Edexcel International AS Biology

Your notes

Inheritance

Contents

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Nature of Mutations

- A **gene mutation** is a change in the sequence of bases in a DNA molecule
- Mutations may result in an altered polypeptide; as the DNA base sequence of a gene determines the sequence of amino acids that make up a polypeptide, **mutations in a gene can sometimes lead to a change in the polypeptide that the gene codes for**
- Mutations occur **spontaneously during** DNA replication
- There are different ways that a mutation in the DNA base sequence can occur, e.g.
  - Substitution
  - Insertion
  - Deletion
- Substitution, insertion, and deletion mutations are all examples of **point mutation**; mutations that involve a change in the DNA base sequence at a **single location**
- Other types of mutation can affect entire genes or entire chromosomes
  - Genes can be replicated or lost
  - Chromosomes can be divided unequally during meiosis, resulting in cells with extra or missing chromosomes

Substitution of nucleotides

- A mutation that occurs when **a base in the DNA sequence is randomly swapped for a different base**
- A substitution mutation will **only change the amino acid for the triplet in which the mutation occurs**, and will have no impact on triplets located elsewhere in the gene
- Substitution mutations include
  - **Silent mutations**
    - The **mutation does not alter the amino acid sequence** of the polypeptide; this is due to the degenerate nature of the genetic code
  - **Missense mutations**
    - The **mutation alters a single amino acid** in the polypeptide chain, e.g. sickle cell anaemia is caused by a single substitution mutation changing a single amino acid in the haemoglobin protein
  - **Nonsense mutations**
    - The **mutation creates a premature stop codon**, causing the polypeptide chain produced to be incomplete and therefore affecting the final protein structure and function, e.g. cystic fibrosis can be caused by a nonsense mutation

- Note that a **stop codon** provides a signal for the cell to **stop translation** of the mRNA molecule into an amino acid sequence

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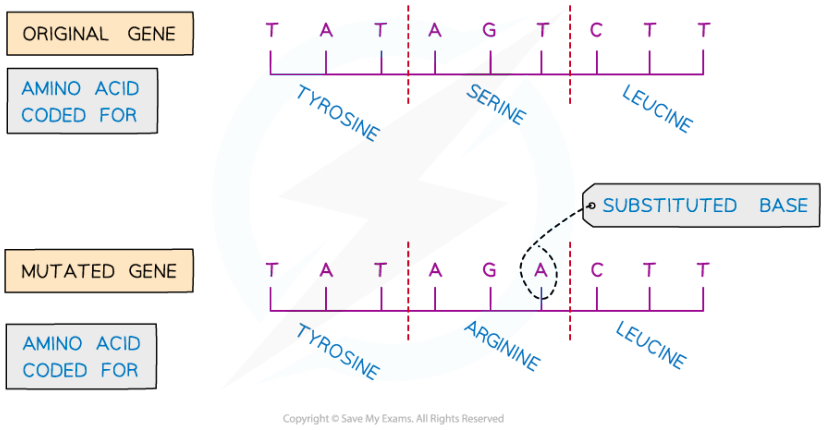
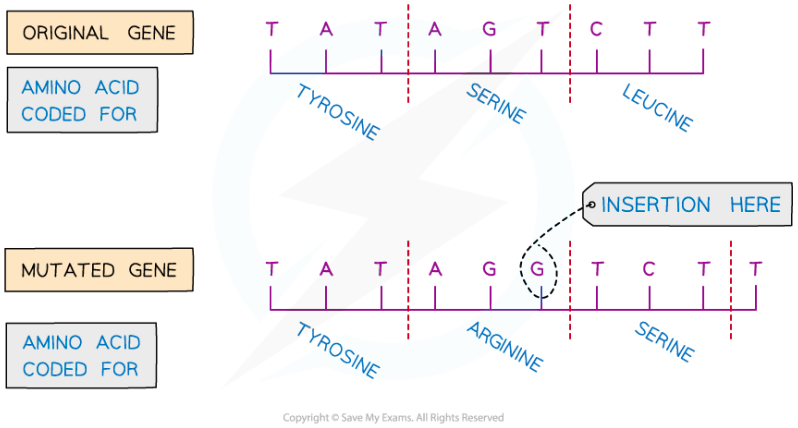


Substitution mutations involve swapping one nucleotide for another

Insertion of nucleotides

- A mutation that occurs when **a nucleotide is randomly inserted** into the DNA sequence is known as an insertion mutation
- An insertion mutation **changes the amino acid that would have been coded for by the original base triplet**, as it creates a **new, different** triplet of bases
  - Remember that every group of three bases in a DNA sequence codes for an amino acid
- An insertion mutation also has a **knock-on effect** on other base triplets by **changing the triplets further on in the DNA sequence**
  - This means that insertion mutations cause what is known as a **frameshift mutation;** they don't only change the triplet where the insertion has occurred, but every triplet downstream of the insertion
- This **may dramatically change the amino acid sequence produced** from this gene and therefore the **ability of the polypeptide to function**



Insertion mutations occur when a new nucleotide is added into a base sequence

Deletion of nucleotides

- A mutation that occurs when **a nucleotide is randomly deleted** from the DNA sequence
- Like an insertion mutation, a deletion mutation **changes the triplet in which the deletion has occurred,** and also **changes every group of three bases further on in the DNA sequence**
  - This is known as a frameshift mutation
- This **may dramatically change the amino acid sequence produced** from this gene and therefore the **ability of the polypeptide to function**

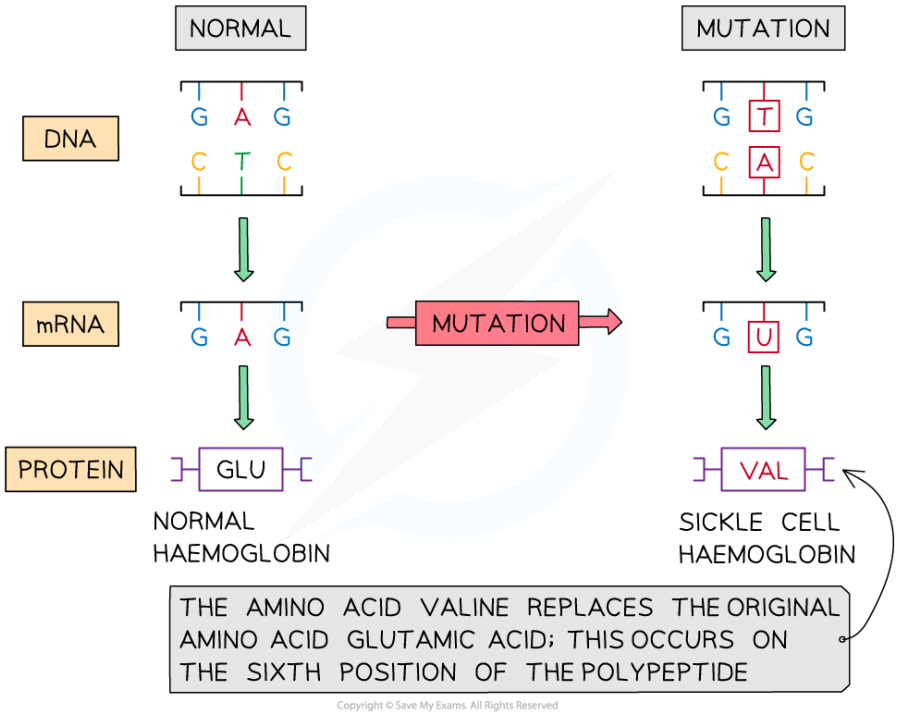
Effects of Mutations

- **Most mutations do not alter the polypeptide** or only alter it slightly so that its appearance or function is not changed
  - This is possible because the genetic code is **degenerate**; the base sequence can be changed without necessarily altering the amino acid
- However, a **small number of mutations** code for a **significantly altered polypeptide**
  - A mutation changes the DNA base sequence
  - One or many amino acids in the primary structure of a protein is altered
  - Different bonds form in the secondary and tertiary structures of the protein
  - The final 3D structure of the protein is altered
- Very rarely this can give rise to a protein that **provides an organism with an advantage**, e.g. resistance to an antibiotic, or the ability to digest a new type of food
  - Mutations that provide an advantage can **drive the process of evolution** by causing **natural selection** to occur
    - Individuals with an advantage are more likely to survive and reproduce

Your notes

- The advantageous mutation is more likely to be passed on
- The mutation becomes more common in the population

- More often, mutations that affect polypeptide structure are likely to be harmful, **affecting the ability of proteins to perform their function,** e.g.
  - In **cystic fibrosis**, a membrane channel protein no longer functions
    - A fault in the CFTR gene leads to production of **non-functional chloride channels, reducing** the movement of **water by osmosis** into cell secretions
    - This results in the production of **thick, sticky mucus** in the air passages, the digestive tract and the respiratory system
  - In **sickle-cell disease**, the haemoglobin protein no longer functions
    - Sickle-cell disease is caused by a single substitution mutation that causes **haemoglobin proteins to clump together**
    - This affects the **shape of red blood cells**, preventing easy blood flow and causing severe pain and problems with blood supply to important organs



Sickle cell disease is caused by a single substitution mutation that changes one amino acid in the haemoglobin protein

- Mutations in the genes that are involved with cell division can lead to **uncontrolled cell division** and the development of **tumours** that can become cancerous
- Mutations that occur in the gametes, or sex cells, can be **passed on to future generations**, meaning that every cell in the body of an organism's offspring will contain the mutation

Your notes

- **Mutagens** can increase the likelihood of a mutation occurring, e.g.
  - Ionising radiation
  - X-rays
  - Some chemicals

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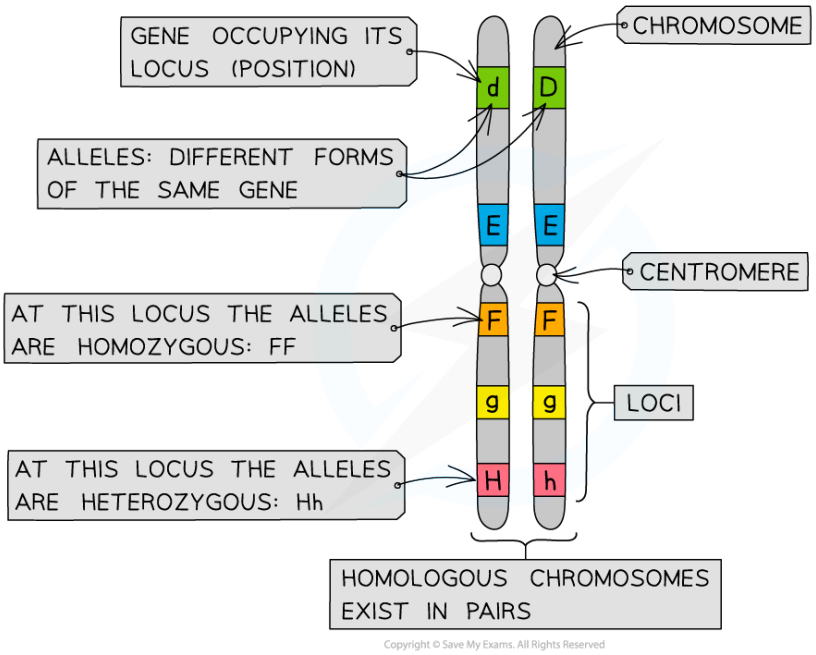
Key Terms: Genetics

Genes & alleles

- A **chromosome** is a long DNA molecule which contains many **genes**
- A **gene** is a length of DNA that codes for a single polypeptide
  - The **position of a gene** on a chromosome is its **locus** (plural loci)
- Each gene can exist in two or more **different forms** called **alleles**
  - Different alleles of a gene have slightly **different nucleotide sequences** but they still occupy the **same locus** on the chromosome
  - Different alleles arise by the process of mutation
  - E.g. each allele might produce a different coat colour in mammals
    - One allele might code for a black coat while the alternative allele might code for a chestnut coat
- When writing about genes it is conventional to use a single letter to represent a gene, while different alleles may be indicated by using upper and lower case letters, e.g. **A** and **a**

Homozygous & heterozygous

- Every individual has two copies of each allele; one on each chromosome in a **homologous pair**
  - A homologous pair of chromosomes is a pair of chromosomes that **match in size and shape**, and that contain **the same genes at the same loci**
    - The chromosomes may not contain the same alleles of each gene
  - One member of a homologous pair of chromosomes comes from one parent, while the other comes from the other parent
- When an individual has **two identical alleles** at a locus they are said to be **homozygous,** or a **homozygote**
  - Homo = the same
- When an individual has **two different alleles** at a locus they are said to be **heterozygous,** or a **heterozygote**
  - Hetero = different



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Chromosomes match up to form homologous pairs which have the same genes at the same loci. While the genes are the same, the alleles may be different, meaning that individuals can be either homozygous or heterozygous at a particular locus

Genotype & phenotype

- The **genotype** of an organism refers to the **alleles of a gene** possessed by that individual
  - E.g. An organism's genotype could be represented by the letters gg
- The genotype of an individual affects their **phenotype**; a phenotype is the **observable characteristics** of an organism
- E.g. every horse has two copies of a gene for coat colour in all of their cells, one on each homologous pair of chromosomes; the gene could be notated using the letters A and a
  - A horse that has two **A** alleles has the **genotype AA** and is homozygous
    - If the **A** allele codes for a black coat, then the **phenotype** of the horse would be black
  - A horse that has two **a** alleles has the genotype **aa** and is also homozygous
    - If the **a** allele codes for a chestnut coat then the phenotype of the horse would be chestnut

Dominant & recessive

- Not all alleles affect the phenotype in the same way
- Some alleles are **dominant;** they are **always expressed** in the phenotype no matter which other allele is present

- This means they are expressed in both heterozygous and homozygous individuals, e.g.
    - A horse with the genotype **AA** would be said to be **homozygous dominant** and would have a black coat phenotype
    - A horse with the genotype **Aa** would be said to be **heterozygous** and would still have a black coat phenotype, as the allele for black coat colour is dominant over the lower case allele
        - It is possible to refer to a heterozygous individual as a **carrier** of the recessive allele; the allele doesn't show in the phenotype but could still be passed on to offspring
- Others are **recessive;** they are **only expressed** in the phenotype **if no dominant allele** is present
    - This means that it is only expressed when present in a homozygous individual, e.g.
        - A horse with the genotype **aa** would be said to be **homozygous recessive** and would have a chestnut coat phenotype due to the absence of the dominant black allele

Codominance

- Sometimes **both alleles can be expressed** in the phenotype at the same time; this is known as **codominance**
    - When an individual is heterozygous they will express both alleles in their phenotype
- When writing the genotype for codominance the **gene** is represented by a **capital letter** and the **alleles** are represented by **different superscript letters**, for example I^A
- An example of codominance can be seen in **coat colour in cattle**
    - The gene for coat colour can be represented by the capital letter C
    - The alleles for coat colour can be represented by letters R (red) and W (white)
    - A cow that is homozygous and has a red coat has the genotype C^RC^R
    - A cow that is homozygous and has a white coat has the genotype C^WC^W
    - A cow that is heterozygous will have a **roan** coat, containing a **mixture of red and white hairs**; the genotype will be C^RC^W

Genetic Pedigree Diagrams

- Family pedigree diagrams can be used to trace the **pattern of inheritance** of a specific trait, e.g. a genetic disorder, **through generations of a family**
- Pedigree diagrams can provide information such as
    - Whether a trait is caused by a **dominant or recessive allele**
    - Whether a trait is more likely to be inherited by **males or females**
    - The **genotypes** of individuals in the family

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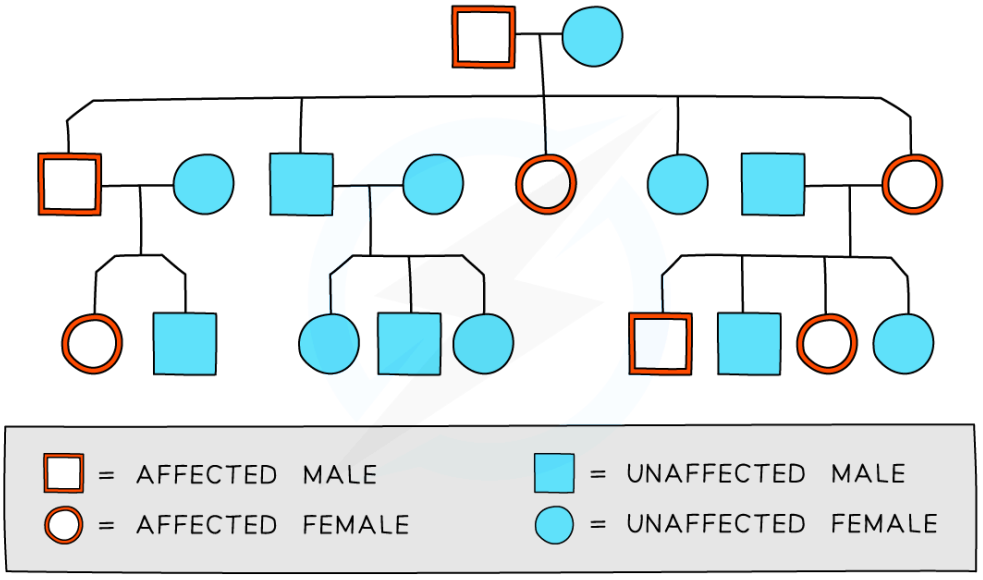
- The **probability** that an individual in the family will inherit a trait



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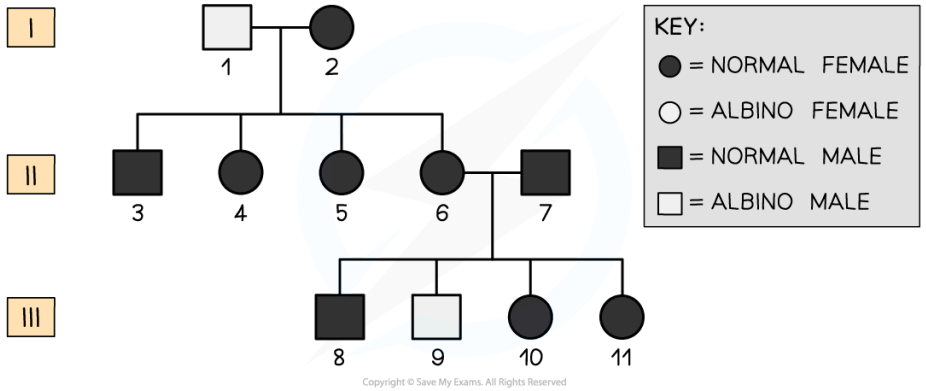
Pedigree diagrams can be used to show the pattern of inheritance of a genetic trait

- **Males** are indicated by the **square shape** and **females** are represented by **circles**
- **Affected** and **unaffected individuals** can be indicated using **colour, shading**, or **cross-hatching**
- **Horizontal lines** between males and females show that they have **produced children**
- **Vertical lines** show the relationship between **parent** and **child**
- Roman numerals may be used to indicate **generations**
- For each generation the eldest child is on the left and **each individual** is **numbered**
- The family pedigree above shows the following
  - Both males and females are affected by the trait in question
  - Every generation has affected individuals
  - The eldest son in the second generation is affected
  - There is one family group that has no affected parents or children
- The diagram above does not contain enough information to show
  - Whether the trait is caused by a dominant or recessive allele
  - The genotypes of the individuals involved

Worked Example

Your notes

The pedigree diagram below traces the inheritance of **albinism** through several generations. Albinism affects the production of the **pigment melanin** leading to lighter hair, skin and eyes.



Using the pedigree chart, deduce and explain the following:

1. The type of allele that causes albinism
2. The genotype of individuals **9** and **7**
3. The possible genotypes of **10** and **11**

Answer:

Question 1

Albinism is caused by a **recessive allele**

Person number 9 is an affected individual despite parents 6 and 7 being unaffected; 6 and 7 must both be carriers of the recessive allele and 9 has inherited one recessive allele from each parent

Question 2

The genotype of person 9 must be **homozygous recessive** (aa) and the genotype of 7 must be **heterozygous** (Aa)

Person 9 is an affected individual with albinism; as this is determined by the recessive allele they must have two copies of the albinism allele

Person 7 must be heterozygous as he does not have albinism but has passed on the recessive allele to person 9

Question 3

The possible genotypes of 10 and 11 are **heterozygous** (Aa) or **homozygous dominant** (AA)

They are both unaffected individuals so must possess at least one dominant allele (A), however, it is possible that they each might have inherited a recessive allele (a) from one parent (both parents must have a copy of the recessive allele in order for person 9 to have albinism)

Your notes

Examiner Tips and Tricks

When answering questions about pedigree charts for genetic diseases, it is always useful to remember which phenotype is caused by the homozygous recessive genotype. You can write these genotypes onto your chart and it will give you a good starting point for working out the possible genotypes of the rest of the individuals in the chart.

Sex Linkage

- Sex-linked genes are located on the sex chromosome
- This means the sex of an individual affects which alleles they pass on to their offspring through their gametes
- If the gene is on the X chromosome, **males** (XY), **will only have one copy** of the gene, whereas **females** (XX) **will have two**
  - The X chromosome has many more genes on it than the Y chromosome, so sex-linkage that involves the Y chromosome is very rare
- Sex linkage is notated using a capital letter to represent the chromosome X or Y and a superscript letter to represent the allele
- There are **three genotypes** for females, e.g. for a genetic trait caused by a recessive allele
  - X^AX^A = unaffected
  - X^AX^a = carrier
  - X^aX^a = affected
- **Males** have only **two genotypes**, e.g.
  - X^AY = unaffected
  - X^aY = affected
- It is not possible for males to be **carriers** of X-linked traits, nor for them to **pass such traits on to their sons**; males only pass Y chromosomes on to their sons

Worked Example

Red-green colour blindness is a well known sex-linked trait in which individuals find it difficult to distinguish between the colours red and green. It is controlled by is a gene **found on the X chromosome;** the dominant B allele codes for normal vision and the recessive b allele results in red-green colour blindness.

Use a genetic diagram to show how two parents with normal vision can have offspring with red-green colour blindness.

Answer:

Step 1: Work out the genotypes of the parents

Both parents have normal vision so each must have a copy of the dominant B allele

The father only has one copy of the X chromosome, so his genotype must be X^BY

The question tells us that the parents must be able to have a child with colour blindness, so this allele must come from the mother; she must therefore have a copy of the b allele and her genotype must be X^BX^b

Step 2: Work out which gametes the parents can produce

The genotype X^BY will produce gametes containing either X^B or Y

The genotype X^BX^b will produce gametes containing either X^B or X^b

Step 3: Use the gametes to complete a Punnett square and then indicate which offspring will be affected

	X^B	Y
X^B	X^BX^B	X^BY
X^b	X^B	X^bY

The individual with genotype X^bY will be affected by red-green colour blindness; they only have only copy of the X chromosome and it contains the colour blindness allele

Examiner Tips and Tricks

Note that in the worked example above the letter B has been chosen to represent colour blindness rather than the letter C. It can often be a good idea to choose letters for which there is a clear difference between the upper and lower case; this avoids losing marks in exams because examiners can't tell the difference between, e.g. C and c, or S and s

Your notes

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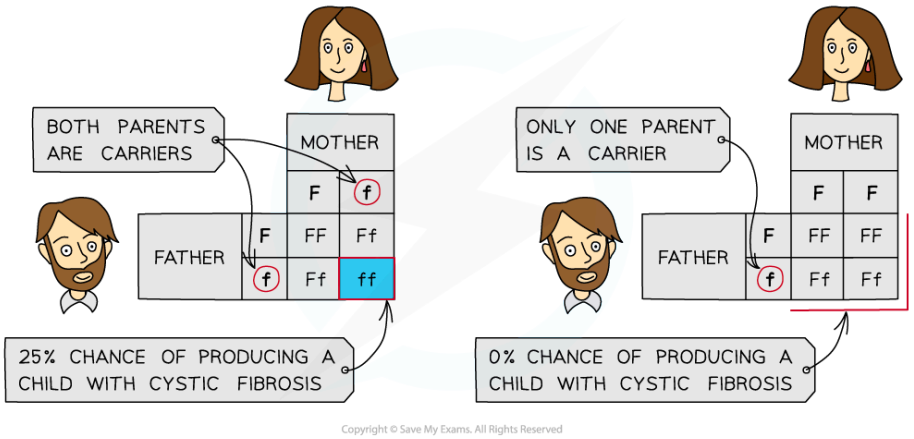
Cystic Fibrosis

- Genes can affect the phenotype of an organism
  - A gene codes for a single polypeptide
  - The polypeptide can affect the phenotype, e.g. it could form part of an enzyme or a membrane transport protein
- **Genetic disorders** are often caused by a mutation in a gene that results in a differently-functioning or non-functioning protein that **alters the phenotype** of the individual

Cystic fibrosis

- Cystic fibrosis is a genetic disorder of **cell membranes** caused by a recessive allele of the **CFTR** (**C**ystic **F**ibrosis **T**ransmembrane Conductance **R**egulator) gene located on chromosome 7
  - This gene codes for the production of chloride ion channels required for secretion of sweat, mucus and digestive juices
  - A mutation in the CFTR gene leads to production of **non-functional chloride channels**
  - This **reduces** the movement of **water by osmosis** into the secretions
  - The result is that the body produces large amounts of **thick, sticky mucus** in the air passages, the digestive tract and the reproductive system
- Because cystic fibrosis is determined by a **recessive allele,** this means
  - People who are heterozygous won't be affected by the disorder but are **carriers**
  - People must be homozygous **recessive** in order to have the disorder
  - If **both parents are carriers** the chance of them producing a child with cystic fibrosis is 1 in 4, or 25 %
  - If only **one of the parents is a carrier** with the other parent being homozygous dominant, there is no chance of producing a child with cystic fibrosis, as the recessive allele will always be masked by the dominant allele



Cystic fibrosis is a genetic disorder caused by a recessive allele

The respiratory system

- Mucus in the respiratory system is a necessary part of keeping the lungs healthy
  - It prevents infection by trapping microorganisms
  - This mucus is moved out of the respiratory tract by cilia
- In people with cystic fibrosis, due to the faulty chloride ion channels, the **cilia are unable to move** as the mucus is so thick and sticky
- This means microorganisms are not efficiently removed from the lungs and lung infections occur more frequently
- Mucus builds up in the **lungs** and can block airways which limits gas exchange
  - The **surface area for gas exchange is reduced** which can cause breathing difficulties
- **Physiotherapy** can support people with cystic fibrosis to loosen the mucus in the airways and improve gas exchange

The digestive system

- Thick mucus in the digestive system can cause issues because
  - The tube to the **pancreas** can become blocked, preventing digestive enzymes from entering the small intestine
    - Digestion of some food may be reduced and therefore **key nutrients may not be made available for absorption**
  - The mucus can cause **cysts** to grow in the pancreas which **inhibit the production of enzymes**, further reducing digestion of key nutrients
  - The **lining of the intestines** is also coated in thick mucus, **inhibiting the absorption of nutrients into the blood**

Your notes

The reproductive system

Your notes

- Mucus is normally secreted in the reproductive system to prevent infection and regulate the progress of sperm through the reproductive tract after sexual intercourse
- The mucus in people with cystic fibrosis can cause issues in both men and women
  - In **men** the tubes of the testes can become blocked, preventing sperm from reaching the penis
  - In **women** thickened cervical mucus can prevent sperm reaching the oviduct to fertilise an egg

Your notes

Uses of Genetic Screening

- Some circumstances, e.g. in a pregnancy where there is a family history of a genetic disorder, may require individuals to determine if they have a particular allele present in their genome
- This can be determined by **genetic screening**
- There are three main uses of genetic screening
  - Identifying individuals who **carry an allele at a gene locus for a particular disorder**
  - The screening of embryos prior to implantation during fertility treatment; this is **Preimplantation Genetic Diagnosis** (PGD)
  - Testing a foetus before birth; this is **prenatal testing**

Identification of carriers

- Carrier testing is offered to individuals with a **history** of genetic disorders in their family
- It can show whether people who have no symptoms **carry the allele** for particular disorders, such as cystic fibrosis
  - Cell samples can be extracted from, e.g. blood or saliva, before being tested for the presence of **specific alleles**
- Couples can be tested prior to having children to **determine the probability of future children inheriting the disorder**
- Some of the benefits of carrying out genetic screening at this stage include
  - Families can make **informed decisions** before having children
  - Women can decide whether to have **prenatal testing** during pregnancy

Preimplantation Genetic Diagnosis (PGD)

- IVF, or *in vitro* fertilisation is a type of fertility treatment during which **fertilisation is carried out in the lab;** embryos produced in this way can be **implanted into the uterus** where they develop into a foetus
- Sometimes a couple might choose to have a child by IVF if they know that they are at **increased risk of certain genetic disorders**, as it allows them to **screen any embryos produced** using PGD
- PGD involves **analysis of the DNA of an embryo** prior to implanting it into the uterus
  - The sample of DNA to be analysed can be obtained by taking **cell samples from embryos** produced during IVF
- Benefits of PGD include
  - Evidence suggests that the process **does not harm the embryo** in any way

- Reduces the chances of having a baby with a genetic disorder
- It **avoids abortion** as it is carried out before implantation of the embryo
    - It is worth noting that some people believe that an **embryo is as worthy of human status as a foetus or a baby**, so the discarding of affected embryos after PGD is **not ethically straightforward** for everyone

Your notes

Prenatal testing

- Prenatal testing is offered to pregnant women with a family history of genetic disorders
- It involves testing the foetus for genetic diseases during the course of a pregnancy
- The DNA can be obtained by **chorionic villus sampling** or **amniocentesis** in the uterus
- Chorionic villus sampling
    - This involves removing and testing a small sample of cells **from the placenta** using a fine needle
    - The cells contain foetal DNA which can be **analysed for genetic disorders**, allowing parents to make informed decisions about the pregnancy and foetus
    - Advantages of this process include
        - It is carried out at around 11–14 weeks of pregnancy, so any problems can be **picked up early on**
        - A relatively large tissue sample can be collected, providing **plenty of cells to analyse**
        - Results are available **rapidly**
    - Potential implications of chorionic villus sampling that should be considered include
        - The process has a **1–2 % risk of miscarriage**
        - The process cannot pick up any disorders that are caused by alleles of genes located on the paternal X chromosome, as **this chromosome is inactive** in the placental cells sampled
- Amniocentesis
    - This involves removing and testing a small sample of cells **from amniotic fluid** using a fine needle
        - The amniotic fluid is the fluid that surrounds the foetus within the uterus
    - The fluid contains **foetal cells** which contain **DNA to be analysed**
    - Potential implications of amniocentesis that should be considered include
        - It is carried out at around 15–20 weeks of pregnancy; this is relatively **late in the pregnancy**, making decisions about abortion more difficult for some parents
        - The procedure has a **1 % risk of miscarriage**

- It takes **2–3 weeks** for results to be available

- Benefits of prenatal testing include
  - The tests allow parents to make informed decisions about the progress of a pregnancy
  - Results can help parents prepare for the future care of the child, including medical treatment

Your notes

Implications of Prenatal Genetic Screening

- Prenatal genetic screening involves **analysis of the DNA of a foetus** taken from the uterus **during pregnancy**
  - Examples of prenatal screening methods include **chorionic villus sampling** and **amniocentesis**
- Both forms of prenatal screening come with associated risks and potential ethical dilemmas, so it is important that parents considering this type of screening have thought about the implications
  - Positive implications
    - Prenatal screening can provide **advance notice** of the birth of a child with a genetic disorder, giving **time** for parents to be **educated** and to **make decisions about medical treatments**
    - The **risk of harm** to the foetus during prenatal screening **are low**; around 1–2 % for both methods
    - Some parents may feel able to make the decision to **end a pregnancy** on discovering that a foetus has a life-limiting or potentially fatal diagnosis
    - Some parents may choose to continue with a pregnancy after receiving a fatal diagnosis, but they have time to process the results and grieve before the birth of a child who may not survive for long outside the uterus
    - **Genetic counsellors** are available to help parents think through the results of prenatal testing
  - Negative implications
    - Both methods of prenatal screening bring a **small risk of miscarriage**
    - Amniocentesis provides results **relatively late in pregnancy**, making decisions about termination of a pregnancy very difficult for some parents
    - Prenatal screening is **not 100 % accurate**
      - False positive results may lead to the termination of a healthy pregnancy
      - False negative results may give false expectations for the health of a foetus

- Parents may experience **pressure** from society or their medical team **to abort a foetus** with a genetic disorder
- Some parents may believe that a foetus has human status even very early on during a pregnancy, meaning that they **would not consider abortion to be an option** even after early testing

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Ethical & Social Issues of Genetic Screening

- Some circumstances, e.g. in a pregnancy where there is a family history of a genetic disorder, may require individuals to determine if they have a particular allele present in their genome; this can be determined by **genetic screening**
- As genetic screening can leave future parents with many questions, **genetic counsellors** are available to help
  - Counsellors can be seen **before screening** has occurred; they may discuss the following with the prospective parents
    - The probability of the couple having a child with a genetic disorder
    - Termination of the pregnancy
    - Therapeutic treatments possible for the child
    - Financial implications of having the child
    - Effect on existing siblings
    - Ethical issues
  - After screening the counsellors will read the results and **explain them** to the future parents
- Each use of genetic screening brings **potential concerns** that should be considered; these concerns will differ depending on someone's **religious, moral**, and **social position**, e.g.
  - Belief that God is in control may mean that a **pregnancy will be continued no matter what** genetic screening might show
  - Belief that embryos are **potential human beings from conception** would mean that the discarding of embryos after embryo screening or the abortion of a foetus at any stage would be considered impossible
  - Belief that **abortion is only acceptable up to a certain stage** of pregnancy may mean that screening techniques that are carried out later in pregnancy can't lead to termination
  - Some may feel that it is unethical to bring a child into the world who will **struggle with health issues**, or who they will be **unable to care for properly**; this may mean that abortion is considered to be the most ethical option
  - Processes that involve screening embryos could allow for embryos to be selected on the basis of **factors other than genetic health**, e.g. sex or intelligence; many are concerned about the **potential future of 'designer babies'**

- Some **cultures may have different traditions** around genetic disorders, e.g. with abortion considered to be more acceptable by some cultures than others
- Positive screening results for non life-threatening conditions, e.g. Down syndrome, can lead to the **abortion of foetuses that could have gone on to live full and happy lives**; some feel that such conditions are being **eradicated from society**
- An embryo or unborn baby has **no ability to give consent or make decisions** about its future; some believe that they are deserving of full human rights while others do not

Your notes

Examiner Tips and Tricks

Make sure that you are able to give a **balance of arguments** from **different ethical viewpoints**; you may have personal views on some the issues covered, but you should avoid sticking to only one side of any argument.