[TOPIC 1] Mendel's Laws of Inheritance

- **Genetics** is the branch of biology, which deals with inheritance and variation of characters from parents to offspring.
- **Inheritance** is the process by which characters or traits are transferred from one generation to the next.
- **Variation** is the degree by which progeny differs from each other and with their parents. Humans knew from as early as 8000-1000 B.C., that one of the causes of variation was hidden in sexual reproduction.
- **Gregor Johann Mendel** for the first time conducted experiments to understand the pattern of inheritance of variation in living beings.

1.1 Mendel's Experiment

Mendel's Experimental Material

(*i*) He conducted experiments on garden pea plant (*Pisum sativum*) for seven years (1856-1863) and proposed the laws of inheritance in living organisms.

(*ii*) He selected garden pea plant as experimental material because of:

(a) easy availability on a large scale.

(b) many varieties are available with distinct characteristics.

(c) they are self-pollinated and can be cross-pollinated easily in case self-pollination does not occur.

(d) pea plant has a shorter life cycle. It is because short life cycle enables the genetecists to study many generations of the organism in a short time period.

(*iii*) Mendel selected **14 true-breeding** (a breeding line which has undergone continuous self-pollination and show stable trait inheritance and expression for several generations) pea plant varieties, as pairs, which were similar except for one character with contrasting traits.

Seven contrasting characters and their traits as taken by Mendel are listed in the table given below:

Contrasting Characters Studied by Mendel in Pea

Character	Contrasting character (Dominant/Recessive)
Stem height	Tall/Dwarf
Flower colour	Violet/White
Flower position	Axial/Terminal
Pod shape	Inflated/Constricted
Pod colour	Green/Yellow
Seed shape	Round/Wrinkled
Seed colour	Yellow/Green

Mendel's Experimental Procedure

(*i*) He studied one trait or character at a time, e.g. he crossed tall and dwarf pea plants to study the inheritance of one gene that confers tallness or dwarfness.

(*ii*) Mendel hybridised plants with alternate forms of a single trait (monohybrid cross). The seeds produced by these crosses were grown to develop into plants of **Filial$_1$** progeny or F_1-generation.

(*iii*) He then self-pollinated the tall F_1 plants to produce plants of **Filial$_2$** progeny or F_2-generation.

(*iv*) In later experiments, Mendel also crossed pea plants with two contrasting characters known such a cross is known as dihybrid cross.

(*v*) Mendel self-pollinated the F_2 plants also.

(*vi*) Mendel used emasculation and bagging like procedures to avoid unwanted pollination in his experiments.

Mendel's Observation in his Experiment

(*i*) In F_1-generation, Mendel found that all pea plants were tall and none was dwarf.

(*ii*) He also observed other pair of traits and found that F_1 always resembled one of its parents while the trait of other parent was always masked.

(*iii*) In F_2-generation, he found that some of the offsprings were dwarf, i.e. the characters which were not seen in F_1-generation were expressed in F_2-generation.

(*iv*) These contrasting traits (tall/dwarf) did not show any mixing either in F_1 or in F_2-generation.

(*v*) Similar results were obtained with the other traits that he studied. Only one of the parental traits was expressed in F_1-generation, while at F_2-generation stage, both the traits were expressed in the ratio of 3 : 1.

(*vi*) Mendel also found identical results in dihybrid cross as in monohybrid cross.

(*vii*) On self-pollinating F_2 plants, he found that dwarf F_2 plants continued to generate dwarf plants in F_3 and F_4-generations.

Inferences of Mendel's Experiments

(*i*) Mendel observed that something was being passed down, from parents to offsprings through the gametes over successive generations. He called these as 'factors'. The Mendelian 'factors' are now known as genes.

(*ii*) Genes are considered to be the units of inheritance. They contain the information required to express a particular trait.

(*iii*) Genes which codes for a pair of contrasting traits are called **alleles** or **allelomorphs**, i.e. they are slightly different forms of the same gene or two alternative forms of a gene are known as allele.

(*iv*) Mendel also proposed that in a true breeding variety, the allelic pair of genes are identical. For example, TT and tt for tall or dwarf pea variety respectively.

(*v*) TT and tt represent **genotype** of a trait.

(*vi*) The observable external feature, e.g. tall and dwarf represent the **phenotype**.

(*vii*) When the tall (TT) and dwarf (tt) pea plants produce gametes, the alleles of the parental pair **segregate** from each other and only one allele is transmitted to a gamete.

(*viii*) The gametes of the tall TT plants have the allele T and the dwarf tt plants have the allele t.

(*ix*) This segregation of alleles is a random process and so there is a 50% chance of a gamete containing either allele, as verified by the results of crossings. After fertilisation of plant with TT and tt traits, hybrids are formed that contain Tt.

(*x*) Mendel found the phenotype of Tt to be similar as TT parent in appearance, he proposed that in a pair of dissimilar factors, one dominates the other (T in this case) and hence, is called the **dominant** factor, while the other factor (t) is **recessive**. In other words, in a pair of dissimilar factor, one factor is able to express itself and is known as dominant, while another factor is not able to express itself and is known as recessive.

(*xi*) Allele can be similar in case of homozygous TT or tt and dissimilar in case of heterozygous Tt.

(*xii*) Dominant character is expressed in homozygous as well as in heterozygous condition, while recessive is expressed only in its homozygous condition.

(*xiii*) Since, the Tt plant is heterozygous for genes controlling one character (height), it is a monohybrid and the cross between TT and tt is a monohybrid cross.

Punnett Square

(*i*) The production of gametes by the parents, the formation of the zygotes, the F_1 and F_2-generations can be understood by a diagram called **Punnett square** developed by a British geneticist **RC Punnett**.

(*ii*) The Punnett square is a graphical representation to calculate the probability of all possible genotypes of offsprings in a genetic cross.

(*iii*) The 1/4 :1/2 :1/4 genotypic ratio of TT : Tt : tt is mathematically condensable to the form of binomial expression $(ax + by)^2$, that has the gametes bearing genes T or t in equal frequency of 1/2.

(*iv*) The expression can be expanded as

$$\left(\frac{1}{2}T+\frac{1}{2}T\right)^2=\left(\frac{1}{2}T+\frac{1}{2}t\right)\times\left(\frac{1}{2}T+\frac{1}{2}t\right)$$

$$=\frac{1}{4}TT+\frac{1}{2}Tt+\frac{1}{4}tt$$

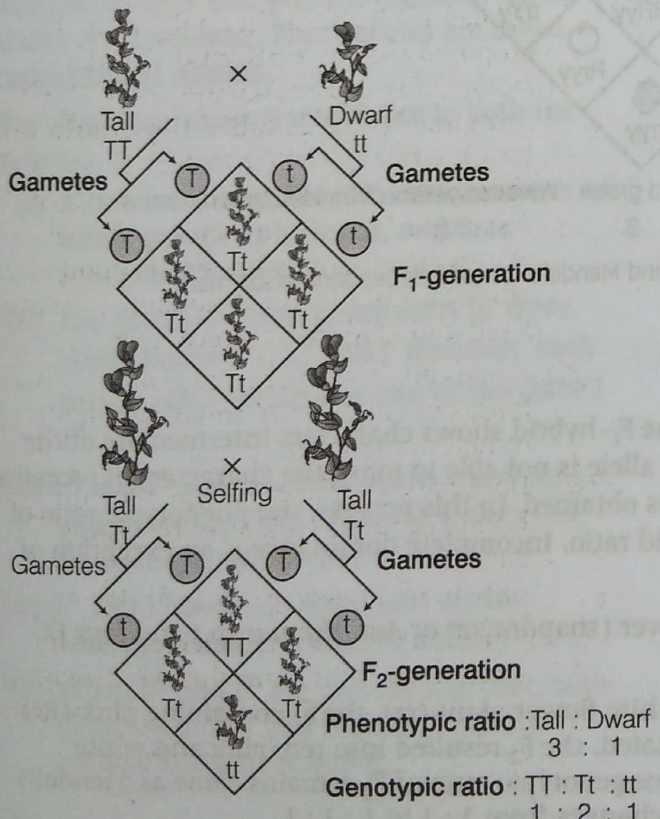


Figure 5.1 A Punnett square used to understand a typical monohybrid cross conducted by Mendel between true-breeding tall plants and true-breeding dwarf plants

1.2 Mendel's laws of Inheritance

Mendel's laws of inheritance are based on his observations on monohybrid and dihybrid crosses. He proposed three laws:

Law of Dominance (First law)

Law of dominance states that characters are controlled by genes which occur in pairs, when two alternate forms of a trait or character (genes or alleles) are present in an organism, only one factor (dominant) expresses itself in F_1-generation.

While, the other factor (recessive) remains hidden. This is known as law of dominance. It explains expression of genes in a monohybrid cross. In such a cross the F_2-generation. Phenotypic ratio is 3 : 1 while genotypic ratio is 1 : 2 : 1. There are two exceptions of law of dominance. These include incomplete dominance and codominance.

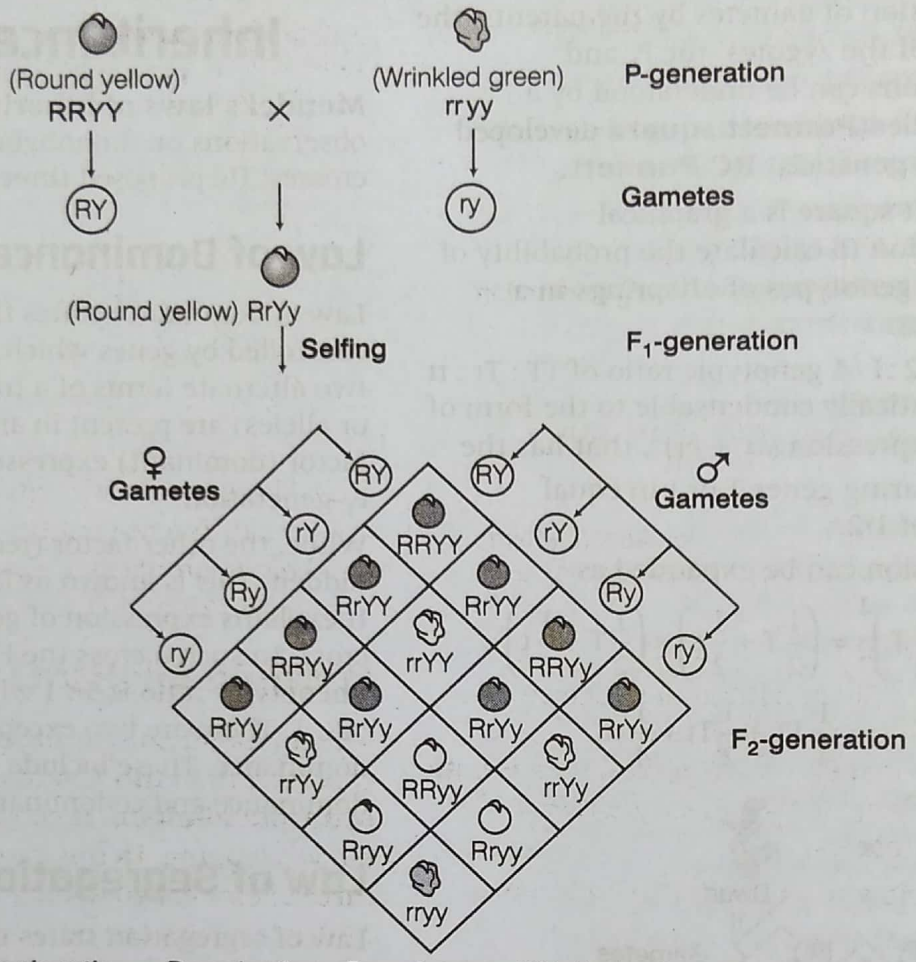
Law of Segregation (Second law)

Law of segregation states that the factors or alleles of a pair segregate from each other during gamete formation, in a way that a gamete receives only one of the two factors. They do not show any blending or mixing. It is also known as law of purity of gametes. There is no exception to law of segregation.

Law of Independent Assortment (Third law)

Law of independent assortment is based on inheritance of two genes, i.e. **dihybrid cross.** It states that when two pairs of contrasting traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters. Thus, the genes randomly rearrange in the offsprings producing both parental and new combinations of characters. Thereforce, the inheritance of one character does not affect the inheritance of another character and both the characters assort independently.

The Punnett square can be used to understand the independent segregation of the two pairs of genes during meiosis. Linkage is the exception to law of independent assortment.



Phenotypic ratio	Round yellow	:	Round green	:	Wrinkled yellow	:	Wrinkled green
	9	:	3	:	3	:	1

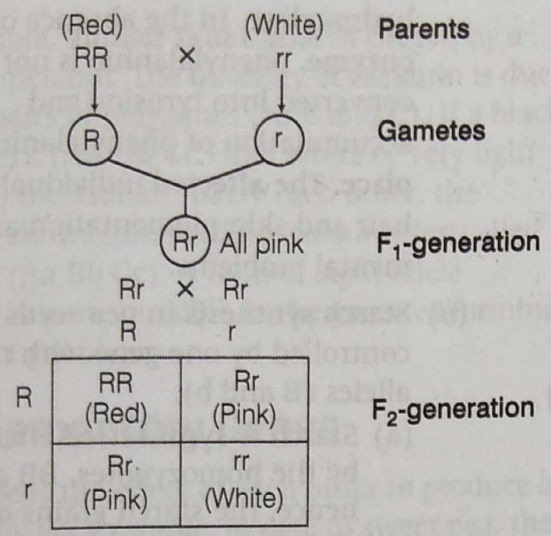
Figure 5.2 A Punnett square used to understand Mendel's law of independent assortment

Incomplete Dominance

Incomplete dominance is a phenomenon in which the F_1-hybrid shows characters intermediate of the parental genes. In incomplete dominance, dominant allele is not able to mask the characters of recessive allele completely hence, an intermediate phenotype is obtained. In this process, the phenotypic ratio of F_2-generation deviates from the Mendel's monohybrid ratio. Incomplete dominance is an exception of Mendel's law of dominance.

Example, inheritance of flower colour in the dog flower (snapdragon or *Antirrhinum* sp.) and four O' clock plant (*Mirabilis jalapa*).

As a result of a cross between red flower (RR) and white flower plant (rr), the F_1 containing pink (Rr) flower was obtained. When F_1 plants were self-pollinated, the F_2 resulted into red, pink and white flowers in the ratio of 1 : 2 : 1. In incomplete dominance genotypic ratio of F_2 remains same as Mendel's monohybrid cross, i.e. 1 : 2 : 1, but phenotypic ratio changes from 3 : 1 to 1 : 2 : 1.



Monohybrid cross in the plant snapdragon, where one allele is incompletely dominant over the other

Codominance

Codominance is a phenomenon in which two alleles are able to express themselves independently when present together, means both alleles are dominant. These alleles are called **codominant alleles.**

The offsprings show resemblance to both the parents.

(*i*) A common example of codominance is ABO blood groups in humans, which is controlled by gene I.

(*ii*) The gene for blood group exist in three allelic forms I^A , I^B and i. However, each person can contain any two of the three I alleles.

(*iii*) I^A and I^B produce RBC surface antigens A and B, respectively, whereas 'i' does not produce any antigen.

(*iv*) I^A and I^B both are dominant alleles, whereas 'i' is the recessive allele.

(*v*) When I^A and I^B are present together, both express equally and produce both the surface antigens A and B.

Genetic Basis of Blood Groups in Human Population

Allele from parent 1	Allele from parent 2	Genotype of offspring	Blood types of offspring
I^A	I^A	I^AI^A	A
I^A	I^B	I^AI^B	AB
I^A	i	I^A i	A
I^B	I^A	I^AI^B	AB
I^B	I^B	I^BI^B	B
I^B	i	I^B i	B
i	i	ii	O

(*vi*) These three different alleles, may produce six different genotypes of human ABO blood group that may show four phenotypes A, B, AB and O.

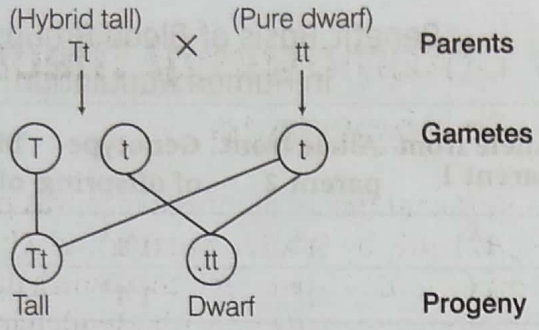
Multiple Allelism

When more then two alleles are present for a character then this condition is known as **multiple allelism.** It can be explained by ABO blood grouping. In this case, more than two, i.e. three alleles are governing the same character. Multiple alleles can be found only when population studies are made since, an individual can have only two alleles.

1.3 Test Cross

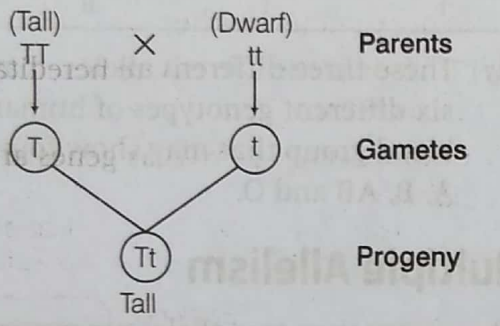
It is a method devised by Mendel to determine the genotype of an organism. Test cross is performed to know whether an organism is homozygous dominant (TT) or heterozygous dominant (Tt). A cross is conducted between unknown dominant genotype and the recessive parent.

(*i*) For example, F_1 hybrid (Tt) heterozygous (of a pure tall plant, i.e. TT and a pure dwarf plant, i.e. tt) is crossed with a pure dwarf plant.

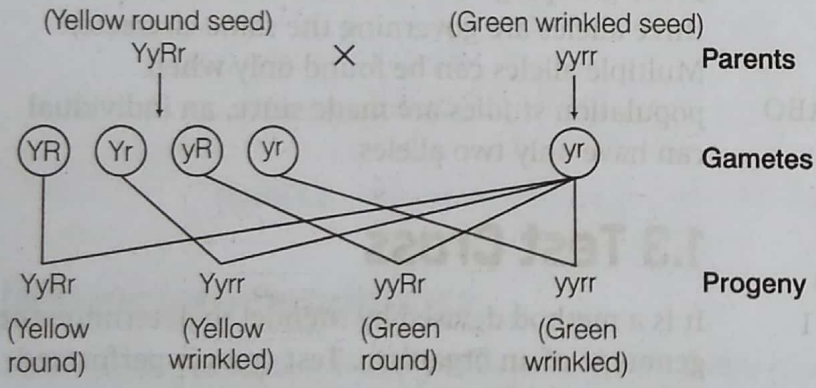


In this example, the progeny consists of tall and dwarf plants in the ratio of 1 : 1. Thus, monohybrid test cross ratio is 1 : 1.

(*ii*) In case of both homozygous parents, i.e. TT, the progeny obtained will have all tall plants.



(*iii*) In case of dihybrid test cross, where two traits are taken, a heterozygous individual is crossed with a homozygous recessive parent.



The dihybrid test cross ratio comes as 1 : 1 : 1 : 1.

1.4 Pleiotropy

Pleiotropy is the phenomenon in which a single gene exhibits multiple phenotypic expressions. It means that a single pleiotropic gene may produce more than one effect.

For example,

(*i*) Phenylketonuria, a disorder caused by mutation in the gene encoding for enzyme phenylalanine hydroxylase. In the absence of this enzyme, phenylalanine is not converted into tyrosine and accumulation of phenylalanine takes place. The affected individuals show hair and skin pigmentation and mental problems.

(*ii*) Starch synthesis in pea seeds is controlled by one gene with two alleles (B and b).

(a) Starch is synthesised effectively by the homozygotes, BB and hence, the starch grains are large and the seeds at maturity are round.

(b) The homozygotes, bb are less efficient in starch synthesis, hence they have small starch grains and the seeds are wrinkled.

(c) The heterozygotes, Bb produce round seeds, indicating that B is the dominant allele, but the starch grains are intermediate in size and hence, for the starch grain size, the alleles show incomplete dominance. It is an example of pleiotropy as the same gene controls two traits, i.e. seed shape and size of starch grains.

(d) Here, it is to be mentioned that dominance is not an autonomous feature of the gene or its product, but it depends on the production of a particular phenotype from the gene product.

1.5 Polygenic Traits

Polygenic inheritance was given by **Galton** in 1833. In this, traits are controlled by three or more genes (multiple genes). Such traits are called **polygenic traits.** The phenotype is produced as a result of participation of several genes and is also influenced by the environment and is called quantitative inheritance as the character/phenotype can be quantified.

For example, human skin colour is caused by a pigment melanin. The quantity of melanin is due to three pairs of polygenes (A, B and C). If a black or very dark (AA BB CC) and white or very light (aa bb cc) individuals marry each other, the offspring shows intermediate colour often called **mulatto** (Aa Bb Cc). A total of eight allele combinations are possible in the gametes forming 27 distinct genotypes.

Complementary Genes

Complement the effect of each other to produce a phenotype. For example, in case of sweet pea, the flower colour is due to complementary genes. Here, one gene complements the expression of another gene.

1.6 Rediscovery of Mendel's Laws

(*i*) Though, Mendel published his work on inheritance of characters in 1865, it remained unrecognised for several reasons till 1900. Some of these reasons are as follows:

(a) Communication was difficult, so his work could not be widely publicised.

(b) His concept of genes as stable unit that controlled the expression of traits and of the pair of alleles which did not blend was not accepted.

(c) His idea of using mathematics to explain biological phenomenon was new and unacceptable.

(d) He could not provide any physical proof for the existence of factors that where these factors are located in the cell.

(*ii*) In 1900, **Hugo de Vries, Correns** and **von Tschermak** rediscovered Mendel's results independently. Due to microscopy, they carefully observed cell division.

(*iii*) This led to discovery of **chromosomes** (structure in the nucleus that appeared to double and divide just before each cell division).

1.7 Chromosomal Theory of Inheritance

Chromosomal theory of inheritance was proposed independently by **Walter Sutton** and **Theodore Boveri** in 1902. They united the knowledge of chromosomal segregation with Mendelian principles and called it **chromosomal theory of inheritance**.

The main points of this theory are as follows:

(*i*) Gametes (sperm and egg) carry and transmit hereditary characters from one generation to another.

(*ii*) Nucleus is the site where hereditary factors are present.

(*iii*) Chromosomes as well as genes are found in pairs.

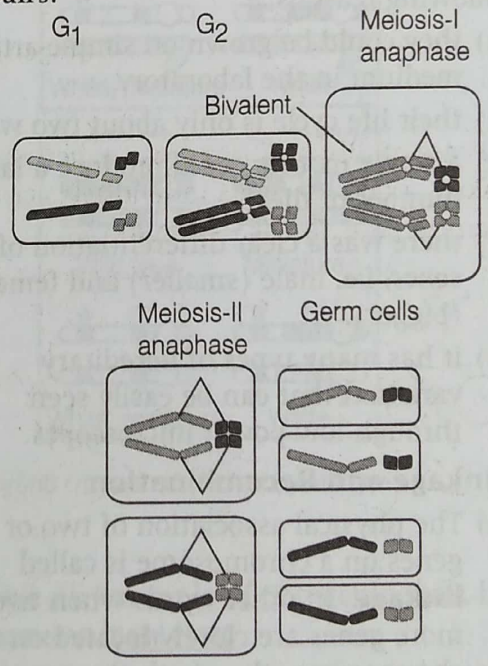


Figure 5.3 Meiosis and germ cell formation in a cell with four chromosomes

(*iv*) The two alleles of a gene pair are located on homologous sites on the homologous chromosomes. During meiotic anaphase-I, separation of homologous chromosomes takes place.

(*v*) The sperm and egg having haploid sets of chromosomes fuse to regain the diploid state.

(*vi*) Homologous chromosomes synapse during meiosis and get separated to pass into different cells. It is the basis of segregation and independent assortment during meiosis. Sutton and Boveri said that the pairing and separation of a pair of chromosomes would lead to the segregation of a pair of factor they carry.

Experimental Verification of the Chromosomal Theory of Inheritance

Experimental verification of the chromosomal theory of inheritance was done by **Thomas Hunt Morgan** and his colleagues.

(*i*) Morgan selected fruit fly, *Drosophila melanogaster* for his experiments because of following reasons:

(a) they could be grown on simple artificial medium in the laboratory.

(b) their life cycle is only about two weeks.

(c) a single mating could produce a large number of flies.

(d) there was a clear differentiation of the sexes, i.e. male (smaller) and female (bigger).

(e) it has many types of hereditary variation that can be easily seen through low power microscopes.

(*ii*) **Linkage and Recombination**

(a) The physical association of two or more genes on a chromosome is called **linkage**. In other words when two or more genes are closely located on a chromosome, then both the genes try to go together in the next generation. This type of inheritance of genes is known as linkage. It is the exception of Mendel's law of independent assortment.

(b) **Recombination** explains the generation of non-parental gene combinations.

(c) To explain the phenomena of linkage and recombination, Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked, i.e. the genes are located on X-chromosome.

(d) He observed that:

- two closely located genes did not segregate independently of each other.
- the proportion of parental gene combinations were much higher than the non-parental types, when two genes in a dihybrid cross were situated on the same chromosome. Morgan concluded this as a physical association or linkage.

Cross A show crossing between genes y and w. Cross B show crossing between genes w and m. Here, dominant wild type alleles are represented with [+] sign.

(e) $\text{Linkage} \propto \frac{1}{\text{Distance between two genes}}$

Means if two genes are very close to each other then they are tightly linked and there are very less chances of recombination. However, if two genes are located far from each other, then they are loosely linked and there are more chances of recombination.

(f) Morgan and his group also found that even when genes were grouped on the same chromosome, some genes were very tightly linked (very low recombination), while others were loosely linked (higher recombination).

(g) Recombination of linked genes is by crossing over, i.e. exchange of corresponding parts between the chromatids of homologous chromosomes.

(h) **Alfred Sturtevant** (Morgan's student) used the frequency of recombination between gene pairs on the same chromosome as a measure of the distance between genes and 'mapped' their position on the chromosome. **Genetic maps** are now used as a starting point in the sequencing of whole genomes as done in case of **Human Genome Sequencing Project**.

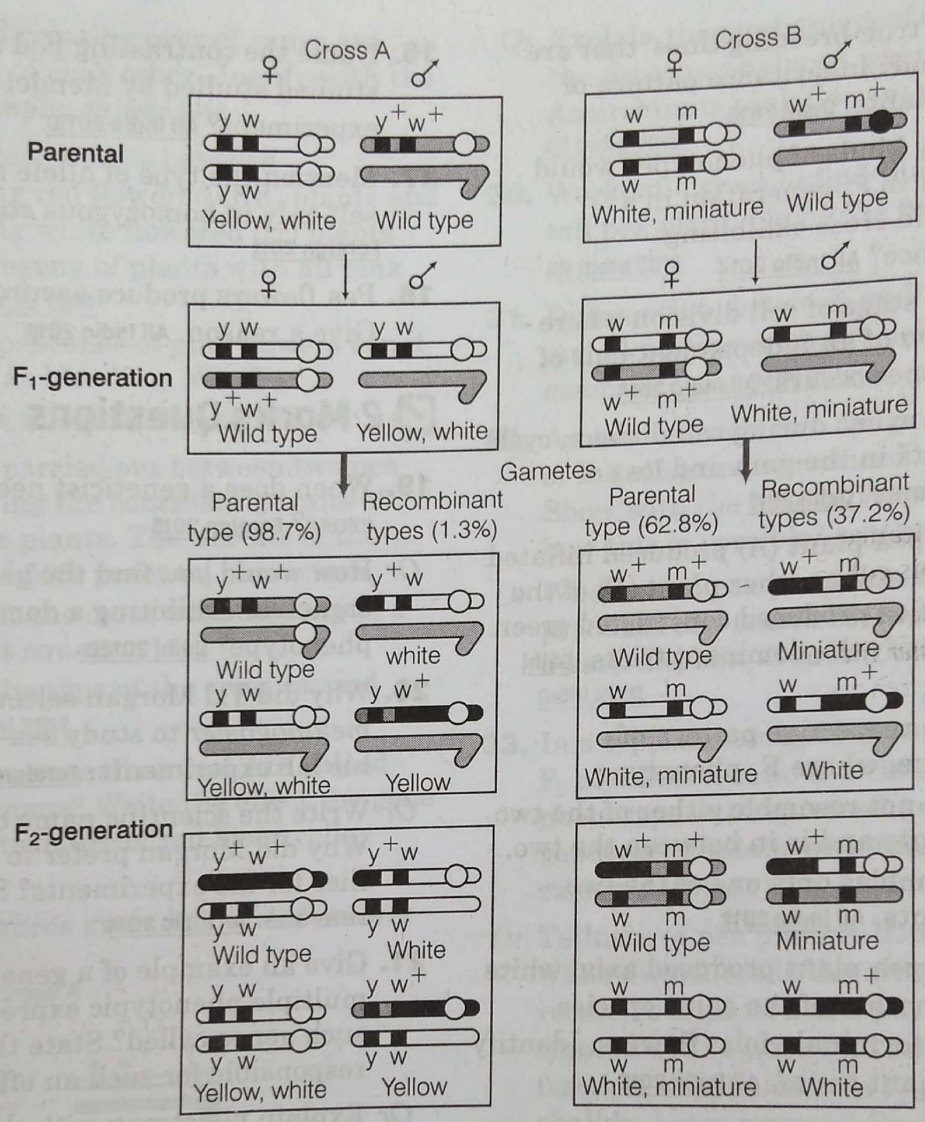


Figure 5.4 Linkage result of two dihybrid crosses conducted by Morgan

[TOPIC 2] Sex-Determination and Genetic Disorders

2.1 Mechanism of Sex-Determination

(*i*) The establishment of sex through differential development in an individual at the time of zygote formation is called **sex-determination**.

(*ii*) **Henking** (1891) could trace a specific nuclear structure all through spermatogenesis in few insects.

(a) He observed that 50% of sperms received this specific structure after spermatogenesis, whereas the other 50% sperms did not receive it.

(b) He named this structure as X-body. Scientists further explained this X-body as **X-chromosome**.

(*iii*) There are different types of sex-determination mechanism observed in various organisms. These mechanisms are mainly dependent on whether the parents are homogametic, i.e. with similar gametes or heterogametic, i.e. with different gametes some of these mechanisms are as follows:

(a) **XO type sex-determination** is found in a large number of insects, e.g. grasshopper, etc. It includes homogametic females and heterogametic males.

- In this type, all the ova bear a pair of X-chromosome, while sperms bears only one X-chromosome along with the other chromosomes (autosomes).
- Eggs fertilised by sperms having an X-chromosome become females and those fertilised by sperms that do not have X-chromosome become males.
- Due to the involvement of the X-chromosome in sex-determination, it was named as **sex chromosome** and rest chromosomes were named as **autosomes**.

(b) **XY type of sex-determination** is present in many insects like *Drosophila melanogaster* and in mammals including man. This type of sex-determination includes homogametic female and heterogametic males.

- In males, an X-chromosome is present along with another chromosome, which is very small and called as **Y-chromosome.**
- Females have a pair of X-chromosomes.
- Both males and females bear same number of autosomes. The males have autosomes plus XY and females have autosomes plus XX-chromosomes. So, male is responsible for determination of the sex of the child.

(c) **XO type and XY type of sex-determination** shows the example of **male heterogamety**. Because in both cases, males produce two different types of gametes:

- Either with or without X-chromosome.
- Some gametes with X-chromosome and some with Y-chromosome.

(d) **ZW type of sex-determination** is found in certain birds, fowls and fishes.

- Females have Z and W-chromosomes along with autosomes and the males have a pair of Z-chromosomes.
- In this type, sex is determined by the type of ovum that is fertilised to produce offspring.

(e) **ZO type of sex-determination** is seen in butterflies and moths. In this type the female have only one Z-chromosome, while the male have a pair of Z-chromosomes.

(f) **ZW type and ZO type of sex-determination** shows the example of **female heterogamety**.

Sex-Determination in Humans

(*i*) In humans, 23 pairs of chromosomes are present, out of which 22 pairs are exactly same in both males and females. These are known as **autosomes**.

(*ii*) A pair of X-chromosome (XX) is present in females, whereas one X and one Y-chromosome (XY) is present in males.

(*iii*) In males, during spermatogenesis, two types of gametes are produced. 50% of the total sperms carry the X-chromosomes while the rest 50% carry Y-chromosomes besides autosomes.

(*iv*) Females produce only one type of ovum with an X-chromosome.

(*v*) In case, the ovum fertilises with a sperm carrying X-chromosome, the zygote develops into a female (XX) and if ovum fertilised the Y-chromosome carrying sperm, zygote formed is a male (XY).

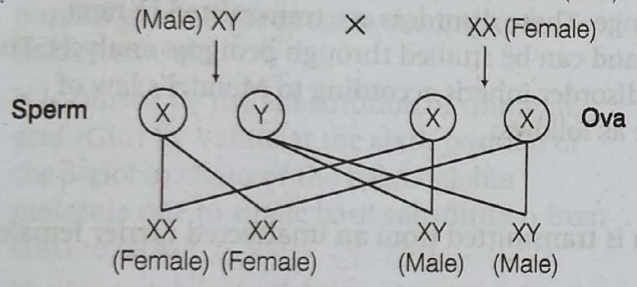


Figure 5.5 Sex-determination in human beings

(*vi*) Hence, the genetic make up of sperm, which fertilises the ovum determines the sex of a child.

(*vii*) There are 50% chances of having male and 50% chances of having female in each pregnancy. So, woman should not be blamed for the sex of a child.

Sex-Determination in Honeybee

(*i*) It is known as **haplo-diploidy method** in which an unfertilised egg develops into male (Arrhenotoky) while fertilised egg develops into female.

(*ii*) This type of sex-determination is seen in certain insects like honeybees, ants, etc.

2.2 Mutation

It is a phenomenon, which causes alteration of DNA sequences resulting in changes in the genotype and the phenotype of an organism. It leads to variation in DNA in addition to recombination.

(*i*) Loss (deletion) or gain (insertion/duplication) of a segment of DNA, results in alteration in chromosomes. As genes are located on chromosomes, alteration in chromosomes results in abnormalities, these are known as **chromosomal alterations**, which are common in cancer cells.

(*ii*) Mutation also occurs due to change in a single base pair of DNA. This is called **point mutation,** e.g. sickle-cell anaemia.

(*iii*) Deletions and insertions of base pairs of DNA, causes **frameshift mutations.**

(*iv*) There are many physical and chemical factors that induce mutation, which are called **mutagens**. For example, UV radiation is a mutagen.

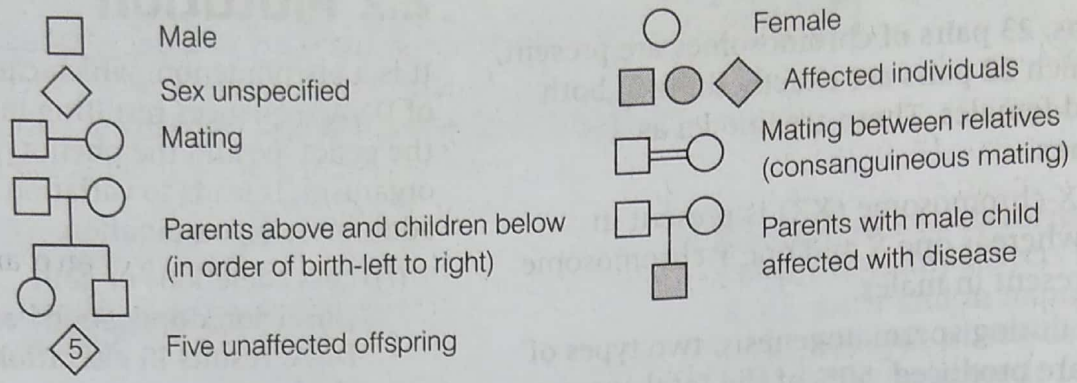
2.3 Pedigree Analysis

It is an analysis of traits in several generations of a family. In this analysis, the inheritance of a particular trait is represented in the family tree over generations.

(*i*) Pedigree study provides a strong tool in human genetics, which is utilised to trace the inheritance of a specific trait, abnormality or disease.

(*ii*) Pedigree analysis is performed for human population because Mendel's monohybrid and dihybrid cross with pure lines are not possible in human.

(*iii*) The symbols used in pedigree analysis are given below:



2.4 Genetic Disorders

A number of disorders in human beings are associated with the inheritance of changed or altered genes or chromosomes. These are called **genetic disorders**. Genetic disorders can be divided into following types:

Mendelian Disorders

Mendelian disorders are mainly determined by alteration or mutation in the single gene. Here, chromosome number and their structure do not change. These disorders are transmitted in next generation according to the principle of inheritance and can be studied through pedigree analysis. They may be dominant or recessive. It means Mendelian disorder inherit according to Mendel's law of inheritance. Some common Mendelian disorders are as follows:

Haemophilia

Haemophilia is a sex-linked recessive disease, which is transmitted from an unaffected carrier female to some of the male offsprings.

- In this disease, a single protein that is a part of cascade of proteins involved in the clotting of blood is affected.
- Due to this, in an affected individual, a small cut results in non-stop bleeding.
- The heterozygous female (carrier) may transmit the disease to sons. The possibility of a female becoming haemophilic is extremely rare because mother of such a female has to be atleast carrier and father should be haemophilic. In haemophilia, male is never a carrier because it is a X-linked recessive disease and male has only one X-chromosome. So, even a single allele will make a male haemophilic.
- Example, the family pedigree of queen Victoria, shows a number of haemophilic descendents as she was a carrier of the disease.

Colour Blindness

It is a recessive sex-linked trait in which eyes fail to distinguish red and green colours.

- The recessive allele is carried on X-chromosomes.
- In female, it appears only when both the sex chromosomes carry the gene (X^cX^c).
- The females function as carriers in the presence of a single recessive gene (XX^c).
- In males, the defect may appear in the presence of a single recessive gene (X^cY) because Y-chromosome does not carry any gene for colour vision.
- Haemophilia and colour blindness show ***criss-cross* inheritance pattern,** in which inheritance of sex-linked characters is transmitted from father to daughter or from mother to son.

Sickle-cell Anaemia

Sickle-cell anaemia is an autosome linked recessive trait that can be transmitted from parents to the offspring when both the partners are carrier for the gene (heterozygous). In this disorder due to a point mutation abnormal haemoglobin is produced, which leads to sickle-cell RBC. This RBC is destroyed hence, person become anaemic.

- This disease is controlled by a single pair of allele, Hb^A and Hb^S. Hb^A codes for normal haemoglobin, while Hb^S codes for sickle-cell haemoglobin.
- Only homozygous individuals for Hb^S ($Hb^S Hb^S$) show the diseased phenotype.
- Heterozygous ($Hb^A Hb^S$) individuals appear unaffected, but they are carrier of the disease as there is 50% chances of transmission of the mutant gene to the progeny leading to sickle-cell trait.
- It is caused by the substitution of Glutamic acid (Glu) by Valine at the sixth position of the β-globin chain of the haemoglobin molecule due to single base substitution from GAG to GUG.
- The mutant haemoglobin molecule undergoes polymerisation under low oxygen tension causing the change in the shape of the RBC from biconcave disc to elongated sickle-like structure.

Carrier male Hb^A Hb^S × Carrier female Hb^A Hb^S

mating

	Hb^A	Hb^S
Hb^A	Hb^A Hb^A	Hb^A Hb^S
Hb^S	Hb^A Hb^S	Hb^s Hb^S

$Hb^A Hb^A$ - Normal
$Hb^A Hb^S$ - Carrier
$Hb^S Hb^S$ - Sickle-cell anaemia affected

Thalassemia

Thalassemia is an autosome linked recessive disease, which occurs due to either mutation or deletion of genes, resulting in reduced rate of synthesis of one of the globin chains of haemoglobin.

- Haemoglobin consists of an α and a β-protein. If body does not produce enough of either of these two protein, the RBC do not form properly and cannot carry sufficient oxygen.
- Anaemia is the main feature of this disease.

Phenylketonuria

Phenylketonuria is an inborn error of metabolism, which is inherited as the autosomal recessive trait.

- The disease is due to the lack of an enzyme phenylalanine hydroxylase that converts the amino acid phenylalanine into tyrosine. In the lack of this enzyme phenylalanine is not converted into tyrosine.
- The phenylalanine is accumulated and gets converted into phenyl pyruvic acid and other derivatives.
- Accumulation in brain results in mental retardation.
- These are also excreted through urine because of its poor absorption by kidney.

Chromosomal Disorders

Chromosomal disorders are caused by the absence or excess or abnormal arrangement of one or more chromosomes. These disorders do not follow Mendel's law of inheritance.

- Failure of segregation of chromatids during cell division resulting in the gain or loss of chromosome(s) is called **aneuploidy**, e.g. Down's syndrome.
- Failure of cytokinesis after telophase stage resulting in an increase in whole set of chromosomes, called **polyploidy**. Often seen in plants.

Some examples of chromosomal disorders are as follows:

Down's Syndrome

Down's syndrome occur due to the presence of an additional copy of the chromosome number 21. This condition is called **trisomy** of 21. So, it is an example of autosomal trisomy. Here, total number of chromosomes become 47 as there is an extra copy of 21 chromosome.

- The disorder was first described by **Langdon Down** (1866).
- Affected individuals are short statured with small round head, furrowed tongue and partially open mouth.
- Palm is broad with characteristic palm crease.
- Physical, psychomotor and mental development is retarded.

Turner's Syndrome

Turner's syndrome is a disorder caused due to the absence of one of the X-chromosome. In this case, the number of chromosomes is 45 with XO. So, it is an example of sex chromosomal monosomy. It is represented by $(2n-1)$.

- The affected females are sterile as ovaries are rudimentary.
- Lack of secondary sexual characters, short stature.

Klinefelter's Syndrome

Klinefelter's syndrome is caused due to the presence of an additional copy of X-chromosome (XXY), resulting into 47 chromosomes. So, it is an example of trisomy of sex chromosome. It is represented by $(2n+1)$.

- Individuals have masculine development, but feminine development (development of breast, i.e. gynaecomastia) also occurs. These are males.
- The individuals are sterile.

All these chromosomal disorders can be easily studied *via* the analysis of karyotypes, i.e. an organised profile of an individual's chromosome according to their shape, size and number.