



# Principles of Inheritance and Variation

## INTRODUCTION

Genetics deals with inheritance and variation of characters from parents to offsprings. Inheritance is the process by which characters are passed from parent to progeny. Variation is the degree by which progeny differ from their parents.

Humans knew that the causes of variation was hidden in sexual reproduction.

## MENDEL'S LAWS OF INHERITANCE

Gregor Mendel conducted hybridisation experiments on garden peas for seven years (1856–1863) and proposed the laws of inheritance.

Mendel selected 14-true breeding pea plant varieties as pairs, which were similar except for one character with contrasting traits.

### Contrasting traits studied by Mendel in Pea

S.No.	Characters	Contrasting Traits
1.	Stem height	Tall/Dwarf
2.	Flower colour	Violet/White
3.	Flower position	Axial/Terminal
4.	Pod shape	Inflated/Constricted
5.	Pod colour	Green/Yellow
6.	Seed shape	Round/Wrinkled
7.	Seed colour	Yellow/Green

### INHERITANCE OF ONE GENE

Mendel found that  $F_1$  always resembled either of the parents but in  $F_2$  (produced by selfing  $F_1$ ) both traits appeared;  $3/4^{\text{th}}$  showed the dominant trait and  $1/4^{\text{th}}$  the recessive.

Both traits were identical to their parental type and did not show any blending, i.e. none were of Intermediate type.

Mendel got similar results for all traits.

To determine the genotype of dominant trait at  $F_2$ , Mendel performed test cross.

### BASED ON MONOHYBRID CROSS, MENDEL PROPOSED TWO GENERAL RULES

**LAW OF DOMINANCE** : Explains the expression of only one parental character in  $F_1$  of monohybrid cross and both  $F_2$ . It also explains the phenotypic ratio of 3 : 1 obtained at the  $F_2$ .

**LAW OF SEGREGATION** : The factors or alleles of a pair segregate from each other such that gametes receive only one of the two factors/alleles.

### INCOMPLETE DOMINANCE

$F_1$  did not resemble either of the parents and was in between the two. Seen in Dog flower (Snapdragon or *Antirrhinum* species.)  
In this case : RR = has red flowers, rr = has white flowers

But Rr has pink flowers

Here Genotypic ratio of  $F_2$  is like Mendelian monohybrid cross 1 : 2 : 1 but phenotypic ratio changed from 3 : 1 to 1 : 2 : 1





## EXPLANATION OF CONCEPT OF DOMINANCE

In diploid organisms, there are two copies of each gene, i.e., a pair of alleles. One of them may be different, i.e., modified

The normal allele produces normal enzyme needed for transformation of substrate.

If, the modified allele produces normal/less efficient enzyme, which produces same phenotype/trait, it is dominant, but if it produces non-functional or no enzyme, the phenotype will be affected and recessive trait is seen.

'Factors' or genes are the units of inheritance. They contain information required to express a particular trait in an organism. British geneticist R.C Punnett developed a graphical representation call Punnett square to calculate possibility of all possible genotype of offsprings in a genetic cross

### CO-DOMINANCE

$F_1$  resembles both parents.

ABO blood group in human being is controlled by Gene-I, having three alleles  $I^A$ ,  $I^B$  and  $i$ .  $I^A$  and  $I^B$  produce slightly different form of sugar, while  $i$  does not produce any sugar.

$I^A$  and  $I^B$  are completely dominant over  $i$ , but when  $I^A$  &  $I^B$  are present together, they express their own sugars, because of Co-Dominance hence RBC have both sugars.

There are six genotypes and four phenotypes in human ABO blood types.

### PLEIOTROPY

A single gene can exhibit multiple phenotypic expression. It is the effect of a gene on metabolic pathways which contribute towards different phenotypes.

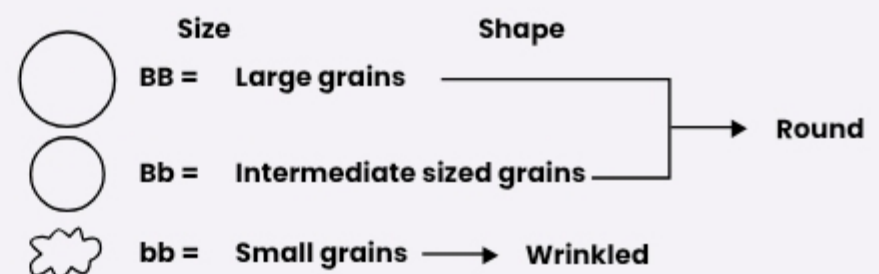
Example :

(a) Phenylketonuria  
(Single gene)

- (i) Mental retardation
- (ii) Reduction in hair & skin pigmentation

(b) Starch Synthesis  
gene in pea-(B)

- (i) Seed shape (Dominance)
- (ii) Size of starch grain  
(Incomplete dominance)



### MULTIPLE ALLELES

More than two alleles governing the same character.

ABO blood grouping is a very good example of multiple alleles. Since in an individual only two alleles are present, multiple alleles can be found only in population studies.

### INHERITANCE OF TWO GENES

Mendel also worked and crossed pea plants that differed into two characters and got a phenotypic ratio of 9 : 3 : 3 : 1 and genotype ratio of 1 : 2 : 2 : 4 : 1 : 2 : 1 : 2 : 1.

Based on these dihybrid crosses Mendel proposed the second set of generalisations that call mendal's law of independent assortment.

### LAW OF INDEPENDENT ASSORTMENT

The 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.





01>

Walter Sutton & Theodore Boveri noted that the behaviour of chromosomes was parallel to behaviour of genes and they used chromosome movement to explain Mendel's Laws.

02>

Sutton united the knowledge of chromosomal segregation with Mendelian principles and called it chromosomal theory of inheritance.

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### CHROMOSOMAL THEORY OF INHERITANCE

### DROSOPHILA MELANOGASTER WERE SUITABLE FOR GENETIC STUDIES

1

They could be grown on simple synthetic medium in laboratory.

2

They complete their life cycle in about two weeks.

3

A single mating could produce a large number of progeny flies.

4

There is a clear differentiation of sexes.

5

Also, it has many types of hereditary variations that can be seen with low power microscopes.

## LINKAGE AND RECOMBINATION

Morgan carried out several dihybrid crosses in *Drosophila* to study genes that were sex-linked, similar to the dihybrid crosses of Mendel in peas.

But the  $F_2$  ratios deviated significantly from 9 : 3 : 3 : 1 (expected when the two genes are independent).

When two genes in a dihybrid cross were situated on the same chromosome, the proportion of parental gene combinations were much higher than non-parental type. Morgan attributes it to physical association or linkage of two genes and used term recombination to describe non-parental gene combinations.

Some genes were very-tightly linked (Showed very low recombinations), while others were loosely linked (Showed higher recombinations).

Morgan's student Alfred Sturtevant used frequency of recombination between genes on same chromosome as a measure of distance between genes and mapped their position on chromosomes.

Today Genetic maps are extensively used as a starting point in sequencing whole genomes as done in the case of Human Genome Project.

## POLYGENIC INHERITANCE

Traits controlled by three or more genes are polygenic traits. It also takes into account influence of environment.

The phenotype reflects the contribution of each allele, i.e., the effect of each allele is Additive. E.g., Human Skin Colour.

AABBCC has darkest skin colour; aabbcc has lightest and AaBbCc intermediate colour. Other example is height in humans.





## SEX-DETERMINATION

### GENETIC/CHROMOSOMAL BASIS

Initial clue came from Insects. The X-body of Henking was in fact X-chromosome

#### TYPES

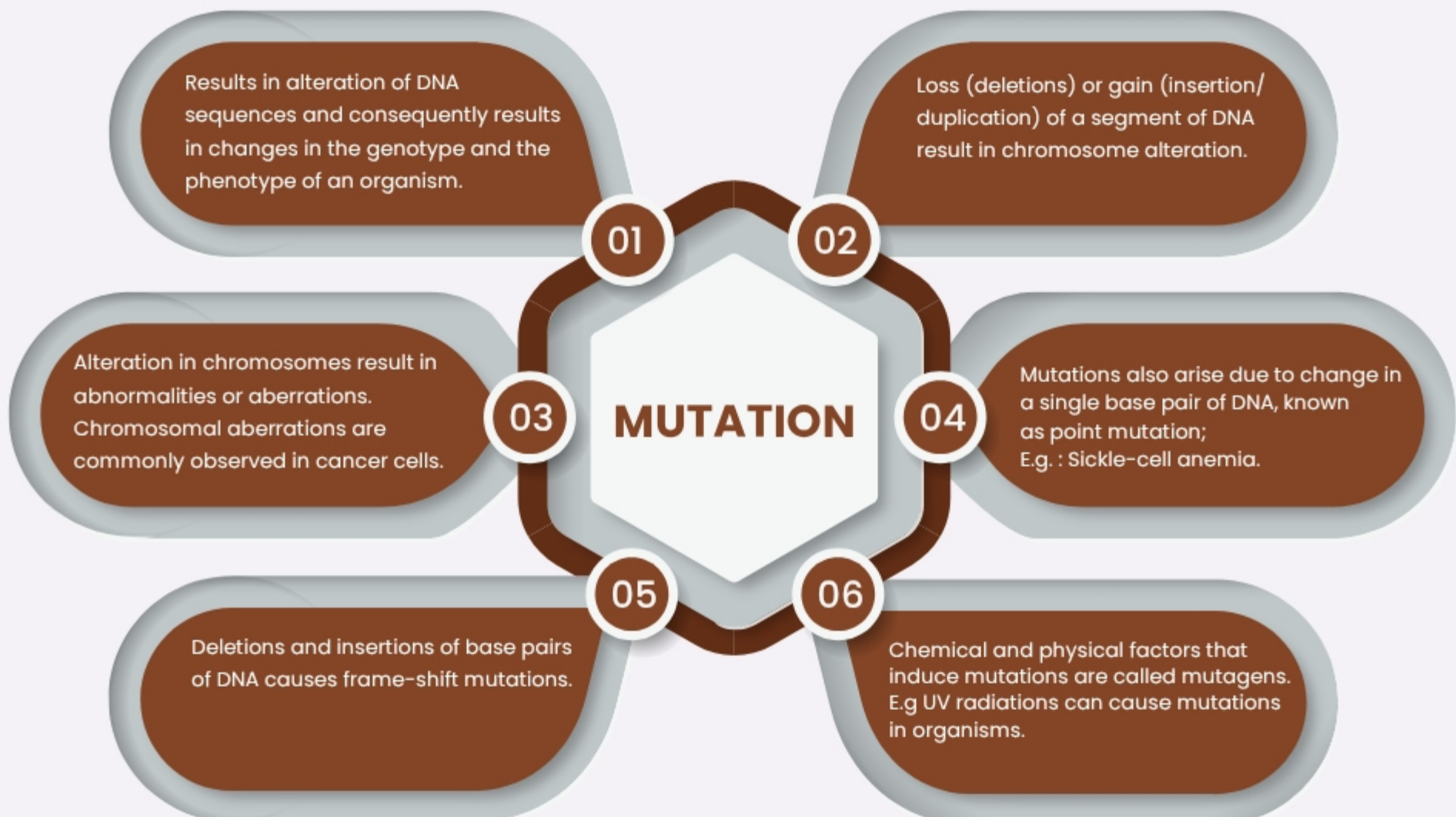
- (a) — XO-type = Male heterogamety  
e.g. = Grasshopper
- (b) — XY-type = Male heterogamety  
e.g. = Insects, Man
- (c) — ZW-type = Female heterogamety  
e.g. = Birds

### SEX-DETERMINATION IN HUMANS

- Genetic make-up of sperm determines sex of the child and in each pregnancy there is always 50% probability of a male or female child.
- It is unfortunate that in our society females are blamed for giving birth to female children.

### SEX-DETERMINATION IN HONEY BEE

- Haplo-diploid sex-determination.
- Unfertilised egg develops as male (drone) i.e. haploid; queen & worker bees (females) are diploid.



## GENETIC DISORDERS

### PEDIGREE ANALYSIS

Controlled crosses are not possible in case of human beings. Study of family history about inheritance of a particular trait provides an alternative. Such analysis on several generations of a family is called pedigree-analysis.



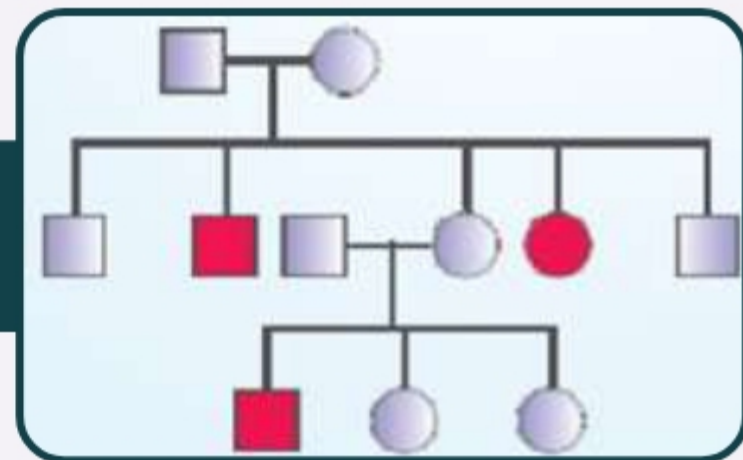
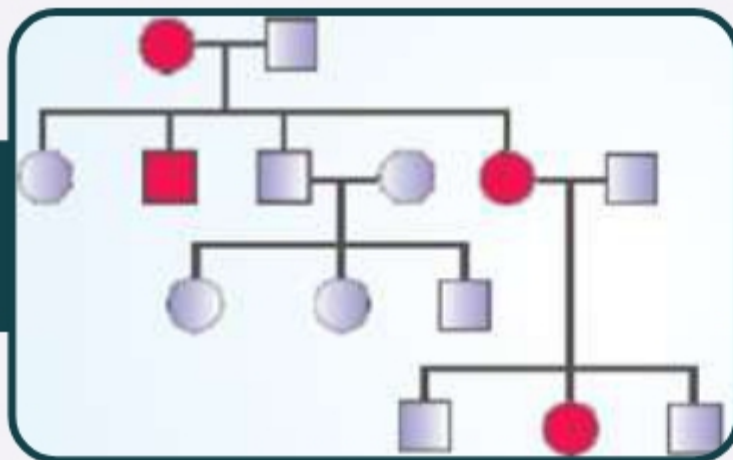
## SYMBOLS USED IN THE HUMAN PEDIGREE ANALYSIS

	Male		Female		Sex unspecified
	Affected individuals		Mating		Mating between relatives (consanguineous mating)
	Parents above and children below		Parents with male child affected with diseases		Five unaffected offspring

## PEDIGREE ANALYSIS OF

(a) Autosomal dominant trait (e.g., Myotonic dystrophy)

(b) Autosomal recessive trait (e.g., sickle-cell anaemia)



T.H. Morgan found that in *Drosophila* the genes for yellow body and white eye were very tightly linked and showed only 1.3 % recombination, while white eye and miniature wing showed 37.2 % recombination.

In Honeybee, males produce sperms by mitosis, they do not have father and thus cannot have sons, but have grand-fathers and can have grandsons.

Cystic fibrosis is autosomal recessive disorder.

Chromosomal disorders can be easily studied by the analysis of karyotypes.

Inheritable mutations can be studied by generating a pedigree of a family.

The family pedigree of Queen Victoria shows a number of haemophilic descendents as she was a carrier of the disease.

Thalassemia differs from sickle-cell anaemia in that the former is a quantitative problem of synthesising few globin molecules while the latter is a qualitative problem of synthesising incorrect globin.





## MENDELIAN DISORDERS

- Mainly determined by alteration or mutation in a single gene.
- It may be dominant or recessive. Autosomal or Sex-linked.

### Example

#### Colour-blindness

- Sex-linked recessive.
- Due to defect in either red or green cone of eye due to mutation in certain genes present on X-Chromosome
- 8% of males and 0.4 % of females affected.

#### Haemophilia

- X-linked recessive
- A single protein that is part of cascade of proteins involved in blood clotting is affected.

#### Sickle-Cell anaemia

- Autosomal linked recessive
- Controlled by single pair of allele  $Hb^A$  and  $Hb^S$

#### Phenylketonuria

Inborn error in metabolism. Autosomal recessive. Affected individual lack enzyme which converts phenylalanine to tyrosine. Results in mental retardation.

#### Thalassemia

- Autosomal recessive, could be due to mutation or deletion.
- $\alpha$ -thalassemia : Controlled by two closely linked genes  $HBA_1$  and  $HBA_2$  on Chr-16.
- $\beta$ -Thalassemia : controlled by single gene  $HBB$  on Chr-11

## CHROMOSOMAL DISORDERS

- Caused due to absence or excess or abnormal arrangement of one or more chromosomes.
- Failure of segregation of chromatids during cell-division cycle resulting in gain or loss of a chromosome(s) is called Aneuploidy.
- Failure of Cytokinesis after telophase stage of cell division results in an increase in a whole set of chromosomes in an organism, this is called Polyploidy, often seen in plants.
- TRISOMY or MONOSOMY leads to very serious consequences in the individual. Common examples of chromosomal disorders.

**(I) Down's Syndrome:** Trisomy of 21 ; was first described by Langdon Down (1866).

Symptoms:

- i) Short Statured
- ii) Small round head.
- iii) Furrowed tongue
- iv) Partially open mouth.
- v) Palm is broad with palm crease
- vi) Physical, psychomotor & mental development is retarded.

**(II) Klinefelter's Syndrome :** Karyotype = 47 XXY, overall masculine development, however Gynaecomastia is also expressed. Such individuals are sterile.

**(III) Turner's Syndrome :** Due to absence of one of the X-chromosomes, i.e., 45 with XO. Such females are sterile as ovaries are rudimentary besides lack of other secondary sexual characters.