Chapter 01 Principles of Inheritance and Variation

CONTENT

- **Mendel's Laws of Inheritance**
- **Inheritance of One Gene**
- **Inheritance of Two Genes**
- **Sex Determination**
- **Genetic Disorders**

INTRODUCTION:

Genetics deals with the inheritance, as well as the variation of characters from parents to offspring. **Inheritance** is the process by which characters are passed on from parent to progeny.

- Inheritance is the basis of heredity.

SPOT LIGHT

- Human knew from as early as 8000 - 1000 B.C. that one of the cause of variation was hidden in sexual reproduction.
- Sahiwal cows (Indian breed) was produced through artificial selection and domestication from ancestral wild cow.

- Variation is the degree by which progeny differ from their parents.
- There two type of variations:

(1) **Somatic variations:** Acquired once in lifetime

(2) **Germinal variations:** Appear in germ cells and are inherited

DETECTIVE MIND

- **Study** of transmission of characters from one generation to another is called heredity.
- To develop a genetical character in any organism, gene should be present. It should express and for expression suitable conditions must be present.

SOME GENETICAL TERMS:

1. Factors:

- Unit of heredity which is responsible for inheritance and appearance of characters (Genetical characters).
- These factors were referred as **genes** by **Johannsen** (1909). Mendel used term **"element"** or **"factor".**
- Dominant factors are represented by capital letter while recessive factor by small letter.

W. Bateson
Father of Modern Genetics. He gave many terms like Genetics, Allele, etc.

2 Allele/Allelomorph:

- Alternative forms of a gene which are located on same position [loci] on the homologous chromosome is called Allele. Term allele was coined by **Bateson**.

3. Homozygous (Pure):

- A zygote is formed by fusion of two gametes having identical factors is called homozygote and organism developed from this zygote is called homozygous. Eg. TT, RR, tt

4. Heterozygous (Impure/Hybrid):

- A zygote is formed by fusion of two different types of gamete carrying different factors is called heterozygote (Tt, Rr) and individual developed from such zygote is called heterozygous.

5. Hemizygous:

- If an individual contains only one gene of a pair then individual is said to be hemizygous. Male individual is always hemizygous for sex linked gene. Eg. Haemophilia in man.

6. Dominant :

- The character expresses itself in both homozygous as well as heterozygous condition.
- **Eg.** Tallness in pea plant appears both in "TT" and "Tt".

A. Garrod :

- Father of human genetics. Garrod is covered first human Metabolic genetic disorder which is called **alkaptonuria** (black urine disease).

7. Recessive:

- The character which usually expresses itself in homozygous condition.
- **Eg.** Dwarfness in pea plant appears in "tt" only.

8. Phenotype:

- It is the external and morphological appearance of an organism for a particular character. Eg. Height of plant, colour of flower.

9. Genotype:

- The genetic constitution or genetic make-up of an organism for a particular character. Eg. TT, Tt, tt

10. Phenocopy:

- If different genotypes are placed in different environmental conditions then they produce same phenotype. Then these genotypes are said to be phenocopy of each other.

11. Hybrid vigour/Heterosis:

- Superiority of offsprings over their parents is called as ***Hybrid vigour*** & it develops due to heterozygosity. Hybrid vigour can be maintained for long time in vegetatively propagated crops.
- Hybrid vigour can be lost by inbreeding (selfing) because inbreeding induces the homozygosity in offsprings. Loss of Hybrid vigour due to inbreeding, is called as **inbreeding depression**.

12 Trait:

- It is defined as individual's feature that are inherited
  Examples – Tall and dwarf plants

13. It was developed by a British geneticist **Reginald C. Punnett**.

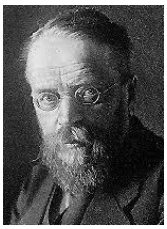
- It is a graphical representation to calculate the probability of all possible genotypes of offsprings in a genetic cross.
- The possible gametes are written on the top row and left column while all possible combinations are represented in the boxes below in the square.

MENDELISM

- **Gregor Johann Mendel** demonstrated the scientific basis of inheritance and variation by conducting hybridisation experiments.
- **Mendel conducted hybridisation experiments on garden peas for seven years (1856- 1863)**
- Mendel published his work on inheritance of characters in **1865** but for several reasons, it remained unrecognised till 1900.
- **Mendel's work was unrecognised because of following reasons:**
- **Firstly,** communication was not easy (as it is now) in those days and his work could not be widely publicised.

G.J. Mendel :
Father of Genetics.

- **Secondly,** his concept of **genes** (or **factors**, in Mendel's words) as stable and discrete units that controlled the expression of traits and, of the pair of alleles which did not 'blend' with each other, was not accepted by his contemporaries as an explanation for the apparently continuous variation seen in nature.
- **Thirdly,** Mendel's approach of using mathematics to explain biological phenomena was totally new and unacceptable to many of the biologists of his time.
- **Finally,** though Mendel's work suggested that factors (genes) were discrete units, he could not provide any physical proof for the existence of factors or say what they were made of.
- After 16 years of Mendel's death in 1900, Mendel's postulates were rediscovered.
- Rediscovery was done by three scientists independently.



Carl Correns

1. **Carl Correns** Germany : **(Experiment on Maize).** He made laws of Mendelism.
2. **Hugo deVries :** (Holland) **(Experiment on Evening Primrose)**
   He republished the Mendel's results in 1901 in **Flora** magazine
3. **Erich von Tschermak** : (Austria) **(Experiment on different flowering plants).**

SPOT LIGHT

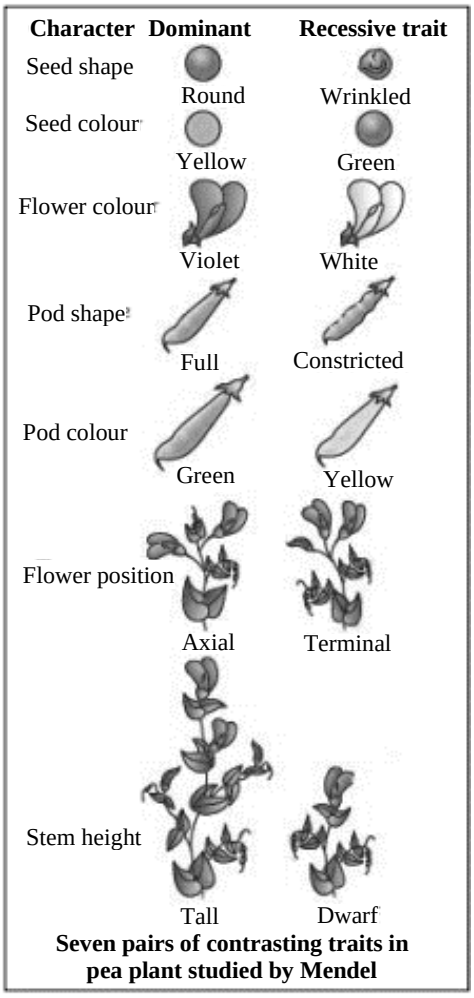
Reasons For Mendel's Success :

- Selection of pea plant for study.
- Mendel studied the inheretance of one or two characters at a time unlike his predecessors who had considered many characters at a time. (Kolreuter-Tobacco plant, John Goss and Knight -Pea plant).
- Use of mathematics and statistics in his experiement.
- Use of pure parents for crosses.
- Mendel quantitatively analysed the inheritance of qualitative characters.
- His experiments had a large sampling size which gave greater credibility to the data that he collected.

Mendel's experiemental materials :

- He selected ***Pisum sativum*** (Garden Pea) plant for his study. The main reasons for adopting garden pea for experiments were as follows :
  (i) Pea plant is easy to cultivate.
  (ii) Pea plant is annual plant with short life cycle of 2-3 months so large number of offsprings can be analysed within a short period of time.
  (iii) It has many contrasting traits.
  (iv) Natural self pollination is present in pea plant.
  (v) Cross pollination can be performed in it artificially so hybridization can be made possible.
  (vi) Pea seeds are large.
- Mendel studied 7 characters in pea plant for carrying out hybridization experiments.

S. No.	Characters	Dominant	Recessive	Chromosome. Number
1.	Stem height	Tall	Dwarf	4th
2.	Colour of flower	Violet	White	1st
3.	Flower position	Axial	Terminal	4th
4.	Shape of pod	Inflated	Constricted	4th
5.	Colour of pod	Green	Yellow	5th
6.	Shape of seed	Round	Wrinkled	7th
7.	Colour of Seed	Yellow	Green	1st



Seven pairs of contrasting traits in pea plant studied by Mendel

TECHNIQUE OF MENDEL :

1. Selection of pure parents :

- Mendel selected 14 true breeding garden pea plant varieties as pairs which were similar except for one character with contrasting traits .
- True breeding variety refers to that plant variety that has undergone continuous self pollination and shows the stable trait inheritance and expression for several generations.
- Mendel developed true breeding varieties of garden pea plant by continuous self pollination and selection.

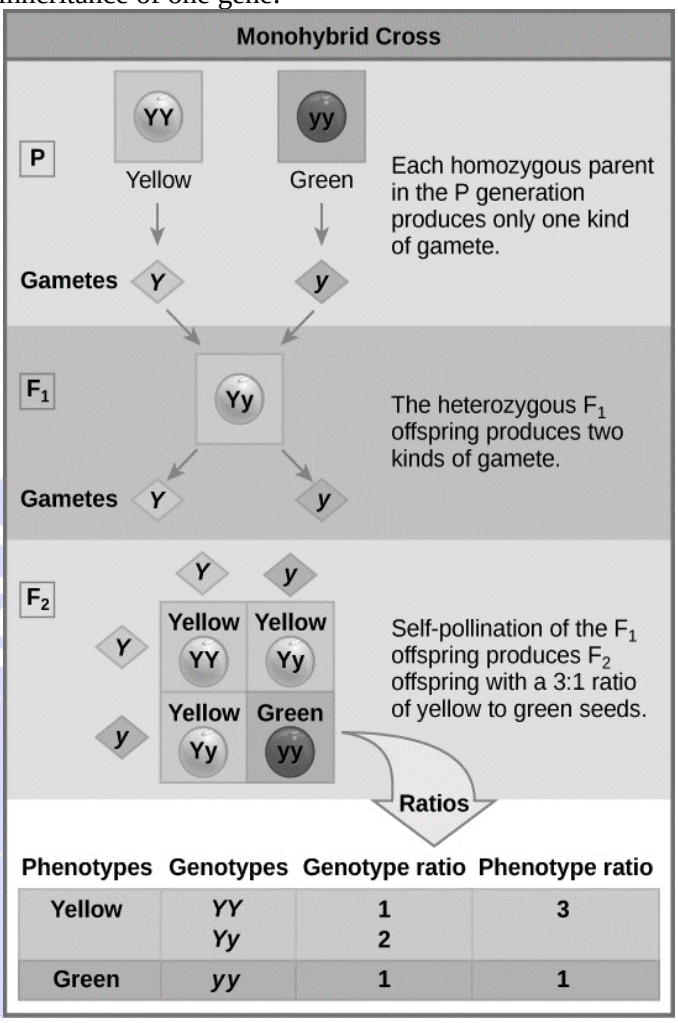
2. Hybridisation between pure plants :

- **Emasculation**
  - Removal of anther from bisexual flower in bud condition so this flower is used as Female flower.
  - It is done to prevent self pollination.
- **Bagging**
  - Emasculated flower is covered with paper bags.
  - This is done to prevent undesirable cross pollination.
- This is the mature pollen grains are collected from male plants and are spread over emasculated flower.
- Seeds are formed in the female flower after pollination.
- The plants that are obtained from these seeds are called First Filial generation or F_1 generation according to Mendel.
- The plants of F_1 generation are self pollinated and F_2 generation is produced.

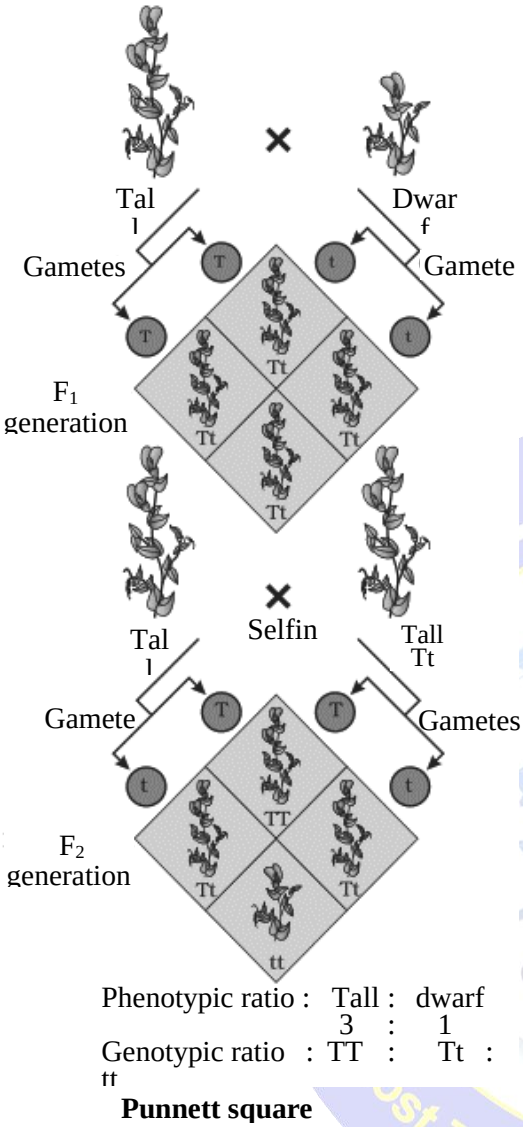
MONOHYBRID CROSS :

- This is the most fundamental cross.

- When we consider the inheritance of one character at a time in a cross, this is called monohybrid cross. Let us take the example of one such hybridisation experiment carried out by Mendel where he crossed tall and dwarf pea plants to study the inheritance of one gene.

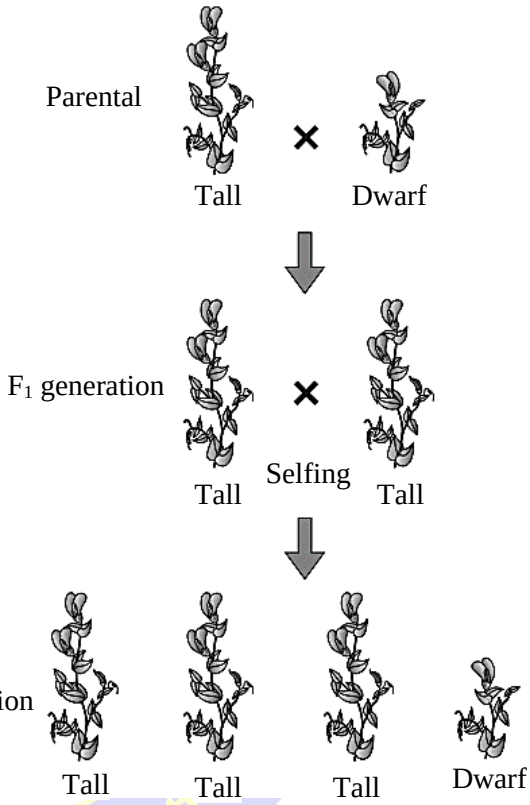


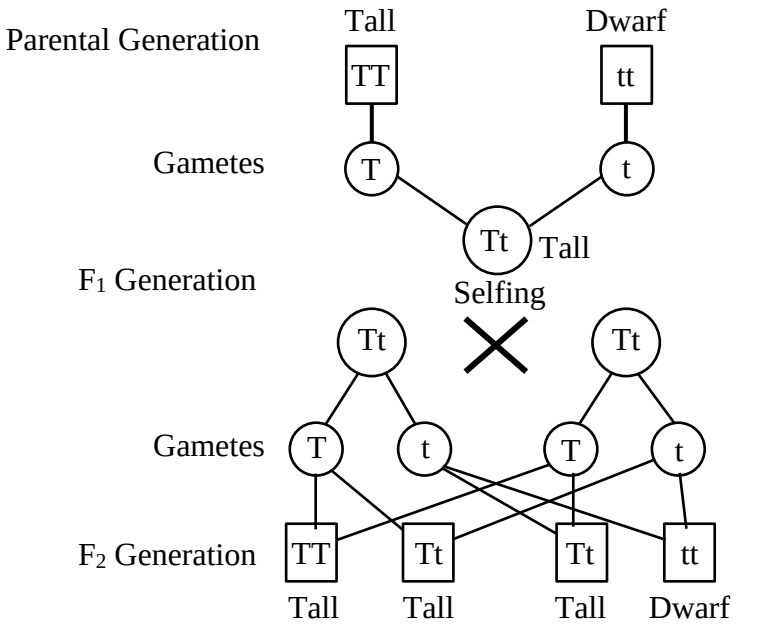
Phenotypes	Genotypes	Genotype ratio	Phenotype ratio
Yellow	*YY* *Yy*	1 2	3
Green	*yy*	1	1



Phenotypic ratio : Tall : dwarf
3 : 1
Genotypic ratio : TT : Tt : tt

Punnett square





MONOHYBRID CROSS (HEIGHT OF PEA PLANT)

Diagrammatic representation of monohybrid cross

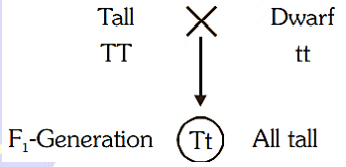
RESULTS OF MONOHYBRID CROSS:

1st Conclusion (Postulate of paired factors):

(a) According to Mendel, each genetic character is controlled by a pair of unit factor.

(b) In this pair, one factor comes from male parent and other from female parent.

2nd Conclusion (Postulate of Dominance):



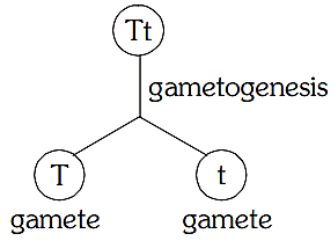
(a) This conclusion is based on F_1 - generation. When two different unit factors are present in single individual, only one unit factor is able to express itself and is known as dominant unit factor.

(b) Another unit factor that fails to express in F_1 generation is the recessive factor.

- The law of dominance is used to explain the expression of only one of the parental characters in a monohybrid cross in the F_1 generation and the expression of both in the F_2 generation. It also explains the proportion of 3 : 1 obtained at the F_2
- There are two exceptions of law of dominance. [A] Incomplete dominance, [B] Co-dominance, Law of dominance = 1st Conclusion + 2nd Conclusion.

3rd Conclusion (Law of segregation):

- This law is the based on the fact that the alleles do not show any blending and that both the characters are recovered as such in F_2 generation though one of these is not seen at the F_1 stage
- During gamete formation, the unit factors of a pair segregate randomly and transfer inside different gametes. Each gamete receives only one factor of a pair; so gametes are pure for a particular trait. It is known as **law of purity of gametes or segregation.**
- There is no exception of Law of segregation. The segregation is essential during the meiotic division in all sexually reproducing organisms. (Nondisjunction could be exception of this law).

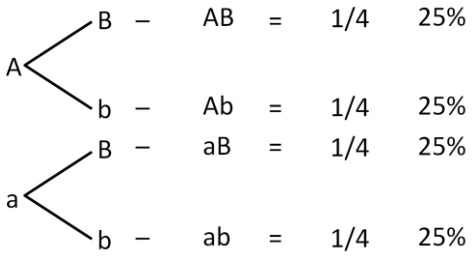


- This law is based on the basis of F_2 generation.

SPOT LIGHT

METHOD FOR GAMETES FORMATION:

- Type of gametes = 2^n
  n = No of hybrid character or heterozygous pair.
- To find out the composition of factors inside the gamete, we use fork line method.
  AaBb = 4 types of gamete



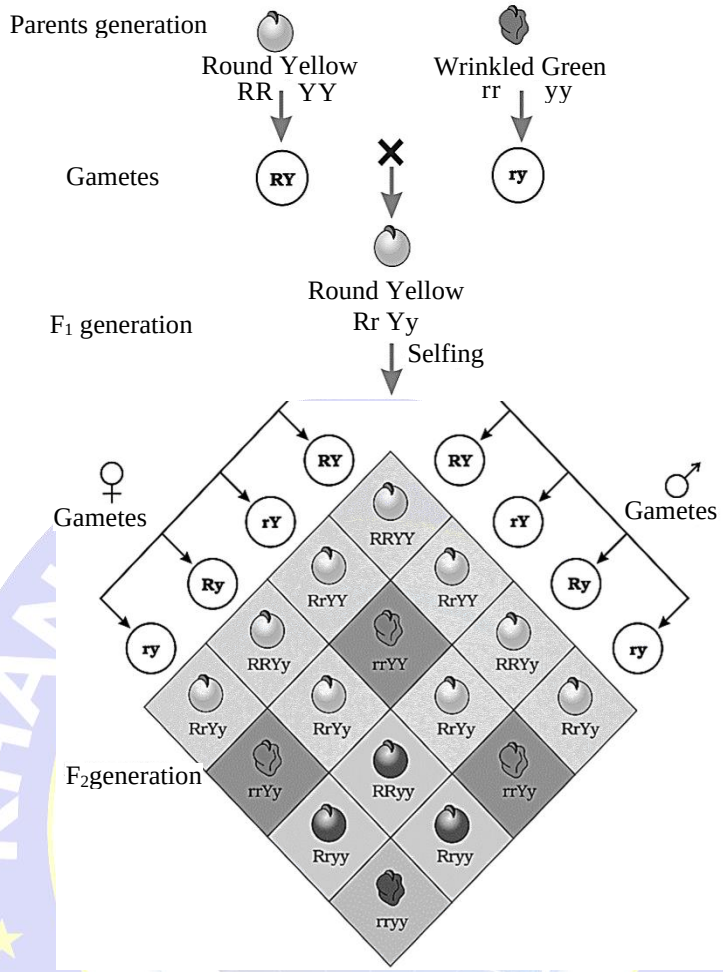
DETECTIVE MIND

Important Formulae

Type of gametes = 2^n
Type of phenotypic category = 2^n
Type of genotype = 3^n
No. of zygote produced by selfing of a genotype = 4^n
Note: n = No. of heterozygous pair in a genotype

DIHYBRID CROSS:

- A cross, in which study of inheritance of two pairs of contrasting traits is done, is called dihybrid cross.
- Mendel wanted to observe the effect of one pair of character on other pair.
- Mendel selected following traits for dihybrid cross -
  [1] Colour of cotyledons → Yellow (Y) & Green (y)
  [2] Seed Shape → Round (R) and Wrinkled (r)
- Yellow and round characters are dominant and green and wrinkled are recessive characters.
- Mendel crossed, yellow and round seeded plants with green and wrinkled seeded plants.
- All the plants in F_1– generation had yellow and round seeds. When F_1 plants were self pollinated to produce four kinds of plants in F_2 generation in the ratio of 9 : 3 : 3 : 1.
- This ratio is known as dihybrid ratio.



Phenotypic ratio: (9:3:3:1)

- Round Yellow: Round Green: Wrinkled Yellow: Wrinkled Green
  9 3 3 1
- Types of phenotype = 4

Genotypic ratio : (1:2:2:4:1:2:1:2:1)

- RRYY RrYY RRYy RrYy rrYY rrYy RRyy Rryy rryy
  1 2 2 4 1 2 1 2 1
- Types of genotype = 9

CONCLUSION (LAW OF INDEPENDENT ASSORTMENT):

→ This law states that 'when two pairs of traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters'.

→ The Punnett square can be effectively used to understand the independent segregation of the two pairs of genes during meiosis and the production of eggs and pollen in the F_1 **RrYy** plant. Consider the segregation of one pair of genes **R** and **r**. Fifty percent of the gametes have the gene **R** and the other 50 per cent have **r**. Now besides each gamete having either **R** or **r**, it should also have the allele **Y** or **y**.

→ The important thing to remember here is that segregation of 50 per cent **R** and 50 per cent *r* is *independent* from the segregation of 50 per cent **Y** and 50 per cent **y**. Therefore, 50 per cent of the **r** bearing gamete has **Y** and the other 50 per cent has **y**.

→ Similarly, 50 per cent of the **R** bearing gamete has **Y** and the other 50 per cent has **y**. Thus there are four genotypes of gametes (four types of pollen and four types of eggs).

→ The four types are **RY**, **Ry**, ***rY*** and **ry** each with a frequency of 25 per cent or 1/4th of the total gametes produced. When you write down the four types of eggs and pollen on the two sides of a Punnett square it is very easy to derive the composition of the zygotes that give rise to the F_2 plants.

→ **Exception: Linkage**

BACK CROSS:

A back cross is a cross in which F_1 individuals are crossed with any of their parents.

(1) Out Cross: When F_1 individual is crossed with dominant parent then it is termed **out cross**.
The generations obtained from this cross, all possess dominant character. So the analysis is not possible in F_1 generation.

(2) Test Cross: When F_1 progeny is crossed with recessive parent then it is called test cross.
The total generations obtained from this cross, 50% having dominant character and 50% having recessive character. [Monohybrid test cross]. Thus, this cross helps to find out the genotype of dominant individual.

[a] Monohybrid Test Cross: The progeny obtained from the monohybrid test cross are in equal proportion, means 50% is dominant phenotypes and 50% is recessive phenotypes. It can be represented in symbolic forms as follows.

F_1 progeny(hybrid) Recessive parent
T t × t t

♀ \ ♂	t
T	Tt
t	tt

Monohybrid test cross ratio = 1 : 1

[b] Dihybrid Test Cross: The progeny is obtained from dihybrid test cross are four types and each of them is 25%.

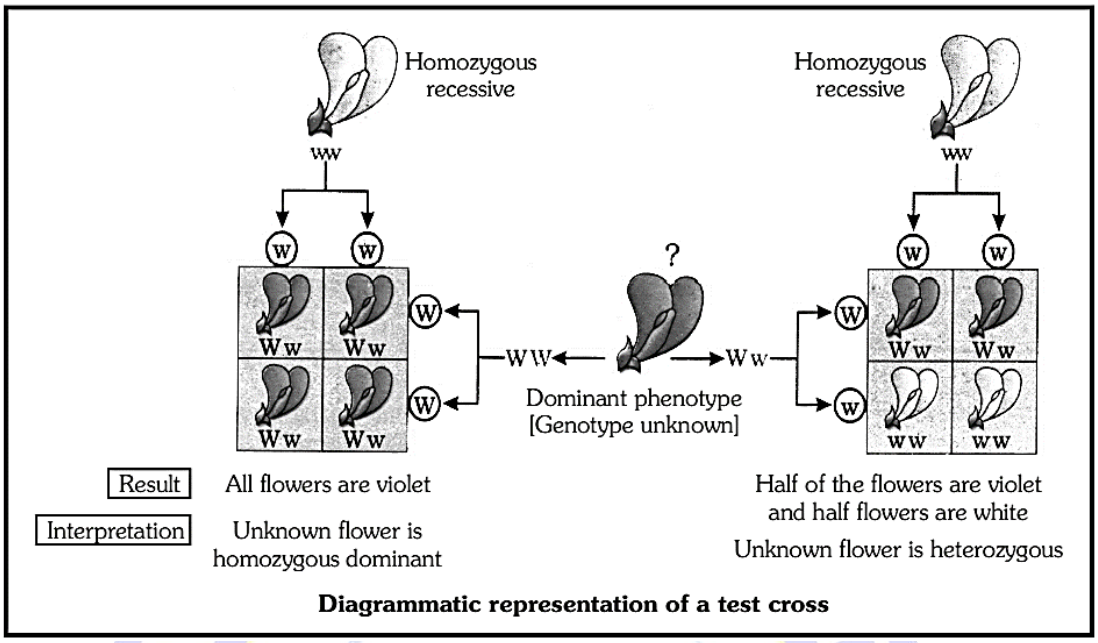
F_1 - dihybrid Recessive parent
T t R r × t t r r

♀ \ ♂	TR	Tr	tR	tr
tr	TtRr	Ttrr	ttRr	ttrr

➢ The ratio of Dihybrid test cross = 1:1:1:1

Conclusion:- In test cross phenotypic and genotypic ratio are same.

Test cross helps to find out the genotype of dominant individual.



Diagrammatic representation of a test cross

POST – MENDELISM/Extensions of basic principles of Mendel's law:

GENE INTERACTION:

Gene interaction is of two types:

(i) Allelic interaction/Intragenic interaction

(ii) Non allelic interaction/Intergenic interaction

(i) Allelic interaction/Intragenic interaction:

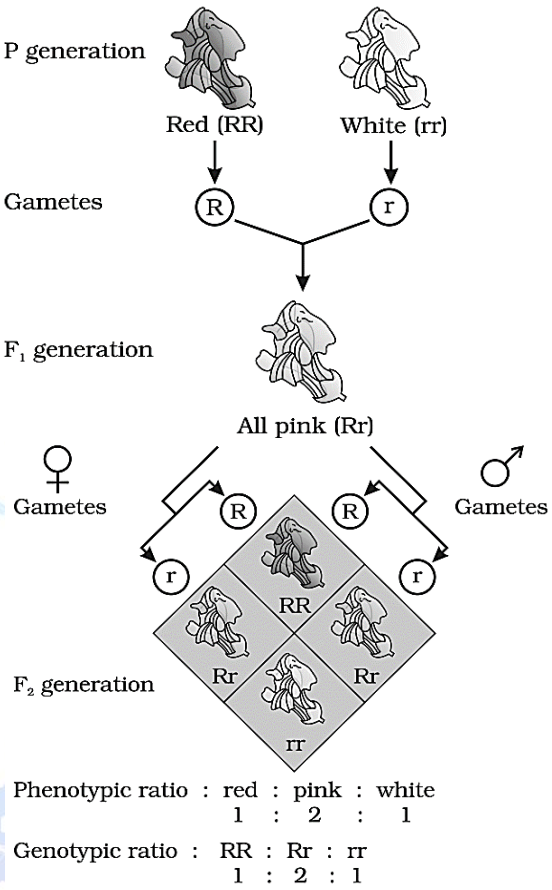
- Majority of gene interaction occurs at product level so only phenotypic ratio will change and genotypic ratio will remain same.
- Allelic interaction takes place between allele of same gene which are present at same locus. Example of allelic interaction are as follows:

[1] Incomplete dominance :

- According to Mendel's law of dominance, dominant character must be present in F_1 generation. But in some organisms, F_1 generation is different from both the parents.
- Both factors such as dominant and recessive are present in incomplete dominance but dominant factors is unable to express its character completely, resulting is intermediate type of generation is formed which is different from both the parents. Some examples are:

(a) Flower colour in *Mirabilis jalapa*:

- Incomplete dominance was first discovered by **Correns** in *Mirabilis jalapa*. This plant is called as **'4 O' clock plant** 'or' **Gul-e-Bans'**. Three different types of plants are found in *Mirabilis* on the basis of flower colour, such as red, white and pink.
- When plant with red flowers is crossed with white flower, plant with pink flower is obtained in F_1 generation.
- The reason of this is that the genes of red colour is incompletely dominant over the genes of white colour and thus new phenotype is expressed.



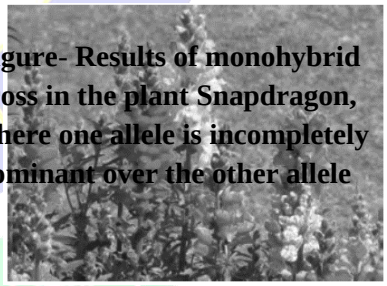


Figure- Results of monohybrid cross in the plant Snapdragon, where one allele is incompletely dominant over the other allele

- When, F_1 generation of pink flower is self pollinated then the phenotypic ratio of F_2 generation is red, pink, white is 1:2:1 ratio in place of normal monohybrid cross ratio 3:1.
- The ratio of phenotype and genotype of F_2 generation in incomplete dominance is always same.

(b) Flower colour in *Antirrhinum majus* :

Incomplete dominance is also seen in flower colour of this plant. This plant is also known as '**Snapdragon** ' or '**Dog flower**'. Incomplete dominance is found in this plant which is same as ***Mirabilis.***

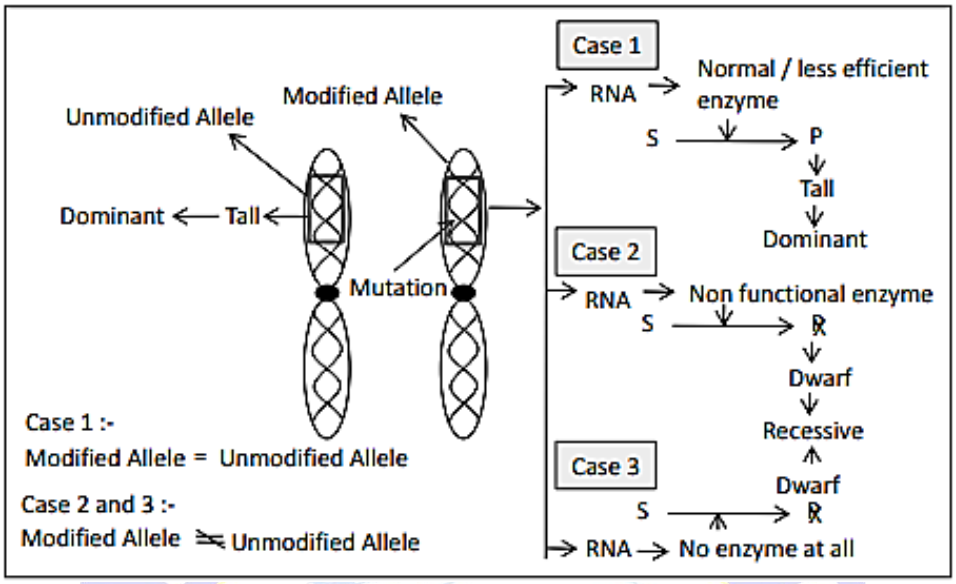
(c) Feather colour in Andalusian Fowls:

When a black colour fowl is crossed with a white colour fowl, the colour of F_1 generation is blue.

(d) Size of starch grain in pea plant :

- When a large size is crossed with small size, the size of starch in F_1 generation is intermediate.

Explanation of the Concept of dominance:



SPOT LIGHT

Size of starch grain in *Pisum sativum*:

- Occasionally, a single gene product may produce more than one effect. For example, starch synthesis in pea seeds is controlled by one gene. It has two alleles **(B and b)**. Starch is synthesised effectively by **BB** homozygotes and therefore, large starch grains are produced. In contrast, bb homozygotes have lesser efficiency in starch synthesis and produce smaller starch grains. After maturation of the seeds, **BB** seeds are round and the **bb** seeds are wrinkled. Heterozygotes produce round seeds, and so **B** seems to be the dominant allele. But, the starch grains produced are of intermediate size in **Bb** seeds. So if starch grain size is considered as the phenotype, then from this angle, the alleles show **incomplete dominance**.

  Therefore, dominance is not an autonomous feature of a gene or the product that it has information for. It depends as much on the gene product and the production of a particular phenotype from this product as it does on the particular phenotype that we choose to examine, in case more than one phenotype is influenced by the same gene.

[2] Co-dominance:

- In this phenomenon, both the genes are simultaneously expressed for a particular character in F_1 hybrid progeny. There is no blending of characters, whereas both the characters are expressed equally.
- **Examples :-**
  - Co-dominance is seen in animals for coat colour.
  - When a black parent is crossed with white parent, a roan colour F_1 progeny is produced. Which show similarity with both parents.
  - When we obtain F_2 generation from the F_1 generation, the ratio of black; black-white (Roan); white animals is 1 : 2 : 1

Note : F_2 generation is obtained in animals by sib-mating cross.

BLACK × WHITE

R_1R_1 ↓ R_2R_2

F_1 generation R_1R_2 (Roan)

Sib-mating cross

	R_1	R_2
R_1	R_1R_1	R_1R_2
R_2	R_1R_2	R_2R_2

R_1R_1 = Black -1 R_1R_2 = Roan - 2 R_2R_2 = White - 1

- It is obvious by above analysis that the ratio of phenotype as well as genotype is 1:2:1 in co-dominance.

Other Examples of Co-dominance:

(i) AB blood group inheritance (I^AI^B)

(ii) Carrier of Sickle cell anaemia (Hb^A Hb^S)

DETECTIVE MIND

In incomplete dominance, characters are blended phenotypically, while in co-dominance, both the genes of a pair exhibit both the characters side by side and effect of both the character is independent from each other.

[3] Multiple Allelism /Multiple Alleles:

- More than 2 alternative forms of a same gene are called as multiple allele. Multiple allele is formed due to mutation.
- Multiple alleles are located on same locus of homologous chromosome.
- A diploid individual contains two alleles and gamete contains one allele for a character.
- If n is the number of allele of a gene then number of different possible genotype = $\frac{n(n+1)}{2}$.

Example of multiple allele :

a. ABO blood group :

- ABO blood groups are controlled by the gene *I*.
- The plasma membrane of the RBC has sugar polymers that protrude from its surface and the kind of sugar is controlled by the gene.
- The gene has three alleles – I^A, I^B, and I^O or i
  I^A = dominant (produce sugar)
  I^B = dominant (produce sugar)
  I^O = recessive (Does not produce any sugar)
- Possible phenotypes - A, B, AB, O

Allele from parent 1	Allele from parent 2	Genotype of offspring	Blood types of offspring
I^A	I^A	I^A I^A	A
I^A	I^B	I^A I^B	AB
I^A	i	I^Ai	A
I^B	I^A	I^A I^B	AB
I^B	I^B	I^B I^B	B
I^B	*i*	I^Bi	B
i	*i*	*i i*	O

Table Showing the Genetic Basis of Blood Groups in Human Population

- When I^A and I^B are present together, they both express their own types of sugars. This represents **Co-dominance.**

b. Coat colour in rabbits.

c. Eye colour in Drosophila → Eye colour in **Drosophila** is controlled by 15 alleles

[4] Pleiotropic gene: Gene which controls more than one character is called pleiotropic gene. This gene shows multiple phenotypic effect.

For example: (1) In Pea plant: Single gene influences
- Seed coat colour
- Red spot in the axil of leaf
- Flower colour

(2) In Pea plant: Single gene influences
- Size of starch grain
- Seed shape

(3) Examples of pleiotropic gene in human - Most of genetical disorders, like sickle cell anaemia, phenyl-ketonuria.

➢ **Phenylketonuria**

- Phenylketonuria is caused by mutation in the gene that codes for the enzyme phenyl alanine hydroxylase (single gene mutation.)
- This manifests phenotypic expression characterised by mental retardation, reduction in skin and hair pigmentation.

(ii) Non allelic interaction/Intergenic interaction

➢ When interaction takes place between non alleles is called non allelic gene interaction. It changes or modifies other non allelic gene.

1. Complementary Gene : Two pair of non allelic genes are essential in dominant form to produce a particular character. Such genes that act together to produce an effect that neither can produce, its effect separately are called complementary genes. Both types of genes must be present in dominant form.

Example : Colour of flowers in *Lathyrus odoratus* (Sweet pea) :-

2. Epistasis:

➢ When, a gene prevents the expression of another non-allelic gene, then it is known as epistatic gene and this phenomenon is known as Epistasis. Gene which inhibits the expression of another non alleleic gene is called epistatic gene and expression of which gene is suppressed by epistatic gene is called hypostatic gene.

Epistasis is of two types: (A) Dominant epistasis (B) Recessive epistasis.

(A) Dominant Epistasis: When the allele of one gene masks the expression of all alleles of another gene. e.g. Fruit colour in Summer squash (*Cucurbita pepo*)

(B) Recessive Epistasis : When the recessive allele of one gene hides the expression of all gene of another gene.

Example :- Coat colour in Mice.

POLYGENIC INHERITANCE:

➢ Inheritance of characters in which one character is controlled by many (3 or more) genes and the intensity of character depends upon the number of dominant allele. Polygenic inheritance also takes into account the influence of environment.

➢ Examples of polygenic inheritance are colour of the skin in human, height in human.

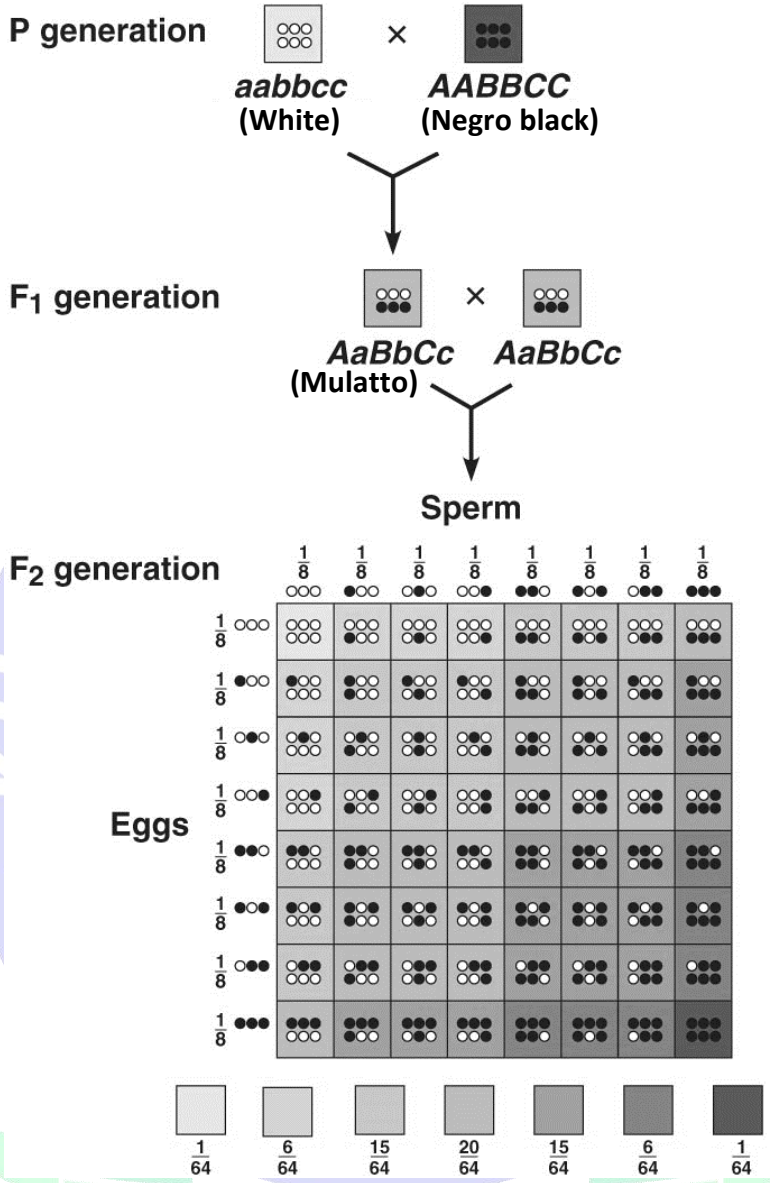
➢ No. of phenotypes = 2n + 1, n = number of genes

Example.

Colour of the skin in Human.

➢ The inheritance of colour of skin in human was studied by **Devenport**. Skin colour in human is regulated by three pairs of genes.

- When a Negro Black **(AABBCC)** phenotype is crossed with white **(aabbcc)** phenotype, intermediate phenotype is produced in F_1 generation.



Polygenic inheritance in human skin pigmentation

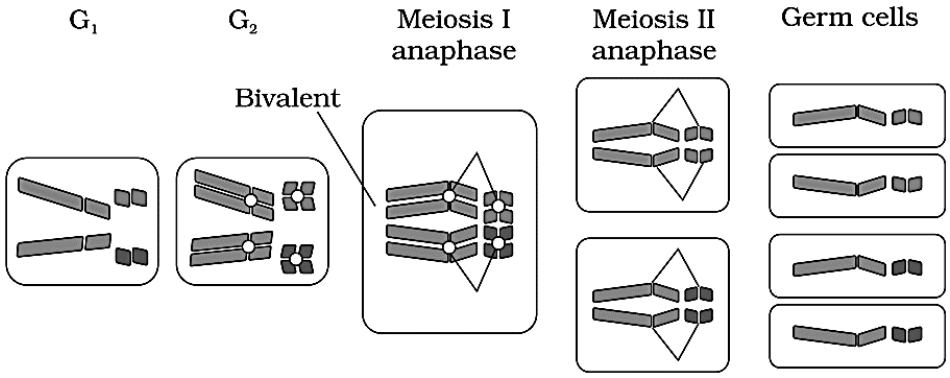
Phenotypic ratio will be:

Negro Black	:	Very Dark Brown	:	Dark Brown	:	Mulatto	:	Light Brown	:	Very Light Brown	:	White
1	:	6	:	15	:	20	:	15	:	6	:	1

CHROMOSOMAL THEORY OF INHERITANCE:

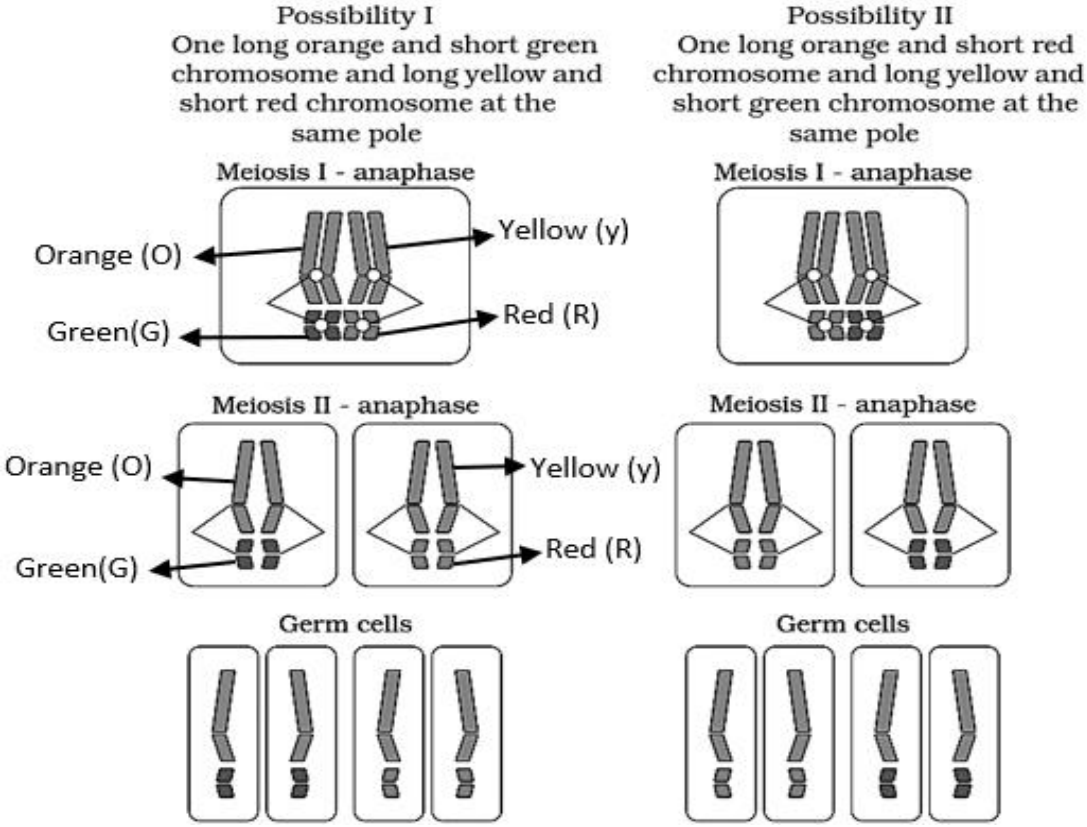
- This theory was proposed by **Walter Sutton** and **Theodor Boveri** (1902).
- Due to the advancement in microscopy, it was discovered that there are some structures in the nucleus that appeared to double and divide just before each cell division. These structures were called chromosomes (*colored bodies*, as they were visualised by staining). By 1902, the chromosome movement during meiosis had been worked out.
- Walter Sutton and Theodore Boveri noted that the behaviour of chromosomes was **parallel** to the behaviour of genes and they used chromosome movement to explain Mendel's laws.

- Chromosomes as well as genes occur in pairs.
- The two alleles of a gene pair are located on homologous sites on homologous chromosomes.



Meiosis and germ cell formation in a cell with four chromosomes

During anaphase of meiosis I, the two chromosome pairs can align at the metaphase plate independently of each other. To understand this, following diagram can be observed.



A comparison between Mendelian Factors (Genes) and Chromosomes

Mendelian Factors (Genes)	Chromosomes
Occur in pairs	Occur in pairs
Segregate at the time of gamete formation such that only one of each pair is transmitted to a gamete	Segregate at gamete formation and only one of each pair is transmitted to a gamete
Independent pairs segregate independent of each other	One pair segregate independently of another pair
Also shows linkage	Never shows linkage

- Sutton and Boveri argued that the pairing and separation of a pair of chromosomes would lead to the segregation of a pair of factors they carried. Sutton united the knowledge of chromosomal segregation with Mendelian principles and called it the **chromosomal theory of inheritance**.
- Following this ideas, experimental verification of the chromosomal theory of inheritance was given by **Thomas Hunt Morgan** and his colleagues, led to discovering the basis for the variation that sexual reproduction produce. Morgan worked with the tiny fruit files, ***Drosophila melanogaster***, which were found very suitable for such studies.

Reasons To Work On *Drosophila melanogaster*

- They could be grown on simple synthetic medium in the laboratory.
- They complete their life cycle in about two weeks, and a single mating could produce a large number of progeny flies.
- There was a clear differentiation of the sexes – the male and female flies are easily distinguishable.
- It has many types of hereditary variations that can be seen with low power microscopes.

LINKAGE AND RECOMBINATION:

- **The physical association of genes on a chromosome is called linkage.**
- Collective inheritance of character is called linkage. Linkage first time seen by **Bateson** and **Punnett** in *Lathyrus odoratus* and gave **coupling and repulsion phenomenon**. The observed ratio in coupling and repulsion Was 7 : 1 : 1 : 7 and 1 : 7 : 7 : 1 respectively
- But they did not explain the phenomenon of linkage.
- Linkage was first described by **Morgan** in *Drosophila*, **Morgan and Castle** proposed the chromosomal theory of linkage.
- Morgan and his group knew that the genes were located on the same chromosome and saw quickly that when the two genes in a dihybrid cross were situated on the same chromosome, the proportion of parental gene combinations were much higher than the non-parental type.

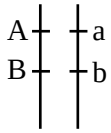
T.H. MORGAN
Father of experimental genetics
Worked on drosophila

- Morgan attributed this due to the physical association or linkage of the two genes and coined the term **linkage** to describe the physical association of genes on a chromosome and the term **recombination** to describe the generation of non-parental gene combinations.
- Morgan and his group also found that even when genes were grouped on the same chromosome, some genes were very tightly linked (showed very low recombination) while others were loosely linked (showed higher recombination).
- Linkage and independent assortment can be represented in dihybrid plant, as –

In case of linkage in dihybrid (AaBb)

It produces two types of gamete

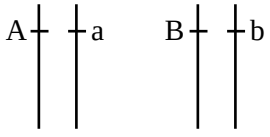
AB : ab



In case of independent assortment

It produces four types of gamete

AB : ab : aB : Ab



Theory of linkage:

1. Linked genes are linearly located on same chromosome. They get separated if exchange (crossing over), takes place between them.

2. Strength of linkage inversely related to distance between the genes. It means, if the distance between two genes is increased then strength of linkage is reduced and it proves that greater is the distance between genes, the greater is the probability of their crossing over.
Crossing over obviously disturbs or degenerates linkage. Linked genes can be separated by crossing over.

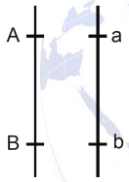
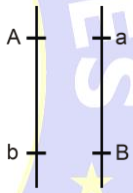
3. **Linkage group :-** All the genes which are located on one pair of homologous chromosome form one linkage group. Genes which are located on homologous chromosomes inherit together so we consider them as linkage group.

Factors affecting crossing over (C.O) and linkage:-

(1) Distance between Two genes = C.O↑ / linkage ↓
(2) Temperature ↑ = C.O.↑/ linkage ↓
(3) Age ↑ = C.O.↓ / linkage ↑
(4) Sex - Male = C.O.↓ (Crossing over totally absent in male *Drosophila*.)
(5) X – Rays = C.O.↑/ linkage ↓

DETECTIVE MIND

- Arrangement of linked genes on chromosomes-

Cis-arrangement	Trans -arrangement
Two dominant genes are located on one chromosome and both recessive genes on another chromosome 	One dominant and one recessive gene on one chromosome while the same on the other. 

- **Cis and Trans arrangement of genes can be interchange due to Crossing Over**
- **Unit conversion –**
  0.1 M (Morgan) = 10 cM (Centimorgan)

Types of Linkage :- There are two types of linkage :

1 COMPLETE LINKAGE :

- Linkage in which genes always show parental combination. It never forms new combination. Crossing over is absent in it.
- Such genes are located very close on the chromosomes. Such type of linkage is very rare in nature. e.g. male *Drosophila*, female silk moth.

2. INCOMPLETE LINKAGE:

- When new combinations also appear along with parental combination in offsprings, this type of linkage is called incomplete linkage, the new combinations form due to crossing over.

SEX LINKAGE:

- When the genes are present on sex-chromosome is termed as sex linked gene and their linkage is known as sex-linkage.
- Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked. The crosses were similar to the dihybrid crosses carried out by Mendel in peas. For example Morgan hybridised yellow-bodied, white-eyed females to brown-bodied, red-eyed males and inter-crossed their F_1 progeny.

- He observed that the two genes did not segregate independently of each other and the F_2 ratio deviated very significantly from the 9:3:3:1 ratio (expected when the two genes are independent).
- He found that the genes white and yellow were very tightly linked and showed only **1.3 percent** recombination while white and miniature wing showed **37.2 percent** recombination.

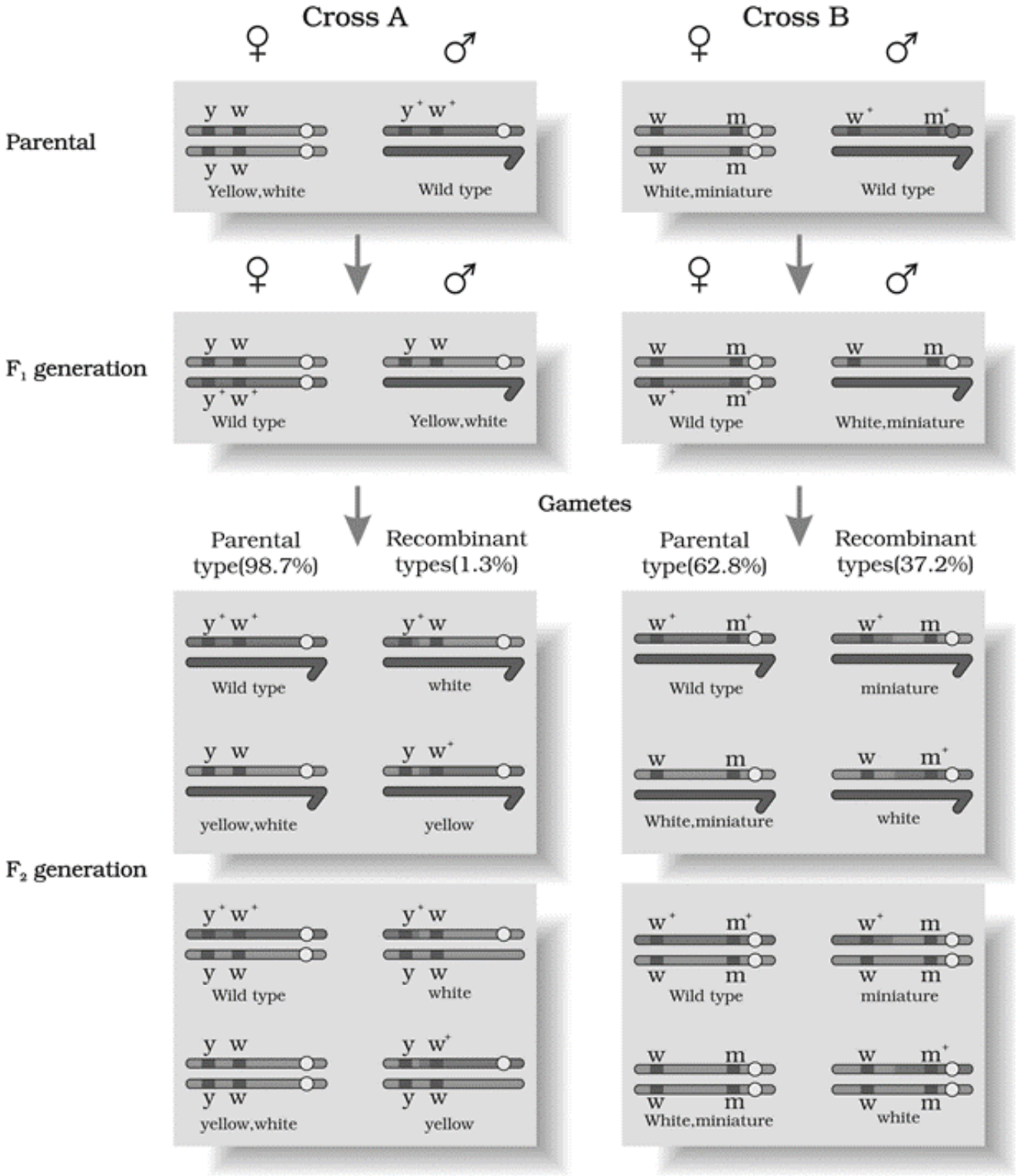


Figure:– Linkage : Results of two dihybrid crosses conducted by Morgan. Cross A shows crossing between gene y and w; Cross B shown crossing between genes w and m. Here dominant wild type alleles are represented with (+) sign in superscript

Note : The strength of linkage between y and w is higher than w and m

SEX LINKAGE IN HUMAN BEING :-

X-LINKAGE

- Genes present on non homologous region of X chromosomes.
- Biparental

TWO TYPES

X- linked Recessive

(a) Hemophilia
(b) Colourblindness

X- linked Dominant

(a) Pseudorickets (Vitamin D resistant rickets)
(b) Defective enamels of teeth

1. X-linkage.

Genes of some characters are found on x- chromosome. The inheritance of x-linked character occurs through the males and females.

Example of X-linkage:

[i] Haemophilia :

Haemophilia is also called **"bleeder's disease"** and first discovered by **John Otto** (1803). The gene of haemophilia is recessive and x-linked gene.

Haemophilic female is very rare as mother of such female has to beat least carrier and father should be haemophilic (unviable in the later stage of life)

On the basis of x-linked, following types of genotype are found.

X^h X = Carrier female

X^hX^h = Affected female

X^hY = Affected male.

(1) Haemophilia : A (Royal disease) - It is due to lack of blood clotting factor -VIII (Antihaemophilic globulin AHG). It shows absolute lethality in female. (Most common type)

(2) Haemophilia : B (Christmas disease) - It is due to lack of blood clotting factor - IX (Plasma thromboplastin component)

(3) Haemophilia : C (Autosomal disorder) - It is due to lack of blood clotting factor - XI (Plasma Thromboplastin antecedent)

[ii] Colour Blindness :-

- The inheritance of colour-blindness is like haemophilia, but it is not a lethal disease so it is found in male and female.(discovered by **Horner**)
- This disease is more common in males due to hemizygous condition.

It occurs in about 8% of males and about 0.4% of female**s.** This is because the genes that lead to red-green colour blindness are on the X chromosome.

- Males have only one X chromosome and females have two. The son of a woman who carries the gene has a 50 per cent chance of being colour blind. The mother is not herself colour blind because the gene is recessive. That means that its effect is suppressed by her matching dominant normal gene. A daughter will not normally be colour blind, unless her mother is a carrier and her father is colour blind.

Question : A colourblind man marries with a women where there is no historical record of colourblindness. Find out the possibility of appearance of colourblindness in the off-springs of this couple.

(1) 25% (2) 100% (3) 50% (4) 0%

DETECTIVE MIND

- **There are three types of colour blindness are-**
  - **[a] Protanopia** : It is for red colour.
  - **[b] Deuteranopia** : It is for green colour
  - **[c] Tritanopia** : It is for blue colour blindness.
- Colour blindness is checked by ishihara cards.
- To check colour blindness ishihara cards are placed at 40 inches distance for 15 seconds

Type of Inheritance of sex linked character:

(1) Criss cross inheritance (Morgan): In criss-cross inheritance, male or female parent transfer a X-linked character to grandson or grand daughter through the offspring of opposite sex.

(a) Diagenic (Diagynic): - Inheritance in which the characters are inherited from father to the daughter and from daughter to grandson.
Father → daughter → grand son.

(b) Diandric: Inheritance in which the characters are inherited from mother to the son and from son to grand daughter. Mother → Son → Grand-daughter.

(2) Non criss-cross inheritance: - In this inheritance male or female parent transfer sex linked character to grand son or grand daughter through the offspring of same sex.

(a) Hologenic (Hologynic): - Mother → Daughter → Grand-daughter (female to female)

(b) Holandric : Father → Son → Grand-son (male to male)

Sex-Limited Character:

- These characters are present in one sex and absent in another sex. But their genes are present in both the sexes and their expression is dependent on sex hormone.
- **Example :-** Secondary sexual characters.

Sex Influenced Characters :

- Genes of these characters are also present on autosomes but they are influenced differently in male and female. In heterozygous condition, their effect is different in both the sexes.
- **Example :-** Baldness :- Gene of baldness is dominant (B).

2. Y- linkage:

- The genes of some characters are located on Y- chromosome. The inheritance of such type of character occurs only in males.
- Genes present on non-homologous region of Y chromosomes.
- Such type of character is called Holandric character.
- These characters are found only in males. Gene which is located on differential region of Y - chromosome is known as Holandric gene.

e.g. (1) Gene which forms TDF /SRY-gene
(2) Hypertrichosis (excessive hair on ear pinna.)

DETECTIVE MIND

Sex-determination on the basis of fertilization

Three types :

1. **Progamic :** Sex is determined before fertilization. eg. : drone in honey bee
2. **Syngamic :** Sex is determined during fertilization. eg. : most of plants & animals
3. **Epigamic :** Sex is determined after fertilization. eg. : Female in honey bee, Crocodile , turtle

Genetic map/Linkage map/chromosome map:

- **Alfred Sturtevant** 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. Today genetic maps are extensively used as a starting point in the sequencing of whole genomes as was done in the case of the Human Genome Sequencing Project.
- In genetic map different genes are linearly arranged according to % of recombination between them. With the help of genetic map we can find out the relative position of a particular gene on chromosome.
- Distance can be identified by the incomplete linkage. Its unit is centi Morgan.

$$\text{Strength of linkage} \propto \frac{1}{\text{Distance b/ w linked gene}} \propto \frac{1}{\text{Crossing Over}}$$

- Absolute/accurate mapping done by sequencing approach is known as "**physical map**".

$$\text{Distance between two gene} = \frac{\text{No. of offsprings (Recombinant)}}{\text{Total No. of offspring}} \text{ cm.}$$

- Maximum Recombination frequency could be 50%

Chromosomal Map provides information about:

1. **Sequence of different linked genes on a chromosome**
2. **Distance between the two linked genes**

SEX DETERMINATION:

- Establishment of sex through differential development in an individual at an early stage of life, is called sex determination.
- The cytological observations made in a number of insects led to the development of the concept of genetic/chromosomal basis of sex-determination.

Chromosomes are of two types:

(a) Autosomes or somatic chromosomes:
These regulate somatic characters.

(b) Allosomes or Heterosomes or Sex chromosomes:

- **Henking** (1891) could trace a specific nuclear structure all through spermatogenesis in a few insects, and it was also observed by him that 50 per cent of the sperm received this structure after spermatogenesis, whereas the other 50 per cent sperm did not receive it.
- **Henking** gave a name to this structure as the **X body** but he could not explain its significance. Further investigations by other scientists led to the conclusion that the 'X body' of **Henking** was in fact a chromosome and that is why it was given the name **X-chromosome**.

Types of Sex Determination:

Chromosomal theory of sex determination (Allosomic determination of sex): Wilson and **Stevens** proposed chromosomal theory for sex determination.

(A) XX female and XY male type or Lygaeus type: – This type of sex determination was first observed by ***Wilson*** and ***Stevens*** in Lygaeus insect. In this type of sex determination female is Homogametic i.e produces only one type of gamete

2A + XX (Female) ⟶ gametes → A + X, A + X

Male is heterogametic (male produces two types of gamete)

2A + XY(Male) ⟶ gametes → A + X, A + Y

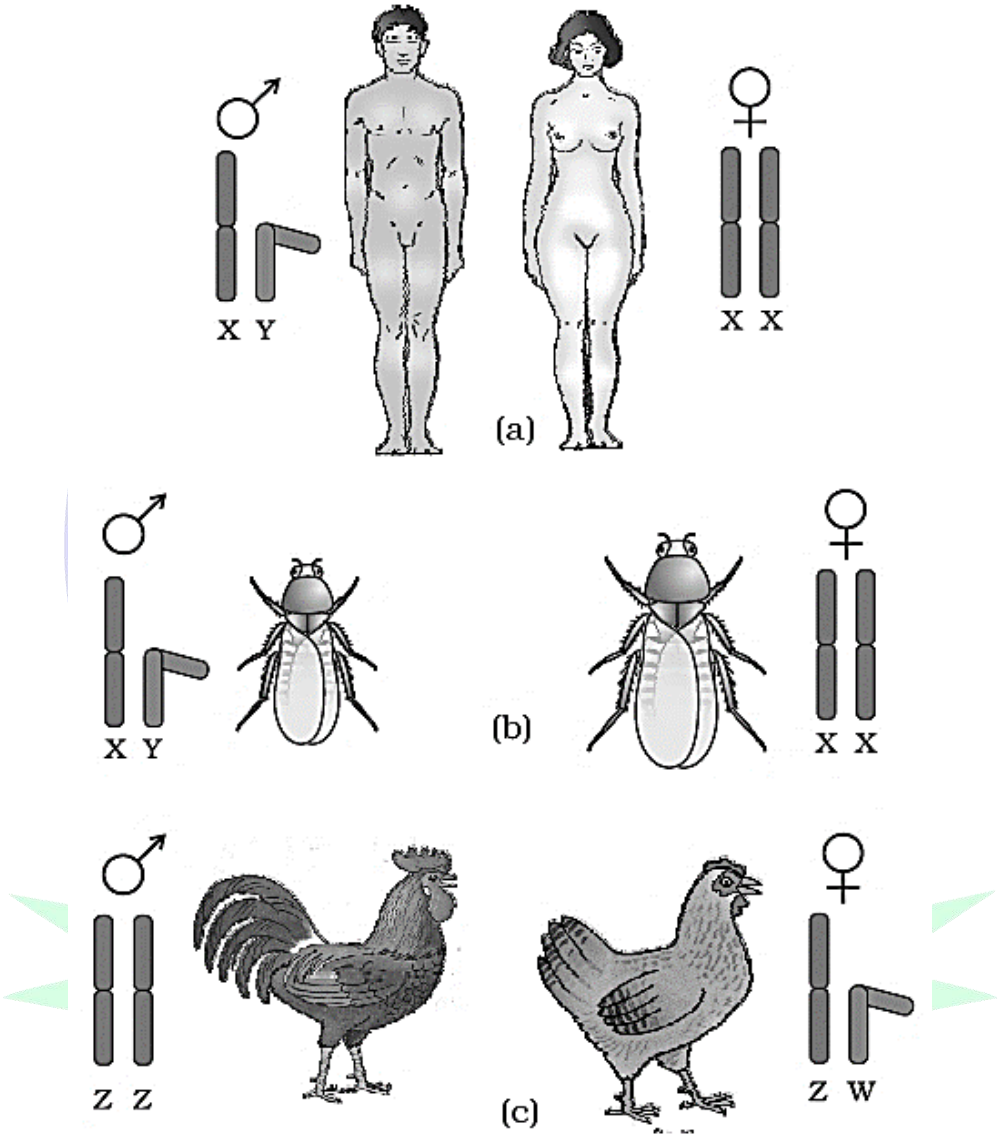


Figure : Determination of sex by chromosomal differences: (a,b) Both in humans and in Drosophila, the female has a pair of XX chromosomes (homogametic) and the male XY (heterogametic) composition; (c) In many birds, female has a pair of dissimilar chromosomes ZW and male two similar ZZ chromosomes.

(B) ZW female and ZZ male : In this type of sex determination, female is heterogametic i.e produces two types of gamete and male individual is homogametic i.e produces one type of gamete. It is found in some insects like **butter flies**, **moths** and **vertebrates** like **birds, fishes** and **reptiles.**

(C) XX female and XO male: or **"Protenor type"**: In this type of sex, determination deficiency of one chromosome in male is found. In this type, female is homogametic and male is heterogametic. **e.g. Grass hopper, Bugs, Cockroach, ascaris**.

Female (2A + XX) → A + X, A + X

(Homogametic)

Male (2A + XO) → A + O, A + X

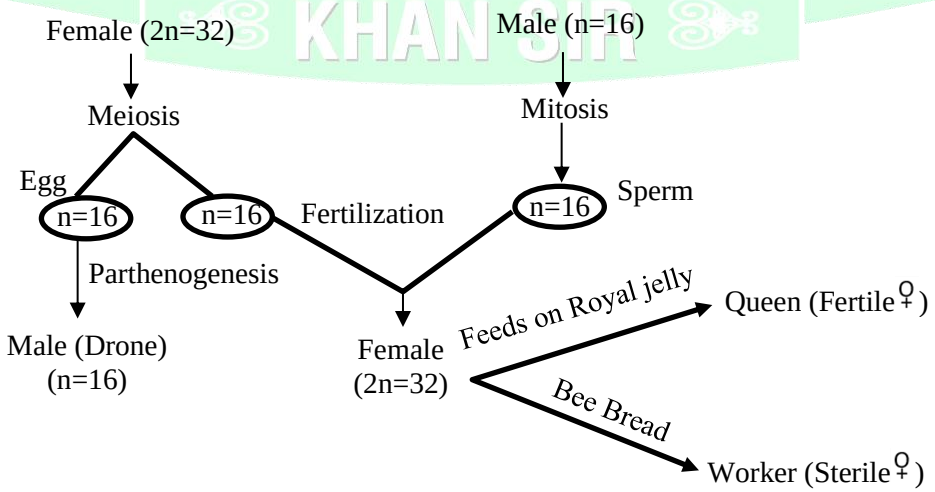
(Heterogametic)

SEX DETERMINATION IN HUMANS

- It has already been mentioned that the sex determining mechanism in case of humans is XY type. Out of 23 pairs of chromosomes present, 22 pairs are exactly same in both males and females; these are the autosomes.
- A pair of X-chromosomes are present in the female, whereas the presence of an X and Y chromosome are determinant of the male characteristic these are called allosomes.
- During spermatogenesis among males, two types of gametes are produced. 50 per cent of the total sperm produced carry the X-chromosome and the rest 50 per cent has Y-chromosome besides the autosomes.
- Females, however, produce only one type of ovum with an X-chromosome.
- There is an equal probability of fertilisation of the ovum with the sperm carrying either X or Y chromosome.
- In case the ovum fertilises with a sperm carrying X-chromosome, the zygote develops into a female (XX) and the fertilisation of ovum with Y-chromosome carrying sperm results into a male offspring.
- Thus, it is evident that it is the genetic makeup of the sperm that determines the sex of the child. It is also evident that in each pregnancy there is always 50 per cent probability of either a male or a female child.
- It is unfortunate that in our society women are blamed for producing female children and have been ostracised and ill-treated because of this false notion.

(D) Haploid - diploid mechanism (Sex Determination in Honey Bee): In insects of order Hymenoptera which includes **ants, honey bees, wasps** etc. Sex determination takes place by sets of chromosomes.

The sex determination in honey bee is based on the number of sets of chromosomes an individual receives. An offspring formed from the union of a sperm and an egg develop as a female (queen or worker), and an unfertilised egg develops as a male (Drone) by means of parthenogenesis. This means that the males have half the number of chromosomes than that of a female. The females are diploid having 32 chromosomes and males are haploid, i.e., having 16 chromosomes. This called as haplodiploid sex determination system and has special characteristic features such as the males produce sperms by mitosis, they do not have father and thus cannot have sons, but have a grandfather and can have grandsons.



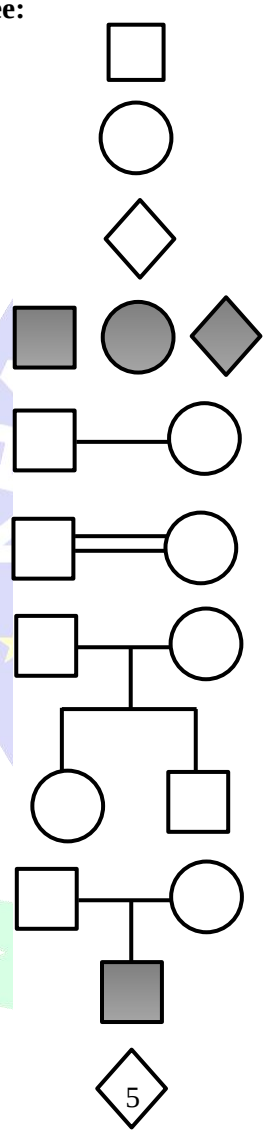
GENETICS DISORDERS:

- The study and analysis of human genetics is performed by many methods like pedigree analysis, statistical analysis and human karyotyping. Of these the important ones, that is, pedigree analysis is being described here.

PEDIGREE ANALYSIS:

- Study of ancestral history of man of transmission of genetic characters from one generation to next, is pedigree analysis. Dwarfism, albinism, colour blindness, haemophilia etc. are genetically transmitted characters. To study and analyse them a pedigree of genetic facts/data and following symbols are used.

Symbol used in Pedigree:



Male

Female

Sex unspecified

Affected individuals

Mating (Marriage)

Mating between relatives (consanguineous mating)

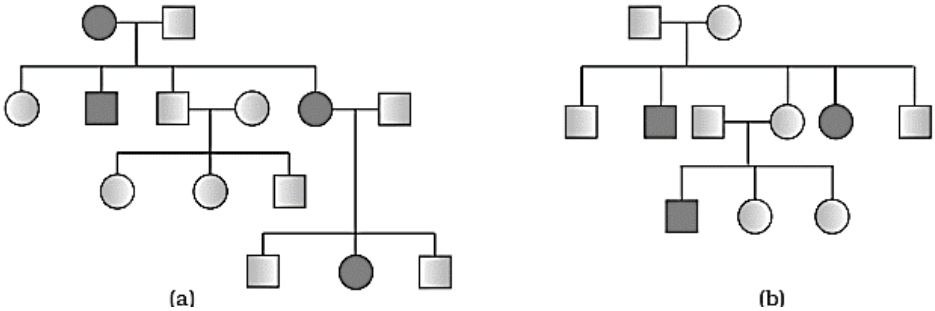
parents above and children below (in order of birth – left to right)

Parents with male child affected with disease

Five unaffected offspring

Figure: Symbols used in the human pedigree analysis

- **Pedigree analysis** provides valuable information regarding genetical make up of human beings. **In the pedigree analysis the inheritance of a particular trait is represented in the family tree over generations.** If any genetic disease is occurring in a family, then pedigree analysis provides guidance to forthcoming parents about their future progenies.
- A representative pedigree is shown in for dominant and recessive traits.



Representative pedigree analysis of (a) Autosomal dominant trait (for example: Myotonic dystrophy) (b) Autosomal recessive trait (for example: Sickle-cell anaemia)

- Each and every feature in any organism is controlled by one or the other gene located on the DNA present in the chromosome. DNA is the carrier of genetic information. It is hence transmitted from one generation to the other without any change or alteration. However, changes or alteration do take place occasionally. Such an alteration or change in the genetic material is referred to as mutation. A number of disorders in human beings have been found to be associated with the inheritance of changed or altered genes or chromosomes.

I. MENDELIAN DISORDERS:

These are mainly determined by mutation in the single gene, therefore also called gene related human disorders. They are transmitted to the offspring as per Mendelian principles. The pattern of inheritance of such disorders can be traced in a family by the pedigree analysis. Some common and prevalent Mendelian disorder are as follows:

S.No.	Disorder	Dominant/Recessive	Autosomal / Sex linked
(1)	Haemophilia	Recessive	X-linked
(2)	Colour blindness	Recessive	X-linked
(3)	Sickle cell anaemia	Recessive	Autosomal
(4)	Phenylketonuria	Recessive	Autosomal
(5)	Cystic fibrosis	Recessive	Autosomal
(6)	Thalassemia	Recessive	Autosomal
(7)	Myotonic dystrophy	Dominant	Autosomal

SOME IMPORTANT MENDELIAN DISORDERS ARE:

Autosomal Recessive Disorders:

1. **Phenylketonuria:** This inborn error of metabolism is also inherited as the autosomal recessive trait. The affected individual lacks a liver enzyme called **phenylalanine hydroxylase** that converts the amino acid phenylalanine into tyrosine. As a result of this phenylalanine is accumulated and converted into phenylpyruvic acid and other derivatives. Accumulation of these in brain results in mental retardation. These are also excreted through urine because of its poor absorption by kidney.

DETECTIVE MIND

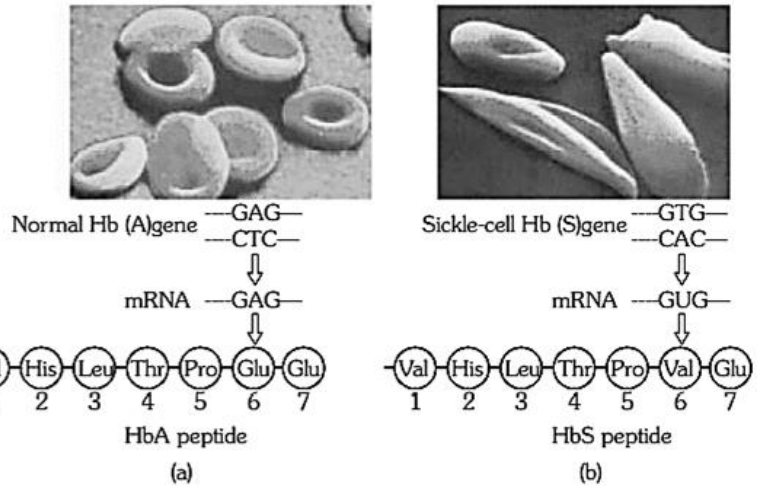
- **Alkaptonuria (Black urine disease):** This disorder occurs due to the deficiency of enzyme homogentisic acid oxidase. Concentration of homogentisic acid increases in blood and tissue like joints, ligament, tendon. cartilage and also excreted in urine. When this urine comes in contact with air, homogentisic acid is oxidised into alkapton (Alkaptonuria) which is black in colour so disease is also called black urine disease.
- **Albinism:** This disorder is due to deficiency of enzyme tyrosinase therefore the body parts like skin, iris of eye etc., become melanin deficient. Melanin provide protection against U. V. rays.
- **Tay-sach's disease:** This disease is first reported by Tay and Sach. This genetic disorder is due to deficiency of enzyme β-N acetyl hexosaminidase, this enzyme is involved in fat metabolism. so, the fat (conjugate lipid) accumulate in brain (ganglioside cell) and spinal cord and damage these cells. This causes mental retardation and paralysis of a normal born child and this child does not survive more than 3-4 years. There is no treatment of Tay-sach's disease.

2. Thalassemia:

- This is also an autosome-linked recessive blood disease transmitted from parents to the offspring when both the partners are unaffected carrier for the gene (or heterozygous).
- The defect could be due to either mutation or deletion which ultimately results in reduced rate of synthesis of one of the globin chains (α and β chains) that make up haemoglobin.
- This causes the formation of abnormal haemoglobin molecules resulting into anaemia which is characteristic of the disease.
- Thalassemia can be classified according to which chain of the haemoglobin molecule is affected.
- In α Thalassemia, production of α globin chain is affected while in β Thalassemia, production of β globin chain is affected.
- α Thalassemia is controlled by two closely linked genes HBA1 and HBA2 on chromosome 16 of each parent and it is observed due to mutation or deletion of one or more of the four genes.
- The more genes affected, the less alpha globin molecules produced.
- While β Thalassemia is controlled by a single gene HBB on chromosome 11 of each parent and occurs due to mutation of one or both the genes.
- Thalassemia differs from sickle-cell anaemia in that the former is a quantitative problem of synthesising too few globin molecules while the latter is a qualitative problem of synthesising an incorrectly functioning globin.

3. Sickle cell anaemia –

- Gene Hb^S_β provide a classical example of pleiotropy.
- It not only causes haemolytic anaemia but also results in increased resistance to one type of malaria that caused is by the parasite *Plasmodium falciparum.* The sickle cell Hb^S_β allele also has pleiotropic effect on the development of many tissues and organs such as bone, lungs, kidney, spleen, and heart.
- It is an autosomal recessive trait.
- The defect is caused by the substitution of Glumatic acid (Glu) by Valine (Val) at the sixth position of the beta globin chain of the haemoglobin molecule
- The substitution of amino acid in the globin protein result due to the single base substitution at the sixth codon of beta globin chain from GAG to GUG
- The mutant haemoglobin molecules undergoes polymerisation under low oxygen tension causing the change in the shape of the RBC from biconcave disc to elongated sickle like structure.



Micrograph of the red blood cells and the amino acid composition of the relevant portion of β-chain of haemoglobin : (a) from a normal individual; (b) From an individual with sickle-cell anaemia

II. CHROMOSOMAL DISORDERS:

- The chromosomal disorders are caused due to absence or excess or abnormal arrangement of one or more chromosomes.

- Failure of segregation of chromatids during cell division cycle results in the gain or loss of a chromosome(s), called **aneuploidy**. For example, Down's syndrome results in the gain of an extra copy of chromosome 21. Similarly. Turner's syndrome results due to loss of an X chromosome in human females.
- Failure of cytokinesis after telophase stage of cell division results in an increase in a whole set of chromosomes in an organism and this phenomenon is known as **polyploidy**. This condition is often seen in plants.
- The total number of chromosomes in a normal human cell is 46 (23 pairs). Out of these 22 pairs are autosomes and one pair of chromosomes are sex chromosomes. Sometimes, though rarely, either an additional copy of a chromosome may be included in an individual or an individual may lack one of anyone pair of chromosomes. These situations are known as trisomy or monosomy of a chromosome, respectively. Such a situation leads to very serious consequences in the individual. Down's syndrome, Turner's syndrome, Klinefelter's syndrome are common examples of chromosomal disorders.

AUTOSOMAL ANEUPLOIDY:

Nullisomic	2n – 2
Monosomic	2n – 1
Trisomic	2n + 1
Tetrasomic	2n + 2

n = Haploid number of chromosomes

2n = Diploid number of chromosomes

- **Down's Syndrome:** The cause of this genetic disorder is the presence of an additional copy of the chromosome number 21 (trisomy of 21). This disorder was first described by Langdon Down (1866). The affected individual is 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.

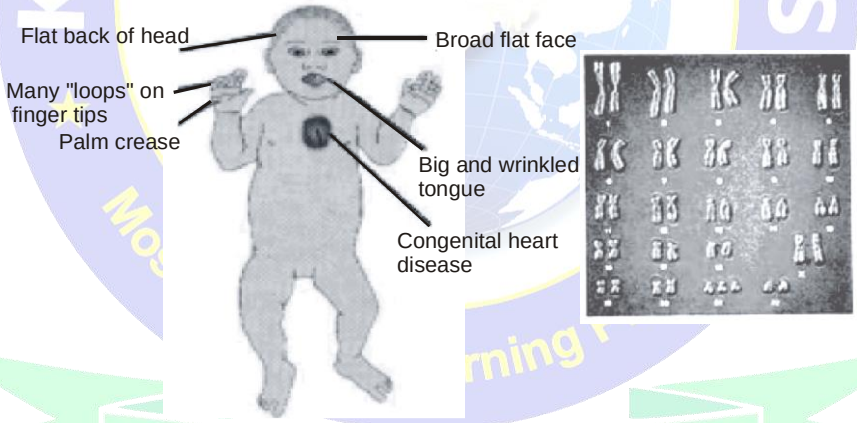
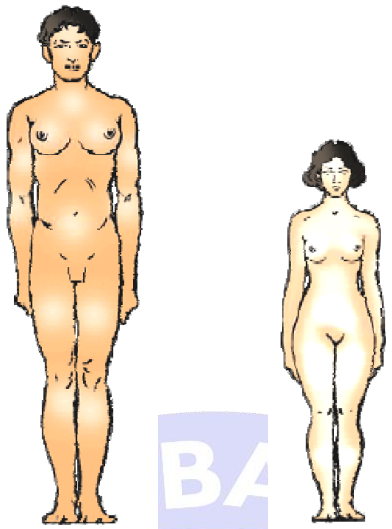


Fig. A representative figure showing an individual inflicted with Down's syndrome and the corresponding chromosomes of the individual

SEX CHROMOSOMAL ANEUPLOIDY:

1. **Klinefelter's Syndrome:** This genetic disorder is also caused due to the presence of an additional copy of X-chromosome resulting into a karyotype of 47, XXY. Such an individual has overall masculine development, however, the feminine development (development of breast, i.e., Gynaecomastia) is also expressed. Such individuals are sterile.
2. **Turner's Syndrome :** Such a disorder is caused due to the absence of one of the X chromosomes, i.e., 45 with X0, Such females are sterile as ovaries are rudimentary besides other features including lack of other secondary sexual characters.



(a) Tall stature with feminised character

(b) Short stature and underdeveloped feminine character

Figure:- Diagrammatic representation of genetic disorders due to sex chromosome composition in humans: (a) Klinefelter Syndrome; (b) Turner's Syndrome

DETECTIVE MIND

- Edward syndrome (18th Trisomy)
- Patau syndrome (13th Trisomy)
- Cat cry syndrome (Cri-du-chat): Partial deletion of short arm of 5th chromosome
- **Super males or Jacob's Syndrome (44 + XYY):** These patients have extra Y-chromosome. So the production of testosterone increased in these patients. These individual have abnormal height, aggressive behaviour, mentally retarded and criminal bent of mind.
- **Super females (44 + XXX):** These females usually have underdeveloped breasts and genital organs. They can often bear children. They have lower-than-average intelligence. Mental retardation is proportional to the Number of X-Chromosomes.