TOPIC 2: GENES AND HEALTH

For the Edexcel Biology A Level (SNAB)

TOPICS COVERED

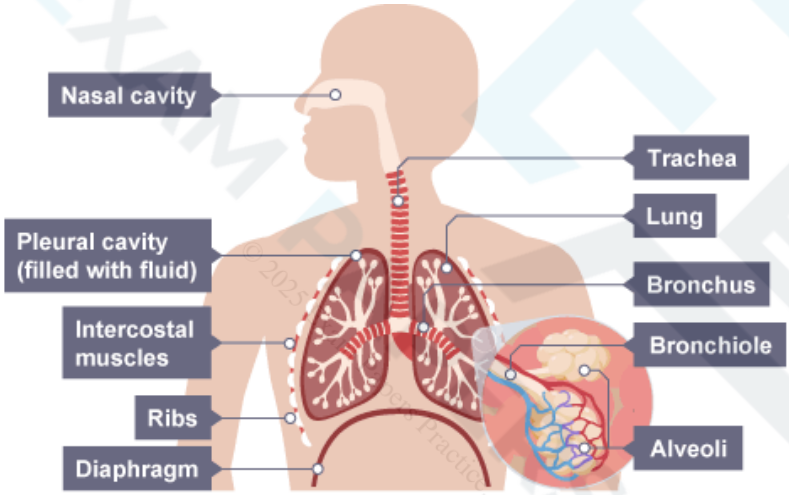
- The Respiratory System
- Gas Exchange and Fick's Law
- The Need for a Circulatory System (SA:V)
- Protein Structure
- Cell Membrane Structure
- Symptoms of Cystic Fibrosis
- Enzymes
- DNA and its Replication
- Protein Synthesis
- Genetics: Mutation and Inheritance
- Genetic Testing
- Treating CF

Respiration

Key Terminology and Equations

Term	Definition
Cystic Fibrosis	A genetic disorder that affects mostly the lungs, but also the pancreas, liver, kidneys, and intestine. The disease causes the production of viscous mucus, which contains low amounts of water, increasing the risk of lung infection
Mucus	Aqueous secretion produced by goblet cells
Ciliated Epithelial Cells	Cells lining the trachea, bronchi and bronchioles which have cilia (hair-like structures) which beat and move substances along the lining, removing debris and pathogens
Squamous Epithelial Cells	Layers of cells sit on a basement membrane, made of protein fibres in a matrix. The thin, flat squamous cells fit together to line systems
Pathogen	A bacterium, virus or fungus which can cause disease
Diffusion	The random, passive movement of particles down a concentration gradient due to the kinetic energy they possess; sometimes referred to as **passive transport**

The Structure of the Respiratory System



To the left is a diagram of the respiratory system. Air is drawn into the lungs through the trachea due to low pressure created by the movement of the ribs and diaphragm. The trachea divides into the bronchi which carry air through narrow tubes called bronchioles to alveoli, tiny air sacs, which are the site of gas exchange.

Mucus is always found in the system linings to remove debris, working with the cilia of the epithelial cells

- However, people with CF have mucus which is drier and stickier which the cilia find difficult to move
- Efficient gas exchange is proportional to the surface area of the lungs. Sticky mucus will block the bronchioles, preventing air reaching alveoli further in the lungs, reducing efficiency of gas exchange
- Eventually, the lungs will lose elasticity, which further reduces surface are and the ability to exchange surfaces across the membranes of alveoli. This can lead people with CF to be short of breath and find exercise very difficult
- CF also increases the chance of lung infection, as the mucus which should normally be coughed out or swallowed, sticks in cilia on the lining of the respiratory system. Mucus builds up and there are low levels of O_2, where trapped pathogens can thrive
- White blood cells fight infections within the mucus but when they die, they break down, releasing DNA which makes mucus stickier. Repeated infection weakens the immune system, causing damage to the gas exchange system

Gas Exchange

Gas exchange is needed for life. Oxygen needs to be absorbed by all body cells for respiration. This process also produces waste products CO_2 and H_2O. If these were not removed, they would react to form carbonic acid, which would destroy cells by lowering the pH

Fick's Law of Diffusion

$$Rate\ of\ Diffusion \propto \frac{Concentration\ Gradient \times Surface\ Area}{Thickness\ of\ Gas\ Exchange\ Surface}$$

- The factors which affect the rate of diffusion all influence the adaptions of the respiratory system
- The alveoli contain many alveoli, increasing the area of exchange. These sacks of air are convex in shape, increasing the surface area to volume ratio. The surface area of contact is increased by the extensive network of capillary vessels
- The concentration gradient is high with fresh air constantly supplied, and with blood being constantly pumped around the alveoli, maintaining this difference
- The thin walls of the alveoli and capillaries reduce the diffusion distance

Surface Area to Volume Ratios

All organisms need exchange surfaces for reasons highlighted previously. In unicellular organisms, the whole cell membrane is the exchange surface. The concentration gradient is maintained by constantly using and producing substances. The surface area is sufficient to account for its volume. However, larger organisms need more exchange to meet greater needs; due to the lower surface area to volume ratio, the exchange would not be efficient enough to only use the external surface. This is the reason for the circulatory and respiratory systems for exchange

Protein Structure, Membranes and Transport

In people with CF, the mucus layer is sticky because of low water content, which is due to abnormal water and salt transport across membranes due to faulty channel proteins.

Key Terminology and Equations

Term	Definition
Primary Structure	The sequence of amino acids in polypeptide chains of protein
Secondary Protein Structure	Interactions between amino acids in chains cause the chains to twist into either α-helices or β-pleated sheets
Tertiary Protein Structure	The final three-dimensional shape of a protein chain, with chemical bonds and hydrophobic interactions maintaining this structure
Quaternary Protein Structure	Association of more than one polypeptide chain, sometimes with the addition of conjugates
Conjugate	The addition of another chemical group associated with a polypeptide chain
Hydrophobic	R Group which is water-repelling; synonymous with **non-polar**
Hydrophilic	R Group which is water-attracting; synonymous with **polar**
Fibrous Proteins	Consist of parallel polypeptide chains held together by cross-links, forming long, rope like fibres with high tensile strength which are usually insoluble
Globular Proteins	Spherical shape caused by highly folded polypeptide chain with a tertiary structure, with hydrophilic groups on the inside
Phospholipid	Type of lipid made from two fatty acid chain tails attached to a phosphate (PO_4^{3-}) group head. The phosphate head is polar while the tails are non-polar
Bilayer	Where hydrophobic fatty acid tails move to the middle and exclude water whilst the polar phosphate heads face the extra- and intra-cellar spaces
Glycoproteins	Intrinsic protein molecules with polysaccharides attached, acting as channels, transporters, receptors and enzymes
Glycolipids	Lipid molecules with polysaccharides attached, important in cell-to-cell recognition.
Facilitated Diffusion	Passive net movement of ionic or large molecules down the concentration gradient, through the use of channel proteins or carrier proteins. This is much faster than diffusion through the phospholipid bilayer
Channel Proteins	Proteins containing water-filled pores, allowing certain ions and molecules in depending on its shape. Some channels can be open or closed based on a signal, such as a hormone, or a change in voltage across a membrane; these are called gated channels
Carrier Proteins	Ion or molecule binds onto specific site. The protein changes shape, allowing the molecule to cross the membrane. Movement can be in either direction
ATP	Energy transfer molecule
Vesicle	Small, membrane-bound sac containing a substance such as a hormone

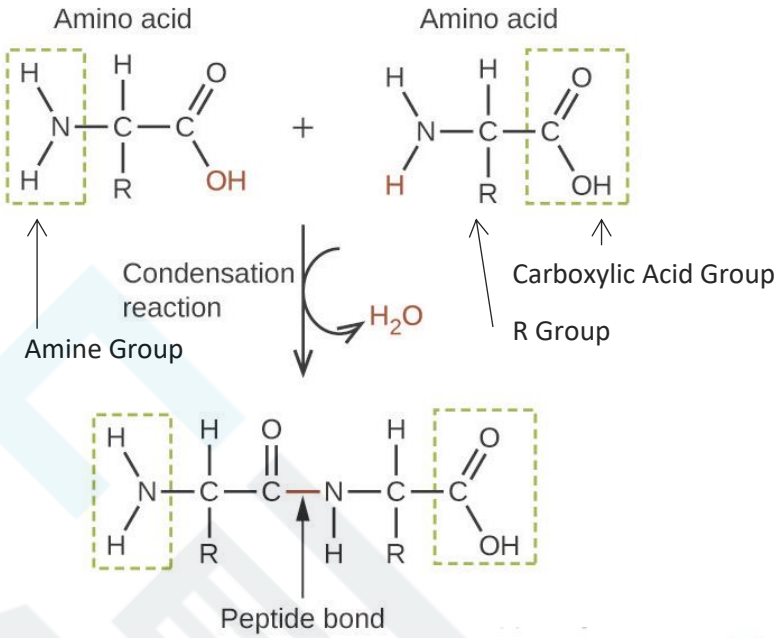
Exocytosis	The release of substances, usually proteins or polysaccharides, from a cell, as vesicles fuse with the cell membrane
Endocytosis	Substances are taken into a cell by the creation of a vesicle. Part of the cell membrane engulfs the substance; in some cases, the substance attaches to a receptor in the membrane
Zwitterion	A molecule or ion having separate positively and negatively charged groups.

Protein Structure

All amino acids contain an amine group, $-NH_2$, a carboxylic acid group, -COOH, and a hydrogen, -H, attached to a central carbon atom. Each amino acid has a varying R or residual group.

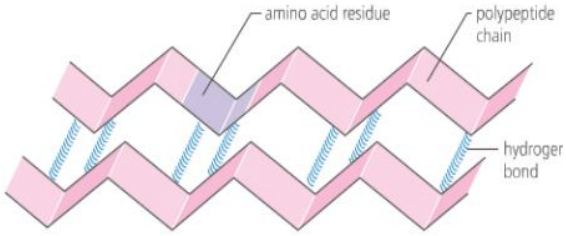
Two amino acids join in a condensation reaction to form a dipeptide, with a peptide bond.

Dipeptides can be hydrolysed through the addition of water, under enzymatic conditions, meaning amino acids are soluble. The hydrogen nucleus of the carboxylic acid group will move to the amine group to leave this side with a positive charge, whilst the carboxylic acid side will have a negative charge. A molecule with opposite charges on either side is called a zwitterion.

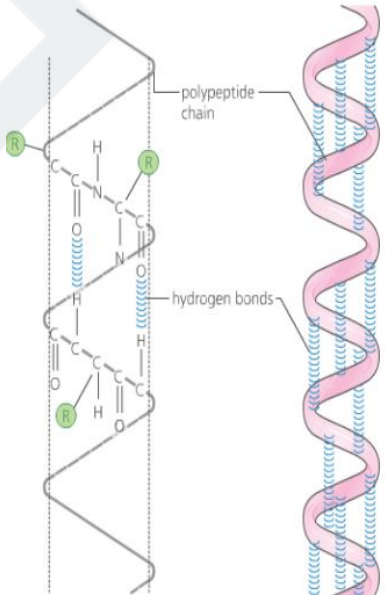


This condensation process can repeat to form polypeptide chains. The sequence of amino acids in a polypeptide chain is known as the **primary sequence of a protein**.

Interactions between the residual groups cause the chain to twist and fold into its secondary structure, either an α-helix or β-pleated sheet.



- In an α-helix, hydrogen bonds form between the C=O of the carboxylic acid group and the -NH of the amine group, stabilising this shape.
- In β-pleated sheets, several chains may link together, with hydrogen bonds holding the parallel chains in this arrangement



In the tertiary structure, the protein chain folds to produce a precise 3D shape. The bonds detailed below maintain this structure.

A protein may be compromised of multiple polypeptide chains held together in a structure which is quaternary, sometimes with conjugates e.g. globular transport protein myoglobin contains an iron within the haem group

Bond/Force	Description	Forms between	Relative Strength	Broken
Hydrogen	Hydrogen atom shared by two atoms	α helices, β-pleated sheets	Weak	Heat, Activity
Ionic	Electrostatic forces of attraction between oppositely charged ions	Polar R-groups	Strong	Changing pH, Heat
Disulfide Bridge	Covalent bond between two thiol groups	R groups containing -SH groups	Strong	Treat with βME

Hydrophobic Interaction	Hydrophobic R groups move to the inside of a protein to exclude water	Non-polar R Groups	Weak	pH, Heat
Van der Waal	Intermolecular forces of attraction	When two or more atoms are very close	Weak	Heat

Proteins can be globular or fibrous. The differences in structure and function are detailed below

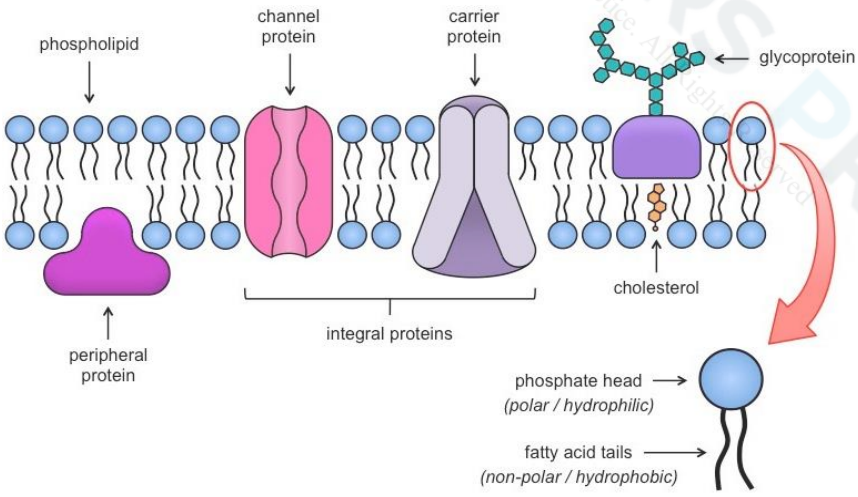
	Globular	Fibrous
Description	Spherical shape usually caused by tightly folded polypeptide chain	Long, rope like fibres with high tensile strength. Formed from parallel polypeptide chains held by cross links
Structure	Tertiary or Quaternary	Secondary, rarely Tertiary
Solubility	Soluble as folding encloses hydrophobic groups on the inside	Insoluble as hydrophobic groups are on the outside
Examples	• Enzymes e.g. Lipase, DNA Polymerase • Transport Proteins e.g. Myoglobin • Hormones e.g. Insulin, Glucagon	• Collagen – main component of connective tissue (ligaments, tendons) • Keratin – used in hair, nails, claws

Cell Membrane Structure

Fluid Membranes cover the surface of every cell, and surround most organelles within cells. Their functions include keeping components within cells, allowing transport of substances in and out of cells, isolating organelles from the cytoplasm, and allowing a cell to move and change shape.

Membranes are composed of phospholipids, a lipid made from two hydrophobic fatty acid chain tails attached to a hydrophilic phosphate group head. The hydrophobic tails form a bilayer in membranes which develop into a liposome. This way the hydrophobic components avoid contact with the aqueous cytoplasm and the extra-cellular space.

This model of a bilayer comes from much evidence. The idea of a bilayer was proposed when an investigation into red blood cells found that the area of the red blood cell membrane was half the area of lipid in the membrane. This was supported by two distinct layers in electron micrographs. Freeze-fracture studies provided evidence for integral proteins and peripheral proteins, as many proteins could only be removed by drastic action, which countered ideas of equal protein layers.



The bilayer contains two type of lipid: unsaturated, containing only C-H bonds, and saturated, containing a C=C bond. The C=C bonds introduce kinks into tails, preventing phospholipids from packing closely together. The higher the concentration of saturated tails, the less fluid the membrane is.

Cholesterol reduces fluidity further, preventing movement by packing into gaps created by these kinks

At high temperatures, lipids have more kinetic energy and are packed more loosely, increasing fluidity

Substances can pass through cell membranes through many transport processes. Substances such as CO_2, H_2O and O_2 are small enough to pass across the plasma membrane freely, as can lipid-soluble steroids. However, the membrane is impervious to large molecules, such as amino acids and glucose, or ionically charged molecules, such as Na^+ and K^+. Below is a summary of the different transport types

Diffusion	Passive net movement of molecules down the concentration gradient
	Lipid-soluble or small molecules
	Through the phospholipid bilayer
	CO_2 and O_2
Facilitated Diffusion	Passive net movement of molecules down the concentration gradient. This is much faster than diffusion through the phospholipid bilayer
	Hydrophilic molecules or Ions

	Either by drifting through the water-filled pores of integral channel proteins, which allow certain ions and molecules in depending on its shape. Some channels can be open or closed based on a signal, such as a hormone, or a change in voltage across a membrane; these are called gated channels. This can also occur via carrier proteins which change shape after a molecule has binded to it to allow transport passively
	e.g. Glucose, Urea, Vitamins
Osmosis	Net passive movement of water molecules from a solution with low to high concentration of a solute through a partially permeable membrane
	Through the phospholipid bilayer
	H_2O
Active Transport	Movement of molecules against the concentration gradient
	Carrier protein uses ATP to change shape, causing a substance to be released on the membrane's other side
	e.g. Na^+, Amino Acids
Exocytosis	The release of substances, usually proteins or polysaccharides, from a cell, as vesicles, small membrane-bound sacs, fuse with the cell membrane
	e.g. Proteins, Polysaccharides, Hormones
Endocytosis	Substances are taken into a cell by the creation of a vesicle. Part of the cell membrane engulfs the substance to be transported; in some cases, the substance attaches to a receptor in the membrane and is then absorbed by endocytosis
	e.g. Cholesterol, Action of White Blood Cells (Macrophages)

Symptoms of Cystic Fibrosis

In healthy people, the amount of water in mucus is regulated to maintain constant viscosity, so that it is runny enough to be moved by cilia but thick enough to only line the airways. The regulation of water content is achieved by the transport of sodium and chloride ions across the epithelial cells.

Excess water	Too little water	With CF
• If the mucus layer contains too much water, the epithelial cells detect this • Carrier proteins in basal membrane actively pump Na^+ ions from cells into tissue fluid, creating a concentration gradient across the apical membrane • Na^+ ions diffuse down the concentration gradient through channel proteins in apical membrane • Raised Na^+ concentration creates an electrical gradient, causing Cl^- ions to diffuse out of the mucus into the tissue fluid through gaps between epithelial cells • Water is drawn out of the cells by osmosis due to high salt concentration in tissue fluid • Water is drawn out of mucus by osmosis	• Cl^- ions pumped into the cell across the basal membrane • Cl^- diffuses through the open CFTR protein channels in apical membrane • Na^+ diffuses down the electrical gradient into the mucus between epithelial cells • High salt concentration in the mucus draws water out of the cell by osmosis • Water is drawn into the cell by osmosis	• CFTR protein is absent or non-functional • When there is too little water in the mucus, Cl^- cannot leave the cell across the apical membrane • Na^+ channel is permanently open and Cl^- is constantly drawn out of the mucus int the tissue fluid • Water is also drawn out of the mucus • The mucus is therefore more viscous, making it ineffective and cannot be moved by cilia • This mucus frequently becomes infected

- Most breakdown and absorption of food occurs at the small intestine. Glands secrete enzymes into the gut, where they break down food molecules. Exocrine glands outside the gut produce enzymes such as at the salivary glands, the liver and the pancreas. Pancreatic cells produce enzymes involved in the breakdown of proteins, carbohydrates and lipids. These enzymes are delivered to the gut in a fluid through the pancreatic duct.
- In a person with CF, the pancreatic duct is blocked by sticky mucus, impairing the release of digestive enzymes; the lower concentration reduces the rate of digestion and not all food is

digested, meaning nutrients cannot be absorbed. This food is lost through excretion. This is called malabsorption syndrome

- CF sufferers may therefore have issues maintaining body mass, and they also have high blood metabolic rates. As a result, people with CF need to take 120-140% of the recommended daily energy intake and supplements containing digestive enzymes
- When the pancreatic enzymes become trapped behind the mucus, they damage the pancreas itself, forming cysts of hard, damaged or fibrosed tissue within the pancreas. If the cells in the pancreas responsible for insulin are damaged, a form of diabetes can result
- Females have a reduced chance of being pregnant with CF as a mucus plug develops in the cervix
- Males with CF lack the vas deferens (sperm duct) on both sides, meaning sperm cannot leave the testes. Where the sperm duct is present, it can be partially blocked by a thick sticky mucus layer, meaning fewer sperm are present in each ejaculate
- In CF sufferers, mucus is viscous, too thick for cilia to clear. It progressively blocks bronchioles and becomes a breeding ground for bacteria, causing a sever cough, wheezing, blocked sinuses and difficult breathing
- In babies, CF sufferers will secrete high amounts of very salty sweat, which may cause salt deposits. They may also get intestinal blockage due to intestinal contents being too thick to expel. Children exhibit stunted growth, have delayed puberty and find exercise difficult

Enzymes are biological catalysts which increase rate of reaction by offering an alternative pathway with a lower activation energy, meaning a higher proportion of substrate collisions will have sufficient energy to cause a reaction. This reaction takes place on the active site, a depression on the surface of the enzyme molecule. Substrate molecules form temporary bonds with amino acids of the active site to form an enzyme-substrate complex. Intracellular enzymes catalyse reactions inside cells. Extracellular enzymes are produced by cells and catalyse reactions outside of cells.

The rate of an enzymatically controlled reaction can be varied by changing the temperature, pH and enzyme or substrate concentrations. Rate is calculated as a change of dependent variable over time.

- As temperature increases there is a higher rate of reaction as the substrate and enzyme require more frequently to form an enzyme-substrate complex. However, as temperature increases beyond the optimum temperature, the temperature at which the enzyme works best, the active site starts to change shape and the enzyme of denatured
- If pH is too high or low, the bonds holding the enzyme together start to break down, making it denatured. Optimum pH depends on the location of the enzyme
- At low substrate concentration, only a few substrate molecules collide with an enzyme, leaving many empty active sites. At higher concentrations, rate is increased as more active sites are filled and more reactions are catalysed. As concentration increases further, some substrate molecules have to wait for an active site to become free, so rate starts to level off
- As enzyme concentration increases, there is a higher frequency of successful collisions with substrates, increasing rate of reaction proportionally

The Lock and Key Model says that a single substrate exactly fits the active site of a particular enzyme and will only be catalysed by this specific enzyme due to the complementary shape. However, the induced fit theory states that the active site is flexible; when the substrate enters, the molecule changes shape slightly. Only a specific substrate will induce a shape change.

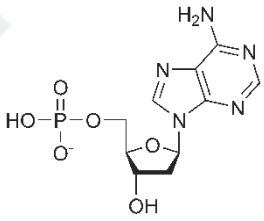
DNA, Genetics and Inheritance

Key Terminology

Term	Definition
DNA	Deoxyribonucleic Acid
Gene	Sequence of bases which codes for the primary sequence of a protein
Genome	All the genes in an individual are known as the genome. A genome includes coding regions and non-coding regions
Exons	DNA sequences coding for amino acids

Introns	DNA sequences which do not code for amino acids
Purine Bases	Adenine and Guanine, with two carbon rings and N atoms
Pyrimidine Bases	Thymine and Cytosine, with one carbon ring and N atoms
5' and 3'	Five prime and three prime, indicating the carbon numbers in the DNA's sugar backbone, giving DNA asymmetry and therefore direction to be read by enzymes
Anti-Parallel	Equidistant but moving in opposite directions
Denaturation	At extreme temperatures, the two DNA strands are pulled apart as the weak hydrogen bonds between complementary bases are overcome
Non-Overlapping	Each base is only ever part of one codon
Degenerate	The genetic code is degenerate as a single amino acid may be coded for using multiple codons
Triplet	Information carried by nucleic acid is carried by sequences of three adjacent bases
Promoter Region	Base sequences that occur upstream of a gene's coding sequence
DNA Polymerase	An enzyme with a number of active sites. It has a helicase function, allowing it to break the hydrogen bonds holding nitrogenous bases together. It can catalyse the formation of phosphodiester bonds between RNA mononucleotides, forming polynucleotides, and can encourage re-formation of DNA double helix
Ribosome	Small organelles in the cytoplasm associated with the rough endoplasmic reticulum. 70S size in prokaryotes, 80S size in eukaryotes. A ribosome has two sub-units composed of ribosomal RNA and protein. Their function is to attach to mRNA and hold two codons in place while tRNA molecules bring amino acids together to synthesise a polypeptide. Ribosomes have catalytic function to catalyse peptide bond formation between amino acids
Semi-Conservative	Half of the strands in each DNA molecule are from the original double helix
Mutation	Change in the genetic material in a cell

DNA and RNA carry genetic code. Nucleotides are their subunits, each containing an organic base, a 5-carbon pentose sugar and a phosphate group. In DNA the sugar is deoxyribose and in RNA it is a ribose sugar. In DNA, there are four bases which are all nitrogenous. Of these, adenine and guanine are purines and cytosine and thymine are pyrimidines. In RNA, uracil replaces thymine. Phosphodiester bonds hold the sugars and phosphate groups of nucleotides together.



Bases exist in complementary base pairs. A and T [two hydrogen bonds] and C and G [three hydrogen bonds] are the two pairings which exist, and are held together by weak hydrogen bonds. This pairing rule exists because the distance between the two DNA strands does not vary and accommodates a purine-pyrimidine pair.

The two polynucleotide chains run anti-parallel to each other, equidistant but moving in opposite directions, hence the double helix shape. Weak hydrogen bonds between bases hold the strands together.

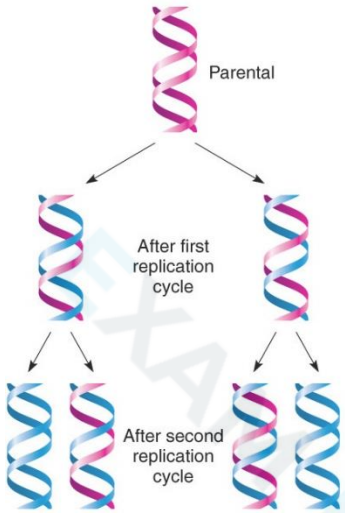
The genetic code is described as non-overlapping, degenerate and triplet. It is used to form protein by the process known as protein synthesis

Protein Synthesis

1. In the nucleus, RNA polymerase binds to promoter regions of DNA. Binding to DNA is controlled by transcription factors and repressors.
2. The enzyme uses its helicase function to unwind the DNA double helix by breaking the hydrogen bonds between bases, exposing bases on the antisense strand
3. Free RNA mononucleotides in the nucleus move above complementary bases on the antisense strand. The RNA polymerase joins the RNA mononucleotides by forming phosphodiester bonds to form the polynucleotide RNA – this means that the gene has been transcribed
4. Once the enzyme reaches the terminating region, it leaves the chromosome and cause it to rewind
5. The mRNA strand formed leaves the nucleus through a nuclear pore, entering the cytoplasm

6. Translation takes place on the ribosome. Ribosomes attach to mRNA, and the small sub-unit clamps the ribosome in place, while a large sub-unit facilitates the binding of tRNA molecules.
7. Unique tRNA molecules carry a variety of bases on the bottom to form the anticodon, which determines the amino acid carried by the tRNA
8. A tRNA molecule with an anticodon complementary to a codon moves into place. The first codon is always AUG, which cods for Met
9. Amino acids are joined to the elongating chain by peptide bonds, created by the catalytic properties of the ribosomes. The chain elongates until the ribosome reaches the stop codon

DNA Replication



- DNA copies itself before cell division by semi-conservative replication; half of the strands in each DNA molecule are from the original double helix
- The enzyme DNA polymerase breaks the hydrogen bonds between bases on the two DNA strands, making the helix unwind to form two single strands
- Each original strand acts as a template for a new DNA double helix. Free nucleotides are attracted to their complementary exposed bases on each original template strand
- Condensation reactions join the nucleotides of the new strands together, forming phosphodiester bonds – this is catalysed by the DNA polymerase. Hydrogen bonds form between the bases on the original and new strands

There were three models for DNA replication – semi-conservative, as detailed above; conservative, where one DNA molecule has two original parent DNA strands, and the other has two new strands; dispersive, where all DNA strands are made up of a mix of original parent DNA and new nucleotides.

Meselson and Stahl used heavy and light strands of DNA by using DNA from bacteria grown in a culture containing only a heave nitrogen isotope, ^{15}N, creating a heavy DNA band when centrifuged. Bacteria and therefore DNA was allowed to replicate in a culture containing only ^{14}N. After the first replication, a hybrid medium band was seen, discounting the conservative model as no pure heavy or light DNA strands were seen. After a second replication, another medium band and a pure light band was seen. This supports the semi-conservative model – the dispersive model would have seen a hybrid between medium and light bands as the original heavy DNA was randomly dispersed with light DNA in a 3:1 ratio

Mutation

Mutation is the change in the genetic material in a cell. Some mutations are concerned with very small changes to an organism's DNA, known as gene mutations. Mutations happen by chance, but certain environmental factors can increase rate of mutation. Mutation is slightly more likely to happen during DNA replication, despite the presence of DNA repair genes and fidelity checking by DNA polymerase. Mutation has led to all genetic variation, and is the basis of variation. All life started by chance with a random mistake.

Type of Mutation	Description	Example from AGT CCC AAA CCA
Insertion	Adding an extra base	AGT **ACC CAA ACC A**
Duplication	Doubling a base during replication	AGT CCC CAA **AAC C**
Substitution	Swapping one base for another	AGT CCC **TAA** CCA
Inversion	Swapping of two bases in a sequence	AGT **CCA CAA** CCA
Deletion	Removal of a base	**ATC CCA AAC CA**

From the above table, it can be seen that different mutations have more serious effects on final protein structure. Deletion, insertion or duplication can cause a frame shift, affecting every codon past the

additional/missing base, leading to a vastly different primary structure and therefore different folding. This will also affect the position of the stop codon. However, inversion or substitution may only affect one or two codons, and due to the degenerate nature of the genetic code, this may eventually code for the same amino acid and will therefore have no effect on the protein structure.

Inheritance

Term	Definition
Homologous Pair	Each chromosome contains DNA for the same genes at the same locus on the chromosome. Alleles may differ (in heterozygotes) or be the same (homozygotes) at given loci in a homologous pair. One chromosome is maternally derived, the other is paternally derived
Autosome	Non-sex chromosome
Autosomal Recessive	Caused by a recessive allele on an autosome. The phenotype is not necessarily shown in offspring, even if one parent is homozygous. Carriers possible
Autosomal Dominant	Caused by a dominant allele on an autosome. The phenotype is shown in approximately 50% of offspring, cannot skip a generation. If one parent is homozygous, all offspring will show the phenotype
Sex-Linked	Allele is sex-linked, found on the X or Y chromosomes. One sex will more likely show the phenotype than the other. Most common are X-linked disorders
Allele	Forms of the same gene
Genotype	Combination of alleles
Phenotype	Observable characteristics as a result of genotype
Recessive	Phenotype only expressed when allele inherited form both parents
Dominant	Characteristic expressed even if only one allele present
Incomplete Dominance	Intermediate inheritance where two dominant alleles are present, causing a blending of phenotypes
Codominance	Intermediate inheritance where two dominant alleles are present, but both are expressed simultaneously without blending e.g. AB Blood Type
Homozygous	Identical alleles on both homologous chromosomes
Heterozygous	Two different alleles on homologous chromosomes

Inheritance can follow patterns and can be represented using pedigree diagrams and Punnett Squares. CF is an autosomal recessive disease and genotypes of offspring can be calculated from inheritance patterns shown on such diagrams.

Genetic Testing

Ideal effective genetic tests are inexpensive, reliable, test for a range of disorders, non-invasive, have low risk of miscarriage, and with proper follow-up with counselling and education if necessary. A test is best when carried at an early stage, as if an abortion is decided on, it is both physically and emotionally easier to abort earlier. However, this cannot be achieved currently, but maternal serum screening is the gold standard at present, as it is non-invasive and inexpensive with low risk of miscarriage.

Technique	When	Risk	Description
Amniocentesis	15 - 17 weeks	0.5-1% risk miscarriage	Removal of small volume of amniotic fluid by injection that bathes the foetus and contains cells from it. The proteins can then be analysed
Chorionic villi sampling	8 – 12 weeks	1-2% risk miscarriage	Removal of small tissue sample from the edge of the placenta, either through the abdomen or through the vagina. Provides more DNA than amniocentesis and most of the tissue is foetal
Preimplantation Genetic Diagnosis	At 8 Cells	No risk	Only for IVF. Removal of one or two cells for testing when zygote is at 8 cells. If genetic disorder is found, embryo is discarded
Maternal Serum Screening	10 weeks	No risk	Tests mother's blood for presence of foetal proteins. DNA then tested for genetic disorders

When making ethical decisions, four frameworks can often be used to justify a decision:

- Rights and Duties – most people feel there are certain human rights that should always be permitted. If a right is owed, then some people feel a duty to fulfil or stand by this right. These rights may originate from religious teachings, and historical social conventions
- Utilitarianism – the option which maximises the happiness in the world should be undertaken, with no moral absolutes imposed
- Informed Autonomous Decisions – people should be able to act autonomously, giving informed consent. This framework is frequently criticised: utilitarians argue that a selfish decision could negatively impact many others, and people who believe in rights may say that we also have a duty to consider the effects of decisions on others
- Virtue – a good decision requires justice, wisdom, temperance, fortitude, faith, hope and charity. An approach which utilises as many of these qualities as possible is the best to pursue

Treating CF

- Bronchodilators –Air is blown through a solution to make a fine mist which is breathed into the lungs using a nebuliser's mouthpiece. The drug relaxes muscles in the airways, opening them up and relieving tightness in the chest
- Antibiotics – early diagnosis and treatment of lung infection is the best form of CF treatment. Many antibiotics are used to kill or prevent growth of bacteria in the lungs
- DNAase Enzymes – infection of the lungs leads to the accumulation of white blood cells in the mucus. The breakdown of these cells releases DNA, increasing stickiness of the mucus. DNAase enzymes are inhaled using a nebuliser and break down DNA, so mucus is easier to clear
- Steroids are used to reduce inflammation of the lungs
- Ivacaftor is a new medication which is a CFTR potentiator. Ivacaftor improves the transport of chloride ions through the ion channel by binding to the channels directly to cause a currently unknown mode of gating which in turn increases the probability that the channel is open
- High-energy diets which include double the normal protein intake, and potentially salt supplements
- Digestive enzyme supplements replace those trapped by the blocked pancreatic duct
- Physiotherapy rhythmically taps the walls of the chest cavity to help loosen mucus and help improve air flow through the lungs
- If lungs become too inefficient, the only option may be a heart and lung transplant

Possible Future Treatments

Gene therapy may offer a future cure to CF by treating the cause of the disease: the genotype and therefore the phenotype of a gene is altered.

1. Normal allele of the gene is inserted into target cells, either using liposomes, which fuse with cell membrane to carry in DNA, or by using a modified virus. A virus with a lytic lifecycle is used and the sequence allowing replication is removed. The normal allele is added, with a promoter sequence to initiate CFTR synthesis. The virus could cause an inflammatory response, but is efficient. The liposome-DNA complexes are inhaled by a nebuliser from an aerosol
2. The normal allele is incorporated into the airway epithelial cell's genome and is transcribed
3. Functioning CFTR channel is produced and incorporated into cell membrane, removing CF

Correction currently has only lasted up to 15 days due to cell replacement and with no evidence of sodium secretion resolution. It is hoped that somatic (body) cells can be edited in the future to remove sickle cell anaemia and thalassaemia. The alternative is germ cell (gamete) editing, so every cell in a new body is corrected. Ethical objections to germ line therapy are concerned with the possible effects in future generations of the inherited new gene.