

Inheritance, cystic fibrosis and genetic screening

Revision notes · Genetic terms, monohybrid inheritance, pedigrees and sex linkage, the effects of cystic fibrosis, genetic screening and the ethical issues it raises.

For Pearson Edexcel International AS Biology XBI11 and International A Level Biology YBI11. **A Level only** is IA2 content (Units 4 to 6), not needed for the International AS.

Inheritance, cystic fibrosis and genetic screening **Spec 2.15-2.18**

Genetic terms **Spec 2.15**

Gene	A sequence of bases on a DNA molecule that codes for a sequence of amino acids in a polypeptide chain, found at a particular locus on a chromosome.
Allele	One of the different forms of a gene.
Genotype	The alleles that an organism has for a particular gene (or genes).
Phenotype	The observable characteristics of an organism, resulting from its genotype and the environment.
Dominant	An allele that is expressed in the phenotype when present in only one copy (in the heterozygote).
Recessive	An allele that is expressed in the phenotype only when two copies are present (in the homozygote).
Codominance	Both alleles are expressed in the phenotype of the heterozygote, because neither is dominant over the other.
Homozygote	An organism with two identical alleles of a gene.
Heterozygote	An organism with two different alleles of a gene.

A person has two alleles of each gene, one inherited from each parent. A **dominant** allele is shown by a capital letter (for example B) and a **recessive** allele by a lower-case letter (b). The **genotype** BB is homozygous dominant, bb is homozygous recessive, and Bb is heterozygous.

Codominance

In **codominance**, two alleles are both expressed. For example, the human ABO blood group gene has alleles I^A , I^B and I^O . I^A and I^B are codominant, so a person with genotype $I^A I^B$ has blood group AB. Both are dominant over I^O , so $I^A I^O$ has group A and $I^B I^O$ has group B, and only $I^O I^O$ has group O. When codominant alleles are used, the capital letter is the gene and the superscripts are the alleles.

Common mistake: A dominant allele is not necessarily common or 'stronger'. It just shows in the phenotype in the heterozygote. Also, a 'carrier' has one copy of a recessive allele and does not show the condition.

Monohybrid inheritance and pedigree diagrams Spec 2.15

A **monohybrid cross** looks at the inheritance of one gene. Each parent makes gametes containing one allele of the gene (as a result of meiosis), and the alleles combine at random when gametes fuse at fertilisation.

A cross between two heterozygotes

Cystic fibrosis is caused by a recessive allele, *f*. Two parents are both heterozygous (*Ff*). Draw a genetic diagram, and find the probability that a child has cystic fibrosis.

1. Parent genotypes: *Ff* × *Ff*.
2. Gametes: *F* or *f* from each parent.
3. Possible offspring: *FF*, *Ff*, *Ff*, *ff* (Punnett square).
4. Phenotypes: *FF* and *Ff* do not have the condition (3), *ff* has cystic fibrosis (1).

Answer: Ratio 3 : 1 (unaffected : affected). Probability of a child with cystic fibrosis is 1 in 4 (25 %).

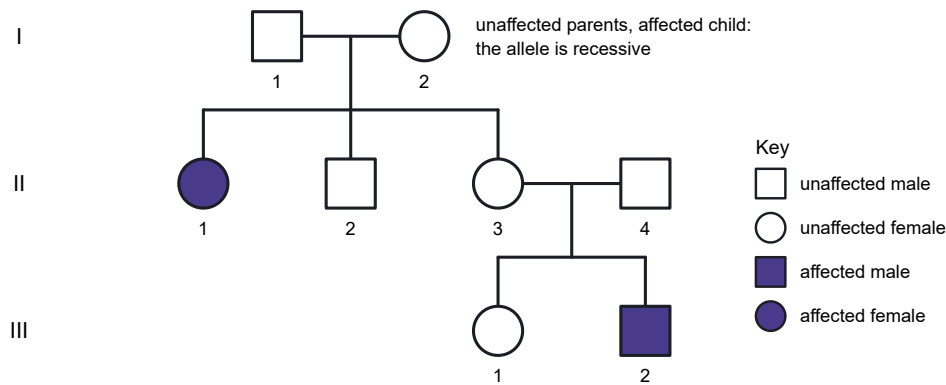
Pedigree diagrams

A **pedigree diagram** shows the phenotypes of family members across generations. Males are usually drawn as squares and females as circles; shaded symbols show people with the condition; horizontal lines join parents and vertical lines lead to their children.

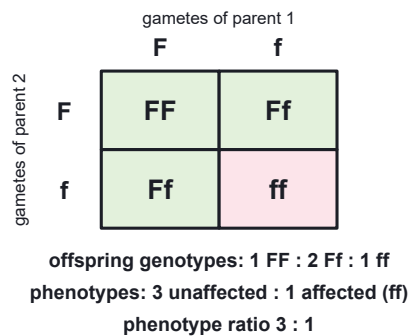
Clues for working out the type of inheritance

Clue in the pedigree	Conclusion
Two unaffected parents have an affected child	The condition is caused by a recessive allele, and both parents are heterozygous carriers.
Two affected parents have an unaffected child	The condition is caused by a dominant allele, and both parents are heterozygous.
Every affected person has an affected parent	Suggests a dominant allele.
Condition skips generations	Suggests a recessive allele.

Exam tip: To prove that an allele is recessive, find a pair of unaffected parents with an affected child, and say so, naming the individuals. To prove dominant, find affected parents with an unaffected child. Give the genotypes of the individuals concerned.



Punnett square for the cross $Ff \times Ff$ (F = unaffected allele, f = recessive allele)



Unaffected parents with an affected child show that the allele is **recessive**. $Ff \times Ff$ gives **3 : 1**.

Sex linkage and red-green colour blindness Spec 2.15

Human females have two X chromosomes (XX) and males have one X and one Y (XY). The Y chromosome is shorter and carries few of the genes found on the X chromosome. A **sex-linked** characteristic is controlled by a gene on a sex chromosome, and here we consider genes on the **X chromosome**.

Red-green colour blindness is caused by a recessive allele on the X chromosome. The alleles are written as superscripts on the X: X^B (normal colour vision, dominant) and X^b (colour blind, recessive).

Genotypes and phenotypes	
Genotype	Phenotype
$X^B X^B$	Female, normal colour vision
$X^B X^b$	Female, normal colour vision, carrier of the allele
$X^b X^b$	Female, colour blind
$X^B Y$	Male, normal colour vision
$X^b Y$	Male, colour blind

A cross involving a carrier mother

A woman who is a carrier of red-green colour blindness ($X^B X^b$) has children with a man with normal colour vision ($X^B Y$). Give the possible genotypes and phenotypes of their children.

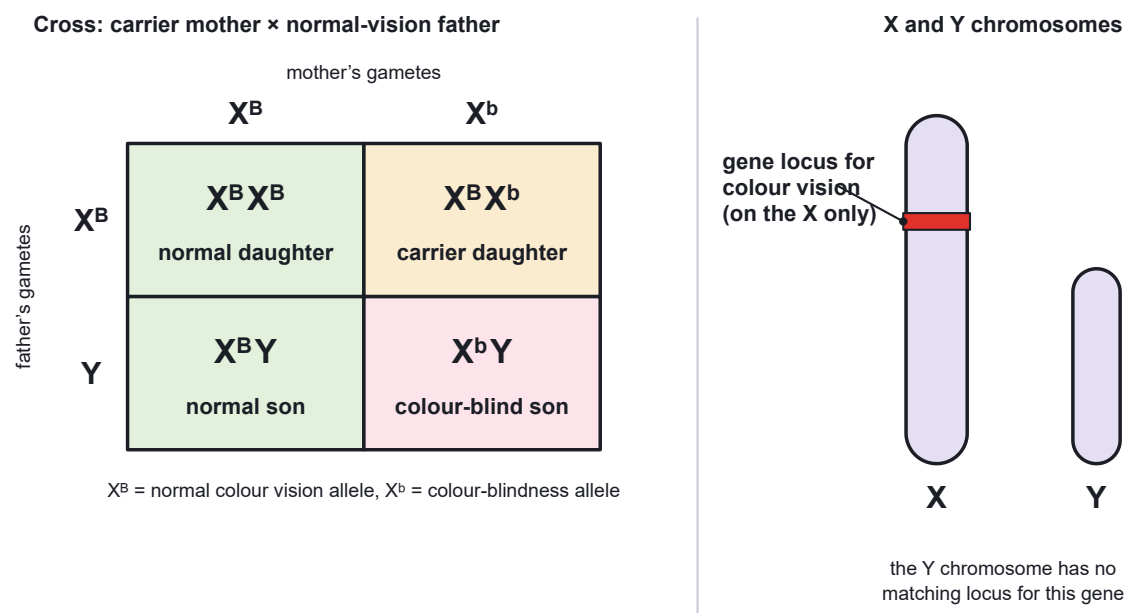
1. Gametes from the mother: X^B or X^b . Gametes from the father: X^B or Y .
2. Daughters: $X^B X^B$ (normal) or $X^B X^b$ (carrier, normal vision).
3. Sons: $X^B Y$ (normal) or $X^b Y$ (colour blind).

Answer: Half of the sons (so 1 in 4 of all children) are colour blind; no daughters are colour blind, but half the daughters are carriers.

Why the condition is more common in males

- A male has only one X chromosome, so a single recessive allele on it is always expressed (there is no second allele to mask it).
- A female must inherit the recessive allele on both of her X chromosomes to show the condition.
- A male inherits his X chromosome from his mother, never from his father. A colour-blind man passes the allele to all of his daughters (who become carriers) and to none of his sons.

Exam tip: Write sex-linked genotypes with the X, and the allele as a superscript, and always include the Y for males. Marks are lost for writing the alleles without the sex chromosomes.



Colour blindness is **sex-linked**: the gene is on the **X chromosome** only.

Cystic fibrosis Spec 2.16

Cystic fibrosis is a genetic disorder caused by a recessive allele of the CFTR gene, on chromosome 7. Someone with the condition has two copies of the faulty allele; carriers (heterozygous) have one copy and do not have symptoms. The commonest mutation is a deletion of three bases, which removes one amino acid from the protein.

From mutation to symptoms

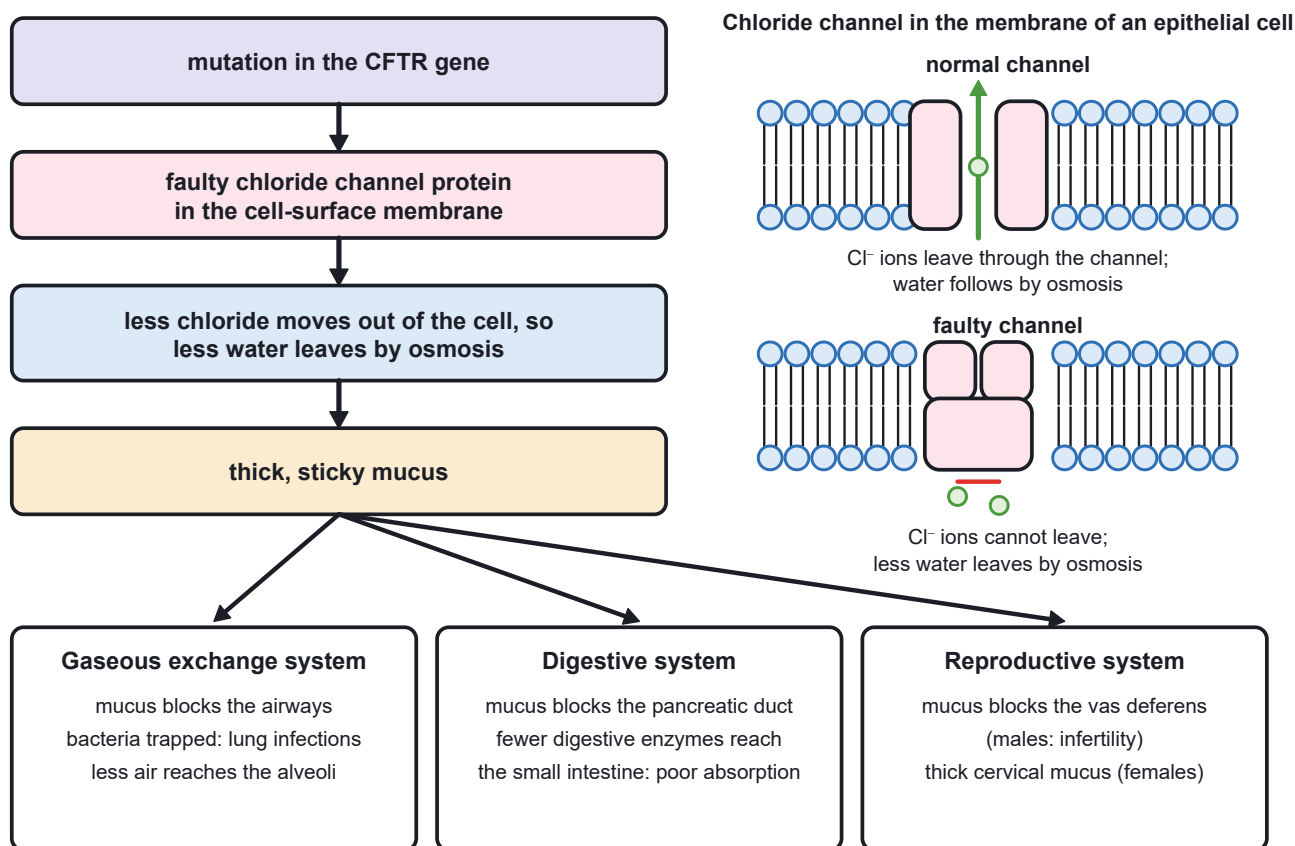
1. The gene mutation changes the primary structure of the CFTR protein, so it folds into the wrong tertiary structure.
2. The faulty protein does not work as a chloride ion channel in the cell-surface membrane (or does not reach the membrane).

- Chloride ions are not secreted out of the epithelial cells, so water does not move out by osmosis (the water potential gradient is reduced).
- The mucus on the surface of the epithelium is therefore thick and sticky, instead of thin and watery.

Effects of cystic fibrosis on body systems

System	Effect
Gaseous exchange	Thick mucus blocks the airways and traps bacteria, which cannot be removed by cilia. This causes repeated lung infections, inflammation and damage, reducing the surface area for gas exchange and making breathing difficult. Less oxygen reaches the blood.
Digestive	Thick mucus blocks the pancreatic duct, so digestive enzymes (amylase, lipase and protease) cannot reach the small intestine. Food is poorly digested and absorbed, which causes poor growth and malnutrition. Mucus may also block the intestine.
Reproductive	In males, the tubes (vas deferens) that carry sperm may be blocked or missing, causing infertility. In females, thick mucus in the cervix can prevent sperm from reaching the egg, reducing fertility.

Exam tip: To score full marks on 'how does a mutation cause these symptoms', follow the chain: **gene mutation** → **faulty channel protein** → **less chloride and water secretion** → **thick mucus** → **blockage of the specific system**.



How a **CFTR mutation** leads to **thick sticky mucus** and the symptoms of cystic fibrosis.

Genetic screening: carriers, PGD and prenatal testing Spec 2.17

Identifying carriers

A DNA sample (from blood or a cheek swab) can be tested for the presence of a particular recessive allele. People with a family history of a condition such as cystic fibrosis can find out if they are **carriers**,

and so assess the risk of having an affected child.

Pre-implantation genetic diagnosis (PGD)

1. Eggs are fertilised in vitro (IVF) and the embryos develop to an early stage (about 8 cells; many clinics now wait until the blastocyst stage at about 5 days).
2. One or two cells (or, at the blastocyst stage, a few cells from the outer layer) are removed from each embryo, and their DNA is tested for the faulty allele.
3. Only embryos that do not carry the allele (or that are not affected) are implanted into the uterus.

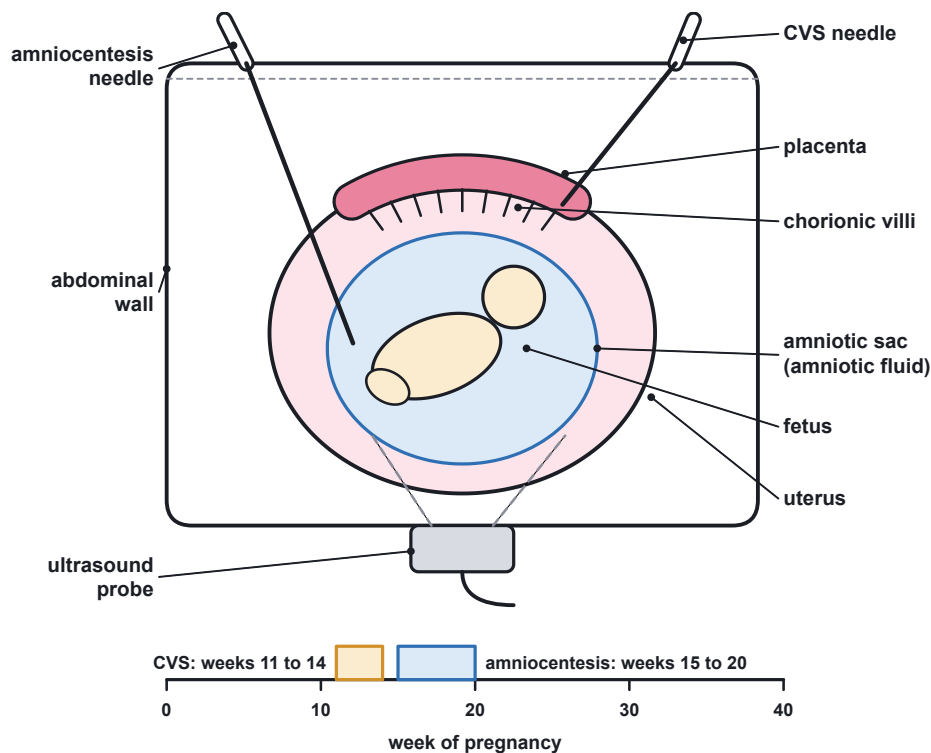
Prenatal testing

Amniocentesis and chorionic villus sampling		
Feature	Amniocentesis	Chorionic villus sampling (CVS)
Sample	Amniotic fluid containing fetal cells.	Cells from the chorionic villi (part of the placenta).
Method	A needle is passed through the abdominal wall and uterus wall, guided by ultrasound, to remove fluid.	A needle is passed through the abdomen (or a tube through the cervix), guided by ultrasound, to remove a small sample of tissue.
Timing	From about 15 weeks of pregnancy.	From about 11 weeks of pregnancy (earlier).
Risk	Small risk of miscarriage.	Small risk of miscarriage (slightly higher than amniocentesis).
After	Fetal cells cultured; DNA or chromosomes analysed.	Fetal cells analysed directly, so results sooner.

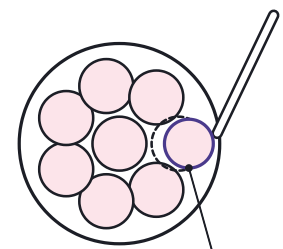
Implications of prenatal screening

- A positive result may lead parents to consider termination of the pregnancy, or to prepare for the birth of a child with the condition.
- Both tests carry a risk of miscarriage, including of an unaffected fetus.
- A result can cause anxiety, and an incorrect result (false positive or false negative) could lead to a wrong decision.
- Results show only that a fetus has a particular allele. They do not show how severe the condition will be, and for many conditions there is no cure.
- Test results about a fetus also give information about the genes of the parents and other relatives.

Exam tip: Do not describe these tests as treatment. They are screening tests: they give information. Be specific about risks, such as miscarriage, rather than saying 'it is dangerous'.



PGD
embryo from IVF, 8-cell stage



one cell removed
with a micropipette

the removed cell is tested for
the faulty allele; only unaffected
embryos are put in the uterus

CVS is done at 11-14 weeks and **amniocentesis** at 15-20 weeks; **PGD** tests an IVF embryo before it is transferred.

Ethical and social issues of genetic screening Spec 2.18

To **discuss** the ethical and social issues, identify the issue, set out arguments on each side from different viewpoints, and reach a reasoned conclusion. The issues come from the fact that screening gives information about people, and about embryos and fetuses that cannot consent.

Viewpoints on genetic screening		
Viewpoint	In favour of screening	Against, or concerns
Religious	Some traditions allow screening to prepare for, or prevent, severe suffering, and to allow informed choices.	Many traditions hold that life is sacred from conception, so discarding embryos in PGD or terminating a pregnancy is wrong. Views differ between and within religions.
Moral	Respect for autonomy: parents have the right to information and to choose. Avoiding the suffering of a child with a severe disorder.	Every life has equal value, including that of a person with a disorder. Embryos may have a right to life. Screening could lead to selection of embryos for other traits (so-called designer babies).
Social	Reduces the number of children born with serious conditions, and reduces demand on families and health services.	Pressure on parents to screen and terminate; stigma towards people living with the condition; cost and unequal access; discrimination by insurers or employers using genetic information; privacy of genetic data.

- Who should have access to the results (the individual, family members, employers, insurers)?
- Should screening be offered for all disorders, including those with late onset or with mild effects?
- How should genetic counselling be provided to help people understand the results and the options?

Exam tip: A discuss answer needs both sides and the named viewpoints (religious, moral and social). Avoid giving a personal opinion without reasons. A balanced conclusion earns credit, such as 'screening is justified for severe disorders, provided counselling and consent are given'.

Common mistake: Do not assume that all religious people share one view. Say 'some religious groups' or 'many religious traditions' to stay accurate.

Quick check

- 1 . What is the difference between genotype and phenotype?
- 2 . What is codominance?
- 3 . Why is red-green colour blindness more common in males?
- 4 . Name the protein that is faulty in cystic fibrosis.
- 5 . Name two methods of prenatal testing.

Quick check answers

Inheritance, cystic fibrosis and genetic screening

1. Genotype is the alleles an organism has; phenotype is its observable characteristics.
2. Both alleles are expressed in the phenotype of a heterozygote.
3. The allele is recessive and on the X chromosome; males have only one X, so one copy is expressed.
4. The CFTR protein, a chloride ion channel in cell-surface membranes.
5. Amniocentesis and chorionic villus sampling (CVS).