Chapter 5: Principles of Inheritance and Variation

"**Genetics is the study of heredity and variation**".

Heredity: Inheritance of characters from generations to generation is called heredity.
Variation: The change in the hereditary characters is called variation. Variations are the raw materials for evolution.

Terminologies

1. Gene: "***Gene is a unit of heredity***". Gene is a segment of DNA that codes for the synthesis of a polypeptide chain or protein and their by control a character.
2. Alleles: A pair of genes occupying a same locus on homologous chromosomes and controlling a single or contrasting character.
3. **Locus**: It is the position occupied by a gene on chromosome.
4. **Homologous chromosome:** Two identical chromosomes in a diploid organism is called homologous chromosome.
5. Phenotype: The external morphological appearance of a character is called phenotype.
6. Genotype: The genetic makeup or genetic constituent of phenotypic character is called genotype.
7. Dominant: When two different alleles are together, one of the allele express its character by suppressing another allele is called dominant. It is represented by capital letter (T).
8. Recessive: The allele which is suppressed by the dominant allele is called recessive and it is represented by small letter (t).
9. Homozygous: When a character is controlled by two identical alleles is called homozygous (TT or tt).
10. Heterozygous: When a character is controlled by two different alleles is called heterozygous (Tt). Heterozygous condition can produce two types of gametes.
11. Incomplete dominance: When two different alleles are together, neither one of the allele is fails to become complete dominance and they produce intermediate character.
12. Co-dominant: When two different alleles are together, both the alleles express their character side by side.
13. Hybrid: It is the progeny or offspring obtained by crossing two parents.
14. Monohybrid: It is the made between two parents in respect to a single character.
15. Dihybrid: It is the cross made between two parents with respect to two character
16. Test cross: It is the cross made between F1 hybrids with its double recessive parent to confirm homozygous or heterozygous condition ofF1hybrids.
17. Back cross: It is the cross made between F1 hybrids with any one of its parents.
18. F1 Generation: It is the hybrid obtained as a first filial generation after crossing two parents.

Mendel's Laws of Inheritance

Gregor John Mendel was born in 1822 in a village called Heinzendorf of Czechoslovakia. He conducted breeding or hybridization experiments on garden pea plants, *Pisum sativum*. He conducted experiments between 1856 to 1864 and postulated two laws such as i) **Law of segregation** ii) **Law of Independent Assortment**. He published the results of the experiments in a scientific journal "**Annals of proceedings of Natural History Society of Brunn**" in 1866. But the work of Mendel was not recognized and he died in 1884.

In 1900, Mendel's principles were rediscovered by three scientists namely, Hugo de Vries of Holland, Karl Correns of Germany and Tschermark of Austria. Since then Mendel is regarded as **Father of Genetics**.

Mendel has chosen garden pea plants for the experiments because of several reasons.

a) The plants are annuals so that one can get the results quickly within one year.
b) The plants are both self and cross pollinating.
c) The plants exhibit several contrasting characters.
d) Handling and growing of these plants is easier and economical.

Mendel has chosen seven contrasting characters from pea plants for the experiment.

Characters	Contrasting characters
1. Height of the plant	Tall and Dwarf
2. Colour of the seed	Yellow and Green
3. Shape of the seed	Round and Wrinkle
4. Colour of the pod	Green and Yellow
5. Shape of the pod	Inflattened and Constricted
6. Colour of flower	Violet and White
7. Position of the flower	Axillary and Terminal

Mendel's proposition:

a) Mendel proposed that something was being stably passed down, unchanged, from parent to offspring through the gametes, over successive generations.
b) He called these materials as **'factors'.**
c) Now a day we call them as **genes.**
d) Gene is therefore are the **units of inheritance.**
e) Genes which codes for a pair of contrasting traits are known as **alleles,** i.e. they are slightly different forms of the same gene.

Law of Dominance:

1) Characters are controlled by discrete units called factors.
2) Factors occur in pairs.
3) In a dissimilar pair of factors one member of the pair dominates (dominant) the other (recessive).

Inheritance of "ONE GENE"

Law of Segregation or Purity of gametes or Monohybrid cross

"When the alleles for two contrasting characters are brought together in F_1 generation, they separate or segregate in F_2 generation during the formation of gametes".

When a tall plant is crossed with dwarf plant, all the F_1 hybrids are tall. Because tall is dominant. When the F_1 hybrids are self crossed, in the F_2 generation there are $3/4^{th}$ (75%) of the plants are tall and $1/4^{th}$ (25%) of the plants are dwarf in the ratio of **3:1**. The genotypic ratio is **1:2:1** where $1/4^{th}$ of the progenies are homozygous tall (**TT**), ½ of the progenies are heterozygous tall (**Tt**) and $1/4^{th}$ of the progenies are homozygous dwarf (**tt**). The 1/4 : 1/2 : 1/4 ratio of (1:2:1) TT:Tt:tt is mathematically condensed to the form of the binomial expression $(ax + by)^2$, that has the gametes bearing genes T or t in equal frequency of ½. The expression is expanded and given as: **$(1/2T + 1/2\ t)^2 = (1/2T + 1/2t) \times (1/2T + 1/2t) = 1/4TT + 1/2Tt + 1/4tt$**.

In these crosses all the gametes produced are carrying a single allele without mixed or contaminated with another allele. Therefore gametes are said to be pure. Hence law of segregation is also called as '**Purity of Gametes**'.

Parents : Tall x Dwarf

Genotype : TT tt

Gametes : T t

F_1 generation : Tt

Tall

Self Cross

F_1 x F_1

Tt Tt

T t T t

	T	**t**
T	TT	Tt
t	Tt	tt

F_2 generation : TT, Tt, Tt, tt

Tall Dwarf

Phenotype ratio: **3 : 1**

Genotype ratio: **1 : 2 : 1**

Test cross

It is the cross made between F_1 hybrids with its double recessive parent to confirm that the F1 hybrids are homozygous or heterzygous. When the test cross is conducted, 50% of the plants are tall and other 50% of the plants are dwarf in the ratio of 1:1. This confirms that F_1 hybrids are heterozygous.

Test Cross

F_1 x drp

Tt tt

T t t t

Tt tt

Tall Dwarf

1 : 1

Inheritance of Two Genes / *Law of Independent Assortment* or *Dihybrid Cross*

"When the alleles for more than two contrasting characters are brought together in F_1 hybrids, they assort independently by one another in F_2 generation during the formation of gametes".

When a plant producing round and yellow coloured seeds is crossed with a plant producing wrinkle and green coloured seeds, all the F_1 hybrids produce round and yellow coloured seeds. This indicates that, alleles for yellow (Y) is dominant over green (y) and allele for round (R) is dominant over wrinkle (r).

When the F_1 hybrids are self crossed to obtain F_2 generation, all the four types of plants are obtained such as **round yellow (9), round green (3), wrinkle yellow (3) and wrinkle green (1)** in the ratio of **9:3:3:1** (phenotypic ratio). The genotypic ratio is **4:2:2:1:2:1:2:1:1**.

When the test is conducted between F1 hybrids with its double recessive parents, all the four types of plants such as Round yellow, Round green, Wrinkle yellow and Wrinkle green are obtained in the ratio of **1:1:1:1:1**. This confirms that F_1 hybrids are heterozygous.

Parents: Round x Wrinkle
Yellow Green

Genotype: RRYY rryy

Gametes: RY ry

F_1 generation: RyYy
Yellow

Self Cross

F_1 x F_1

RrYy RrYy

Gametes: RY Ry RY Ry
rY ry rY ry

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

Round Yellow – 9

Round Green – 3

Wrinkle Yellow – 3

Wrinkle Green – 1

Phenotypic ratio: 9 : 3 : 3 : 1

Genotypic ratio : 4:2:2:1:2:1:2:1:1

Test Cross

F_1 x drp

Genotype: RrYy rryy

Gametes: RY Ry ry
rY ry

RrYy Rryy Rryy rryy

Round Yellow | Round Green | Wrinkle Yellow | Wrinkle Green

1 : 1 : 1 : 1

Incomplete Dominance (Partial dominance or Blending inheritance)

"It is a process in which the dominant gene is incompletely dominant over the recessive gene and produces a phenotype which is intermediate to the parental type".

The phenotype of F1 generation does not resemble either of the two parents and the expression is in between the two. It is noticed in the inheritance of flower colour in the **dog flower** or **snapdragon** (***Antirrhinum*** sps.) is a good example for incomplete dominance. In a cross between true breeding **red** flowered (RR) plant and true breeding **white** flowered (rr) plants, the F1 hybrids produce **pink** coloured flowers (Rr). When the F1 hybrids are self pollinated (self cross), the F2 generation resulted in the ratio of **1 : 2 : 1** [**1Red (RR) : 2 Pink (Rr): 1White (rr)**]. Here the phenotype ratio does not resemble the Mendelian monohybrid cross but the genotype ratio is exactly similar to that of Mendelian monohybrid cross.

Parents : Red x White

Genotype : RR x rr

Gametes : R r

F_1 generation : Rr

Pink

Self cross

F_1 x F_1

Rr Rr

R r R r

F_2 generation : RR, Rr, Rr, rr

Red Pink White

1 : 2 : 1

Codominance

"When the alleles for two contrasting characters are together in heterozygous condition, both the alleles express their character together is called codominance".

Ex: Blood group in man, coat color in rabbit etc.

Multiple alleles: More than two alternative forms of a single gene occupying same locus on the homologous chromosome and control a single character is called multiple alleles.

Karl Landsteiner (1900) classified human blood into four groups such as A, B, AB and O. The blood group of man is determined by two kinds of proteins present in the blood such as antigens and antibodies.

Antigens (Agglutinogens): These are the glycoprotein's (polymer of sugars) present on the membrane of RBC. There are two types of antigens such as antigen A and antigen B.

Antibody (Agglutinins): These are the protein present in blood plasma. There are two types of antibodies present in the blood such as antibody – a and antibody – b.

"Due to immunological response the blood of a man doesn't contains same type of antigen and antibody".

The type of blood group in man is determined by the presence or absence of antibodies or antigens in blood.

Blood Group	Antigen	Antibody
A	A	b
B	B	a
AB	A and B	- Nil -
O	- Nil -	a and b

The following table shows the type of donor and recipient

Donor	Recipient
A	A, AB
B	B, AB
AB	AB
O	A, B, AB, O

'O' blood group is called <u>universal donor</u> and 'AB' blood group is called <u>universal recipient</u>.

Inheritance of blood groups in man

The blood group in man is controlled by 'I' gene which exists in three allelic forms such as I^A, I^B and i.

I^A and I^B are dominant over 'i', I^A and I^B are co-dominant.

Genotypes of Blood groups in man

Blood Group	Genotypes
A	I^AI^A, I^Ai
B	I^BI^B, I^Bi
AB	I^AI^B
O	ii

Problems:

1. Identify the blood group of children whose father is heterozygous A and mother

is homozygous A.

2. Father is homozygous B and mother is AB.

3. Father is heterozygous A and mother is O.

4. Father is homozygous A and mother is homozygous B.

5. Father heterozygous A and mother is heterozygous B.

A single gene product may produce more than one effect:

a) Starch synthesis in pea seeds is controlled by one gene.
b) It has two alleles **B** and **b.**
c) Starch is synthesized effectively by **BB** homozygote and therefore, large starch grains are produced.
d) The **'bb'** homozygous has less efficiency hence produce smaller grains.
e) After maturation of the seeds, **BB seeds** are **round** and the **bb seeds** are **wrinkle.**
f) **Heterozygous (Bb)** produce round seed and so B seems to be dominant allele, but the starch grains produced are of intermediate size.
g) If starch grain size is considered as the phenotype, then from this angle the alleles show incomplete dominance.

Chromosomal Theory of Inheritance

The idea of chromosome theory of inheritance was put forth in the year 1902 by **Sutton** and **Boveri** and was confirmed by **T.H. Morgan** in the year 1933. According to this theory, the material of inheritance (gene) is present on the chromosomes and it is the chromosomes that segregate and assort independently during meiosis and recombine during the process of fertilization.

Chromosomes and genes: Some of the similarities recognized by Sutton and Boveri between Mendel's factors (gene) and the behavior of chromosomes are as follows.

Genes	Chromosomes
1.Occur in pairs	1.Occur in pairs
2.Separate during gamete formation and only one of each pair is present in gamete	2.Separate during gamete formation and only one of each pair is present in gamete

3.Pairs assort independently	3.Pairs assort independently

In a typical dihybrid cross between round yellow and wrinkled green pea, segregation of alleles of two genes (shape and color) located on different chromosomes takes place during gamete formation. It also shows that the paired homologous chromosomes assembled at **metaphase I** can separate in two possible ways. This leads to independent assortment of chromosomes as well as the genes located on them in four possible ways. Thus, four types of gametes are formed in equal proportions, at the end of meiosis, each with half the number of chromosomes and genes. Of the four types, two have parental combinations while the other two are recombinants or new combinations. These gametes give rise to F_2 progeny exhibiting dihybrid phenotypic ratio **9:3:3:1**.

During Anaphase of meiosis I, the two chromosome pairs can align at the metaphase plate independently of each other. To understand this, compare the chromosomes of four different colours in the left and right columns. In the left column (Possibility I) orange and green chromosomes are segregating together. But in the right column (Possibility II) the orange and red chromosomes are segregating together. This results in the formation of four types of gametes. Of the four types, two have parental combinations while the other two are recombinants or new combinations. These gametes give rise to F_2 progeny exhibiting dihybrid phenotypic ratio **9:3:3:1**.

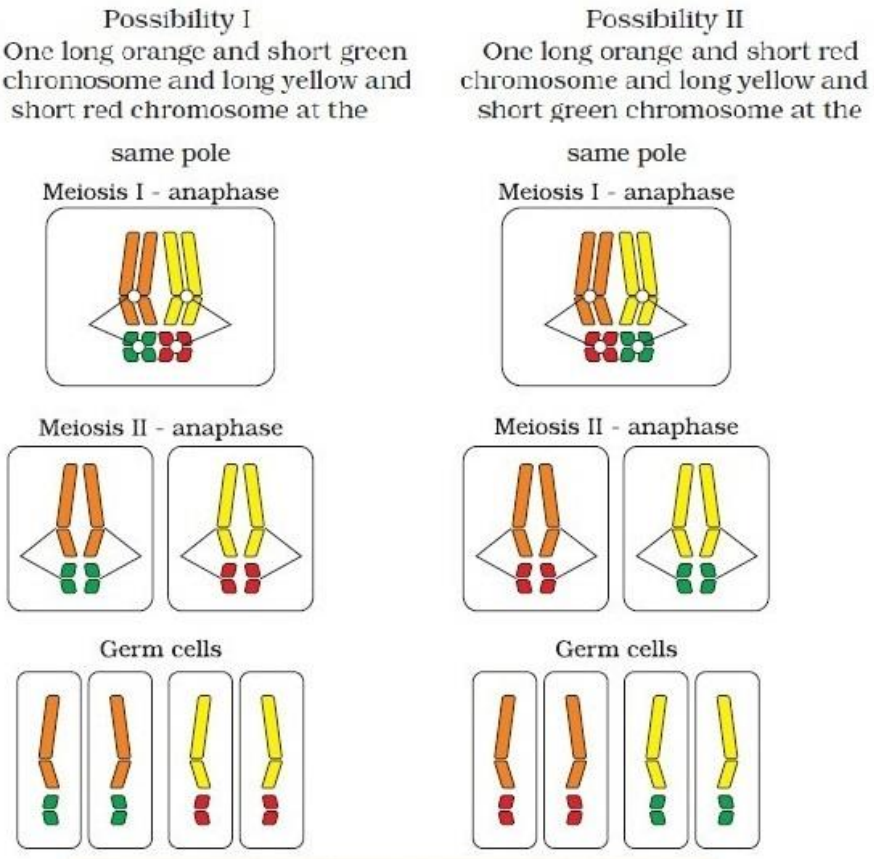


Figure 9. Independent assortment of chromosomes

Chromosomal theory of inheritance was experimentally proved by Thomas Hunt Morgan and his colleagues. Morgan worked with the tiny fruit flies, ***Drosophila melanogaster*** popularly known as "**Cinderella of Genetics**" which were found very suitable for such studies.

- They could be grown easily on synthetic medium in the laboratory.
- They complete their life cycle within 15 days.
- A single mating can produce large number of progenies.

- They exhibit sexual dimorphism i.e., clear differentiation between male and female sexes (males are smaller in size and females are larger).
- Many hereditary variations can be seen in microscopes.
- They have limited number of chromosomes i.e., 2n = 8.

Linkage, crossing over and Recombination

Genetic studies after Mendel revealed that, some of the genes do not follow the law of independent assortment during gamete formation. This is because these genes are present on the same chromosome and are transmitted as a single unit. Hence, presence of two or more genes on the same chromosome are said to be linked genes and their pattern of inheritance is called **linkage**.

Morgan's experiments on linkage

Morgan carried out a dihybrid cross in *Drosophila*. In the cross 'A', he took a normal wild type male with **brown body (y^+)** and **red eye (w^+)** and crossed it with **yellow body (y)** and **white eye (w)** which is a mutant female. In the F_1 generation, all females were wild type (brown body and red eye) while the males expressed both the mutant traits (yellow body and white eye).

When these F_1 females and males were crossed, the F_2 progeny consisted of 98.7% parental type (yellow bodied white eye type and brown bodied red eyed type). The remaining 1.3% consisted of new combinations or recombinants like yellow body and red eye as well as brown body and white eye type.

In the cross 'B', Morgan crossed **white eyed** and **miniature winged female** with normal wild male (**red eye** with **normal wing**). In F1 generation, all females were **wild type** while the males were **white miniature**. When the F1 male and female were crossed the F2 progeny consisted of 62.8% parental type and 37.2% recombinant type. The above observations raised two questions. **How do genes get separated or recombined? And why is the difference in the frequency of recombination in different genes?** Morgan was able to answer both the questions. Genes separated or shifted because of crossing over and the difference in the frequency of recombination depends on the distance between two genes on the chromosome.

Crossing Over and recombination:

It is defined as the "**interchange of chromosomal segments (parts) between non-sister chromatids of homologous chromosomes results in recombination of genes".** It occurs during pachytene stage of prophase I during meiosis while the chromosomes are closely paired. During this stage each chromosome has two chromatids called sister chromatids and the homologous chromosomes have four chromatids (tetrad). The non sister chromatids twisted above one another and there occurs breakage at identical levels and a reattachment of the same portions of the chromatids from homologous chromosomes.

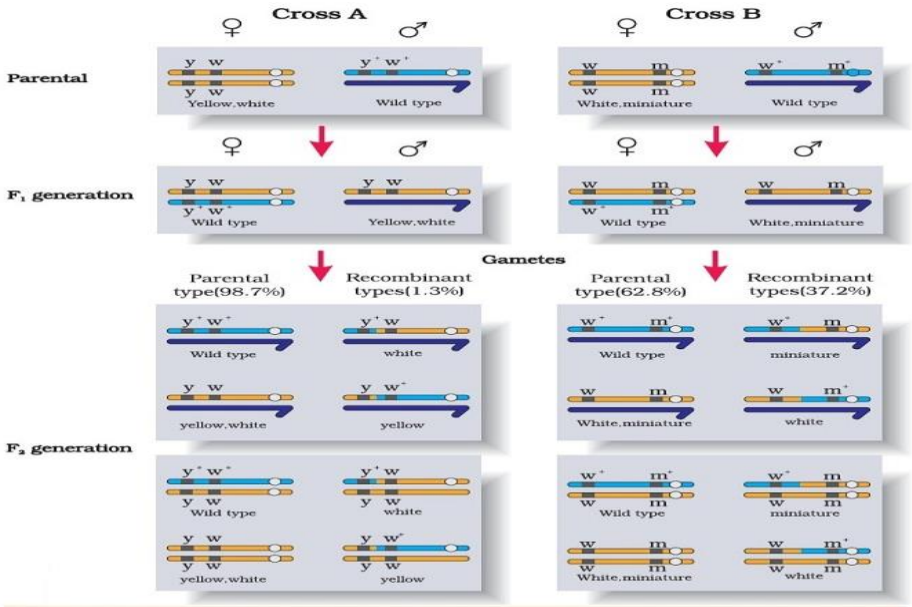


Figure 11. Linkage: Results of two dihybrid crosses conducted by Morgan. Cross A shows crossing between gene y and w; Cross B shows crossing between genes w and m. Here dominant wild type alleles are represented with (+) sign in superscript Note: The strength of linkage between y and w is higher than w and m.

Linkage: "**It is the tendency of two or more genes to remain together in the original combination on the same chromosome during the process of inheritance for generations".** Thus, linked genes occur in the same chromosomes and lie in linear sequence. There are two types of linkages namely complete and incomplete linkages.

a) Complete linkage: "If the two genes are placed close to each other, and are inherited for number of generations" is called complete linkage. Here there is no crossing over and recombination of genes. As a result the young ones inherit only the parental characters. But this condition is very rare.

b) Incomplete linkage: "It is when two genes are placed far apart and they separate due to the breakage of chromosomes (crossing over) during gametogenesis". This leads to the appearance of new combinations.

"The strength of linkage between two genes depends on the distance between the genes on the chromosome".

Sex Determination

The process by which sexuality of an organism is decided is called sex determination. Sex consists of two alternatives male and female. A German biologist, **Henking** (1891) while conducting experiments in the wasp insects noticed that, some wasps had 12 chromosomes and few wasps had 11 chromosomes. Further he observed that the mysterious 12th chromosome looked and behaved differently than the other 11chromosomes. Hence he named the 12th chromosome the **'X body'** to represent its unknown nature. Based on his observations, Henking hypothesized that this extra chromosome, the X body, must play some role in determining the sex of insects.

Types of sex determination

One of the most common methods of sex determination is chromosomal mechanism of sex determination. Here, the sex of an individual is determined by the type of chromosome. Basically, there are two types of chromosomes namely, **autosomes** and **allosomes**.

- Autosomes (Somatic chromosomes) contain genes which determine somatic characters or body characters.
- Allosomes (Sex chromosomes) determines sex of an organism.
- There are two types of sex chromosomes namely, X and Y chromosomes.
- Based on the type of gametes an individual produces in terms of sex, Correns in 1906 put forth a theory called **Theory of heterogamesis**.
- According to this theory there are two types of sex determination mechanisms namely, **male heterogamety** and **female heterogamety**.

1. <u>Male Heterogamety</u>

XX-XY type sex determination

Ex: Drosophila and man

In this type, sex is determined by the presence of 'X' and 'Y' chromosomes. Here the female carries XX chromosomes (homogameteic) and they produce similar types of gametes carrying 'X' chromosome. While the males carry XY chromosome and produce two different types of gametes hence they are called heterogametic. Among the gametes they produce, 50% of gametes carry 'X' chromosome and other 50% of gametes carry 'Y' chromosome.

Parents	Female	Male
	AA + XX	AA + XY
Gametes	A + X	A + X A + Y
Offspring	AA + XX	AA + XY
	Female	Male

XX-XO type of sex determination

Ex: Grasshopper

In this type, the females are homogametic and have 'XX' chromosomes and produce only one type of egg carrying 'X' chromosomes, while the males are heterogametic and have only one 'X' chromosomes without the partner. Hence they produce two types of sperms where 50% of the sperms carry 'X' chromosome with autosomes (A+X) and other 50% of the sperms carry only autosomes but no allosome (A+O).

Parents	Female	Male
	AA + XX	AA + XO
Gametes	A + X	A + X A + O
Offspring	AA + XX	AA + XO
	Female	Male

2. <u>Female Heterogamety</u>

a) ZZ – ZW type of sex determination Ex: Birds

In this type, female is heterogametic (ZW) and the male is homogametic (ZZ). The female produce two types of eggs carrying 'Z' and 'W' chromosomes. Whereas, the male (ZZ) produce only one type of sperm carrying 'Z' chromosome. If the sperm carrying 'Z' chromosome fertilise with the egg carrying 'Z' chromosome the zygote develops into **male.** If the sperm carrying 'Z' chromosome fertilise with the egg carrying 'W' chromosome the zygote develops into **female**.

Parents	Male	Female
	AA + ZZ	AA + ZW
Gametes	A + Z	A + Z A + W
Offspring	AA + ZZ	AA + ZW
	Male	Female

b) ZZ – ZO type of sex determination Ex: Butterfly

In this type, female is heterogametic having ZO chromosomes and the male is homogametic with having ZZ chromosomes. Hence, the female produces two types of gametes (A+Z) and (A+O), whereas, the male produce only one type of gametes (A+Z).

Parents	Male	Female
	AA + ZZ	AA + ZO

Gametes	A + Z	A + Z A + O
Offspring	AA + ZZ Male	AA + ZO Female

Sex Determination in Humans

Sex determination in man is XX-XY type, where male is heterogametic and the female is homogametic. Out of 23 pairs of chromosomes present, 22 pairs of autosomes are similar in both male and female individuals. Regarding sex chromosomes female have XX and male have XY chromosomes. Hence, the chromosome complement of male individual is 44A + XY and that of female is 44A+XX. During spermatogenesis among males, two types of sperms produced such as 50% of the sperms carry X chromosome and other 50% of the sperms carry Y chromosome besides 22 autosomes, hence male is called heterogametic. Females, however, produce only one type of ovum with X chromosome besides 22 autosomes. There is an equal probability of fertilisation of the ovum with the sperm carrying either X or Y chromosome. If the ovum carrying X chromosome fertilise with the sperm carrying Y chromosome, the child will become male. If the ovum carrying X chromosome fertilise with the sperm carrying X chromosome, the child will become female. Thus it is evident that, the genetic makeup of the sperm decides the sex of a child. It is clear that in each pregnancy there is always 50 % probability of either a male or female child. But it is unfortunate that in our society women are blamed for producing female children. With the evident one can say that the sex of a child is determined by the father but not by the mother.

Parents	Female	Male
	AA + XX	AA + XY
Gametes	A + X	A + X A + Y
Offspring	AA + XX	AA + XY
	Female	Male

Mutation: It is defined as*, 'a spontaneous and permanent change in the genetic makeup of an individual'*.

- This change may produce an alteration in the character.
- According to Dobzhansky mutation is a mistake or misprint during cell division.
- Mutations may be caused due to errors during DNA duplication or due to environmental factors like chemicals, radiation etc.
- If these mutant genes are in the somatic cells they may not be of **evolutionary significance**. If they are in the germ cells they are passed on to the next generation and are of **evolutionary significance**.
- Hence mutations are considered as the **raw materials** for evolution.

Types of mutation

a) Gene mutation/point mutation: When the mutation occurs at the gene level is called gene mutation or point mutation. It happens due to change in the nucleotide sequences of a gene (DNA) molecule. For example, in defective haemoglobin, the amino acid glutamic acid is replaced by valine, where GAG codon is altered as GUG codon on mRNA. This results in genetic disorder **sickle cell anaemia**.

b) Chromosomal mutation: It is a kind of mutation caused by the change in the chromosomal number. It could be due to addition or deletion of 1 or 2 chromosomes in the diploid set called **aneuploidy**. The addition of one extra 'x' chromosome results in Klinefelter's syndrome (feminine male), whereas deletion of one 'x' chromosome results in Turner's syndrome (a sterile female).

Pedigree Analysis: "It is an analysis of inheritance of traits or characters for several generations in a family is called the pedigree analysis".

In the pedigree analysis the inheritance of a particular trait is represented in the family tree over generations.

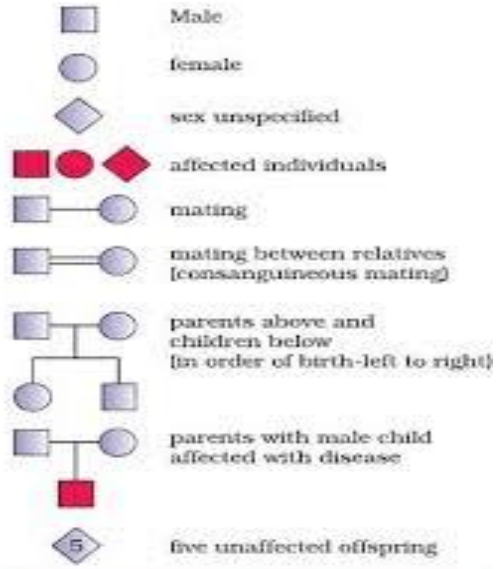
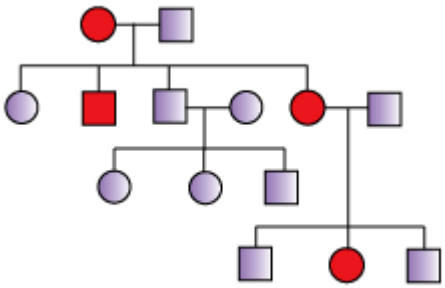


Figure 13. Symbols used in the human pedigree analysis

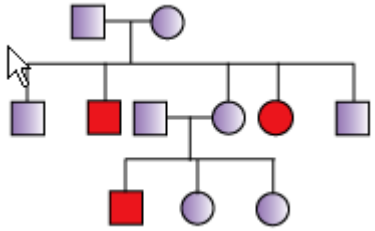
Autosomal Dominant:

- Affected individuals have at least one affected parent
- The phenotype generally appears every generation
- Two unaffected parents only have unaffected offspring
- Traits are controlled by dominant genes
- Both males and females are equally affected
- Traits do not skip generations
- **e.g. polydactyly, tongue rolling ability etc**



Autosomal recessive:

- Unaffected parents can have affected offspring
- Traits controlled by recessive genes and appear only when homozygous
- Both male and female equally affected
- Traits may skip generations
- 3:1 ratio between normal and affected.
- Appearance of affected children from normal parents (heterozygous)
- All children of affected parents are also affected.
- **e.g.- Albinism, sickle cell anemia etc.**



Genetic Disorders: A genetic disorder in human society is studied under a specialized branch called "Human genetics". It is a branch of science that deals with the study of inheritance of characters in humans.

Mendelian Disorders

Mendelian disorders are mainly due to alteration or mutation in the single gene. They are also known as **monogenic diseases**. The pattern of inheritance is very clear and straight forward in them. These disorders are transmitted to the offspring as per the Mendelian principles of inheritance. The pattern of such inheritance can be traced in a family by the pedigree analysis. Most common Mendelian disorders are Haemophilia, Cystic fibrosis, Sickle cell anaemia, Colour blindness, Phenylketonuria, Thalesemia etc. Such Mendelian disorders may be dominant or recessive. Similarly, the trait (character) may also be linked to the sex chromosome as in case of haemophilia. It is evident that, this X-linked recessive trait shows transmission from carrier female to male progeny.

1. Haemophilia

It is also known as bleeder's disease. It takes a prolonged time for clotting due to absence of clotting factors. This results in profuse and prolonged bleeding even from a small wound. It is due to the presence of a recessive gene on X chromosome. Hence it is an example for X-linked inheritance. Therefore, haemophilia is a hereditary disease.

Haemophilia was first reported by **John Conrad Otto** (1803) in the royal family of Europe. Hence haemophilia is also known as **royal disease**. The family pedigree of **Queen Victoria** shows a number of haemophilic descendents as she was a carrier of the disease.

Types of Haemophilia

a. Haemophilia A: It is due to a defective x-linked gene. It is a typical sex linked disease that accounts for 80% of hemophilic cases. The affected individual has least number of **AHF (**Anti Haemophilic Factors**),** clotting factor VIII.

b. Haemophilia B: It is a mild form of disease exhibited by 20% of haemophilics. It is due to a recessive gene present on x chromosome. It is due to the reduction in **PTC (**Plasma Thrombo Plastin Components), clotting factor IX.

c. Haemophilia C: It is a mildest form of haemophilia exhibited by 1% of haemophilics. It is due to the presence of rare autosomal gene which interferes in the production of **PTA** (Plasma Thrombo Plastin antecedents)**.**clotting factor XI.

2. Colour blindness

It is a common X-linked inheritance caused by a recessive gene which prevents development of colour sensitive retina cells in eyes.

Types of colour blind

a. Monochromatism: The affected individuals are totally colour blind and is unable to differentiate colours even in bright light.

***b. Dichromatatism*:** The affected individual is partially colour blind and is unable to differentiate some colours. The most common among them is the 'red and green' colour blindness also called '**Daltonism'**. The red blindness is called protonopia where the individuals see grey instead of red. While the green blindness is called deuteronopia here, the individuals see grey instead of green.

3. Sickle cell anaemia

It is an autosomal disorder due to the presence of a recessive gene. It is an inborn error where the normal biconcave RBC's are transformed into crescent (half moon) or sickle shape. It is due to the production of 'S' haemoglobin which is defective.

The production of normal haemoglobin is controlled by the gene Hb^A, whereas other allele Hb^S controls the production of defective 'S' haemoglobin. When Hb^A occur in homozygous condition (Hb^AHb^A) normal haemoglobin is produced and the person is health. Whereas, persons of Hb^S allele in homozygous condition (Hb^SHb^S) make the person to suffer from chronic haemophilic anemia. It is due to the production of defective 'S' haemoglobin which contain an amino acid **valine** in place of **glutamic acid** in β chain. This defective haemoglobin cannot transfer enough oxygen, such sickle shaped RBC's are not able to move through the smaller blood capillaries that cause an internal bleeding and pain. Such patients become anaemic and die.

If it is heterozygous condition (Hb^AHb^S) both the normal and 'S' haemoglobin are produced and the affected individual will not have severe problem like those of homozygous condition but they suffer from periodic discomfort and develop anemia in higher altitude.

4. Thalassemia

It is an autosomal disorder due to the presence of a recessive gene present of 16^{th} chromosome. This causes the formation of abnormal haemoglobin resulting in anaemia similar to the sickle cell anaemia. The disorder results in destruction of excessive RBC which leads to anaemia. Haemoglobin is made up of two chains namely α chain and β chain and controlled by two individual genes. Thalassemia can be classified according to which chain of haemoglobin is affected. Thalassemia differs from sickle cell anaemia in that the former is a quantitative problem of synthesizing few globin molecules while the latter is a qualitative problem of synthesizing an incorrectly functioning globin.

Types of Thalassemia

i. α Thalassemia: It is due to mutation of a gene that codes for α chain.
ii. β Thalassemia: It is due to mutation of a gene that codes for β chain.
iii. Thalassemia major: It occurs when a person inherits the defective gene from both the parents
iv. Thalassemia minor: It occurs when a person receives the defective gene from only one parent. Persons with this form of disorder are carriers of the disease and usually do not have symptoms.

5. Phenylketonuria

It is an autosomal disorder due to the presence of a recessive gene. It is an inborn error of metabolism and inherited through the autosomal recessive trait. The affected individual lacks an enzyme ***phenylalanine hydroxylase*** that converts the essential amino acid **phenylalanine,** a substance found in our food into **tyrosine**. As a result of this phenylalanine is accumulated and converted into **phenylpyruvic acid** and other derivatives. Accumulation of these in brain results in mental retardation. These are also excreted through urine because of its poor absorption by kidney. Infants have lighter skin, hair and eyes than their siblings (brothers or sisters) without this disease.

Chromosomal Disorder

Several diseases arise due to chromosomal anomalies. It happens because of change in the chromosomal number due to **aneuploidy**.

Aneuploidy is a condition, which involves addition or deletion of one or two chromosomes in the diploid set. It is due to non-disjunction or non-separation of chromosome during the formation of gamete. As a result one gamete receives both the chromosomes of that pair and other without the chromosome of that pair. This is called non-disjunction of chromosome occur either in autosomes or in allosomes.

Types of Aneuploidy

$2n + 1$ = Trisomy
$2n - 1$ = Monosomy
$2n + 2$ = Tetrasomy
$2n - 2$ = Nullisomy

A. Down's syndrome *or* Mongolism *or* Mongoloid Idiocy (Autosomal hyper aneuploidy**)**

It is the most familiar human autosomal abnormalities. It was first noticed by a British Physician, Langdon Down (1856). It occurs in one among 1000 births. This incidence occur in the babies who born invariably to the old mothers. Such babies will have an extra chromosome from 21st pair of autosomes. Therefore, the affected individual has 47 chromosomes. Hence it is a ***trisomy*** condition (2n+1). It is due to non-disjunction of chromosomes during the formation of gametes in old females.

Characters

1. They are small statured
2. They have small and slant eye balls like those of Mongolian race (epicanthus).
3. They have sagging and salivating mouth.
4. Swollen lips and tongue.
5. Enlarged forehead.
6. Flattened nose.
7. Stubby fingers and spongy toes.
8. Low IQ (Intelligent quotient) and mental retardation.

B. Klinefelter syndrome (Aullosomal hyper aneuploidy**)**

This syndrome was reported by Harry Klinefelter. This is an allosomal abnormality due to addition of one extra 'X' chromosome. Hence it is a ***trisomy*** condition (2n+1). The chromosomal complement in such individual is 44A + XXY. Henceforth such individuals are sterile males.

Characters

1. They are tall statured.
2. The body shows obesity.
3. Scanty hairs on the body.
4. They show tendency towards female characters like enlargement of breast, underdeveloped testis and low production of androgen.
5. There is no production of sperms, hence they are sterile.

C. Turner's syndrome (Allosomal hypo aneuploidy**)**

This syndrome was reported by Henry Turner. This is an allosomal abnormality due to absence of one 'X' chromosome. Hence it is a ***monosomy*** condition (2n-1).

The chromosomal complement of such individual is 44A + XO. Henceforth such individuals are sterile females.

Characters

1. They are small statured.
2. They possess large chest.
3. They show webbed neck.
4. Do not attain puberty.
5. There is no menstrual cycle.
6. Breasts are underdeveloped.
7. Ovaries are rudimentary (underdeveloped).
8. They do not produce ovum, hence they are sterile female.