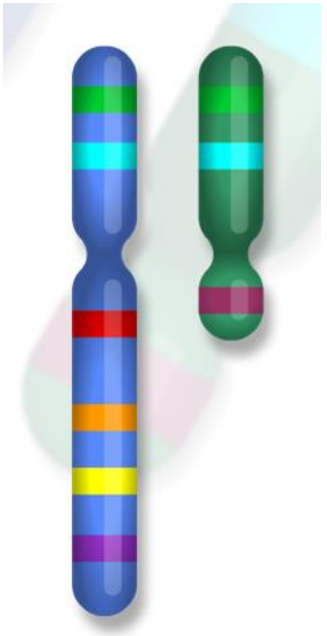
5.5 Genes and patterns of inheritance



Mendel's laws of Inheritance:

1st Law = The law of segregation of factors states that "*when any individual produces gametes, the alleles separate, so that each gamete receives only one allele".* Shown by the separation of homologous chromosomes, carrying the alleles, during anaphase 1 of meiosis.

2nd Law = The law of independent assortment states that *"during gamete formation, the segregation of the alleles of one gene is independent of the segregation of the alleles of another gene".* Shown by the random arrangement of the homologous pairs on the equator of the spindle at metaphase 1 of meiosis and then their separation during anaphase 1.

Homework for Friday/study work tomorrow:

- **Finish Monohybrid crosses**
- **Complete q5 of PPQ (at back)**
- **Read to p8 and attempt any questions in pencil**

5.5.1 Understand the terms genotype and phenotype

- Genetics is the study of **inheritance**.
- Much of our understanding of genetics is due to the work of Gregor **Mendel**, a Czechoslovakian monk, who in the 1850s carried out a vast number of breeding experiments in the garden of his monastery. He concentrated on the garden pea because it had many distinct and easily identifiable characteristics; including flower colour, pea shape and pea colour that varied from plant to plant.

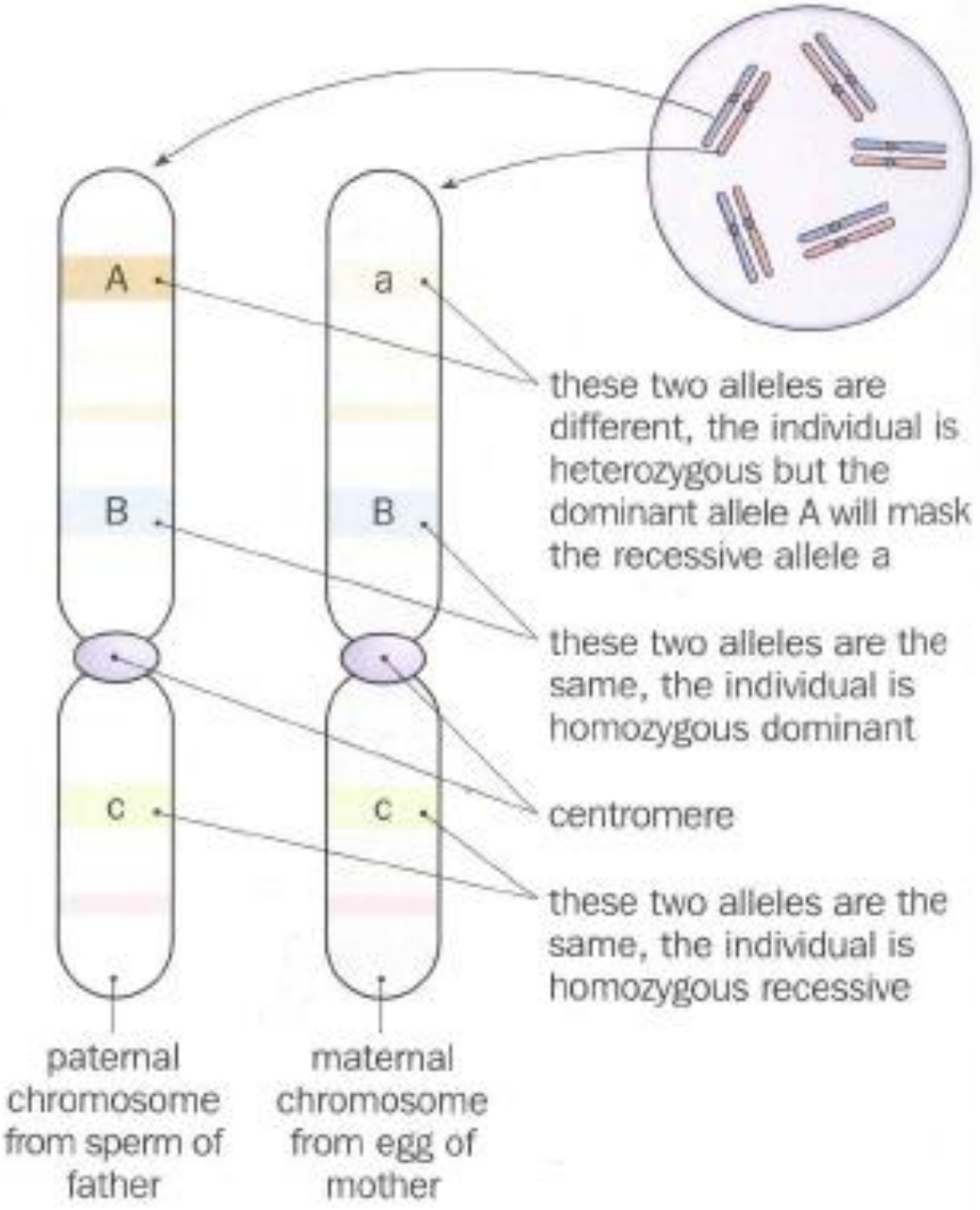
Figure 3.7 Round and wrinkled peas

- Mendel carried out a range of breeding experiments in which he crossed plants carrying particular characteristics that he was interested in. By careful observation of the offspring, he was able to draw conclusions about the nature of inheritance.
- Mendel completed his work without being aware of the existence of chromosomes or genes. Although he published his work in 1866, it was largely ignored and it was only at the start of the 20th Century when chromosomes were discovered under the microscope that the significance of his findings was appreciated. Although additional research and knowledge has increased our understanding of genetics in recent times, it is important to note that this knowledge has built on Mendel's findings, not contradicted them.
- In recognition of his work, the genetics that we study is called **Mendelian** Genetics.

Useful Definitions

- **Genes** are lengths of DNA which code for a particular polypeptide or trait. They carried on the chromosomes and as chromosomes are found in pairs, the genes are also found in pairs. For any characteristic there are alternative or different forms of the gene and these are called **alleles**.
- **Alleles** occur in the same position on the chromosome called the **locus**, many genes have two alternative alleles but some may have more.
- An allele that is always expressed (shows its effect) is said to be **dominant** – given with a capital letter.

- An allele that is only expressed when no dominant is present is said to be **recessive** – given with a lower case letter.
- If the individual has two alleles the same they are **homozygous** for that characteristic (either dominant or recessive).
- If the individual has two different alleles they are **heterozygous** for that characteristic.
- The genetic make up of an individual is known as its **genotype**.
- The expression of the genotype (the characteristics we can see) is called its **phenotype**. This may of course also be influenced by the **environment** (diet, sunlight etc.)


A
a
B
B
c
c
these two alleles are different, the individual is heterozygous but the dominant allele A will mask the recessive allele a
these two alleles are the same, the individual is homozygous dominant
centromere
these two alleles are the same, the individual is homozygous recessive
paternal chromosome from sperm of father
maternal chromosome from egg of mother

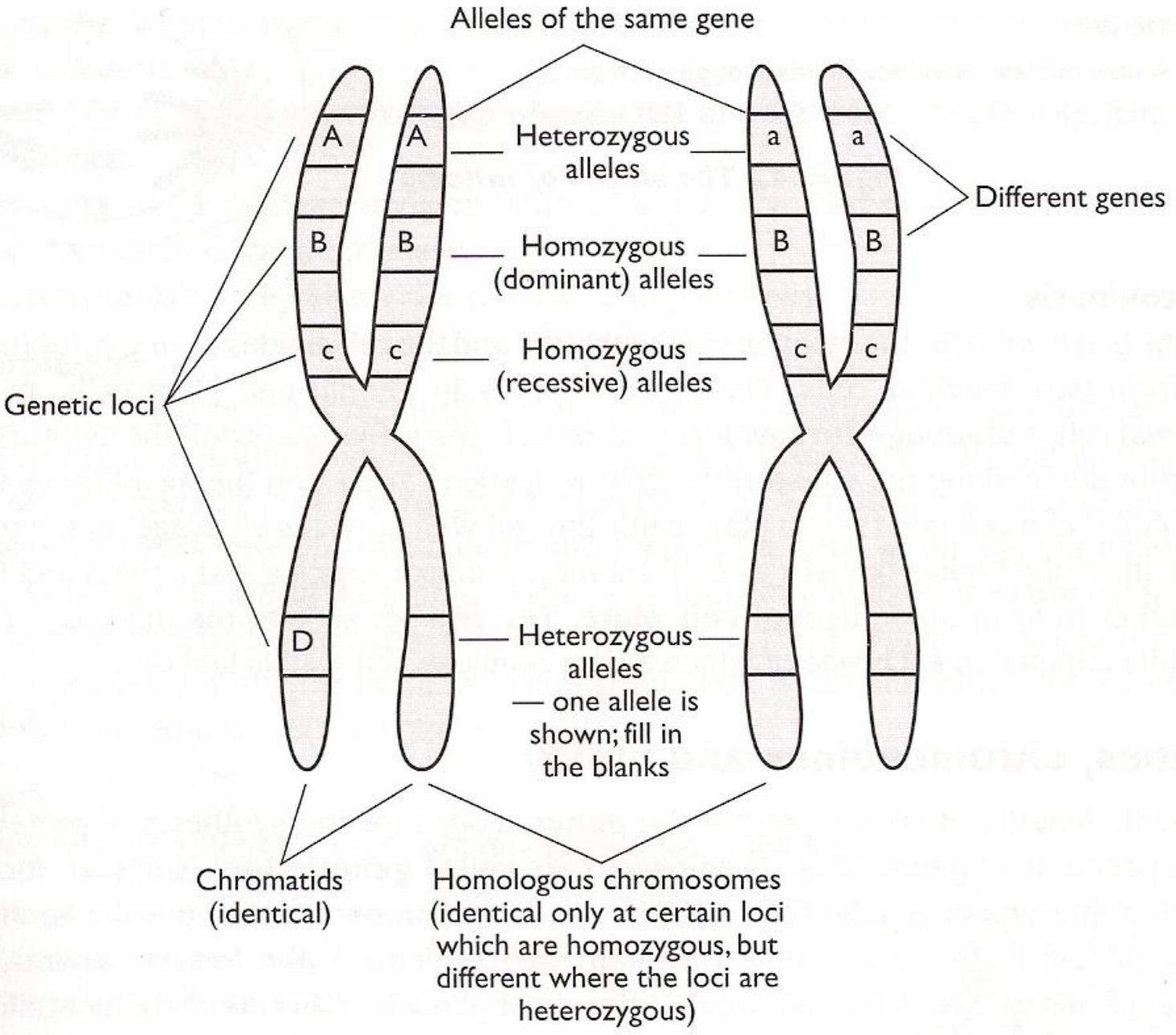


Figure 43 Genes, alleles, chromatids and homologous chromosomes

5.5.2 Understand the relationship between chromosomes, genes & alleles

- Many people find the concept of alleles and genes confusing. A **gene** is a short length of DNA on a chromosome coding for a specific polypeptide. An individual gene may have more than one form that differs slightly from the others in the sequence of nucleotide bases that make it up. These different forms of the gene are known as **alleles**. It is the nature of these alternatives that some are more likely to express themselves than others (dominant) and that our **genotype** is the allele combination that we possess.

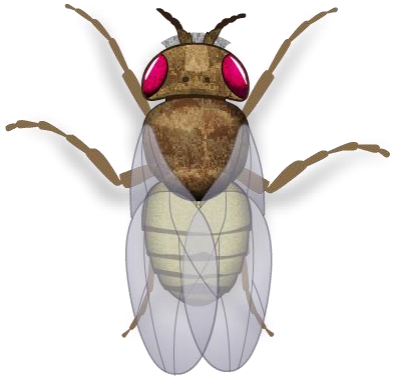
- The phenotype which is ultimately expressed depends upon which allele is dominant. A **dominant** allele has its instructions followed and so its effect is produced in the heterozygous condition. The recessive allele does not have its instruction followed in the heterozygous condition.

Representing alleles

A gene can be represented using a letter: upper case for the dominant allele, and lower case for the recessive allele.

For example, the allele for wing length in *Drosophila* can be either long (L) or short (l).

Genotype		**Phenotype**
LL	homozygous dominant	long wings
Ll	heterozygous	long wings
ll	homozygous recessive	short wings

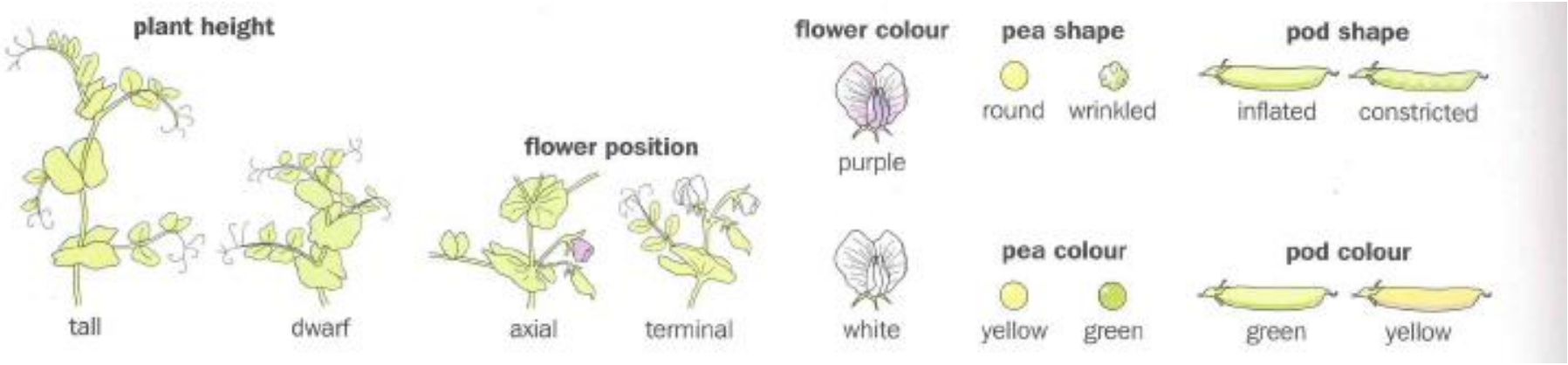


For example, humans possess a gene that determines the ability to taste phenylthiocarbamide (PTC). The PTC gene, TAS2R38, was discovered in 2003 as a consequence of work carried out during the Human Genome Project. There are two alleles: one (designated by the symbol **T**) is the tasting allele; while, the other (designated **t**) is the non-taster allele. The tasting alle (**T**) codes for a bitter taste receptor protein to which PTC can bind. The non-tasting allele (**t**) codes for a non-functional protein. **T** is dominant over **t**, since a heterozygote, **Tt**, possesses the allele **T** and produces the taste receptor protein. Things are never so simple, and environmental factors can affect PTC tasting ability – for example having a dry mouth may make it more difficult to taste PTC and what is eaten or drunk beforehand may also affect tasting ability.

Practical – who has the PTC "taster" allele?

5.5.3 Understand the inheritance of traits showing discontinuous variation

- **Monohybrid Inheritance**
- **Heredity** is the transfer of genetic factors from one generation to the next, i.e. from parents to their offspring. The first breeding experiments carried out by Mendel were on **monohybrid inheritance**. This involves the inheritance of the alleles of a **single gene.** Mendel used pea plants for his experiments because they had a number of clearly identifiable characteristics such as height, flower colour and pea colour and shape (see below). More importantly, peas self-pollinate (they are true breeding). Mendel cross bred the peas by removing the anthers of one type of plant so that it could not self pollinate and then used feathers to artificially pollinate it with pollen from another type of plant.


plant height
tall
dwarf
flower position
axial
terminal
flower colour
purple
white
pea shape
round
wrinkled
pea colour
yellow
green
pod shape
inflated
constricted
pod colour
green
yellow

- To begin with he crossed tall pea plants with short ones, he expected medium plants in the first generation but to his surprise they were all tall, when he allowed these first generation plants to self-pollinate, the second generation was ¾ tall and ¼ short.
- Tall x short (parental type P)
- All tall (selfed) (first generation F1)
- Tall (787) Short (277) (second generation F2)

Genetic crosses: a history

One of the first people to study genetics was an Austrian monk called Gregor Mendel in the 1850s and 1860s.

He experimented with thousands of pea plants and established the basic foundations of inheritance, such as dominant and recessive characteristics.

Mendel had no knowledge of DNA or genes but he did identify that inheritance is particulate, i.e. it depends on the transfer of separate (discrete) factors from parents to offspring.

Complete the diagram:

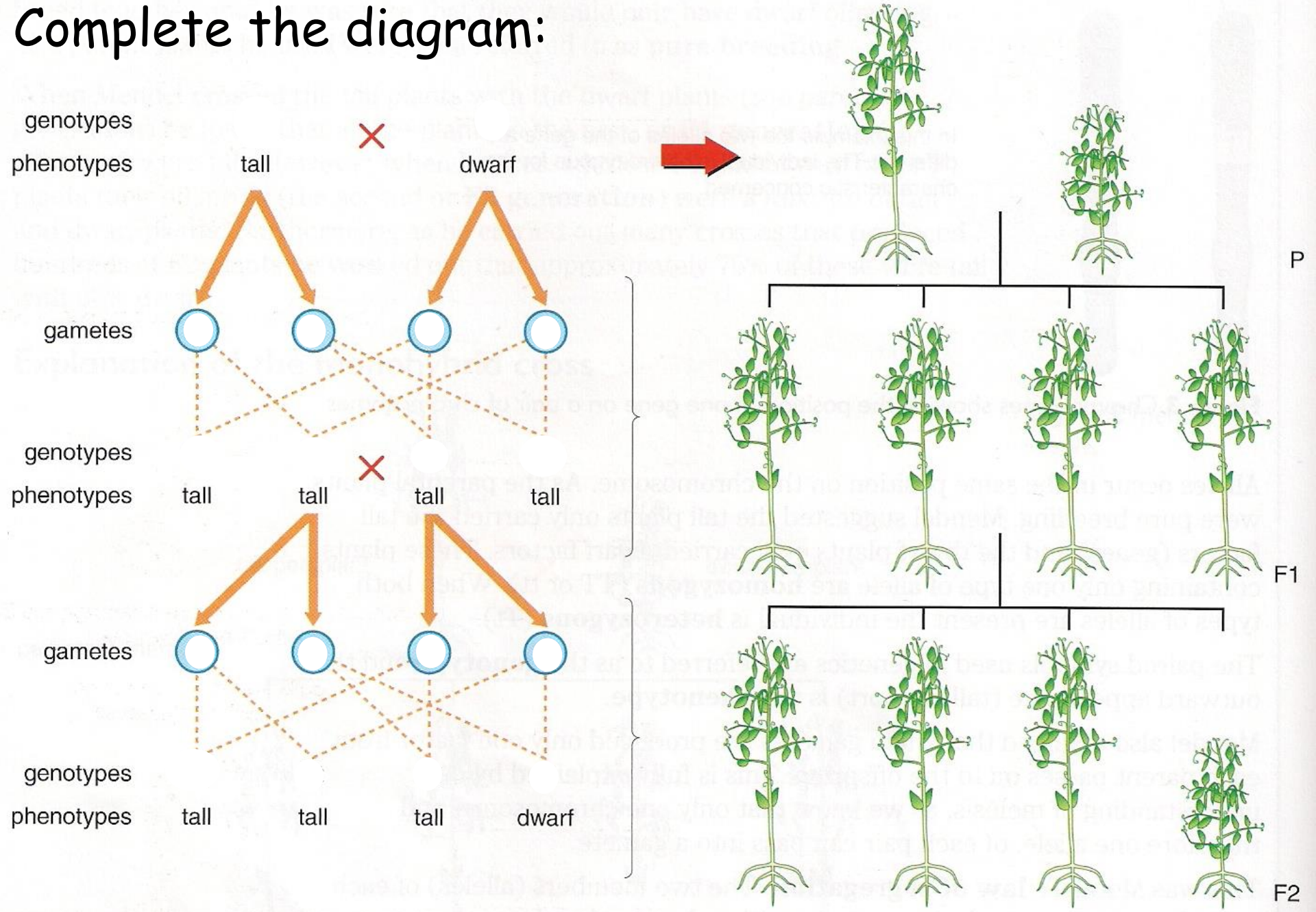


Figure 4 Explaining Mendel's results

Conclusion 1

- Note that in all his breeding experiments Mendel never got plants that showed an intermediate form (medium height in the example above). From this we can conclude that inheritance is not a process in which the features of the two parents are blended but rather a process in which **chromosomes**, carrying the alleles for characteristics (which may or may not show themselves) are transmitted from parents to offspring.

Conclusion 2

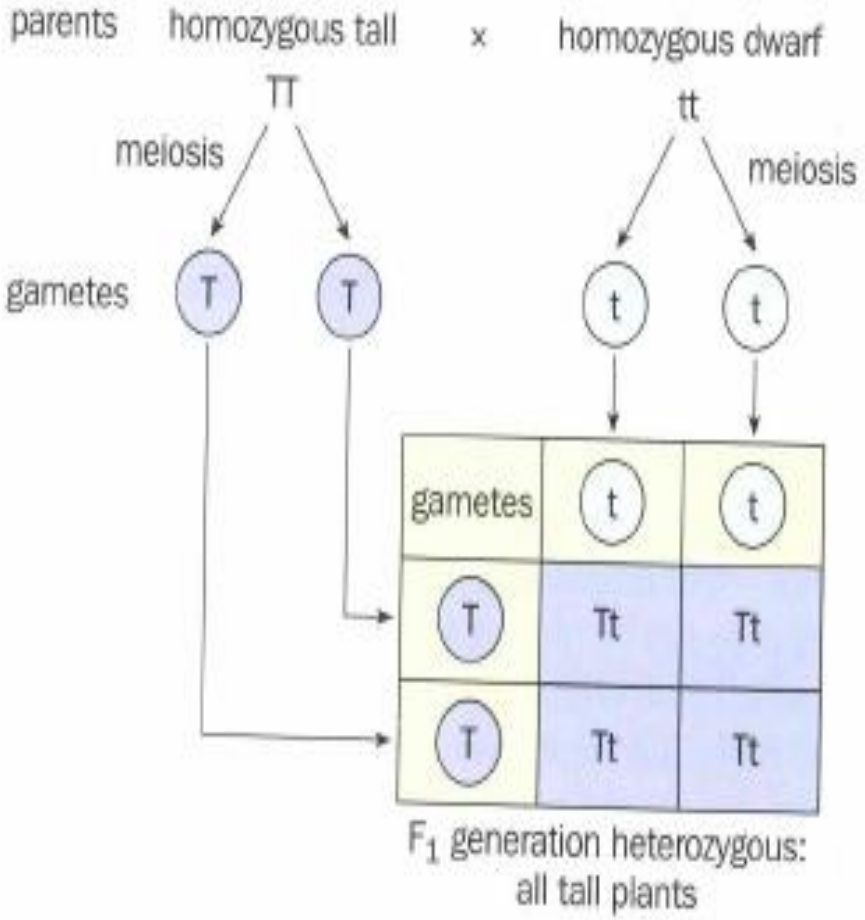
- There were no short plants in the F1 generation although they did reappear in the F2. From this we can conclude that although the F1 plants are tall, they do possess an allele for shortness that remains ‘hidden’ in the heterozygote F1 plants, confirming that **two** alleles are at work.

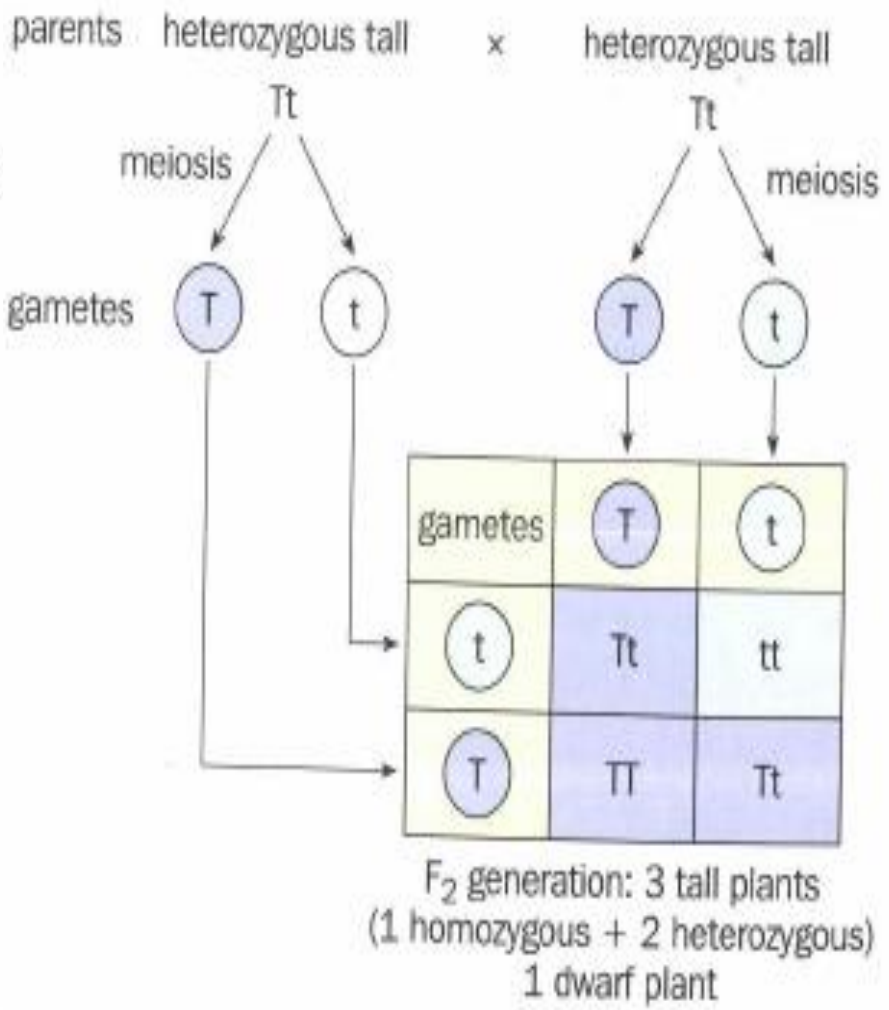
Conclusion 3

- As all the plants in the F1 generation were tall we can conclude that the allele for shortness was somehow swamped by the allele for tallness. The tallness is the **dominant** characteristic and the shortness is described as **recessive** because it does not exert its effects in the heterozygote.

Mendel's first law of inheritance – Law of Segregation
Alleles segregate so that only one of a pair of alleles is transmitted via each gamete.

Mendel's monohybrid cross

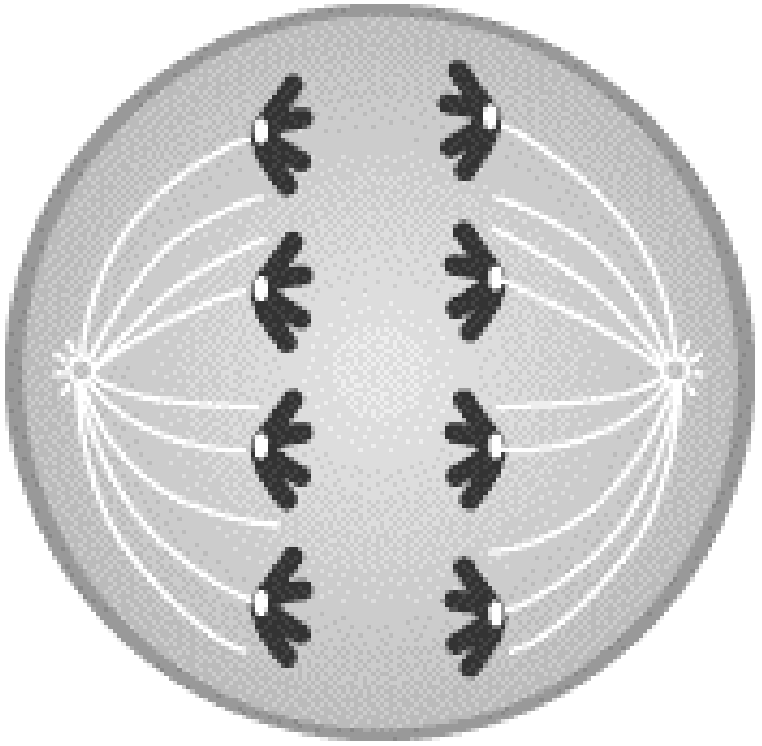




Law of segregation further explained

- In sexual reproduction, new individuals develop from a zygote produced by the fusion of male and female gametes. Since gametes are haploid (possess only one set of chromosomes) they only contain one allele of each gene. Thus, while an organism has a pair of alleles for any genetic condition in the somatic cells, only one allele of the pair is passed on via one gamete. If an individual is homozygous, (for example TT in tall plants as shown above) then there can only be one type of gamete produced. i.e “T”. If the individual was homozygous tt, then only “t” gametes could be produced. If an individual is heterozygous e.g. Tt, then half the gametes produced will contain one type of allele (T) and half will contain the other (t). This segregation can be explained by the separation of homologous chromosomes, carrying the alleles, during anaphase 1 of meiosis.

- During fertilisation, the gametes combine to form a zygote and the individual alleles are restored to a pair: one from female parent, the other from the male parent. Fertilisation is a random event as any of the gametes from the female parent can combine with any of the gametes from the male.



Alternative patterns of inheritance

1. Dominance

- Mendel's experiments on pea plants revealed the principles of inheritance. Regardless of what feature he was testing for, he bred plants through two generations and in large numbers so that reliable ratios could be calculated. One experiment crossed white-flowered and purple-flowered plants. He found that the **F1** (First generation offspring) were all purple (we now know that this was due to a dominant allele) but that when the F1 were interbred the **F2** (second generation) showed a mixture of purple and white-flowered plants in a ratio of 3:1.

- If **P** codes for the production of purple pigment and **p** coding for no pigment, then fill out the following table with the possible genotypes and phenotypes of flower colour in pea plants.

Genotypes	Phenotypes

Using these combinations Mendel carried out the following experiment to give an understanding of Dominance.

Parental phenotype	Purple flowers	White flowers	Plants from pure-breeding lines are cross-pollinated
Parental genotype			Both are homozygous
Parental gametes			Gametes are haploid, so contain only one allele from a pair — only one type of gamete from each parent
F_1 genotype			All F_1 plants are heterozygous with purple flowers — purple allele is dominant
F_1 gametes			All F_1 plants can produce two types of gamete — half with the purple flower allele and half with the white flower allele (two sets are shown to represent male and female gametes)
Fertilisations possible and F_2 genotypes			This is the standard way of showing all the possible fertilisations and possible combinations of alleles in the F_2 generation
F_2 phenotypes			In this instance, three of the possible four combinations contain at least one dominant allele and so have purple flowers, while only one of the four has two recessive alleles to give white flowers

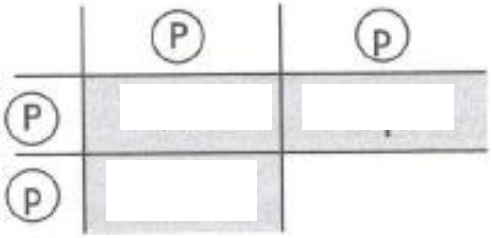
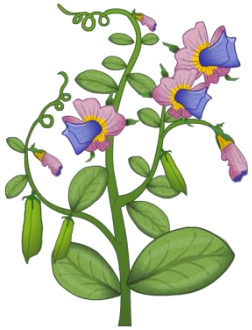


Figure 25 A cross between pure-breeding white-flowered and pure-breeding purple-flowered pea plants

Test cross

To determine whether an organism showing the dominant characteristic of a trait is homozygous or heterozygous, a **test cross** can be performed. This involves crossing the organism with another that is homozygous recessive for the trait.

TT or Tt?  ×  **tt**

if TT

	T	**T**
t	Tt	Tt
t	Tt	Tt

all tall

if Tt

	T	**t**
t	Tt	tt
t	Tt	tt

2 tall, 2 short

If any of the offspring show the homozygous recessive trait in the phenotype, the parent must have been heterozygous.

Test Crosses

- Sometimes it is difficult to know what the genotype of a plant may be by simply looking at it. For example in Mendel's experiments the purple flowers which he used may have had the genotype PP or Pp. To ascertain what the genotype is, a **test cross** has to be carried out. This is simply crossing with the homozygous recessive individual and observing the offspring.

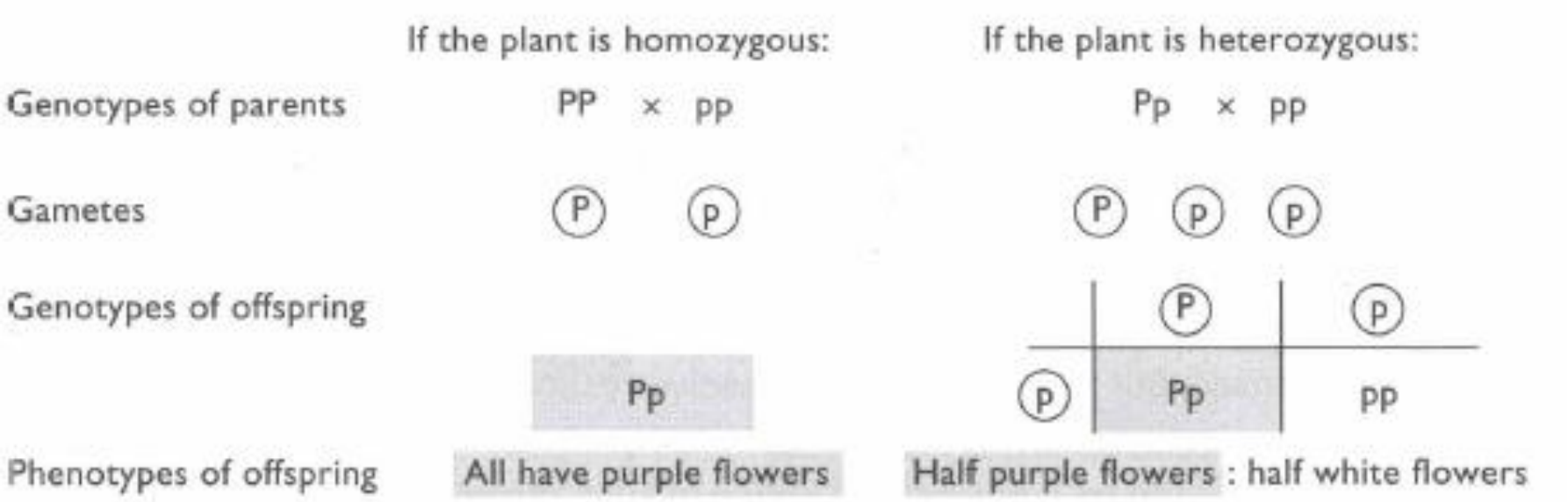


Figure 26 The test cross (testing the genotype of a purple-flowered plant)

- As can be seen from the results above if the offspring produce no variation, then the parent genotype is **homozygous dominant** (e.g PP). If there is variation within the offspring produced then the genotype of the parent is **heterozygous** (e.g Pp)

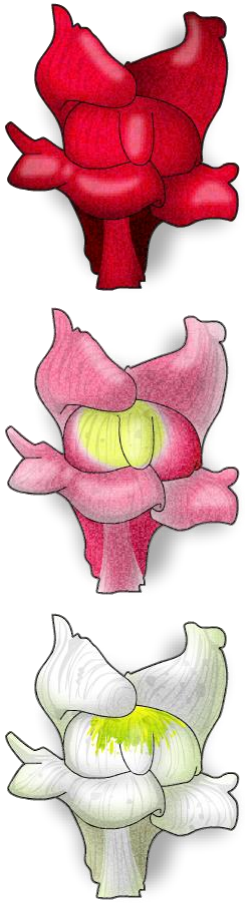
Codominant alleles

Alleles are **codominant** if they are both expressed in the phenotype of a heterozygote. They can be represented by two capital letters superscript to the letter representing the gene.

For example, flower colour in snapdragons *Antirrhinum majus*.

C^R = red flowers C^W = white flowers

Genotype		Phenotype
C^RC^R	homozygous	red flowers
C^RC^W	heterozygous	pink flowers
C^WC^W	homozygous	white flowers



Codominance

- Mendel's experiments might lead us to assume that alleles are always dominant and recessive; this is not always the case.
- Some alleles will have equal dominance and the heterozygote will show a mix of the parental characteristics, this is called **codominance**. An example is the flower snapdragon where a red parent crossed with a white parent will produce pink offspring in the F1
- Between the extremes of complete dominance and absence of dominance, there are various shades of partial or incomplete dominance e.g. snap dragons

Add this:

- Snapdragon flowers show co dominance as there is a mix of both phenotypes. The heterozygote shows a distinct intermediate of the two homozygous phenotypes

- Let Red = C^R and White = C^W

Table 8 The genotypes and phenotypes of flower colour in snapdragons

Genotypes	Phenotypes
C^RC^R	Red flowers
C^RC^W	Pink flowers
C^WC^W	White flowers

- Complete the cross and work out the F2 of a cross between two F1

Parental Phenotype

Parental Genotype C^RC^R x C^WC^W

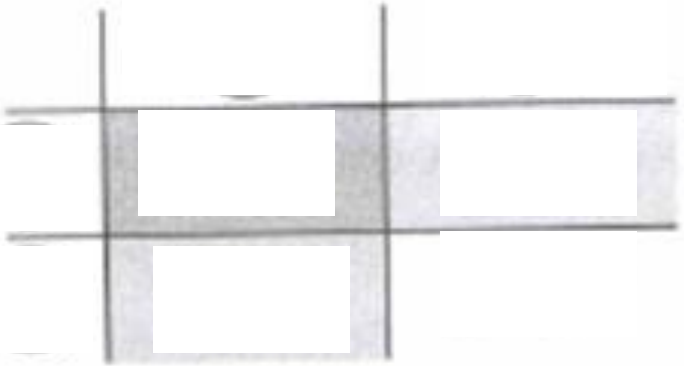
Gametes

Genotype of F1 offspring:

Genotype of parents

Gametes

Fertilisations possible and genotypes of offspring



Phenotypes of offspring

3. Lethal Allele combinations

- It is probably true that in genetic studies more has been learned about genes from abnormal ratios than from normal ones. Such is the case with **lethal** alleles which cause the death of individuals. This allele may only exert it's effect when in a certain combination eg. homozygous dominant or heterozygous. This is the case in the inheritance of fur colour in mice.
- The allele **A** codes for a signalling protein.
- The allele $\mathbf{A^Y}$ does not code for this protein

- The lethal allelic combination causes death at an early stage of development but it's presence is evident in the heterozygote where it displays a distinctive phenotype.
- The genotypes and phenotypes of coat colour are shown in Table 9.

Table 9 The genotypes and phenotypes of coat colour in mice

Genotypes	Phenotypes
AA	Agouti coat colour
AA^Y	Yellow coat colour
A^YA^Y	Lethal: embryonic death

- Fig. 28 shows how a cross between two heterozygote's produces a distinctive 2:1 ratio. This is shown in a cross between yellow mice, with the lethal allele combination clearly labelled.

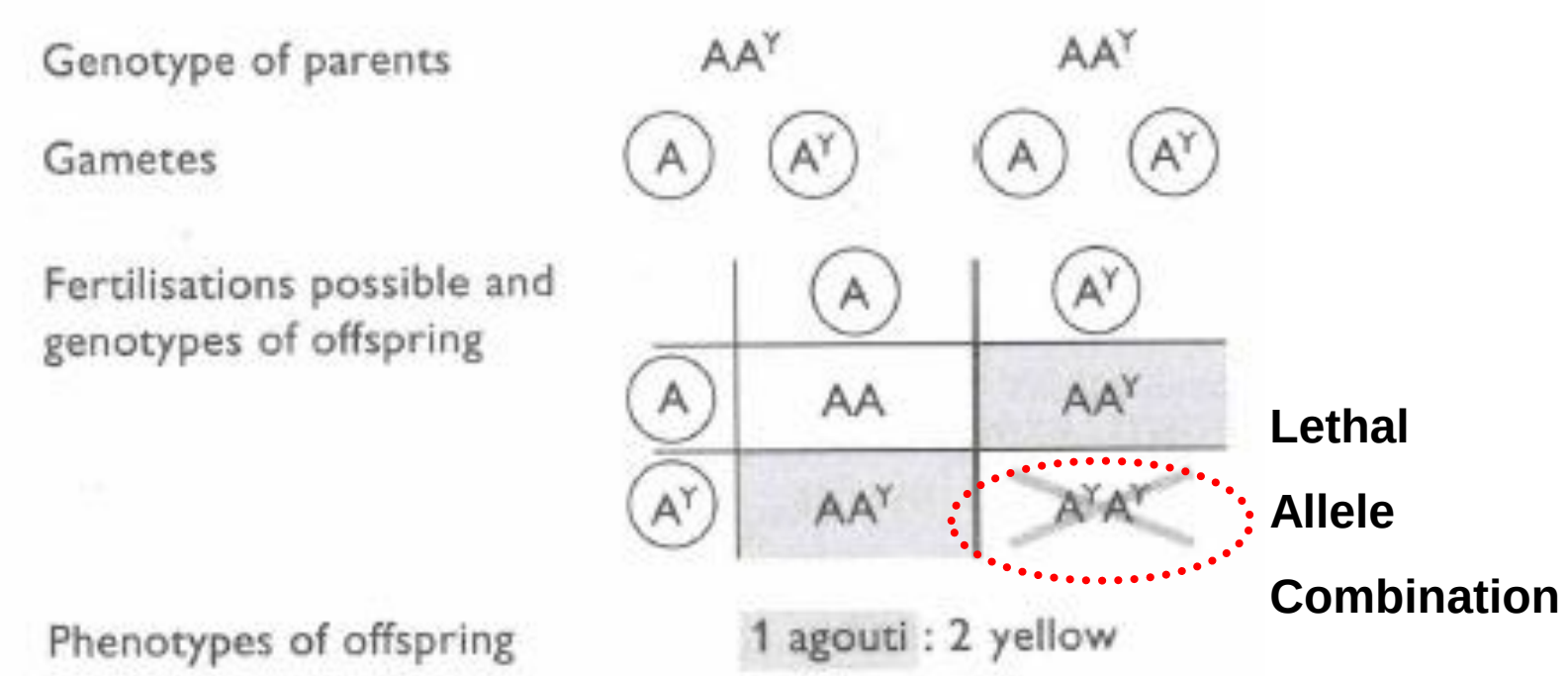


Figure 28 A cross between yellow mice

Other types of lethality are recognised including:

- The lethal allelic combination causes death of either the zygote or an early embryonic stage so there is no obvious evidence that the lethal allelic combination ever occurred.
- The lethal allelic combination causes death after a reduced lifespan. For example Tay-Sachs disease is a rare genetic disorder of the central nervous system in humans, which causes progressive damage to the nerve cells, resulting in death in early childhood.

4. Multiple alleles

- Often genes have more than two alleles at a given locus, though in any one individual only two alleles can be present. An example of such multiple alleles is provided by the three alleles that control the ABO blood group system.

ABO blood group

Some genes have multiple alleles (i.e. more than two), but only two can be present in an individual. For example, the ABO blood group gene (immunoglobulin) in humans.

- I^A produces antigen A on the surface of red blood cells
- I^B produces antigen B on the surface of red blood cells
- I^O produces no antigen.

Genotype	Phenotype
I^AI^A and I^AI^O	blood group A
I^BI^B and I^BI^O	blood group B
I^AI^B	blood group AB
I^OI^O	blood group O

A and B are codominant and O is recessive to both.

- The fact that there are more than two alleles responsible for determining the blood groups makes no difference to their transmission, which take place in the normal Mendelian way.
- Thus a child whose parents are blood group O must be blood group O. However, offspring may result whose genotypes are different from their parents.

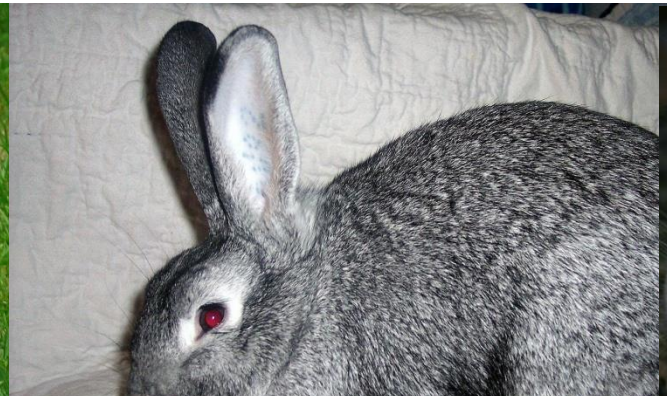
I^AI^O x I^BI^O

Another well known example of multiple alleles is provided by fur type in rabbits. There are four alleles with a dominance hierarchy:

- **C** – dominant to $\mathbf{c^h}$, $\mathbf{c^{ch}}$ and $\mathbf{c^a}$
- $\mathbf{c^h}$ – dominant to $\mathbf{c^{ch}}$ and $\mathbf{c^a}$
- $\mathbf{c^{ch}}$ – dominant to $\mathbf{c^a}$
- $\mathbf{c^a}$ – recessive

Genotypes	Phenotypes
CC, Cc^h, Cc^{ch}, Cc^a	
c^hc^h, c^hc^{ch}, c^hc^a	
$c^{ch}c^{ch}$, $c^{ch}c^a$	
c^ac^a	






Only a rabbit with albino fur has a known genotype – c^ac^a. Others would require a test cross to ascertain their genotype.

Cystic fibrosis

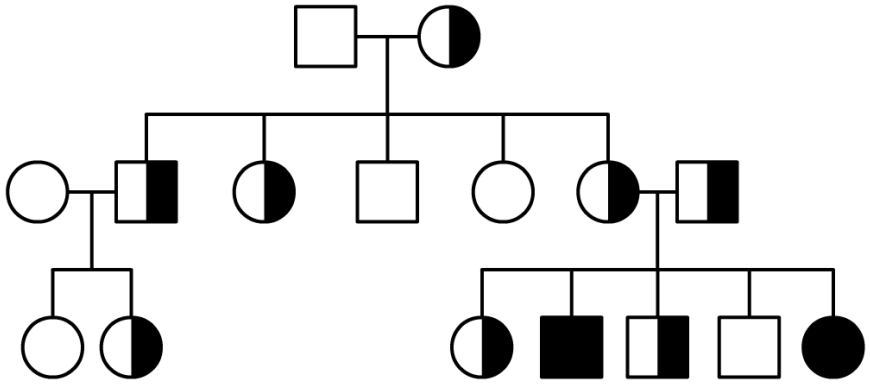
A 3:1 ratio is typical of the results of a monohybrid cross between two heterozygotes where one of the alleles is dominant and the other recessive. This fact is very useful when considering human genetic disorders and genetic counselling is being given.

For example, **cystic fibrosis** (CF) is a disease that occurs due to a recessive allele of a gene on chromosome 7.
The normal allele controls the production of a membrane protein essential for the proper functioning of epithelial cells.

Cystic fibrosis: pedigree diagram

If a person is homozygous for the recessive CF allele, thick and sticky mucus is produced in their lungs and pancreas, causing breathing problems and malnutrition. Very salty sweat is also a symptom of the disease.

Pedigree diagrams show how alleles, like the one for CF, have been inherited through families.



- unaffected male
- male carrier (heterozygote)
- affected male (has CF)
- unaffected female
- female carrier (heterozygote)
- affected female (has CF)

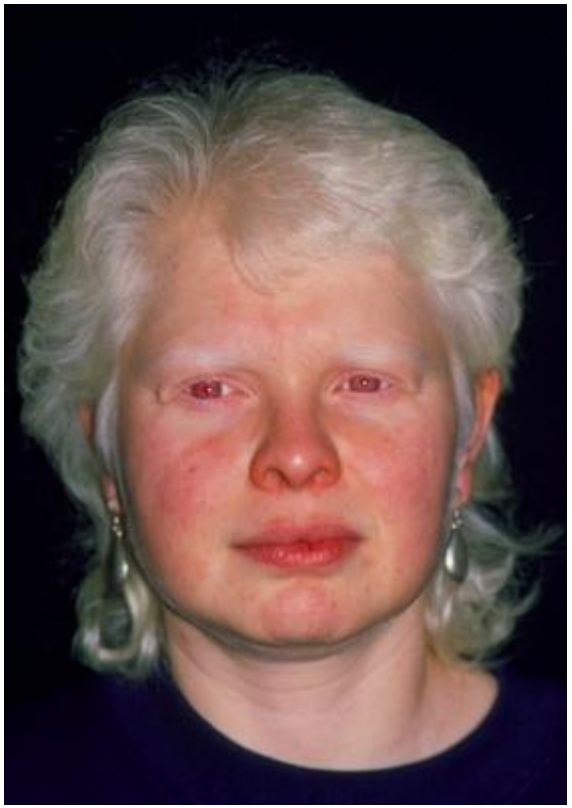
Thalassaemia

Thalassaemia is the name given to a group of inherited blood disorders that affect the body's ability to create red blood cells.
In cases of thalassaemia, the bone does not produce haemoglobin, causing anaemia and reduced oxygen-carrying capacity.

In sickle cell anaemia the structure of the globin chain is affected, i.e it is qualitative, the haemoglobin molecule does not function properly, whereas thalassaemia is quantitative.

Albinism

Albinism is an inherited condition in which there is a lack of the pigment melanin in structures that are normally coloured. Albinos therefore have pinkish skin, deep red pupils and pink irises, photophobia and pale yellow hair.



It is caused by a single recessive gene on an autosome, resulting in a malfunctioning tyrosinase enzyme. This prevents tyrosine from being converted into melanin.

Dominant allele: Huntington's disease

Huntington's disease

Some diseases are caused by dominant alleles. One example is Huntington's chorea, an incurable and fatal neurological disease.

The dominant allele shows delayed penetrance, i.e. the nervous system does not usually start to degenerate until after the age of 25, by which time the person may already have had children.

	father		
mother	gametes		

1. Complete the Punnett square for a father who is heterozygous for Huntington's and a mother who is normal.
2. What is the chance that a child has Huntington's?

S C

Codominant crosses

Codominant cross

Roan cows have red coats with white blotches (C^RC^W), and are the result of a cross between a parent with red fur and another with white fur. The gene for coat colour has codominant alleles.

	father (roan) C	C
mother (roan) C C	gametes C	C
C	C C	C C
C	C C	C C

1. What are the genotype and gametes of each parent (A–H)?

2. What are the genotypes of the possible offspring (I–P)?

3. What is the ratio of the offspring? red roan white

S C ?

Multiple allele crosses

Multiple allele cross

Complete the Punnett square for a father who is blood group O and a mother who is blood group AB.

	father		
mother	gametes		

1. What are the genotype and gametes of the parents?

1. What is the probability of having a child with blood group A?

2. What is the probability of having a child with blood group B?

3. What is the probability of having a child with blood group O?

S C

Dihybrid inheritance

Dihybrid inheritance

Mendel extended his work by looking at **dihybrid inheritance** – the inheritance of two characteristics that are controlled by different genes at different loci.

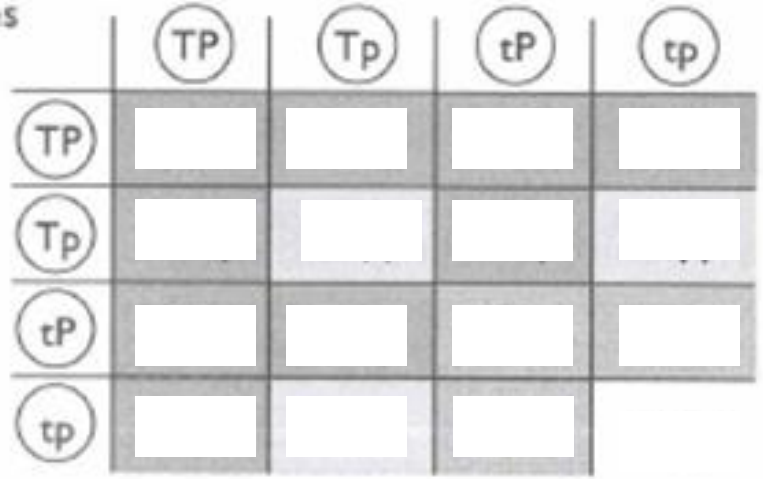
Press **play** to find out more.

5. Dihybrid Inheritance

- This is where the inheritance of two characteristics is considered. In one experiment Mendel crossed a pure-bred tall pea plant with purple flowers with a short plant possessing white flowers.

Parental phenotype	Tall, purple	Short, white	Plants from pure-breeding lines are cross-pollinated
Parental genotype	TTPP	ttpp	Both are homozygous
Parental gametes	(TP)	(tp)	Gametes are haploid, so contain only one allele from a pair — only one type of gamete from each parent
F_1 genotype	TtPp		All F_1 plants are heterozygous tall, purple — tall and purple alleles are dominant
F_1 gametes	(TP) (Tp) (tP) (tp)		All F_1 plants can produce four types of gamete — either of the 'height' alleles may be separated with either of the 'flower colour' alleles (only one set is shown)

Fertilisations possible and F_2 genotypes



With four types of gamete, there are 16 possible combinations — nine have both dominant traits, three are tall but white, three are short but purple, while only one of the 16 has both recessive traits

F_2 phenotypes

Homework for tomorrow:

Complete monohybrid questions

Complete qu3-7 codominance

Complete 1-2 of lethal

In the F1 generation all the plants produced were tall with purple flowers.
In the F2 generation four different phenotypes in different ratios:

Tall purple	Dom / dom	9/16
Tall white	Dom / rec	3/16
Short purple	Rec/ dom	3/16
Short white	Rec/ rec	1/16

In other words the offspring showed the two pairs of characteristics combined in every possible way. This is called the classic 9:3:3:1 ratio and indicates a heterozygous (4x4) cross.

Dihybrid inheritance

Mendel also looked at plant height (T = tall, t = dwarf) and flower colour (P = purple, p = white) together.

	tall, purple	**tall, white**	**dwarf, purple**	**dwarf, white**
Possible genotypes	TTPP, TTPp, TtPP, TtPp	TTpp, Ttpp	ttPP, ttPp	ttpp
Mendel's results	96	31	34	11
Ratio	9	3	3	1

He concluded that the factors (height, flower colour) are transmitted independently of each other. He called this the **law of independent assortment**. Today we say that each pair of alleles for a particular gene can combine randomly with either of another pair of alleles from another, different gene.

Conclusions from the dihybrid cross

- The alleles are transmitted **independently** of each other from parent to offspring and therefore assort freely; gametes must each contain **one** allele for each characteristic.
- Our knowledge of **meiosis** would confirm this; chromosomes line up on the spindle in their homologous pairs and separate to form the gametes. However the order in which the chromosomes line up is a matter of chance, and this is a major source of genetic variation.

Mendel's Second Law of Inheritance – Law of Independent Assortment

Pairs of alleles assort independently so that any one allele can be segregated with any one allele of another pair.

Independent assortment occurs during metaphase I of meiosis, to produce a gamete with a mixture of the organism's maternal and paternal chromosomes. Along with chromosomal crossover, this process aids in increasing genetic diversity by producing novel genetic combinations.

Recombination

Recombination is the re-assortment of genes or traits into different combinations from those of the parents.

Offspring with genotypes unlike either parent are known as recombinants.
Recombination is an important source of genetic variation as it gives rise to the differences between individuals in a natural population.

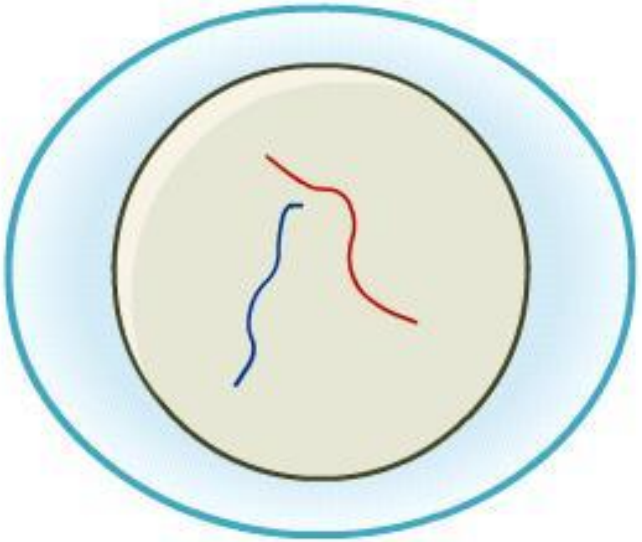
Recombination is achieved by three different mechanisms: **crossing over**, **independent assortment of alleles** and **random fertilization**.

Crossing over

How does genetic exchange occur during meiosis?

Crossing over occurs during prophase I of meiosis. It results in variation by altering the type of alleles carried by a chromosome.

Press **play** to find out how it works.

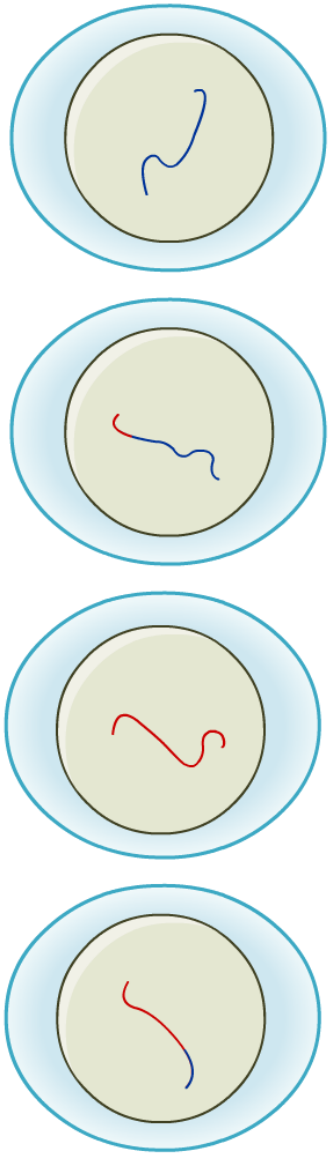


interphase

Independent assortment of alleles

Independent assortment describes the random arrangement and separation of chromosomes (and all the alleles and genes therein) during meiosis. It is random chance how the chromosomes migrate during anaphase I and II.

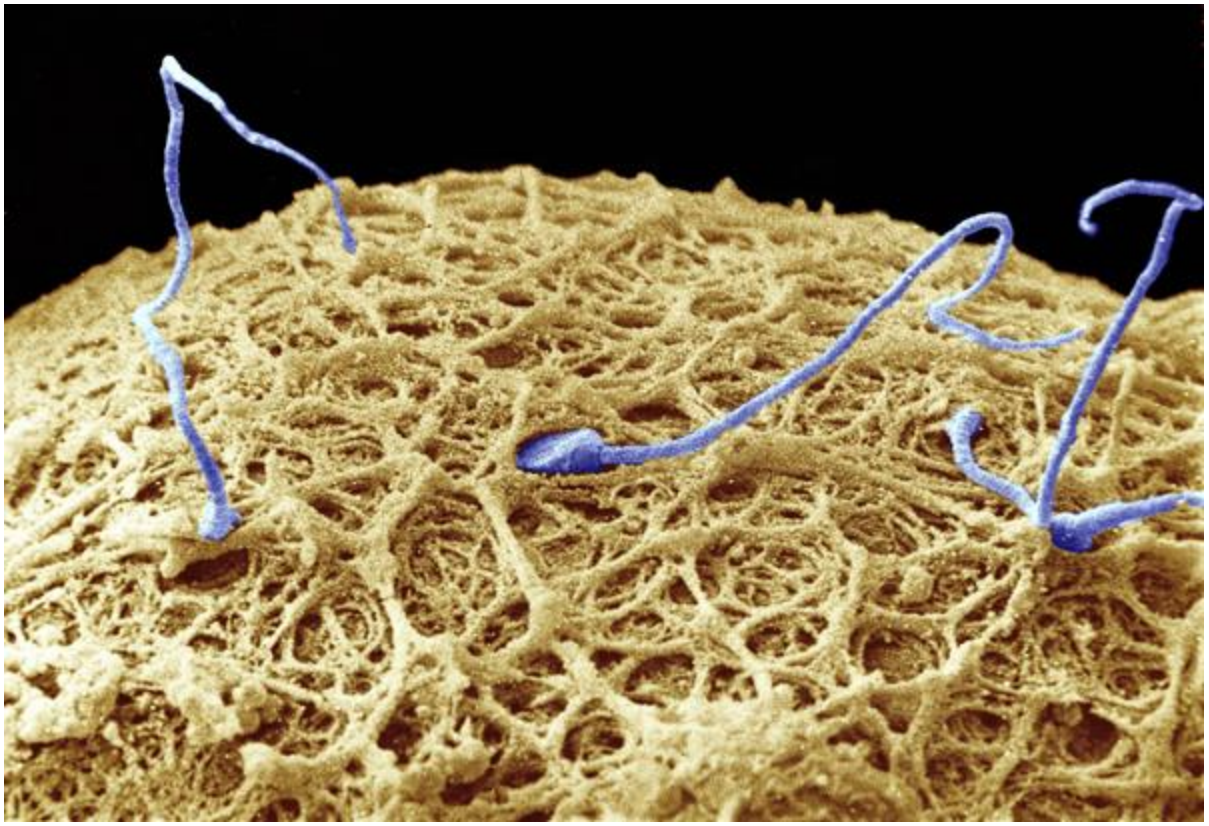
It was after Mendel had studied the inheritance of two characteristics that he described his law of independent assortment: each of a pair of alleles for a particular gene can combine randomly with either of another pair of alleles for a different gene.



- In independent assortment the chromosomes that end up in a newly-formed gamete are randomly sorted from all possible combinations of maternal and paternal chromosomes. Because gametes end up with a random mix instead of a pre-defined "set" from either parent, gametes are therefore considered assorted independently. As such, the gamete can end up with any combination of paternal or maternal chromosomes. Any of the possible combinations of gametes formed from maternal and paternal chromosomes will occur with equal frequency. For human gametes, with 23 pairs of chromosomes, the number of possibilities is 2^{23} or 8,388,608 possible combinations. The gametes will normally end up with 23 chromosomes, but the origin of any particular one will be randomly selected from paternal or maternal chromosomes. This contributes to the genetic variability of progeny.

Random fertilization

It is random as to which gametes will fertilize each other, i.e. which pollen grain will fertilize which ovum, and which sperm will fertilize which egg. This further adds to the possibility of increasing the genetic variation in the population.

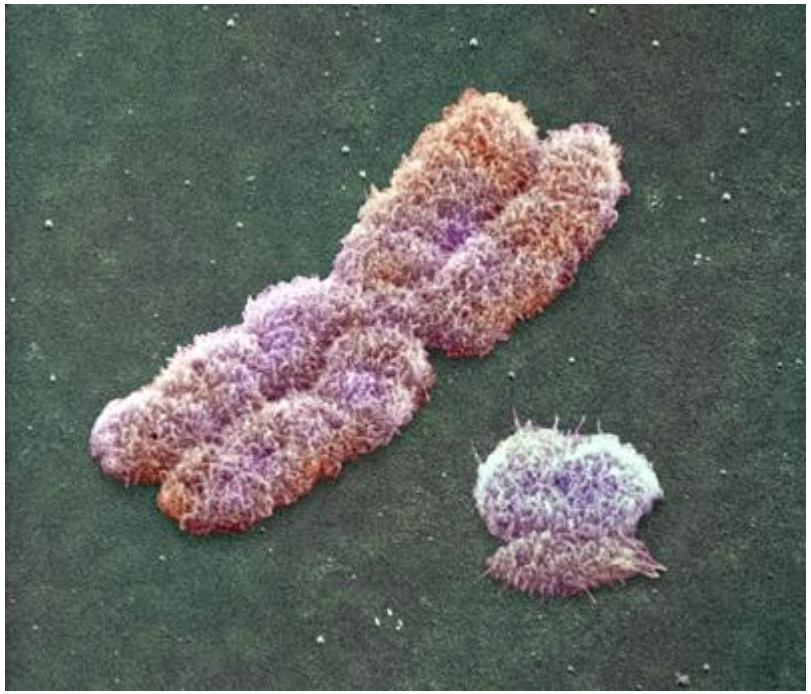


Variation: increase or decrease?

Sex determination

Sex in mammals is determined by two chromosomes, known as the **sex chromosomes** or **heterosomes**.

The X chromosome is larger and contains about 2000 genes, whereas the Y chromosome contains fewer than 100.



- Females (XX) are the homogametic sex.
- Males (XY) are the heterogametic sex.

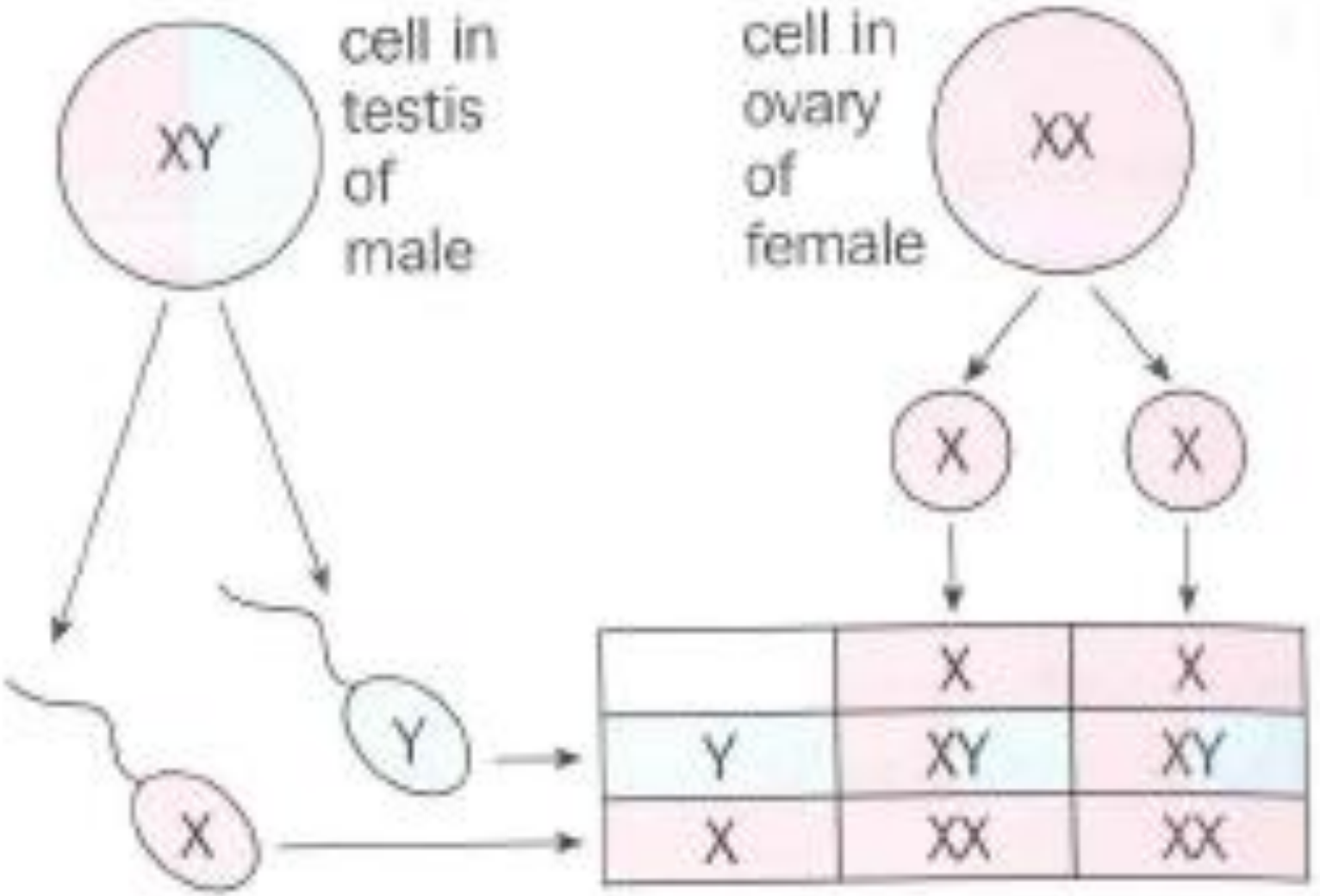
5.5.4 Understand sex determination & sex linkage

Sex determination

- In humans sex is determined by the sex chromosomes. These chromosomes are an exception to the rule that homologous chromosomes are identical in appearance; all the other pairs (1-22) which are identical are called **autosomes**.

- Female is **XX** (has two similar chromosomes)
- Male is **XY** (has two different chromosomes)

- In the human, female characteristics are initiated by special genes on the X chromosome and these must be present in a double dose. Maleness is determined by the Y chromosome.
- The sex of the child is **determined by the male** and there is a 50% chance of having a boy or a girl.


XY
cell in testis of male
XX
cell in ovary of female
X
X
Y
X
X
X
Y
XY
XY
X
XX
XX

- There is considerable variation between species as to how sex is determined. For example in **birds**, the males are XX and the females are XY.

- A quite different system of sex determination is found in **alligators** and **crocodiles**. Here the males and females do not differ in their chromosomes; rather it is the environmental **temperature** that determines the sex of the individual. During the early development of the egg, there is a critical period during which high temperatures lead to males and lower temperatures to females. In some species this pattern is reversed.

Sex linkage

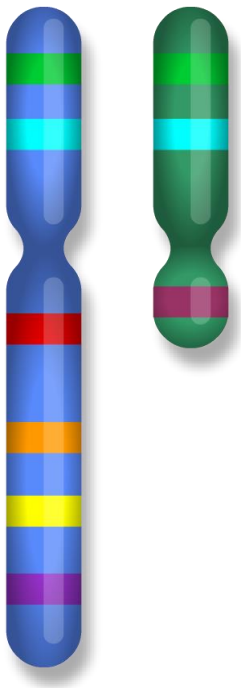
Genes are located on the sex chromosomes are described as **sex linked**. The study of their inheritance involves examining both the sex of the offspring and the genetic trait of interest.

X-linked diseases	Y-linked diseases
Haemophilia Duchenne muscular dystrophy Red–green colour blindness	Rare and debatable! It is argued that there is little room on the Y chromosome for anything other than genes controlling testes formation and function.

Sex linkage: X linkage

X linkage is more common because:

- the X chromosome is larger
- part of it does not have a homologous section on the Y chromosome, therefore only one allele of a gene will be present and so will always be expressed.



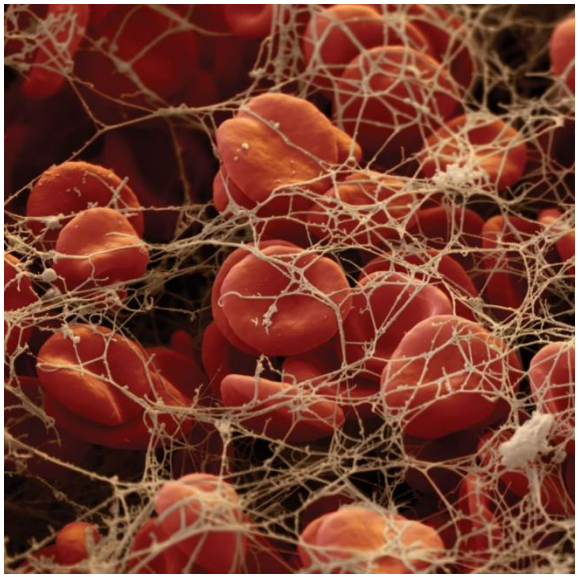
homologous regions
do not carry sex-determining genes

non-homologous regions
carry sex-determining genes
and other genes

Sex linkage

- In organisms with sex chromosomes (including humans and *Drosophila*) all the genes carried on the sex chromosomes are transmitted along with those determining sex – they are **sex linked**. In most conditions the genes are carried on the X chromosome, but not on the Y. Indeed in humans, the Y chromosome carries very few genes (in general those concerned with the development of maleness), compared to over a thousand carried on the X chromosome. **Y-linked inheritance** is confined to males and is relatively rare. **X-linked traits** are relatively common.

- **Haemophilia** (a condition where blood takes an abnormally long time to clot) and **red-green colour blindness** (where individuals are unable to distinguish between these two colours) are sex-linked characteristics.



- This is because the gene is carried on one of the sex chromosomes. In both cases the normal gene is dominant and these conditions are caused by a **recessive** gene carried on the X chromosome.
- For a male to be afflicted he need only inherit **one** recessive allele but a female needs **two** recessive alleles to be affected and this is a much more unusual occurrence. For this reason, many **more** men are affected by sex-linked conditions than females.

Example: haemophilia

Normal blood condition - X^H

Haemophiliac condition - X^h

As the male lacks a second X chromosome the following genotypes occur:

Females		Males	
X^HX^H	Normal female	X^HY	Normal male
X^HX^h	Carrier female		
X^hX^h	Haemophiliac female	X^hY	Haemophiliac male

Sex Link crosses

These are carried out in the normal Mendelian way.

carrier female x normal male

X^HX^h X^HY

X^H X^h X^H Y

Male gametes

Female gametes	X^H	Y
X^H		
X^h		

Sex linkage: haemophilia

Haemophilia

Haemophilia is an X-linked, recessive condition where the blood does not clot normally, resulting in excessive bleeding.

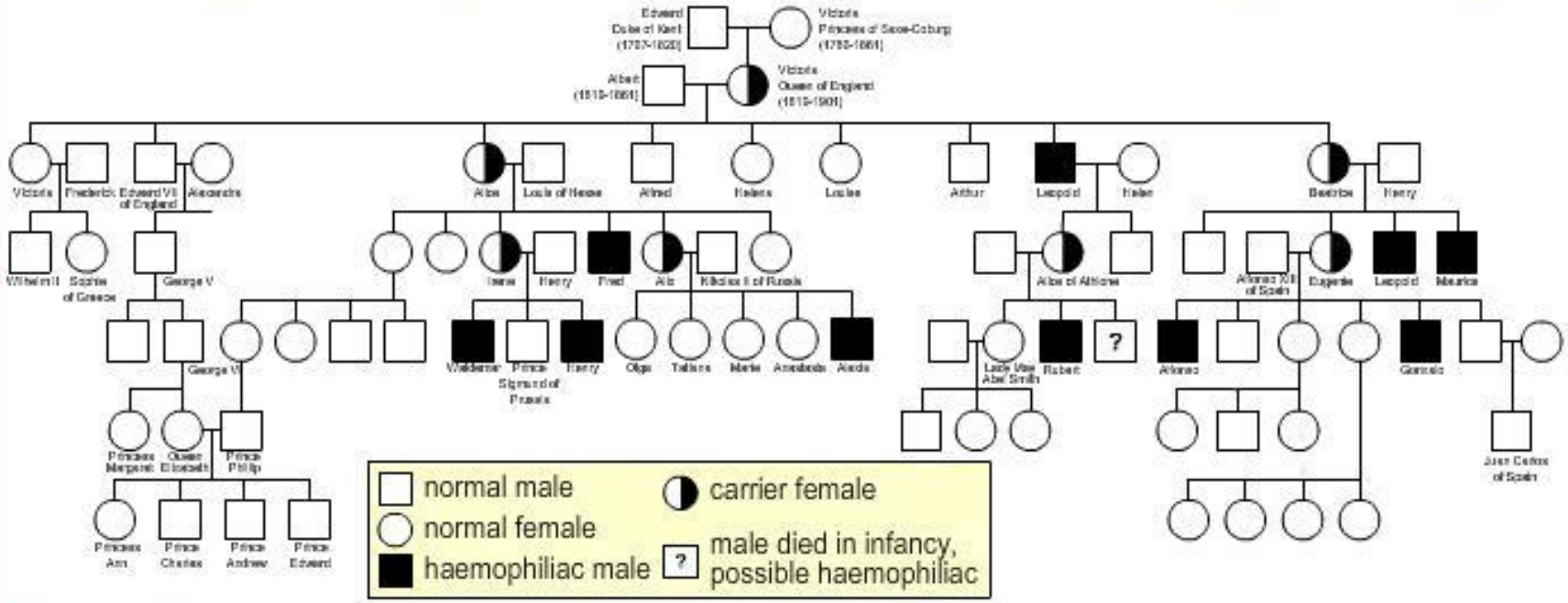
		father (normal) X^HY	
mother (carrier) X^HX^h	gametes	X^H	Y
	X^H	X^HX^H	X^HY
	X^h	X^HX^h	X^hY

X^H = normal, dominant X^h = haemophiliac, recessive

What are the phenotypes of the children of the above parents?

Haemophilia in the Royal Family

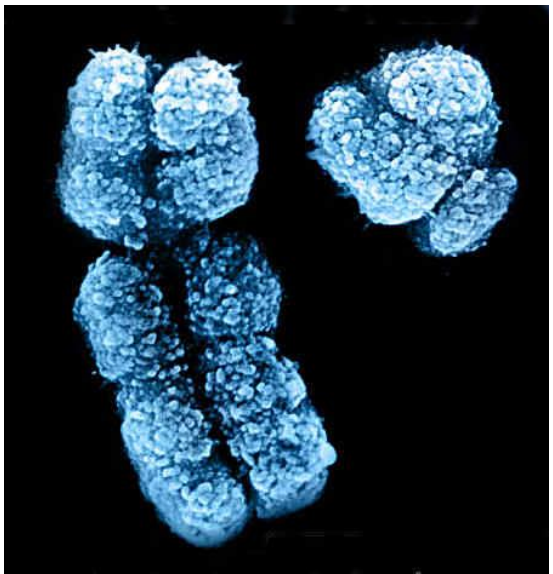
Pedigree diagram: haemophilia in the Royal family



1. Are there any haemophiliac females?
2. How could a haemophiliac female be produced?

- It is interesting to note that in **all species** where the females are XX and the males XY that males never inherit their father's X chromosome and so can never inherit their father's sex-linked traits.
- Daughters however, always receive their father's X chromosome and there is therefore a 50% chance that they will transmit this condition to their offspring.

- Y chromosome Inheritance
- If a gene is carried on the Y chromosome we would expect only males to show the effects; this is essentially what maleness is! The Y chromosome has several copies of a testicular differentiating gene. This gene acts on the gonads of the young embryo and causes them to differentiate into testes. In the absence of the products made by these genes, the gonads develop into ovaries!



X-linked recessive traits share the following features:

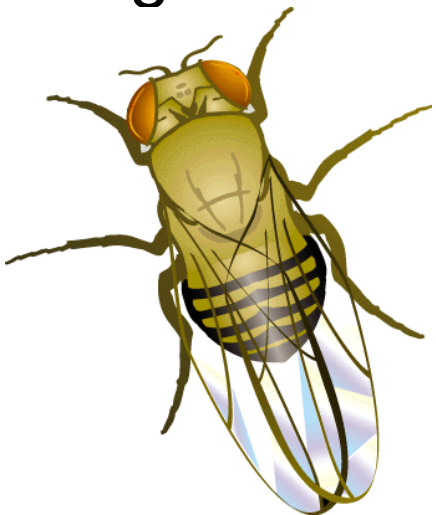
- Reciprocal crosses produce different results and are used in testing for sex linkage
- They are more common in males than females. This is because the allele only has to appear once in a male but has to be inherited from both parents in an affected female.
- Affected males inherit the allele from the female parent since the Y chromosome is inherited from the male carrier (and most commonly from a heterozygous – carrier)
- Affected females inherit the allele from both parents (and so the male must also be affected).

- There are a number of X-linked recessive traits in humans – for example, red-green colour blindness and haemophilia. In ca**T**s there is the interesting example of a coat colour called tortoiseshell. The condition is codominant and so tortoiseshell cats are heterozygotes. It only occurs in females since males cannot have both alleles.

- X-linked dominant traits **exist, such as Huntington's chorea in humans. The trait is passed from an affected father to all his daughters (since a daughter always inherits her father's X chromosome).**

Recognising sex linkage

- Sex linkage is usually recognised by the results of a **reciprocal** cross: a male of one type crossed with a female on another will give a **different** result from the opposite one.
- **Example**: In Drosophila the females are XX and the males XY. The normal eye colour (wild type) is red but white-eyed forms are caused by a recessive gene carried on the X chromosome.



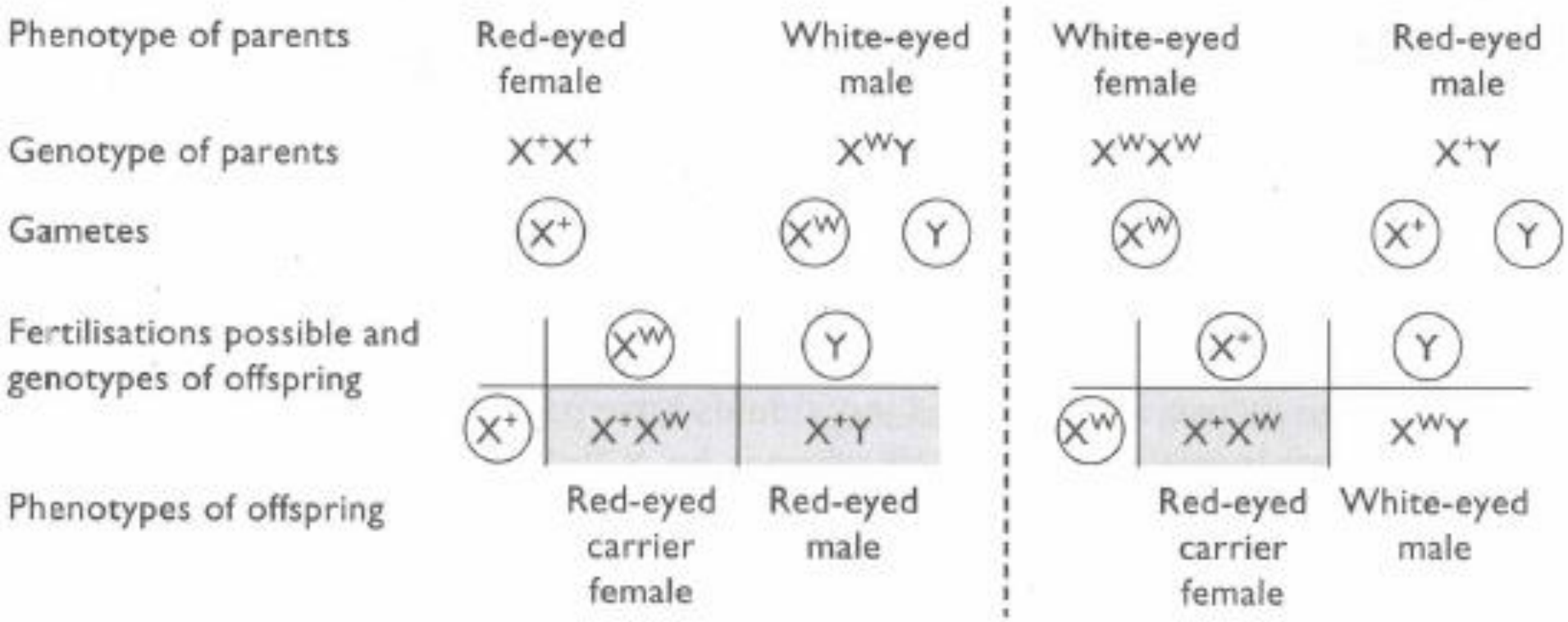


Figure 30 Reciprocal crosses between red-eyed and white-eyed fruit flies

Human genetics and pedigrees

- A pedigree charts the transmission of a genetic trait over several generations in a family. Pedigrees can be used to analyse the pattern of inheritance of genetic disorders. Two pedigrees are illustrated in Fig. 31.

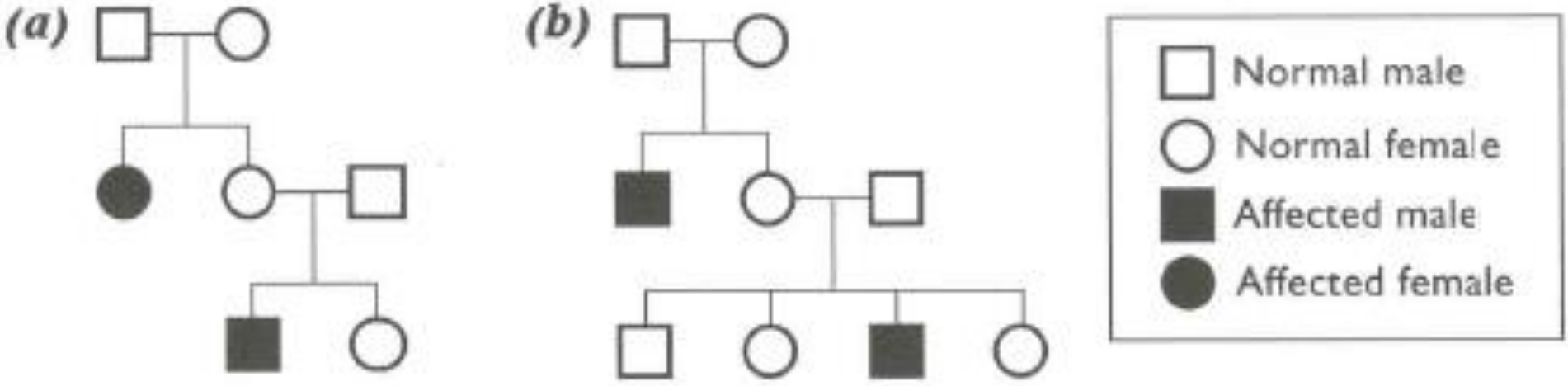


Figure 31 Pedigrees for (a) cystic fibrosis, and (b) Duchenne muscular dystrophy

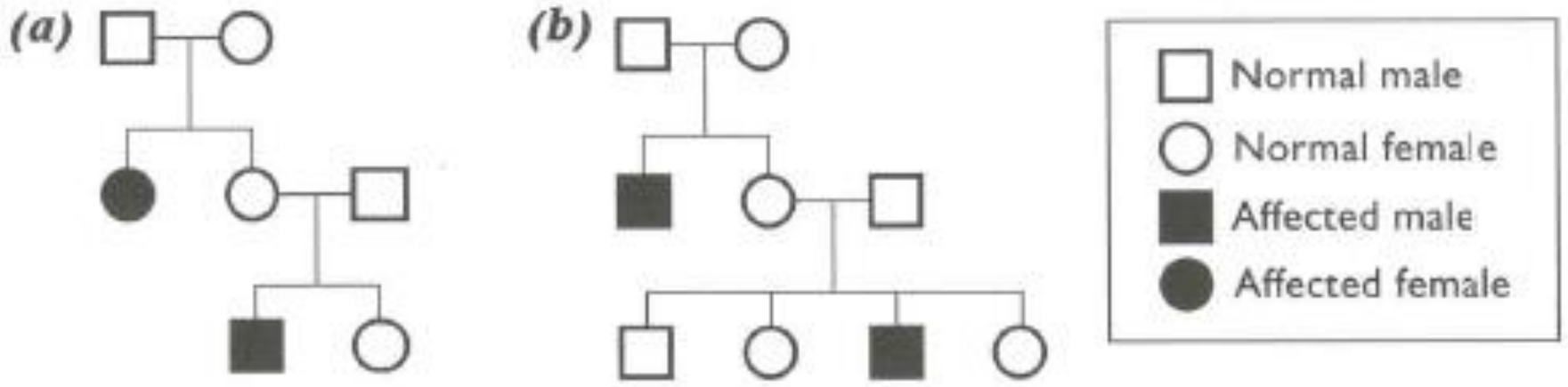
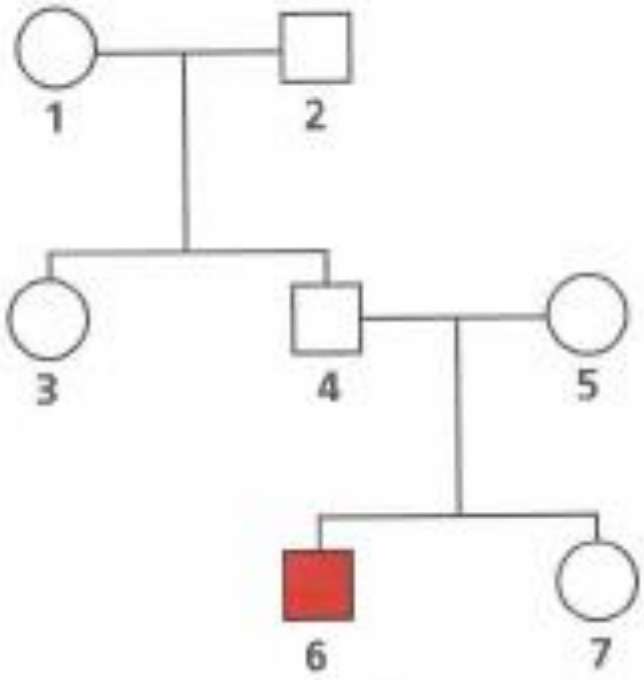


Figure 31 Pedigrees for (a) cystic fibrosis, and (b) Duchenne muscular dystrophy

- Both traits are recessive – affected individuals have parents without the trait. Cystic fibrosis is autosomal recessive – it cannot be X–linked since an affected female has a father who is unaffected (see Fig 31 (a)). Duchenne muscular dystrophy is X-linked recessive – Figure 31 (b) shows that the trait is more common in boys. However, a more extensive pedigree would be required to determine X-linkage with any degree of certainty.

Pedigree Chart for Cystic Fibrosis

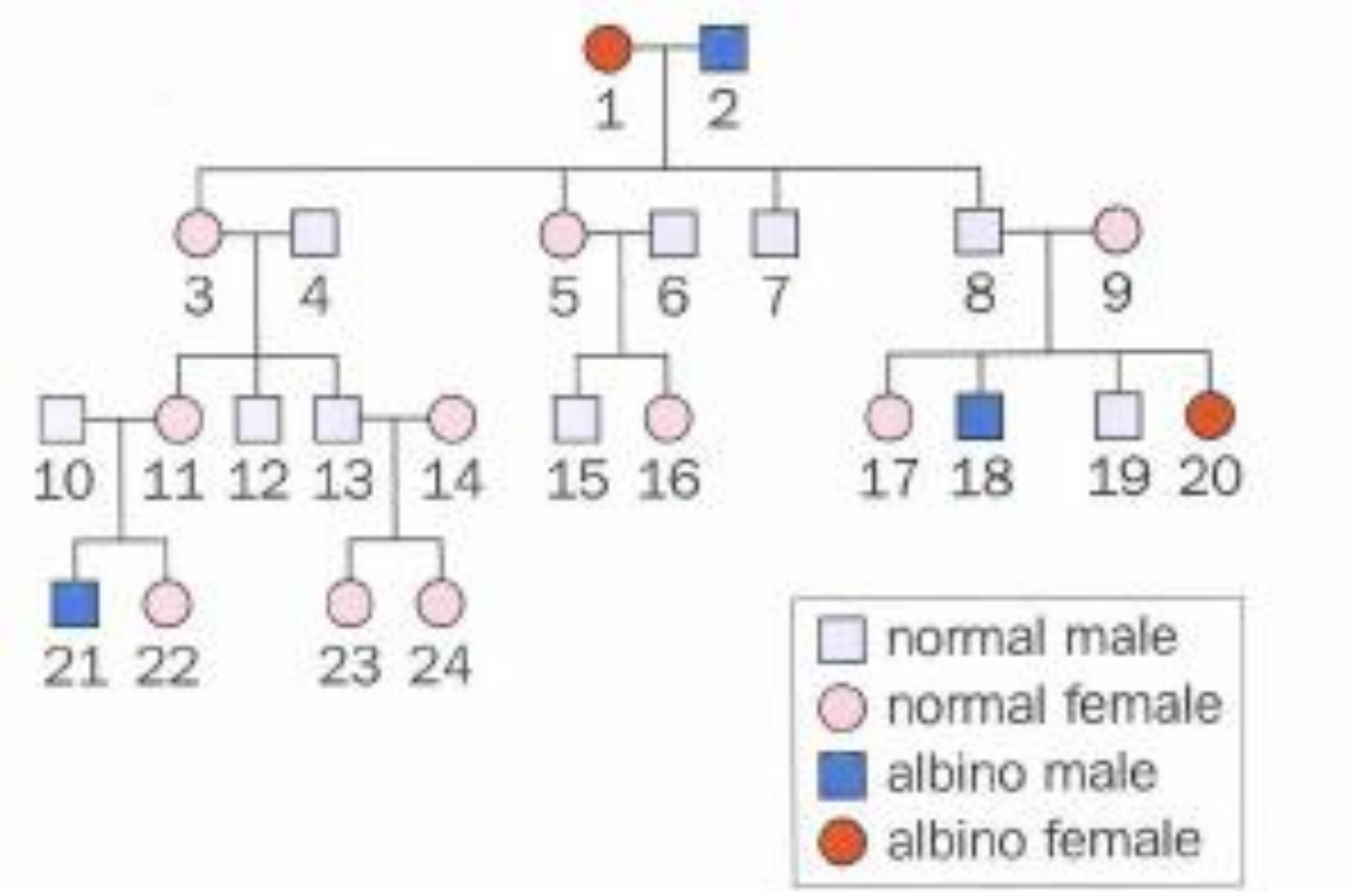


Key

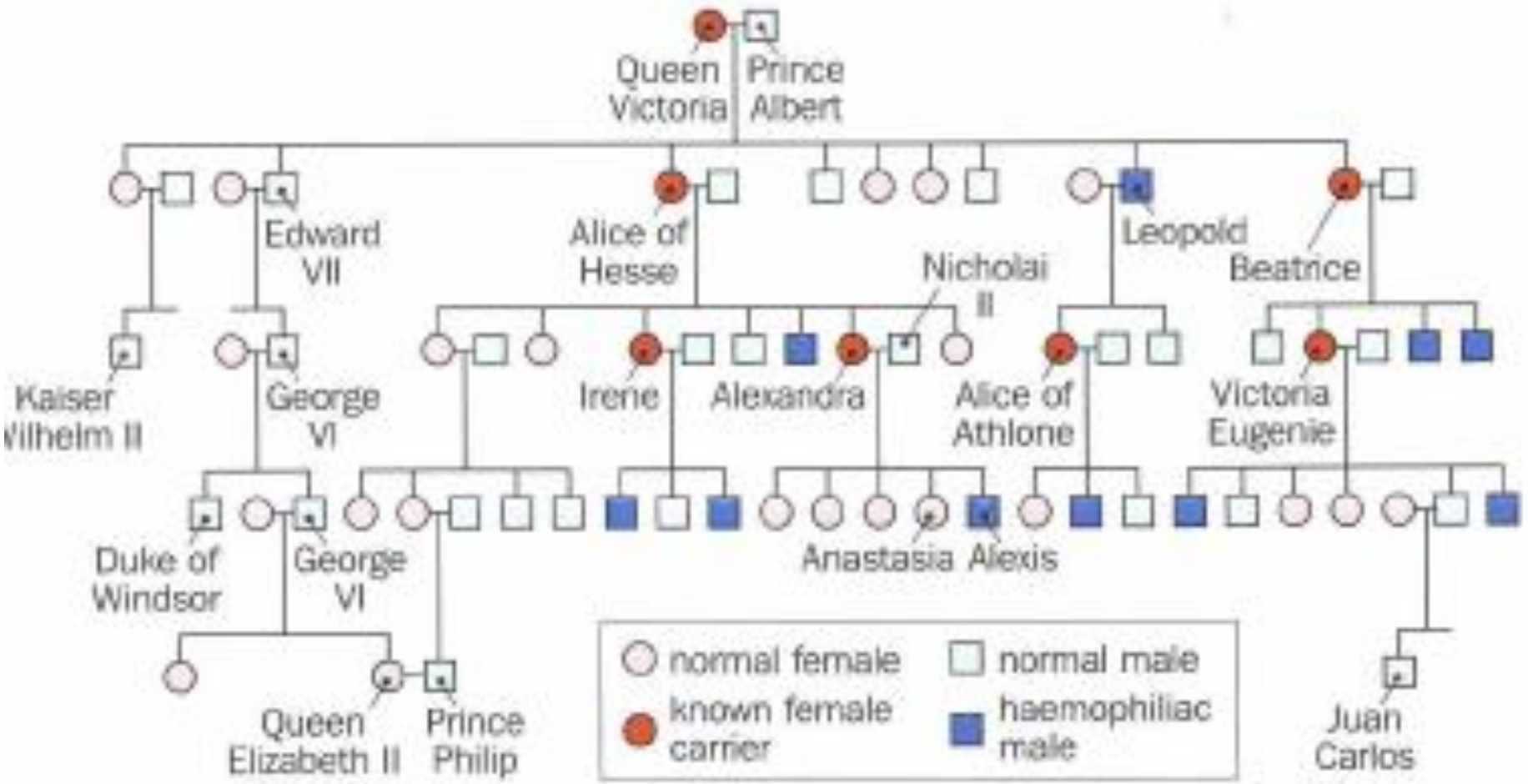
- unaffected male
- male with cystic fibrosis
- unaffected female
- female with cystic fibrosis

Note: Individuals 4 and 5 must both be carriers, each passing a recessive allele to child 6.

Albino Pedigree Chart



Haemophilia Pedigree Chart



The transmission of haemophilia from Queen Victoria

Considerations when analysing pedigrees include:

- **Autosomal recessive** – parents of an affected individual may not be affected, i.e. the trait may appear to skip a generation.
- **X-linked recessive** – as for autosomal recessive but:
  - more common in males that females (passed on from carrier mothers
  - for a female to be affected the father must also be affected.
  - an affected female will pass the trait on to all her sons.
- **Autosomal dominant** – at least one parent must be affected (though if both parents are affected not all children would necessarily be affected, since the parents could be heterozygous)
- **X-linked dominant** – as for autosomal dominant but an affected father will pass the trait on to all his daughters.

Epistasis

What is epistasis?

Epistasis is a form of genetic interaction in which one gene interferes with the expression of a gene at a different loci.

Press **play** to find out more about epistasis in mice fur colour.

5.5.5 Gene Interaction

- Another sort of gene interaction is seen when one gene modifies or masks the action of another gene. This is known as **epistasis**, and it can give rise to unusual ratios in genetic crosses.
- **We are not talking about dominant and recessive alleles which by definition occur on the same loci on homologous chromosomes, the genes in epistasis occur at different loci.**

- An example of epistasis is provided by the inheritance of certain coat colours in mice; most mice have a coat colour called agouti, a greyish brown colour. However some mice are black or white. The following pathway explains the inheritance of coat colour.

Gene 1 (W) Gene 2 (A)

- White molecules → Black pigment → Agouti colour



- If Gene 1 is lacking; the coat colour will be white irrespective of the actions of Gene 2 because coloured molecules are not present
- Therefore **white** coat colour is due to the presence of a double recessive **ww** in other words **no W**
- **Agouti** colour will only result if both **W and A** are present
- **Black** colour is formed when there is a **W** to create colour but **no A (aa)** to move the colour on to agouti.

Fill in the table below and then on a page complete cross WwAa x WwAa

Phenotype	Genotype
Agouti	
Black	
White	

Polygenic inheritance

Many phenotypic characteristics are controlled by more than one gene and are therefore affected by alleles at many loci as well as the environment. This is **polygenic inheritance**.

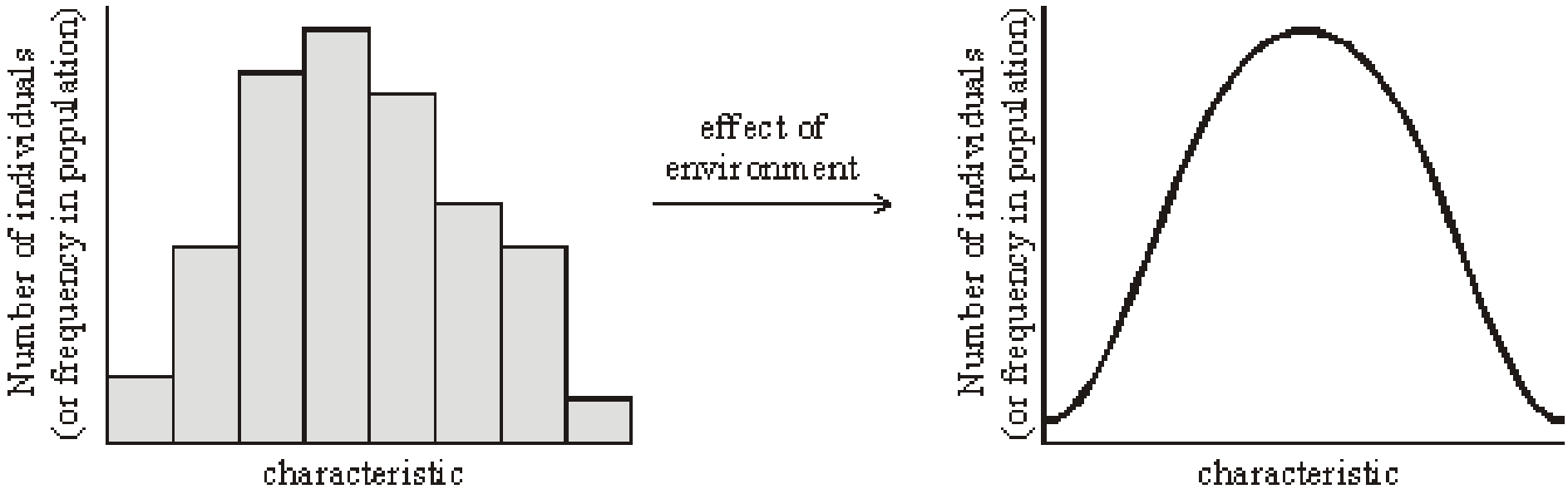
Most examples involve more than two codominant genes. As the number of genes increases, the number of possible phenotypes increases, resulting in characteristics showing continuous variation.

One example is human skin colour, which depends on the quantity of the pigment melanin. It is thought at least four genes are involved.

5.5.6 Understand the inheritance of traits showing continuous variation (polygenic inheritance)

- The **phenotype** is the appearance of a trait resulting from the interaction of a given genotype with the environment. So far we have only dealt with cases where a characteristic is controlled by the alleles of **one** gene. Sometimes however, a single characteristic is controlled by the alleles of **two** or more genes interacting with each other. The transmission of many human characteristics is controlled by the additive effect of more than one gene (called **polygenic inheritance**) and it is a cause of **continuous variation**. A character is said to vary continuously if individuals show a range of phenotypes with a smooth graduation from one extreme to another, rather than falling into a small number of discrete categories. Continuous variation gives us a ‘bell shaped’ **normal distribution** curve.

Continuous variation – bell curve



Example of continuous variation:-

- The grain colour in wheat is determined by the additive effects of the alleles of two genes, **A/a** and **B/b**. The more **A** and **B** alleles that are present in a genotype the deeper the shade of red in the grain. The absence of **A** and **B** alleles causes the grain to be white. Indeed, five shades of colour are possible: darkest-red, dark red, red, light-red and white. The results of a cross between two individuals of genotype AaBb, red grain colour, are shown below.

Parental phenotypes	Red grain	Red grain	Plants with the intermediate colour of grain
Parental genotypes	AaBb	AaBb	Both are heterozygous
Parental gametes	(AB) (Ab) (aB) (ab)	(AB) (Ab) (aB) (ab)	Each produces four types of gamete — A and a are segregated with either of B and b

Fertilisations possible and F2 genotypes

	(AB)	(Ab)	(aB)	(ab)
(AB)	AABB	AABb	AaBB	AaBb
(Ab)	AABb	AAbb	AaBb	Aabb
(aB)	AaBB	AaBb	aaBB	aaBb
(ab)	AaBb	Aabb	aaBb	aabb

Phenotypes of offspring

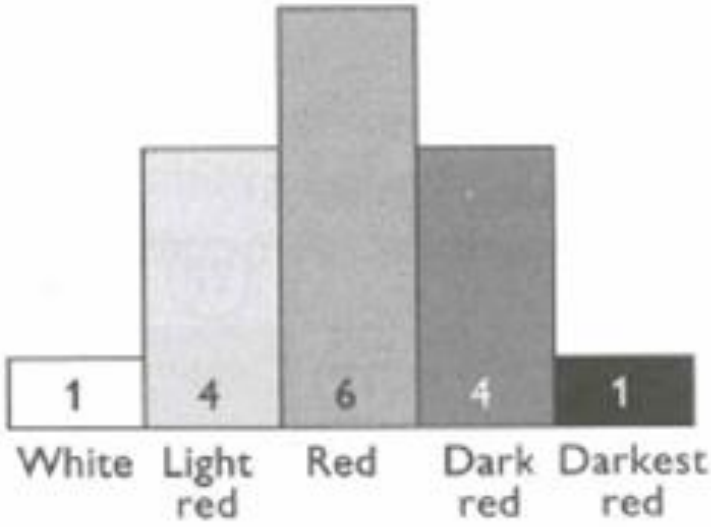


Figure 33 A cross between two red-grained wheat plants of genotype AaBb

Other factors can account for continuous variation:

- **Multiple alleles** – multiple alleles occur at one locus (as opposed to polygenic inheritance where the genes are at many different loci) but the combination of the multiple alleles can lead to a wide variety of types.
- **Environmental effects** – may also be important. This can be seen in human height; people's height depends not only on their genotypes but also on the environment (eg. nutrition levels). The environment can have a very great effect on the phenotype.

Genes and the environment

Genes interact with each other and with their environment. An organism's phenotype is a result of the interaction between its genotype and its environment, but the relative contributions are often difficult to interpret.

In addition, the level of interaction will vary between organisms and will therefore affect variation within a species.

For example, the potential height of a person is genetically determined, but an individual cannot reach this height without an adequate diet.

Gene–environment interaction: fur colour

The distribution of dark and light fur colour in Siamese cats (known as **point colouration**, a form of partial albinism) is a result of the effect of the environment on the functioning of a mutated enzyme, tyrosinase, involved in melanin production.

The mutated enzyme is inactive at normal body temperature, resulting in white fur across most of the body. The enzyme is active at lower temperatures, resulting in darker fur at the extremities: nose, face, ears, feet, tail and scrotum.

Linkage

Genes that are closely located on the same chromosome tend to be inherited together and are known as a **linkage group**.

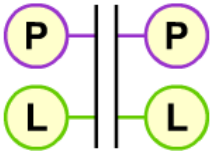
As a consequence, fewer genetic combinations of their alleles are possible, reducing the variation in offspring.

In crosses where linkage is a contributing factor, a large proportion of the offspring are of the parental type. If the genes had been on separate chromosomes, there would be more genetic variation in the gametes and therefore in the offspring.

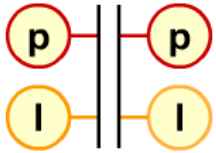
Linkage in pea plants

Flower colour and pollen shape are linked in sweet pea plants.

parents



purple, long



red, short

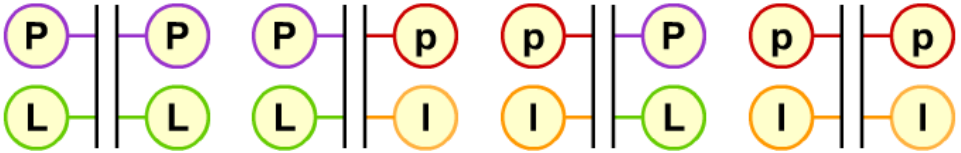
P = purple flowers
p = red flowers
L = long pollen grains
l = short pollen grains

F_1

all purple, long

All F_2 phenotypes are parental types: there are no new combinations of flower colour and pollen shape.

F_2



3 purple, long; 1 red, short

Linkage in pea plants

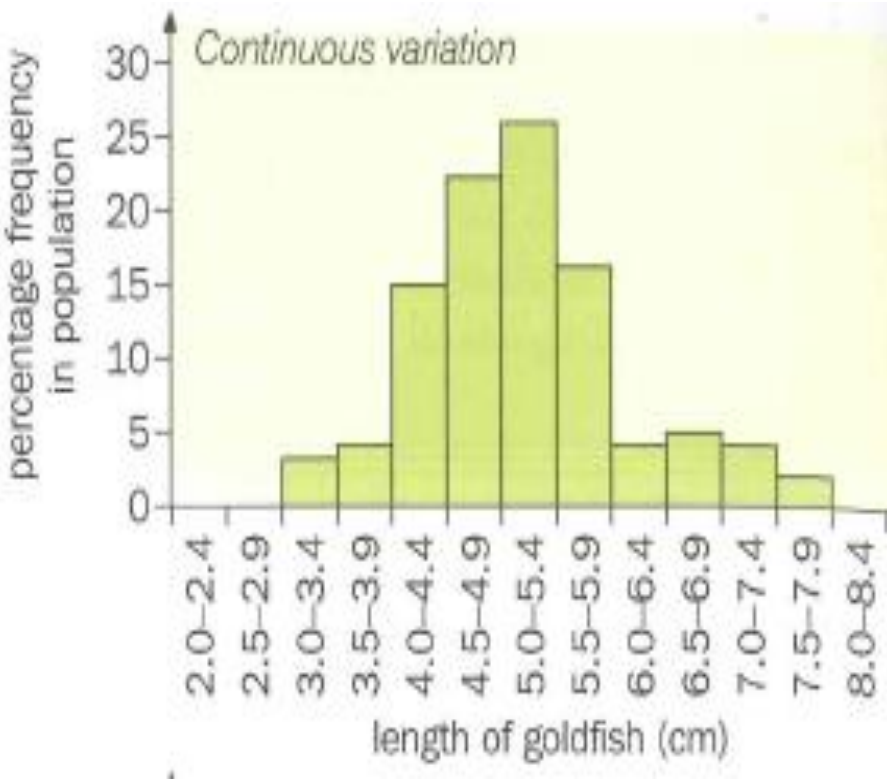
If flower colour and pollen length were NOT linked, what ratio of phenotypes would you expect from an F_2 cross of PpLl?

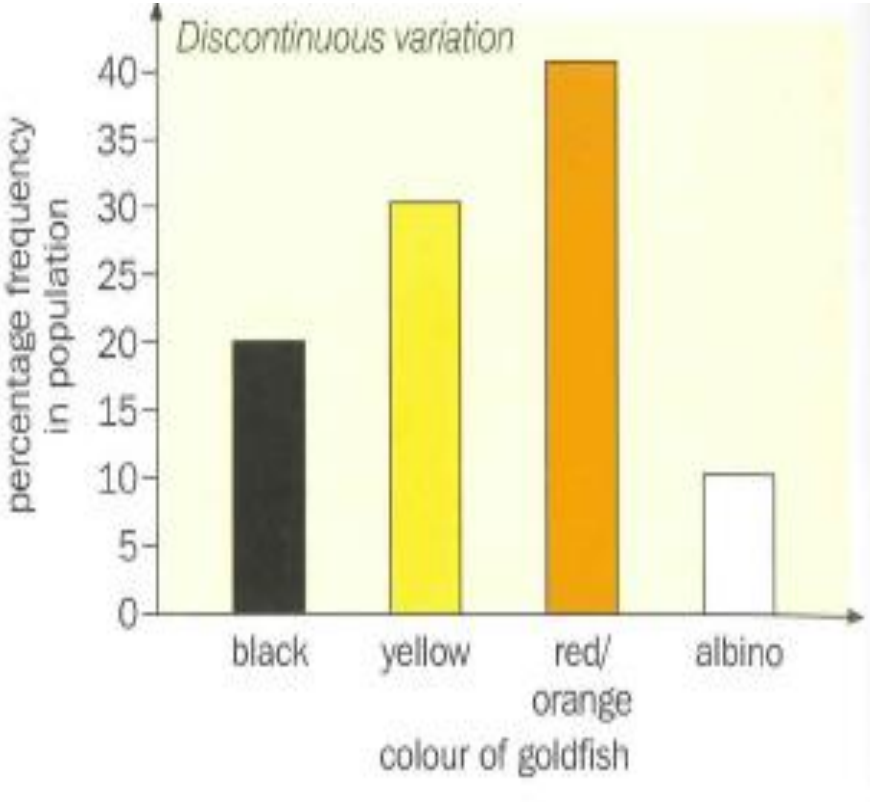
The geneticists Bateson and Punnett performed this cross and produced 427 pea plants. What are the expected results?

The actual results were significantly different. An alternative hypothesis (linkage) was needed to explain the results. A ratio of 12:1:1:2 is more typical of some linked characters, but it depends on the distance between the two genes.

	purple, long	**purple, short**	**red, long**	**red, short**
expected ratio	9	3	3	1
expected results	240	80	80	27
actual results	296	19	27	85

- Other characteristics such as those studied by Mendel in his garden peas show **discontinuous variation.** Mendel could unambiguously assign all his pea plants to a small number of phenotypes such as tall or short. This is because only **one** gene is involved, and it is quite different from continuous variation. When characteristics show discontinuous variation it is usually because they are controlled by only one gene and so there can only be a limited number of outcomes eg. tongue rolling, flower colour in peas.


Continuous variation
percentage frequency in population
0
5
10
15
20
25
30
2.0–2.4
2.5–2.9
3.0–3.4
3.5–3.9
4.0–4.4
4.5–4.9
5.0–5.4
5.5–5.9
6.0–6.4
6.5–6.9
7.0–7.4
7.5–7.9
8.0–8.4
length of goldfish (cm)


Discontinuous variation
percentage frequency in population
0
5
10
15
20
25
30
35
40
black
yellow
red/ orange
albino
colour of goldfish

Complete the PPQs

Easter work:

1. **Finish and correct genetics PPQs (we will review after Easter)**
2. **Complete animal classification definitions from Powerpoint (weebly)**
3. **Complete summary page of animal classification**
4. **Complete animal classification PPQs**