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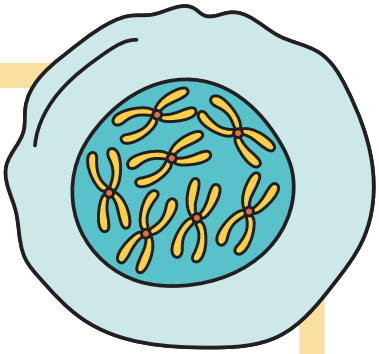

Principles of Genetics

B.Sc., Zoology
Semester -III

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SEMESTER-III

COURSE 6: PRINCIPLES OF GENETICS

Theory Credits: 3 3 hrs/week

SYLLABUS

UNIT-I:

1.1 History of Genetics- Concepts of Phenotype, Genotype, Heredity, Variation, Pure lines and Inbreed Lines

1.2 Mendelian Principles on Monohybrid cross, back cross and Test cross

1.3 Mendelian Principles on Dihybrid cross

UNIT-II:

2.1 Linkage - Definition, Types of linkage-complete linkage and incomplete linkage, Significance of linkage.

2.2 Crossing over - definition; Mechanism of crossing over: Chiasma Interference and coincidence

2.4 Gene Interactions: Incomplete dominance, codominance, Pleiotropy

2.5 Gene Interactions**:** Lethal alleles, Epistasis, Non- Epistasis

UNIT-III:

3.1 Polygenes (General Characteristics & examples)

3.2 Multiple Alleles (General Characteristics and Blood group inheritance)

3.3 Rh inheritance erythroblastosis foetalis

3.4 Extra chromosomal inheritance- Kappa particles in Paramecium and Shell coiling in snails

UNIT-IV:

4.1 Sex determination- Chromosomal theory and Genic Balance theory

4.2 Sex determination- Hormonal, Environmental and Haplo-diploidy types

4.3 Sex linked inheritance: X-linked inheritance

4.4 Sex linked inheritance: Y-linked & XY-linked inheritance

UNIT-V:

5.1 Human karyotyping, Pedigree Analysis(basics)

5.2 Autosomal Recessive disorder-Sickle cell anaemia – causes, treatment, inheritance pattern, modes of testing and prevention

5.3 Autosomal Dominant disorder- Huntington disease

5.4 Basics on Genomics and Proteomics.

Unit-I

History of Genetics

19th Century

1856-1863: Gregor Mendel's Experiments

- Gregor Mendel conducted experiments with pea plants and discovered the fundamental laws of inheritance. His work laid the foundation for the field of genetics.

1869: Discovery of DNA

- Friedrich Miescher isolated "nuclein" (DNA) from the nuclei of white blood cells, marking the first identification of DNA.

Early 20th Century

1900: Rediscovery of Mendel's Work

- Hugo de Vries, Carl Correns, and Erich von Tschermak independently rediscovered Mendel's laws of inheritance, which led to the wider recognition of his work.

1902: Chromosome Theory of Inheritance

- Walter Sutton and Theodor Boveri proposed that chromosomes are the carriers of genes and the basis for Mendelian inheritance.

1910: Discovery of Gene Linkage

- Thomas Hunt Morgan discovered that genes are located on chromosomes and can be linked, demonstrating that they do not always assort independently.

1928: Griffith's Experiment

- Frederick Griffith discovered the phenomenon of transformation, suggesting that genetic information could be transferred between bacteria.

Mid 20th Century

1944: Avery-MacLeod-McCarty Experiment

- Oswald Avery, Colin MacLeod, and Maclyn McCarty demonstrated that DNA is the substance that causes bacterial transformation, identifying it as the carrier of genetic information.

1950: Chargaff's Rules

- Erwin Chargaff discovered that DNA composition is species-specific and that the amount of adenine equals thymine, and the amount of cytosine equals guanine.

1952: Hershey-Chase Experiment

- Alfred Hershey and Martha Chase provided further evidence that DNA is the genetic material through experiments with bacteriophages.

1953: Watson and Crick's Model of DNA

- James Watson and Francis Crick proposed the double helix structure of DNA, with critical contributions from Rosalind Franklin and Maurice Wilkins.

Late 20th Century

1961: Genetic Code Cracked

- Marshall Nirenberg and Heinrich Matthaei deciphered the first codon of the genetic code, showing how DNA sequences determine amino acid sequences in proteins.

1970: Discovery of Restriction Enzymes

- Hamilton Smith and Daniel Nathans discovered restriction enzymes, which became essential tools in genetic engineering and molecular cloning.

1977: DNA Sequencing

- Frederick Sanger developed a method for sequencing DNA, revolutionizing genetics and leading to rapid advances in genetic research.

1983: Polymerase Chain Reaction (PCR)

- Kary Mullis developed PCR, a technique that allows for the amplification of specific DNA sequences, greatly enhancing genetic research and forensic science.

1990: Human Genome Project

- The Human Genome Project, an international research effort to map and sequence the entire human genome, was launched.

21st Century

2003: Completion of the Human Genome Project

- The Human Genome Project was completed, providing a complete map of all human genes and opening new avenues for research in genetics and medicine.

2012: CRISPR-Cas9

- The development of the CRISPR-Cas9 gene-editing technology by Jennifer Doudna, Emmanuelle Charpentier, and others provided a powerful tool for precise genetic modifications.

Genotype

- Genotype is the complete set of genes carried by a particular organism.
- Genotype is one factor that determines the characteristics, appearance and behavior of a particular organism.
- The appearance and the behavior can be altered by inherited epigenetic factors and environmental factors.
- Therefore, two individuals carrying similar genotypes can be different in observable characteristics. However, the genotype is inherited through the progeny via reproduction.
- In polyploid organisms, the genotype of a particular trait is determined by a combination of alleles.
- These alleles can either be homozygous or heterozygous for the locus. Alleles can also be either dominant or recessive depending on the phenotype they exhibit.
- Three genotypes, BB, Bb and bb, determine the colour of the flower in pea plants as shown in figure.
- The dominant phenotype for the flower color is purple; White is the recessive phenotype.
- Thus, the dominant allele is identified as 'B' whereas the recessive allele is identified as 'b'.

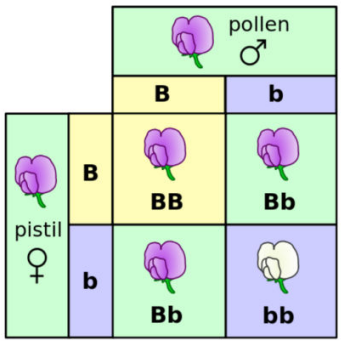


Figure 1: Genotypes of Mendel flowers

Phenotype

The phenotype is the observable characteristics or traits of an organism, such as its physical appearance, behavior, and biochemical properties. These traits result from the interaction of the organism's genotype (its genetic makeup) with the environment. Examples of phenotypes include eye color, height, leaf shape in plants, and blood type.

Heredity

Heredity is the process by which genetic information is passed from parents to their offspring. This transmission of traits and characteristics occurs through the genes, which are units of heredity found in the DNA of living organisms. Spencer was first used the term 'Heridity'.

Variation

Variation refers to the differences in traits and characteristics among individuals within a species. These differences can be observed in physical appearance, behavior, physiology, and genetic makeup. Variation is essential for the survival and evolution of species as it

enables populations to adapt to changing environments. Here are key points about variation:

1. **Genetic Variation:**
   - Differences in DNA sequences among individuals contribute to genetic variation. This can result from mutations, recombination during sexual reproduction, and gene flow between populations.
2. **Environmental Variation:**
   - The environment can influence the traits of organisms, leading to variation even among genetically similar individuals. Factors like climate, diet, and experiences play a role.
3. **Continuous and Discontinuous Variation:**
   - **Continuous Variation:** Traits that show a range of values, such as height or skin color, and are usually influenced by multiple genes (polygenic inheritance).
   - **Discontinuous Variation:** Traits that have distinct categories, such as blood type or flower color, and are often controlled by a single gene or a small number of genes.
4. **Sources of Genetic Variation:**
   - **Mutation:** Random changes in DNA that can introduce new genetic material.
   - **Recombination:** During sexual reproduction, the mixing of parental genes creates new combinations.
   - **Gene Flow:** Movement of genes between populations through migration.
5. **Importance in Evolution:**
   - Variation provides the raw material for natural selection to act upon. It allows some individuals to have traits better suited to their environment, increasing their chances of survival and reproduction.

Variation within a species is crucial for biodiversity and the adaptability of organisms to their surroundings, driving the evolutionary processes that shape life on Earth.

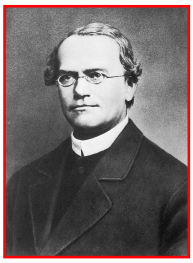
Pure Lines

- Pure lines are groups of organisms that have been bred to be genetically identical for specific traits.
- **They're Created** by mating individuals with the same traits over many generations, resulting in offspring that consistently exhibit those traits.
- Often used in plant and animal breeding to ensure consistent, predictable traits, like a specific flower color or crop yield.
- **Examples:** A strain of wheat that always produces the same type of grain, or a breed of dog that always has the same coat color.

Inbred Lines

- Inbred lines are similar to pure lines but refer more to the process of breeding closely related individuals to achieve genetic uniformity.
- These are created by mating siblings or parent-offspring pairs over several generations to concentrate desired traits.
- Helps in studying specific traits and maintaining genetic uniformity in research.
- Drawback is itcan lead to inbreeding depression, where harmful genetic traits become more common, leading to health problems.
- **Examples:** Lab mice used in scientific research, where genetic consistency is crucial, or certain crops that have been inbred to ensure uniformity.

Mendelism



The pattern of inheritance obeying the Mendelian inheritance is called as Mendelism, proposed by Bateson.

Gregor Johan Mendel (1822-1884) carried out his experiments on garden pea or *Pisum sativam* (Garden pea) and published the experimental results in the proceedings of the Natural history society of Bruno under the title "**Hybridization experiments in plants".**

Garden pea exhibits the following features that are suitable for the genetic experiments.

- It contains bisexual flowers and as a result self pollination is the preferred mode of pollination this character is very useful in carrying out selfing experiments.
- Either for generating pure lines or for obtaining F2, F3, F4 generations, cross pollination can be induced by **emasculation** (removal of stamens from bisexual flowers).
- The plant contains 7 pairs of contrasting characters that exhibit independent assortment.
- Generation time is relatively small so that 2-3 generations can be obtained in one year.

Table: Seven Contrasting characters studied by Mendel in Garden pea.

Sl. No	Charcter	Dominant	Recessive	F_1 Phenotype
1	Height	Tall	Dwarf	Tall *(T>t)*
2	Flower position	Axillary	Terminal	Axillary *(A>a)*
3	Flower Colour	Purple	White	Purple *(P>p)*
4	Pod shape	Inflated	Constricted	Inflated *(I>i)*
5	Fruit Colour	Green	Yellow	Green *(G>g)*
6	Cotylydon shape	Round	Wrinkled	Round (R>r)
7	Cotylydoncolour	Yellow	Green	Yellow *(Y>y)*

Hybridization

"Across between two homozygous pure line individuals having One or more contrasting pairs of characters".

- The generation of individuals taken for hybridization constitutes ***parental generation*** where is the progeny formed from the hybridization is called ***F1 generation*** or ***F1 hybrid***
- ***Law of uniformity in F1***: All the individuals in the F_1 generation from a hybridization experiment will have the same genotype and the same phenotype.

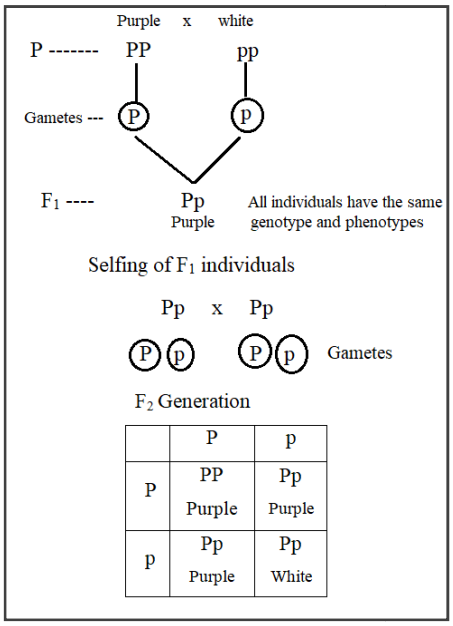
Mono hybridisation:

Cross between two pure line individuals, contrasting in one pair of characters.

Example: - Flower color; Purple is dominant over white flowers (P>p)

F_2 Phenotypic ratio = ¾ Purple: ¼ White = (3:1)

F_2 Genotypic ratio= ¼ PP: 2/4 Pp : ¼ pp = (1:2:1)



	P	p
P	PP Purple	Pp Purple
p	Pp Purple	Pp White

Di hybridization

"Cross between two pure line individuals, contrasting in two pairs of characters".

- Cotyledon colour: Yellow is dominant over green (Y>y)
- Cotyledon shape: Round is dominant over wrinkled (R>r)
- When we cross two pure lines of Yellow colour, round cotyledons and Green colour, wrinkled cotyledons, all the F_1 individuals have same phenotypes.
  - After selfing of F_1individuals,
  - F_2Phenotypic ratio

    9/16 – Yellow, Round

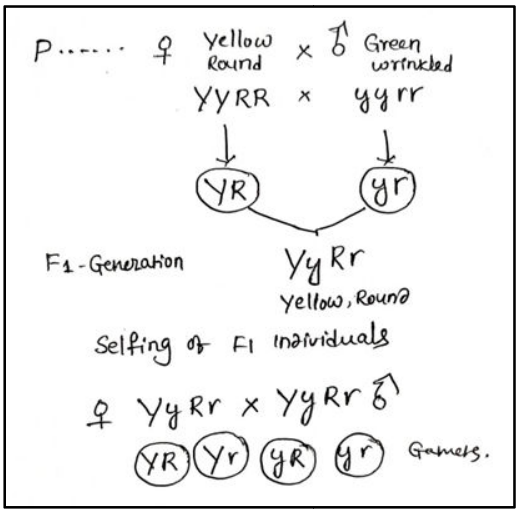
    3/16 – Yellow, Wrinkled

    3/16 –Green, Round

    1/16 - Green, Wrinkled

F_2 Phenotypic ratio = 9:3: 3:1

F_2Genotypicratio =1:2:1:2:4:2:1:2:1

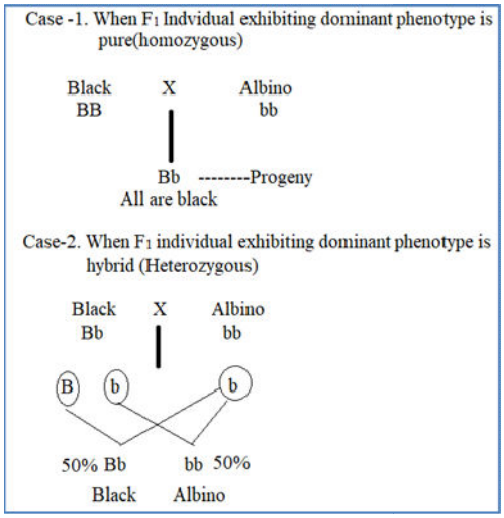


Male/ Female	YR	Yr	yR	yr
YR	YYRR Yellow,round	YYRr Yellow,round	YyRR Yellow,round	YyRr Yellow,round
Yr	YYRr Yellow,round	YYrr Yellow,wrinkled	YyRr Yellow,round	YYrr Yellow,wrinkled
yR	YyRR Yellow,round	YyRr Yellow,round	yyRR green, round	yyRr green, round
yr	YyRr Yellow,round	Yyrr Yellow,round	yyRr green, round	yyrr green,wrinkled

Test Cross

This cross is called test cross because it can be used to assess the purity of an individual (homozygous or not) exhibiting a dominant phenotype in F_1 generation: If an individual is homozygous dominant then the cross with the homozygous recessive produces a progeny exhibiting only the dominant phenotype; if an individual exhibiting a dominant phenotype is heterozygous then the cross with homozygous recessive genotype generates 50% of the progeny is with dominant phenotype and remaining 50% with recessive phenotype.

- **Monohybrid test cross ratio= 1:1**
- **Phenotypic ratio= Genotypic ratio**
- ½ dominant phenotype= ½ recessive phenotype
- ½ Heterozygous = ½ homozygous recessive



Back cross

- It is a cross between the F1 individual and either of 2 parents.
- It is the crossing of a hybrid with one of its parents, or an adult genetically identical to the parent, to achieve offspring with a genetic identity closer to parents.
- It is generally used in horticulture, animal breeding, & gene knockout organism development.
- It is generally used to improve a variety or breed by making a number of backcrosses.

Mendelian principles

- **Principles (Laws) based on monohybridization:**

Mendel proposed 2 laws based on nanohybridization experiments.

1: Law of dominance:

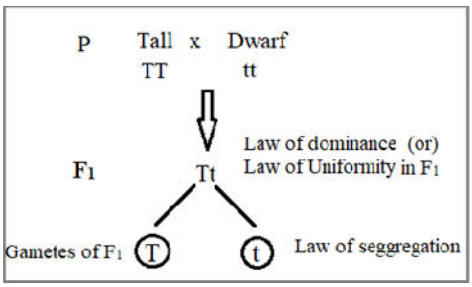
When two homozygous pure line individuals differing in one contrasting pair of characters are crossed, then all the F_1 individuals have the same genotype and phenotype (uniformity in F_1). And the phenotype exhibited was that of **dominant phenotype** (dominance).

Even though the F_1 hybrid comprise the two alternative forms (alleles) of the heredity factor (gene) only the phenotype corresponding to the dominant allele was physically manifested (dominant phenotype) where as the phenotype expression of the other allele (recessive allele) was masked in the F1 **(recessive phenotype).**

2: Law of segregation:

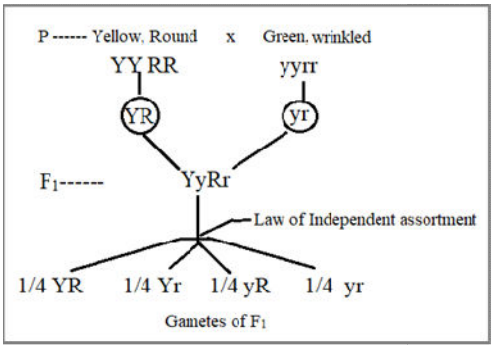
(Law of purity gametes):

Even though the recessive allele was mask by the dominant allele (with respect to the phenotypic expression) in the F1 hybrid the two alleles segregate into two different gametes without influencing each other, in other words, the presence of dominant allele has the masking effect only on the phenotypic expression of the recessive allele and it has no effect on the segregation of the recessive allele during gametogenesis.



3. Law of independent assortment:

- During the gametogenesis in a F1 dihybrid the assortment of one gene is independent of a second gene located on a non homologous chromosome.
- Law of independent assortment is valid for genes located on non homologous chromosomes.
- Independent assortment occurs due to the separation and movement of homologous chromosomes to opposite poles in Ana phase-1 of meiosis.
- Independent assortment is involved in the formation of recombinants when the genes are located on non homologous chromosomes.
- In independent assortment, the frequency of recombinant gametes (50%) = the frequency of parental gametes (50%).
- Genes present on the same chromosome (linked genes) violate Law of independent assortment.



Unit II

Linkage

"Linkage is the phenomenon of certain genes staying together during inheritance through several generations without any change or separation due to their presence on same chromosomes".

(Or) "The tendency of Genes present on the same chromosome to move together into the same gamete during gametogenesis is called the linkage".

- The principle of linkage was discovered by English Scientists **William Bateson** and **R.C. Punnet** in 1906 in Sweet Pea (*Lathyrus odoratus*). However, it was put forward as a regular concept by **Morgan** in 1910 from his work on fruit fly (*Drosophila melanogaster).*
- Linkage involves two or more genes which are linked in same chromosomes in a linear fashion.
- Linkage reduces variability.
- It may involve either dominant or recessive alleles (coupling phase) or some dominant and some recessivealleles (repulsion phase).
- It usually involves those genes which are located close to each other.
- All the genes present on a single chromosome constitutes a linkage group
- The number of linkage group in case of bacteria and viruses is usually one as the genetic material is organized into a single unit
- The number of linkage groups in eukaryotes corresponds to the number of chromosomes present in a haploid set (or) the number of chromosomes in the gametes.

Organism	Diploid number of Chromosomes (2n)	No.of Linkage groups
Drosophila	8	4
Pisum sativum	14	7
Zeamaize	20	10
Homo sapeans	46	23

- The strength of linkage depends on the distance between the linked genes; 'lesser the distance higher the strength of linkage'.

Types of Linkage

ON THE BASIS OF CROSSING OVER

i. Complete Linkage

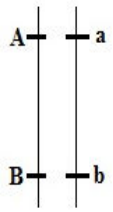
- The genes located in the same chromosome are inherited together over the generations due to absence of crossing over. It is rare but has been reported in male *Drosophila*.

ii. Incomplete Linkage

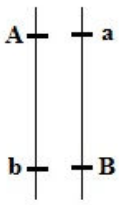
- Genes present on thesame chromosomeshave a tendency to separate due to crossing over. They produce recombinant progeny beside the parental types.

ON THE BASIS OF GENES INVOLVED

i. **Coupling phase/ Cis phase:** Dominant alleles and recessive alleles present on the same chromosomes shows coupling phase.



Cis Phase



Trans phase

ii. **Repulsion/ Trans phase:** Dominant alleles of same genes are linked with recessive

alleles of other genes on same chromosomes shows repulsion phase.

Significance of linkage

- It reduces the chances of formation of new combinations of genes in gametes.
- It helps keeping the parental, racial and specific traits together.
- It also useful for maintaining the good character of newly developed variety.
- Linkage plays an important role in determining the nature and scope of hybridization.

Crossing over

- Crossing over or (chromosomal cross over) is the exchange of genetic material between homologous chromosomes that results in recombinant chromosomes.

  Or

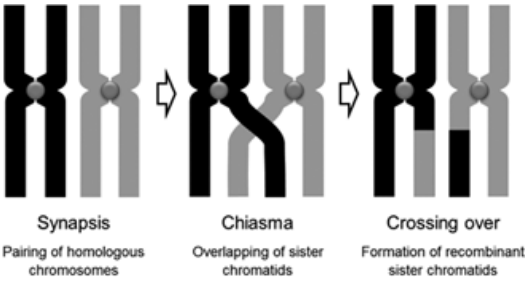
- The physical exchange of chromatid segments between two nonsister chromatids of a homologous pair of a chromosome in the Tetrad stage (4 Chromatid stage) is called Crossing over.
- Crossing over occurs during the Pachytene sub stage of prophase-I of Meiosis-I.
- Crossing over is responsible for the formation of recombinants when genes are present on the same chromosome (Linked genes).

MECHANISM OF CROSSING OVER

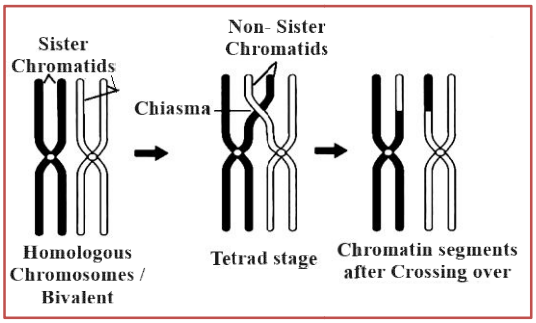
- Synapsis
- Tetrad formation
- Exchange of chromatid segments
- Terminalization

- **Synapsis**

  In the Zygotene or pairing stage of prophase-I, the homologous chromosome of eachpair come together and line up side by side.This pairing of homologous chromosomes is called synapsis.



- **Tetrad formation:** The two chromatids of chromosome are referred to as **dyad**. A group of four homologous chromatids (two dyad) of two synapsed homologous chromosome is known as **tetrad**. The two chromatids of same chromosome are called **sister chromatids**. The two chromatids, one of the one chromosome and other of its homologue, are termed **non-sister chromatids.**



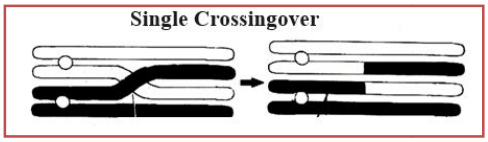
- **Exchange of chromatid segments:**
  - Two non-sisterchromatids in a tetrad break at equivalent locations.
  - The broken ends transpose and join the respective broken ends of opposite chromatid.
  - This completes the process of crossing over.
  - The unchanged chromatids are called parental ornon-cross overs.
  - The changed chromatids are called recombinants.
- **Terminalization :**
  - Completion of crossing over marks the end of pachytene stage and beginning of diplotene stage.
  - Synaptic forces end and the homologous chromosomes separate.

- The point at which the separation does not occur is called **chiasmata.**
- The chromatids separate progressively from the centromere towards the chiasma which moves like a zipper towards the end of tetrad.
- The slipping of chiasmata towards the ends of the bivalents is called terminalization.

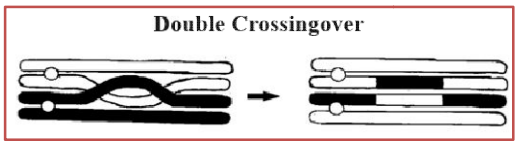
Types of Crossing over

Crossing over is classified into different types based on the number of crossing over events occurring between two genetic loci.

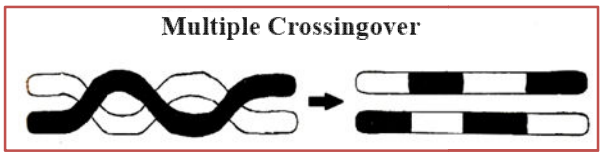
i) **Single Crossing over**: if only one crossing over event occurs between two genetic loci, the phenomenon is Single crossing over and the products are called as Single Cross Overs (SCOs).



ii) **Double Crossing over**: If two crossing over events occur simultaneously between two genetic loci, the phenomenon is double crossing over and the products are called as Double Cross Overs (DCOs).



iii) **Multiple Crossing over**: If more than one two crossing over events occur between two genetic loci at the same time, the phenomenon is called Multiple Crossing Over and the products are called Multiple Cross Overs (MCOS)



Since the Crossing over event involves the X-Shaped chiasma between the non sisters chromatids, the occurrence of One Crossing over event usually suppress the simultaneous occurrence of Second Crossing over and as a result the Frequency of MCOs will be less than that of DCOs, which will be less than that of SCOs.

NCOs > SCOs > DCOs > MCOs

Factors affecting crossing over

1. Gene Distance: Genes that are farther apart on a chromosome have a higher chance of crossing over.
2. Chromosomal Regions: Certain regions, known as hot spots, are more prone to crossing over.
3. Species: Different species exhibit varying frequencies and patterns of crossing over.
4. Age: The age of the organism can affect the likelihood and location of crossing over.
5. Environment: External factors like temperature and chemicals can influence crossing over rates.
6. Sex: There can be differences in crossing over rates between males and females in some species.

Chiasma Interference and Coincidence

Chiasma Interference:

Chiasma interference refers to the phenomenon where the occurrence of one crossover event affects the likelihood of another crossover event occurring nearby. This is a crucial concept in genetics, particularly in the study of recombination during meiosis.

- **Positive Interference**: If the presence of one crossover decreases the probability of another crossover occurring nearby, it is known as positive interference. This often leads to fewer double crossovers than expected if crossovers were independent.

- **Negative Interference:** If the presence of one crossover increases the probability of another crossover occurring nearby, it is termed negative interference. This leads to more double crossovers than expected.
- **No Interference:** if the occurrence of crossovers is independent, meaning one crossover does not affect the likelihood of another, there is any interference.

Coefficient of Coincidence (c):

The coefficient of coincidence is a measure used to quantify the degree of interference. It is defined as the ratio of observed double crossovers to expected double crossovers.

Coefficient of Coincidence =

$$= \frac{\text{Observed Double Cross overs}}{\text{Expected Double Cross overs}}$$

Interference (I):

Interference (I) can be calculated from the coefficient of coincidence:

Interference (I) = 1 − ***Coefficient of coinsidence***

- **Positive Interference**: If the coefficient of coincidence is less than 1 (c < 1), it indicates positive interference.
- **Negative Interference**: If the coefficient of coincidence is greater than 1 (c > 1), it indicates negative interference.
- **No Interference:** If the coefficient of coincidence is equal to 1 (c = 1), there is no interference.

Examples

1. Drosophila Melanogaster: In fruit flies, positive interference is commonly observed, meaning that double crossovers are rarer than expected.
2. Yeast: In yeast, regions with negative interference have been identified, where the presence of one crossover increases the likelihood of another nearby.

Significance of crossing over

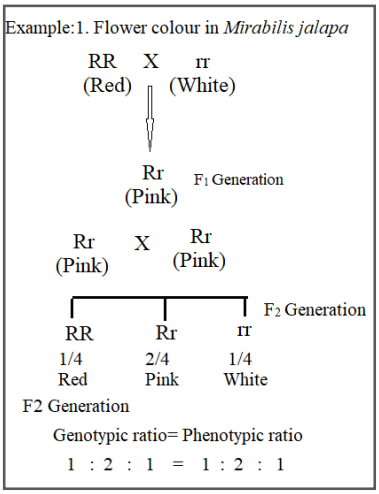
- Crossing over has helps in establishing the concept of liner arrangements of genes.
- The frequency of Crossing over helps in mapping of chromosomes i.e. determining the location of genes on the chromosomes.
- It is an important factor in sexual reproduction.
- It increases the variation which is vital for evolution.
- It helps in plant breeding also.

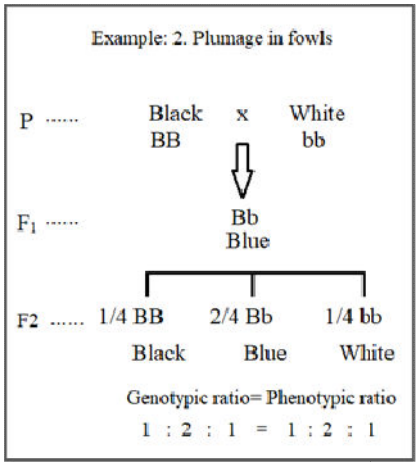
Gene Interactions

Incomplete dominance

- "When the F1 hybrid or heterozygote exhibits a phenotype i.e. intermediate between the two homozygous parental phenotypes, the condition is said to be ***incomplete dominance or partial dominance or semi dominance***".
- In case of incomplete dominance, for the complete manifestation of the dominant phenotype two doses of the dominant allele (homozygous dominant condition) are required, when the dominant allele is present in single dose (heterozygous condition) its phenotype is partially expressed and as a result the heterozygote has an intermediate phenotype.
  - In incomplete dominance, the genetic locus is represented by a dominant and a recessive allele.

Eg: 1. Flower colour in ***Mirabilis jalapa*** ($4^{'0'}$ clock plant).



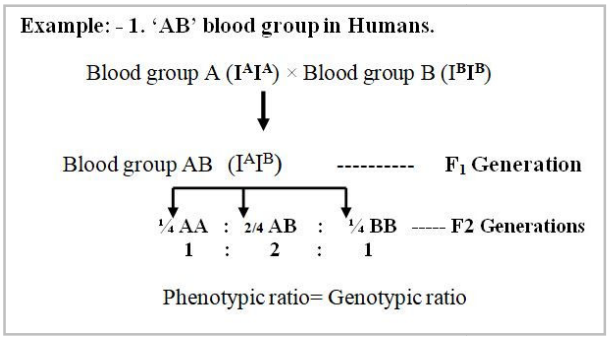


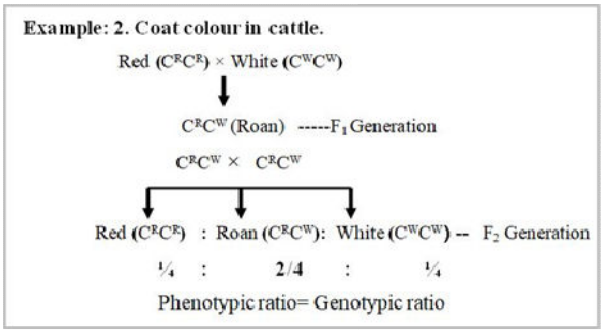
Codominance

When the F_1 heterozygote has a phenotype that is a mixture of both the homozygous genotype, the phenomenon is called **co dominance** and the alleles are said to be codominant.

In the F_1 heterozygote, both the alternative forms of the gene are phenotypically expressed and this phenotype is distinct from either of the homozygotes.

- In co dominance both the alternative forms act as dominant alleles and as a result recessive allele is absent.
- Similar to incomplete dominance, the F_2 phenotypic ratio in co dominance is equal to the F_2 genotypic ratio and is 1:2:1.
- Since recessive alleles are absent in co dominance the two alleles are designated as superscripts using a common symbol.





Pleotropy

"When a single pair of a gene controls the production of many characters then it is called Pleotropism. The gene is called Pleotropic gene".

- The term Pleotropy was coined in 1910 by Festschrift.
- Pleotropy describes the genetic effect of a single gene on multiple phenotypic traits.
- Mutation in Pleotropic gene may have an effect on some or all traits
- Mechanism of Pleotropy in most cases is the effect of a gene in metabolic pathways that contribute to different phenotypes.

  Example: Phenylketonuria
- **Phenylketonuria (PKU)** disease is an example of pleiotropy in human.
- Phenylketonuria is due to mutation in a single gene (pp) that codes for the enzyme ***Phenylalanine hydroxylase.***
- Phenylalanine hydroxylase converts the amino acid phenylalanine to tyrosine.
- Due to mutation conversion of phenylalanine to tyrosine is reduced or ceased entirely.
- This disease can also cause **mental retardation** and **reduced hair and skin pigmentation.**

Lethal alleles

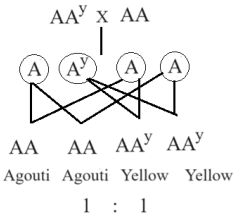
Lethal alleles (also referred to as **lethal** or **lethals**) are alleles that cause the death of the organism that carries them.

They are usually a result of mutations in genes that are essential for growth or development.

Lethal alleles were first discovered by ***Lucien Cuenot*** in 1905 while studying the inheritance of coat color in mice.

- The *agouti* gene in mice is largely responsible for determining coat colour.
- The wild-type allele produces 'agouti' (yellow and black blend) colour.
- One of the mutant alleles of the *agouti* gene results in mice with a much lighter, yellowish colour.

When these yellow mice were crossed with homozygous wild-type mice, a 1:1 ratio of yellow and dark grey offspring were obtained. This indicated that the yellow mutation is dominant, and all the parental yellow mice were heterozygote for the mutant allele.



By mating two yellow mice, Cuenot expected to observe a usual 1:2:1 Mendelian ratio of homozygous agouti to heterozygous yellow to homozygous yellow.

Instead, he always observed a 1:2 ratio of agouti to yellow mice.

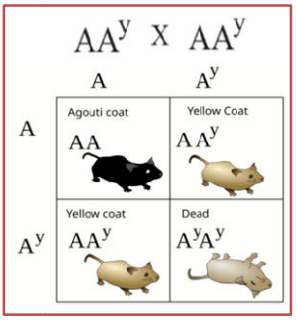
He was unable to produce any mice that were homozygous for the yellow agouti allele.

Lethal alleles may be recessive, dominant, or conditional depending on the gene or genes involved.

Recessive lethals: A pair of identical alleles that are both present in an organism that ultimately results in death of that organism are referred to as recessive lethal alleles.

The recessive lethal may code for dominant or recessive traits, they are only fatal in the homozygous condition.

Example: Achondroplasia, Cystic fibrosis



Dominant lethals:

Alleles that need only be present in one copy in an organism to be fatal are referred to as dominant lethal alleles. These alleles are not commonly found in populations because they usually result in the death of an organism before it can transmit its lethal allele on to its offspring. An example in humans of a dominant lethal allele is Huntington's disease, a rare neurodegenerative disorder that ultimately results in death.

However, because of its late onset (i.e., often after reproduction has already occurred), it is able to be maintained in populations.

EPISTASIS

The interaction between two genes present on non homologous chromosomes at their product level to generate a specific phenotype called gene interaction.

It may also involve more than two genes located on non homologous chromosomes.

Since the Interaction at the level of gene products rather than the gene sequences, the ***genotype ratios are not affected in gene interactions however in epistatic interactions the phenotypic ratios are modified from the conventional 9:3:3:1.***

Intergenic interactions are broadly divided into two major types

- Non epistatic interactions - F2 phenotypic ratio 9:3:3:1.
- Epistatic interactions - F2 phenotypic ratio changed.

1. Non epistatic interactions:

In this type of interactions one gene has no inhibitory or suppressive of another gene the two genes have independent phenotypic effect when present alone but interact to produce a new phenotype in present together.

Example: **Combs in fowls**

Epistatic interactions:

Epistasis is an intergenic interaction in which one gene suppresses the phenotypic expression of a second gene located on non homologous chromosomes i.e. epistasis is an intergenic suppression.

- An ***epistatic gene*** is the gene that suppresses the phenotypic expression of a second gene.
- ***Hypostatic gene*** is the gene whose phenotype expression is the supressed by an '***epistatic gene'.***

The term ***Epistasis*** was first used by **Bateson** and literally means ***sitting above***.

The Epistatic interactions are further divided into the following types

- Dominant epistasis -12:3:1
- Recessive epistasis -9:3:4
- Duplicate dominant epistasis- 15:1
- Duplicate recessive epistasis (Complementary gene interaction)- 9:7
- Dominant recessive epistasis (Inhibitory gene interaction) – 13:3
- Duplicate gene and cumulative effect Dominant gene interaction- 9:6:1

Dominant Epistasis:

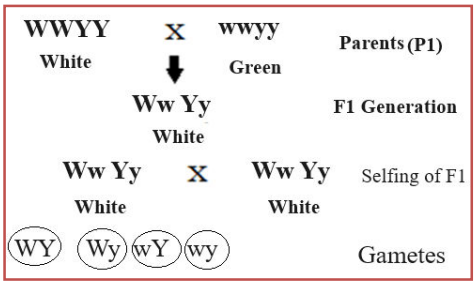
In dominant epistasis the epistatic gene suppresses the phenotypic expression of the hypostatic gene whenever the epistatic gene is present in Dominant condition (Homozygous or Heterozygous).

The hypostatic gene can express its phenotype only when the Epistatic gene is homozygous recessive.

Example:Fruit colour in summer squash (*Cucurbita pepo*)

In summer squash White, Yellow, Green colored fruits are common the White color is dominant over Yellow and Green; Yellow color is dominant over Green color.

When the cross between two plants having White (WWYY) and Green (wwyy) colored fruits all the plants in F1 generation are with White colored fruits.



Male/ Female	WY	Wy	wY	wy
WY	WWYY White	WWYy White	WwYY White	WwYy White
Wy	WWYy White	WWyy White	WwYy White	Wwyy White
wY	WwYY White	WwYy White	wwYY Yellow	wwyy Yellow
wy	WwYy White	Wwyy White	wwYy Yellow	Wwyy Green

Phenotypic ratio changed from 9:3:3:1 to 12:3:1 due to dominant gene interactions.

Recessive epistasis

In this type of interaction the Epistatic gene suppresses the phenotypic expression of the hypostatic gene whenever the epistatic gen is homozygous recessive. For the phenotypic expression of the hypostatic gene, the epistatic gene should be either homozygous dominant or heterozygous. i. e. The epistatic gene should be dominant

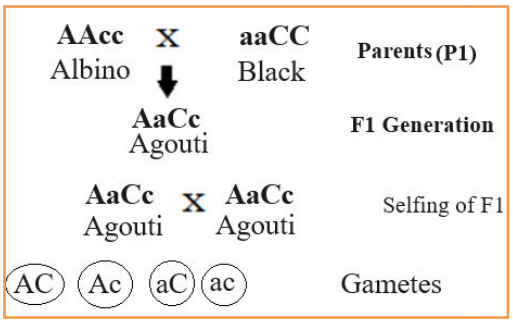
Example: Coat colour in albino series of mice

Coat color in albino mice is of 3 types (Agouti, Black & Albino).

Agouti color- 'A' Gene, Black- 'C' Gene

'c' – Epistatic gene

'A' - Hypostatic



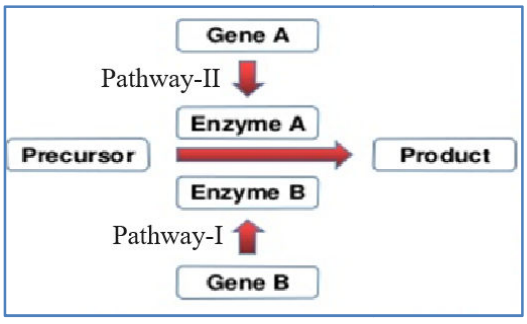
F2 Generation

Male/ Female	AC	Ac	aC	ac
AC	AACC Agouti	AACc Agouti	AaCC Agouti	AaCc Agouti
Ac	AACc Agouti	AAcc Albino	AaCc Agouti	Aacc Albino
aC	AaCC Agouti	AaCc Agouti	aaCC Black	aaCc Black
ac	AaCc Agouti	Aacc Albino	aaCc Black	aacc Albino

In F2 generation the phenotypic ratio of Agouti, Black and Albino is 9:3:4 due to recessive epistasis.

Duplicate dominant Epistasis - 15:1

In this type of interaction the formation of specific phenotype occurs by two independent mechanisms controlled by two dominant genes; the presence of any one of the gene or both the genes can lead to the formation of a specific phenotype. Only double recessive cannot form this phenotype.



Example: Fruit shape in Shepherd purse (*Capsella bursapastoris*).

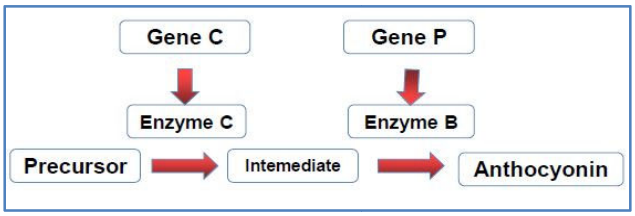
15:1 (15- Triangular, 1- Elongated)

Duplicate recessive Epistasis 9:7
(Complementary gene interaction)

In this type of interaction for the formation of specific phenotype to non homologous genes should be present in the dominant state. If anyone gene is present in the recessive condition then the phenotype will correspond to the double recessive condition.

In this type of interaction the product forms as a result of the first gene activity serves as the substrate for the enzyme coded by the second gene the phenotypic effect can be seen only when the final product is formed**.**

Example: Flower color in sweet pea (*Lathyrus odoratus*).

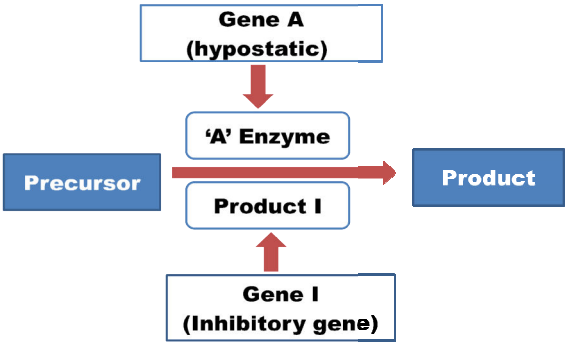


Dominant recessive Epistasis
(Inhibitory gene interaction 13:3)

Dominant gene (inhibitory gene) suppresses the phenotypic expression of the hypostatic gene in such a way that the phenotype resembles double recessive.

Hypostatic gene expresses the phenotype when epistatic gene is resistive.

Example: Kernel colour in Maize

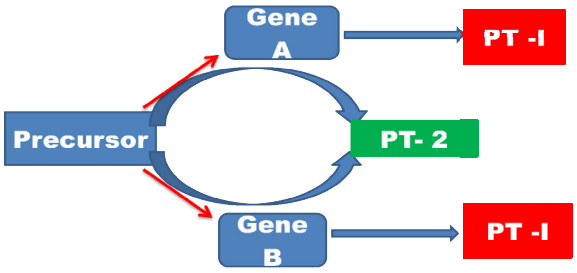


Duplicate genes and cumulative effect or Dominant gene interaction (9:6:1)

In this type of interaction two distinct dominant genes produce the same phenotype when they are present individually where as when they are together interaction between the gene products results in the formation of a new phenotype.

Examples:

- Fruit shape in Cucurbita
- Coat colour in pigs
- Fruit shape in summer squash



UNIT-III

Polygenes("poly", meaning "many")

Polygenic inheritance is a nonMendelian pattern of inheritance in which ***a particular trait is produced by the interaction of genes at many loci*** (i.e. polygenes). (Or) Polygenic inheritance, in simple terms, implies a character or phenotypic trait, which is regulated by more than one gene.

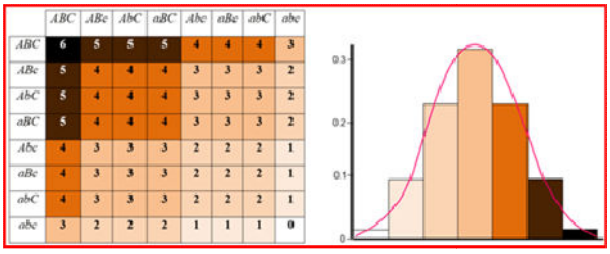
Characteristics of Polygenic Inheritance:

- A gene that employs a minor effect on a phenotype along with other genes is referred to as polygenes.
- The effect of an individual gene is too minor and often remains undetected.
- Numerous genes exert an equal effect.
- Individually, each allele contributes to the result in a cumulative or additive manner
- The expression of one gene is not masked by the presence of the other genes, i.e., epistasis is not involved.
- The gene involved in polygenic inheritance is either ***contributing*** (active allele) or ***non-contributing*** (null allele); there are no genes as dominant or masked genes.
- There is a continuous variation of the phenotype of a trait in a polygenic inheritance
- The polygenic inheritance pattern is difficult to predict and it is highly complex.
- The statistical analysis of polygenic inheritance patterns can help to provide an estimate of population parameters.
- Most of the polygenic inheritance follows the ***normal distribution curve***, wherein the majority of the people fall in the middle range of the curve.
- Polygenic inheritance is different from multiple alleles. In multiple alleles, on the same locus, three or more alleles are present an organism, e.g. human blood group system, i.e., the ABO system, is controlled by three alleles.

Polygenic Inheritance Examples

1. Skin color and pigmentation in Humans

- It is controlled by around 60 loci.
- To understand the inheritance pattern of skin color let us consider an example of pair of three different alleles present at unlinked loci represented as A and a, B and b, C and c.
- Accordingly, the greater number of "capital letters" in the genetic pattern indicates dark skin color whereas the presence of a greater number of "small letters" represents the lighter colour of the skin.

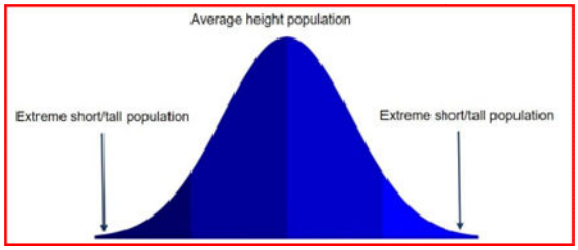


	ABC	ABc	AbC	aBC	Abc	aBc	abC	abc
ABC	6	5	5	5	4	4	4	3
ABc	5	4	4	4	3	3	3	2
AbC	5	4	4	4	3	3	3	2
aBC	5	4	4	4	3	3	3	2
Abc	4	3	3	3	2	2	2	1
aBc	4	3	3	3	2	2	2	1
abC	4	3	3	3	2	2	2	1
abc	3	2	2	2	1	1	1	0

- The progeny of the parents with genotype ***AABBCC and aabbcc*** will have intermediate colour in the F1 generation, i.e. genotype would be ***AaBbCc.*** Further, in the F2 generation of two triple heterozygotes parents — AaBbCc x AaBbCc — will produce varying skin colours ranging from ***very dark to very light***, the ratio of which would range in 1:6:15:20:15:6:1.

2. Human height:

Human height is a polygenic trait that is controlled by three genes that have six alleles. So, a tall person would have all dominant alleles whereas a short person will have the most number of recessive alleles. Like all the polygenic inheritance patterns, human height inheritance also follows a normal distribution curve wherein the extreme ends of the curve represent either extremely short or tall people, while the middle portion of the curve represents the population with average height .



3. Polygenic inheritance of the human eye color:

The eye color follows a polygenic inheritance pattern. In humans, 9 eye colors are recognized. Phenotypic expression of eye color is controlled by two major genes and 14 additional genes, which are linked to X chromosomes. The eye color is due to the presence of melanin in the front portion of the iris.

Dominant allele (BBGG) contributes to the melanin synthesis in the iris those results in black eye color while the combination of all recessive alleles (bbgg) results in blue eye color. The rest of all the eye colors are the combination of these dominant and recessive alleles. See below:

- ***BBGG*** results in Black eyes
- ***BBGg***or***BbGG***results in Dark Brown eyes
- ***BbGgorBBggorbbGG*** results in Light Brown eyes
- ***Bbgg***or***bbGg*** results in green eyes
- ***Bbgg*** results in blue eyes

Multiple Alleles

- The presence of more than two alleles or alternative forms for a genetic locus is called as multiple alleles.
- Multiple alleles can be studied only in population.
- The Maximum number of alleles possible in diploid individual, when a genetic locus exhibits multiple alleles is two.
- In a multiple allelic series, dominance, incomplete dominance, co dominance and recessive are possible. Even though in a given multiple allelic series all of these may not be present.
- The number of genotypes possible for genetic locus or gene having 'n' number of alleles equals to $\frac{n(n+1)}{2}$.
- If incomplete dominance and codominance are absent then the number of phenotypes possible for the multiple allelic series is equal to the number of alleles.
  - If a multiple allelic series having ***'n'***- alleles exhibits incomplete dominance and co dominance then the number of phenotypes possible will be equal to '***n+ m***'

- Where ***'m'*** represents the number of incomplete and or codominant events.

Examples:

- A, B, AB and O blood groups in humans
- The coat colour of rabbits,
- The eye colour in Drosophila.

A, B, AB and O blood groups in humans:

- Carl Landsteiner discovered ABO blood group system in 1900. The gene responsible for the ABO system is present on the 9th chromosome.
- The alleles are I^A,I^B and i^O.
- I^A and I^B are dominant over i^O, whereas both I^A and I^B are codominant.
- I^A and I^B code for functional galactosyl transferaseenzyme.
- The recessive allele 'i' is generated by a 'deletion' in the functional gene.
- Number of genotypes possible = $\frac{n(n+1)}{2}$.
- Where 'n'= 3. = $\frac{3(3+1)}{2}$= 6.
- Number of possible phenotypes = n+m = 4;
- where 'n'=3 (number of alleles);
- '***m***'=1(number of codominance and incomplete dominance).

Genotype	Phenotype Blood group	Antigen on RBC	Antibodies in Plasma	Blood can be accepted from	Blood donates to
I^AI^A / I^Ai^O	'A' Group	Antigen-'A'	Antibody-b	A, O	A, AB
I^BI^B / I^Bi^O	'B' Group	Antigen-'B'	Antibody-a	B, O	B, AB
I^A,I^B	'AB' group	Both-'A'& 'B'.	NONE	A, B,AB and O	AB
i^Oi^O	'O' Group	NONE	Both-'a'& 'b'.	O	A, B,AB and O

- Universal donor lacks both the antigens 'A' and 'B'= 'O' group
- Universal acceptors contain both the antigens 'A' and 'B' = AB group.

Rh inheritanceand Erythroblastosisfetalis

Landsteiner and Weiner generated Antibodies for blood antigens of Rhesus monkey and tested various mammalian blood samples for the presence of Rh antigen; they found 85% of the tested human population was positive for the presence of Rh antigen, whereas the remaining 15% were negative.

- Rh^{+ve}individuals produce Rh antigen, whereasRh^{-ve}individuals neither produce Rh antigen nor Rh antibodies.
- The fundamental difference between ABO blood group system and Rh system is that the ABO system has natural antibodies whereas Rh system lacks natural antibodies.
- Rh^{-ve} individuals generate Rh antibodies when they were transferred with Rh^{+ve} blood.
- Rh^{-ve} women generates Rh antibodies during pregnancy when the foetus is Rh^{+ve}(Maternal foetal blood Incompatability)

Genetics of Rh blood group

Two hypotheses were proposed to explain the genetics of Rh blood group.

1. **Multiple allele system proposed by Weiner:**
   According to this system the gene responsible for Rh blood group contains 8 different alleles out of which 4 are dominant and code for functional Rh antigen whereas other four are mutated forms that codes for non-functional proteins.

   Rh alleles (R>r)

   R^0, R^1, R^2, R^Z – codes Rh^{+ve}

   r, r^I, r^{II}, r^y – codes Rh^{-ve}

2. Pseudo allele system – Proposed by Fischer & Race

This is the accepted hypothesis for Rh blood group system.

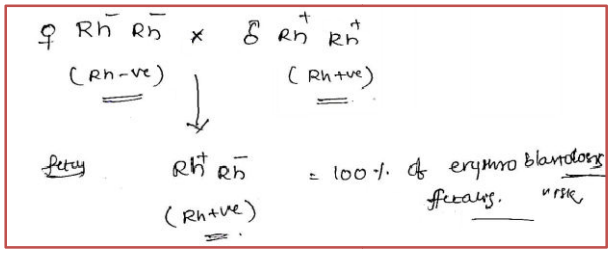
Pseudo alleles or Non alleles - Genes that are closely located and control the same primary character and behaves as alleles.

According to this system 3 closely linked genes C, D and E are responsible for various Rh genotypes, among these three genes the pseudo allele 'D' is primarily responsible for the Antigen production; individuals homozygous (DD) and heterozygous (Dd) for 'D' are capable of producing Rh antigen (Rh^{+ve}) whereas homozygous recessive individuals (dd) are Rh^{-ve}.

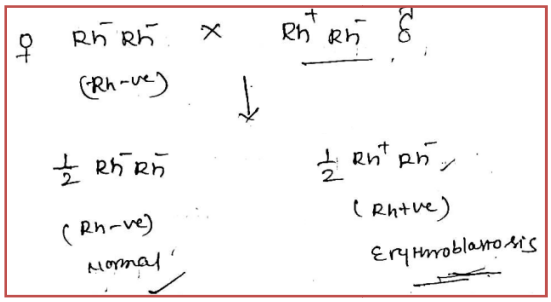
Genotypes	Phenotype
CC D_ EE	Rh^{+ve} (Rh Positive)
Cc D_ Ee	
cc D_ EE	
cc D_ Ee	
cc D_ ee	
CC dd EE	Rh^{-ve} (Rh Negative)
Cc dd EE	
Ccdd Ee	
cc dd EE	
cc dd ee	

Erythroblastosis fetalis (or)
Hemolytic disease of Newborn (HDN)

- It is the Condition that arise due to incompatibility between the mother and fetus; when Rh^{+ve} fetus develops in Rh^{-ve} mother.
- The incompatibility leads to production of Rh antibodies by Rh^{-ve} mother and these antibodies will cause clumping of foetal erythrocytes leading to their lysis and fetal death.
- In order to prevent sensitization of an Rh^{-ve} mother and to prevent hemolysis of the fetus, ***Rhogam*** is administered in the first trimester of pregnancy.
- Rhogam is Rh gamma globulin that neutralizes Rh antibodies developed by a sensitized Rh^{-ve} mother.
- Erythroblastosis risk will be maximum when the mother is Rh^{-ve} and father is homozygous Rh^{+ve}; in this case fetus will be always Rh^{+ve} and incompatible with mother Rh type.



- The risk of Erythroblastosis is 50% when women is Rh^{-ve} and the men is heterozygous Rh^{+ve}.



- The risk of Erythroblastosis is 0% for the following combinations

- Rh^{-ve} female x Rh^{-ve} male
- Rh^{+ve} female x Rh^{+ve} male
- Rh^{+ve} female x Rh^{-ve} male

0% } **HDN**

Extra chromosomal inheritance

Inheritance due to genes located in cytoplasm (plasmagenes) is called cytoplasmic inheritance.

(Or)

The Transmission of characters controlled by plasma genes is called Cytoplasmic Inheritance or Extra Chromosomal Inheritance. Described by Correns in 1908.

Since genes governing traits showing cytoplasmic inheritance are located outside the nucleus and in the cytoplasm, they are referred to as plasmagenes.

Plasmogenes are Self-replicating and transmitted by cytoplasm only.

The off springs receive Cytoplasm only from female gamete, not frommale gamete. As a result, Cytoplasmic inheritance is known asMaternal Inheritance (Plasma genes of female parent alone arecontributed to the off springs)

Example 1: Kappa particles in Paramecium

Sonneborn (1938) described the inheritance of some cytoplasmic particles known as Kappa and their relation to nuclear gene in paramecium.

There are twostrains in Paramecium one is Killer and the other is sensitive.Killer Strain produces toxic substance***Paramecin***, which kills the othertype.

Production of ***Paramecin*** in killer type controlled by cytoplasmic Particles "Kappa".

Sensitive Strain lacks Kappa Particles.

The Kappa Particles pass from one generation to other during cell division.

These particles also multiply during division & transmitted throughCytoplasm.

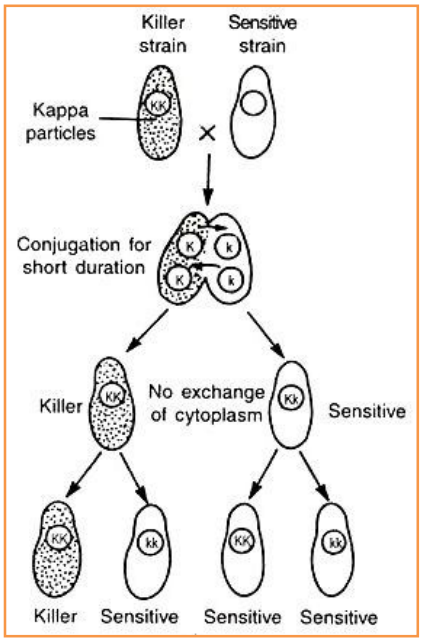
The multiplication of Kappa particles is controlled by dominant nucleargene "K" can only maintain Kappa particles but cannotinitiate its production.

When killersKK conjugate with non-Killers kk, the ex-conjugants are Kk

The development of particular type depends on the ***duration ofCytoplasmic exchange***.

In normal case of Conjugation, the nuclearmaterial alone is exchanged & there is no exchange of Cytoplasmicmaterial.

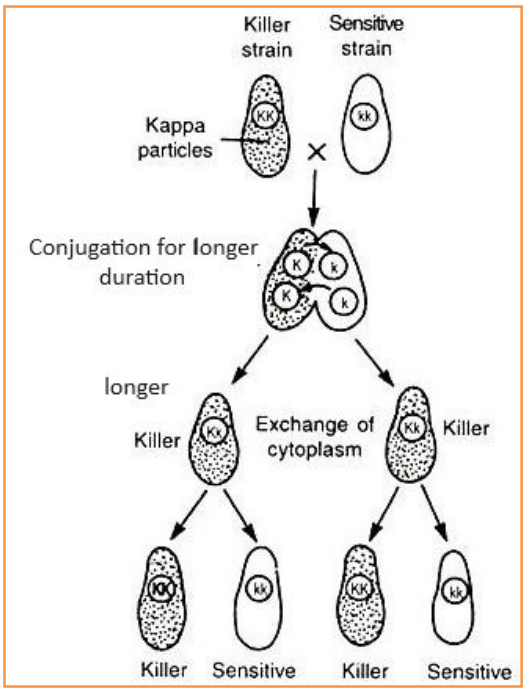
In such cases, each ex conjugant gives rise to the one killer strain and three sensitive strains.



Sometimes the conjugation period is prolonged & cytoplasmic bridge between the two conjugant is larger.

In such cases, in addition to the nuclear material, thecytoplasmic material is also exchanged. During this time, the Kappa particles present in the cytoplasm of the killer type enter the non killer type & convert it into killer type. Hence, the offspring produced bythe ex conjugates are killer type.

This shows that Paramecium becomes a killer, when it receives Kappaparticles & it becomes sensitive when it does not receive Kappa Particles.



Example 2: Shell coiling in snails

In Snail Shell coiling is of two types

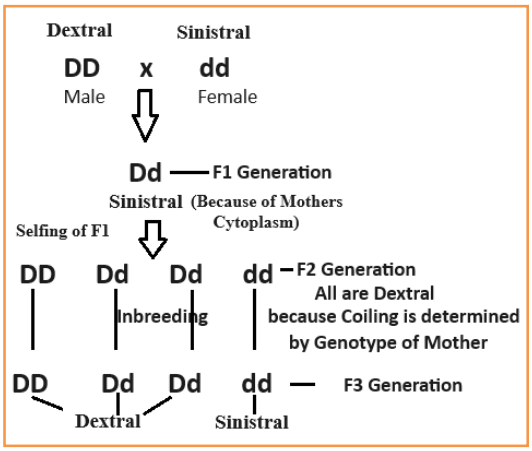
i. Dextral: Shell coiling is clockwise (towards right)

ii. Sinistral: Shell is coiled is anticlock wise (Towards left)

Shell coiling is determined by a pair of nuclear genes. Derxtral coiling is shown by DD or Dd and sinistral by dd. Because D is dominant over d

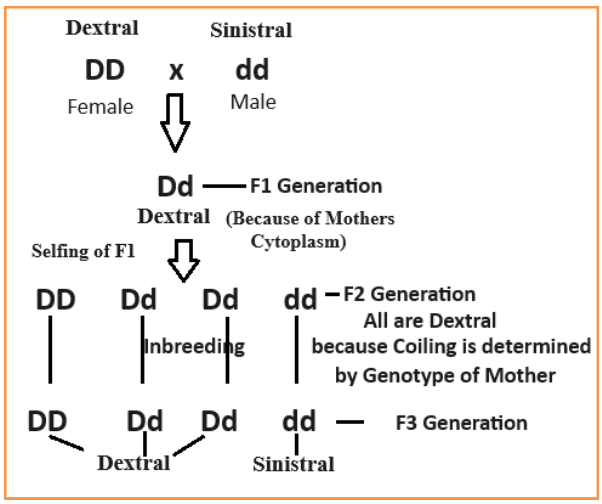
character of Coiling is determined by the gene of mother and not by the individual's own gene.

Cross between Sinistral female and Dextral Male



This maternal effect lasts only forone generation because for next generation Phenotype is determined by the Genotype i.e. 'Dd' in F1and 'dd' in F2.

Cross between Female Dextral (DD) and Male Sinistral (dd)



Unit-IV

***** Sex determination *****

Sex determination is the process of sex differentiation by which whether a particular individual will develop into male or female sex.

In unisexual animals, chromosomes are of two types, viz., autosomes and allosomes.

- **Autosomes -** Chromosomes which do not differ in morphology and number in male and female.
- **Allosomes or sex chromosomes**- Chromosomes which differ in morphology and number in male and female and contain genes that determine sex (XX Female; XY Male).
- Male and female reproductive organs are found in the different individuals is called as ***monoecious/ bisexual/ hermaphrodite s***(Nematodes and Earthworm).
- In some animals male and female reproductive organs are present in differentorganisms is called as***Dioecious***(Humans and other mammals)

Mechanism of Sex determination

Three important mechanisms:

I) Chromosomal sex determination

II) Environmental sex determination

III) Hormonal sex determination

(I) Chromosomal sex determination:

Three types of chromosomal sex determination:

(a) Sex determination by allosomes

(b) Diploid-haploid system of sex determination

(c) Genic balance system.

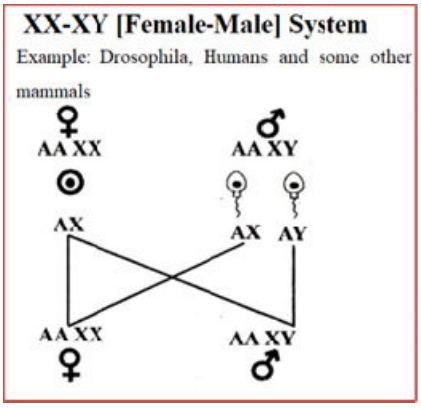
(a) Allosomal Sex Determination

- Allosomes or sex chromosomes are generally of X and Y types, but in some birds, they are of Z and W types.
- Sex with similar type of sex chromosomes (XX) is known as homogametic sex and with dissimilar type of sex chromosomes (XY) as heterogametic sex.
- There are four different types of allosomal sex determination systems:

1. XX-XY [Female-Male] System

(Drosophila, Humans and some other mammals)

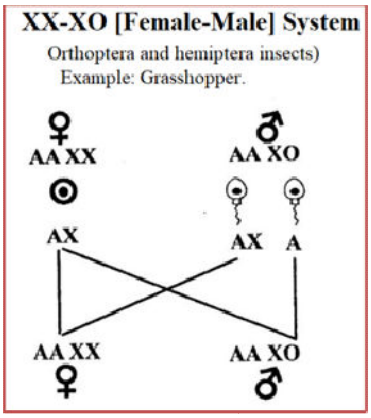
- In this system female has two X- chromosomes, is homogametic and produces only one type of gamete, i.e. X.
- The male has one X and one Y-chromosome, is heterogametic and produces two types of gametes, viz., Xand Y.
- Union of X ovum with X sperm leadsto development of female (XX) sex.
- If X ovum units with Y sperm, it produces male (XY) sex.



2. XX-XO [Female-Male] System

(Grasshoppers and many orthoptera insects and Hemiptera)

- In this system, female has double Xchromosomes (XX) and male has single Xchromosome (XO).
- Female is homogametic and produces all the eggs with X chromosome.
- The male is heterogametic, which produces sperms half of which have X chromosome and other half have none.
- Union of egg with sperm having X-chromosome will give rise to female sexand with sperm having none results in development of male sex.

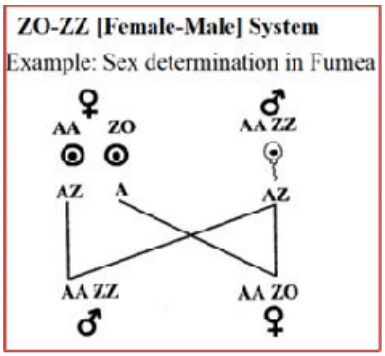


3. ZO-ZZ [Female-Male] System

(Very few species of insects like ***Fumea***)

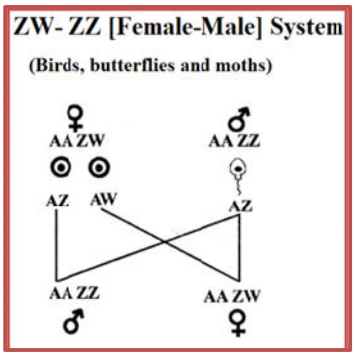
- In this system, female has only one X-chromosome and hence is heterogametic.

- As a result of meiosis, 50% eggs of suchfemale carry an X chromosome andremaining 50% have none.
- On the other hand, male has two Xchromosomes and produces the entire spermswith one X chromosome. Thus, male sex is***homogametic.***
- Union of X sperm with ovum having X-chromosome gives rise to male sex andunion of X sperm with ovum having noneleads to development of female.



4. ZW- ZZ [Female-Male] System (Birds, butterflies and moths)

- Female is heterogametic and produces two types of gametes - Z and W types.
- Male is homogametic and produces all the sperms of same type carrying one Z chromosome.
- Union of Z sperm with ovum having Z chromosome gives rise to male and union of Z sperm with ovum carrying W chromosome leads to the development of female sex.



Genic Balance Theory of Sex Determination

- Calvin. Bridges experiments demonstrated that Y-chromosome is not importantfor determination of sex in Drosophila. Instead autosomes play some role in sex determination.
- Bridges in the year 1922 came across certain Drosophila individuals which were TriploidFemales and has 3 sets of chromosomes (3A + XXX). These triploid individuals were found tobe normal females.
- He crossed them with normal diploid males (2A + XY). From this cross he found normaldiploid males and females, superfemales, supermales and intersexes.
- The presence of Triploid intersexes (3A + XX) proves that autosomes also play role in sexdetermination.
- According to this theory the ratio between number of X-chromosomes and number ofcomplete sets of autosomes will determine the sex.
- The X-chromosome believed carry female tendency genes while autosomes carry male tendency genes.
- X/A ratio determines maleness and femaleness in Drosophila.

If X/A ratio is -

- <0.5 -Meta male/Supermale (Sterile)
- = 0.5 - Normal male (Fertile)
- Between 0.5 and 1.0 - Intersex/ Gynandromorphs (Sterile).
- = 1.0 - Normal Female (Fertile)
- >1.0 - Meta female/ Superfemale (Sterile)

Chromosome Complement	X / A Ratio	Sexual Morphology
X XX + 2A	3/2 or 1.5	Metafemale
X XX + 3A	3/3 or 1.0	Female
XX + 2A	2/2 or 1.0	Female
X X + 3A	2/3 or 0.67	Inter sex
X XX + 4A	3/4 or 0.75	Inter sex
XO + 2A	1/2 or 0.5	Male
XY + 2A	1/2 or 0.5	Male
XY + 3A	1/3 or 0.33	Metamale

Hormonal sex determination

- Another classical example of hormonal control of sex determination has been found in cattles.
- In cattle, when twin calves of different sexes occur, the female member is usually a sterile intersex called a ***freemartin***. The freemartin has external female genitalia but internal sex organs are more or less like those of male. The male twin is usually normal.
- In birds only one gonad of a normal female develops into a functional ovary. The other gonad remains rudimentary. If the functional ovary of a hen is destroyed, the rudimentary gonad develops into a testis **(Crew, 1923).** Thus, the female sex is reversed into male sex due to the phenomenon called sex reversal.

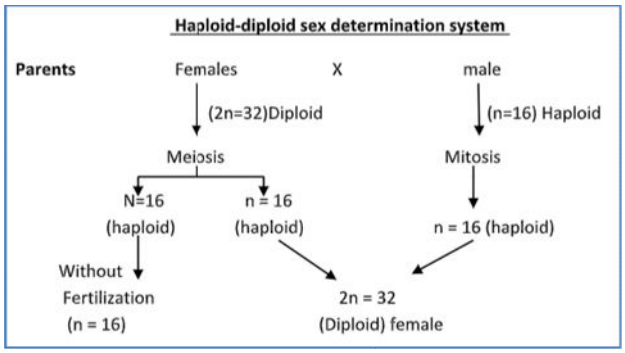
Environmental Sex Determination

- Sex determination in some organisms such as sea worm (***Bonellia and Dinophilus***) is governed by environmental conditions and also includes some hormonal effects.
- All larvae of ***Bonellia*** are genetically and cytologically similar. The males live as parasites in the uterus of the females. The larvae which remain free in the sea water and settle on the sea bottom are differentiated into females while those larvae which settle on the proboscis of female develop into tiny males (***F. Baltzer***, 1935). Further, if incompletely developed male is detached from the proboscis of female, it becomes an intersex.
- **Temperature:** In turtle, Alligators and Crocodiles incubation temperature determines the sex of the eggs. If incubation temperature of egg is high (30-35ºC) the egg develops into Female. If it is low (23-28ºC) egg is develops as male.

Haplo-Diploid (Male-Female) System

(Honey bees, ants and termites)

- In honey bees, the females have diploid (2n = 32) chromosomes and drones or males have haploid (n= 16) chromosomes.
- Females are queen and workers.
- The females which feed on royal jelly develop into queen. The queen is fertile and workers are sterile females.
- The queen produces haploid eggs. However, haploid male bees produce haploid sperms by mitosis rather than by meiosis. Union of egg with sperm gives rise to diploid larvae which become female.



SEX- LINKED INHERITANCE

Inheritance of a trait (phenotype) that is determined by a gene located on one of the sex chromosomes.It was discovered by T. H. Morgan in 1910.

Types of sex-linked Inheritance

Sex-linked inheritance is of three types.

1. **X-linked inheritance:**

The phenotypes controlled by X-linked genes are called X-linked characters and inheritance is called X-linked inheritance.

a) Dominant X-linked inheritance:

- Both the homozygous dominant and heterozygous individuals are affected; only the homozygous recessive individuals are normal.
- Carriers are not possible because heterozygous individuals are phenotypically affected.

Examples: -

1. Constitutional thrombopathy (delayed blood clotting due to reduced number of platelets)
2. Hypophosphatemia – (Vit-D resistant rickets)
3. Defective enamel-fragile teeth

b) Recessive X-linked inheritance:

- Since males have single X-chromosome and the females have two X-chromosomes, X-linked trait is more common in one sex compared to another.
- X-linked dominant traits are more frequently expressed in females. Whereas X-linked recessive traits are more common in males.
- Male to male transfer from one generation to another is not possible because a male contributes only Y-chromosome to his son. Whereas X-chromosome is derived from the mother's gamete.
- Criss-cross pattern of inheritance is exhibited by X-linked traits
- Both the homozygous dominant and heterozygous individuals are normal but homozygous recessive individuals are affected.
- Heterozygous individuals are phenotypically normal but contain the recessive allele and hence are called carriers. In case of autosomal traits both the males and females can act as carriers, but in case of X-linked traits only the females can act as carriers.
- Some of the generations will not exhibit a recessive trait (heterozygosity) and as a result skipping of generations is commonly seen.

Examples-

1. **Red- Green colour blindness**- failure to recognise various shades of red/ green colour
2. **Haemophilia** – delayed blood clotting due to defective in blood clotting factors
3. **Duchenne's muscular dystrophy**- defective protein Dystrophin, degeneration of muscles.

2. Y-linked inheritance-

- Genes that control body characters are located on Y chromosomes, are called as Y-linked genes.
- The Y -linked genes are confined to males only, hence they called as ***Holandric genes***.
- Their mode of inheritance is called Y -linked inheritance.
- The transmission of characters is directly from father to the son.

Examples- 1. Hypertrichosis, Ichthyosis hysterix, etc.

3. XY Linked inheritance:

- Genes that control body characters are located on X chromosome and Y chromosomes both are called as XY -linked genes.
- The phenotypes controlled by XY -linked genes are called XY -linked characters and inheritance is called XY -linked inheritance.
- These homologous region on X and Y chromosomes are called ***Pseudo Autosomal Regions*** (PARs).
  - There are two pseudo autosomal regions; PAR1 and PAR2.
  - Their mode of inheritance is called XY -linked inheritance.
  - XY -linked genes located on PARs follow autosomal inheritance.

Examples- Xeroderma pigmentosum, Nephritis, Retinitis pigmentosa, etc.

Unit-V

Human karyotyping

Karyotyping is a laboratory technique used to visualize an individual's complete set of chromosomes. It

involves arranging and photographing chromosomes to detect abnormalities in number, structure, and form.

Karyotyping is commonly used in diagnosing genetic disorders, understanding chromosomal abnormalities, and in prenatal testing.

A **karyotype** is the characteristic number, size and shape of chromosomes of a species. A **karyogram** is a photographic representation of these chromosomes stained and arranged in order. An ***idiogram*** is a diagrammatic representation or interpretive drawing of the chromosomes based on the physical features seen in the karyogram. The karyotype of normal humans is 46. Human autosomal chromosomes are divided into seven groups (*Table*) on the basis of their sizes and the positions of their centromeres.

Chromosome Group	Chromosome Numbers	Description
A	1 to 3	Long Metacentric
B	4 to 5	Long, Submetacentric
C	6 to 12, X	Medium Submetacentric
D	13 to 15	Medium, Acrocentric
E	16 to 18	Short, Submetacentric
F	19 to 20	Short, Metacentric
G	21 to 22	Very short Acrocentric

- **Procedure**

a) **Sample Collection:** Karyotyping usually requires a sample of cells, which can be obtained from blood, amniotic fluid, or bone marrow.

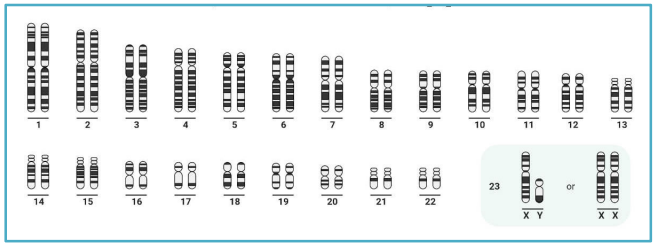
b) **Cell Culture:** The collected cells are cultured to encourage them to divide, as chromosomes are most visible during cell division (metaphase).

c) **Chromosome Staining:** Cells are stained using a technique like Giemsa staining (G-banding), which produces a pattern of light and dark bands unique to each chromosome.

d) Microscopic Analysis: A microscope is used to photograph the stained chromosomes, which are then arranged in pairs according to size, banding pattern, and centromere position.

- **Karyotype Interpretation:**

Normal Karyotype: A normal human karyotype contains 46 chromosomes, arranged in 23 pairs, including 22 pairs of autosomes and 1 pair of sex chromosomes (XX for females, XY for males).



Abnormal Karyotype:

Abnormalities in a karyotype can include:

Aneuploidy: Extra or missing chromosomes (e.g., Down syndrome with an extra chromosome 21).

Structural Abnormalities: Deletions, duplications, translocations, or inversions of chromosome segments.

Clinical Applications:

Prenatal Testing: Karyotyping is used in prenatal diagnosis to detect chromosomal abnormalities such as Down syndrome, Edwards's syndrome, or Turner syndrome.

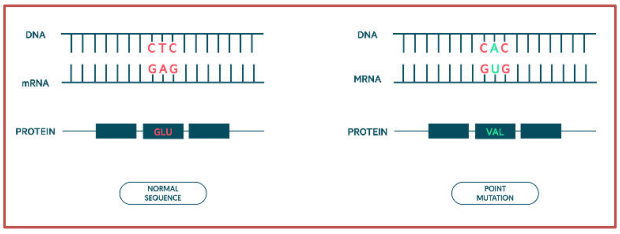
Cancer Diagnosis: Certain cancers, like leukemia, are associated with specific chromosomal abnormalities that can be detected through karyotyping.

Infertility and Miscarriages: Karyotyping can identify chromosomal causes of infertility and recurrent miscarriages.

Sickle Cell Anemia

Genetic mutation:

Sickle haemoglobin is due to a ***point mutation in the beta-globin gene*** located on chromosome 11. A point mutation refers to a single base substitution. In sickle haemoglobin, this affects the sixth amino acid that causes the amino acid glutamic acid to be converted to valine.



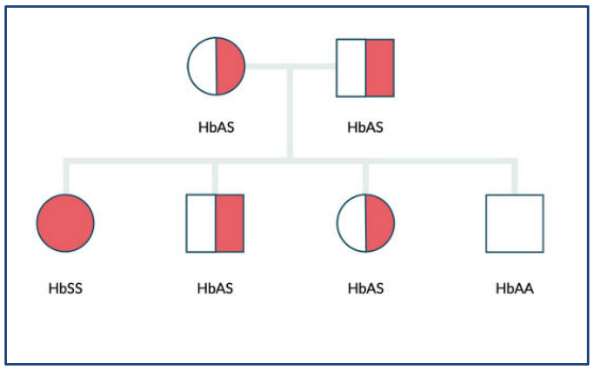
Inheritance

Sickle haemoglobin is inherited in an autosomal recessive pattern. Inheritance of two abnormal sickle haemoglobin genes is known as sickle cell anaemia and patients are homozygous (e.g. HbSS).

1. Causes: Sickle cell anemia is an autosomal recessive genetic disorder caused by a mutation in the HBB gene, which encodes the beta-globin subunit of hemoglobin. This mutation leads to the production of abnormal hemoglobin known as hemoglobin S (HbS). Under low oxygen conditions, HbS polymerizes, causing red blood cells to assume a characteristic sickle shape. These sickle-shaped cells are less flexible, can block blood flow in small vessels, and have a shorter lifespan, leading to various complications.

2. Inheritance Pattern:

- **Autosomal Recessive Inheritance:** Sickle cell anemia follows an autosomal recessive inheritance pattern. This means that a person must inherit two copies of the mutated HBB gene (one from each parent) to develop the disorder.



- **Carrier State (Sickle Cell Trait):** Individuals with only one copy of the mutated gene (heterozygotes) are carriers and typically do not show symptoms but can pass the mutated gene to their offspring.

3. Modes of Testing:

- **Newborn Screening:** Most countries with high prevalence of sickle cell disease have mandatory newborn screening programs. A blood test can detect abnormal hemoglobin.
- **Hemoglobin Electrophoresis:** This test identifies the different types of hemoglobin in the blood, helping to diagnose sickle cell anemia.
    - **Genetic Testing:** DNA analysis can confirm mutations in the HBB gene, useful for prenatal diagnosis or carrier screening.
    - **Prenatal Testing:** Procedures like chorionic villus sampling (CVS) or amniocentesis can detect sickle cell disease in a fetus.

4. Treatment:

- **Pain Management:** Painful crises, a common symptom, are managed with painkillers, hydration, and sometimes oxygen therapy.
- **Hydroxyurea:** This medication increases the production of fetal hemoglobin (HbF), which reduces the frequency of sickling crises.
- **Blood Transfusions:** Regular transfusions can treat or prevent complications such as stroke or severe anemia.

- **Bone Marrow or Stem Cell Transplantation:** The only potential cure for sickle cell anemia, though it is not widely available and carries risks.
- **Gene Therapy:** Experimental treatments are being developed to correct the defective gene responsible for sickle cell anemia.

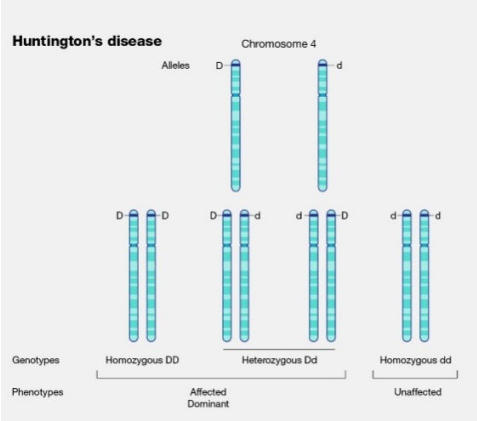
5. Prevention:

- **Genetic Counseling:** Couples with a family history of sickle cell anemia can receive genetic counseling to understand their risk of having a child with the disease.
- **Prenatal Testing:** Testing during pregnancy can inform parents if the fetus has sickle cell disease or is a carrier.
- **Carrier Screening:** Individuals in populations with a high prevalence of sickle cell trait can be screened before conception to assess their risk of having an affected child.

Huntington disease

Cause: Huntington's disease (HD) is an autosomal dominant genetic disorder caused by a mutation in the HTT gene, leading to abnormal expansion of CAG trinucleotide repeats.

Inheritance: HD is inherited in an autosomal dominant pattern, meaning each child of an affected parent has a 50% chance of inheriting the disorder.



Symptoms:

- **Motor:** Involuntary movements (chorea), muscle rigidity, and balance problems.
- **Cognitive:** Memory loss, impaired judgment, and difficulty concentrating.
- **Psychiatric:** Depression, mood swings, and irritability.

Diagnosis: Confirmed through genetic testing to identify the number of CAG repeats in the HTT gene. Neurological exams and brain imaging can also assist in diagnosis.

Treatment: No cure; treatment focuses on managing symptoms with medications for motor and psychiatric symptoms, as well as physical, occupational, and speech therapy.

Prevention: Genetic counseling and prenatal testing options like preimplantation genetic diagnosis (PGD) can help at-risk couples make informed decisions.

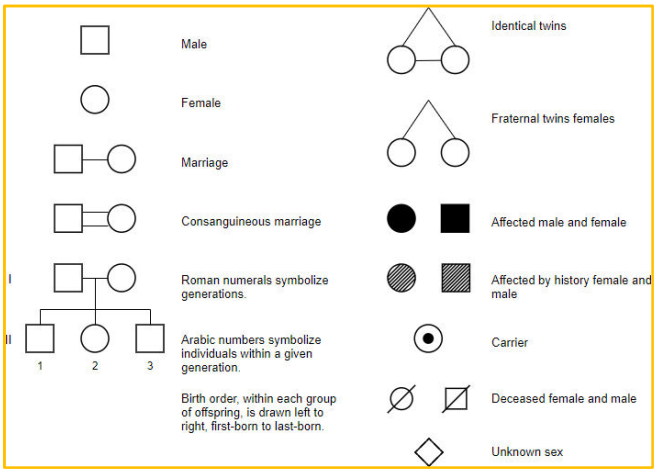
Pedigree Analysis (basics):

The study of Mendelian genetics in humans is difficult due to the following reasons

- Controlled hybridization experiments and random mating is not possible in humans or difficult to perform.
- The generation time needed from one generation to the next generation is relatively large (16-20 years) and as a result it is not possible to carry out the studies for more than three generations in once life time.
- Hence the one way of studying Mendelian genetics in humans is to carryout pedigree analysis.
- **FALANI** was the first to carry out pedigree analysis in humans.
- A pedigree analysis involves the analysis of family ancestry with respect to given trait.
- A pedigree chart is the symbolic representation of a family ancestry with respect to a genetic trait

- A pedigree analysis can be carried out by a genetic counselor or Eugeneticist
- The individual who had first approached the genetic counselor with respect to pedigree analysis is called the ***'PROBAND'***.
- A female proband is '***PROPOSITA'***; male proband is '***PROPOSITUS'***

Fig: Common Symbols used in pedigree analysis



Genomics and Proteomics

Genomics:

Genome: The total DNA (genetic information) contained in an organism or a cellis regarded asthe genome. Thus, the genome is the storehouseof biological information. It includes thechromosomes in the nucleus and the DNA inmitochondria, and chloroplasts.

Genomics: The study of the structure andfunction of genome is genomics.

Functional genomicsis used to represent thegene expression and relationship of genes withgene products.

Structural genomics refers to the structural motifs and complete protein structures.

Comparative genomics involves the study ofcomparative gene function and phylogeny.

Metagenomics refers to the study of genomes ofwhole communities of microscopic life (microorganisms, viruses).

Applications:

- To understand and finds cures for diseases.
- To study genetic variability in human population
- The study of whole sequence data helps in Identification of
    - Open reading frames
    - Gene splicing sites (Introns)
    - Gene annotation

Proteomics

Genome function can be studied at the translation level as well as the transcription level. The entire collection of proteins that an organism produces is called its ***proteome***. Thus proteomics is the study of the proteome or the array of proteins an organism can produce.

Much of the research in this area is referred to as functional proteomics.

It is focused on determining the function of different cellular proteins, how they interact with one another, and the ways in which they are regulated.

- ***Expression proteomics-*** is a novel approach that studies the quantitative and qualitative expression of proteins.
- ***Structural proteomics-***determine the three-dimensional structure and structural complexities of functional proteins.
- ***Functional proteomics-*** This type of proteomics studies the protein functions and molecular mechanisms in the cell and determines the protein partner's interactions.

Methods used in proteome analysis:

- Two-dimensional gel electrophoresis
- SDS polyacrylamide gel electrophoresis (SDS-PAGE)

Applications:

Personalized medicine: Disease treatment to each patient based on their genetic and epigenetic makeup, so as to improve efficacy and reduce adverse effects. **Biomarker discovery:**

Identification of protein markers for e.g., the diagnosis and prognosis of glioblastoma, and evaluating patients' response to therapeutic interventions such as stem cell transplantation.

Drug discovery and development: Identifying potential drug targets, examining the drugability of selected protein targets.

Systems biology: System-wide investigations of disease pathways and host–pathogen interactions to identify potential biomarkers and therapeutic targets.

Agriculture: Investigations of plant–pathogen interactions, crop engineering for increased resilience to e.g., flooding, drought and other environmental stresses.

Food science:Food safety and quality control, allergen detection and improving the nutritional value of foods.

Paleoproteomics: The study of ancient proteins to further our understanding of evolution and archeology.

Astrobiology: Investigations of how mammals' immune systems may respond to exomicrobes found in space and studies of the prebiotic organic matter found on meteorites.