CORE IDEA 2: GENETICS & INHERITANCE
TOPIC 2.12: INHERITANCE

Learning Outcomes

(u) Explain the terms, *locus, allele, dominant, recessive, codominant, incomplete dominance, homozygous, heterozygous, phenotype* and *genotype and linkage.*

(v) Explain how genes are inherited from one generation to the next via the germ cells or gametes.

(w) Explain how genotype is linked to phenotype.

(x) Use genetic diagrams to solve problems in dihybrid crosses, including those involving codominance, incomplete dominance, multiple alleles, sex linkage, autosomal linkage and epistasis.

(y) Use genetic diagrams to solve problems involving test crosses.

(z) Explain the meaning of the terms linkage and crossing over and explain the effect of linkage and crossing over on the phenotypic ratios from dihybrid crosses.

(aa) Describe the interaction between loci (epistasis) and predict phenotypic ratios in problems involving epistasis (knowledge of the expected ratio for various types of epistasis is not required; focus of this section is on problem solving).

(bb) Explain how the environment may affect the phenotype (including how diet affects the differentiation of honeybees and how temperature affects fur colour of Himalayan rabbits).

(cc) Explain the difference between genetic variation that is continuous (many, additive genes control a characteristics) and genetic variation that is discontinuous (one or a few genes control a characteristics).

(dd) Use the chi-squared test to test the significance between observed and expected results.

Use the knowledge gained in this section in new situations or to solve related problems.

Textbooks and References

Campbell, Urry, Cain, Wasserman, Minorsky, Reece (2018) **Biology – A Global Approach (11th Edition)(Global Edition) Chapter 14: Mendelian Genetics pg. 319 – 340, Chapter 15: Linkage & Chromosomes pg. 344 - 361** (Pearson Publication) ISBN-10 1-292-17043-3

Note: This textbook is available in our library. You may wish to borrow them to supplement your reading when necessary.

Contents

1. Introduction

- Different cells in a multicellular organism contains different number of sets of chromosomes inside the nucleus. Cells are either:
    - **haploid**
        - containing 1 set of chromosomes
        - e.g. gametes like sperm and ovum
        - note that haploid ≠ monoploid
    - **diploid**
        - containing 2 sets of chromosomes
        - e.g. somatic cells like skin cell
        - diploid number varies among organisms. e.g. cucumber 2n = 14, dog 2n = 78

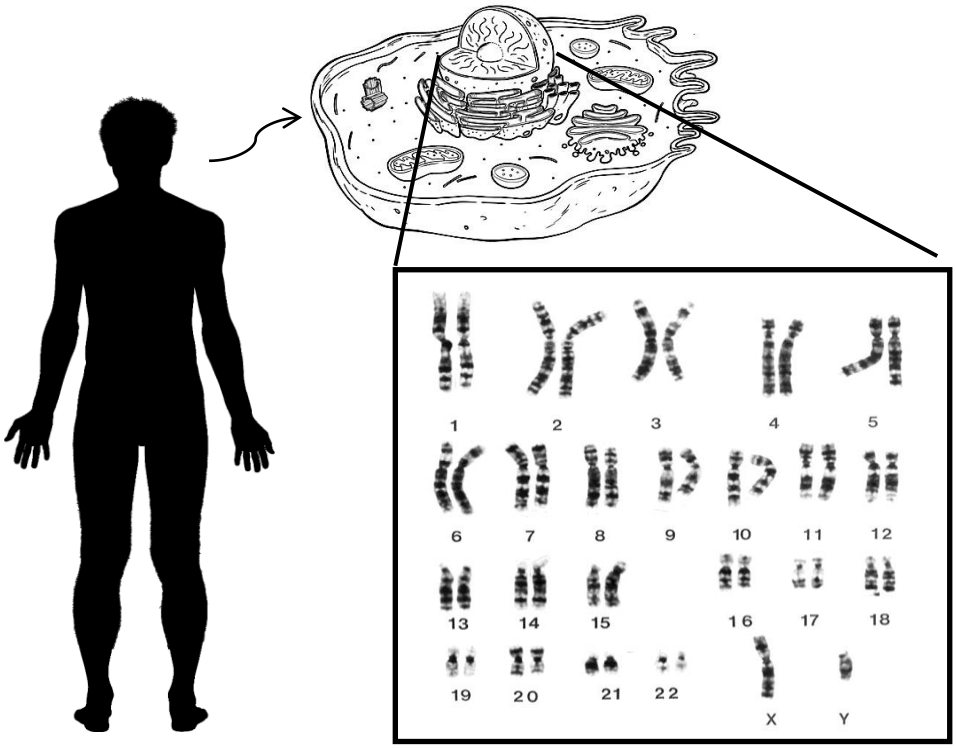


Fig. 1 Human karyotype

CHECKPOINT 1:

- The complete set of chromosomes is displayed in the _____ (arrangement of chromosomes based on length and number).

- Each chromosome contains hundreds to thousands of genes, which code for the different proteins and RNA products. The total genetic information carried by a cell, or an organism is known as the _____. It is equivalent to the DNA of a haploid set of chromosomes from that organism.

- The _____ pattern for each pair of chromosomes observed in the karyotype is similar. That is because the genes within these chromosomes are at similar positions (_____). Hence, they are known as _____pair of chromosomes (homologous = “same locus”).

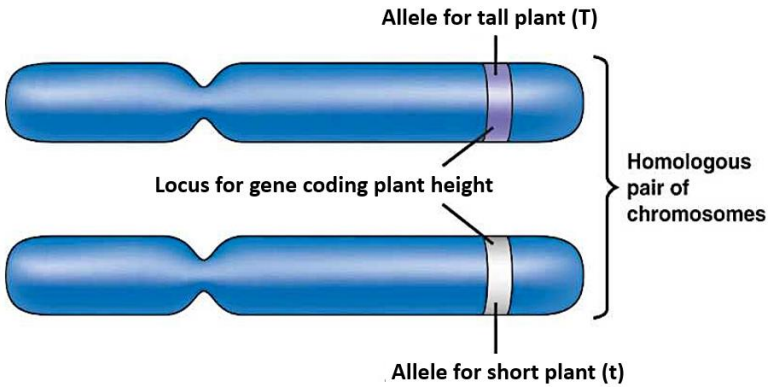
In the next section, you will learn that the genes at these loci can slightly differ, bringing about variation.

Learning Outcome 2(u):

Explain the terms, locus, allele, dominant, recessive, codominant, incomplete dominance, homozygous, heterozygous, phenotype and genotype and linkage.

2. Glossary of terms

Term	Explanation
Gene	• A gene is a **specific nucleotide sequence** of DNA that occupies a **specific locus** in a chromosome. • It codes for a **functional protein or RNA product**, and hence determines a specific phenotype of an individual. • It is a **discrete unit of inheritance** ○ E.g. gene coding for height in plants

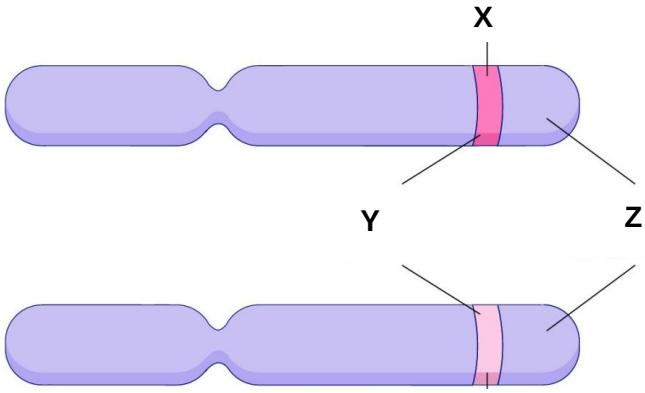
Allele	• An allele is an **alternative form of a gene** and is responsible for determining the contrasting characteristics of a gene.
	  ○ For instance, there is <u>one gene</u> responsible for the stem height of pea plants; however, there are <u>2 forms</u> of it:
	  ▪ allele for <u>tall</u> stem (T)
	  ▪ allele for <u>short</u> stem (t)
	• Occupy the **same gene locus** in a diploid cell
	• Different alleles of the same gene have their **own unique nucleotide sequence** and therefore codes for a different form of the gene product.
	  ○ Alleles are found to be identical in most of their sequences and <u>differ only at one/few nucleotides</u> of the thousand nucleotides that make up the gene.
	  ○ The following diagram represents the DNA of two alleles of one gene and their difference in the nucleotide sequence.
	Allele 1 AACCG
	Allele 2 AATTG
	• A pair of homologous chromosomes has a **pair of alleles**, occupying the same gene locus.
	 
	
	Fig. 2 A pair of homologous chromosomes

Locus	• It refers to the **specific location of a gene** along the length of a **chromosome.**

Term	Explanation
Homozygous	• The condition in which a pair of **identical alleles** for a gene are present at the same gene locus on a pair of homologous chromosomes in a diploid cell. o E.g. TT or tt
Heterozygous	• The condition in which two **different alleles** for a gene are present at the same gene locus on a pair of homologous chromosomes in a diploid cell. o E.g. Tt
Dominant *Represented by capital letter	• An allele which can **exhibit its phenotypic effect regardless of the other allele** at the same locus. • Dominant allele is fully expressed in the phenotype in a heterozygote (Tt) o E.g. The tall allele, T is dominant to the short allele, t.
Recessive *Represented by lower case letter	• An allele whose phenotypic effect is completely **masked in the presence of a dominant allele.** • Recessive alleles' phenotypic effect can only be observed when two copies are present in homozygous recessive (tt) or in the absence of a dominant allele. o E.g. The short allele, t is recessive to the tall allele, T. o E.g. The sex-linked recessive haemophilia allele, X^hY
Genotype	• Refers to **the allelic makeup of various genes**, found in a cell / organism.
Phenotype	• Observable trait (physical or physiological) of an organism. • The phenotype of an individual is determined by the genotype and may be influenced by environmental factors. o E.g. <u>physical traits</u> like hair colour o E.g. <u>physiological traits</u> like blood group
Codominant alleles	• An allele that can exhibit its phenotypic effect **with** another allele. • In a heterozygote, codominant alleles are **simultaneously and fully expressed** in the phenotype. o I^AI^B results in blood group AB
Incomplete dominance	• Occurs when alleles do not show complete dominance over each other. • Heterozygote displays a **blended, intermediate phenotype** between the homozygous dominant and recessive traits. o Presence of allele for red flower and white flower in snapdragon results in pink flowers
Linkage	• When two genes are located on the **same chromosome**, they are described as being linked o E.g. Gene for plant height and flower colour found on the same chromosome

CHECKPOINT 2

1 Which of the following descriptions matches X, Y and Z in the diagram?



	X	Y	Z
A	Locus	Allele	Homologous Chromosomes
B	Allele	Locus	Homologous Chromosomes
C	Locus	Homologous Chromosomes	Allele
D	Homologous Chromosomes	Allele	Locus

2 Which of the following statement **correctly** describes gene and an allele?

A A gene is a DNA segment that codes for a specific trait, while an allele is another gene that can influence the same trait.
B A gene is a segment of DNA that codes for a specific trait, whereas an allele is a version of that gene that can lead to different expressions of the trait.
C A gene can have only one allele in an organism, as alleles are unique to specific individuals.
D A gene and an allele are the same thing, as both refer to the DNA coding for a characteristic.

3 Match each statement to the correct genetic term.

1. A condition in which two identical alleles for a gene are present on a pair of homologous chromosomes in a diploid cell.
2. A condition in which two different alleles for a gene are present on a pair of homologous chromosomes in a diploid cell.
3. An allele that is fully expressed in the phenotype, even when only one copy is present.
4. An allele whose phenotypic effect is observed only when two copies are present or when no dominant allele is present.

	Statement 1	Statement 2	Statement 3	Statement 4
A	Dominant	Recessive	Homozygous	Heterozygous
B	Recessive	Dominant	Heterozygous	Homozygous
C	Homozygous	Heterozygous	Dominant	Recessive
D	Heterozygous	Homozygous	Recessive	Dominant

Learning Outcome 2(w):

Explain how genotype is linked to phenotype.

3. Genotype influence on phenotype

- The phenotype of an organism is mainly determined by the gene(s) controlling that particular characteristic (i.e. genotype determines the phenotype).

- Alleles of a gene specify the primary structure of polypeptides. The polypeptide folds to form the specific three-dimensional tertiary structure of proteins, due to bond formation between R groups of amino acids. The three-dimensional structure of proteins determines its function, and the subsequent phenotype.

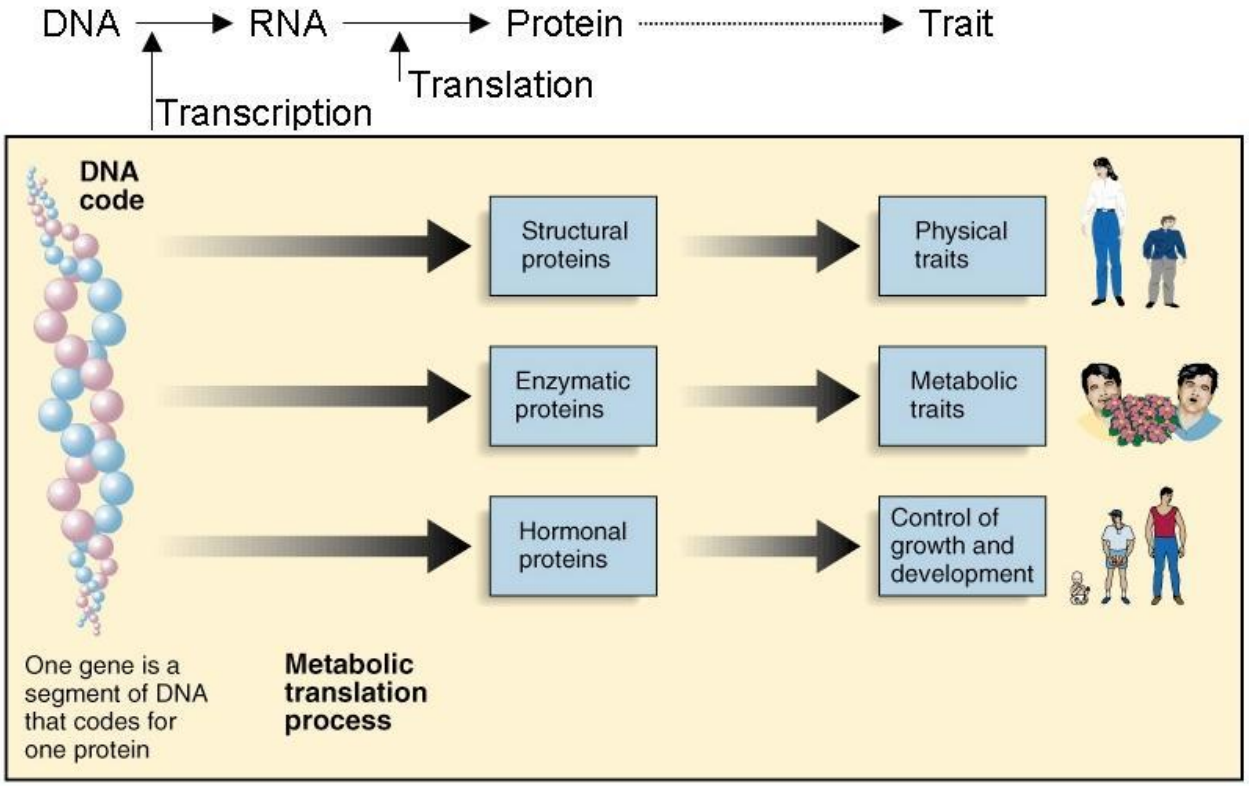


Fig. 3 Genotype influence on phenotype.

Learning Outcome 2(v):

Explain how genes are inherited from one generation to the next via the germ cells or gametes.

4. Inheritance of gene from parents via sexual reproduction

- In sexual reproduction, haploid gametes are formed, by meiosis from the nucleus of diploid cells in gonads. Each gamete contains only one copy of each gene.

- At fertilisation, male and female gametes fuse to form a zygote, restoring the diploid number. The zygote is a diploid cell with two sets of chromosomes (known as homologous pairs) one from each parent.

- Thus, there are two copies of each gene. These lie in the same position, or loci, on the two homologous chromosomes. There are at least two alleles of every gene.

- The genes control different characteristics of organisms. The alternative versions of genes (different alleles) account for variation in inherited characters.

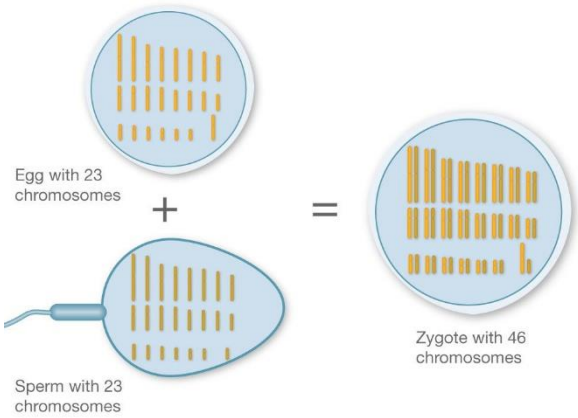


Figure 4. Fusion of a haploid egg cell and haploid sperm cell to form a diploid zygote

5. Mendel's Experiment (Further Reading, but Useful)

Gregor Mendel (1822 – 1884), an Austrian monk often called the 'Father of modern genetics', is known for his study of the inheritance of traits in pea plants.

In 1856, Mendel discovered the basic principles of heredity through hybridisation (cross-pollination) experiments with *Pisum sativum* (garden peas).

The garden pea, *Pisum sativum*, was chosen as the experimental organism due to:

(a) True-breeding/pure-breeding lines available
- A true-breeding or pure-breeding organism is one that is homozygous at the gene locus under investigation (i.e. TT or tt)

(b) Relatively easy to cross varieties to produce offspring (Fig. 4)
- The structure of the plant's flower naturally allowed for self-fertilisation to occur.
- The large flowers were easy to manipulate, which allows artificial cross-fertilisation.

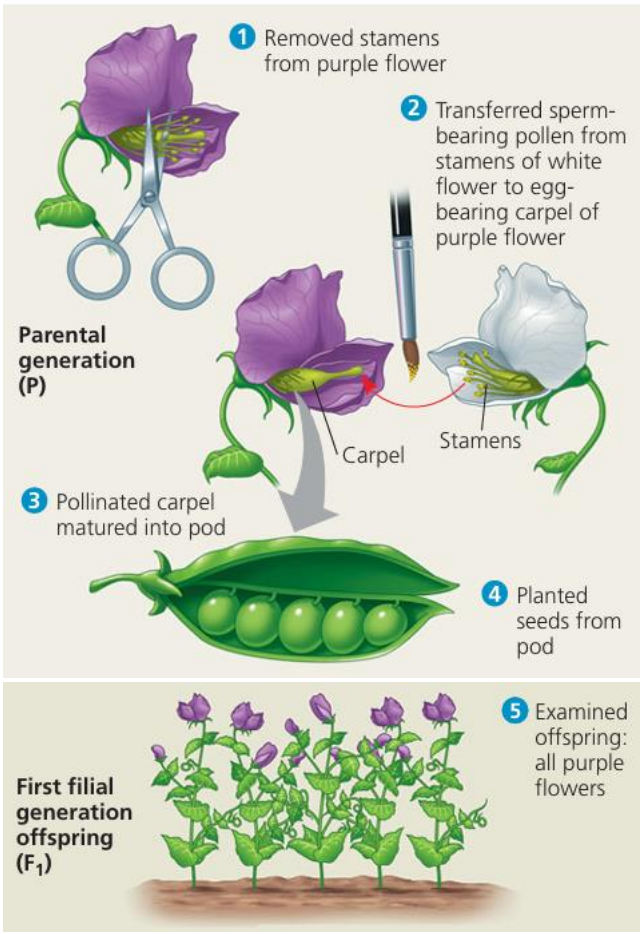
(c) Distinct phenotypes for chosen characteristics
- Clear, easily distinguishable traits present, such as stem length, seed shape, seed colour, pod shape, pod colour, flower colour, and flower position.

(d) Reproduce quickly with a large number of offspring
- This allows experimental results to be obtained within a short period of time.
- A large number of offspring is required to obtain a fair and accurate result in testing of hypotheses.

(e) Common, cheap and easily available

(f) Easy to cultivate

Mendel's experiment proceeds as such:



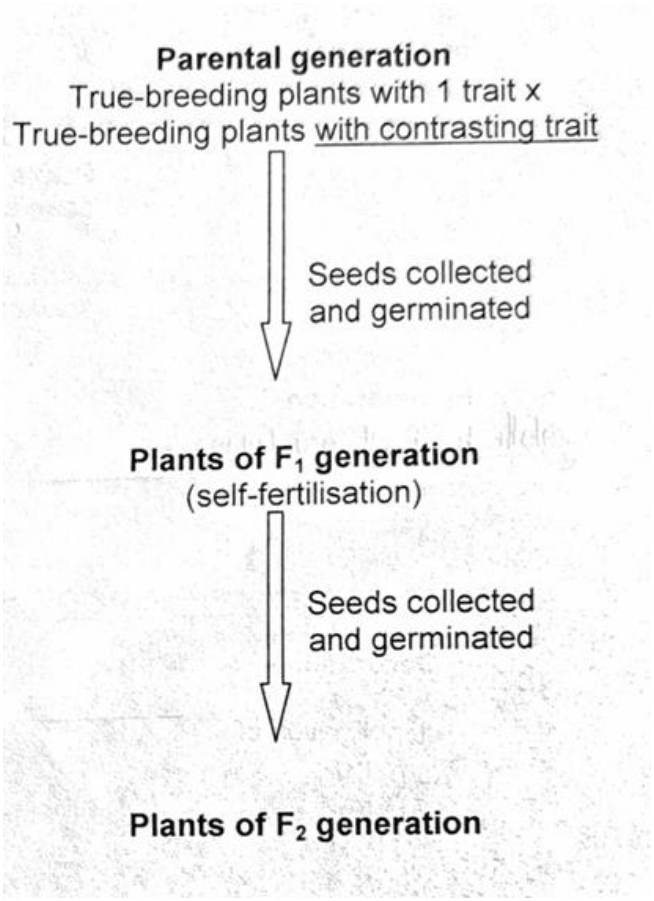
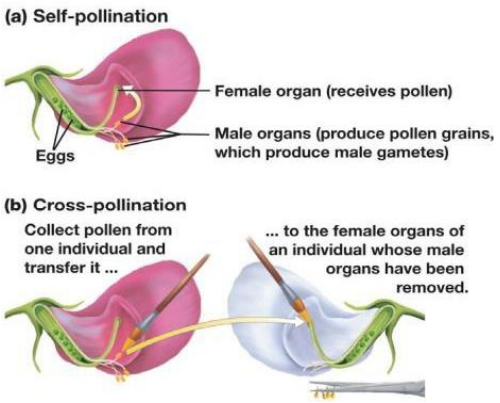


Figure 5. Crossing of the Pea Plant

1. Mendel observed seven characters, each of which occurred in two alternative forms. For example, Purple vs White flowers, Round vs Wrinkled Seeds, Tall vs Short stems.

2. To study how a particular character would be transmitted from the parent plant to the next generation, Mendel started his experiments with true-breeding plant varieties with contrasting traits (*Fig. 4*). The true-breeding parental plants are called the **Parental generation**.

   - **True-breeding / pure breeding** – always producing offspring with the same traits as the parents when the parents are self-fertilized/self-pollinated. Individuals are either homozygous dominant or homozygous recessive.



3. Following cross-fertilization, the seeds were collected and germinated. The resulting hybrid offspring comprised the **F_1 generation** (first filial generation, the word *filial* from the Latin word for "son").

4. F_1 generation plants **self-pollinate/self-fertilize** to produce the next generation, the **F_2 generation** (second filial generation).

5. Mendel observed the transmission of selected traits for at least three generations and arrived at two principles of heredity that are now known as the **law of segregation** and the **law of independent assortment**.

6. Monohybrid Inheritance (Review of O Level Foundation) & Mendel's Law of Segregation

Monohybrid crosses investigate the inheritance of a **<u>one</u>** characteristic, involving **one pair of alleles at one gene locus**. (e.g. Aa x Aa)

6.1 Mendel's Experiment

Pure-breeding plants with **purple flowers** were crossed with pure-breeding plants with **white flowers.** <u>All offspring of the F_1 generation had purple flowers</u>. The genetic cross below helps to illustrate the expected phenotypic ratio of 3:1 in the F_2 generation resulting from the self-fertilisation of F_1 plants

Let **P** be the allele for purple flowers
Let **p** be the allele for white flowers.

The allele for purple flowers, **P**, is dominant to the allele for white flowers, **p**.

<table>
<tr><td>Step 1: Write_____ _____involved</td><td>Parental phenotypes</td><td></td><td>X</td><td></td></tr>
<tr><td>Step 2: Write_____ _____involved</td><td>Parental genotypes</td><td></td><td>X</td><td></td></tr>
<tr><td>Step 3: Write gametes produced from meiosis.

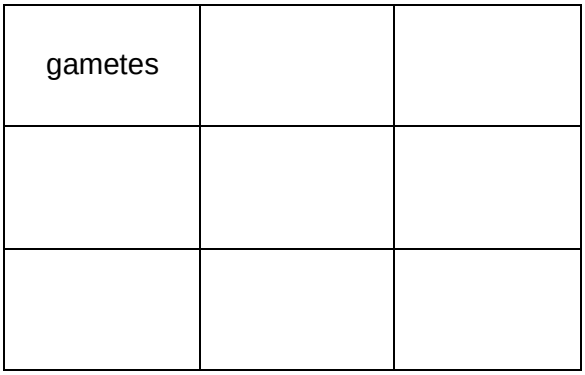
_____ all gametes.</td><td>Parental Gametes</td><td></td><td></td><td></td></tr>
<tr><td>Step 4: Use Punnett Square to illustrate _____of gametes process

_____ all gametes in the Punnett Square.

_____ circle the diploid genotype

Write _____ below the genotypes

Draw the lines in the table properly</td><td>Punnett Square</td><td colspan="3"><table><tr><td>gametes</td><td></td></tr><tr><td></td><td></td></tr></table></td></tr>
<tr><td>Step 5: Write down the _____ and _____</td><td>F_1 genotypic ratio</td><td colspan="3"></td></tr>
<tr><td>Step 6: Write down _____ and _____</td><td>F_1 phenotypic ratio</td><td colspan="3"></td></tr>
</table>

Step 1: Write_____ _____involved	Selfing of F_1 phenotypes		X	
Step 2: Write_____ _____involved	F_1 genotypes		X	
Step 3: Write _____ _____ gametes produced from meiosis. _____ all gametes.	F_1 Gametes			
Step 4: Use Punnett Square to illustrate _____ _____ of gametes process _____ all gametes in the Punnett Square. _____circle the diploid genotype Write _____ below the genotypes Draw the lines in the table properly	Punnett Square			
Step 5: Write down the _____ and _____	F_2 genotypic ratio			
Step 6: Write down _____ and _____	F_2 phenotypic ratio			

*Recall, you were required to predict the results of Monohybrid Cross (expected ratios of 3:1), using the terms homozygous, heterozygous, F1 generation and F2 generation back in O levels.

6.2 Mendel's First Law: Law of Segregation

- The law of segregation states that two different alleles in a diploid organism will randomly segregate (separate) during meiosis to end up in different gametes.

- Each cell of an individual carries two alleles at any one gene locus found on two homologous chromosomes (one from each parent).

- Separation of homologous chromosomes during anaphase I of meiosis results in the segregation of the pair of alleles. Thus, each gamete inherits only **one allele** of each gene.

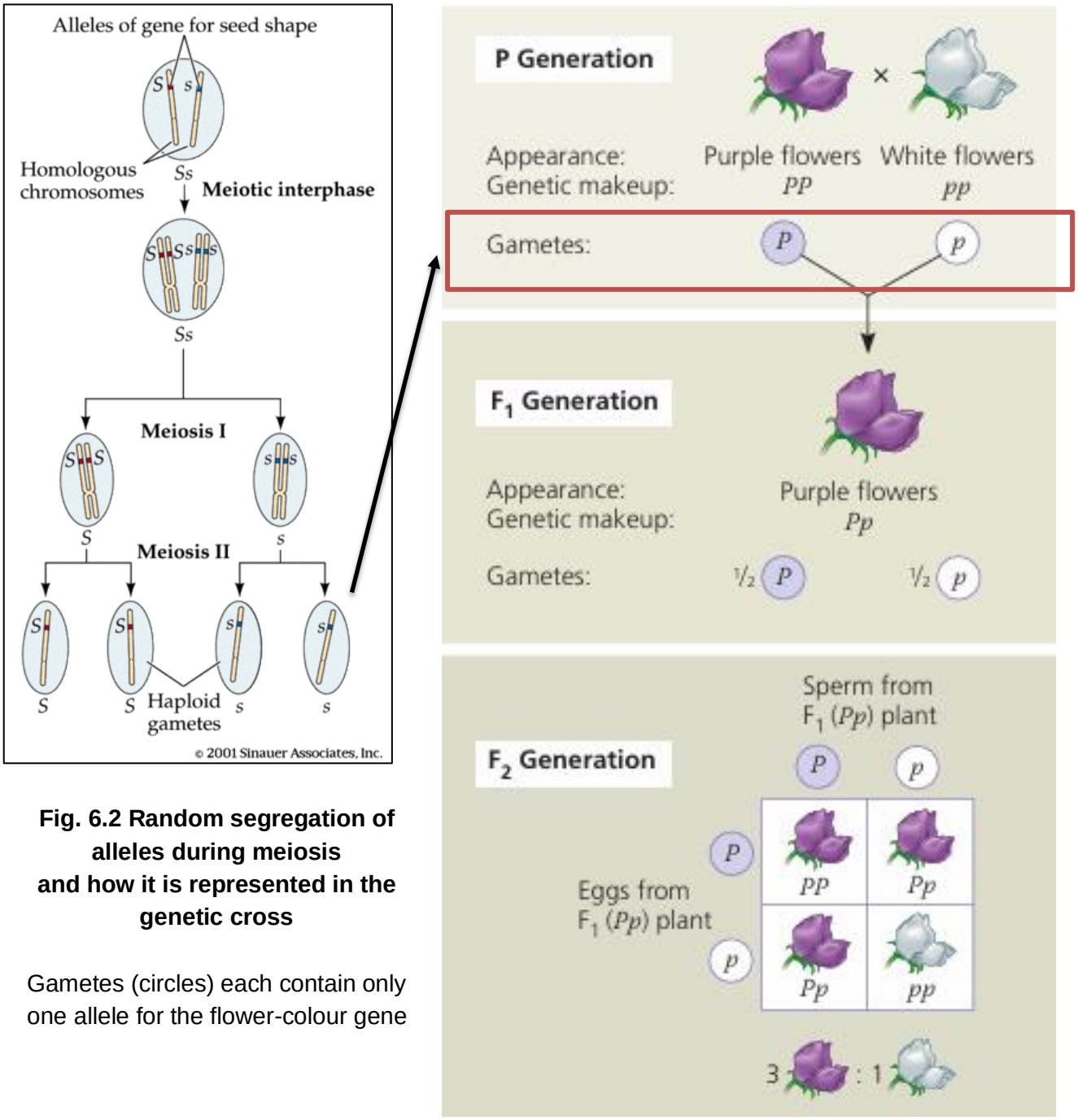


Fig. 6.2 Random segregation of alleles during meiosis and how it is represented in the genetic cross

Gametes (circles) each contain only one allele for the flower-colour gene

CHECKPOINT 6.2: Monohybrid Inheritance in Plants (Stem Height)

Practice drawing the gene cross from scratch!

i. Define the symbols if it is not provided in the question.
Write " Let **T** be the allele for _____, **t** the allele for _____"

ii. Take note of the pattern of the headings:
Parental Phenotype → Parental Genotype → Gamete → Punnett's Square (fertilisation) → Offspring Genotypic ratio, Offspring Phenotypic Ratio.

iii. Take note that gametes must be drawn in circles. Use a ruler for Punnett's square!

Pure-breeding plants with **tall stem** were crossed with pure-breeding plants with **short stem**. All offspring of the F_1 generation had tall stems. Illustrate the expected phenotypic ratios in the F_2 generation resulting from the self-fertilisation of F_1 plants.

The allele for tall stem, **T,** is dominant to the allele for short stem, **t.**
Let **T** be the allele for tall stem.
Let **t** be the allele for short stem.

Learning Outcome 2(x):

Use genetic diagrams to solve problems in dihybrid crosses.

7. Dihybrid Inheritance & Mendal's Law of Independent Assortment

- **Dihybrid crosses** investigate the inheritance of **<u>two</u>** characteristics, involving **two pairs of alleles at two gene loci**.
  E.g. AaBb x AaBb

- Using the garden pea plant, Mendel investigated how two different characteristics (e.g. seed colour and seed shape) were inherited.

Example

Pure-breeding pea plants with **yellow** and **round** seeds were crossed with pure-breeding pea plants with **green**, **wrinkled** seeds. <u>All offspring of the F_1 generation had yellow and round seeds</u>. Illustrate the expected phenotypic ratios in the F_2 generation resulting from the self-fertilisation of F_1 plants.

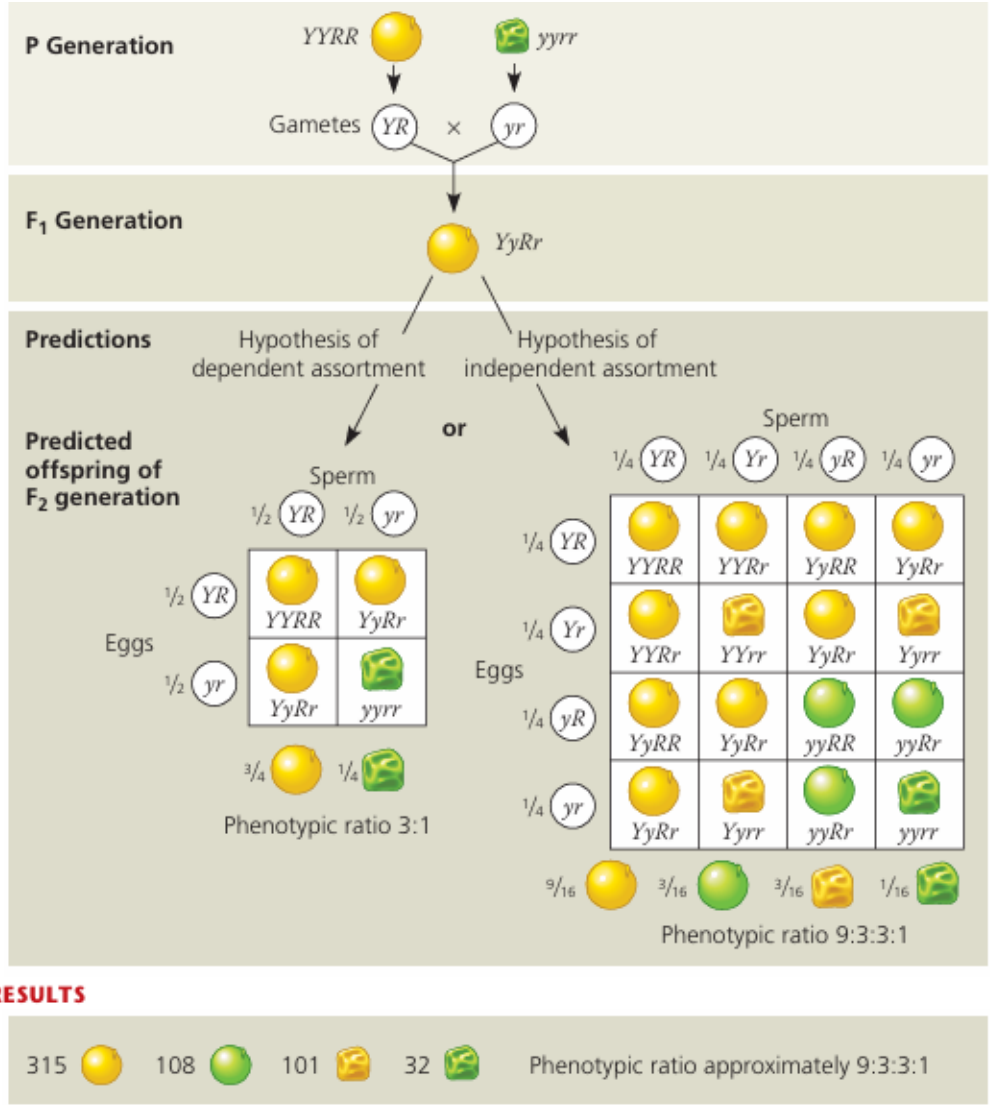


Fig. 7.1 Dihybrid inheritance

Legend

Let **Y** represent the dominant allele for yellow seed in pea plant.

Let **y** represent the recessive allele for green seed in pea plant.

Let **R** represent the dominant allele for round seed shape in pea plant.

Let **r** represent the recessive allele for wrinkled seed shape in pea plant.

<table>
<tr><td>Step 1:
Write_____
_____involved</td><td>Parental phenotype</td><td></td><td>X</td><td></td></tr>
<tr><td>Step 2:
Write_____
_____involved</td><td>Parental genotype</td><td></td><td>X</td><td></td></tr>
<tr><td>Step 3: Write gametes produced from meiosis.

_____ all gametes.</td><td>Parental gametes</td><td></td><td></td><td></td></tr>
<tr><td>Step 4: Use Punnett Square to illustrate
_____
__of gametes process

_____ all gametes in the Punnett Square.

_____ circle the diploid genotype

Write _____ below the genotypes

Draw the lines in the table properly</td><td>Random fertilization</td><td colspan="3"><table><tr><td>gametes</td><td></td></tr><tr><td></td><td></td></tr></table></td></tr>
<tr><td>Step 5: Write down the
_____
and _____</td><td>F_1 genotypic ratio</td><td colspan="3"></td></tr>
<tr><td>Step 6: Write down
_____
and _____</td><td>F_1 phenotypic ratio:</td><td colspan="3"></td></tr>
</table>

<table>
<tr><td>Step 2: Write <u>F_1 genotypes</u> involved</td><td>F_1 x F_1</td><td colspan="3"></td><td>X</td><td colspan="4"></td></tr>
<tr><td>Step 3: Write <u>all different</u> gametes produced from meiosis in a <u>single row</u>

<u>Circle</u> all gametes.</td><td>F_1 gametes</td><td colspan="3"></td><td></td><td colspan="4"></td></tr>
<tr><td>Step 4: Use Punnett Square to illustrate <u>random fertilization</u> of gametes process

<u>Circle</u> all gametes in the Punnett Square.

<u>Do not</u> circle the diploid genotype

Write <u>phenotype</u> below the genotypes

Draw the lines in the table properly</td><td>Random fertilization</td><td colspan="7"><table><tr><td>gametes</td><td></td><td></td><td></td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td></tr></table></td></tr>
<tr><td>Step 5: Write down the <u>F_2 genotype</u> and <u>ratio</u>

Dashes indicate _____ allele (e.g. Y or y, R or r)

*If the question asks for genotype, do not give dashes. Dashes only help to determine genotypic ratio</td><td>F_2 genotypic ratio</td><td colspan="3"></td><td></td><td colspan="4"></td></tr>
<tr><td>Step 6: Write down <u>F_2 phenotype</u> and <u>ratio</u></td><td>F_2 phenotypic ratio</td><td colspan="3"></td><td></td><td colspan="4"></td></tr>
</table>

7.1 Mendel's Second Law: Law of Independent Assortment

- The law of independent assortment states that the segregation of alleles from one gene **does not influence** the inheritance of the alleles of another gene, i.e. inheritance of alleles of each gene is **independent** of each other.

- The arrangement of each pair of homologous chromosomes at metaphase plate in metaphase I of meiosis is independent of the next pair. During anaphase I, the separation of each pair of homologous chromosomes is independent of the next pair.

- This applies to **unlinked genes** (genes found on different pairs of chromosomes).

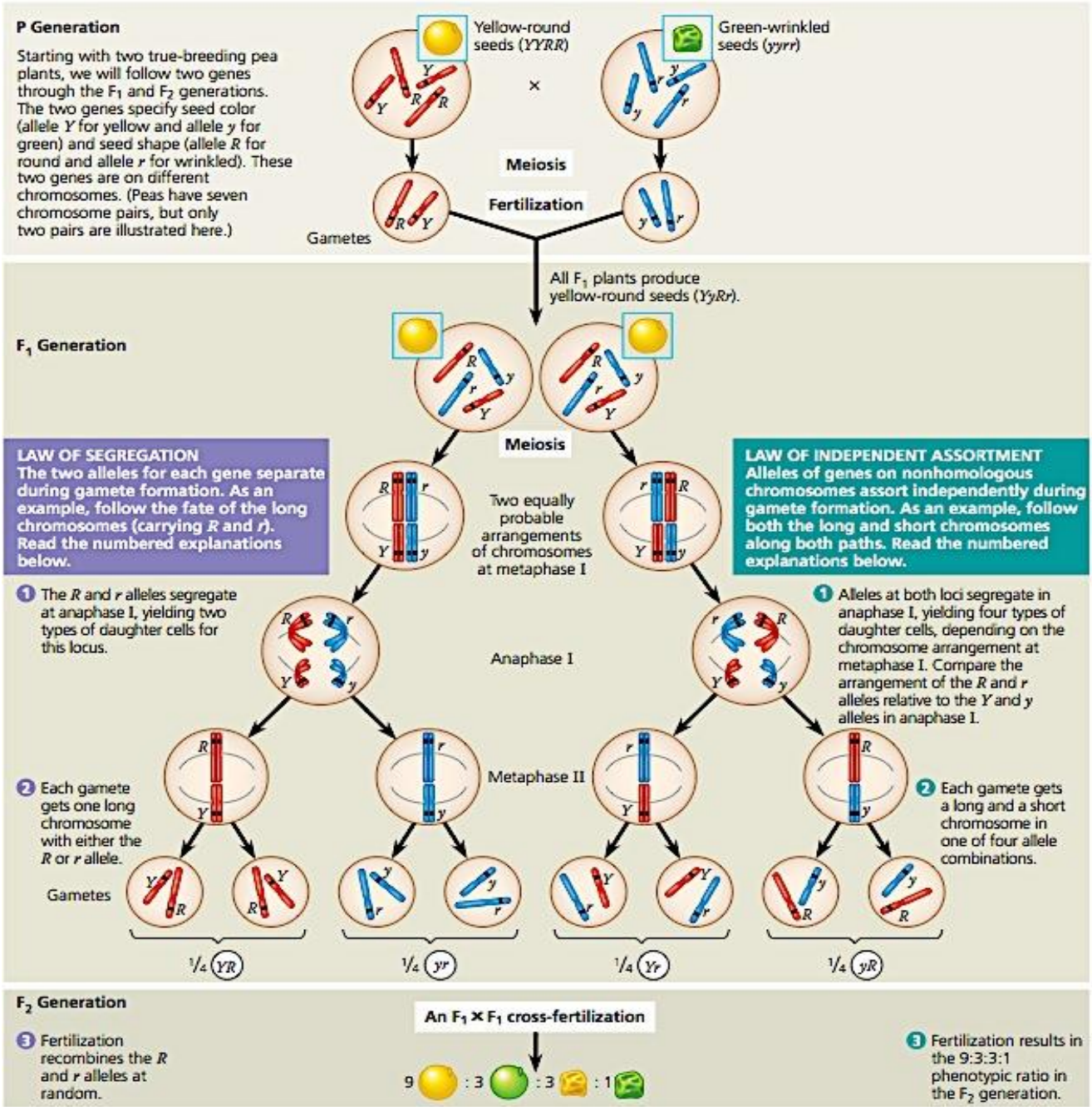


Fig. 7.2 Independent assortment

CHECKPOINT 7.1: Dihybrid Inheritance (Guinea Pig Hair Length and Colour)

A cross between pure-breeding short black-haired guinea pig and pure-breeding, long white-haired guinea pig produced all short and black hair guinea pigs in the F_1 generation.

Use a genetic diagram to illustrate the expected phenotypic ratio in the F_2 generation resulting from sibling crosses of the F_1 offspring.

Legend

Let A represent the dominant allele for short hair length in guinea pig

Let a represent the recessive allele for long hair length in guinea pig.

Let B represent the dominant allele for black hair colour in guinea pig.

Let b represent the recessive allele for white hair colour in guinea pig.

Parental phenotype			
Parental genotype			
Parental Gametes:			
Punnett square	Gametes		
F_1 genotype			
F_1 phenotype			
F_1 x F_1 (phenotype)			
F_1 x F_1 (gametes)			

Punnett square					
	Gametes				

F_2 genotypic ratio	
F_2 phenotypic ratio	

If there were a total of 576 guinea pigs in the F_2 generation, how many individuals of each phenotype would you expect to observe?

Phenotype	Expected Ratio	Expected Number (E)

Learning Outcome 2(y):

Use genetic diagrams to solve problems involving test crosses.

8. Test Cross

- A test cross is a cross between any individual organism and a **homozygous recessive** (for all the genes that are being investigated) individual.

- Test cross can be used to:
  - <u>determine the unknown genotype</u> of an individual organism

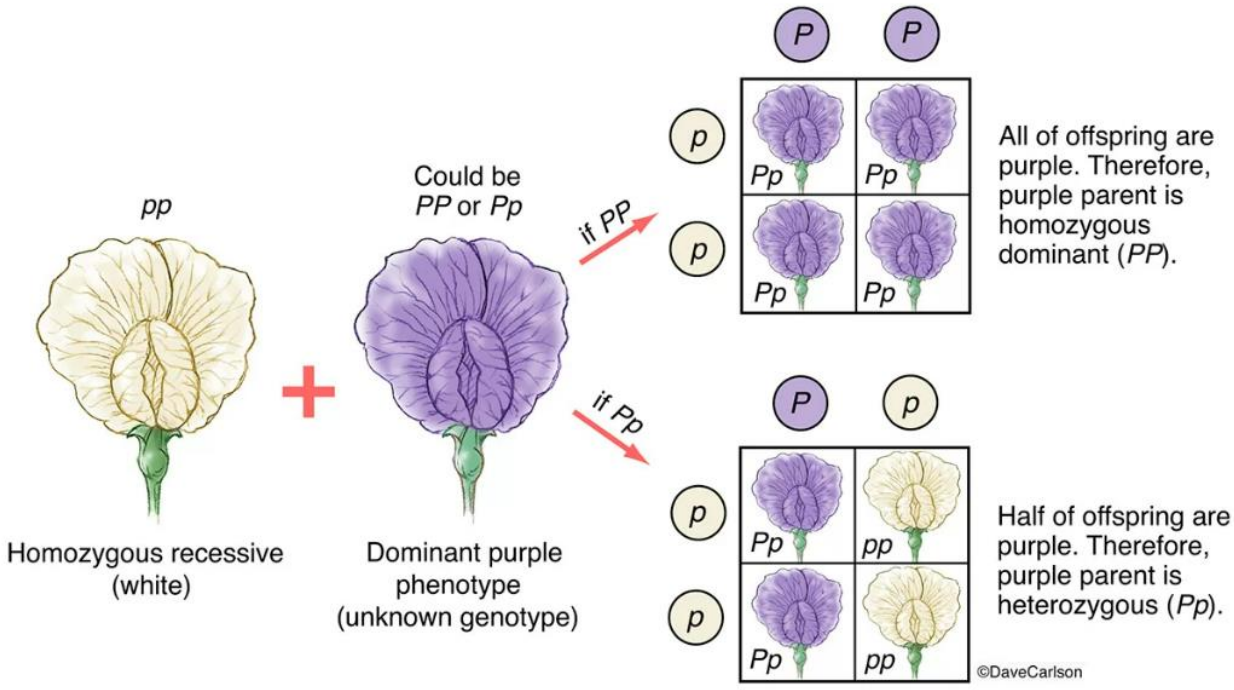


Figure 8: Test cross involves crossing an unknown genotype with a homozygous recessive The resultant ratio helps to determine if the unknown genotype is Pp or PP.

8.1 Determining Unknown Genotype

Organisms with **dominant phenotype** may have a few possible genotypes which includes **homozygous dominant for both traits (e.g. AABB), homozygous dominant for one trait AND heterozygous for the other trait (e.g. AABb or AaBB) or heterozygous for both traits (e.g. AaBb)**. To determine the genotype of an organism with dominant phenotype, a test cross is used.

Example

For pea plant exhibiting dominant phenotype yellow and round seeds may have genotype RRYY, RrYy, RRYy or RrYY. A test cross can be used to decipher the genotype of the plant by observing the phenotypes of the test cross offspring

If the parental genotype is RRYY,

Parental phenotype	round, yellow seed	x	wrinkled, green seed
Parental genotype	RRYY	x	
Parental gametes	(RY)		(ry)

Random fertilization

Gametes	(RY)
(ry)	RrYy

Offspring genotype	
Offspring phenotype	

If the parental genotype is RrYy,

Parental phenotype	round, yellow seed	x	wrinkled, green seed
Parental genotype	RrYy	x	
Parental gametes	(RY) (Ry) (rY) (ry)		(ry)

Random fertilization

Gametes	(RY)	(Ry)	(rY)	(ry)
(ry)	RrYy	Rryy	rrYy	rryy

Offspring genotypic ratio	
Ofspring phenotypic ratio	

If the parental genotype is RRYy,

Parental phenotype	round, yellow seed	x	wrinkled, green seed
Parental genotype	RRYy	x	
Parental gametes	RY Ry		ry

Random fertilization

Gametes	RY	Ry
ry	RrYy	Rryy

Offspring genotypic ratio	
Offspring phenotypic ratio	

If the genotype is RrYY,

Parental phenotype	round, yellow seed	x	wrinkled, green seed
Parental genotype	RrYY	x	
Parental gametes	RY rY		ry

Random fertilization

Gametes	RY	rY
ry	RrYy	rrYy

Offspring genotypic ratio	
Offspring phenotypic ratio	

CHECKPOINT 8

These are some crosses that were performed.

1. aa X AA
2. Aa X Aa
3. CC X CC
4. cc X cc
5. Bb x bb

Which of the following is/are test cross(es)?

(a) 1 and 2 **(b)** 1 and 5 **(c)** 3 and 4 **(d)** 3 and 5

Learning Outcome 2(x):

Use genetic diagrams to solve problems in dihybrid crosses, including those involving codominance, incomplete dominance, multiple alleles, sex linkage, autosomal linkage and epistasis.

9. Non-Mendelian Inheritance

Inheritance patterns are often more complex than the predicted Mendelian ratios. Mendel chose pea plant characters that turn out to have a **relatively simple genetic basis**: Each character is determined by one gene, for which there are only two alleles, one completely dominant and the other completely recessive.

However, not all heritable characters are determined so simply, and the **relationship between genotype and phenotype is rarely so straightforward**. There are many characters which are controlled by more than one gene, or more than two alleles, and have alleles which are not completely dominant or recessive.

This does not diminish the utility of Mendelian genetics however, because the basic principles of segregation and independent assortment still apply to more complex patterns of inheritance. In this section, we will **extend Mendelian genetics** to hereditary patterns that were not reported by Mendel.

To **observe Mendelian inheritance dihybrid ratio of 9:3:3:1**, the characteristics investigated must be controlled by genes that	**Deviation from the Mendelian ratio** is observed for:
alleles have a complete dominant-recessive relationship	incomplete dominance and codominance
have only two possible alleles per gene locus	multiple alleles
are autosomal i.e. found on autosomes (not sex chromosomes)	sex linkage
are unlinked i.e. found on different chromosomes	autosomal linkage
do not interact with each other	epistasis

9.1 Incomplete Dominance

- Incomplete dominance occurs when an allele does not show complete dominance over another allele.
- A heterozygote exhibits a blended**, intermediate phenotype** between the homozygous dominant and recessive conditions.
- It occurs when a single dominant allele does not express sufficient gene product, i.e. proteins to control the characteristic completely.
- Neither allele is dominant, so rather than using upper and lowercase letters, we use the letter C with a superscript to indicate an allele for flower colour: C^R for red and C^W for white.

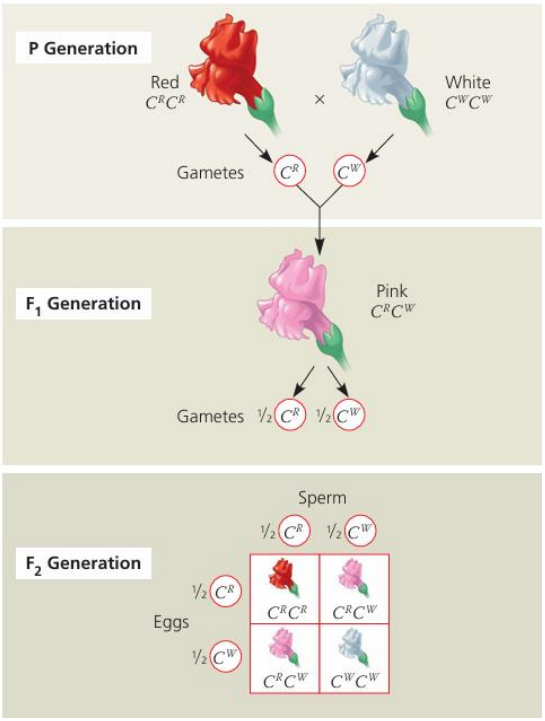


Figure 9.1 Incomplete dominance in snapdragon colour.

Example

A pure-breeding red snapdragon (*Antirrhinum majus*) with **red flowers** is crossed with a pure-breeding one with **white flowers**. The F_1 generation all have pink flowers. Illustrate the phenotypic ratio in the F_2 generation using a genetic diagram.

Legend

Let C^R represent the allele for red flower

Let C^W represent the allele for white flower

Parental phenotype	Red Flower	x	White Flower
Parental genotype	$C^R C^R$		$C^W C^W$
Parental gametes	C^R		C^W
F_1 genotype		$C^R C^W$	
F_1 phenotype		Pink	
F_1 x F_1	$C^R C^W$	x	$C^R C^W$
F_1 gametes	C^R C^W		C^R C^W
Random fertilization			

	C^R	C^W
C^R	$C^R C^R$	$C^R C^W$
C^W	$C^R C^W$	$C^W C^W$

F_2 genotypic ratio	1 $C^R C^R$: 2 $C^R C^W$: 1 $C^W C^W$
F_2 phenotypic ratio	1 Red : 2 Pink: 1 White

9.2 Codominance

Codominance occurs when alleles of a gene are **simultaneously expressed** in the phenotype. A heterozygote will **express both phenotypes**.

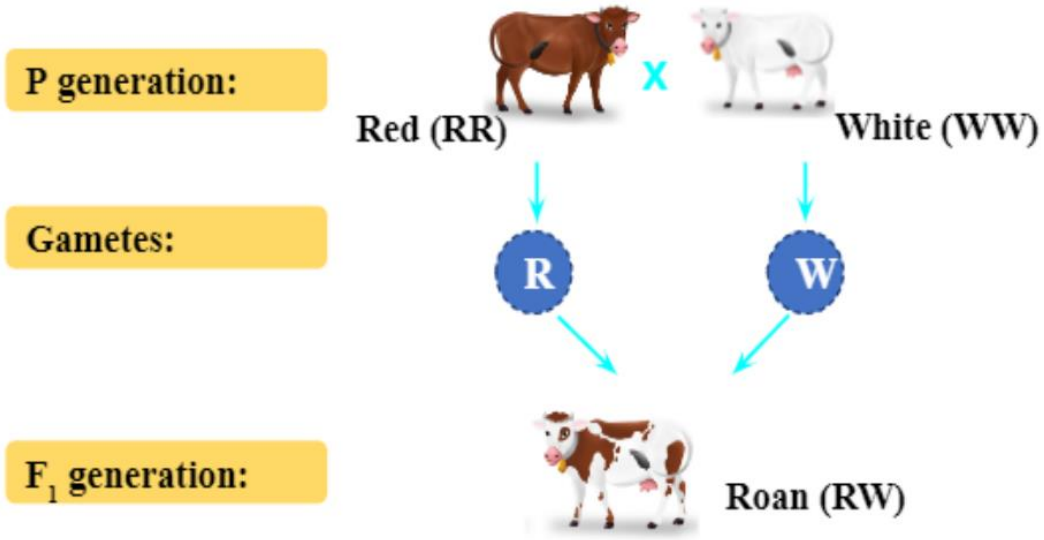


Figure 9.2 Co-Dominance observed in short horn cattle

Example

A pure-breeding short horn cattle with **red** coat was crossed with another pure-breeding short horn cattle with **white** coat. All F1 offspring have roan coats.

Legend

Let R represent the allele for Red Coat (codominant)

Let W represent the allele for White Coat (codominant)

Parental phenotype	Red Coat	x	White Coat
Parental genotype	RR		WW
Parental gametes	(R)		(W)
F_1 genotype		RW	
F_1 phenotype		All Roan coat	
F_1 x F_1	RW	x	RW
F_1 gametes Random fertilization	(R) (W)		(R) (W)

	(R)	(W)
(R)	RR	RW
(W)	RW	WW

F_2 genotypic ratio	1 RR : 2 RW : 1 WW
F_2 phenotypic ratio	1 Red : 2 Roan 1 White

9.3 Multiple Alleles

- If a gene controlling a characteristic has **three or more possible alleles**, the gene is considered to have multiple alleles.

- However, in a diploid organism, only **two** alleles may occupy one gene locus on a pair of homologous chromosomes at a time.

Example

- ABO blood group in humans is determined by **multiple alleles** (I^A, I^B and i) of a single gene. In each individual, a maximum of two of these alleles are present at the gene locus.

- Alleles I^A and I^B are **codominant**, coding for enzymes that add different glycoproteins (antigens) to the surface of red blood cells. The **allele I^A** codes for **type A antigen**, and the **allele I^B** codes for **type B antigen**.

- The **allele i** is **recessive** to both I^A and I^B and codes for a non-functional enzyme that does not add any antigen to the surface of red blood cells.

(a) The three alleles for the ABO blood groups and their carbohydrates

Allele	I^A	I^B	i
Carbohydrate	A △	B ○	none

(b) Blood group genotypes and phenotypes

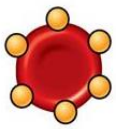
Genotype	I^AI^A or I^Ai	I^BI^B or I^Bi	I^AI^B	ii
Red blood cell appearance				
Phenotype (blood group)	A	B	AB	O

Fig. 9.3 Multiple alleles in ABO blood group system in humans.

Worked Example: Multiple Alleles which are co-dominant

A man with blood group A marries a woman with blood group B.
(a) If they have a child with blood group O, identify the genotype of both parents.
(b) What is the probability of their second child having blood group A?

Legend
Let I^A represent the allele for blood group A.
Let I^B represent the allele for blood group B.
Let i represent the allele for blood group O.

Parental phenotype	blood group A	x	blood group B
Parental genotype	I^Ai	x	I^Bi
Parental gametes	I^A i		I^B i

Random fertilization

Gametes	I^A	i
I^B	I^AI^B	I^Bi
i	I^Ai	ii

Offspring genotypic ratio	1 I^AI^B	1 I^Ai	1 I^Bi	1 ii
Offspring phenotypic ratio	1 blood group AB	1 blood group A	1 blood group B	1 blood group O

CHECKPOINT 9.3 – Multiple Alleles which have different levels of dominance

The chinchilla has white hair on the body and black hair on the feet, tail, ears and face. The allele for the chinchilla pigment pattern, c^h, is recessive to the allele for dark chinchilla (all hair dark grey), c^{chd}, which is in turn recessive to normal colour (all hair agouti), C. The allele for Himalayan pigment pattern is dominant to the allele for albino (all hair white, no pigment production), c. All the alleles of this gene produce different versions of the same enzyme involved in pigment production.

(a) List the alleles controlling pigment production in order of dominance (dominant series)

(b) List the possible genotypes for the following phenotypes:

Phenotypes	Possible genotype(s)
Agouti	
Chinchilla	
Himalayan	
Albino	

9.4 Sex-linkage

9.4.1 Sex determination in humans

- The first 22 pairs of chromosome are known as **autosomes** or autosomal chromosomes. The 23rd pair of chromosomes is known as the sex chromosomes. The X chromosome is larger than the Y chromosome.

- The genotype of the female is XX and that of the male is XY. The sex having genotype XX is **homogametic** as it produces gamete cells containing only X chromosome. The sex having genotype XY is **heterogametic** as half their gametes contain the X chromosome and half the Y chromosome.

Fig. 9.4.1.1 Relative sizes of human sex chromosomes

- The sex of an offspring is determined by the sex chromosome carried by the sperm that fertilizes the egg.

- Sex determination generally proceeds in the direction of female development. A gene on the Y chromosome called sex-determining region of Y (SRY) is responsible for the development of testes. Without the gene SRY, the gonads will develop into ovaries.

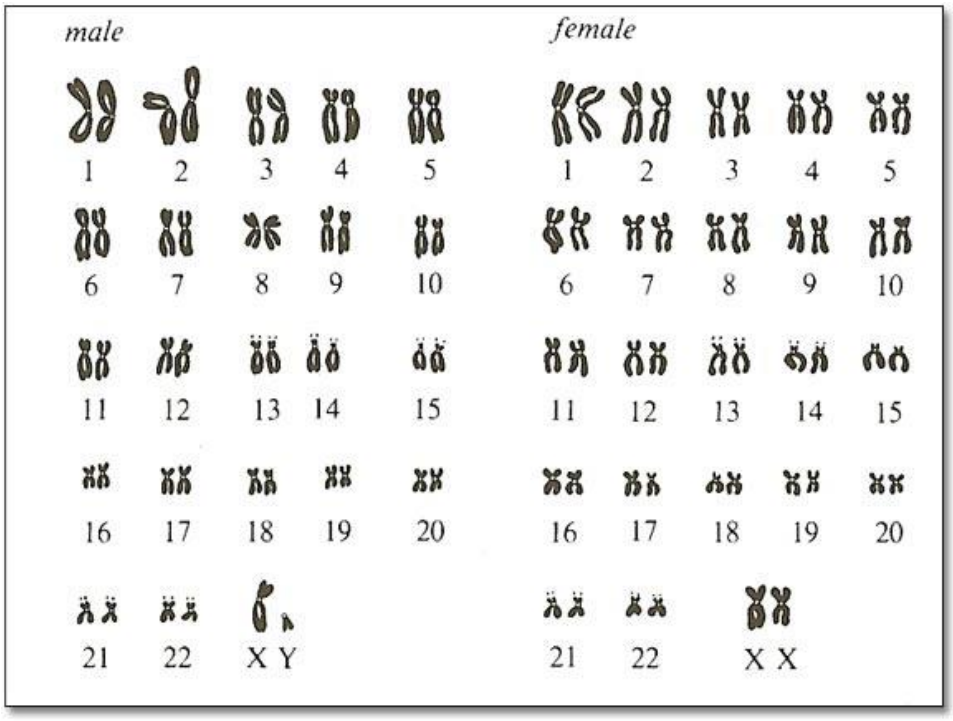


Fig. 9.4.1.2 Karyotype of a male and female human.

9.4.2 Sex determination in other organisms

- **The X-Y system**: Similarly, in ***Drosophila***, the female is XX and the male is XY.

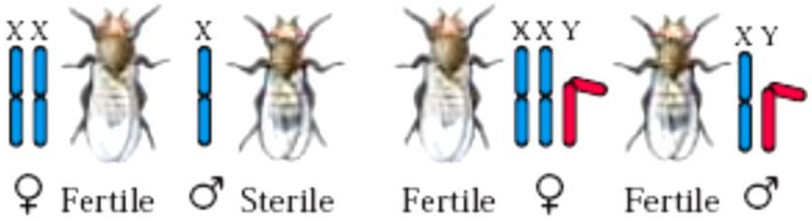


Fig. 9.4.2.1. Sex determination in *Drosophila melanogaster.*

The Z-W system. In birds, some fishes, and some insects, the **sex chromosomes present in the egg** (not the sperm) **determine the sex** of offspring. The sex chromosomes are designated Z and W. Females are ZW (heterogametic) and males are ZZ (homogametic).

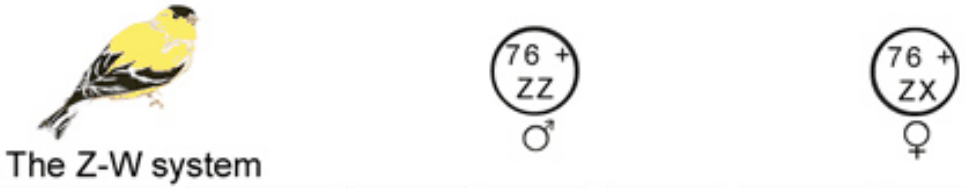


Fig 9.4.2.2. Sex determination in birds.

- **The haploid-diploid system**: There are no sex chromosomes in most species of bees and ants. For example, in **honeybees**, females develop from fertilized eggs and are thus **diploid**. **Males** develop from unfertilized eggs and are **haploid**..

  Note that the female has twice as many chromosomes as the male.

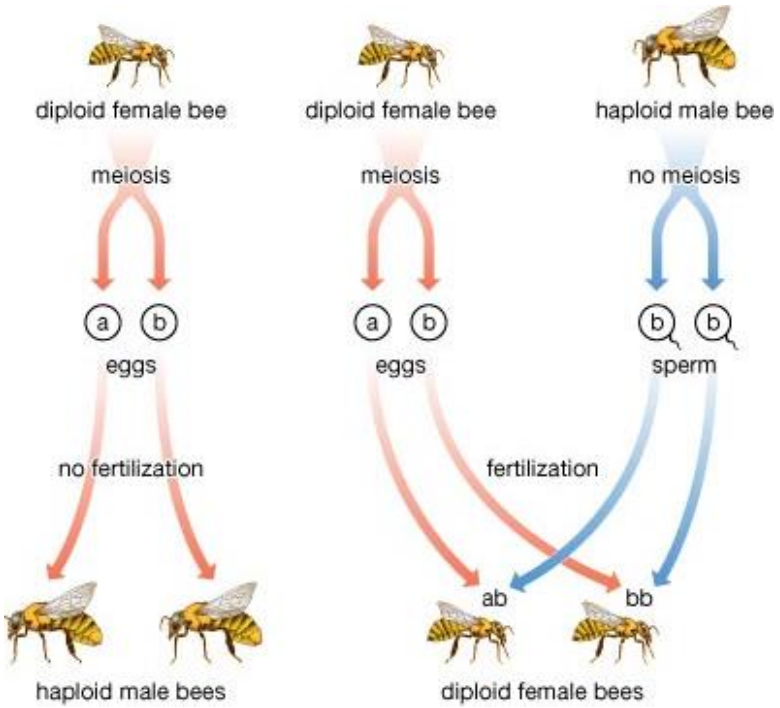


Fig. 9.4.2.3 Sex determination in honeybees.

9.4.3 Sex Linkage in Humans

- Sex-linked genes refer to genes whose loci is found on the sex chromosomes. As the Y chromosome is much smaller than the X, very few genes carried on the Y chromosome. Most sex-linked genes are on the X chromosome thus known as X-linked genes.

- Sex-linked characteristics controlled by X-linked genes include:
  - haemophilia
  - red-green colour blindness

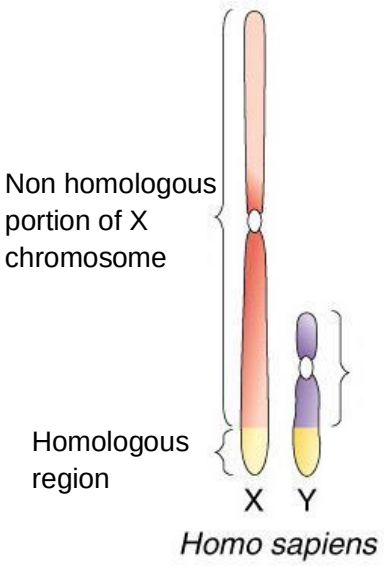


Fig. 9.4.3 Human sex chromosomes

- Males only have one allele for genes carried on the X chromosome that is non-homologous to the Y chromosome while females have two alleles for the same gene.

- Therefore, even if a male has only one copy of the recessive allele on the X chromosome, he will suffer from diseases like haemophilia because there is no corresponding gene on the Y chromosome to mask the recessive allele.

- A female with one recessive allele of the X chromosome would not suffer from the disease if the other X chromosome carried the normal dominant allele of the gene. This female is known as a **carrier** of the disease.

How do we write the alleles for sex linkage?

When it comes to sex-linked genes, the alleles are not represented by a capital letter (for dominant allele) or a small letter (recessive allele) but rather by X^A for a sex-linked dominant allele and X^a for a sex-linked recessive allele.

9.4.4 Sex Linkage with Haemophilia

Haemophilia is a genetic disorder that affects blood clotting. Deficiency of blood clotting factors can result in excessive bleeding, leading to death. This disease occurs more in males than females.

DID YOU KNOW?

Haemophilia has often been called the "Royal Disease." Queen Victoria of England (1837-1901) was a carrier of the haemophilia allele and subsequently passed the disease on to several royal families. Queen Victoria's haemophilia gene had far-reaching consequences, extending even to the Russian monarchy. Through her descendants, the disease was passed on to her granddaughter Alexandra, who became Empress of Russia upon marrying Tsar Nicholas II. Their only son, Alexei, inherited haemophilia, a condition that made him prone to life-threatening bleeding. Desperate to protect their son, Alexandra placed her faith in the mystic Rasputin, who claimed to have healing powers. Rasputin's influence over the royal family, coupled with growing public mistrust and dissatisfaction, weakened the monarchy and fuelled unrest. This turmoil contributed to the Russian Revolution and the eventual downfall of the Romanov dynasty.

Legend

X^H represents the X chromosome allele for normal clotting
X^h represents the X chromosome allele for haemophilia
Y represents the Y chromosome with neither allele

Scenario 1: Mother is a haemophiliac

Parental phenotypes	haemophiliac female	x	normal male
Parental genotypes	$X^h X^h$		$X^H Y$
Parental gametes	X^h		X^H Y

Random fertilization

	X^h
X^H	$X^H X^h$
Y	$X^h Y$

Offspring genotypic ratio	$X^H X^h$	:	$X^h Y$
Offspring phenotypic ratio	1 normal female (carrier) : 1 haemophiliac male		

Probability of a haemophiliac son = 0.5

$X^H X^H$: Normal female that experiences normal blood clotting
$X^H X^h$: Carrier female that experiences normal blood clotting, but can transmit X^h allele to offspring Does not have haemophilia as X^h allele can be masked by X^H allele
$X^h Y$: Haemophiliac male, as X^h allele is enough to cause the disease since the Y chromosome does not carry an allele for normal blood clothing to mask the recessive allele. Hence this disease occurs more in males than females.

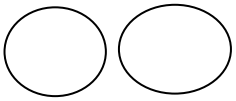
CHECKPOINT 9.4.4

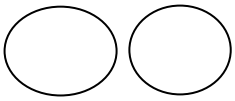
Scenario 2: Mother is a Carrier

Parental phenotypes Carrier female x normal male

Parental genotypes

Parental gametes





Random fertilization

Offspring genotypic ratio

Offspring phenotypic ratio

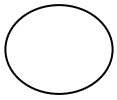
Probability of a haemophiliac son =

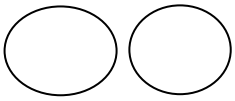
Scenario 3: Father is a Haemophiliac

Parental phenotypes Normal female x Haemophiliac male

Parental genotypes

Parental gametes





Random fertilization

Offspring genotypic ratio

Offspring phenotypic ratio

Probability of a haemophiliac son =

Conclusion:

- The allele for haemophilia is passed from one sex to the other at each generation.
- The father passes it to his daughters who thus become carriers
- The daughters may pass it to their sons who will thus have haemophilia.

*To better understand this, you can draw another cross: Carrier Female X Normal Male

9.4.5 Reciprocal Cross : Is the mode of inheritance sex-linked?

- Used to determine if the mode of inheritance of a particular trait is sex-linked
- A cross where the same genetic features are used but the sexes are reversed.
    - a female without the trait will be crossed with a male expressing the trait
        - e.g. (a) normal (red eye) female x white-eyed male
    - a female expressing the trait is crossed with a male without the trait
        - e.g. (b) white-eyed female x normal (red eye) male
- The results of the 2 crosses will be different.
    - If the gene is sex-linked, the phenotypic ratio observed in the different sexes will be different in the reciprocal crosses.
    - If the gene is autosomal, sexes do not display different distributions of phenotypes.

Worked Example 1: **Red-eyed female X White-eyed male**

Legend

X^R represents the X chromosome with the allele for red eye (dominant)
X^r represents the X chromosome with the allele for white eye (recessive)
Y represents the Y chromosome with neither allele

Parental phenotypes: Red-eyed female x White-eyed male

Parental genotypes: $X^R X^R$ x $X^r Y$

Parental gametes: X^R ; X^r, Y

Random fertilization

	X^R
X^r	$X^R X^r$
Y	$X^R Y$

F_1 genotypic ratio: $X^R X^r$: $X^R Y$

F_1 phenotypic ratio: 1 red-eyed female : 1 red-eyed male

F_1 phenotypes: Red-eyed female x Red-eyed male

F_1 genotypes: $X^R X^r$ x $X^R Y$

F_1 gametes: X^R, X^r ; X^R, Y

Random fertilization

	X^R	X^r
X^R	$X^R X^R$	$X^R X^r$
Y	$X^R Y$	$X^r Y$

F_2 genotypic ratio: $X^R X^R$: $X^R X^r$: $X^R Y$: $X^r Y$

F_2 phenotypic ratio: **2 red -eyed females : 1 red-eyed male : 1 white-eyed male**

Worked Example 2 : **White-eyed female X Red-eyed male**

Legend

X^R represents the X chromosome with the allele for red eye (dominant)

X^r represents the X chromosome with the allele for white eye (recessive)

Y represents the Y chromosome with neither allele

Parental phenotypes: White-eyed female x Red-eyed male

Parental genotypes: $X^r X^r$ x $X^R Y$

Parental gametes: X^r x X^R Y

Random fertilization

	X^r
X^R	$X^R X^r$
Y	X^r Y

F_1 genotypic ratio: $X^R X^r$: X^r Y

F_1 phenotypic ratio: 1 red-eyed female : 1 white-eyed male

F_1 phenotypes: Red-eye female x White-eyed male

F_1 genotypes: $X^R X^r$ x X^r Y

F_1 gametes: X^R X^r x X^r Y

Random fertilization

	X^R	X^r
X^r	$X^R X^r$	$X^r X^r$
Y	X^R Y	X^r Y

F_2 genotypic ratio: $X^R X^r$: $X^r X^r$: X^R Y : X^r Y

F_2 phenotypic ratio: **1 red-eyed female : 1 white-eyed female: 1 red-eyed male : 1 white-eyed male**

Comparing both crosses

Reciprocal Cross	**Phenotypic Ratio**
Red-eyed female x White-eyed male	
White-eyed female x Red-eyed male	
Since the phenotypic ratio observed in the different sexes is _____ in the reciprocal crosses, the trait (eye-colour) is sex-linked. If the eye colour gene were to be unrelated to sex, the phenotypic ratios would be the _____ for both crosses.	

(a)

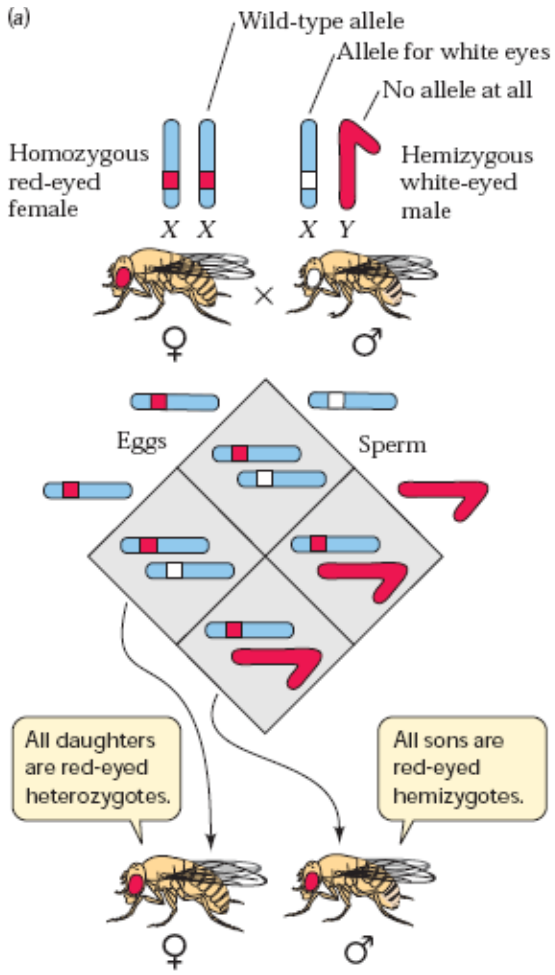


Fig. 9.4.5.1. female without the trait will be crossed with a male expressing the trait.

(b)

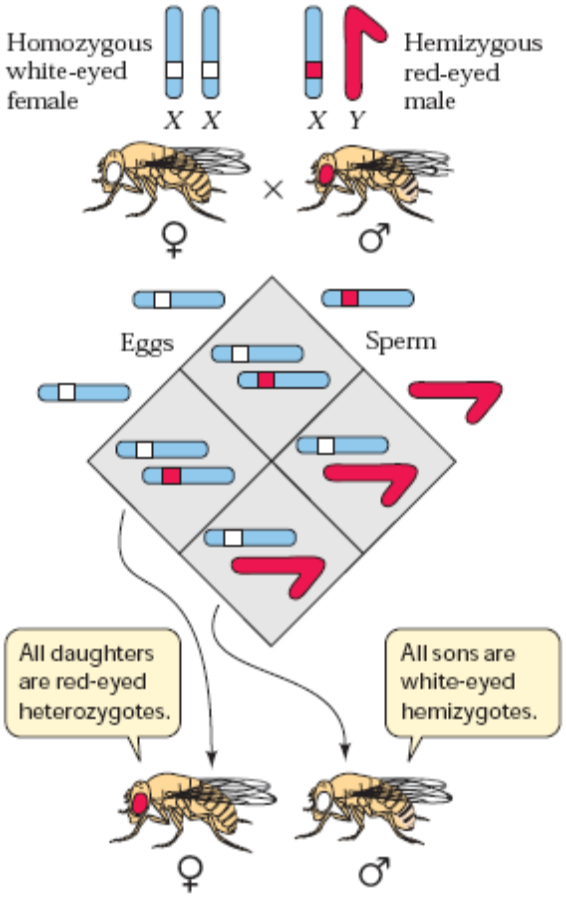


Fig. 9.4.5.2. a female expressing the trait is crossed with a male without the trait.

9.4.6 Pedigree Analysis

You are expected to acquire the skill of comprehending and analysing a given pedigree.

- Investigation of inheritance patterns in humans is done by collecting information about one's family history for a particular trait and assembling this information into a **pedigree chart** (a diagram of a family tree over several generations).

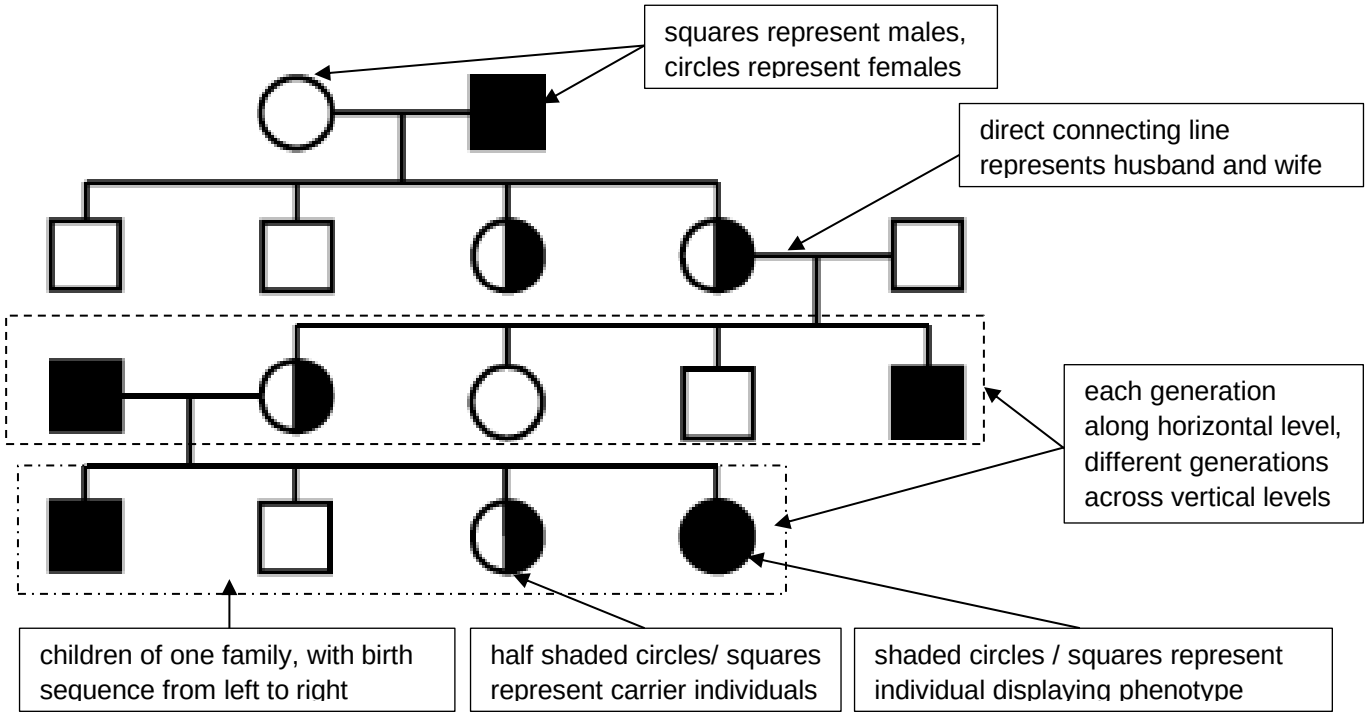


Fig. 12. Pedigree chart

- Pedigrees are often used to **determine the mode of inheritance** (dominant / recessive, autosomal dominant / recessive, sex-linked dominant / recessive etc.) of genetic diseases.

9.4.6.1 Autosomal dominant

- An autosomal dominant trait is a phenotype that is due to a dominant allele on an autosome.
  E.g. Huntington's disease

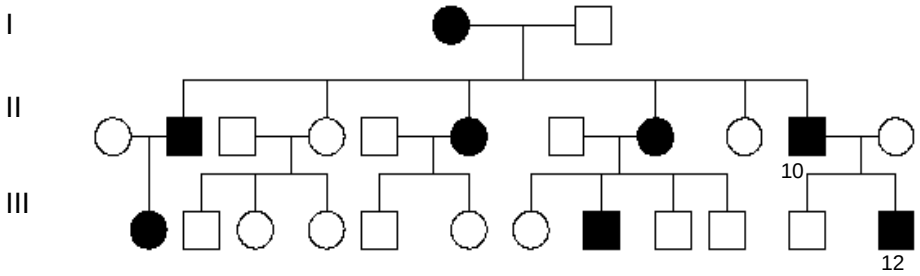


Fig. 9.4.6.1 Autosomal dominant inheritance pattern

- The pedigree shows that this trait is due to a dominant allele because:
  - the trait appears in every generation
  - every affected individual has an affected parent.
- This trait is autosomal because:
  - approximately equal number of males and females being affected.
  - affected male (II10) with a normal female passes the trait to his son (III12) therefore is not sex-linked.

9.4.6.2 Autosomal recessive

- An autosomal recessive trait is a phenotype that is due to a recessive allele on an autosome.
  E.g. albinism, cystic fibrosis, sickle-cell anaemia, phenylketonuria (PKU)

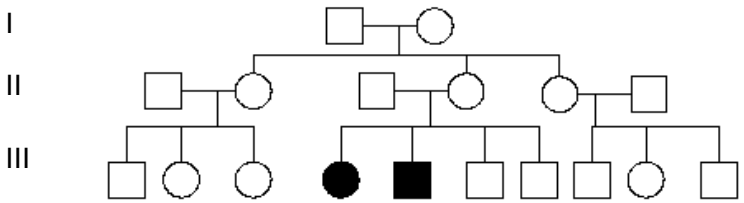


Fig. 9.4.6.2. Autosomal recessive inheritance pattern

- The pedigree shows that this trait is due to a recessive allele because:
  - the trait skips generations i.e. an affected individual (III4) may have unaffected parents (II3 and II4). This shows that both parents are carriers of the trait.

9.4.6.3 Sex-linked dominant

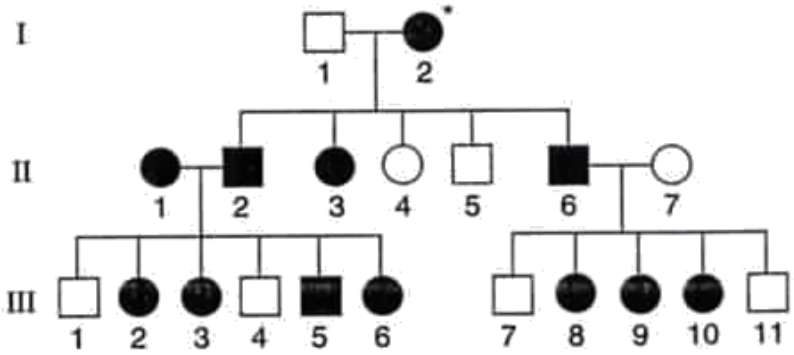


Fig. 9.4.6.3. Sex-linked dominant inheritance pattern

- Example: Vitamin D resistant rickets
- A sex-linked dominant trait is a phenotype that is due to a dominant allele on the sex chromosome.
- The pedigree shows that this trait is due to a X-linked dominant allele because:
  - affected males (II2) pass the trait to all daughters (III2,3 and 6).
  - affected males (II6) with normal females do not pass the trait to the sons (III 7 and III 11).

9.4.6.4 Sex-linked recessive

- Example: red-green colour blindness, haemophilia
- A sex-linked recessive trait is a phenotype that is due to a recessive allele on the sex chromosome.

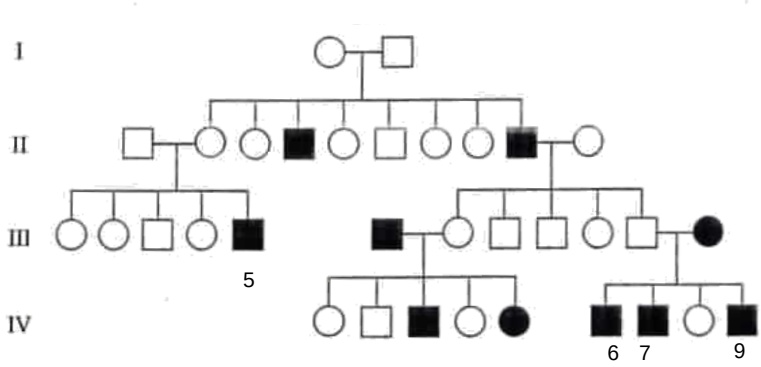
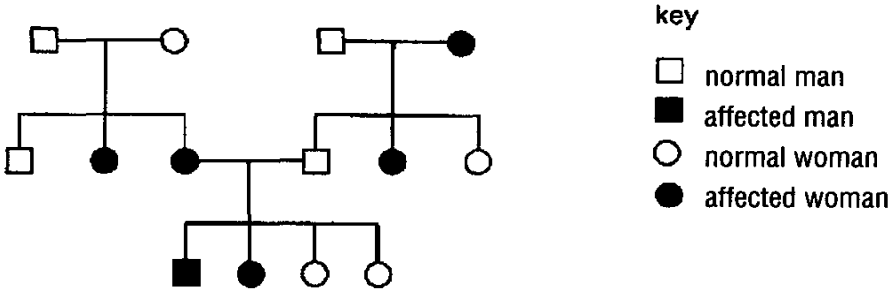


Fig. 9.4.6.4. Sex-linked recessive inheritance pattern

- The pedigree shows that this trait is due to an X-linked recessive allele because:
  - more males than females are affected
  - phenotypically normal parents produce affected sons because the mother is a carrier (III5).
  - all the sons of an affected female will be affected (IV6, IV7 and IV9).

Practice Question (N96/P1/Q22)

The family tree shows the inheritance of a skin condition.



What is the genetic basis of the skin condition?

A autosomal dominant

B sex-linked dominant

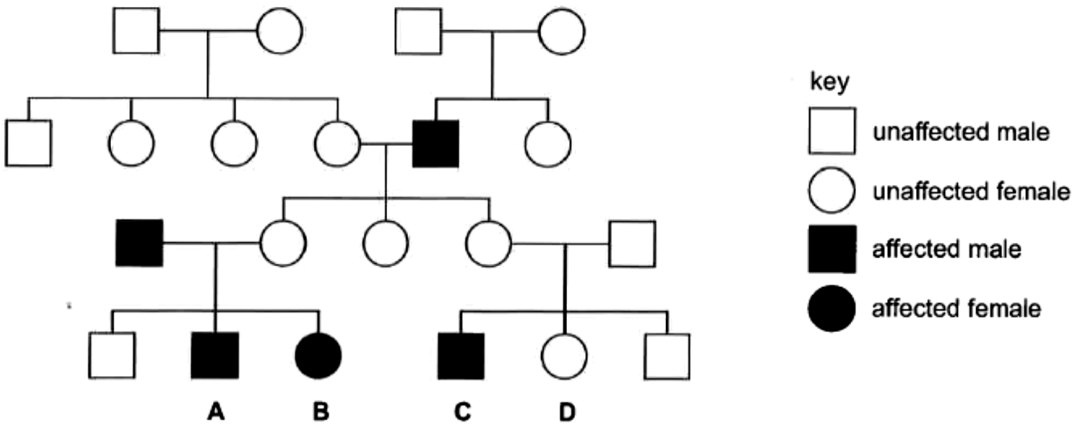
C autosomal recessive

D sex-linked recessive

Practice Question (N17/H1/P1/Q13)

The pedigree diagram shows the inheritance of an X-linked recessive trait in humans.

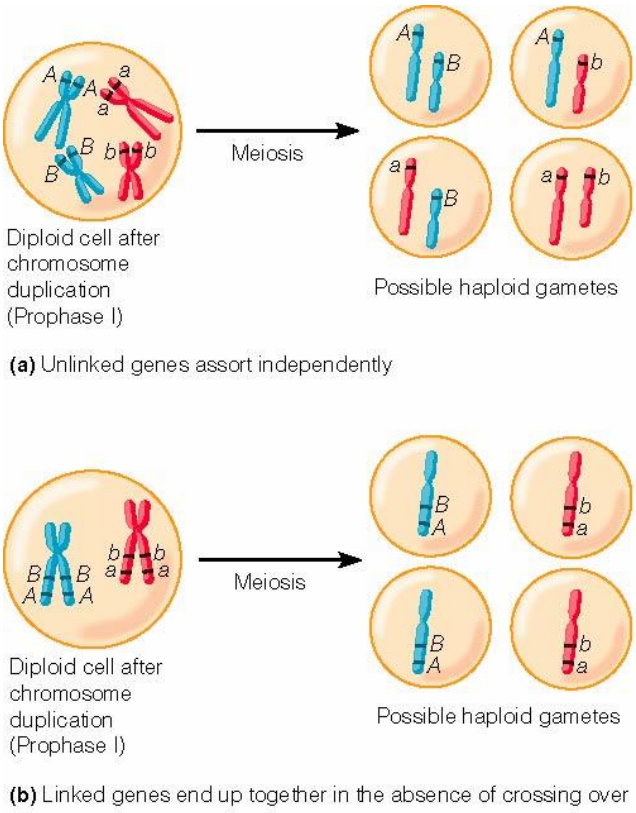
If the recessive allele is r, which individual possess the genotype rr?



9.5 Autosomal Linkage

- When two genes are located on the **same chromosome**, they are **linked**.

- **Linked genes are usually inherited together** in genetic crosses because they are part of a single chromosome. As a result, linked genes **do not exhibit independent assortment**.



(a) Unlinked genes **assort independently**

(b) **Linked genes end up together** in the absence of crossing over

* If the genes are not too close to one another (incomplete linkage), crossing over may break the linkage, and they would be inherited separately

*If the genes are very close to one other (complete linkage), crossing over would not break the linkage, and they would be inherited as a unit.

Fig. 9.5. Inheritance of linked genes

9.5.1 Autosomal *incomplete* linkage

Worked Example: Flowers in Pea Plants

Pure-breeding pea plants with red flowers and long pollen are crossed with pure-breeding pea plants with white flowers and short pollen. All F_1 generation plants had red flower and long pollen. F_1 plants were test crossed to give offspring of the following phenotypes:

red flowers, long pollen	35
red flowers, short pollen	15
white flowers, long pollen	17
white flowers and short pollen	33

Explain the results of the test cross generation using a genetic diagram.

Legend
R represent allele for red flower
r represent allele for white flower
L represent allele for long pollen
l represent allele for short pollen

Tips:
- ✓ For linked genes, draw **'stick' diagrams.**
- ✓ Gametes of 'stick' diagrams must also be circled.

Parental phenotype red flower, long pollen x white flower, short pollen

Parental genotype $\frac{R\ L}{R\ L}$ $\frac{r\ l}{r\ l}$

Parental gametes (RL) (rl)

F_1 Genotype $\frac{R\ L}{r\ l}$

Test cross $\frac{R\ L}{r\ l}$ x $\frac{r\ l}{r\ l}$

Gametes (RL) (Rl) (rL) (rl) (rl)

due to crossing over

Random fertilization

	(RL)	(Rl)	(rL)	(rl)
(rl)	$\frac{R\ L}{r\ l}$	$\frac{R\ l}{r\ l}$	$\frac{r\ L}{r\ l}$	$\frac{r\ l}{r\ l}$

Expected test cross genotypic ratio 1 $\frac{R\ L}{r\ l}$: 1 $\frac{R\ l}{r\ l}$: 1 $\frac{r\ L}{r\ l}$: 1 $\frac{r\ l}{r\ l}$

Expected test cross phenotypic ratio	1 red flower long pollen :	1 red flower, short pollen :	1 white flower, long pollen :	1 white flower, short pollen
Expected phenotypic nos.	**25**	**25**	**25**	**25**
Observed phenotypic nos.	**35**	**15**	**17**	**33**
	parental phenotypes	recombinant phenotypes		parental phenotype

- If the genes are linked i.e. presence of **autosomal incomplete linkage**, the observed phenotypic ratio will **deviate significantly** from the expected ratio.

- **Parental phenotypes** (i.e. red flower, long pollen and white flower, short pollen) **will occur in higher numbers than expected while recombinant phenotypes** (i.e. white flower, long pollen and red flower, short pollen) would occur in lower numbers than expected.

- **Alleles of linked genes found on the same chromosome are inherited together**. Thus, there are **more gametes with the parental allelic makeup** leading to more offspring with parental phenotypes.

- However, during prophase I of meiosis, non-sister chromatids of homologous chromosomes can undergo crossing over. **The exchange of alleles give rise to recombinant gametes which has a different combination of alleles as the parents**. Fertilisation of these recombinant gametes gives offspring with recombinant phenotypes.

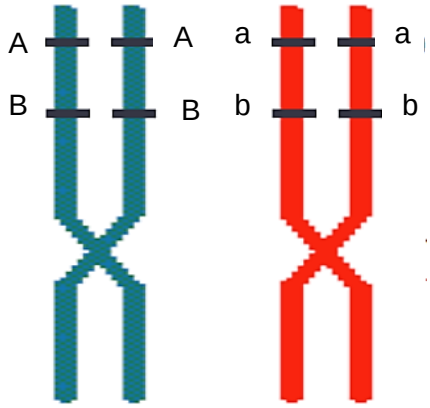
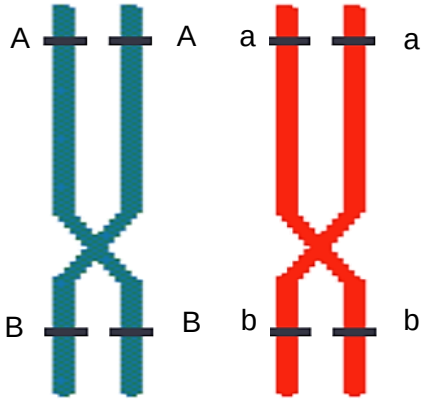
- The **frequency of crossing over is dependent on the distance** between the two gene loci on the chromosome. The further apart the genes, the higher the possibility of crossing over occurring between the two gene loci.

- By calculating **recombinant frequencies**, **a linkage map** showing the relative locations of genes along a chromosome can be constructed.

Recombination frequency = <u>No. of recombinants</u> X 100%
total no. offspring

**** need not memorise formula, if required, will be provided in assessments***

- The recombination frequency indicates how far apart the two linked genes are on the **same chromosome**, measured in centimorgans, cM

	
The shorter the distance between the two linked gene loci ⬇ The shorter the length (along the chromosome) where chiasma formation can occur ⬇ Lower chance of crossing over occurring ⬇ Lower chance of recombinant gametes forming ⬇ Low frequency of recombinant phenotypes	The longer the distance between the two linked gene loci ⬇ The longer the length (along the chromosome) where chiasma formation can occur ⬇ Higher chance of crossing over occurring ⬇ Higher chance of recombinant gametes forming ⬇ High frequency of recombinant phenotypes

CHECKPOINT 9.5.1: Incomplete Linkage

Long wings and grey bodies in *Drosophila melanogaster* are dominant over vestigial wings and black bodies. Long wing, black body females are mated with male having vestigial wings with grey bodies. All flies in the F_1 generation have long wings with grey bodies. A test cross was conducted on the F_1 generation.

The following numbers of offspring were observed:

64	long wing, black body
26	long wing, grey body
18	vestigial wing, black body
44	vestigial wing, grey body

Tips:
- ✓ For linked genes, draw 'stick' diagrams.
- ✓ Gametes of 'stick' diagrams must also be circled.

Legend

L represent allele for long wings
l represent allele for vestigial wings
G represent allele for grey body
g represent allele for black body

Parental phenotypes	
Parental genotypes	
Parental gametes produced	
F_1 Genotype	
F_1 Phenotype	
Testcross genotypes	
Random fertilization	
Expected genotypic ratio	
Expected phenotypic ratio	
Expected phenotypic nos.	
Observed phenotypic nos.	

gametes				

What are some conclusions that can be drawn from the expected and observed phenotypic numbers?

- Since most offspring had a _____phenotype, it can be concluded that the genes for body color and wing size are genetically _____ on the same chromosome.
- The production of a relatively small number of offspring with _____phenotypes indicated that _____occurred.
- Crossing over occasionally _____between specific alleles of genes on the same chromosome, producing gametes with non-parental genotypes, allowing for recombinant phenotypes to be observed in offspring.

9.5.2 Autosomal complete linkage

- The phenotypic offspring ratio for **fully linked genes (i.e. complete linkage) resembles a monohybrid cross.** This is because **tightly linked genes determining the two different characters** are **located relatively near each other** on the **same chromosome**.
- When two genes are **tightly linked**, a **chiasma will not form** between them, and they will not be separated by crossing over. **The two genes tend to be inherited together as one unit**, resulting in only **parental gametes.**
- Two tightly linked genes can be thought of as only one gene and not two, and so the **F_2 generation gives a phenotypic ratio of 3:1** (when pure breeding parents are used for crossing in the parental generation, giving rise to heterozygotes in the F_1 generation).

Note that this ratio is the same as that for monohybrid inheritance.

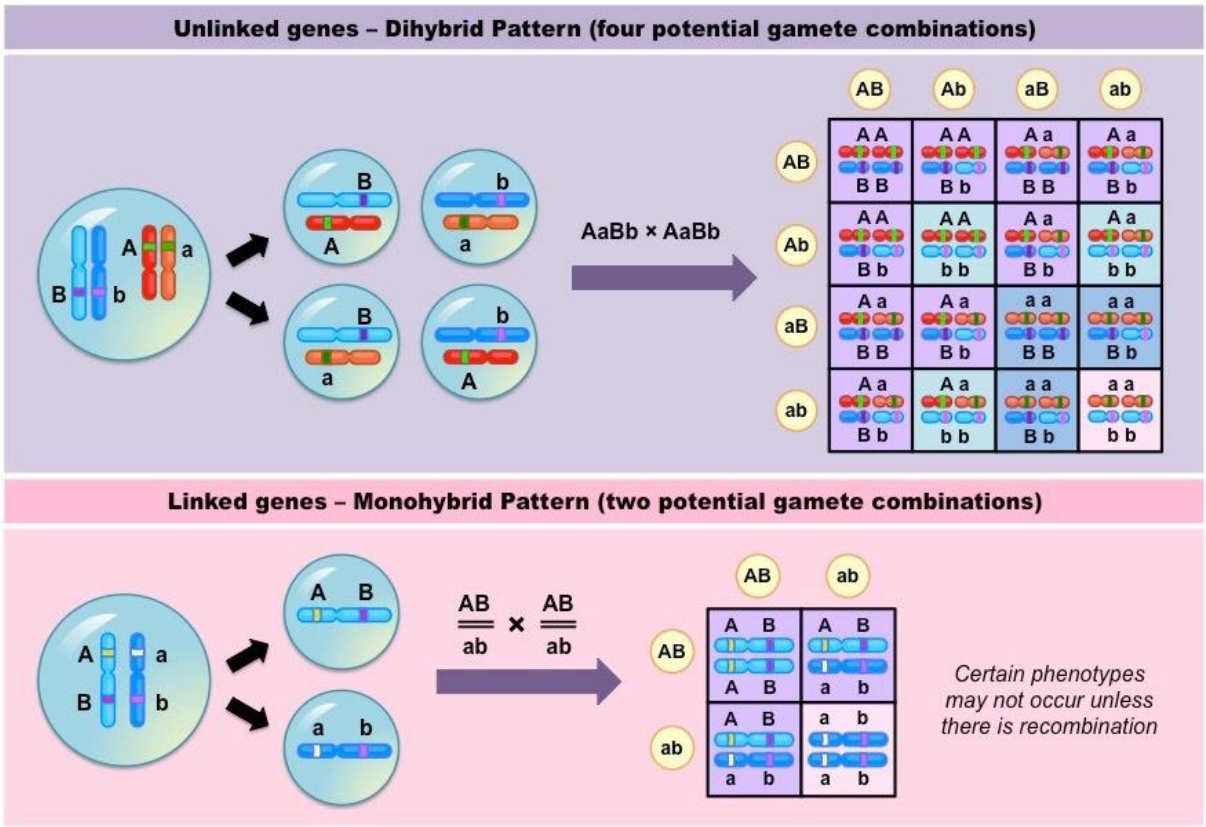


Fig. 9.5.2. Results of genetic crosses involving linked versus unlinked genes.

- The cross below illustrates the **complete linkage** in *Drosophila* by crossing flies with two different traits: between a **pure-breeding long wing, grey body fly** and a **pure-breeding short (vestigial) wing, ebony body fly**.

- The resultant F_2 generation have a phenotypic ratio of **3 long winged, grey bodied flies: 1 short winged, ebony body fly.**

Legend
L represent allele for long wings
l represent allele for vestigial wings
G represent allele for grey body
g represent allele for ebony body

Tips:
- ✓ For linked genes, draw 'stick' diagrams.
- ✓ Gametes of 'stick' diagrams must also be circled.

Parental phenotypes: long wings, grey body x vestigial wings, ebony body

Parental genotypes: $\frac{L\ G}{L\ G}$ x $\frac{l\ g}{l\ g}$

Parental gametes produced: (LG) (lg)

F_1 Genotype: $\frac{L\ G}{l\ g}$

F_1 Phenotype: All long wings, grey body

Selfing F_1: $\frac{L\ G}{l\ g}$ x $\frac{L\ G}{l\ g}$

gametes: (LG) (lg) (LG) (lg)

Punnet square

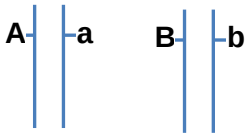
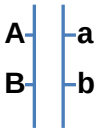
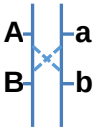
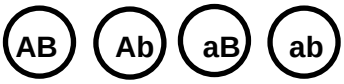
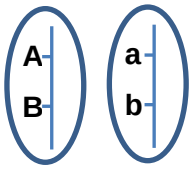
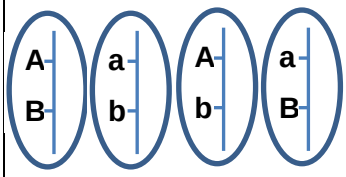
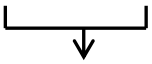
	(LG)	(lg)
(LG)	$\frac{LG}{LG}$	$\frac{LG}{lg}$
(lg)	$\frac{LG}{lg}$	$\frac{lg}{lg}$

F_2 genotypic ratio: $\frac{L\ G}{LG}$ $\frac{L\ G}{l\ g}$ $\frac{L\ G}{l\ g}$ $\frac{l\ g}{l\ g}$

F_2 phenotypic ratio: 3 long wing, grey body : 1 vestigial wing, ebony body

- The two genes are located on the **same chromosome** and are **tightly linked**. As a result, no chiasma is formed, and thus **no crossing over** occurred between the gene loci for wing size and body colour. The paternal and maternal homologues segregated unchanged into the gametes, carrying the linked combinations of alleles with them.

- As a result, there are no recombinant gametes formed and the two alleles are **transmitted together as a unit** to produce the two phenotypic groups observed in the ratio of **3:1.**

SUMMARY:			
	If genes are on separate chromosomes 	**Complete linkage – no crossing over because of close proximity of the 2 gene loci** 	**Incomplete Linkage – recombinants formed because crossing over occurs** 
Gametes of F_1 individual with genotype AaBb			
F_2 generation (F_1 X F_1)	9A_B_:3A_bb:3aaB_:1aabb	AABB: 2AaBb: aabb  3 : 1	A_B_: aabb: A_bb: aaB_ Deviates from 9:3:3:1
Test cross (F_1 X aabb)	1:1:1:1	1:1	Deviates from 1:1:1:1

Learning Outcome 2(aa):

Describe the interaction between loci (epistasis) and predict phenotypic ratios in problems involving epistasis.

9.6 Epistasis

- When two or more different genes code for gene products that control enzymatic reactions of related metabolic pathways, there is **gene interaction**.

- The gene that masks the expression of another gene and expresses its own phenotype is the **epistatic** gene, while the other gene is **hypostatic**.

- **Epistasis <u>reduces</u> the number of different phenotypes** for the character, so instead of having 4 phenotypes for 2 genes, there will be 3 or 2.
  ***** For all the examples, please assume that all the crosses are made from the selfing of the F_1 heterozygotes that result from a cross between pure bred parents.***

9.6.1 Recessive Epistasis

- Recessive epistasis occurs when the presence of a **homozygous recessive genotype** in the epistatic gene results in a **single phenotype** regardless of the allelic makeup of the hypostatic gene (i.e. two recessive alleles at epistatic gene locus masks the expression of all alleles at the hypostatic gene locus).

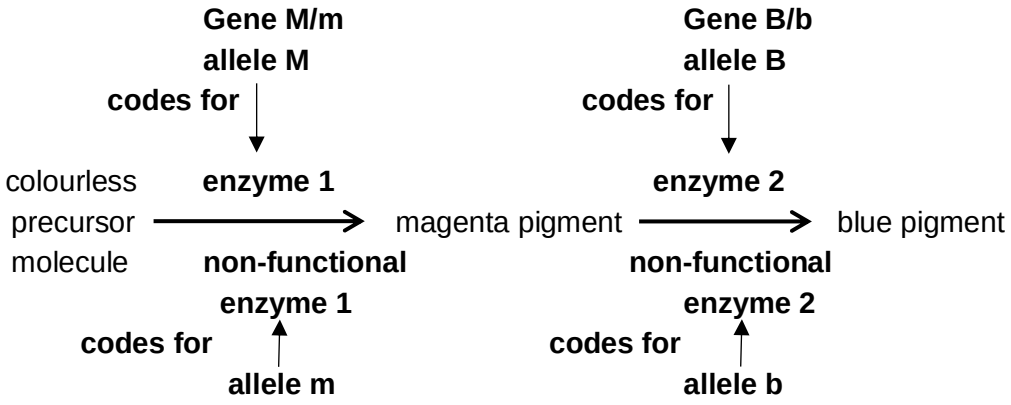
- This results in the following phenotypic ratio:

9 A _ B _	**9**
3 A _ bb	**3**
3 **aa** B _	**4**
1 **aa**bb	

Worked Example: Recessive Epistasis

In the plant blue-eyed Mary (*Collinsia parviflora*), two genes interact to result in the flower colour.

Metabolic pathway



Genotype	Colour	Result of Gene Interaction
9 M_B_		Blue pigment (B_) deposited
3 M_bb		Magenta pigment deposited
3 mmB_		Recessive alleles (mm) masks expression of B allele due to the production of non-functional enzyme 1
1 mmbb		Recessive alleles (mm) masks expression of b allele due to the production of non-functional enzyme 1 and 2

In the plant blue-eyed Mary (*Collinsia parviflora*), the dominant allele M codes for enzyme synthesizing magenta pigment, which is subsequently converted to a blue pigment by enzyme coded by a dominant allele of another gene, B. When the plant is homozygous recessive at gene M, its flowers are white instead.

Use a genetic diagram to illustrate the results of self-fertilization of a blue-eyed Mary that is heterozygous at both loci.

Legend

Let M represent the dominant allele coding for enzyme synthesizing magenta pigment.
Let m represent the recessive allele coding for non-functional enzyme synthesizing magenta pigment.
Let B represent the dominant allele coding for enzyme synthesizing blue pigment.
Let b represent the recessive allele coding for non-functional enzyme synthesizing blue pigment.

Parental phenotype: Blue flower colour x Blue flower colour

Parental genotype: MmBb x MmBb

Parental gametes: MB Mb mB mb | MB Mb mB mb

Random fertilization

Gametes	MB	Mb	mB	mb
MB	**MMBB** *Blue*	**MMBb** *Blue*	**MmBB** *Blue*	**MmBb** *Blue*
Mb	**MMBb** *Blue*	**MMbb** *Magenta*	**MmBb** *Blue*	**Mmbb** *Magenta*
mB	**MmBB** *Blue*	**MmBb** *Blue*	**mmBB** *White*	**mmBb** *White*
mb	**MmBb** *Blue*	**Mmbb** *Magenta*	**mmBb** *White*	**mmbb** *White*

F_1 genotypic ratio: 9 M_B_ : 3 M_bb : 3 mmB_ : 1 mmbb

F_1 phenotypic ratio: 9 Blue flower : 3 Magenta flower : 4 White flower

***Similar to the steps done in dihybrid cross, the key difference here is the interpretation of genotypes to phenotypes, which requires a good understanding of the biochemical pathway.**

9.6.2 Dominant Epistasis

- Dominant epistasis occurs when presence of a **dominant allele** in the epistatic gene results in a **single phenotype** regardless of the allelic makeup of the hypostatic gene (i.e. the dominant allele at epistatic gene locus masks the expression of all alleles at hypostatic gene locus).

- This results in the following F_2 phenotypic ratio:

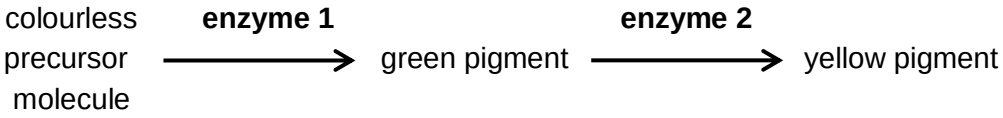
9 **A** _ B _ 3 **A** _ bb	**12**
3 aa B _	**3**
1 aabb	**1**

Worked Example

In the summer squash (*Cucurbita pepo*) fruit, two genes interact to result in the fruit colour. The dominant allele W at the epistatic gene locus results in white fruit colour regardless of the genotype at gene locus, Y/y. Allele Y results in yellow colour which is dominant to y which gives green colour.

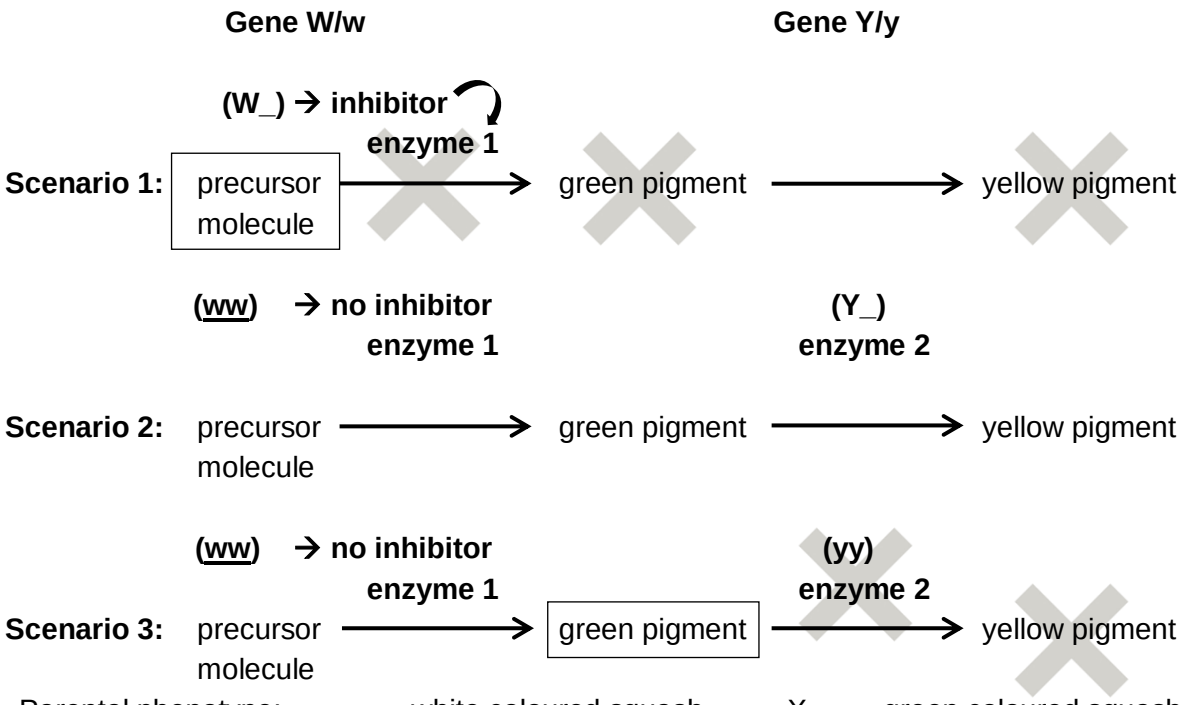
Genotype	Fruit Colour	Result of Gene Interaction
9 W_Y_		Dominant W allele (white) masks expression of Y allele due to expression of inhibitor that inhibits enzyme 1
3 W_yy		Dominant W allele (white) masks expression of y allele due to expression of inhibitor that inhibits enzyme 1
3 wwY_		Y allele allows expression of yellow colour
1 wwyy		Absence of Y allele allows expression of green colour

Metabolic pathway:



Gene W, when expressed, inhibits enzyme 1.

Gene Y, when expressed synthesizes enzyme 2.



Parental phenotype: white coloured squash X green coloured squash

Parental genotype: WWYY X wwyy

Gametes (n): (WY) (wy)

F_1 generation genotype: WwYy

F_1 generation phenotype: All white coloured squash

Selfing of F_1 generation: WwYy X WwYy

Gametes (n): (WY) (Wy) (wY) (wy) (WY) (Wy) (wY) (wy)

Random Fertilisation:

**Refer to the metabolic pathways above to interpret phenotype for each genotype*

Gametes	(WY)	(Wy)	(wY)	(wy)
(WY)	WW YY	WW Yy	Ww YY	WwYy
(Wy)	WW Yy	WW yy	Ww Yy	Ww yy
(wY)	Ww YY	Ww Yy	**ww** YY	**ww** Yy
(wy)	WwYy	Ww yy	**ww** Yy	**ww** yy

Genotypic ratio of F_2 generation: 9 W_Y_ : 3 W_yy : 3 wwY_ : 1 wwyy

Phenotypic ratio of F_2 generation: **12 white : 3 yellow : 1 green**

9.6.3 Duplicate recessive epistasis

- Duplicate recessive gene action occurs when the presence of **dominant alleles in both genes** results in a single phenotype i.e. both genes are epistatic to each other. When either gene is homozygous recessive, its masks the expression of the other gene.

- This results in the following phenotypic ratio:

9 **A _ B _** **9**
3 A _ bb
3 aa B _ } **7**
1 aabb

Worked Example: Duplicate recessive epistasis

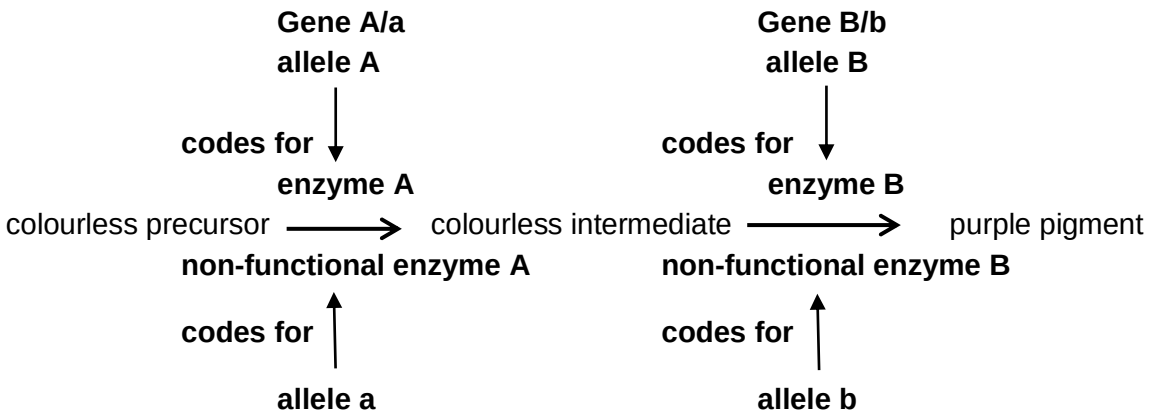
In the sweet pea plant, two genes interact to result in the flower colour.

Presence of **both** the **dominant allele A** at the first locus and the **dominant allele B** at the second locus results in **purple flower colour**.

Absence of either of the dominant alleles A or B at both gene loci (i.e. **one or both genes are homozygous recessive**) results in **white flower colour**.

Genotype	Colour	Result of Gene Interaction
9 A_B_		Dominant allele codes for functional enzymes A and B
3 A_bb		Enzyme B is non-functional, i.e. masks expression of gene A/a
3 aaB_		Non-functional enzyme A is expressed, unable to convert colourless precursor to colourless intermediate
1 aabb		Non-functional enzyme A is expressed, unable to convert colourless precursor to colourless intermediate

Metabolic pathway:



In an experiment by Bateson and Punnett, two different white flowered sweet pea plants were crossed and the resulting F_1 generation plants that all had purple flowers. When the F_1 generation were allowed to self-fertilise, the F_2 generation contained purple and white flowers in the ratio of 9 purple: 7 white. Draw a genetic diagram to illustrate the self-fertilisation of F_1 to give F_2 generation.

F1 phenotype: purple flower x purple flower

F1 genotype: WwYy x WwYy

F1 gametes: **WY** **Wy** **wY** **wy** x **WY** **Wy** **wY** **wy**

Random fertilization

Gametes	**WY**	**Wy**	**wY**	**wy**
WY	WWYY	WWYy	WwYy	WwYy
Wy	WWYy	WWyy	WwYy	Wwyy
wY	WwYY	WwYy	wwYY	wwYy
wy	WwYy	Wwyy	wwYy	wwyy

F_2 genotypic ratio: 9 W_Y_ : 3 W_yy : 3 wwY_ : 1wwyy

F_2 phenotypic ratio: 9 purple flowers : 7 white flowers

<u>Summary of Epistasis biochemical pathway summary</u>

Genotypes	**Biochemical pathway**
Dominant epistasis [12:3:1] *as long as **A**_ present, they all have phenotype 1, since you just need one allele A to code for an inhibitor (12 phenotype 1 observed)	Allele A → Protein A (inhibitor) ⊘ Allele B → Protein B Phenotype 1 ⊘ Phenotype 2 → Phenotype 3
Recessive epistasis [9:3:4] *as long as **aa** present, they all have phenotype 1 (4 phenotype 1 observed)	Allele A → Protein A → Phenotype 1 → Phenotype 2 Allele B → Protein B → Phenotype 3
Duplicate recessive epistasis [9 : 7] *as long as **aa** or **bb** present, they all have phenotype 1 (7 phenotype 1 observed)	Allele A → Protein A → Phenotype 1 → Intermediate (same as phenotype 1) Allele B → Protein B → Phenotype 2

10. Environmental Influence on Phenotype

Learning Outcome 2(bb):

Explain how the environment may affect the phenotype (including how diet affects the differentiation of honeybees and how temperature affects fur colour of Himalayan rabbits)

- Phenotypic characteristic is mainly determined by the gene(s) controlling that particular trait. However, **environmental conditions** may also affect the phenotype of an individual.

- Variables such as light intensity, temperature and nutrition can affect the translation of genotype into phenotype. Such phenotypic characters are referred to as **multifactorial**, as the phenotype is collectively determined by genetic and environmental factors.

Example 1. Effect of Diet on Differentiation of Honeybees

- A bee colony consists of three types of individuals: drones, queens and workers.
  Drones are males developed from unfertilized **haploid** eggs.
  Queens and workers are females developed from fertilized **diploid** eggs.

Fig. 10.1. Morphological differences between honeybees.

- After hatching, all larvae are fed with royal jelly. On the third day, larvae destined to be **workers** are switched to a diet consisting of **honey and pollen**. Larvae destined to be **queen** continue with **royal jelly**. The high protein content of royal jelly stimulates the formation and maturation of the female reproductive system, which is required by the queen honeybee.

- Although the queen and workers have the same amount of genetic material, they are **phenotypically different**. The workers are sterile, smaller in size, and have larger mouthparts and modified legs as compared to the queen.

- These phenotypic differences between queen and workers are due to the **diet of the larvae**.

Example 2. Effect of Temperature on Fur Coat of Himalayan Rabbits

- Himalayan rabbits have white bodies with black ears, nose, feet and tail.
- Tyrosinase is an enzyme involved in the synthesis of the pigment melanin which gives rabbits its black colour.
- The recessive c^h allele codes for a heat-sensitive form of tyrosinase. This enzyme does not function above 33°C.
- Himalayan rabbits homozygous with the c^h allele at the tyrosinase gene locus have
    - white fur at the rabbit's body as the central part of the body is above 33°C, thus tyrosinase is inactivated. No melanin is produced, giving rise to light coloured fur.
    - black extremities, such as the ears, nose, feet and tail as the temperature in these regions are below 33°C, thus tyrosinase is active. Melanin is produced, giving rise to dark coloured fur.
- Thus, temperature affects the coat colour of Himalayan rabbits.

Fig. 10.2. Effects of temperature on expression of a gene for coat colour in the Himalayan rabbits. (a) Normally, only the feet, tail, ears and nose are black. (b) Fur is plucked from a patch on the back, and an ice pack is applied to the area. (c)The new fur grown under the artificially low temperature is black.

11. Variation

11.1 Discontinuous variation

- A characteristic showing **discontinuous variation** can be grouped into **distinct / discrete** phenotypic classes (clear-cut characteristics).
  E.g. ABO blood group in humans
  E.g. flower colour in sweet pea

- In discontinuous variation, the phenotype is determined:
  - by **one or two major genes**
  - mainly by **genetic factors** and not affected by the environment or only to a small extent

11.2 Continuous variation

- A characteristic showing **continuous variation** can be grouped into a **range** of phenotypes. It does not show distinct / discrete phenotypes.
  E.g. height and weight of humans

- Phenotypes vary only marginally from one another, and the entire population shows a gradual change from one extreme to the other. Most individuals in the population fall in the middle of the range. Hence, plotting the frequency distribution gives a normal distribution curve.

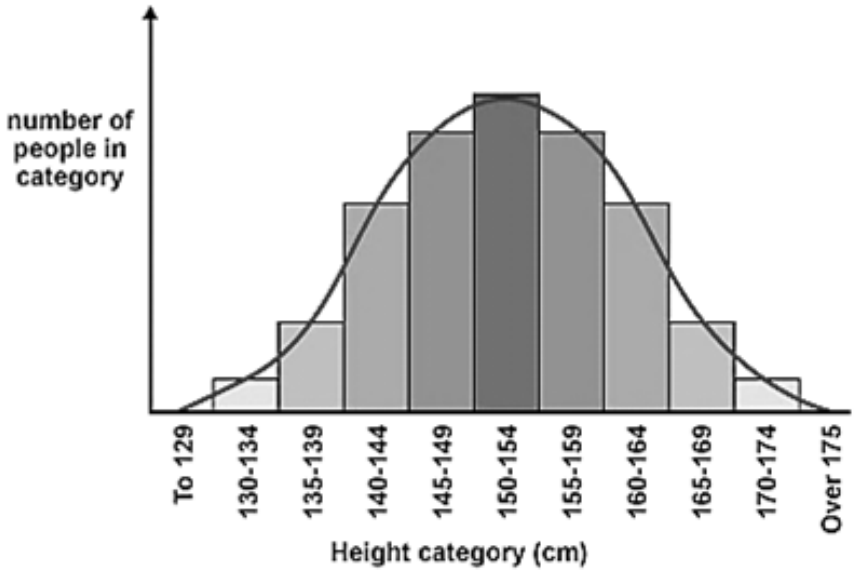


Fig. 11.2.1 Continuous variation as shown in height of humans

- In continuous variation, the phenotype is determined:
  - by many genes (i.e. **polygenic**)
  - by the **additive effect** of the different genes
  - to a large extent by the **environment**.

Thus, continuous variation is determined by both **genetic and environmental factors**.

Example of continuous variation : Skin Colour (Further Reading)

- Skin pigmentation in humans is controlled by at least three separately inherited genes.

- For each gene, a dark-skin allele (**A, B, C**) contributes one "unit" of darkness to the phenotype and is incompletely dominant to the other alleles (**a, b, c**).

- An **AABBCC** person would be very dark, while an **aabbcc** individual would be very fair.

- An **AaBbCc** person would have skin of an intermediate shade. Because the alleles have a cumulative effect, the genotypes **AaBbCc** and **AABbcc** would make the same genetic contribution (three units) to skin darkness.

- Environmental factors, such as exposure to the sun, also affect the skin-colour phenotype and help make the graph a smooth curve rather than a stair-like histogram.

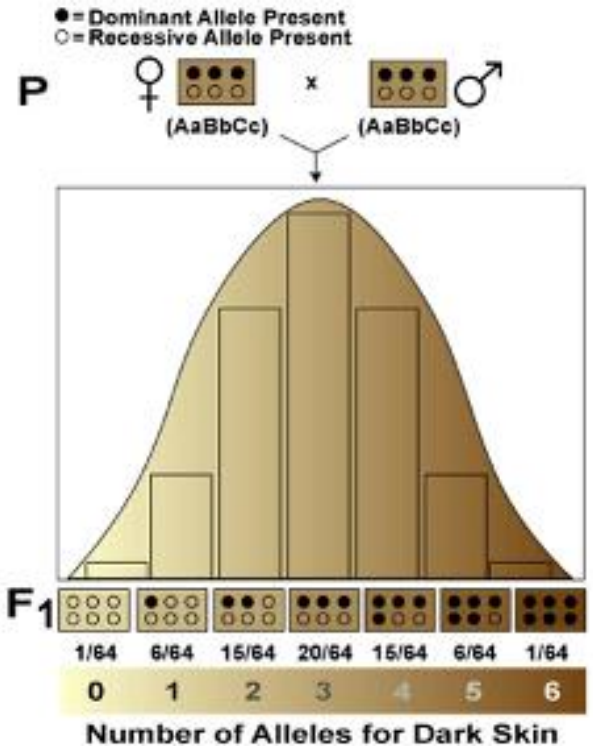


Fig. 11.2.2 Continuous variation as shown in the skin colour of humans

CHECKPOINT 10:

How does continuous and discontinuous variation differ?

Continuous	Discontinuous
Give a _____	Give _____
Effect of individual polygenes cannot be observed; Effect of polygenes is _____	Effect of _____ genes can be observed
The environment has a _____ effect on the phenotype	The environment has a _____ effect on the appearance of the phenotype
Mechanisms of inheritance investigated using _____	Mechanisms of inheritance investigated by counting and comparing _____ in the offspring
Examples: height in humans, skin pigmentation in humans	Examples: ABO blood groups , height of Mendel's pea plant, coat colour in mice, flower colour in sweet pea

12. Chi-Squared (χ^2) Statistical Test

Learning Outcome 2(dd):

Use the chi-squared (χ^2) test to test the significance between observed and expected results.

- A **hypothesis** is a well-formulated scientific idea.
- To verify the hypotheses, scientists test their hypotheses using data collected from observations / experiments to determine if a particular hypothesis should or should not be rejected.
- The extent of deviation between the observed ratio and the hypothetical expected ratio is used to determine the validity of the hypothesis.
- The data is subjected to statistical tests, like **chi-squared (χ^2) test**, to determine whether there is statistically significant deviation between the observed ratio and the expected ratio.

<table>
<tr><th colspan="2">Brief overview of the importance of chi-squared (χ^2) test in Inheritance</th></tr>
<tr><td colspan="2">Aim of experiment: What is the mode of inheritance for pea plants?
Could it be monohybrid/ dihybrid/ incomplete dominance / co-dominance/ complete linkage/ incomplete linkage/ epistasis? We need their ratios to help us solve our question.</td></tr>
<tr><td colspan="2">Theoretically, we know that we if get the expected ratio of 9:3:3:1 for our experiments, the pea plants most likely undergo a dihybrid mode of inheritance.
These ratios give us an expected number of offspring, for instance
90 yellow round : 30 yellow wrinkled : 30 green round : 10 green wrinkled

*Other ratios can be used as well, e.g. test cross 1:1:1:1, depending on the aim of the experiment.</td></tr>
<tr><td colspan="2">However, when we do an actual experiment on peas in real life, we may not get the exact ratio.
We might get 100 yellow round: 20 yellow wrinkled: 31 green round: 9 green wrinkled</td></tr>
<tr><td colspan="2">Key Question: Can we just assume that 100: 20: 31: 9 follows the Mendalian ratio of 9:3:3:1, and conclude that the peas we experimented on follows the dihybrid mode of inheritance?
↓
Do a statistical test (chi-squared (χ^2) test) to check if there is a significant difference between these two ratios.</td></tr>
<tr><td>Significant difference observed between observed and expected ratios
↓
The difference observed might be due another mechanism of inheritance, such as linkage.</td><td>Significant difference NOT observed between observed and expected ratios
↓
The difference observed might be due to chance, we can still conclude that the peas undergo a dihybrid mode of inheritance</td></tr>
</table>

12.1 Conducting a chi-squared (χ^2) test

Step 0: Understanding the context

Yellow and round seeds in pea plants are dominant over green and wrinkled seeds. Pure-breeding pea plants with yellow and round seeds are crossed with pure-breeding pea plants with green and wrinkled seeds. All plants in the F1 generation have yellow and round seeds. After selfing the F1 generation, the expected phenotypic ratio of the dihybrid cross is shown in Table 12.1.

Table 12.1: Expected phenotypic ratio of dihybrid cross

Expected offspring phenotypic ratio	**yellow round**	**yellow wrinkled**	**green round**	**green wrinkled**
Expected number of offspring	**90**	**30**	**30**	**10**

*Recall that the phenotypic ratio of test cross with 2 traits is 1:1:1:1. Refer back to section 8.

The following numbers of offspring were **observed**:

100 yellow and round
20 yellow and wrinkled
31 green and round
9 green and wrinkled

Using the chi-square test, determine if the **observed ratio** differ significantly from the **expected ratio**.

Step 1: State the null hypothesis (H_o)

The null hypothesis (H_o) always states that there is no significant difference between expected and observed ratios

- **H_0: There is no significant different between the observed and expected ratio.**
- H_a: There is no significant different between the observed and expected ratio.

In this context, H_0 means that there is no significant difference between 100 : 20 : 31 : 9 and the expected 9 : 3 : 3 : 1 ratio obtained from the dihybrid cross. H_0 can also be rephrased as

- H_0 : the phenotypic ratio in the F_2 generation is 9 yellow, round : 3 yellow, wrinkled : 3 green, round : 1 green, wrinkled

2. Calculate the chi-squared (χ^2) value, using the formula:

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

χ^2 = chi-sq. value
O = observed
E = expected
$\sum$ = sum of

Phenotype	Expected ratio	Observed (O)	Expected (E)	$\frac{(O-E)^2}{E}$
yellow and round	9	100	90	1.11
yellow and wrinkled	3	20	30	3.33
green and round	3	31	30	0.03
green and wrinkled	1	9	10	0.1
			χ^2 = 4.57	

3. Calculate the degrees of freedom (ν or df), using the formula:

df = n – 1 (where n = no. of phenotypic categories)

In this context, there are a total of 4 phenotypes, hence **df = 4 -1 = 3**

4. Refer to chi-squared table to obtain critical chi-squared value at p = 0.05 (probability = 5%).

degrees of freedom	probability, p				
	0.10	0.05	0.02	0.01	0.001
1	2.71	3.84	5.41	6.64	10.83
2	4.61	5.99	7.82	9.21	13.82
3	6.25	7.82	9.84	11.35	16.27

5. Compare the critical chi-squared value to the calculated chi-squared value and conclude whether to reject the null hypothesis.

If calculated χ^2 value < critical value χ^2 at p = 0.05, the deviation between observed and expected ratio is **statistically insignificant**.
The difference is **due to chance alone.**
H_o is **not rejected.**

If calculated χ^2 value > critical value χ^2 at p = 0.05, the deviation between observed and expected ratio is **statistically significant**.
The difference is **NOT due to chance alone.**
H_o is **rejected.**

In this context, since **χ^2 value of 4.57 < χ^2 value of 7.82** (at p = 0.05), the deviation between observed and expected ratio is **not statistically significant**. The difference is **due to chance alone,** H_o is not **rejected.**

6. State conclusions

At p = 0.05, degree of freedom = _____,

χ^2 calculated **<** = χ^2 critical, _____ < _____

Therefore, deviation between observed and expected ratio is statistically **significant / insignificant** .

The difference is **due to / not due to** chance alone.

Hence, H_o is **rejected / not rejected.**

The observed ratio **is / is not** _____ .

What is the *p* value?

The *p* value is the probability of observing certain data, given that the null hypothesis is true (i.e. the probability that the observed ratio is obtained, given that the expected ratio is true).

At *p* = 0.1, there is 10% probability that the observed ratio is obtained.
At *p* = 0.001, there is a 0.1% probability that observed ratio is obtained.

Statisticians like to be at least 95% certain before drawing any conclusions. Therefore, the *p* value is normally set to 0.05, and χ^2 values that fall within the region indicate that there is a ≤5% probability that the observed ratio is obtained. This difference is regarded as statistically significant, and the null hypothesis is rejected (i.e. not due to chance).

But deviation will definitely occur as events such as random segregation, independent assortment and random fertilisation are chance events**.**

Presence of such deviation does not imply that the hypothesis is incorrect as **deviation could be due to chance events**.

SUMMARY

1. State the null hypothesis (H_o)

The null hypothesis (H_o) always states that there is no significant difference between expected and observed ratios.

2. Calculate the chi-squared (χ^2) value, using the formula:

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

χ^2 = chi-sq value
O = observed
E = expected
$\sum$ = sum of

3. Calculate the degrees of freedom (ν or df), using the formula:

df = n – 1 (where n = no. of phenotypic categories)

4. Refer to chi-squared table to obtain critical chi-squared value at p = 0.05 (probability = 5%).

degrees of freedom	probability, p				
	0.10	0.05	0.02	0.01	0.001
1	2.71	3.84	5.41	6.64	10.83
2	4.61	5.99	7.82	9.21	13.82
3	6.25	7.82	9.84	11.35	16.27

5. Compare the critical chi-squared value to the calculated chi-squared value and conclude whether to reject the null hypothesis.

If calculated χ^2 value < critical value χ^2 at p = 0.05, the deviation between observed and expected ratio is **statistically insignificant**.
The difference is **due to chance alone.**
H_o is **not rejected.**

If calculated χ^2 value > critical value χ^2 at p = 0.05, the deviation between observed and expected ratio is **statistically significant**.
The difference is **NOT due to chance alone.**
H_o is **rejected.**

6. State conclusions

At p = 0.05, degree of freedom = _____,

χ^2 calculated **(> / <)** = χ^2 critical, _____ > / < _____

Therefore, deviation between observed and expected ratio is statistically **(significant / insignificant)**.

The difference is **(due to / not due to)** chance alone.

Hence, H_o is **(rejected / not rejected)**.

The observed ratio **(is / is not)** _____ .

CHECKPOINT 12.1 : Investigating for gene linkage in tomatoes

A widespread application of chi-square test is in testing for linkage. If the observed results cause rejection of the hypothesis of no linkage, then we can infer linkage.

In an investigation to determine whether the genes for leaf shape and colour of the stem are linked, **pure breeding normal-leafed, purple-stemmed tomato** was crossed with a **potato-leafed, green-stemmed tomato.** All of the F_1 offspring had normal leaves and purple stems. One of these offspring was crossed with a potato-leafed, green-stemmed tomato (test cross).

The results of the F_2 are given below. A chi-squared test was carried out to find out if these are two pairs of segregating alleles at two loci.

1. State null hypothesis

H_0: There is no significant difference between the observed and expected numbers; these are two pairs of segregating alleles at two loci.

H_a: There is a significant difference between the observed and expected numbers; these are not two pairs of segregating alleles at two loci.

2. Calculate chi-square value

Appearance/ Phenotype	Observed Number (O)	Expected Number (E)	$\frac{(O-E)^2}{E}$
Normal leaves and purple stems	100	80	
Normal leaves and green stems	60	80	
Potato leaves and purple stems	60	80	
Potato leaves and green stems	100	80	

*The second cross was a test or back cross, so it was expected that the ratio in the F_2 would be 1:1:1:1. The expected numbers are calculated by adding up the observed numbers and dividing by 4.

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

3. Calculate degrees of freedom Df:

4 & 5: Refer to chi-square table & compared to critical chi-squared value

degrees of freedom	probability, p				
	0.10	0.05	0.02	0.01	0.001
1	2.71	3.84	5.41	6.64	10.83
2	4.61	5.99	7.82	9.21	13.82
3	6.25	7.82	9.84	11.35	16.27

6. Conclude

- At p = 0.05, degree of freedom = _____
- χ^2 calculated _____ χ^2 critical, _____
- Therefore, deviation between observed and expected ratio is statistically _____
- The difference is _____ chance alone.
- Hence, H_o is _____
- The observed ratio _____ 1:1:1:1, _____ is likely to be present

Summary

Monohybrid crosses		Phenotypic Ratio	Genotypic Ratio
General	**AA** x aa	ALL heterozygous dominant	
	Aa x **A**a	3:1	1:2:1
Test Cross	**A**a x aa	1:1	
	AA x aa	ALL heterozygous dominant	
Incomplete dominance / Codominance	**A**a x **A**a	1:2:1	
	AA/aa x **A**a	1:1	

Dihybrid crosses		Phenotypic Ratio	Genotypic Ratio
General	**AaBb** x **AaBb**	9: 3: 3: 1	too many
Test Cross	**AABB** x aabb or **LG | LG** x lg | lg	ALL dominant double heterozygote	
	AaBb x aabb	1:1:1:1	
	LG | lg x lg | lg (linkage)	1:1	1:1
Complete Linkage	**LG | lg** x **LG | lg**	3:1 (only 2 parental phenotypes)	1:2:1
Incomplete Linkage	4 different phenotypes : 2 parental, 2 recombinant ● parental >> recombinant		

Type of Gene Interaction	Phenotypic and Genotypic Ratio			
	A_B_	**A_bb**	**aaB_**	**aabb**
Non-epistatic/ Dihybrid	9	3	3	1
Recessive epistasis (aa codes for non-functional gene product)	9	3	4	
Dominant epistasis (A codes for inhibitor)	12		3	1
Duplicate recessive epistasis (aa and bb codes for non-functional gene product)	9	7		

Dihybrid inheritance	Gene interaction
two characteristics controlled by **two** genes (**one** gene one characteristic)	**one** characteristic controlled by **two or more** genes (**many** genes, one characteristic)
Same basic ratio (9:3:3:1)	

Complete dominance	Epistasis
masking alleles at the **same** gene locus	suppress/ inhibit the effect of a gene at a **different** locus
no recessive or dominant	can be recessive or dominant in their effects

X-linked recessive inheritance	X-linked dominant inheritance
X-linked because:	
males more often display the disease phenotype more often than females ● males only have one X chromosome ● 1 disease-causing allele on X chromosome will cause the male to display the disease phenotype ○ even if it is recessive because Y chromosome is shorter and carries very few genes ○ does not carry a dominant allele to mask the recessive allele	
affected mothers produce affected sons with 100% chance	affected father produce affected daughters with 100% chance
affected females are the result of a mating between affected father and affected/ carrier mother	affected females are the offspring of affected mothers OR fathers
half of the sons of carrier females should be affected	affected mothers produce affected sons (50% chance, assuming father is normal and mother is heterozygous)
Recessive because:	**Dominant because:**
if fathers are not affected, daughters will not be affected but may be carriers	approximately half of the children of affected heterozygous females are affected
trait skips generations	trait does not skip generations
unaffected parents can produce affected individuals	unaffected parents should not have affected children

Autosomal recessive inheritance	Autosomal dominant inheritance
Recessive because:	**Dominant because:**
unaffected parents can produce affected individuals	unaffected parents should not have affected children
when unaffected people (**AA**/ **A**a) mate with affected (aa) individuals, ● AA: all children are unaffected ● Aa: at least half are affected	when an affected **A**a individual mates with an unaffected individual, 50% of their offspring should be affected
trait often skips generation	trait should not skip generations
if both parents are affected, all children should be affected	
Autosomal because: males and females are affected with equal probability	

Comparison between Discontinuous & Continuous Variations

Feature	Discontinuous	Continuous
Observable phenotype	phenotypes are definite and clear	phenotypes not clear cut
	can be divided into discrete phenotypic classes	cannot be grouped into distinct contrasting groups as there is a range of an infinite phenotypic varieties
	intermediates are not observed	intermediates observed
No. of genes controlling phenotypic variation	single or a few genes	multiple additive genes (polygenic inheritance) where effects of single genes are too slight to be detected
Effect of environment on phenotypes	little to no environmental effect	phenotypes can be modified by cumulative effect of varying environmental factors acting on the different genotype ● genotype is determined at fertilisation, but degree of expression depends on environmental factors
Mode of measurement and example	bar graphs with distinct phenotypic classes	normal distribution curve that as a continuous range of intermediates formed between two extremes represented on a histogram
	qualitative: counts and ratios	quantitative: estimate population parameters e.g. mean and standard deviation
	e.g. blood type in humans	e.g. height, weight and intelligence in humans

Annex

(Further Reading that can better prepare you for novel questions in A levels)

Monohybrid Inheritance in Humans – Albinism (O level knowledge)

Examples of monohybrid inheritance in humans include the following conditions:

- Albinism
- Cystic fibrosis
- Haemophilia
- Rhesus blood groups
- Sickle-cell anaemia

Albinism is a condition in which the skin is pink and fails to tan, the hair is white and the iris pink.

- The reason is that albinos are unable to make the black pigment melanin because they lack an enzyme (tyrosinase) required for its synthesis. They therefore lack the protection from ultraviolet light which melanin normally confers on the skin.

- The allele for albinism is recessive (a) and so only exerts its effect in the homozygous state (aa). The allele for enzyme involved in melanin production (A) is dominant. The genotype of a person with normal pigmentation is therefore AA or Aa.

Suppose a couple each with normal pigmentation has an albino child. For this to happen, each parent must be heterozygous (Aa). In other words, the parents, though not themselves albino, carry the albino allele, for which reason they may be described as carriers. The couple wants to know the likelihood of their next child also being an albino.

Let **A** be the allele for enzyme involved in melanin production
Let **a** be the allele for defective enzyme involved in melanin production

The allele for enzyme production, A, is dominant to the allele for defective enzyme, a.

Parental phenotypes	Carrier Father		Carrier Mother
Parental genotypes Parental Gametes	Aa (A) (a)	X	Aa (A) (a)

Punnett Square to show fusion of gametes produced

	(A)	(a)
(A)	AA Normal	Aa Normal
(a)	Aa Normal	aa Normal

Offspring phenotypic ratio	Normal 3	:	Albino 1

Q: What would be the likelihood of their next child being an albino? [25%]

Monohybrid Inheritance in Humans – Sickle Cell Anaemia (Relevant to past TYS questions)

Suppose a couple each without sickle cell anaemia has a child with the disease. For this to happen, each parent must be heterozygous (Hb^AHb^S). The couple wants to know the likelihood of their next child also being an albino.

Let **Hb^A** be the allele for normal haemoglobin
Let **Hb^S** be the allele for defective haemoglobin

The allele for production of normal haemoglobin, **Hb^A** is dominant to the allele for defective haemoglobin, **Hb^S**

Parental phenotypes	Carrier Father		Carrier Mother
Parental genotypes Parental Gametes	**Hb^AHb^S** **Hb^A** **Hb^S**	X	**Hb^AHb^S** **Hb^A** **Hb^S**

Punnett Square to show fusion of gametes produced

	Hb^A	**Hb^S**
Hb^A	**Hb^AHb^A**	**Hb^AHb^S**
Hb^S	**Hb^AHb^S**	**Hb^SHb^S**

Offspring genotypic ratio	1 **Hb^AHb^A**:	2 **Hb^AHb^S**	: 1 **Hb^SHb^S**
Offspring phenotypic ratio	Normal 3	:	Sickle Cell Anaemia 1

Q: What would be the likelihood of their next child having sickle cell anaemia? [25%]

Knowing the mode of inheritance for sickle cell anaemia would be helpful for topics

- DNA mutation
- Molecular Techniques

Lethal Genes (appeared in 2024 H1 Paper 2)

- A gene that leads to the death of an individual; these can be either dominant or recessive in nature.

- The effects of a lethal gene are clearly illustrated by the inheritance of fur colour in mice: If two yellow mice are crossed with each other, the offspring produced is always in the ratio 2 yellow : 1 agouti fur.

- These results can be explained on the basis that yellow is dominant to agouti and that all the yellow coat mice are heterozygous.

- A cross between two heterozygotes would be expected to yield a monohybrid genotypic ratio of 1:2:1.

- However, if all the mice in one of the homozygous classes died before birth, the live births would then show a 2:1 ratio of heterozygotes to the surviving homozygotes, **i.e., Fetal death of homozygous yellow coat (YY) mice.**

Legend
Let Y represent the allele for yellow fur (dominant)
Let y represent the allele for agouti fur (recessive)

Parental phenotype	Yellow	x	Yellow
Parental genotype	Yy		Yy
Parental gametes	Y y		Y y

Random fertilization

	Y	y
Y	YY	Yy
y	Yy	yy

F_2 genotypic ratio **1 YY** : 2 Yy : 1 yy

F_2 phenotypic ratio **1 yellow (dead)** : 2 yellow 1 agouti

*The cross is similar to a monohybrid cross. However, the interpretation of the phenotype will be different, according to the question.

Sex Linked Inheritance: Colour Blindness in Males

Red-green colour blindness is the inability to distinguish between the colours red and green.

Legend
X^B represents the X chromosome with the allele for normal vision (dominant)
X^b represents the X chromosome with the allele for colour blindness (recessive)
Y represents the Y chromosome with neither allele

Parental phenotypes	Normal female	x	Colour blind male
Parental genotypes	$X^B X^B$		$X^b Y$
Parental gametes	X^B X^B		X^b Y

Random fertilization

	X^B
X^b	$X^B X^b$
Y	X^B Y

Offspring genotypic ratio	$X^B X^b$	:	X^B Y
Offspring phenotypic ratio	1 normal carrier female	:	1 normal male

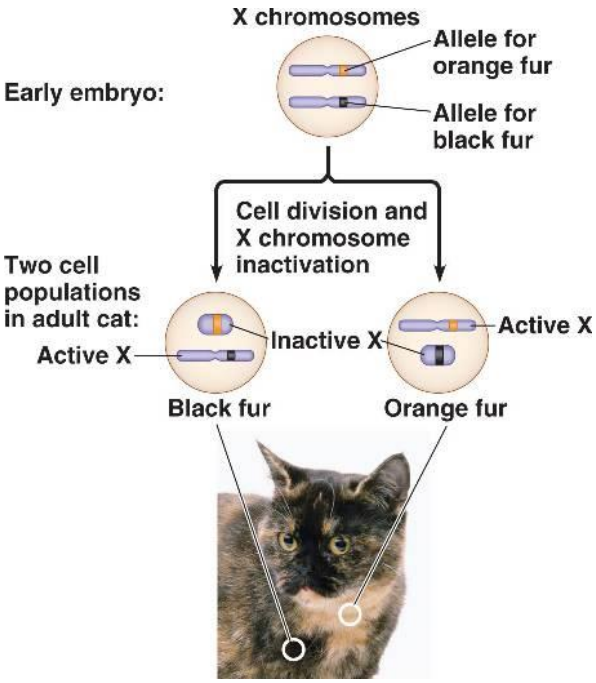
Conclusion:

- The allele for colour blindness is passed from one sex to the other at each generation.
- The father passes it to his daughters who thus become carriers
- The daughters may pass it to their sons who will thus be colour blind.

*To better understand this, you can draw another cross: Carrier Female X Normal Male in the space below

Sex Linked Inheritance: X-inactivation in Female Mammals

- **Female mammals**, including humans, inherit **two X chromosomes** which is twice the number inherited by males.
- Most of **one X chromosome** in each cell in female mammals becomes **inactivated** during early embryonic development. Thus, the cells of females and males have the same effective dosage of most X-linked genes.
- The inactivated X chromosome in each cell of a female condenses into a compact object called the **Barr body** which lies along the inside of the nuclear envelope.
- Most of the **genes of Barr body** are **not expressed**. Reactivation of Barr body only occurs in the ovaries so that every female gamete has an active X chromosome.
- The selection of which X chromosome will form the Barr body occurs **randomly** and **independently** in each embryonic cell present at the time of X-inactivation.
- Therefore, a female consists of a **mosaic of two types of cells**: those with active X derived from the father and those with active X derived from the mother. After an X chromosome is inactivated in a particular cell, all mitotic descendants of that cell have the same inactive X chromosome.



X-inactivation and the tortoiseshell cat

The tortoiseshell gene is on the X chromosome, and the tortoiseshell phenotype requires the presence of two different alleles, one for orange fur and one for black fur. Normally, only females can have both alleles, because only they have two X chromosomes. If a female cat is heterozygous for the tortoiseshell gene, she has tortoiseshell coat colour. Orange patches are formed by populations of cells in which the X chromosome with the orange allele is active; black patches have cells in which the X chromosome with the black allele is active.

Fig. 8.3.5.1. Genetic basis of tortoiseshell cat.

Other Modes of Epistasis

a. Dominant epistasis with recessive interaction (for interest only)

- Dominant epistasis with recessive interaction occurs when presence of a **dominant allele** in the epistatic gene results in the **same phenotype** as a homozygous recessive individual for both genes.

- This results in the following F_2 phenotypic ratio:

9 **A** _ B _	**13**
3 **A** _ bb	
1 aabb	
3 aa B _	**3**

Example

The production of the pigment malvidin (which creates blue-coloured flowers) in the plant *Primula* is controlled by gene K, yet production of this pigment can be suppressed by gene D, which is found at completely different locus.

- At the 1st gene locus: Allele **K** codes for malvidin production and is dominant to allele **k** which does not code for malvidin production.

- At the 2nd gene locus: Allele **D** codes for a gene product which suppresses the allele **K** and is dominant to **d** which does not code for the gene product and thus will not suppress malvidin synthesis.

- Malvidin production is only possible if gene D is homozygous recessive and there is at least one K allele (**K_dd**). Plant with the genotype **KkDd** will not produce malvidin because of the presence of the dominant D allele. Similarly, plant with the genotype **kkdd** will not produce malvidin due to absence of K allele.

Parental phenotype: blue flower X non-blue flower

Parental genotype: KKdd X kkDD

Gametes (n): (Kd) (kd)

F_1 generation genotype: KkDd

F_1 generation phenotype: All non-blue flowers

Selfing of F_1 generation: KkDd X KkDd

Gametes (n): (KD) (Kd) (kD) (kd) (KD) (Kd) (kD) (kd)

Random fertilisation:

		Female Gametes			
		(KD)	(Kd)	(kD)	(kd)
Male Gametes	(KD)	KKDD	KKDd	KkDD	KkDd
	(Kd)	KKDd	KKdd	KkDd	Kkdd
	(kD)	KkDD	KkDd	kkDD	kkDd
	(kd)	KkDd	Kkdd	kkDd	kkdd

Phenotype of the F_2 : no malvidin : malvidin

Phenotypic ratio of F_2: **13 : 3**

Genotype	**Phenotype and genetic explanation**
9 K_D_	no malvidin because dominant *D* allele is present
3 K_dd	malvidin productions because dominant *K* allele present
3 kkD_	no malvidin because recessive *k* and dominant D alleles present
1 kkdd	no malvidin because recessive *k* allele present

Genotypes	**Phenotype**	**F_2 ratio**
KKDD, KKDd, KkDD, KkDd, kkDD, kkDd, kkdd	**No malvidin**	**13**
KKdd,Kkdd	**malvidin**	**3**

b. Duplicate dominant Epistasis

- Duplicate recessive gene action occurs when the presence of **dominant alleles in either genes** result in a single phenotype i.e. both genes are epistatic to each other. Therefore, only one dominant allele at either of the two loci is required to generate the product.

- This results in the following phenotypic ratio:

9 **A** _ **B** _	**15**
3 **A** _ bb	
3 aa **B** _	
1 aabb	**1**

Example

To produce a coloured-kernel, a functional enzyme A or B can convert a common precursor to a product. Therefore, only one dominant allele at either of the two loci is required to generate the product.

Thus, if a pure line wheat plant with a coloured kernel (genotype = **AABB**) is crossed to plant with white kernels (genotype = **aabb**) and the resulting F1 plants (**AaBb**) are selfed, what will be the resulting phenotypic ratio?

Parental phenotype: coloured-kernel X white kernel

Parental genotype: AABB X aabb

Gametes (n): (AB) (ab)

F_1 generation genotype: All AaBb

F_1 generation phenotype: All coloured-kernel

Selfing of F_1 generation: AaBb X AaBb

Gametes (n): (AB) (Ab) (aB) (ab) (AB) (Ab) (aB) (ab)

Gametes	(AB)	(Ab)	(aB)	(ab)
(AB)	AA BB	AA Bb	Aa BB	Aa Bb
(Ab)	AA Bb	AA bb	Aa Bb	Aa bb
(aB)	Aa BB	Aa Bb	aa BB	aa Bb
(ab)	Aa Bb	Aa bb	aa Bb	**aa bb**

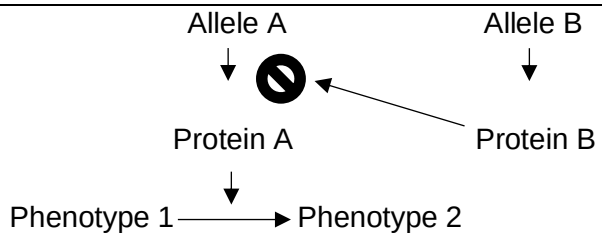
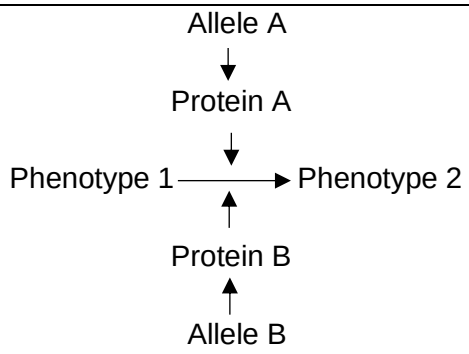
Phenotype of the F_2 : Coloured kernel : White kernel

Phenotypic ratio of F_2: **15 : 1**

Genotype	Kernel Colour	**Enzyme activity**
9 *A_B_*	kernels coloured;	A and B enzyme both functional; Coloured kernels
3 *A_bb*	kernels coloured;	B enzyme non-functional; Coloured kernels
3 *aaB_*	kernels coloured;	A enzyme non-functional; Coloured kernels
1 *aabb*	White kernel	A and B enzymes non-functional; white kernels

Genotypes	**Phenotype**	**F_2 ratio**
AABB, AABb, AaBB, AaBb, AAbb, Aabb, aaBB, aaBb	**Coloured kernels**	**15**
aabb	**White kernels**	**1**

Summary of Epistasis biochemical pathway summary

Genotypes	**Biochemical pathway**
Dominant epistasis and recessive interaction (for interest only)	
Duplicate dominant epistasis (for interest only)	

Other Applications of chi-square test

A student had read that the smooth periwinkle, *Littorina obtusata*, was more likely to be found on bladder wrack than on other seaweeds. In order to test this preference, the students located 100 smooth periwinkles in a 25 m² sample area of rocky shore. For each periwinkle, the students noted the seaweed on which it was found.

1. State null hypothesis

H_0: There is no significant difference in the numbers of smooth periwinkles on the different seaweeds.
H_a: There is a significant difference in the numbers of smooth periwinkles on the different seaweeds.

2. Calculate chi-square value

Groups	Observed Frequency (O)	Expected Frequency (E)	(O-E)	$\frac{(O-E)^2}{E}$
Spiral wrack	2	25	-23	21.16
Egg wrack	30	25	5	1.00
Bladder wrack	61	25	36	51.84
Serrated wrack	7	25	-18	12.96

*The second cross was a test or back cross, so it was expected that the ratio in the F_2 would be 1:1:1:1. The expected numbers are calculated by adding up the observed numbers and dividing by 4.

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$ **= 21.16 + 1.00 + 51.84 + 12.96 = 86.96**

3. Calculate degrees of freedom **Df: 4 – 1 = 3**

4 & 5: Refer to chi-square table & compared to critical chi-squared value

degrees of freedom	probability, p				
	0.10	0.05	0.02	0.01	0.001
1	2.71	3.84	5.41	6.64	10.83
2	4.61	5.99	7.82	9.21	13.82
3	6.25	7.82	9.84	11.35	16.27

6. Conclude

- At p = 0.05, degree of freedom = **3,**
- χ^2 calculated **>** χ^2 critical**, 86.96 > 7.82**
- Therefore, deviation between observed and expected ratio is statistically **significant.**
- The difference is **NOT due to** chance alone.
- Hence, H_o is **rejected .**
- Smooth periwinkles are unlikely to be equally distributed around different sea beds.