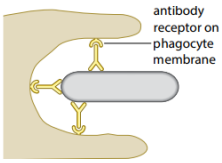
    - Agglutination (clumping together) of bacteria reducing the chances of spread throughout the body.



    - Punch holes in the cell wall of bacteria, causing them to burst when they absorb water by osmosis.



    - Antibodies coat bacteria, making it easier for phagocytes to ingest them; phagocytes have receptor proteins for the heavy polypeptide chains of antibodies.



- **Monoclonal antibodies**: highly specific and identical antibodies made by identical B cell clones.
  - **Monoclonal antibody formation:**
    - A mouse is injected with relevant antigen, stimulating immune response.
    - Plasma cells specific to antigen are extracted from the spleen and fused with cancerous cells forming hybridoma cells.
    - Hybridoma cells that produce the required antibody are cloned.
  - **Diagnosis with monoclonal antibodies:**
    - Radioactive chemicals are attached to each antibody that binds to fibrin. Radioactivity emitted by these antibodies can be detected by gamma rays camera, thus finding the position of a clot.
    - The same method can be used to locate cancer cells and identify the exact strain of a virus or bacterium during an infection.
  - **Treatment with monoclonal antibodies**
    - Mabs from rats into humans trigger an immune response as they are non-self. This is overcome by altering genes that code for polypeptide chains of antibodies into human sequences and the type/position of sugar groups into human antibodies.
    - Used in cancer therapy by marking cancerous cells for their destruction or binding to protein produced by T cells that reduces immune response.
    - Controls over/inappropriate production of B cells, preventing leukaemia and autoimmune diseases.

- **Active immunity:** long term immunity gained when an antigen enters the body, (initially, primary) immune response occurs, antibodies are produced by plasma cells and memory cells are produced.
  - **Natural active immunity:** obtained as a result of an infection where the body has manufactured its own antibodies.
  - **Artficial active immunity:** achieved by injecting small amounts of antigens or attenuated (harmless) pathogen such as vaccines. This stimulates the production of antibodies against the antigen.
- **Passive immunity:** immediate but temporary immunity gained without an immune response; antibodies/antitoxins are injected (artificial) or pass from mother to child across the placenta or in breast milk (natural). No antigen is encountered thus no memory cells are produced.
- **Vaccination:** an antigenic material, which could be a live, dead or attenuated micro-organism, or perhaps a harmless form of a toxic (toxoid) or simply surface antigens. This allows our immune system to produce the requisite B and T cells without actually suffering the disease, mimicking natural immunity.
  - Less effective vaccines do not mimic an infection as they are dead bacteria or viruses that do not replicate inside the body. They need booster injections to stimulate secondary responses that give enhanced protection.
- **Poor response due to:**
  - Defective immune system, so doesn't produce necessary B and T cell clones.
  - Suffer from malnutrition and don't have enough protein to make antibodies.
- **Live virus and herd immunity:** people may also be injected with a live virus and could potentially pass it out in their faeces during the primary response,evolve by mutation in environment, infecting others. This is why we vaccinate everyone at the same time, known as herd immunity. Herd immunity interrupts transmission in a population, so that those who are susceptible never encounter the infectious agents concerned.
- **Antigenic variation:** viruses are constantly mutating and changing - the reason we cannot create a vaccine against the common cold or influenza is because it mutates very frequently and the vaccine will not be effective eg in AIDS/HIV. These mutations are known as antigenic drift (minor changes in antigen structure still recognised by memory cells) or shift (major changes not recognised). Plasmodium parasites are eukaroytic in nature and have far more genes and thus antigens on their cell surfaces.
- **Antigenic concealment:** pathogens that evade attack by the immune system by living inside host cells, proteins and are beyond the reach of the antibodies or don't give enough time for antibodies to react before concealment.
- **Small pox eradicated because:**
  - Variola virus did not mutate and change its surface antigen so same vaccine could be used everywhere, being cheap to produce.
  - The vaccine was made from a harmless strain of a similar virus (vaccinia) and was effective because it was a 'live' vaccine
  - Infected people were easy to identify.
  - The vaccine was easy to administer
  - The smallpox virus did not linger in the body after an infection
  - The virus did not infect animals, which made it easier to break the transmission cycle.
- **Why measles is not eradicated:**
  - Poor response to the vaccine shown by some children who need several boosters to develop full immunity.
  - It can be difficult to give boosters, follow up cases of measles and trace contacts in large cities.
  - Migrants and refugees can form reservoirs of infection, experiencing epidemics within their communities and spreading the disease to surrounding populations.

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