

Chapter 4: Principles of Inheritance and Variations

Genetics — Comprehensive Study Notes

1. Introduction to Genetics

- **Genetics:** It is a branch of biology which deals with the study of inheritance and variations.
- **Father of Genetics:** Gregor Johann Mendel.
- **Inheritance:** It is a process in which genetic characters are transferred from parents to offspring. It is a basis of heredity.
- **Heredity:** Process of transfer of genetic traits from one generation to next generation.
- **Heredity trait:** Some specific trait which transfers from one generation to next generation.
- The study of genetics and heredity was done by Gregor Johann Mendel from 1856 to 1863 firstly.
- **Variation:** The difference b/w parents and progeny or the difference b/w two or more than two progeny.
- Mendel selected a garden pea plant (*Pisum sativum*) for hybridisation experiment and inheritance. So inheritance study was done by Mendel on garden pea plant.

2. Reasons for Selection of Pea Plant

- Many types of variations are present in pea plant.
- It is a bisexual plant.
- It is an annual plant / half yearly plant.
- In this plant both self and cross pollination can occur.
- It can develop in a small geographical area.

3. Contrasting Traits Studied by Mendel in Pea Plant

There are seven pairs of contrasting traits which were studied by Mendel in pea plant:

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

4. Inheritance of One Gene (Monohybrid Cross)

- Mendel crossed homozygous tall and dwarf pea plant to study the inheritance of one gene. This cross is known as **Monohybrid cross**. In this, Mendel crossed b/w one pair of contrasting traits. He collected the seed produced as a result of this cross and grew them to generate plants of the first hybrid generation.
- This generation is called filial 1 progeny or F_1 generation.
- Cross pollination was done by Mendel b/w tall & dwarf plant to obtain F_1 generation.
- Mendel observed that all F_1 generation plants were heterozygous tall plant but none of them were dwarf.
- After that Mendel did self pollination b/w two F_1 generation plants to obtain F_2 generation. Then some offspring were dwarf and some offspring were tall.
- The tall & dwarf traits were identical to their parental type and did not show any blending, so all the offspring were either tall or dwarf.
- On the basis of the result of F_2 generation, Mendel obtained a phenotype ratio & genotype ratio:
 - **Phenotype ratio:** 3 Tall : 1 Dwarf (3 : 1)
 - **Genotype ratio:** 1 Homozygous Tall : 2 Heterozygous Tall : 1 Homozygous Dwarf (1 : 2 : 1)

Gene Representation & Alleles

If we use alphabetical symbols for each gene, then the capital letter is used for the trait expressed in F_1 generation & the small letter is used for other trait.

For e.g., " T " is used for tall trait, " t " is used for dwarf trait. " T " & " t " are alleles of each other, so Mendel told that tall or dwarf pea variety are the allelic pair of genes for height and homozygous such as " TT " and " tt " respectively. A genotype where " T " allele and " t " allele both are present (Tt) is called **Heterozygous**.

According to Mendel, traits which are seen in F_1 generation are called **Dominant traits**, and the traits which are not seen in F_1 generation are called **Recessive traits**.

Monohybrid Cross Diagram

Parents: Tall Plant (TT) × Dwarf Plant (tt)

Gametes: T and t

F_1 Generation: Tt (All Heterozygous Tall Plants)

Selfing of F_1 : $Tt \times Tt$

Punnett Square for F_2 Generation:

Gametes	T	t
T	TT (Tall)	Tt (Tall)
t	Tt (Tall)	tt (Dwarf)

Ratios in F_2 :

- **Phenotype Ratio:** 3 Tall : 1 Dwarf (75% Tall : 25% Dwarf)
- **Genotype Ratio:** 1 **TT** : 2 **Tt** : 1 **tt** (25% **TT** : 50% **Tt** : 25% **tt**)

5. Punnett Square

F_1 and F_2 generation plants can be understood from a diagram which is called **Punnett Square**. It was developed by a British geneticist, **Reginald C. Punnett**. It is a graphical representation to calculate the probability of all possible genotypes of offspring in a hybrid cross. The possible gametes are written on two sides, usually the top row and left columns. All possible combinations are represented in boxes below in the square.

6. Inheritance of Two Genes (Dihybrid Cross)

- Mendel crossed b/w round shape, yellow colour of seed plant and wrinkled shape, green colour of seed plant to study the inheritance of two genes. We can say that Mendel took two different pairs of contrasting traits for the study. So this cross is called **Dihybrid cross**.
- Mendel found that the seeds resulting from this cross were round shape and yellow coloured seeds in F_1 generation. In F_1 generation, round shape and yellow colour was dominant over the wrinkled shape & green colour.
- This result was identical when he made separate monohybrid crosses b/w yellow & green seeded plants and b/w round & wrinkled seeded plants.
- Genotypic symbols:
 - **Y** for dominant yellow seed colour, **y** for recessive green seed colour
 - **R** for dominant round seed shape, **r** for recessive wrinkled seed shape
- Parental genotype: **RRYY** × **rryy**
- Gametes: **RY** and **ry**
- F_1 Generation: **RrYy** (Heterozygous round shaped & yellow coloured seeded plants)
- After self-pollination b/w F_1 progeny to produce F_2 generation, totally 16 plants/combinations are formed.

F_2 Generation Results in Dihybrid Cross:

- Round & Yellow plants: 9
- Round & Green plants: 3
- Wrinkled & Yellow plants: 3
- Wrinkled & Green plants: 1

Phenotypic Ratio: 9 : 3 : 3 : 1

Genotypic Ratio: 1 : 2 : 2 : 4 : 1 : 2 : 1 : 2 : 1

Checker Board (F_2 Generation):

Selfing: $RrYy \times RrYy$ | Gametes: RY, Ry, rY, ry

Gametes	RY	Ry	rY	ry
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

7. Mendel's Laws of Inheritance (Mendelism)

Based on experimental observations, Mendel proposed three inheritance laws in 1865. These laws are called The Principles or Laws of Inheritance or Mendelism:

i. Law of Dominance

- Proposed on the basis of results of monohybrid cross.
- According to this law, characters of organisms are controlled by specific units called 'factors'.
- Factors occur in pairs.
- In a dissimilar pair of factors, one member of the pair is dominant and the other is recessive.
- Dominant traits are seen in F_1 generation & recessive traits are unseen in F_1 generation of monohybrid cross.
- It explains the expression of only one of the parental characters in F_1 progeny and expression of both in F_2 progeny.

ii. Law of Segregation

- Proposed on the basis of results of monohybrid cross.
- According to this law, when the parents contain two different alleles, during gamete formation, the factors or alleles of a pair segregate from each other such that a gamete receives only one of the two factors.
- A homozygous parent produces all similar gametes, while a heterozygous parent produces two kinds of gametes, each gamete having one allele with equal proportion.
- Because of segregation of gametes from each other, this law is also known as '**Law of Purity of Gametes**'.

iii. Law of Independent Assortment

- Proposed on the basis of results of dihybrid cross.
- According to this law, when two pairs of traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters (when genes are present on different chromosomes).
- In a dihybrid cross, the segregation of 50% **R** and 50% **r** is independent from the segregation of 50% **Y** and 50% **y**.

- Therefore, 50% of *r*-bearing gametes have *Y* and the other 50% have *y*. Similarly 50% *R*-bearing gametes have *Y* and other 50% have *y*.
- Four genotypes of gametes are formed: ***RY, Ry, rY, ry*** in equal frequency (25% each).

8. Test Cross

When F_1 progeny is crossed with recessive parental trait, this cross is called '**Test Cross**'. In a typical test cross, a pea plant showing a dominant phenotype is crossed with the recessive parent. The progeny can be easily analyzed to find out the genotype of the dominant phenotype.

Case 1: If Unknown Genotype is Homozygous Dominant (WW)

$WW \times ww \rightarrow$ All offspring are *Ww* (100% Violet flowers).

Case 2: If Unknown Genotype is Heterozygous Dominant (Ww)

$Ww \times ww \rightarrow$ 50% *Ww* (Violet) and 50% *ww* (White).

Phenotypic & Genotypic Ratio of Test Cross: 1 : 1 (or 50% : 50%)

9. Rediscovery of Mendelism

Rediscovery of Mendelism was done by three scientists in **1900**:

1. **Hugo de Vries** (Holland)
2. **Carl Correns** (Germany)
3. **Erich von Tschermak** (Austria)

10. Exceptions / Deviations from Mendelism

i. Incomplete Dominance

- When experiments on pea plant were repeated using other traits in other plants, it was found that sometimes the F_1 generation had a phenotype that did not resemble either of the two parents and was intermediate b/w the two parents.
- **Example:** Inheritance of flower colour in Snap Dragon / Four O'clock plant (*Mirabilis jalapa* / *Antirrhinum majus*).
- In a cross b/w true breeding red-flowered (***RR***) & true breeding white-flowered (***rr***) plant, the F_1 progeny was pink-flowered (***Rr***) plants.
- When F_1 progeny was self pollinated, F_2 progeny resulted in:
 - 1 Red (***RR***) : 2 Pink (***Rr***) : 1 White (***rr***)
- Here, both **Phenotypic ratio (1 : 2 : 1)** and **Genotypic ratio (1 : 2 : 1)** are identical. Red colour trait was not completely dominant over white colour trait.

ii. Co-dominance

- When the F_1 generation resembles both parents, or when two alleles express themselves independently and equally in heterozygous condition, it is called **Co-dominance**.
- **Example:** ABO blood grouping in human beings (controlled by Gene I).
- Gene I has three alleles: I^A , I^B , i (or I^O).
- The plasma membrane of RBCs has sugar polymers that protrude from its surface. Alleles I^A and I^B produce slightly different forms of sugar, while allele i does not produce any sugar.
- I^A and I^B are completely dominant over i . But when I^A and I^B are present together, both express their own types of sugars due to co-dominance.

Genotypes and Phenotypes of ABO Blood Group in Humans:

Blood Group (Phenotype)	Genotype(s)
Blood Group A	$I^A I^A$ or $I^A i$
Blood Group B	$I^B I^B$ or $I^B i$
Blood Group AB	$I^A I^B$
Blood Group O	ii

Total possible genotypes = 6; Total phenotypes = 4.

iii. Multiple Alleles

- When more than two alleles control the expression of a single trait in a population, they are known as **Multiple alleles**. E.g., I^A , I^B , i in human ABO blood group, coat colour in rabbit, eye colour in *Drosophila*.
- Multiple alleles can be observed only when population studies are made.
- **Single gene product producing multiple effects:** E.g., Starch synthesis in pea seeds is controlled by one gene with two alleles (B and b).
 - BB : Large starch grains produced, seeds round.
 - bb : Small starch grains produced, seeds wrinkled.
 - Bb : Intermediate size starch grains produced (shows incomplete dominance for starch grain size, but round shape shows dominance).

iv. Pleiotropy

- When a single gene exhibits multiple phenotypic expressions, such a gene is called a **Pleiotropic gene**, and the phenomenon is called **Pleiotropy**.
- **Example:** Disease **Phenylketonuria (PKU)** in humans.
- Caused by mutation in the gene that codes for the enzyme *phenylalanine hydroxylase*.
- Due to this, phenylalanine is not converted to tyrosine, but converts into *phenylpyruvic acid* (ketone body), which accumulates and is excreted via urine.
- **Symptoms:** Mental retardation, reduction in hair, and skin pigmentation.

v. Polygenic Inheritance

- Traits that are controlled by three or more genes are called **Polygenic traits**, and their inheritance is **Polygenic inheritance** (e.g., human height, human skin colour).
- In human skin colour, controlled by three genes **A, B, C**:
 - **AABBCC** → Darkest skin colour
 - **aabbcc** → Lightest skin colour
 - **AaBbCc** → Intermediate skin colour

11. Chromosomal Theory of Inheritance

- Proposed by **Walter Sutton and Theodore Boveri** in 1902.
- They argued that the behaviour of chromosomes was parallel to the behaviour of genes and used chromosome movement to explain Mendel's laws.
- Chromosomes as well as genes occur in pairs. Homologous chromosomes segregate during gamete formation.

Comparison between Behaviour of Chromosomes and Genes:

Chromosomes	Genes
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 independently of each other.	One pair segregates independently of another pair.

12. Experimental Verification & Linkage Theory

- Experimental verification of the Chromosomal Theory of Inheritance was done by **Thomas Hunt Morgan** (1910) using fruit fly (*Drosophila melanogaster*).
- **Father of Experimental Genetics:** T.H. Morgan.
- **Reasons for selecting *Drosophila*:**
 1. Male and female are easily distinguishable.
 2. Has many types of hereditary variations visible under low power microscope.
 3. Short life span (about 2 weeks).
 4. Single mating produces a large number of progeny flies.
 5. Grows easily on synthetic medium in laboratory.
 6. Has 4 pairs (8) of chromosomes: 6 autosomes + 2 sex chromosomes (**XX** in female, **XY** in male).

Linkage and Recombination

- **Linkage:** Physical association or coexistence of two or more genes on the same chromosome. Such genes are called *linked genes*. Linkage is an exception to the Law of Independent Assortment.
- **Recombination:** Generation of non-parental gene combinations due to crossing over during Meiosis I (Prophase-I).

- Morgan observed in *Drosophila* dihybrid cross:
 - **Cross 1 (Body colour & Eye colour):** Yellow body, white eye (yw) $\times$ Wild type brown body, red eye (y^+w^+).
→ Parental type = **98.7%**, Recombinant type = **1.3%** (Tightly linked).
 - **Cross 2 (Eye colour & Wing size):** White eye, miniature wing (wm) $\times$ Wild type red eye, normal wing (w^+m^+).
→ Parental type = **62.8%**, Recombinant type = **37.2%** (Loosely linked).
- **Alfred Sturtevant** (student of Morgan) 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 Mapping).
- $Distance\ b/w\ genes \propto Recombination\ Frequency \propto 1 / Linkage\ strength.$

13. Sex Determination

- **Henking (1891):** Discovered the 'X-body' during spermatogenesis in insects. Later it was found to be a chromosome, named **X-chromosome**.

Types of Sex Determination Mechanisms:

1. XO Type (Male Heterogamety):

- Males have only one X chromosome (**Autosomes + XO**); Females have two X chromosomes (**Autosomes + XX**).
- Sperms carry either X or no X (O).
- **Examples:** Grasshopper, Cockroach.

2. XY Type (Male Heterogamety):

- Males have XY (**Autosomes + XY**); Females have XX (**Autosomes + XX**).
- **Examples:** Humans, *Drosophila*.

3. ZW Type (Female Heterogamety):

- Females have two different sex chromosomes (ZW); Males have a pair of similar sex chromosomes (ZZ).
- **Examples:** Birds, Reptiles, Fishes.

4. Haplodiploidy System (Honey Bees):

- Female (Queen/Worker) is diploid ($2n = 32$), develops from fertilized egg.
- Male (Drone) is haploid ($n = 16$), develops from unfertilized egg by **Parthenogenesis**.
- Drones produce sperms by *mitosis*. Drones do not have father and cannot have sons, but have a grandfather and can have grandsons.

14. Sex Determination in Humans

- Human beings have 23 pairs of chromosomes: 22 pairs of autosomes + 1 pair of sex chromosomes (XX in female, XY in male).
- Male produces two types of sperms: 50% carrying $22 + X$ and 50% carrying $22 + Y$.
- Female produces only one type of ovum: $22 + X$.

- Fertilization with X -sperm $\rightarrow$ Female ($44 + XX$); Fertilization with Y -sperm $\rightarrow$ Male ($44 + XY$).
- Sex of the child is determined by the male parent (father). 50% probability for either male or female in each pregnancy.

15. Mutation

- **Mutation:** A sudden inheritable change in the DNA sequence / genetic material.
- **Point Mutation:** Mutation due to change in a single base pair of DNA. Example: Sickle cell anaemia.
- **Frame-shift Mutation:** Deletion or insertion/addition of base pairs in DNA/chromosome.
- **Mutagens:** Physical or chemical factors that induce mutations (e.g., UV rays, X-rays, gamma rays, Colchicine alkaloid).

16. Genetic Disorders

Genetic disorders are broadly grouped into two categories:

A. Mendelian Disorders

Caused by alteration/mutation in a single gene. Transmitted to offspring as per Mendelian laws. Can be traced using Pedigree Analysis.

Type	Examples
Autosomal Recessive	Sickle cell anaemia, Phenylketonuria, Thalassemia, Cystic fibrosis
Autosomal Dominant	Myotonic dystrophy
Sex-Linked Recessive (X-linked)	Haemophilia, Colour blindness

1. Haemophilia:

- Sex-linked recessive disease (X-linked).
- Transmitted from unaffected carrier female (X^hX) to male progeny.
- A single protein involved in the cascade of blood clotting is affected. A simple cut results in non-stop bleeding.
- Shows Criss-Cross inheritance. Also called 'Royal disease' (traced in family tree of Queen Victoria).
- **Genotypes:** XX (Normal Female), X^hX (Carrier Female), X^hX^h (Haemophilic Female), XY (Normal Male), X^hY (Haemophilic Male).

2. Colour Blindness:

- Sex-linked recessive disorder due to defect in red or green cone cells of eye, leading to failure to discriminate between red and green colour.
- Gene present on X-chromosome. Affects ~8% of males and ~0.4% of females.

3. Sickle-Cell Anaemia:

- Autosomal linked recessive disease. Transmitted when both parents are carriers ($Hb^A Hb^S$).
- Controlled by single pair of allele: Hb^A and Hb^S .
 - $Hb^A Hb^A$: Normal individual
 - $Hb^A Hb^S$: Carrier individual (unaffected)
 - $Hb^S Hb^S$: Affected individual
- **Point Mutation:** Substitution of Glutamic acid by Valine at the 6th position of the β -globin chain of haemoglobin (mRNA codon change from **GAG** to **GUG**).
- RBC shape changes from biconcave disc to elongated sickle-like structure, leading to reduced oxygen transport and anemia.

4. Phenylketonuria (PKU):

- Autosomal recessive disorder. Lack of enzyme *phenylalanine hydroxylase*.
- Phenylalanine converts to phenylpyruvic acid. Excreted in urine. Causes mental retardation, reduction in hair & skin pigmentation.

5. Thalassemia:

- Autosomal recessive quantitative blood disorder (less synthesis of globin chains).
- **α -Thalassemia:** Controlled by genes **HBA1** & **HBA2** on chromosome 16.
- **β -Thalassemia:** Controlled by gene **HBB** on chromosome 11.

B. Chromosomal Disorders

Caused due to absence, excess, or abnormal arrangement of one or more chromosomes.

- **Aneuploidy:** Gain or loss of individual chromosome(s) due to non-segregation during cell division.
 - **Down's Syndrome:** Trisomy of 21st chromosome ($2n + 1 = 47$). First described by Langdon Down (1866). Short statured, small round head, furrowed tongue, open mouth, broad palm with characteristic palm crease, mental retardation.
 - **Klinefelter's Syndrome:** Presence of an extra X-chromosome in males ($44 + XXY = 47$). Overall masculine development with feminine characteristics like breast development (Gynaecomastia). Individuals are sterile.
 - **Turner's Syndrome:** Absence of one X-chromosome in females ($44 + XO = 45$). Sterile females, ovaries rudimentary, short stature, lack of secondary sexual characters.
- **Polyploidy:** Increase in a whole set of chromosomes due to failure of cytokinesis after telophase stage of cell division ($3n, 4n$ etc.). Often seen in plants.

17. Pedigree Analysis

The analysis of traits / genetic disorders in several generations of a family represented in a family tree is called **Pedigree Analysis**. Used in human genetics to trace inheritance of specific traits or diseases.

Standard Symbols in Pedigree Analysis:



Male



Female



Sex Unspecified



Affected Male



Affected Female



Affected Unspecified

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