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Inheritance

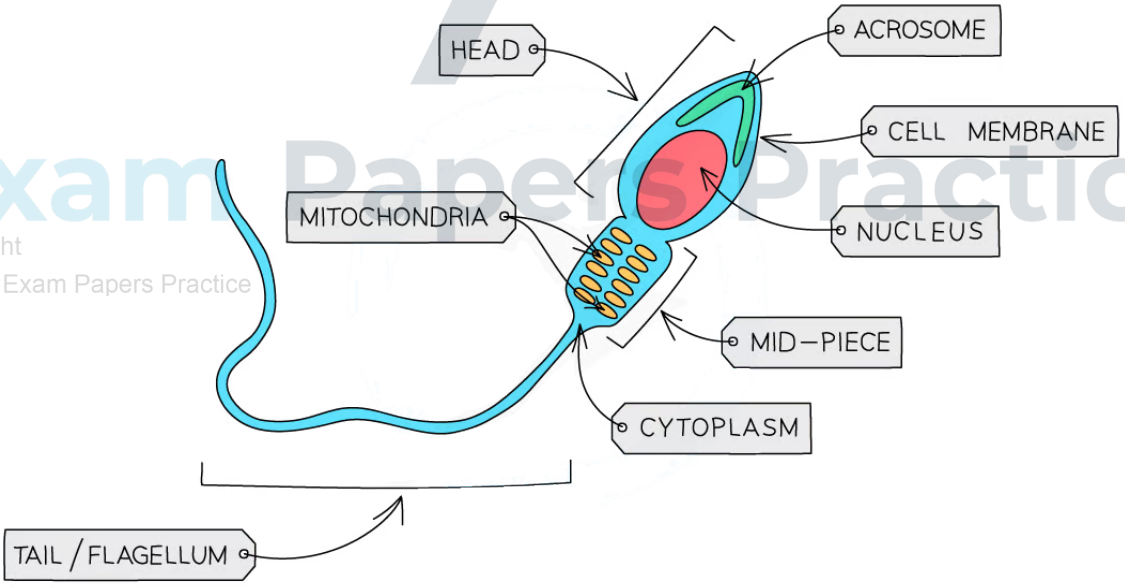
IB Biology - Revision Notes

Genetic Inheritance & Genetic Crossing

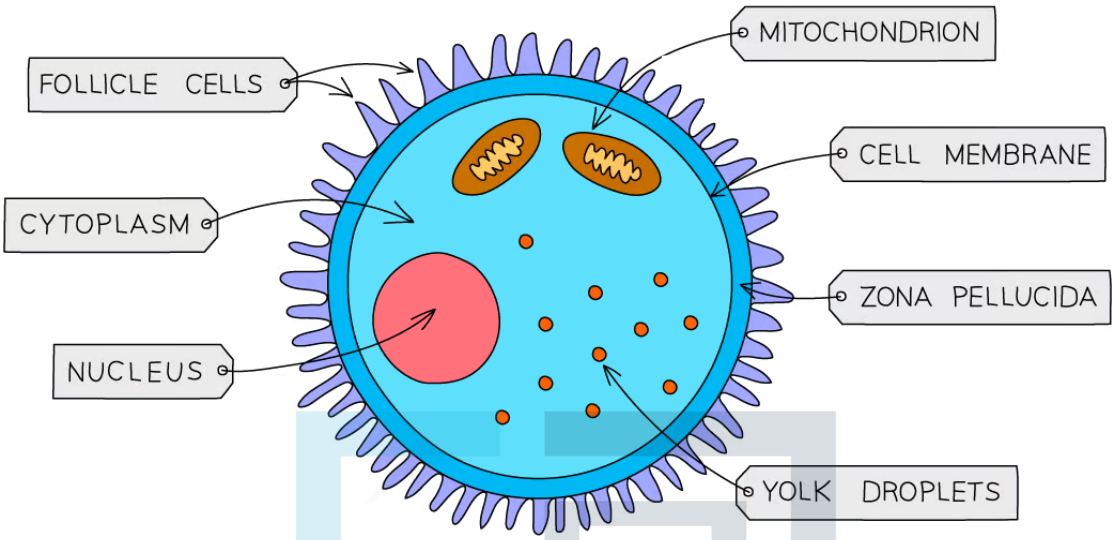
Inheritance: Gametes & Fertilisation

- Gametes are the **sex cells** of an organism
- For example, the **sperm** and **egg** (ovum) cells in humans
  - The **egg is larger than the sperm** as most of its space contains food to nourish a growing embryo
  - The sperm cell contains **many mitochondria** to release energy for its motion
- Gametes **fuse** during fertilization to form a **zygote** (fertilised egg cell)
- These sex cells are formed during **meiosis** and only have **one** copy of each chromosome and so are **haploid** cells
  - For humans, that means the sperm and egg cells contain **23 single chromosomes** in their nucleus (as opposed to diploid cells which contain 46 chromosomes, or 23 pairs)
  - As there is only **one chromosome from each homologous pair** there is only **one allele** of each gene present
    - This allele may be dominant, recessive or **co-dominant**

Sperm cell diagram



Egg cell diagram



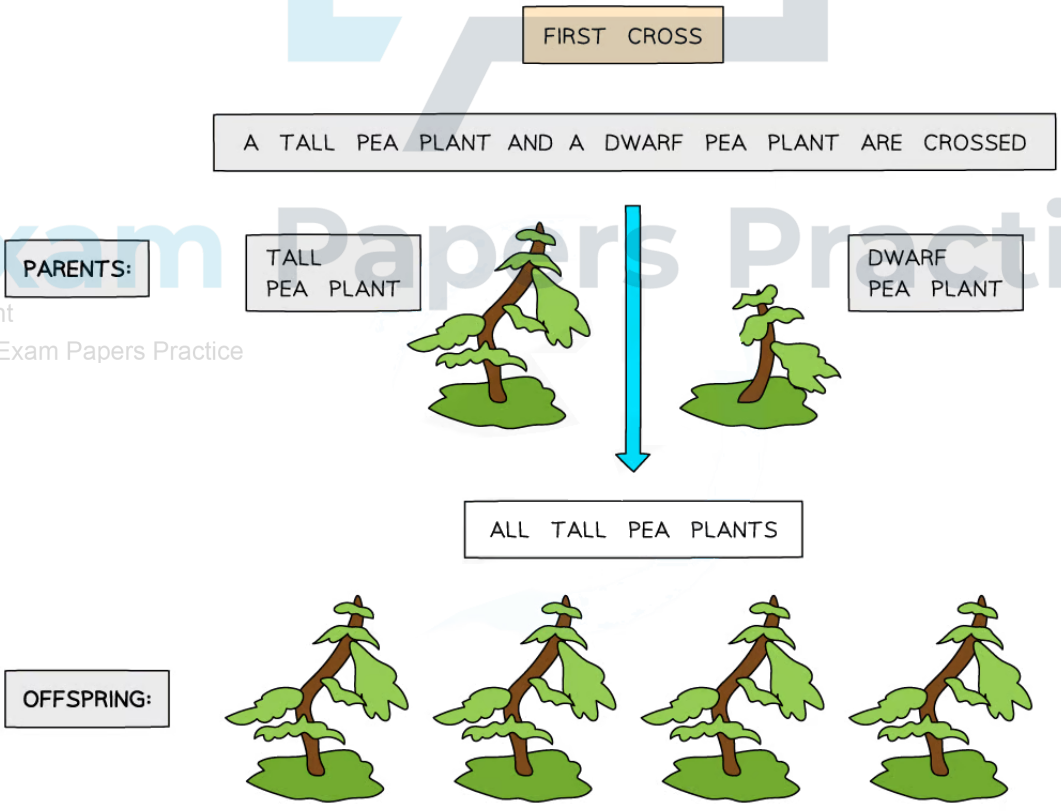
The structure of human gametes – the sperm and egg

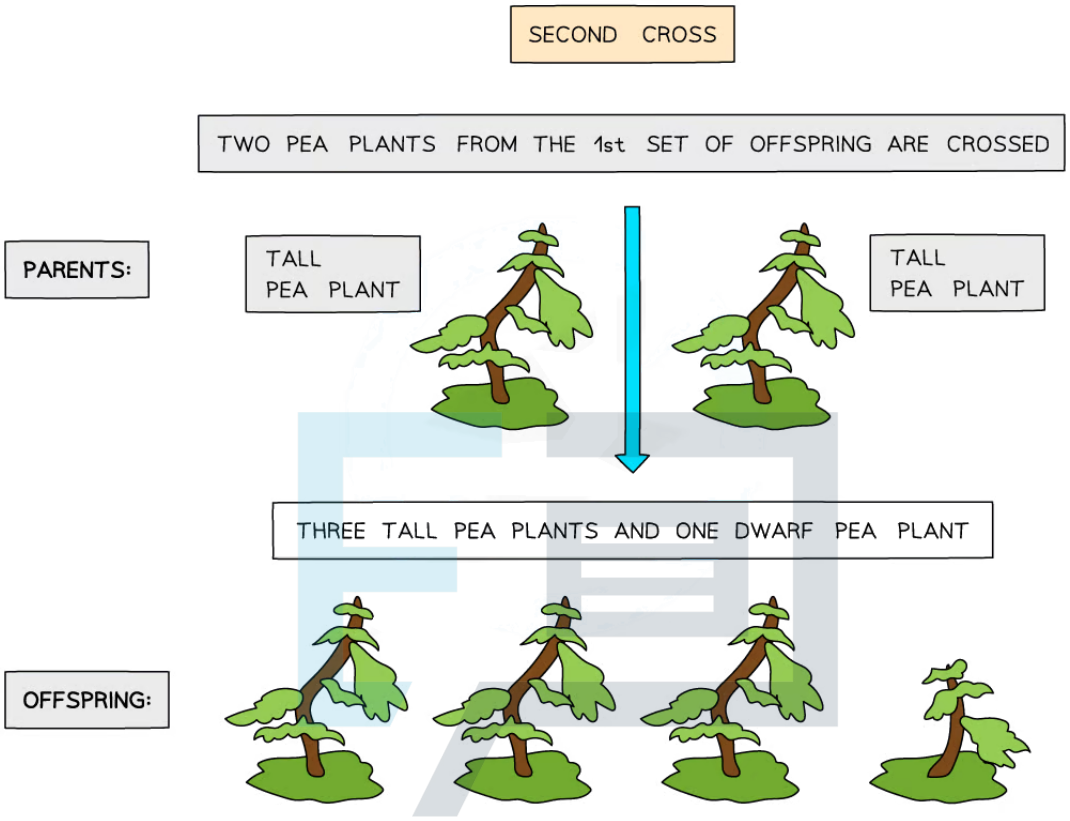
- Fusion of gametes results in diploid zygotes with two alleles of each gene that may be the same allele **or** different alleles
- Sexual reproduction is **a process involving the fusion of the nuclei of two gametes (sex cells) to form a zygote** (fertilised egg cell) and the production of offspring that are **genetically different from each other**
- Fertilisation is defined as the **fusion of gamete nuclei**, and as each gamete comes from a different parent, there is **variation** in the offspring
- When a male and female gamete fuse their **chromosomes are combined**
- This means the resulting zygote is **diploid**
  - The zygote contains two chromosomes of each type
- It will therefore have **two alleles** of each gene
  - If the two alleles for a particular gene are the **same** then the genotype is described as **homozygous**
  - If the two alleles for a particular gene are **different** then the genotype is described as **heterozygous**

Genetic Crosses in Flowering Plants

- **Gregor Mendel** was an Austrian monk
- In the mid-19th century, Mendel carried out **breeding experiments** on large numbers of pea plants whilst looking after the monastery gardens
- He studied how **characteristics were passed on between generations of plants**
- Due to his extensive work on the understanding of inheritance, he is sometimes called the **Father of Genetics**
- Mendel carefully **transferred pollen** from one pea plant to the reproductive parts of another
  - **Pollen contains the male gamete** and is located on the anther of the flower
  - The female gametes are located in the **ovary**
  - The plants reproduce sexually and require **pollination** for fertilisation
  - This technique **eliminated any uncertainty** from his data since he knew which pollen had fertilised each of the plants
- He **collected the pea seeds from these plants** and grew them in favourable conditions to find out their characteristics
- He also **cross-bred offspring peas** in order to find out which, if any characteristics would appear in future generations
- Mendel investigated the **height** of pea plants, the **colours of their flowers** and the **smoothness of their seed coat**

Mendel's breeding experiments of pea plants diagram





Mendel's pea plant crosses

Mendel's Pea Plant Results Table

Parental characteristics	Characteristics of first generation plants	Chraracteristics of second generation plants	Ratio of characteristics in second generation
Tall plant × dwarf plant	100% tall plants	868 tall plants and 277 dwarf plants	3.1 : 1
Round seed coat × wrinkled seed coat	100% Round seed coat	5474 round seed coat and 1850 wrinkled seed coat	3 : 1
Purple flowers × white flowers	100% Purple flowers	705 purple flowers and 224 white flowers	3.1 : 1

- Mendel found that characteristics were **inherited** in a **predictable pattern**
- **All** pea plants in the **first generation** had the same characteristic as **one** of the parental plants
- The offspring plants in the **second generation** had characteristics of **both** parent plants in a **3:1 ratio**
- Without knowing it, **Mendel had discovered genes**, he referred to them as **'units of inheritance'**
- He also discovered that some genes are **dominant** and some genes are **recessive**
- Different forms of the same gene are called **alleles**

- A **monohybrid trait** is one that is controlled by only **one gene**
- Generally, we consider that such a gene has **two alleles**
  - Either: one allele is dominant and the other is recessive
  - Or: the alleles are co-dominant
- A monohybrid cross starts with **pure-breeding parents** (homozygous), each displaying a different phenotype
  - This generation is known as the parental generation, denoted as the **P generation**
- The **purpose of a Punnett grid** is to predict the probability of a certain offspring displaying a certain genotype or phenotype
  - In the case where multiple offspring are produced, Punnett grids can **predict the numbers of offspring** that will display a certain genotype or phenotype after a cross

Steps in constructing a Punnett Grid

1. Write down the **parental phenotypes** and **genotypes**
2. Write down all the **possible gamete genotypes** that each parent could produce for sexual reproduction
   - A useful convention is to write the gamete genotypes **inside a circle** to denote them as gametes (haploid cells)
3. Place each parental genotype **against one axis** of a Punnett grid (2 x 2 table)

4. In the boxes of the Punnett grid, combine the gametes into the possible genotypes of the offspring
   - This gives the offspring of the **F_1 generation** (1^{st} filial generation)
5. List the **phenotype** and **genotype ratios** for the offspring

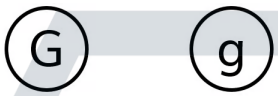
Worked example

Sweet peas grow pods that are either green or yellow. The allele for green, **G**, is dominant to the allele for yellow, **g**. Construct a Punnett grid to predict the outcome when crossing green and yellow pure-bred plants to show the F_1 generation offspring. Using plants from the F_1 generation, construct a second Punnett grid to show the outcomes of the F_2 generation.

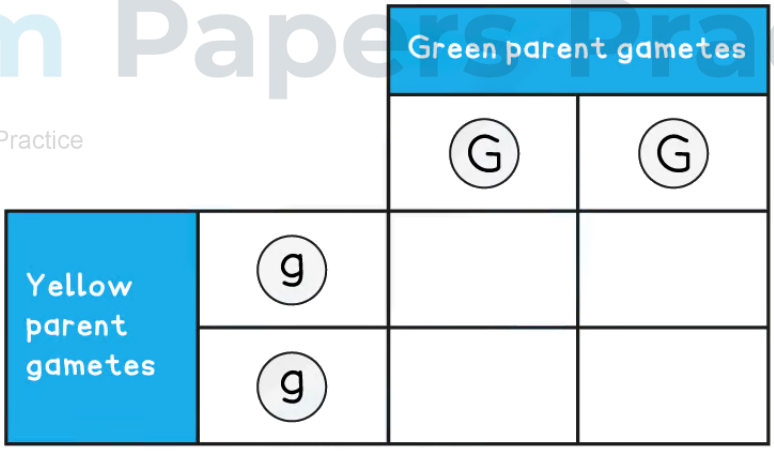
Step 1: Write down the parental phenotype and genotypes

Green coloured pods	Yellow coloured pods
GG	gg

Step 2: Write down all the possible gamete genotypes that each parent could produce



Step 3: Place each parental genotype against one axis of a Punnett grid (2 x 2 table)



Step 4: Combine the gametes in each box of the Punnett grid

		Green parent gametes	
		G	G
Yellow parent gametes	g	Gg	Gg
	g	Gg	Gg

Genotypes of the F1 cross between homozygous green (GG) and homozygous yellow (gg) pea plants. All offspring (100%) have the genotype Gg and the phenotype is green.

Step 5: Take two heterozygous offspring from the F_1 generation and cross them

		Heterozygous parent gametes	
		G	g
Heterozygous parent gametes	G		
	g		

Step 6: Combine the gametes in each box of the Punnett grid

		Heterozygous parent gametes	
		G	g
Heterozygous parent gametes	G	GG	Gg
	g	Gg	gg

Punnett grid showing the results of the F2 generation

Phenotype ratio is 3:1 green: yellow, Genotype ratio is 1 GG: 2 Gg: 1 gg

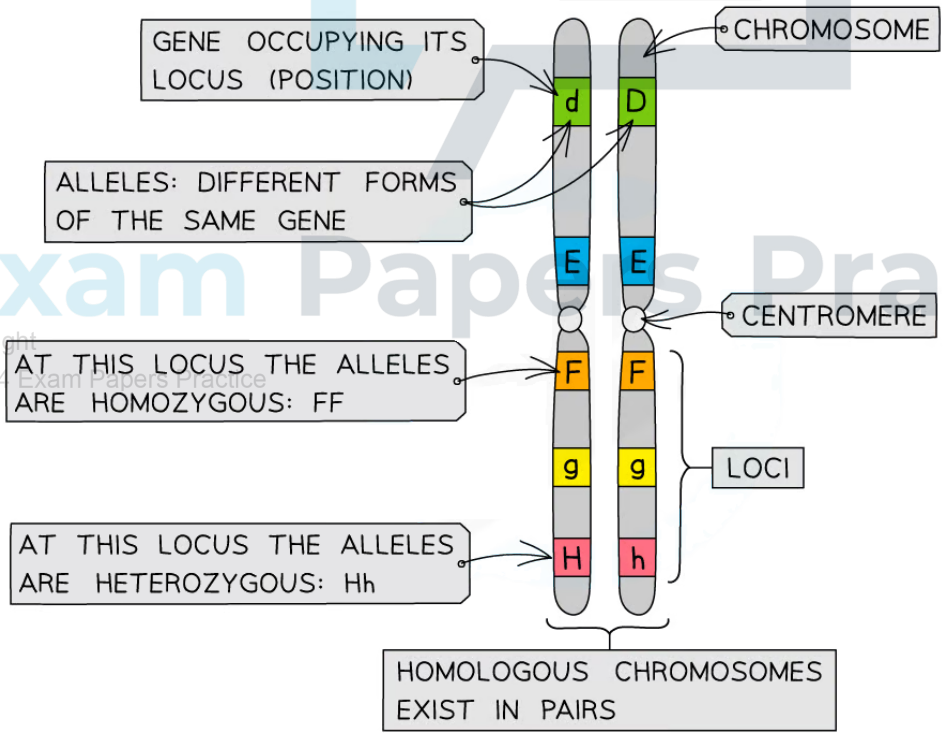
- Plants can sexually reproduce in different ways:
  - Some plants have the male and female reproductive parts within the **same flower**
  - Others have male flowers and female flowers on the **same plant**
  - Others have **different male and female plants**
- Plants with male and female reproductive parts on the same plant can be capable of **self-pollination and self-fertilisation**
- Farmers and ornamental plant growers can control the way their plants reproduce by **artificially pollinating** them
  - If a grower thinks a trait is useful or profitable they may choose to **self-pollinate** the favoured plants to keep the desirable traits in the next generation
  - Growers can also **cross-pollinate** by artificial pollination between different plants with favoured traits, with the goal to create new generation of plants will possess the desirable traits from both parent plants
  - **Genetic crosses** can be used to **predict** and plan for these outcomes

Inheritance: Terminology

Genotype

- A **gene** is a short length of DNA found on a chromosome that codes for a particular **characteristic** (by coding for the production of a specific protein)
- **Alleles** are variations of the same gene
  - As we have two copies of each chromosome, we have two copies of each gene and therefore every individual will have two alleles of each gene
  - One of the alleles is inherited **from the mother** and the other **from the father**
  - The alleles may be the same as each other, or they might be different. e.g. an individual has two copies of the gene for eye colour but **one allele could code for brown eyes** and **one allele could code for blue eyes**
- The combination of alleles that an individual organism inherits is its **genotype**
  - When the two alleles at a locus are the **same/identical**, an individual is said to have a **homozygous** genotype
  - When the two alleles at a locus are **different** the genotype is said to be **heterozygous**

Chromosome diagram



Chromosomes showing genes, loci and alleles

Exam Tip

Make sure to not use the words allele and gene interchangeably. They both have different definitions and need to be used correctly in your exams in order to gain marks.

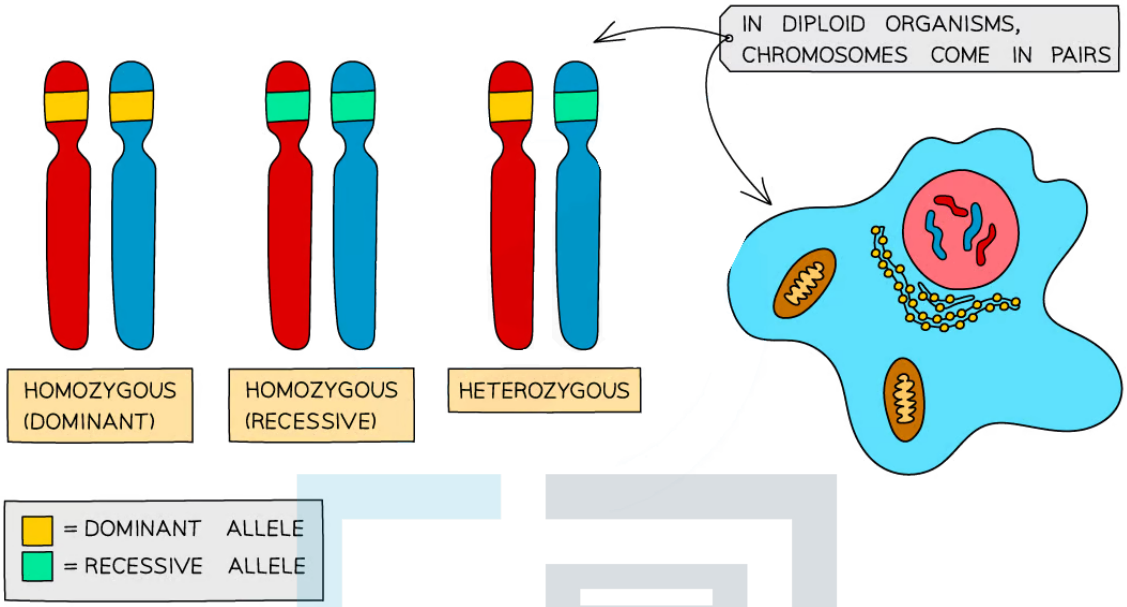
Phenotype

- The **observable characteristics** of an organism (seen just by looking - like eye colour, or found – like blood type) is called the **phenotype**
- The phenotype of all characteristics is determined by the following factors:
  - The **genotype** only - the combination of the two alleles for the gene for the characteristic, for example blood group is determined this way
  - The **environment** only - surroundings such as chemical or radiation exposure, diet or exercise can affect physical characteristics, for example scars and accent are determined this way
  - **Interaction** between **both** the genotype and the environment, for example height and skin colour are determined this way

Dominant & Recessive Alleles

- Alleles can be **dominant** or **recessive**
  - A **dominant** allele **only needs to be inherited from one parent** in order for the characteristic to be expressed in the phenotype
  - A **recessive** allele needs to be **inherited from both parents in order** for the characteristic to be expressed in the phenotype.
  - If there is only one recessive allele, it will **remain hidden** and the dominant characteristic will show
- If the two alleles of a gene are the same, we describe the individual as being **homozygous** (homo = same)
  - An individual could be **homozygous dominant** (having two copies of the dominant allele), or **homozygous recessive** (having two copies of the recessive allele)
- If the two alleles of a gene are different, we describe the individual as being **heterozygous** (hetero = different)

Different forms of allele pairs diagram



Alleles are different forms of the same gene. You can only inherit two alleles for each gene, and they can be the same (homozygous) or different (heterozygous). Alleles can be dominant or recessive.

Incomplete & Codominance

- **Co-dominant alleles** have a combined effect on the phenotype
  - The alleles are **both expressed to an equal extent** in the phenotype
- An example of codominance is in speckled chickens
  - Chickens can have different alleles for gene that determines the colour of their feathers
    - We can denote the gene for **colour** using the capital letter **C**
  - The two alleles for this gene are **white** for white feather colour, and **black** for black feather colour
    - We denote the two alleles using superscript letters, C^W **and** C^B
  - A chicken with the genotype C^WC^W has white feathers as their phenotype
  - A chicken with the genotype C^BC^B has black feathers as their phenotype
  - A chicken with the genotype C^WC^B has a combination of **both** feather colours, they are called **speckled colour chickens**
  - Because both alleles are expressed in the phenotype this is called **codominance**

Example of codominance in chickens diagram

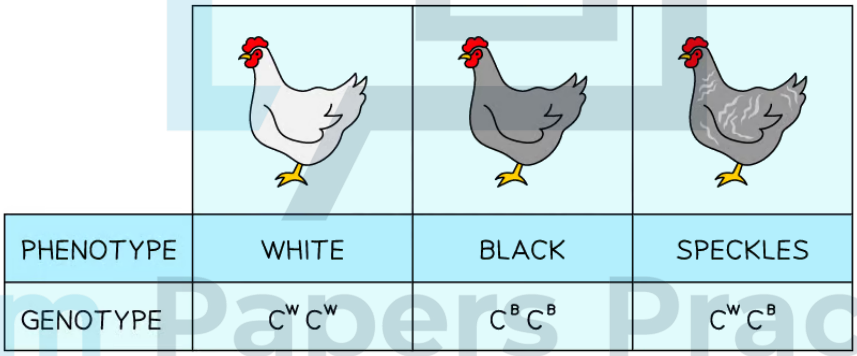


Diagram showing the phenotypes and genotypes of white, black and speckled chickens, which is an example of codominance

- **Incomplete dominance** is **similar to codominance** because two alleles are expressed together instead of just one dominant allele being expressed
- However, instead of both alleles being expressed, both alleles are **partially expressed** leading to a phenotype which is a **blend o**f both phenotypes or an **intermediate** phenotype between the two
- An example is incomplete dominance can be found in the four o'clock flower or marvel of Peru (*Mirabilis jalapa*)
  - Marvel of Peru can have different alleles for gene that determines the colour of their flowers
    - We can denote the gene for **colour** using the capital letter **C**
  - The two alleles for this gene are **white** for white flower colour, and **red** for red flower colour

- We denote the two alleles using superscript letters, C^W and C^R
- A plant with the genotype C^WC^W has white flowers as their phenotype
- A plant with the genotype C^RC^R has red flowers as their phenotype
- A plant with the genotype C^WC^R has a blend of both colours, which is expressed in the phenotype as a **pink flower colour**
- Because the flowers are neither white or red, but an **intermediate** between this two, this is **incomplete dominance**

Example of incomplete dominance in marvel of Peru diagram

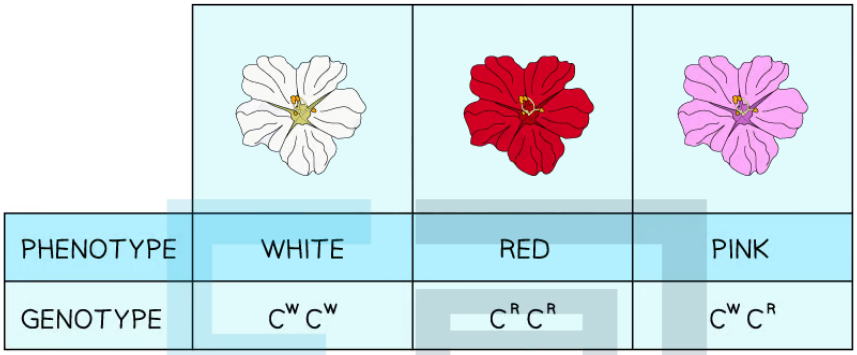


Diagram showing the phenotypes and genotypes of white, red and pink flowers of the marvel of Peru, which is an example of incomplete dominance

Exam Tip

When referring to different species examples in an exam you can use either the common name or the scientific name to gain marks. For example you could say 'four o'clock flower' or 'marvel of Peru' or '*Mirabilis jalapa*' to be awarded the mark.

Inheriting Alleles

Phenotypic Plasticity

- Phenotypic plasticity is the idea that although **genotype remains fixed** throughout an organism's lifetime, the way that the **phenotype is expressed** can **vary** during this time
- An organism's internal or external **environment can influence gene expression** patterns, and therefore phenotype
- The levels of regulatory proteins or transcription factors can be affected **in response to environmental stimuli** such as light, and chemicals including **drugs** and **hormones**
- For example, enzymes are activated in response to ultraviolet radiation and increase the **expression and production of melanin,** leading to skin pigmentation
- **Temperature** can also influence gene expression as demonstrated by organisms
  - The Himalayan rabbit (*Oryctolagus cuniculus L.*) possesses a gene for the development of pigmentation in its fur
    - The gene is inactive above 35°C but active between 15°C and 25°C
    - In the parts of the body that are cooler such as ears, feet and nose the gene becomes active making these areas black

Inheriting Recessive Alleles: Phenylketonuria

- **Phenylketonuria** (PKU) is an inherited condition caused by a **recessive allele** on an autosome
- It is a condition that can lead to symptoms such as mental disorders and seizures
- It is caused by a build-up of the **amino acid phenylalanine** in the body
  - Phenylalanine comes from broken down protein from diet and our cells
  - The enzyme phenylalanine hydroxylase breaks down phenylalanine
  - This enzyme is coded for by the PAH gene
  - PKU is caused by a **mutation** to the PAH gene that results in a **non-functional enzyme** so that the phenylalanine does not get broken down
- In the UK around 1 in 10,000 people are born with PKU

- In order for a child to have PKU, they must first inherit **two recessive alleles** from each of their parents
- Because it is caused by a recessive allele it means that two non-PKU sufferers could have a child with PKU if **both** parents are **heterozygous carriers** of the mutated PAH gene
- An example genetic cross is shown below:

A genetic cross between two PKU carrier parents diagram

	Father	Mother
Parental Phenotypes	Non-PKU	Non-PKU
Parental Genotypes	Pp	Pp
Gametes	P p	P p

		Non-PKU Mother	
		P	p
Non-PKU Father	P	PP	Pp
	p	Pp	pp

Diagram showing the parental phenotypes, genotypes, gametes and a Punnett square predicting the possible genotypes of their offspring. Both parents are PKU carriers and their offspring have a 25% chance of inheriting the disorder.

- The genetic cross shown on the **Punnett square** above demonstrates that the offspring of the PKU carrier parents have a **75% chance of not having PKU** and a **25% chance of inheriting 2 PKU alleles** and therefore having the condition
- This pattern of inheritance is the same with any autosomal **recessive condition**, for example cystic fibrosis
- Every baby born in the UK and in many other countries around the world are **tested** for several genetic conditions including PKU

- The babies have a small prick of blood taken from the sole of their foot a few days after being born in order to be screened for the condition

Exam Tip

It should be the case that in most exams letters will be chosen for genetic crosses that have very different upper and lowercase appearances. If you are ever asked to use a letter in an exam that has a similar upper and lowercase appearance, such as P and p, make sure to overly exaggerate the difference to ensure there is no ambiguity during marking.

Single Nucleotide Polymorphisms & Multiple Alleles

- Many genes have **more than two alleles**
- However, a **diploid individual** will still **only inherit two of the possible alleles**
- Alleles differ from each other by **one or only a few bases**
- Even a very **small change in base sequence** can bring about a **large effect in gene function**, with a large knock-on effect on the phenotype
- Even though different alleles of a gene have slightly **different base sequences**, they still occupy the **same** locus on the chromosome
- Since the Human Genome Project, **sophisticated techniques** can analyse different alleles
- The exact positions where bases differ between alleles are called **SNPs** or **snips** (Single Nucleotide Polymorphisms)
  - An allele **can have several SNPs** but still only **differ by a few bases** from its other allele

Multiple Alleles: ABO Blood Groups

- Inheritance of blood group is an example of **co-dominance** with **multiple alleles**
- This is of critical importance when deciding to give **blood transfusions** following injury or illness
- Use of the wrong blood group can cause an immune response that coagulates (solidifies) blood, leading to clots and serious illness/death
- There are **three alleles** of the gene controlling a person's blood group instead of the usual two
  - I represents the **gene**
  - **Superscripts** A and B represent the **codominant** alleles, I^A for example
  - Lowercase **i** with no superscript represents the **recessive** allele
- I^A results in the production of **antigen A** on the surface of red blood cells
- I^B results in the production of **antigen B** on the surface of red blood cells
- i results in **no antigens** being produced on the surface of red blood cells
- These three possible alleles can give us the following genotypes and phenotypes

Blood Genotype & Phenotype Table

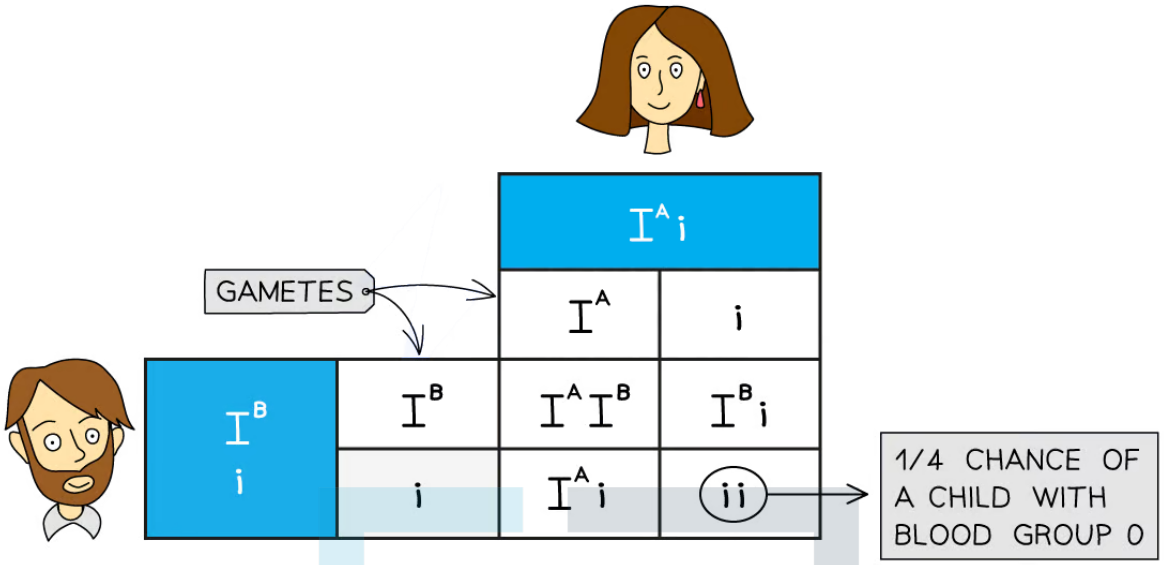
Genotype	Phenotype
I^AI^A or I^Ai	A
I^BI^B or I^Bi	B
I^AI^B	AB
ii	O

- We can use genetic diagrams to predict the outcome of crosses that involve the codominant alleles controlling blood groups

Worked example

Show how a parent with blood group A and a parent with blood group B can produce offspring with blood group O.

Punnett square of the inheritance of blood group



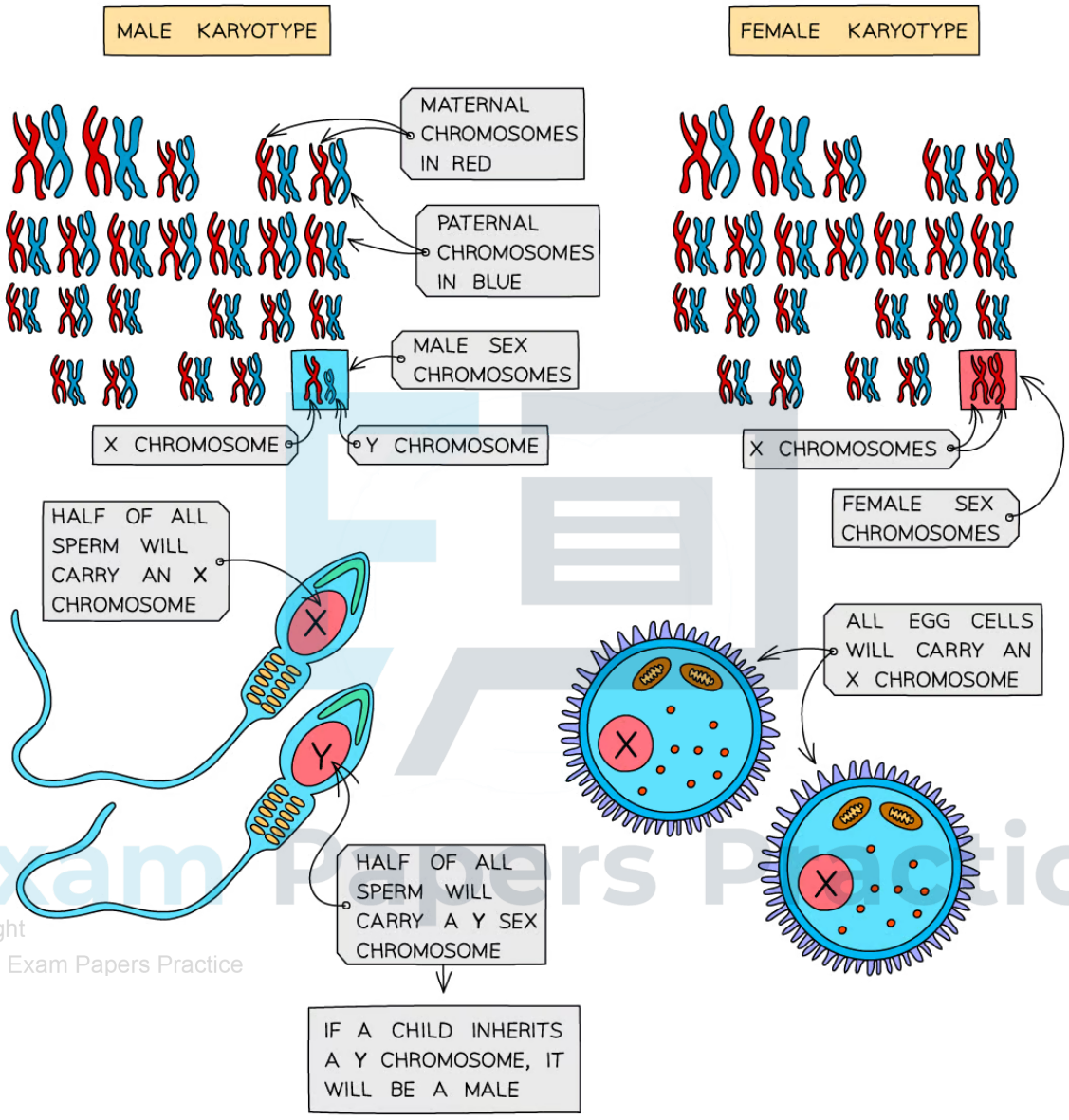
Punnett square showing the inheritance of blood group with two heterozygous parents, type A and type B

Sex Determination

Sex Determination in Humans

- Sex is determined by an **entire chromosome pair** (as opposed to most other characteristics that are just determined by one or a number of genes)
- **Females** have the sex chromosomes (pair 23 in humans) **XX**
- **Males** have the sex chromosomes (pair 23 in humans) **XY**
  - Note that the rule XX for females and XY for males applies to mammals, but not to all species
- All other chromosomes (pairs 1 - 22 in humans) are autosomes and have **no influence on determining the sex** of offspring
- Because only a father can pass on a Y chromosome, he is **responsible for determining the sex of the child**
  - Due to **meiosis**, half of his sperm cells will carry his X chromosome, half his Y chromosome
  - The chromosome carried by **the sperm that fertilises the egg** will determine the sex of the child
  - His daughters receive a copy of his X chromosome
  - His sons receive a copy of his Y chromosome

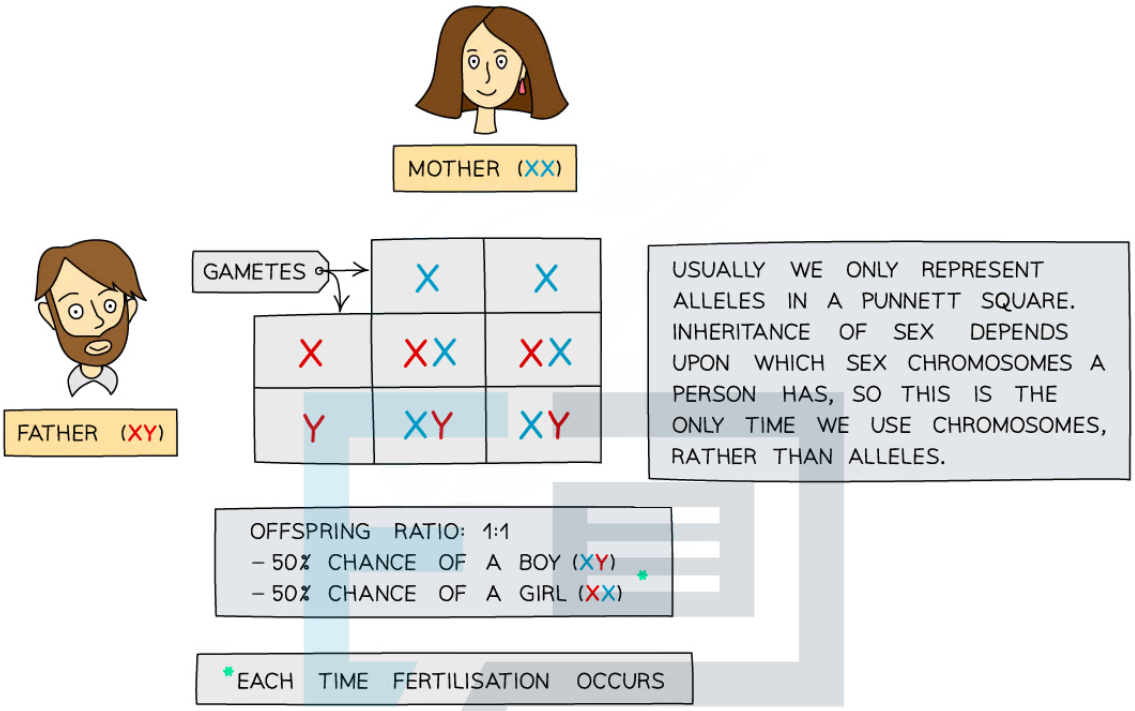
Sex determination in humans diagram



Sperm cells determine the sex of offspring

- The inheritance of sex can be shown using a **genetic diagram** (known as a **Punnett square**), with the X and Y chromosomes taking the place of the alleles usually written in the boxes

Sex determination Punnett square



Punnett square showing the inheritance of sex due to the combination of the X and Y chromosomes from each of the gametes

Genes carried by X and Y chromosomes

- The **X chromosome is larger than the Y**, and has its centromere more central than on the Y chromosome
  - Fewer genes are coded for on the Y chromosome as a result
    - The **X carries around 16 × more genes than the Y** chromosome
  - Non-sex phenotypic traits, including **certain blood clotting factors**, are coded for on the X chromosome but not on the Y
- The Y chromosome carries genes that **code for male characteristics**
- One of these genes is the **SRY gene** which is involved in
  - Development of testes in male embryos
  - Production of testosterone
- Females don't receive these genes, so instead, **ovaries develop** and **female sex hormones** are expressed

Sex Linked Disorders: Haemophilia

- Some genetic diseases in humans are sex-linked
- Inheritance of these diseases is different in males and females
  - Sex-linked genes are only **present on one sex chromosome and not the other**
  - This means the sex of an individual affects what 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
- There are **three phenotypes for females:**
  - normal
  - carrier
  - has the disease,
- **Males have only two phenotypes**
  - norma
  - has the disease

- **Haemophilia** is a well known sex-linked disease
- There is a gene **found on the X chromosome** that codes for a protein called factor VIII. Factor VIII is needed to make blood clot
- There are two alleles for factor VIII
  - The **dominant F** allele which codes for **normal factor VIII**
  - The **recessive f** allele which results in a **lack of factor VIII**, meaning a person has haemophilia
- When a person possesses only the recessive allele **f**, they don't produce factor VIII and their blood can't clot normally
- If males have an abnormal allele, f, they will **have the condition** as they have only one copy of the gene
- Females can be heterozygous for the faulty gene and not suffer from the condition but act as a **carrier**
- This means that haemophilia is a potentially fatal genetic disease which **affects males more than females**

Exam Tip

The expected notation when writing about sex linked alleles is to use upper case 'X' and 'Y' for the chromosome, next to superscript letters to represent the allele. For example

- X^fX^f Homozygous female who has haemophilia or X^FX^f Heterozygous female who is a carrier
- X^fY Male who has haemophilia

Worked example

The genetic diagram below shows how two parents with normal factor VIII can have offspring with haemophilia

Parental phenotypes: carrier female x normal male

Parental genotypes: X^FX^f X^FY

Parental gametes: X^F or X^f X^F or Y

Monohybrid Punnett Square with Sex-linkage Table

		Male gametes	
		X^F	Y
Female gametes	X^F	X^FX^F / female with normal blood clotting	X^FY / male with normal blood clotting
	X^f	X^FX^f / carrier female	X^fY / male with haemophilia

Predicted ratio of phenotypes in offspring

1 female with normal blood clotting : 1 carrier female : 1 male with haemophilia : 1 male with normal blood clotting

Predicted ratio of genotypes in offspring: $1X^FX^F : 1X^FX^f : 1X^FY : 1X^fY$

Exam Tip

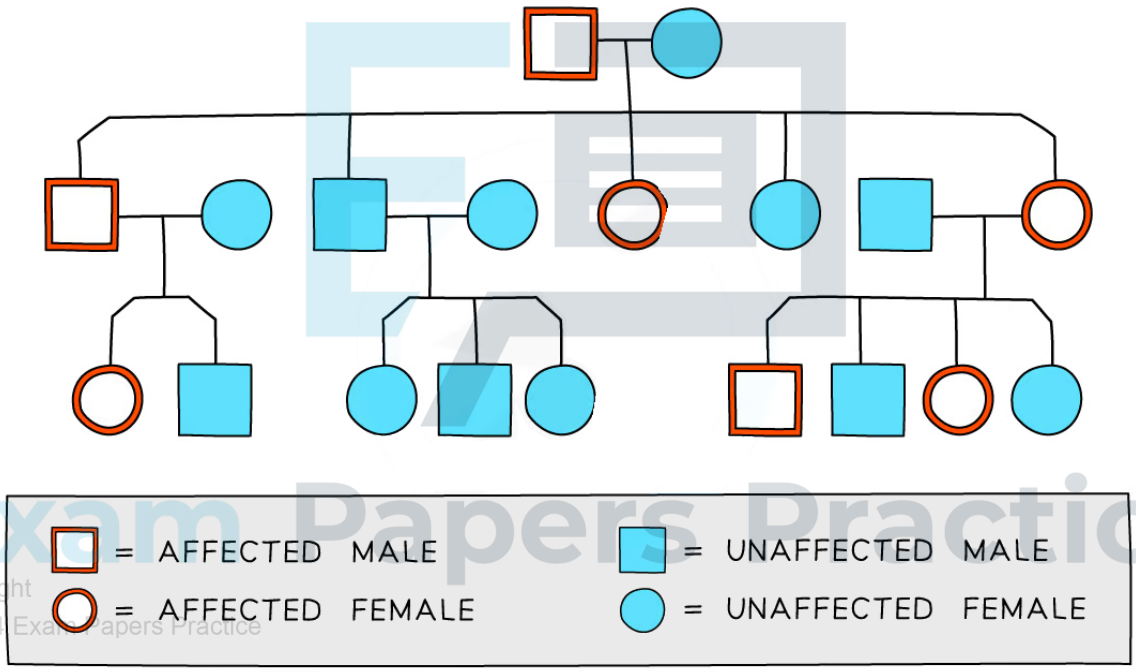
Make sure to include all of your working out when constructing genetic diagrams. It is not enough just to complete a Punnett grid, you need to show that you have thought about the **possible gametes** that can be produced by each parent. Also, remember to state the **phenotype** as well as the genotype of the offspring that result from the cross. Read the questions carefully when answering sex-linked inheritance questions – is the question asking for a probability for **all** children or is it asking about a specific sex (males or females).

Pedigree Charts

Pedigree Charts

- Family pedigree diagrams are usually used to trace the **pattern of inheritance** of a specific characteristic (usually a disease) **through generations of a family**
- This can be used to work out the probability that someone in the family will inherit the **genetic disorder**

Pedigree chart diagram



A family pedigree chart

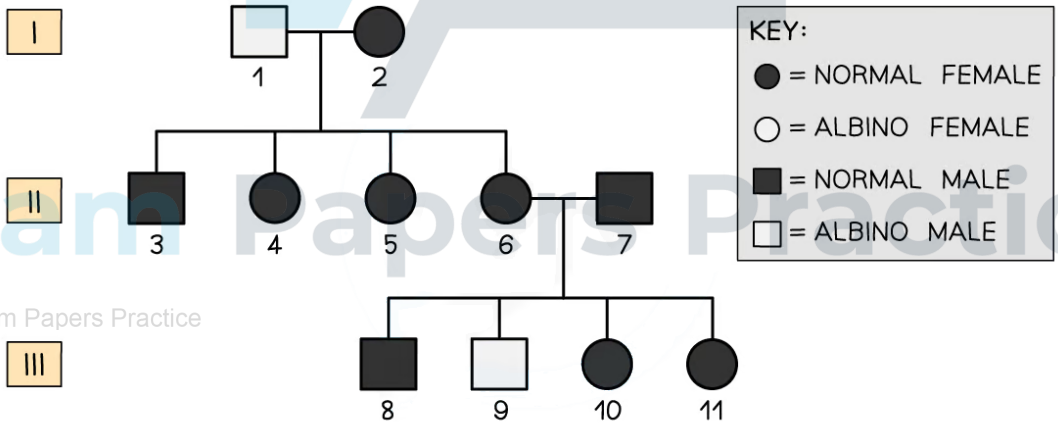
- **Males** are indicated by the **square shape** and **females** are represented by **circles**
- In this diagram, **affected** individuals are **red** and **unaffected** are **blue**
  - **Shading or cross-hatching** may also be used to show affected individuals
- **Horizontal lines** between males and females show that they have **produced children** (which are linked underneath each couple)
- **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:
  - Both males and females are affected
  - Every generation has affected individuals
  - The eldest son (in the second generation) is affected
  - That there is one family group that has no affected parents or children
  - The other two families have one affected parent and affected children as well
- The study of pedigree charts provides an opportunity to appreciate why marriage between close relatives is **prohibited** in many countries
  - Reproducing with close relatives increases the chance that both individuals possess **harmful recessive alleles** that can be passed onto the offspring
  - This causes the offspring to have a much **higher chance** of inheriting **genetic diseases**

Worked example

Worked example: Pedigree charts

- Below is a pedigree chart which traces the inheritance of **albinism** across 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. What type of allele causes albinism?
  2. The genotype of individuals named **9** and **7**
  3. The possible genotypes of **10** and **11**

1. Albinism is caused by a **recessive allele**
   - **Explanation**: We can tell this from the pedigree chart because expression of the disease skips generation II. Also, person number 9 is an affected individual despite his 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.
    - It is unlikely to be a **sex-linked disease as both females and males** have the condition
2. The genotype of person 9 must be **homozygous recessive** (aa) and the genotype of 7 must be **heterozygous** (Aa)
    - **Explanation**: 9 is an affected individual with albinism (which is determined by the recessive allele). 7 must be heterozygous in order for him to pass on the recessive allele to person 9
3. The possible genotypes of 10 and 11 are **heterozygous** (Aa) or **homozygous dominant** (AA)
    - **Explanation**: This is because they are unaffected individuals so must possess at least one dominant allele (A), however, it is possible that they each inherited a dominant allele from each parent

Exam Tip

When answering questions about pedigree charts for genetic diseases, it is always useful to remember which phenotype is caused by the recessive allele. 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.

NOS: Scientists draw general conclusions by inductive reasoning

- **Inductive reasoning** is the idea of making **generalised conclusions** based on **specific evidence** taken from a small sample
    - For example, we could observe a sample of evidence from a pedigree chart and if that observation **deviated from what we would expect** we **could** surmise that the condition could be sex-linked
- **Deductive reasoning** is making **specific deductions** about something unknown based on **known evidence**
    - For example, if two non-affected parents have a child that is affected by a genetic condition we can deduce that the condition is caused by a recessive allele, and that the parents are both carriers of the allele

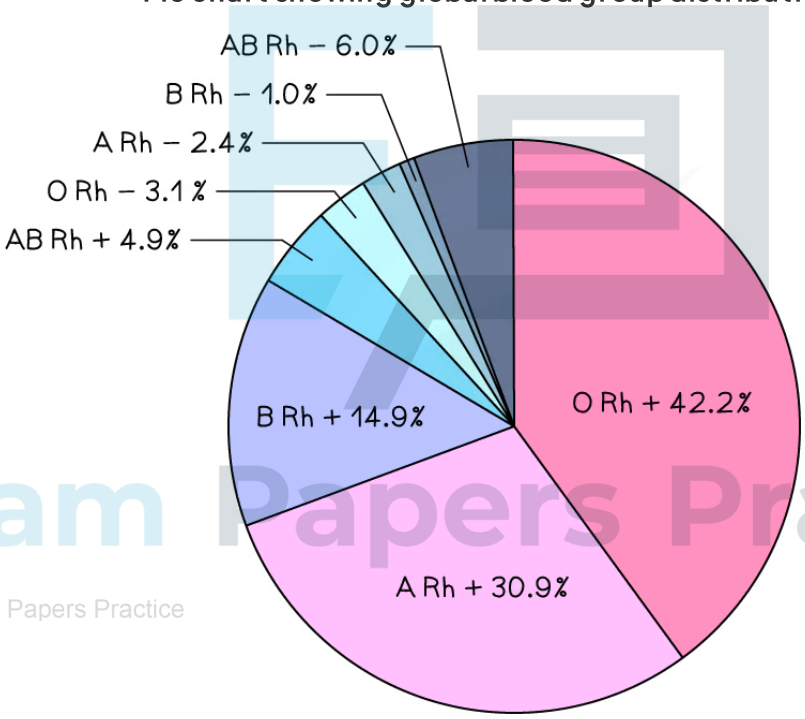
Continuous Variation: Skills

Continuous Variation

Variation can be discrete or continuous

- **Discrete variation** is variation that falls into two or more clear-cut categories with no overlap or in-between categories
  - Blood group is an example of discrete variation
  - All human blood is either group O, A, B or AB, each with a Rhesus factor (+ or -)
- This gives just 8 distinct blood groups:

Pie chart showing global blood group distribution



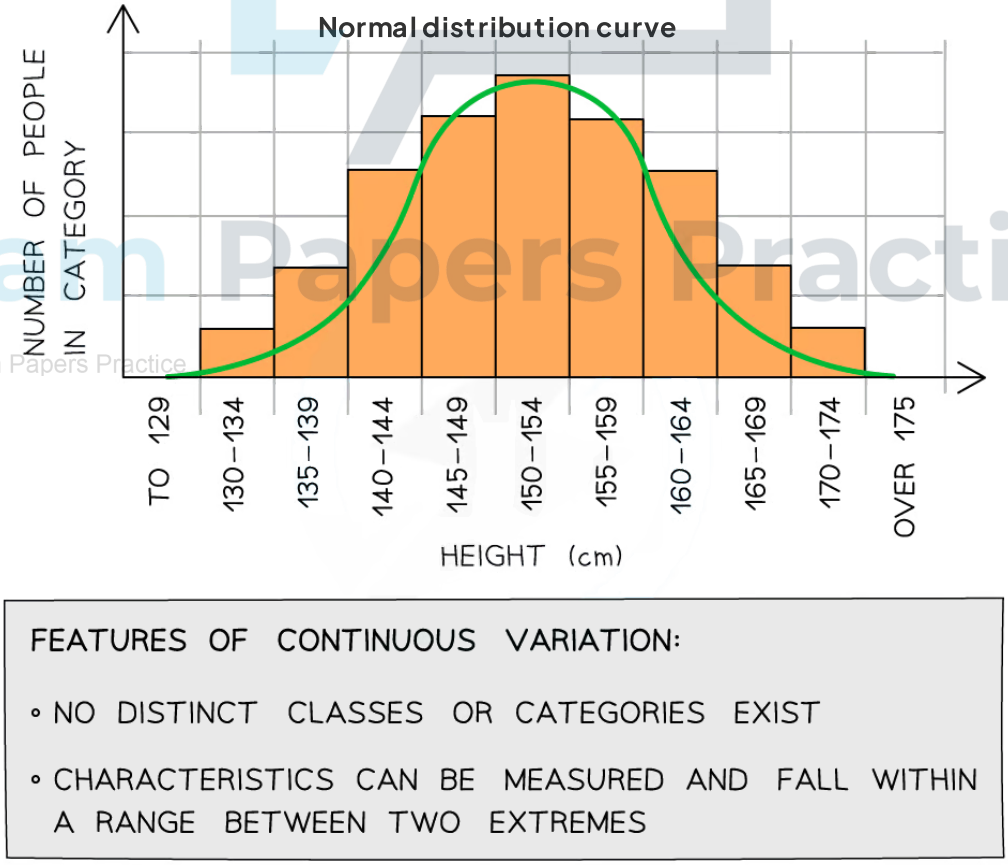
Worldwide A, B, O blood group distribution by percentage, 2019

(data varies regionally with ethnicity)

Continuous Variation

- **Continuous variation** occurs when **two or more genes** affect the final characteristic
- For example, height in humans is determined by **many genetic factors**:

  - Bone length
  - Skeletal muscle structure
  - Ability to absorb food substances effectively
  - Hormone production
  - ...As well as environmental factors like diet, exercise, prenatal nutrition, lifestyle etc
- Most characteristics are determined by more than one gene - a **polygenic** characteristic
- Even **grouped data** like shoe size appears to be discrete but in fact, peoples' feet vary continuously in size
  - Shoe size is merely a practicality for shoe manufacturers, who cannot make exactly the right-sized shoes for everybody
- Continuous variation in birth mass results in the population displaying a **normal distribution** (bell-shaped curve)
  - Environmental factors can also affect birth mass, e.g. mother's diet, presence of a twin, smoking etc
- Continuous variation occurs when there are **quantitative differences** in the phenotypes of individuals within a population for particular characteristics
- Quantitative differences do not fall into discrete categories like in discontinuous variation
  - For example, the mass or height of a human is an example of continuous variation
  - Instead for these features, a **range of values** exist between two extremes within which the phenotype will fall
- The lack of categories and the presence of a range of values can be used to **identify continuous variation** when it is presented in a table or graph



Graph showing population variation in height: an example of continuous variation with quantitative differences

Genetic basis of continuous variation

- This type of variation is caused by an **interaction between genetics and the environment**
- Phenotype = **genotype + environment**
- At the genetic level:
  - Different **alleles** at a single locus have a **small effect** on the phenotype
  - Different **genes** can have the **same effect** on the phenotype and these add together to have an **additive effect**
  - If a large number of genes have a combined effect on the phenotype they are known as **polygenes**
- An example of a **continuous polygenic trait** is **skin colour**
- Skin colour is **determined by several genes** that cause the production of a protein called **melanin**
  - The more melanin is produced, the darker the skin pigmentation becomes
- Skin colour is also influenced by **environmental factors** such as UV exposure, which can cause the skin colour to become darker

Box & Whisker Plots

What are box plots and when should they be used?

- **Box plots** are also known as **box-and-whisker diagrams**
- They are used when we are interested in splitting data up into **quartiles**
- Using quartiles and drawing a box plot allows us to see what is happening at the **low, middle and high points and consider any possible extreme values**

How to draw a box plot

- You need to know **five values** to draw a box plot
  - Lowest data value
  - First quartile
  - Median
  - Third quartile
  - Highest data value
- Usually on **graph paper**, box plots are drawn accurately with the five points marked by **short vertical lines**
  - The middle three values then form a box with the **median line inside**
    - The median will not necessarily be in the middle of the box
  - The box represents the **interquartile range** (middle 50% of the data)
  - The **lowest** data value and **highest** data value are joined to the box by **horizontal lines**
    - These are often called **whiskers**
    - They represent the **lowest 25%** of the data and the **highest 25%** of the data
- You may be given a box plot
  - From which you can read off the five values
  - Calculate other statistics like the **range** and **interquartile range** (IQR)

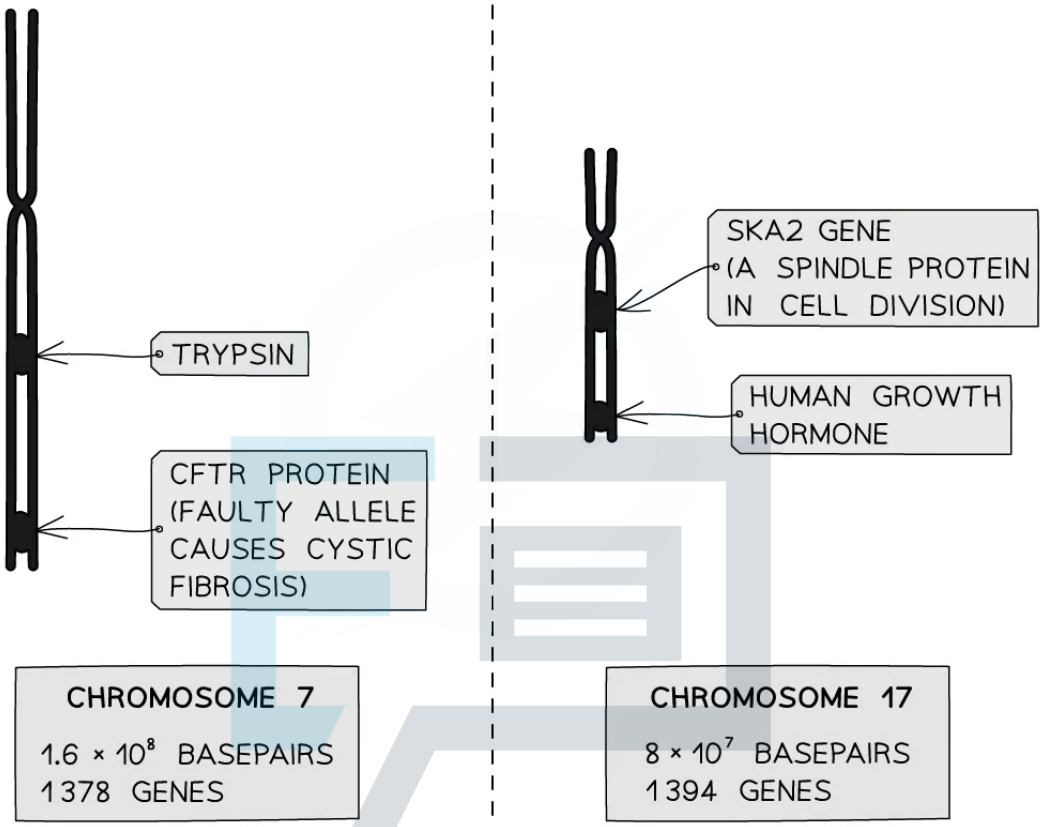
Dihybrid Crosses & Unlinked Genes (HL)

Segregation & Independent Assortment

Unlinked genes segregate independently as a result of meiosis

- **Unlinked genes** are genes that an organism carries on **separate chromosomes**
  - Not on homologous copies of the same chromosome
- An example of a pair of unlinked genes in fruit flies (*Drosophila melanogaster)* is
  - The gene for curly wings on **chromosome 2**, and
  - The gene for mahogany eyes on **chromosome 3**
- An example of a pair of unlinked genes in humans is
  - The gene for trypsin (a stomach enzyme) on chromosome **7**, **and**
  - The gene for human growth hormone on chromosome **17**
- **Assortment** of chromosomes refers to their **alignment** in metaphase I of **meiosis**
  - Each bivalent assorts (aligns) itself **independently** of all the others
- **Segregation** of chromosomes (i.e. how they get separated) is governed by their pattern of assortment
  - Segregation just refers to **which pole of the cell** the whole chromosomes are pulled to in anaphase I
  - Segregation determines **which combinations of alleles** end up in which gamete cells by the end of meiosis II
- We call this Mendel's **Law of Independent Assortment** which states that
  - alleles of different genes are **inherited independently** of one another; in other words inheriting a particular allele for one gene doesn't affect the ability to inherit any other allele for another gene
- By contrast, linked genes (on the same chromosome) tend to be **inherited together**

Linked and unlinked genes diagram



The loci of selected genes in the human genome

Trypsin and CFTR are linked genes (both on the same chromosome);

Human Growth Hormone and trypsin are unlinked genes (both on different chromosomes)

Dihybrid Crosses

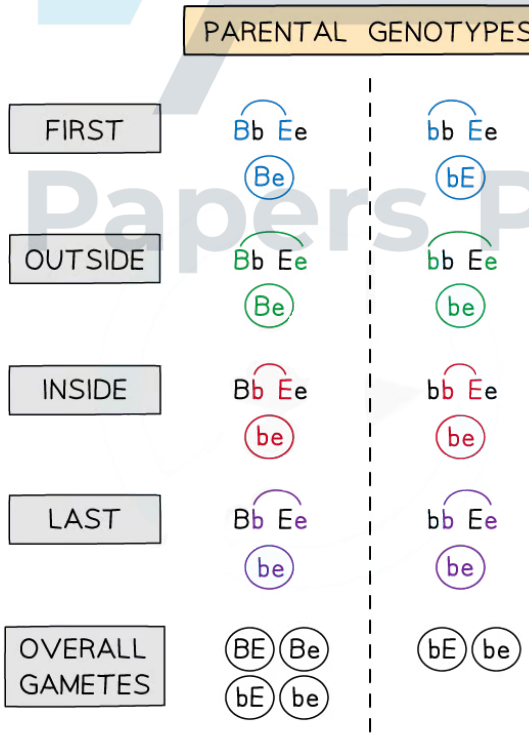
- **Mono**hybrid crosses look at how the alleles of **one** gene transfer across generations
- **Di**hybrid crosses look at how the alleles of **two** genes transfer across generations
  - i.e. dihybrid crosses can be used to show the **inheritance** of **two completely different characteristics** in an individual, for example **unlinked genes**
- The genetic diagrams for both types of cross are very similar
- For dihybrid crosses, there are several more genotypes and phenotypes involved
- When writing out the different genotypes, write the **two alleles for one gene**, followed immediately by the **two alleles for the other gene**
- Do not mix up the alleles from the different genes
  - For example, if there was a gene with alleles **Y** and **y** and another gene with alleles **G** and **g** an example genotype for an individual would be **YyGg**
- Alleles are usually shown side by side in dihybrid crosses e.g. **TtBb**

Worked example

Worked example 1: Dihybrid genetic diagram

- Horses have a single gene for coat colour that has two alleles:
  - **B**, a dominant allele produces a black coat
  - **b**, a recessive allele produces a chestnut coat
- Horses also have a single gene for eye colour
  - **E**, a dominant allele produces brown eyes
  - **e**, a recessive allele produces blue eyes
- Each of these genes (consisting of a pair of alleles) are **inherited independently** of one another because the two genes are located on different non-homologous chromosomes
  - Such characteristics are said to be **unlinked**
- In this example, a horse that is **heterozygous** for both genes has been **crossed** with a horse that is **homozygous** for one gene and **heterozygous** for the other

Parental phenotypes:	black coat, brown eyes	x	chestnut coat, brown eyes
Parental genotypes:	**BbEe**	x	**bbEe**
Parental gametes:	**BE** or **Be** or **bE** or **be**	x	**bE** or **be**



Determining the Alleles Carried by Gametes Based on the Parental Genotypes Using the FOIL (First, Outside, Inside, Last) Method

Dihybrid Cross Punnett Square Table

		Gametes from Parent Two	
		bE	be
Gametes from Parent One	BE	BbEE / black coat, brown eyes	BbEe / black coat, brown eyes
	Be	BbEe / black coat, brown eyes	Bbee / black coat, blue eyes
	bE	bbEE / chestnut coat, brown eyes	bbEe / chestnut coat, brown eyes
	be	bbEe / chestnut coat, brown eyes	bbee / chestnut coat, blue eyes

- Predicted ratio of phenotypes in offspring
  - **3** black coat, brown eyes :
  - **3** chestnut coat, brown eyes :
  - **1** black coat, blue eyes :
  - **1** chestnut coat, blue eyes
- Predicted ratio of genotypes in offspring = **3 BbEE : 3 bbEE : 1 Bbee : 1 bbee**

Statistical Analysis of Dihybrid Crosses (HL)

Chi-squared Test & Dihybrid Crosses

Use of a chi-squared test on data from dihybrid crosses

- The difference between **expected** and **observed** results in experiments can be statistically **significant** or **insignificant** (happened by chance)
- If the difference between results is statistically significant it can suggest that something else is happening in the experiment that isn't being accounted for
  - For example, linkage between genes
- A statistical test called the **chi-squared** test determines whether there is a **significant difference** between the **observed and expected** results in an experiment
- The chi-squared test is completed when the data is **categorical** (data that can be grouped)

Calculating chi-squared values

1. Obtain the **expected and observed results** for the experiment
2. Calculate the **difference** between each set of results
3. Square each difference (as it is irrelevant whether the difference is positive or negative)
4. Divide each squared difference by the expected value and get a sum of these answers to obtain the chi-squared value

THE CHI-SQUARED VALUE, χ^2 IS GIVEN BY THE FORMULA

$$\chi^2 = \Sigma \frac{(O - E)^2}{E}$$

Σ = SUM OF

O = OBSERVED VALUE

E = EXPECTED VALUE

Analysing chi-squared values

- To work out what the chi-squared value means, **a table that relates chi-squared values to probabilities** is used
- If the chi-squared value represents a **larger probability than the critical probability** then it can be stated that the differences between the expected and observed results are **due to chance**
- If it represents a **smaller probability than the critical probability** then the differences in results are **significant** and something else may be causing the differences
- To determine the critical probability biologists generally use a probability of **0.05** ($p = 0.05$)
  - They allow that chance will cause five out of every 100 experiments to be different

- The number of comparisons made must also be taken into account when determining the critical probability. This is known as the **degrees of freedom**

- Every hypothesis test **must** begin with a clear **null hypothesis** (what we believe to already be true) and **alternative hypothesis** (how we believe the data pattern or probability distribution might have changed)
- The **null hypothesis** is denoted $\mathbf{H_0}$ and sets out the assumed population parameter given that no change has happened
  - The standard null hypothesis is that there is **no significant difference** between the expected and observed frequencies, and any difference that does occur is **due to chance**
- The **alternative hypothesis** is denoted $\mathbf{H_1}$ and sets out how we think the population parameter could have changed
  - The standard alternative hypothesis is that there **is a significant difference** between the expected and observed frequencies
- When a hypothesis test is carried out, the null hypothesis is **assumed to be true** and this assumption will either be **accepted** or **rejected**

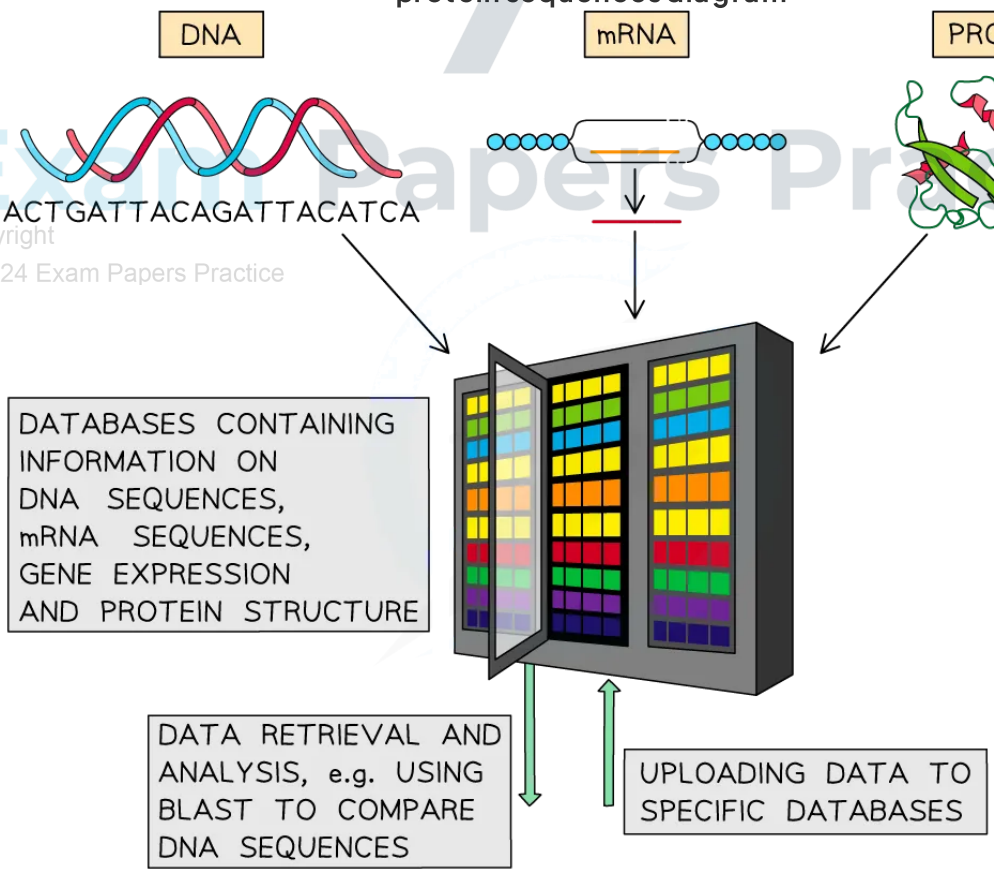
Genes & Polypeptides: Skills (HL)

Genes & Polypeptides: Skills

Use of databases to identify the locus of a human gene and its polypeptide product

- Following the **sequencing of the whole human genome**, we now know the **exact locus** (position) of every gene across the 23 pairs of chromosomes
- Online databases have been built that are able to **locate any known gene or allele**
- Anyone can access these loci
  - One example is the **European Molecular Biology Laboratory** database (EMBL)
- Examples of genes that can be located are
  - The **CFTR protein**, critical to **cystic fibrosis**, on chromosome 7
  - **HBB**, a faulty allele of which is the cause of **sickle-cell anaemia**, on chromosome 11
- If we know the locus of a particular gene, medicine can establish **the location of a faulty allele**, which is often recessive
  - A faulty allele can be cut out of the chromosome by genetic engineering using recombinant DNA technology
  - Replacing a faulty allele could lead to **genetic therapy**
  - Location databases of **cancer-related genes** are often vital information to researchers, doctors and patients involved in cancer genetics

Databases can be used to find and compare information about DNA, mRNA and protein sequences diagram



The use of databases to compare base sequences (and protein sequences) between species

Worked example

- Let's take the example of the gene that has a mutated version that causes cystic fibrosis, called CFTR
- The location of this gene, which can be searched for in the **database**, is **7q31.2**
  - The 7 represents the fact it is found on **chromosome 7**
  - The q represents the fact it is found of the long arm of the chromosome, which is called q
    - The short arm is p
  - 31.2 represents how far away the gene is from the location of the **centromere of the chromosome**
    - The smaller the number, the closer it is to the centromere
- We can compare this information to another gene, which encodes a protein that helps with blood clotting, coagulation factor X. If this gene is mutated it can lead to haemophilia
  - The location of the coagulation factor X gene is **13q34**
  - This is found on chromosome 13
- A conclusion that can be made about these two genes is that they are found on **different chromosomes** and so their inheritance is **not linked**

- Remember that when genes are **located close together** they are **likely** to be inherited together due to **autosome linkage**
- For example, a gene located at 3p24.1 is **not** going to be linked to a gene at 6q13.2 because they are found on **different chromosomes**
- However, a gene located at 3p24.1 **is likely** to be **linked** to a gene found at 3q27.8, and even more likely to be linked to a gene found at 3p18.9, because they are not only on the **same chromosome**, but on the same arm of the chromosome and located close together (a similar distance from the centromere)

Exam Tip

You may be asked to compare this data in an exam and comment on the likelihood of linkage.

Gene Linkage (HL)

Autosomal Gene Linkage

Gene loci are said to be linked if they are on the same chromosome

- **Loci** (singular: locus) refers to the **specific linear positions** on the chromosome that genes occupy
- If genes are on the sex chromosome, they are said to be **sex-linked**
  - Sex-linked genes have characteristics that generally **only affect one gender** of a species
  - These genes are usually **on the X chromosome** because the Y chromosome contains very few genes
  - In humans, **colour-blindness** and **haemophilia** are notable examples of genetic conditions that only affect males
- Linked genes located on the chromosomes 1–22, or any chromosome that is not a sex chromosome (called **autosomes**) are said to be examples of **autosomal linkage**
- The likelihood of genes being inherited together, or the extent to which they are linked, is measured in units called **centimorgans**, in honour of Thomas Hunt Morgan's work

Notation for linked genes

- A common way of denoting linked alleles is to link them with lines, representing the homologous chromosomes
  - E.g. in a cross between a double heterozygous individual where the **dominant alleles G and R are linked** and the **recessive alleles g and r are linked**, the notation would be:

$$\frac{GR}{gr} \times \frac{GR}{gr}$$

Autosomal linkage

- Dihybrid crosses and their predictions rely on the assumption that the genes being investigated behave **independently of one another** during meiosis
- However, **not all genes assort independently** during meiosis
- Some genes which are located on the **same chromosome** display autosomal **linkage** and **stay together in the original parental combination**
- Linkage between genes affects how parental alleles are passed onto offspring through the gametes

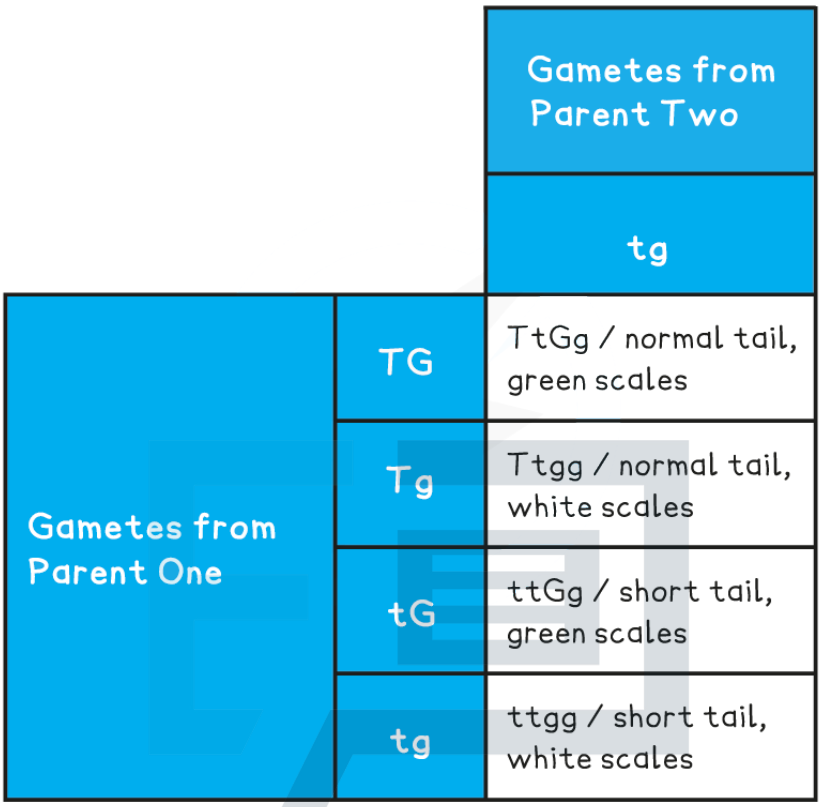
Identifying autosomal linkage from phenotypic ratios

- In the following **theoretical example**, a dihybrid cross is used to predict the inheritance of **two different characteristics** in a species of newt
  - The genes are for **tail length** and **scale colour**
- The gene for tail length has two alleles:
  - Dominant allele **T** produces a normal length tail
  - Recessive allele **t** produces a shorter length tail
- The gene for scale colour has two alleles:
  - Dominant allele **G** produces green scales
  - Recessive allele **g** produces white scales

Without linkage

- The outcomes for this dihybrid cross if the genes are **unlinked** are as follows

Dihybrid Cross without Linkage Punnett Square Table



- Predicted ratio of phenotypes in offspring =
  - 1 normal tail, green scales : 1 normal tail, white scales : 1 short tail, green scales : 1 short tail, white scales
- Predicted ratio of genotypes in offspring =
  - 1TtGg : 1Ttgg : 1ttGg : 1ttgg

With linkage

- However, if the **same dihybrid cross** is carried out but this time the genes are **linked**, we get a **different phenotypic ratio**
  - There would be a **1** : **1** phenotypic ratio (**1** normal tail, green scales : **1** short tail, white scales)
  - This change in the phenotypic ratio occurs because the genes are located on the **same chromosome**
  - The **unexpected phenotypic ratio**, therefore, shows us that the genes are **linked**
- The explanation for this new phenotypic ratio is given in the worked example below:

Worked example

Worked example: Explaining autosomal linkage

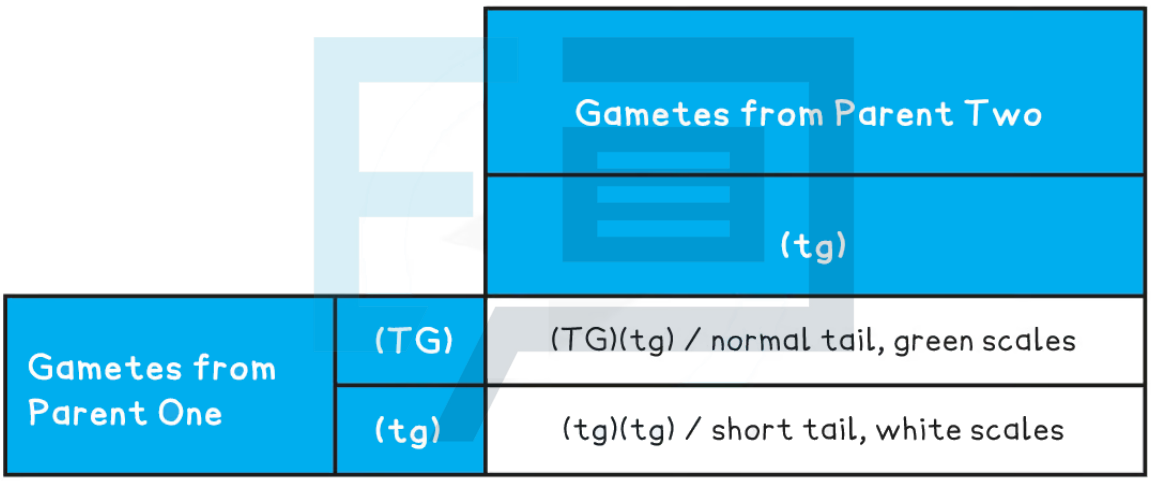
- In reality, the genes for tail length and scale colour in this particular species of newt show autosomal linkage

  Parental phenotypes: normal tail, green scales x short tail, white scales

  Parental genotypes: **(TG)(tg)** **(tg)(tg)**

  Parental gametes: **(TG)** or **(tg)** **(tg)**

Dihybrid Cross with Linkage Punnett Square Table



- Predicted ratio of genotypes in offspring =
  - **1** (TG)(tg) : **1** (tg)(tg)
- Predicted ratio of phenotypes in offspring =
  - **1** normal tail, green scales : **1** short tail, white scales

Exam Tip

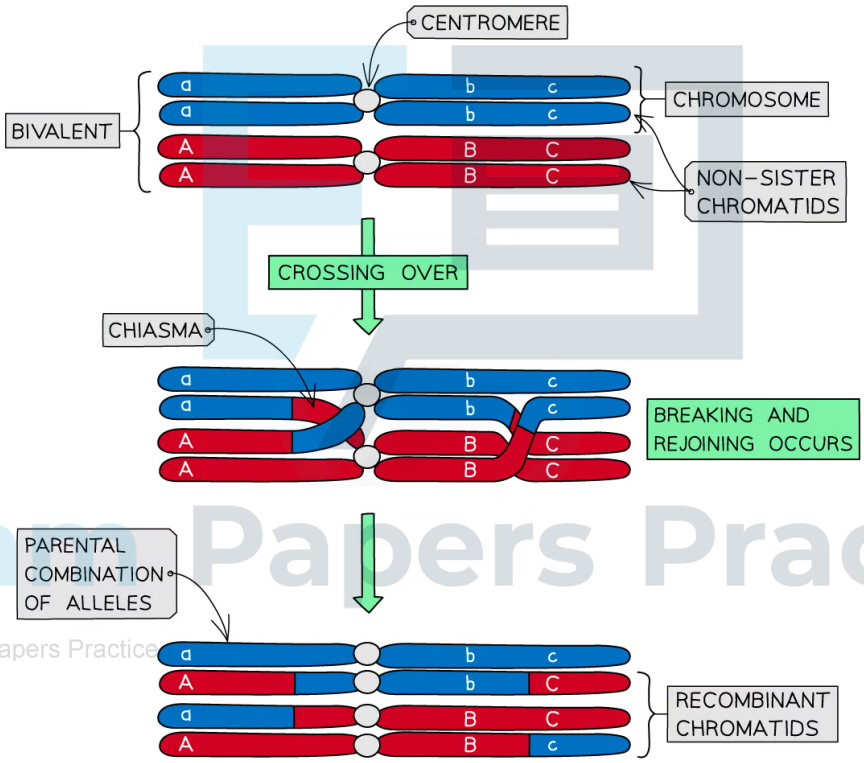
When you are working through different genetics questions you may notice that test crosses involving autosomal linkage predict solely **parental type** offspring (offspring that have the same combination of characteristics as their parents). However in reality **recombinant** offspring (offspring that have a different combination of characteristics to their parents) are often produced. This is due to the **crossing over** that occurs during meiosis. The crossing over and exchanging of genetic material **breaks the linkage** between the genes and recombines the characteristics of the parents. So if a question comes along that asks you why recombinant offspring are present you now know why!

Identifying Recombinants (HL)

Identifying Recombinants

- Genetic diagrams involving autosomal linkage often predict solely **parental type** offspring (offspring that have the same combination of characteristics as their parents)
- However in reality **recombinant** offspring (offspring that have a different combination of characteristics to their parents) are often produced
  - This is due to the **crossing over** that occurs during **meiosis**
  - The crossing over and exchanging of genetic material **breaks the linkage** between the genes and recombines the characteristics of the parents

Crossing over of bivalents diagram



The process of crossing-over results in recombinant phenotypes that can differ from the parental phenotype.

- The frequency of recombinants within a population will nearly always be less than that of non-recombinants
  - Crossing over is **random** and chiasmata form at different locations with each **meiotic** division
- **Recombination frequency** between two linked genes is **greater when genes are further apart** on the same chromosome
  - There are more possible locations for a **chiasma** to form between the genes

Identifying recombinants using test crosses

- **Test crosses** are often used to determine unknown genotypes
- Similarly, they can be used to **identify recombinant phenotypes in offspring**
- An individual is crossed with a **homozygous recessive individual (for both traits)**
  - If **any** of the offspring possess a **non-parental phenotype** then they are labelled as **recombinants**
    - These individuals have **new allele combinations** due to the process of crossing over during meiosis leading to the exchange of genetic material between chromosomes

Drawing a Punnett square to show dihybrid inheritance of linked genes

- A number of sweet pea plants were generated by crossing double-homozygous dominant plants (**PL**)(**PL**) with double-homozygous recessive plants (**pl**)(**pl**) to produce a 100% heterozygous F_1 generation (**PL**)(**pl**) as expected
- Members of this generation then interbreed to produce the F_2 generation
- Alleles:
  - **P** = purple flowers, dominant to **p** = red flowers
  - **L** = long seeds, dominant to **l** = round seeds

Possible Gametes Table

Grandparent of F2 generation – genotypes	$\frac{PL}{PL}$ x $\frac{pl}{pl}$
Gametes	PL pl
F1 generation genotype	$\frac{PL}{pl}$
Due to crossing over, the F1 generation will produce some recombinant gametes as well as a majority of parental ones	
F1 x F2 cross – genotypes	$\frac{PL}{pl}$ x $\frac{PL}{pl}$
Gametes – parental These will be abundant	PL pl PL pl
Gametes – recombinant These will be scarce	pL Pl pL Pl

F_2 Punnet Square Showing Possible Genotypes

		Gametes from F_1 generation, parent 1			
		P L	p l	p L	P l
Gametes from F_1 generation, parent 2	P L	P L / P L	P L / p l	P L / p L	P L / P l
	p l	p l / P L	p l / p l	p l / p L	p l / P l
	p L	p L / P L	p L / p l	p L / p L	p L / P l
	P l	P l / P L	P l / p l	P l / p L	P l / P l

- According to Mendelian ratios and the Punnett square, the F_2 generation should follow the typical 9:3:3:1 ratio
- However, in reality, the **frequency of recombinant gametes will be much lower** than that of parental gametes
  - This affects the resulting offspring phenotypes, with **fewer recombinant phenotypes occurring** than expected

Expected vs Predicted Phenotypes Table

EXPECTED phenotype % in F_2 offspring (9 : 3 : 3 : 1 ratio)	ACTUAL phenotype % in F_2 offspring	Phenotype	Observations
56%	70%	Purple flower, long pollen grains	More than expected
19%	5%	Purple flower, round pollen grains	Less than expected
19%	6%	Red flower, long pollen grains	Less than expected
6%	19%	Red flower, round pollen grains	More than expected

Observations

- More of the F_2 offspring than expected showed the **parental phenotypes**
- **Fewer** plants with **recombinant phenotypes** were produced than the 9:3:3:1 ratio would suggest

- The actual ratios found were referred to as '**non-Mendelian**' as they didn't follow Mendel's pattern
- However, this was not zero; **some recombinants** were still being produced

Possible Theories to Explain These Findings

- At the time, it was known that **many genes were carried on a few chromosomes**
- The idea that certain genes **share the same chromosome** was being developed by many scientists
- This suggested that genes **could be inherited together**, not by the law of independent assortment as put forward by Mendel
- The idea of linkage of genes was developed to explain the non-Mendelian ratios
  - The frequency of recombinant phenotypes is **lower** because **crossing over is a random process** and the chiasmata do not always form in the same place for each meiotic division
  - The frequency of recombinant gametes also depends on the **closeness of linkage** between the two genes
    - Genes located **close together** on a chromosome are **less likely** to be separated by crossing over
    - So recombinants of those two genes will be less frequent
- Thomas Hunt Morgan later provided proof of linkage to explain non-Mendelian ratios in his experimentation with fruit flies (*Drosophila melanogaster*)

Exam Tip

Remember to distinguish between sex linkage and autosomal linkage. The explanation of non-Mendelian ratios falls into the domain of autosomal linkage for IB.