INHERITANCE

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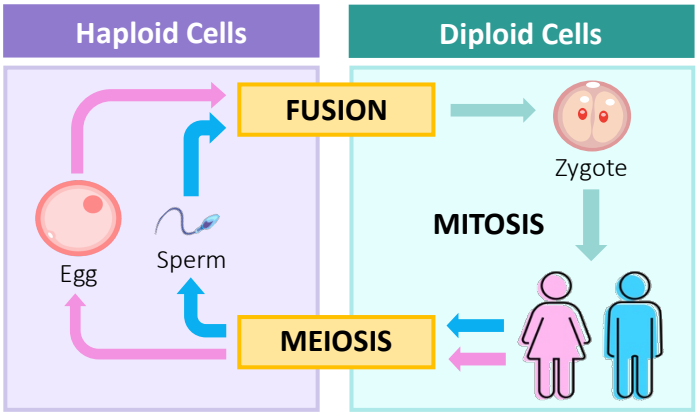
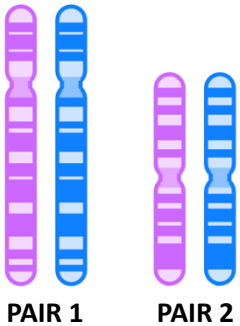
SEXUAL LIFE CYCLE

Gametes are sex cells formed by the process of meiosis – males produce sperm and the females produce ova. The gametes are **haploid**, meaning they only possess one copy of each chromosome. When egg and sperm fuse during fertilisation, the resulting offspring will contain two copies of each chromosome (these cells are classed as **diploid**). These new diploid cells will be genetically unique as they contain chromosomes from two sources.



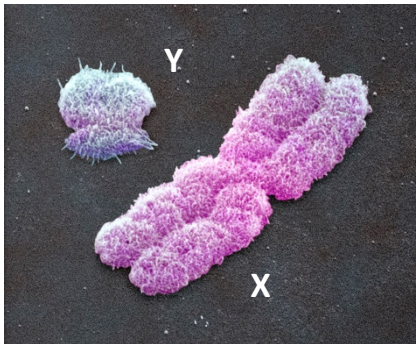
AUTOSOMES

In all sexually reproducing organisms, chromosomes will exist as homologous pairs (i.e. a maternal copy and a paternal copy). The homologous pairs will have identical structures (same size, same centromere position, same banding patterns) and will also carry the same sequence of genes at the same loci positions. However, as the paired chromosomes came from different origins (maternal versus paternal copy), the two alleles at each gene locus may be different. Any chromosome that *always* exists as a matched pair is called an **autosome** (i.e. not the sex chromosomes).



SEX CHROMOSOMES

In diploid organisms, sex is determined by a pair of chromosomes called sex chromosomes (**heterosomes**). Unlike autosomes, sex chromosomes are not homologous and possess different genes. Sex in humans will be determined by the **XY system**. Males possess an X chromosome and a much shorter Y chromosome (XY), while females possess two copies of the larger X chromosome (XX). The Y chromosome contains the genes responsible for developing the male sex characteristics. In its absence, the female sexual characteristics will alternatively continue to develop.



GENOTYPE

All members of a single species will share identical genes, but individuals may possess different versions of a specific genetic characteristic. These alternate forms of a gene are called **alleles**. Alleles typically differ by only one or a few bases and new alleles can be made via **gene mutations**. The complete set of alleles that a given organism possesses is called the genotype – it reflects the genetic identity of a particular individual.

Gene: Eye

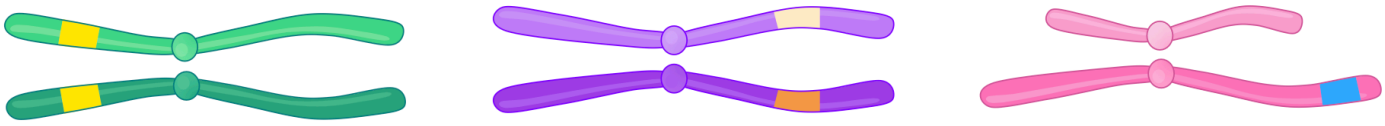
Alleles: Different shades (brown, blue, green, etc.)

TYPES OF ZYGOSITY

For any given gene, the combination of alleles (genotype) can be categorised as follows:

- **Homozygous:** If maternal and paternal alleles are the **same**, the genotype is said to be homozygous
- **Heterozygous:** If maternal and paternal alleles are **different**, the genotype is said to be heterozygous

Males have different sex chromosomes (XY), meaning they have only one allele for each sex-linked gene. When there is only **one copy** of an allele for a gene, the individual is said to be **hemizygous** for that gene. Individuals who are hemizygous cannot be carriers of recessive disease conditions – this is the reason why X-linked recessive disorders occur more commonly in males.



HOMOZYGOUS
Alleles are the same

HETEROZYGOUS
Alleles are different

HEMIZYGOUS
Only one allele (males)

PHENOTYPE

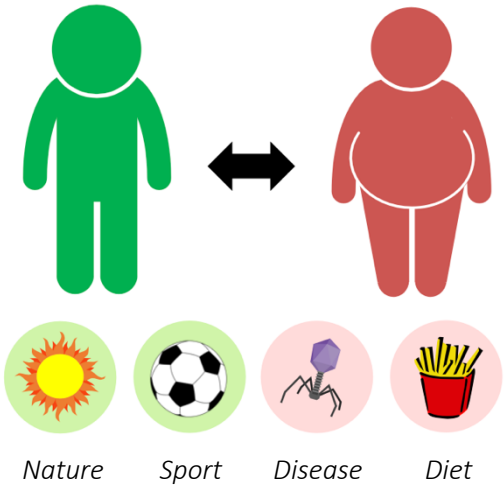
Phenotype describes all of the **observable characteristics** of a given organism, and will be influenced by both the genotype and the environment. Unlike the genotype, which represents the gene sequences, the phenotype is a reflection of the proteins that are produced. The type of proteins produced by a cell will be determined by the genotype, but the activity or expression of the proteins can be impacted by a variety of environmental factors. For example, production of skin pigment (melanin) is influenced by sun exposure.

EPIGENETICS

While the genotype is an important factor in determining the physical expression of inheritable characteristics (phenotype), it is not the only contributing factor. A phenotype can also be influenced by the patterns of expression of particular genes.

Epigenetics describes differences that are caused by changes in gene expression, rather than by changes within the allele sequence (**phenotypic plasticity**). There are various factors that determine whether a given gene is switched on or off:

- **Diet:** Certain foods trigger specific metabolic responses
- **Lifestyle:** Gene expression is influenced by activity levels
- **Environment:** External conditions (UV) can activate genes
- **Pathogens:** Diseases result from a loss of homeostasis



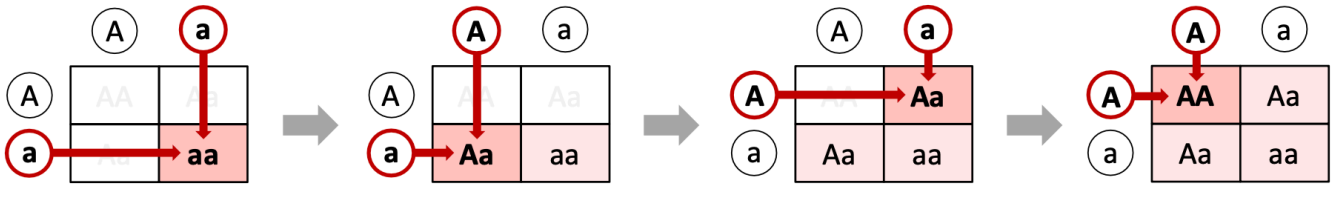
Epigenetics can influence phenotype

GENETIC CROSSES

Genetic crosses determine the allele combinations and phenotypes for potential offspring. Genetic crosses are often conducted using plants, as pollen transfer requires external agents that can easily be controlled and this allows breeding to be carefully manipulated. Plants also have the benefit of being able to produce many seeds in short periods of time. Genetic crosses can be performed according to the following steps:

- Designate potential alleles (dominant = capital letter, recessive = lowercase, codominant = superscript)
- Write down the genotype and phenotype of the prospective parents (this is the P generation)
- Draw a grid with maternal gametes on the top and paternal gametes on the left (this is a **Punnett grid**)
- Complete the Punnett grid to determine the genotypes and phenotypes of offspring (F_1 generation)

Parental Generation: Aa × Aa



F_1 Generation: 1 AA : 2 Aa : 1 aa (3 dominant : 1 recessive)

MODES OF INHERITANCE

A monogenic trait describes a characteristic that is encoded by a **single gene**. The two alleles may interact in different ways to affect the physical expression of the trait (phenotype). The way in which alleles are expressed is called the mode of inheritance. Different patterns can arise depending on the allele behaviour:

- **Complete dominance:** One allele is expressed (dominant) over another allele (recessive)
- **Codominance:** Both alleles are autonomously expressed to create a dual phenotype (both present)
- **Incomplete dominance:** Neither allele is completely expressed, resulting in a blended phenotype
- **Sex-linkage:** The gene is on a sex chromosome and so the inheritance will demonstrate sex bias

1. COMPLETE DOMINANCE

Most traits follow a classical dominant / recessive pattern of inheritance, whereby one allele is expressed over the other allele. The dominant allele will mask the recessive allele when in a heterozygous state and the homozygous dominant and heterozygous forms will therefore be phenotypically indistinguishable (the recessive allele will only ever be able to be expressed within the phenotype when in a homozygous state).

When representing alleles, the convention is to capitalise the dominant allele and use a lowercase letter for the recessive allele (same letter must be used as the alleles are alternative versions of the same gene).

- **Example:** Mouse colour coats – black fur coats (BB or Bb) are dominant to brown fur coats (bb)

PHENOTYPE (Coat colour)			
GENOTYPE	BB (black)	Bb (black)	Bb (brown)

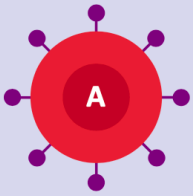
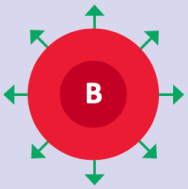
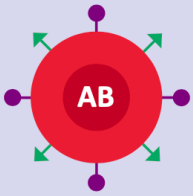
An example of a genetic disorder caused by a recessive allele is **phenylketonuria**. This disorder is caused by a mutation to the gene that codes for an enzyme needed to convert phenylalanine into tyrosine. The excess phenylalanine is instead converted into phenyl ketone – which builds up to toxic levels within the blood and urine. Untreated PKU can lead to brain damage and mental retardation, as well as other serious medical issues. PKU is treated by enforcing a strict diet that restricts the intake of phenylalanine to prevent its build up within the body. This low-protein diet should include certain types of fruits, grains and vegetables, along with precise quantities of amino acid supplements. Because the condition is recessive, both parents must either have the condition themselves or be heterozygous carriers in order to pass the disease to offspring.

2. CODOMINANCE

Codominance occurs when pairs of alleles are *both expressed equally* in the phenotype of a heterozygote. Heterozygous individuals therefore have a different phenotype in comparison to homozygous dominant individuals as the alleles are having a joint effect.

When representing alleles, the convention is to use a common capital letter with **superscripts** to represent the different versions of the dominant allele (recessive alleles are still represented with a lowercase letter).

- **Example:** Human blood groups – I^A and I^B alleles are codominant, allowing for an AB blood group ($I^A I^B$)

BLOOD TYPE	A	B	AB	O
GENOTYPE	$I^A I^A$ or $I^A i$	$I^B I^B$ or $I^B i$	$I^A I^B$	ii
PHENOTYPE				

Fun fact: As the immune system targets foreign markers, O blood is the universal donor type (no markers).

3. INCOMPLETE DOMINANCE

Incomplete dominance occurs when two characteristics *blend together* in the phenotype of a heterozygote. An example of incomplete dominance can be seen in the flower colour of *Mirabilis jalapa* (commonly called the four o'clock flower or the marvel of Peru). When plants with dark pink flowers ($C^P C^P$) are crossed with white-flowered plants ($C^W C^W$), the offspring will have light pink flowers ($C^P C^W$). This reflects the fact that neither allele for flower colour (dark pink or white) is wholly dominant or recessive, so the heterozygous combination will produce a blended trait. The lighter colouration is caused by the fact that only the allele for a dark pink flower codes for pigment (white flowers produce no pigment), so heterozygotes produce less amounts of pigment overall – leading to the lighter colouration.

4. SEX LINKAGE

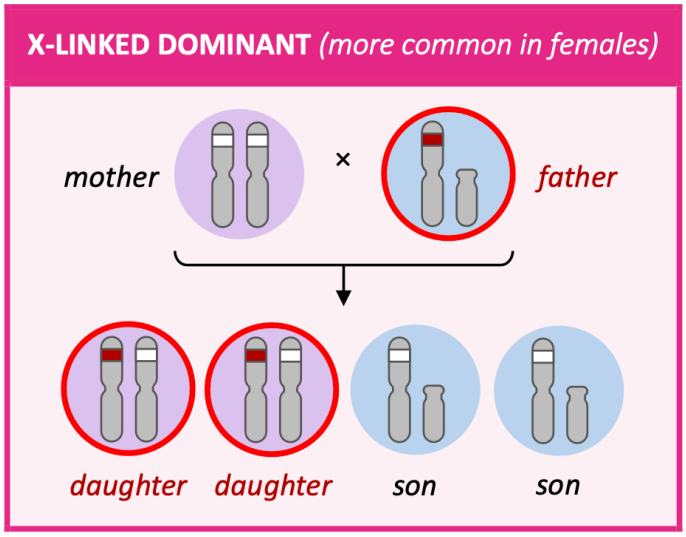
Sex linkage refers to when a gene is found on a sex chromosome (X or Y). Because males and females have different combinations of sex chromosomes (males = XY ; females = XX), the patterns of inheritance will be different according to the sex of the offspring. Sex linkage typically refers to **X-linked genes** specifically, as the Y chromosome is very short and has very few genes present (< 100). Sex linked alleles are represented as superscripts attached to the relevant sex chromosome (example: X^A or X^a).

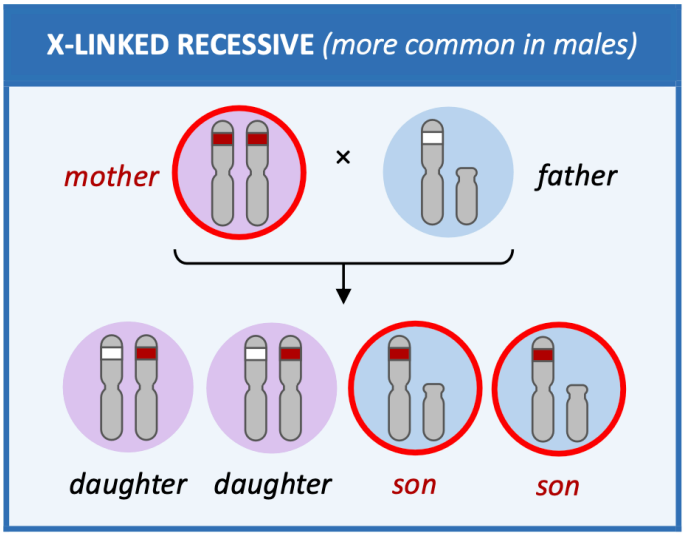
X-Linked Dominant Traits:

- As females possess two X chromosomes, an X-linked dominant trait will be more common in women
- An affected father always has affected daughters (daughters must inherit the father's X chromosome)
- Sons only inherit the condition if the mother is affected (sons inherit their X chromosome from mother)

X-Linked Recessive Traits:

- As males only possess one X chromosome, an X-linked recessive trait will be more common in men
- This is because males cannot be carriers for X-linked recessive traits (they cannot be heterozygous)
- Affected mothers always have affected sons, while unaffected fathers cannot have affected daughters





An example of an X-linked recessive disorder is **haemophilia**. Haemophilia is a genetic disorder whereby the body's ability to control blood clotting (and hence stop bleeding) is impaired. The gene responsible for controlling the clotting cascade is located on the X chromosome, meaning it occurs more frequently in males. Females can only develop haemophilia if they possess two recessive alleles (one from each parent), which means that the father must be a haemophiliac for the daughter to be affected.

PEDIGREE CHARTS

A pedigree is a chart of the genetic history of a family over several generations. Males are represented as squares (☐), while females are represented as circles (○). **Shaded symbols** denote a condition of interest. A horizontal line between man and woman represents mating, and all offspring are shown as offshoots. Generations are listed using roman numerals (I, II, III, IV, etc.) and individuals are numbered from eldest to youngest (for example: the youngest of three grandchildren would be labelled as III-3).

Certain patterns in a pedigree chart can be used to identify the mode of inheritance for a given condition:

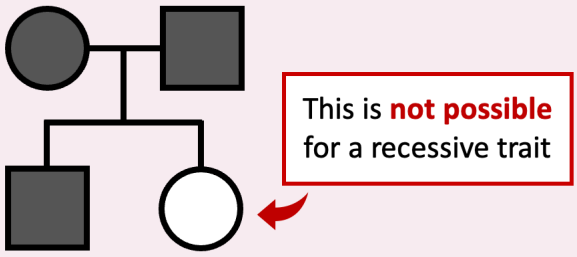
- **Autosomal dominant:** If both parents are *affected* and any offspring are not, the condition must be dominant (unaffected offspring are homozygous recessive and both parents must be heterozygous).
- **Autosomal recessive:** If both parents are *unaffected* and any offspring are not, the condition must be recessive (affected offspring are homozygous recessive and both parents must be heterozygous).

It is <u>not</u> possible to conclusively determine sex linkage from pedigree charts, as autosomal traits could potentially generate the same results. However certain trends can show that a trait is **not** sex-linked:

- **X-linked dominant:** If a male is affected, all daughters must be affected. An unaffected mother cannot have an affected son (or an affected father). Traits will tend to occur more frequently in females.
- **X-linked recessive:** If a female is affected, all sons must be affected. An unaffected mother can have affected sons if she is a carrier (heterozygous). Traits will tend to occur more commonly in males.

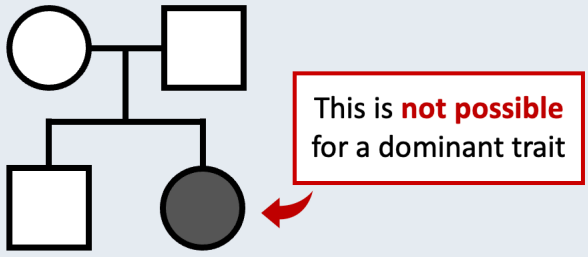
For Dominant Traits:

Both parents affected and any offspring are not



For Recessive Traits:

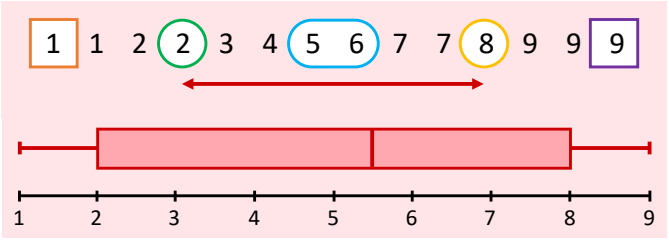
Neither parent is affected and any offspring are



POLYGENIC INHERITANCE

Some characteristics are determined by the interaction of **multiple genes** (polygenic traits). These traits will consequently exhibit a far greater spectrum of variation (i.e. **continuous variation**). Traits that exhibit continuous variation will be normally distributed and include human height, weight and skin colouration.

Continuous variation can be represented graphically via **box-and-whisker** plots. These plots can show the spread of data by identifying minimum, maximum and median values. Outliers can be identified as falling outside the first or third quartiles by a value of more than 1.5 times the interquartile range (IQR).



Min = 1	Max = 9	Median = 5.5
Q1 = 2	Q3 = 8	IQR = 8 – 2 = 6

Minimum Outlier = 2 – (1.5 × 6) = less than –7

Maximum Outlier = 8 + (1.5 × 6) = more than 17