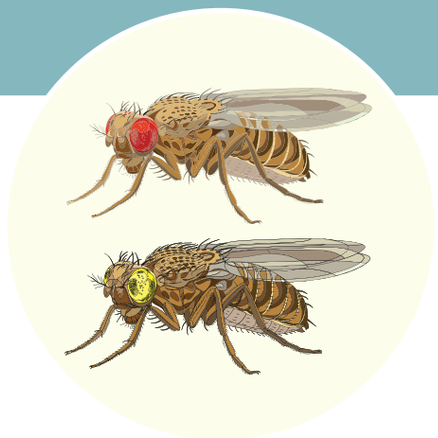
UNIT - II

CHAPTER 4

Principles of Inheritance and Variation



Drosophila are ideal for the study of genetics and development

Chapter outline

Learning objectives

- *Learns the inheritance of multiple alleles with reference to human blood groups.*
- *Understands the mechanism of sex determination in human beings, insects and birds.*
- *Learns about sex linked (X and Y) inherited diseases in human beings.*
- *Understands the Mendelian disorders and diseases associated with chromosomal abnormalities.*
- *Gains knowledge on extra chromosomal inheritance.*
- *Realises the significance of the applications of genetics in the improvement of human race.*

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Genetics is a branch of biology that deals with the study of heredity and variations. It describes how characteristics and features pass on from the parents to their offsprings in each successive generation. The unit of heredity is known as the gene. Gene is the inherited factor that determines the biological character of an organism. A variation is the degree by which the progeny differs from their parents.

In this chapter, we are going to learn about multiple alleles with reference to the human blood groups, sex determination in man, insects and birds, sex linked inherited traits, genetic disorders and extra chromosomal inheritance. The betterment of human race can be achieved by methods like eugenics, euthenics and euphenics.

4.1 Multiple alleles

The genetic segregations in Mendelian inheritance reveal that all genes have two alternative forms – dominant and recessive alleles e.g. tall versus dwarf (T and t). The former is the normal allele or wild allele and the latter the mutant allele. A gene can mutate several times producing several alternative forms. When three or more alleles of a gene that control a particular trait occupy the same locus on the homologous chromosome of an organism, they are called multiple alleles and their inheritance is called **multiple allelism**.

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4.2 Human Blood Groups

Multiple allelism occurs in humans, particularly in the inheritance of different types of blood groups. The blood group inheritance in human can be understood by learning about antigens and antibodies. The composition of blood, different types of blood groups (ABO) the blood antigens and antibodies were discussed in chapter 7 of class XI.

4.2.1 ABO blood types

Multiple allele inheritance of ABO blood groups

Blood differs chemically from person to person. When two different incompatible blood types are mixed, agglutination (clumping together) of erythrocytes (RBC) occurs. The basis of these chemical differences is due to the presence of antigens (surface antigens) on the membrane of RBC and epithelial cells. Karl Landsteiner discovered two kinds of antigens called antigen 'A' and antigen 'B' on the surface of RBC's of human blood. Based on the presence or absence of these antigens three kinds of blood groups, type 'A', type 'B', and type 'O' (universal donor)were recognized. The fourth and the rarest blood group 'AB' (universal recipient) was discovered in 1902 by two of Landsteiner's students Von De Castelle and Sturli.

Bernstein in 1925 discovered that the inheritance of different blood groups in human beings is determined by a number of multiple allelic series. The three autosomal alleles located on chromosome 9 are concerned with the determination of blood group in any person. The gene controlling blood type has been labeled as 'L' (after the name of the discoverer, Landsteiner) or I (from isoagglutination). The I gene exists in three allelic forms, I^A, I^B and I^O. I^A specifies A antigen. I^B allele determines B antigen and I^O allele specifies no antigen. Individuals who possess these antigens in their fluids such as the saliva are called secretors.

Each allele (I^A and I^B) produces a transferase enzyme. I^A allele produces N-acetyl galactose transferase and can add N-acetyl galactosamine (NAG) and I^B allele encodes for the enzyme galactose transferase that adds galactose to the precursor (i.e. H substances) In the case of I^O/I^O allele no terminal transferase enzyme is produced and therefore called "null" allele and hence cannot add NAG or galactose to the precursor.

From the phenotypic combinations it is evident that the alleles I^A and I^B are dominant to I^O, but co-dominant to each other ($I^A=I^B$). Their dominance hierarchy can be given as ($I^A=I^B > I^O$). A child receives one of three alleles from each parent, giving rise to six possible genotypes and four possible blood types (phenotypes). The genotypes are I^AI^A, I^AI^O, I^BI^B, I^BI^O, I^AI^B and I^OI^O.

- Antigens similar to those found among human beings have been recognized in the blood of other organisms. A-type antigens have been found in chimpanzees and in gibbons, A, B and AB antigen in orangutans.
- New world monkeys (Platyrrhina) and lemurs have a substance similar but not identical with B antigen in humans.
- Three blood groups have been distinguished in cats with a genetic system similar to those in humans.
- The secretors (antigens found in the body fluids) can be detected in tears, saliva, urine, semen, gastric juice and in the milk of animals.

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Table 4.1 Genetic basis of the human ABO blood groups

Genotype	ABO blood group phenotype	Antigens present on red blood cell	Antibodies present in blood plasma
I^AI^A	Type A	A	Anti -B
I^Ai^o	Type A	A	Anti -B
I^BI^B	Type B	B	Anti -A
I^Bi^o	Type B	B	Anti -A
I^AI^B	Type AB	A and B	Neither Anti -A nor Anti-B
i^oi^o	Type O	Neither A nor B	Anti -A and anti - B

Rhesus or Rh – Factor

The Rh factor or Rh antigen is found on the surface of erythrocytes. It was discovered in 1940 by Karl Landsteiner and Alexander Wiener in the blood of rhesus monkey, *Macaca rhesus* and later in human beings. The term 'Rh factor' refers to "immunogenic D antigen of the Rh blood group system. An individual having D antigen are Rh D positive (Rh^+) and those without D antigen are Rh D negative (Rh^-)". Rhesus factor in the blood is inherited as a dominant trait. Naturally occurring Anti D antibodies are absent in the plasma of any normal individual. However if an Rh^- (Rh negative) person is exposed to Rh^+ (Rh positive) blood cells (erythrocytes) for the first time, anti D antibodies are formed in the blood of that individual. On the other hand, when an Rh positive person receives Rh negative blood no effect is seen.

4.3 Genetic control of Rh factor

Fisher and Race hypothesis:

Rh factor involves three different pairs of alleles located on three different closely linked loci on the chromosome pair. This system is more commonly in use today, and uses the 'Cde' nomenclature.

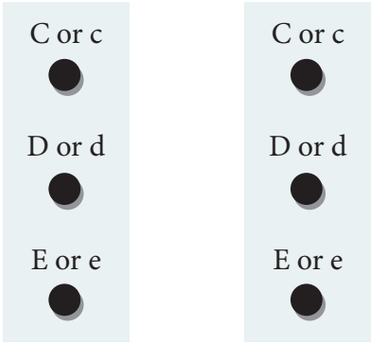

Fig. 4.1 Fischer and Race hypothesis – Rh Blood Type - Homologous Chromosome pair (showing 3 loci and 2 alleles per locus)

In the above Fig. 4.1, three pairs of Rh alleles (Cc, Dd and Ee) occur at 3 different loci on homologous chromosome pair-1. The possible genotypes will be one C or c, one D or d, one E or e from each chromosome. For e.g. CDE/cde; CdE/cDe; cde/cde; CDe/CdE etc., All genotypes carrying a dominant 'D' allele will produce Rh^+positive phenotype and double recessive genotype 'dd' will give rise to Rh^- negative phenotype.

Wiener Hypothesis

Wiener proposed the existence of eight alleles (R^1, R^2, R^0, R^z, r, r^1, r^{11}, r^y) at a single Rh locus. All genotypes carrying a dominant 'R allele' (R^1, R^2 ,R^0 ,R^z) will produce Rh^+positive' phenotype and double recessive genotypes (rr, rr^1, rr^{11}, rr^y) will give rise to Rh^-negative phenotype.

4.3.1 Incompatibility of Rh $^-$ Factor – Erythroblastosis foetalis

Rh incompatability has great significance in child birth. If a woman is Rh negative and

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the man is Rh positive, the foetus may be Rh positive having inherited the factor from its father. The Rh negative mother becomes sensitized by carrying Rh positive foetus within her body. Due to damage of blood vessels, during child birth, the mother's immune system recognizes the Rh antigens and gets sensitized. The sensitized mother produces Rh antibodies. The antibodies are IgG type which are small and can cross placenta and enter the foetal circulation. By the time the mother gets sensitized and produce anti 'D' antibodies, the child is delivered.

Usually no effects are associated with exposure of the mother to Rh positive antigen during the first child birth, subsequent Rh positive children carried by the same mother, may be exposed to antibodies produced by the mother against Rh antigen, which are carried across the placenta into the foetal blood circulation. This causes haemolysis of foetal RBCs resulting in haemolytic jaundice and anaemia. This condition is known as **Erythoblastosis foetalis or Haemolytic disease of the new born (HDN).**

Prevention of Eryhroblastosis foetalis

If the mother is Rh negative and foetus is Rh positive, anti D antibodies should be administered to the mother at 28th and 34th week of gestation as a prophylactic measure. If the Rh negative mother delivers Rh positive child then anti D antibodies should be administered to the mother soon after delivery. This develops passive immunity and prevents the formation of anti D antibodies in the mothers blood by destroying the Rh foetal RBC before the mother's immune system is sensitized. This has to be done whenever the woman attains pregnancy.

4.4 Sex Determination

Sex determination is the method by which the distinction between male and female is established in a species. Sex chromosomes determine the sex of the individual in dioecious or unisexual organisms. The chromosomes other than the sex chromosomes of an individual are called autosomes. Sex chromosomes may be similar (homomorphic) in one sex and dissimilar (heteromorphic) in the other. Individuals having homomorphic sex chromosomes produce only one type of gametes (homogametic) whereas heteromorphic individuals produce two types of gametes (heterogametic).

Y CHROMOSOME

The human Y chromosome is only 60 Mb in size with 60 functional genes whereas X chromosomes are 165 Mb in size with about 1,000 genes.

Chromosomal basis of sex determination

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Heterogametic Sex Determination:

In heterogametic sex determination one of the sexes produces similar gametes and the other sex produces dissimilar gametes. The sex of the offspring is determined at the time of fertilization.

Heterogametic Males

In this method of sex determination the males are heterogametic producing dissimilar gametes while females are homogametic producing similar gametes. It is of two kinds XX-XO type and XX-XY type.

XX-XO Type

This method of sex determination is seen in bugs, some insects such as cockroaches and grasshoppers. The female with two X chromosomes are homogametic (XX) while the males with only one X chromosome

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are heterogametic (XO). The presence of an unpaired X chromosomes determines the male sex. The males with unpaired 'X' chromosome produce two types of sperms, one half with X chromosome and other half without X chromosome. The sex of the offspring depends upon the sperm that fertilizes the egg **(Fig. 4.2)**.

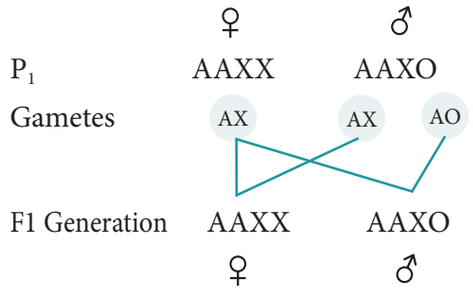

Fig. 4.2 XX-XO Type of sex determination

XX-XY type (Lygaeus Type)

This method of sex determination is seen in human beings and in *Drosophila*. The females are homogametic with XX chromosome, while the males are heterogametic with X and Y chromosome. Homogametic females produce only one kind of egg, each with one X chromosome, while the heterogametic males produce two kinds of sperms some with X chromosome and some with Y chromosome. The sex of the embryo depends on the fertilizing sperm. An egg fertilized by an 'X' bearing sperm produces a female, if fertilized by a 'Y' bearing sperm, a male is produced **(Fig. 4.3).**

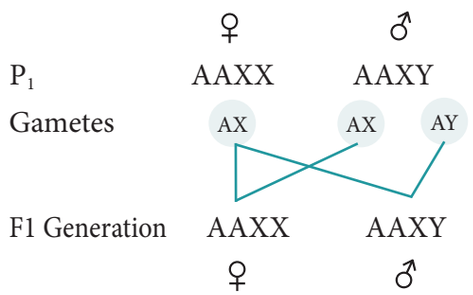

Fig. 4.3 XX-XY Type of sex determination

Heterogametic Females

In this method of sex determination, the homogametic male possesses two 'X' chromosomes as in certain insects and certain vertebrates like fishes, reptiles and birds producing a single type of gamete; while females produce dissimilar gametes. The female sex consists of a single 'X' chromosome or one 'X' and one 'Y' chromosome. Thus the females are heterogametic and produce two types of eggs. To avoid confusion with the XX-XO and XX-XY types of sex determination, the alphabets 'Z' and 'W' are used here instead of X and Y respectively. Heterogametic females are of two types, ZO-ZZ type and ZW-ZZ type.

ZO-ZZ Type

This method of sex determination is seen in certain moths, butterflies and domestic chickens. In this type, the female possesses single 'Z' chromosome in its body cells and is heterogametic (ZO) producing two kinds of eggs some with 'Z' chromosome and some without 'Z' chromosome, while the male possesses two 'Z' chromosomes and is homogametic (ZZ) **(Fig. 4.4).**

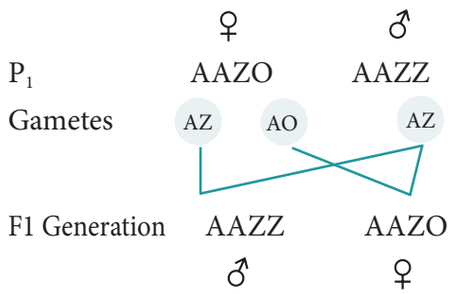

Fig. 4.4 ZO-ZZ type of sex determination

ZW-ZZ type

This method of sex determination occurs in certain insects (gypsy moth) and in vertebrates such as fishes, reptiles and birds. In this method the female has one 'Z' and one 'W' chromosome (ZW) producing two types of eggs, some carrying the Z chromosomes and some carry the W chromosome. The male sex

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has two 'Z' chromosomes and is homogametic (ZZ) producing a single type of sperm **(Fig .4.5).**

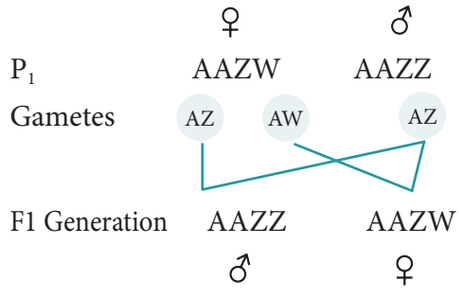

Fig. 4.5 ZW-ZZ type of sex determination

Sex determintion in human beings

Genes determining sex in human beings are located on two sex chromosomes, called allosomes. In mammals, sex determination is associated with chromosomal differences between the two sexes, typically XX females and XY males. 23 pairs of human chromosomes include 22 pairs of autosomes (44A) and one pair of sex chromosomes (XX or XY). Females are homogametic producing only one type of gametes (egg), each containing one X chromosome while the males are heterogametic producing two types of sperms with X and Y chromosomes. An independently evolved XX: XY system of sex chromosomes also exist in *Drosophila*. **(Fig. 4.6)**.

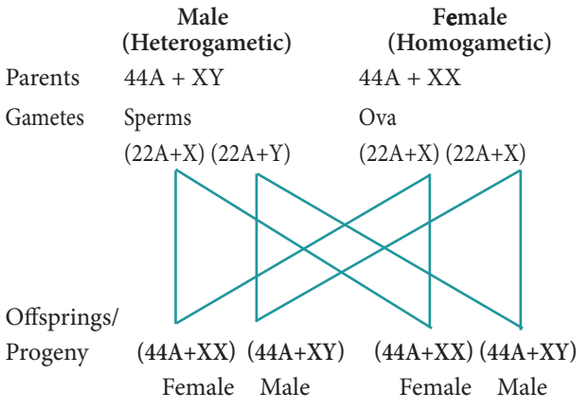

Fig. 4.6 Sex determination in human beings

The Y Chromosome and Male Development

Current analysis of Y chromosomes has revealed numerous genes and regions with potential genetic function; some genes with or without homologous counterparts are seen on the X. Present at both ends of the Y chromosome are the pseudoautosomal regions (PARs) that are similar with regions on the X chromosome which synapse and recombine during meiosis. The remaining 95% of the Y chromosome is referred as the Non - combining Region of the Y (NRY). The NRY is divided equally into functional genes (euchromatic) and non functional genes (heterochromatic). Within the euchromatin regions, is a gene called **Sex determining region Y (SRY)**. In humans, absence of Y chromosome inevitably leads to female development and this SRY gene is absent in X chromosome. The gene product of SRY is the testes determining factor (TDF) present in the adult male testis.

4.4.1 Genic balance in Drosophila

Genic balance mechanisms of sex determination in *Drosophila* was first studied by C.B. Bridges. In *Drosophila*, the presence of Y chromosome is essential for the fertility of male sex, but does not determine the male sex. The gene for femaleness is located on the X chromosome and those for maleness are located on the autosomes. When geneticist C.B. Bridges, working with *Drosophila*, crossed a triploid (3n) female with a normal male, he observed many combinations of autosomes and sex chromosomes in the offspring. From his results Bridges in 1921 suggested that sex in *Drosophila* is determined by the balance between the genes for femaleness located on the 'X' chromosomes and those for maleness located on the 'autosomes' . Hence the sex of an individual is determined by the ratio of its X chromosome to that of its autosome sets. This ratio is termed **sex index** and is expressed as:

$$\text{Sex index} = \frac{\text{Number of X Chromosomes}}{\text{Number of Sets of Autosomes}} \left(\frac{\mathbf{X}}{\mathbf{A}}\right)$$

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Change in this ratio leads to a changed sex phenotype. The results obtained from a cross between triploid female *Drosophila* (3A:3X) with a diploid male (2A: XY) is shown in tables 4.2. and 4.3.

Table: 4.2 Bridges classical cross of a triploid (3A+XXX) female fly and a diploid (2A+XY) male fly

	Triploid ♀	Diploid ♂
Parent	3A + XXX	2A + XY
Gametes	(2A + XX) (A + X) (2A + X) (A + XX)	(A + X) (A + Y)

	A+X	A + Y
2A+XX	3A + XXX Triploid Female	3A + XXY Triploid Intersex
2A+X	3A + XX Triploid Intersex	3A + XY Super Male
A+XX	2A + XXX Super female	2A + XXY Diploid Female
A+X	2A + XX Diploid Female	2A + XY Diploid Male

When the X **:** A ratio is 1.00 as in a normal female, or greater than 1.00, the organism is a female. When this ratio is 0.50 as in a normal male or less than 0.50 the organism is a male. At 0.67, the organism is an intersex. metamales (X/A = 0.33) and metafemales (X/A=1.50) are usually very weak and sterile.

A sex–switch gene in *Drosophila* directs female development. This gene, sex–lethal (SxL) located on the X chromosome, has two states of activity. When it is 'on' it directs female development and when it is 'off' maleness ensures. Other genes located on the X chromosome and autosomes regulate this sex-switch gene. However, the Y- chromosome of *Drosophila* is required for male fertility.

- X-Chromosome was discovered by Henking (1891)
- Y-Chromosome was discovered by Stevens (1902)

Table: 4.3 Different doses of X chromosomes and autosome sets and their effect on sex determination in *Drosophila*

Phenotype		Number of 'X' Chromosomes (X)	Number of Autosome sets (A)	Sex Index = Number of X chromosome / Number of autosome sets
Meta female / Super female		3	2	3/2 = 1.5
Normal Female	Tetraploid	4	4	4/4 = 1.0
	Triploid	3	3	3/3 = 1.0
	Diploid	2	2	2/2 = 1.0
	Haploid	1	1	1/1 = 1.0
Inter sex		2	3	2/3 = 0.67
Normal male		1	2	½ = 0.50
Meta male / Super male		1	3	1/3 = 0.33

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Gynandromorphs

These individuals have parts of their body expressing male characters and other parts of the body expressing female characters. The organism is made up of tissues of male and female genotype and represents a mosaic pattern.

4.4.2 Dosage compensation - Barr body

In 1949, Barr and Bertram first observed a condensed body in the nerve cells of female cat which was absent in the male. This condensed body was called sex chromatin by them and was later referred as **Barr body**. In the XY chromosomal system of sex determination, males have only one X chromosome, whereas females have two. A question arises: how does the organism compensate for this dosage differences between the sexes? In mammals the necessary dosage compensation is accomplished by the inactivation of one of the X chromosome in females so that both males and females have only one functional X chromosome per cell.

Mary Lyon suggested that Barr bodies represented an inactive chromosome, which in females becomes tightly coiled into a heterochromatin, a condensed and visible form of chromatin (Lyon's hypothesis). The number of Barr bodies observed in cell was one less than the number of X-Chromosome. XO females have no Barr body, whereas XXY males have one Barr body.

- The number of Barr bodies follows N-1 rule (N minus one rule), where N is the total number of X chromosomes present.

Haplodiploidy in Honeybees

In hymenopteran insects such as honeybees, ants and wasps a mechanism of sex determination called haplodiploidy mechanism of sex determination is common. In this system, the sex of the offspring is determined by the number of sets of chromosomes it receives. Fertilized eggs develop into females (Queen or Worker) and unfertilized eggs develop into males (drones) by parthenogenesis. It means that the males have half the number of chromosomes (haploid) and the females have double the number (diploid), hence the name haplodiplody for this system of sex determination.

This mode of sex determination facilitates the evolution of sociality in which only one diploid female becomes a queen and lays the eggs for the colony. All other females which are diploid having developed from fertilized eggs help to raise the queen's eggs and so contribute to the queen's reproductive success and indirectly to their own, a phenomenon known as **Kin Selection**. The queen constructs their social environment by releasing a hormone that suppresses fertility of the workers.

4.5 Sex Linked Inheritance

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The inheritance of a trait that is determined by a gene located on one of the sex chromosomes is called sex linked inheritance. Genes present on the differential region of X or Y chromosomes are called sex linked genes. The genes present in the differential region of "X" chromosome are called X linked genes. The X–linked genes have no corresponding alleles in the Y chromosome. The genes present in the differential region of Y chromosome are called Y- linked or **holandric genes**. The Y linked genes have no corresponding allele in X chromosome. The Y linked genes inherit along with Y chromosome and they phenotypically express only in the male sex. Sex linked inherited traits are more common in males than females because, males are hemizygous and therefore express the trait when they inherit one mutant allele.

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The X – linked and Y – linked genes in the differential region (non–homologus region) do not undergo pairing or crossing over during meiosis. The inheritance of X or Y linked genes is called sex-linked inheritance.

4.5.1 Inheritance of X - linked genes

Red-green colour blindness or daltonism, haemophilia and Duchenne's muscular dystrophy are examples of X-linked gene inheritance in humans.

1. Haemophilia

Haemophilia is commonly known as bleeder's disease, which is more common in men than women. This hereditary disease was first reported by John Cotto in 1803. Haemophilia is caused by a recessive X-linked gene. A person with a recessive gene for haemophilia lacks a normal clotting substance (thromboplastin) in blood, hence minor injuries cause continuous bleeding, leading to death. The females are carriers of the disease and would transmit the disease to 50% of their sons even if the male parent is normal. Haemophilia follows the characteristic criss - cross pattern of inheritance.

2. Colour blindness

In human beings a dominant X – linked gene is necessary for the formation of colour sensitive cells, the cones. The recessive form of this gene is incapable of producing colour sensitive cone cells. Homozygous recessive females (X^cX^c) and hemizygous recessive males (X^cY) are unable to distinguish red and green colour. The inheritance of colour blindness can be studied in the following two types of marriages.

(i) **Marriage between colour blind man and normal visioned woman**

A marriage between a colour blind man and a normal visioned woman will produce normal visioned male and female individuals in F_1 generation but the females are **carriers**. The marriage between a F_1 normal visioned carrier woman and a normal visioned male will produce one normal visioned female, one carrier female, one normal visioned male and one colour blind male. Colour blind trait is inherited from the male parent to his grandson through carrier daughter, which is an example of criss-cross pattern of inheritance **(Fig. 4.7).**

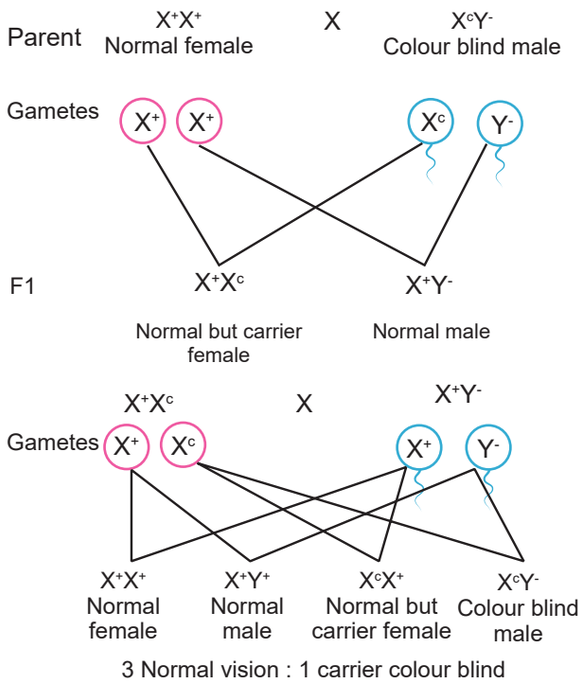

Fig. 4.7 Marriage between colour blind man and normal visioned woman

ii) Marriage between normal visioned man and colour blind woman

If a colour blind woman (X^cX^c) marries a normal visioned male (X^+Y), all F_1 sons will be colourblind and daughters will be normal visioned but are carriers.

Marriage between F_1 carrier female with a **colour blind** male will produce normal visioned carrier daughter, colourblind daughter, normal visioned son and a colourblind son in the F_2 generation **(Fig. 4.8).**

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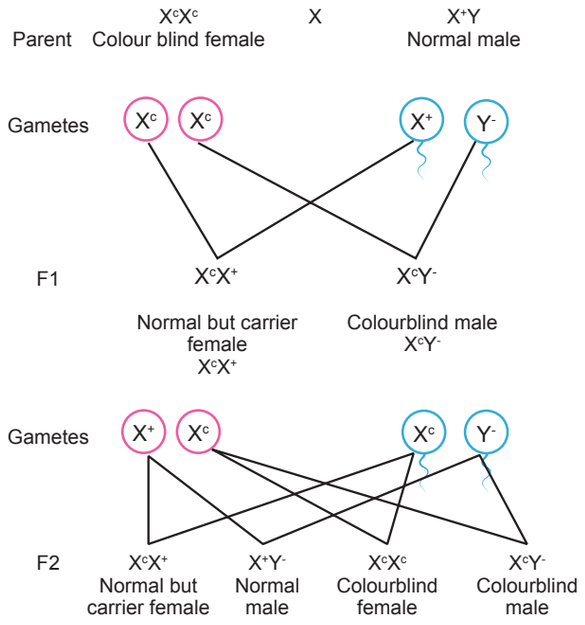

Fig. 4.8 Marriage between normal visioned man and colour blind woman

4.5.2 Inheritance of Y- linked genes

Genes in the non-homologous region of the Y-chromosome are inherited directly from male to male. In humans, the Y-linked or holandric genes for hypertrichosis (excessive development of hairs on pinna of the ear) are transmitted directly from father to son, because males inherit the Y chromosome from the father. Female inherits only X chromosome from the father and are not affected.

4.6 Karyotyping

Karyotyping is a technique through which a complete set of chromosomes is separated from a cell and the chromosomes are arranged in pairs. An idiogram refers to a diagrammatic representation of chromosomes.

Preparation of Karyotype

Tjio and Levan (1960) described a simple method of culturing lymphocytes from the human blood. Mitosis is induced followed by addition of colchicine to arrest cell division at metaphase stage and the suitable spread of metaphase chromosomes is photographed. The individual chromosomes are cut from the photograph and are arranged in an orderly fashion in homologous pairs. This arrangement is called a **karyotype**. Chromosome banding permits structural definitions and differentiation of chromosomes.

Applications of Karyotyping:

- It helps in gender identification.
- It is used to detect the chromosomal aberrations like deletion, duplication, translocation, nondisjunction of chromosomes.
- It helps to identify the abnormalities of chromosomes like aneuploidy.
- It is also used in predicting the evolutionary relationships between species.
- Genetic diseases in human beings can be detected by this technique.

Human Karyotype

Depending upon the position of the centromere and relative length of two arms, human chromosomes are of three types: Metacentric, sub metacentric and acrocentric. The photograph of chromosomes are arranged in the order of descending length in groups from A to G **(Fig. 4.9).**

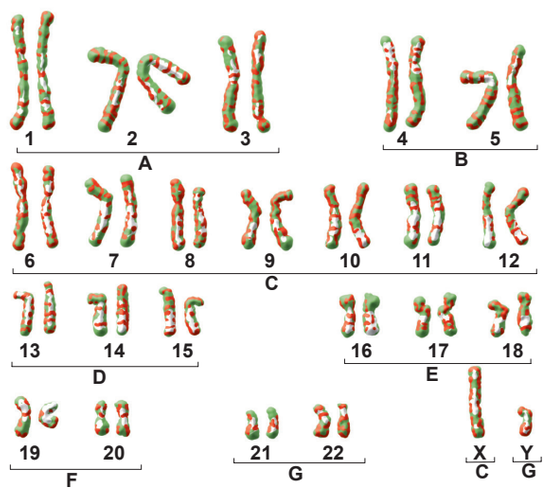

Fig. 4.9 - Human karyotype (male)

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4.7 Pedigree Analysis

Pedigree is a "family tree", drawn with standard genetic symbols, showing the inheritance pathway for specific phenotypic characters.**(Fig. 4.10).** Pedigree analysis is the study of traits as they have appeared in a given family line for several past generations.

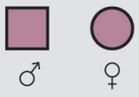
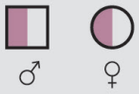
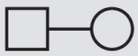
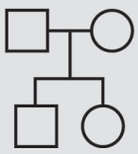
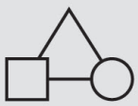
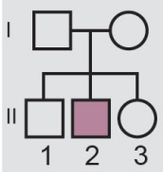
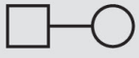
Symbol	Explanation	Symbol	Explanation
	Male		Affected individuals
	Female		Heterozygotes for autosomal recessives
	Mating		Carrier of sex-linked recessives
	Parents and children (1 boy: 1 girl in order of birth)		Death
	Dizygotic twins		Abortion or still birth (sex unspecified)
	Monozygotic twins		Propositus (proband)
	Sex unspecified		Method of identifying persons in a pedigree : here the propositus in child 2 in generation 2 or II 2
	Number of children of sex indicated		Consanguineous marriage

Fig. 4.10 Symbols commonly used in pedigree charts

Genetic Disorders

A genetic disorder is a disease or syndrome that is caused by an abnormality in an individual DNA. Abnormalities can range from a small mutation in a single gene to the addition or subtraction of an entire chromosome or even a set of chromosomes. Genetic disorders are of two types namely, Mendelian disorders and chromosomal disorders.

4.8 Mendelian disorders

Alteration or mutation in a single gene causes Mendelian disorders. These disorders are transmitted to the offsprings on the same line as the Mendelian pattern of inheritance. Some examples for Mendelian disorders are Thalassemia, albinism, phenylketonuria, sickle cell anaemia, Huntington's chorea, etc., These disorders may be dominant or recessive and autosomal or sex linked.

Thalassemia

Thalassemia is an autosomal recessive disorder. It is caused by gene mutation resulting in excessive destruction of RBC's due to the formation of abnormal haemoglobin molecules. Normally haemoglobin is composed of four polypeptide chains, two **alpha** and two **beta** globin chains. Thalassemia patients have defects in either the alpha or beta globin chain causing the production of abnormal haemoglobin molecules resulting in anaemia.

Thalassemia is classified into alpha and beta based on which chain of haemoglobin molecule is affected. It is controlled by two closely linked

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genes HBA1 and HBA2 on chromosome 16. Mutation or deletion of one or more of the four alpha gene alleles causes **Alpha Thalassemia**. In **Beta Thalassemia,** production of beta globin chain is affected. It is controlled by a single gene (HBB) on chromosome 11. It is the most common type of Thalassemia and is also known as Cooley's anaemia. In this disorder the alpha chain production is increased and damages the membranes of RBC.

Phenylketonuria

It is an inborn error of **Phenylalanine** metabolism caused due to a pair of autosomal recessive genes. It is caused due to mutation in the gene PAH (phenylalanine hydroxylase gene) located on chromosome 12 for the hepatic enzyme "phenylalanine hydroxylase" This enzyme is essential for the conversion of phenylalanine to tyrosine. Affected individual lacks this enzyme, so phenylalanine accumulates and gets converted to phenylpyruvic acid and other derivatives. It is characterized by severe mental retardation, light pigmentation of skin and hair. Phenylpyruvic acid is excreted in the urine.

Phenylalanine $\xrightarrow{\text{phenylalanine hydroxylase}}$ Tyrosine

Albinism

Albinism is an inborn error of metabolism, caused due to an autosomal recessive gene. Melanin pigment is responsible for skin colour. Absence of melanin results in a condition called albinism. A person with the recessive allele lacks the tyrosinase enzyme system, which is required for the conversion of dihydroxyphenyl alanine (DOPA) into melanin pigment inside the melanocytes. In an albino, melanocytes are present in normal numbers in their skin, hair, iris, etc., , but lack melanin pigment.

3, 4 dihydroxy phenylalanine (DOPA) $\xrightarrow{\text{Tyrosinase}}$ Melanin

Huntington's chorea

It is inherited as an autosomal dominant lethal gene in man. It is characterized by involuntary jerking of the body and progressive degeneration of the nervous system, accompanied by gradual mental and physical deterioration. The patients with this disease usually die between the age of 35 and 40.

4.9 Chromosomal Abnormalities

Each human diploid (2n) body cell has 46 chromosomes (23 pairs). Chromosomal disorders are caused by errors in the number or structure of chromosomes. Chromosomal anomalies usually occur when there is an error in cell division. Failure of chromatids to segregate during cell division resulting in the gain or loss of one or more chromosomes is called aneuploidy. It is caused by non-disjunction of chromosomes. Group of signs and symptoms that occur together and characterize a particular abnormality is called a syndrome. In humans, Down's syndrome, Turner's syndrome, Klinefelter's syndrome, Patau's syndrome are some of the examples of chromosomal disorders.

a. Autosomal aneuploidy in human beings

Several autosomal aneuploidies have been reported in human beings. eg. Down's syndrome (21-Trisomy), Patau's syndrome (13-Trisomy).

1. Down's Syndrome/Trisomy – 21

Trisomic condition of chromosome - 21 results in Down's syndrome. It is characterized by severe mental retardation, defective development of the central nervous system, increased separation between the eyes, flattened nose, ears are malformed, mouth is constantly open and the tongue protrudes.

2. Patau's Syndrome/Trisomy-13

Trisomic condition of chromosome 13 results in Patau's syndrome. Meiotic non

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disjunction is thought to be the cause for this chromosomal abnormality. It is characterized by multiple and severe body malformations as well as profound mental deficiency. Small head with small eyes, cleft palate, malformation of the brain and internal organs are some of the symptoms of this syndrome.

b. Allosomal abnormalities in human beings

Mitotic or meiotic non-disjunction of sex chromosomes causes allosomal abnormalities. Several sex chromosomal abnormalities have been detected. Eg. Klinefelter's syndrome and Turner's syndrome.

1. Klinefelter's Syndrome (XXY Males)

This genetic disorder is due to the presence of an additional copy of the X chromosome resulting in a karyotype of 47,XXY. Persons with this syndrome have 47 chromosomes (44AA+XXY). They are usually sterile males, tall, obese, with long limbs, high pitched voice, under developed genitalia and have feeble breast (gynaecomastia) development.

2. Turner's Syndrome (XO Females)

This genetic disorder is due to the loss of a X chromosome resulting in a karyotype of 45,X. Persons with this syndrome have 45 chromosomes (44 autosomes and one X chromosome) (44AA+XO) and are sterile females. Low stature, webbed neck, under developed breast, rudimentary gonads lack of menstrual cycle during puberty, are the main symptoms of this syndrome.

4.10 Extra chromosomal / cytoplasmic inheritance

Certain characters are controlled by non-nuclear genomes found in chloroplast, mitochondria, infective agents and plasmids. These characters do not reveal Mendelian pattern of inheritance. The inheritance of the extra chromosomal genes are found to exhibit maternal influence. Maternal effect is due to the asymmetric contribution of the female parent to the development of zygote. Although both male and female parents contribute equally to the zygote in terms of chromosomal genes, the female parent usually contributes the zygote's initial cytoplasm and organelles, since the sperms contain very little cytoplasm. If there are hereditary units in the cytoplasm, these will be transmitted to the offsprings through the egg, so the offsprings exhibit maternal effect.

The cytoplasmic extranuclear genes have a characteristic pattern of inheritance which do not resemble the genes of nuclear chromosomes and is known as extra chromosomal or extra nuclear or cytoplasmic inheritance and exhibit maternal influence. In extra nuclear inheritance, male and female parents contribute equally their nuclear genes to the progeny but do not make equal contribution of extra chromosomal genes hence, the crosses can yield different (or) non Mendelian results. Cytoplasmic inheritance in animals can be studied with reference to shell coiling in *Limnaea* and kappa particles in *Paramecium.*

1. Shell coiling in *Limnaea*

Limnaea peregra is a freshwater snail. The shell of these animals are spirally coiled. The coiling of the shell is clockwise (dextral) or anticlockwise (sinistral). Both type of coilings are produced by two different types of genetically controlled cleavages namely, dextral cleavage and sinistral cleavage.

In *Limnaea*, dextral coiling is normal and sinistral coiling is a mutant character. Direction of coiling is determined by a pair of nuclear genes, D(dextral) and d (sinistral). The gene for dextral (D) being dominant over

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sinistral coiling (d). In **Fig.4.11** a dextral snail provides the eggs and a sinistral snail provides the sperm. The offsprings are all dextral (Dd), in the F_1 generation.

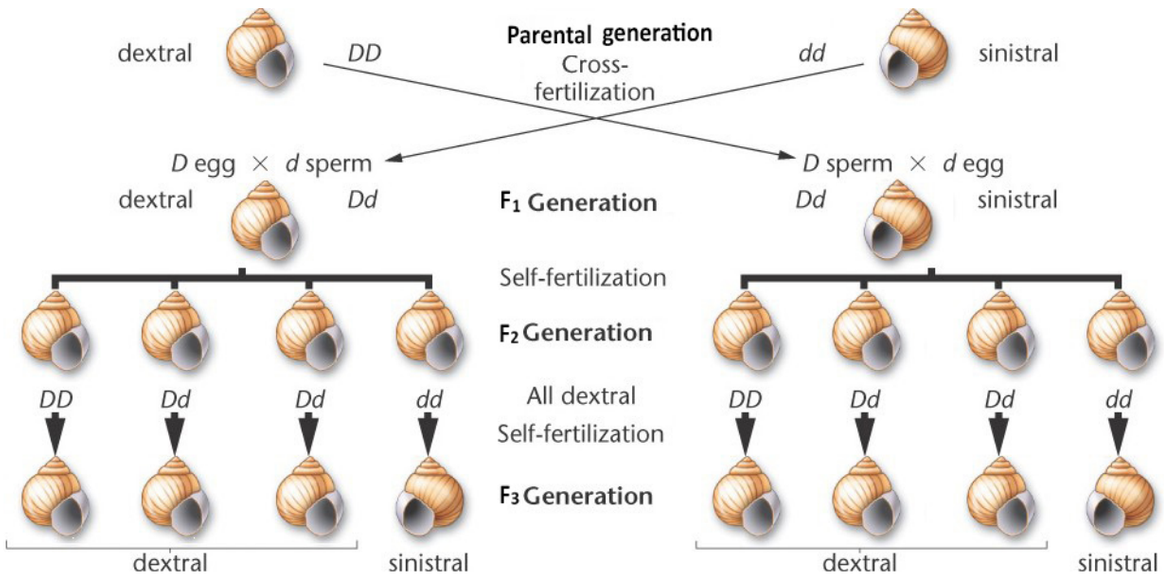
When the F_1 heterozygous dextral individual (Dd) were self crossed the F_2 generation showed dextral coiling with genotype of 1DD, 2Dd and 1dd (**Fig-4.11** left).

When a reciprocal cross is made (**Fig. 4.11**-right) The F_1 individuals have Dd genotype but are coiled sinistrally, as in the female parent. In both the crosses the F_1 are phenotypically similar to the female parent, though the offsprings in both crosses have the same genotype Dd. This is because the genotype of the maternal parent determines the phenotype of the offspring.

maturation division of the oocyte nucleus and by the influence of the maternal genotype. The direction of coiling of the shell depends upon the orientation of the mitotic spindle during the first cleavage. Obviously, maternal control affects only one generation. In each generation the coiling is dependent on the maternal genotype.

2. Kappa particles in *Paramecium*

Sonneborn and his associates have reported the transmission of the cytoplasmic kappa particles in *Paramecium aurelia*. The kappa particles are cytoplasmic symbionts occurring in some strains of the ciliated *Paramecium*. The strains possessing the kappa particles are known as "killer Paramecia".



3 dextral: 1 sinistral

Fig. 4.11 Shell coiling in *Limnaea*

When the F_1 sinistral individuals were self crossed, the shell coiling in the F_2 generation, were all dextral (**Fig-4.11** right). This is because the genes do not segregate in the F_2 generation. Only in the F_3 generation segregation occurs in the ratio of 3 dextral : 1 sinistral.

Why does this pattern occur? The type of cleavage depends on the organization of the egg which is established before the

The kappa liberates a toxin, **paramecin** which is lethal to other individuals called "sensitives".

Kappa particles appear to be either parasites or more possible symbionts since they do not harm their hosts. A killer *Paramecium* may contain hundreds of kappa particles which have their own DNA and which in turn are dependent on a dominant

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gene 'K' for its presence in the killer *Paramecia*. *Paramecia* with nuclear genotype "kk" are unable to produce kappa particles. The inheritance of killer trait does not follow the Mendelian pattern of inheritanc.

When a killer *Paramecium* KK conjugates with sensitive "kk", the exconjugants are all heterozygous for Kk genes. The Kk genotype suggest that both exconjugants should be killers. But this is not seen. If conjugation lasts only for a short period of time, there is no exchange of cytoplasm between the two *Paramecia* resulting in both killers (Kk) and sensitives. However prolonged conjugation permits mixing of cytoplasm of both the conjugants resulting in killers only. This confirms that the killer trait is determind cytoplasmically. Dominant chromosomal genes (KK) are required to maintain the cytoplasmic kappa particles. Without a dominant gene this particle would disappear from the cytoplasm of the host.

The kappa appears to be a bacterium, C*aedobacter taeniospiralis* that has its own DNA and replicates autonomously. Kappa particle occurs in atleast two forms; N and B forms. The N form is the infective form that passes from one *Paremicium* to another and confers the killer specificity to the host cell. The "N" form is attacked by a bacteriophage that induces the formation of inculsions called "R" bodies, inside the kappa particles

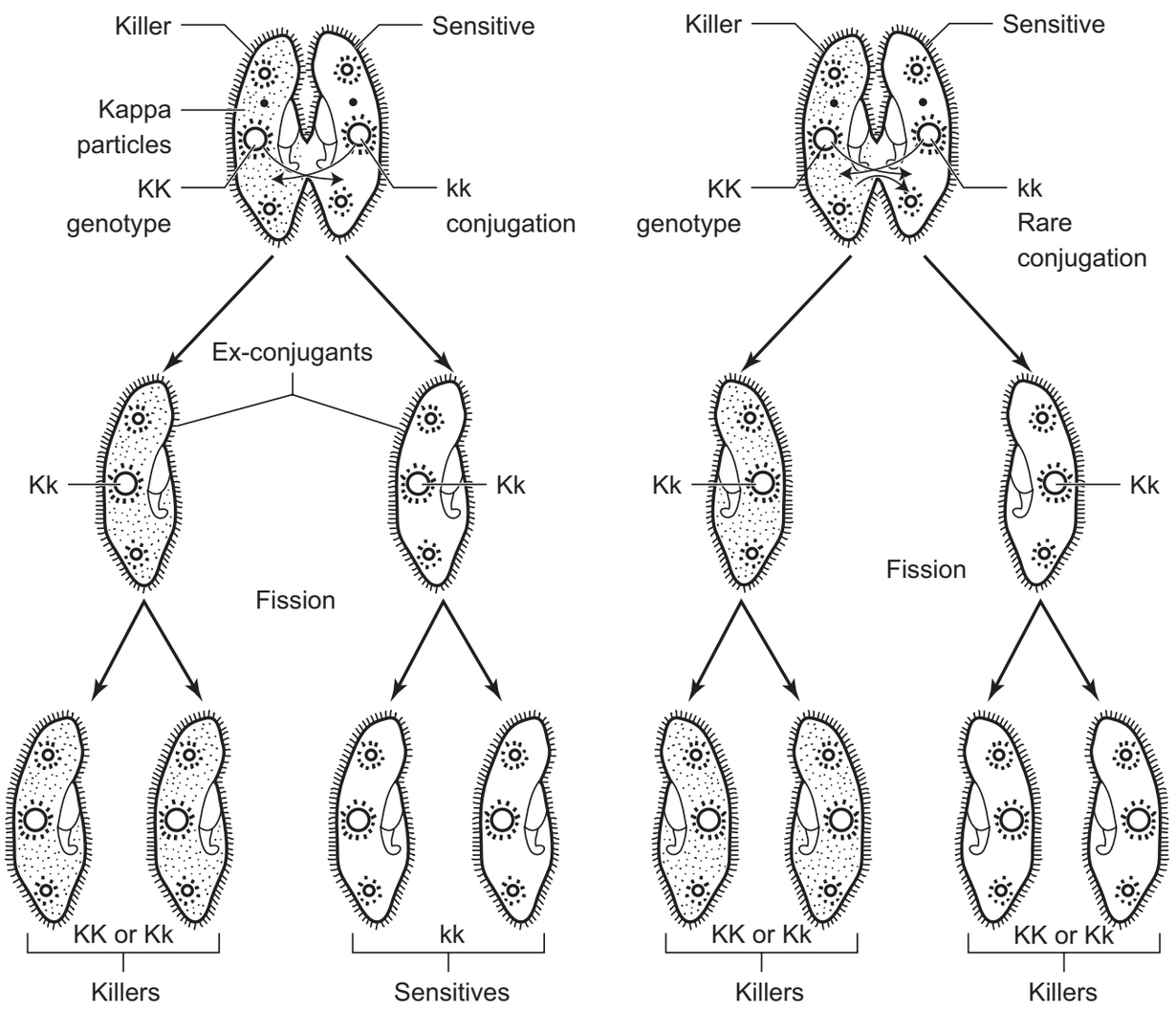

Fig .4.12 Kappa particles in *Paramecium*

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and convert it to the "B" form. These "R" bodies are visible under the light microscope as refractile bodies. In the "B" form, kappa can no longer replicate, it is offen lysed within the cell, however, it confers killer specificity on the host cell. Whether viral DNA or kappa DNA codes the toxin paramecin is not known at present.

4.11 Eugenics, Euphenics And Euthenics

Eugenics

Application of the laws of genetics for the improvement of human race is called **eugenics**. The term **eugenics** means "well born" and was coined by **Francis Galton** in 1885. For the betterment of future generations it is necessary to increase the population of outstanding people and to decrease the population of abnormal and defective people by applying the principles of eugenics.

Two methods of Eugenics

(i) Constructive method or Positive eugenics

(ii) Restrictive method or Negative eugenics

(i) Positive eugenics

Positive eugenics attempts to increase consistently better or desirable germplasm and to preserve the best germplasm of the society. The desirable traits can be increased by adopting the following measures:

(i) Early marriage of those having desirable traits

(ii) Subsiding the fit and establishing sperm and egg banks of precious germplasm

(iii) Educating the basic principles of genetics and eugenics

(iv) Improvement of environmental conditions

(v) Promotion of genetic research

(ii) Negative eugenics

Negative Eugenics attempts to eliminate the defective germplasm of the society by adopting the following measures:

(i) Sexual separation of the defectives

(ii) Sterilization of the defectives

(iii) Control of immigration and

(iv) Regulation of marriages

Euphenics

The symptomatic treatment of genetic disease of man is called Euphenics or Medical engineering. In 1960 Joshua Lederberg coined the term Euphenics. It means normal appearing. It deals with the control of several inherited human diseases especially the inborn errors of metabolism. Eg. Phenylketonuria (PKU)

Euthenics

The science of improvement of existing human race by improving the environmental conditions is called euthenics. It can be achieved by subjecting them to better nutrition, better unpolluted ecological conditions, better education and sufficient medical facilities.

Summary

Genetics is a branch of biology that deals with the study of heredity and variation. It describes how characteristics and features pass on from the parents to their offsprings in successive generations. Variation is the degree by which progeny differ from their parents. A set of three or more alleles of the same gene occupying the same locus in a given pair of homologous chromosomes controlling a particular trait is called Multiple allele. ABO blood grouping in man is a good example for multiple allelism. Apart from A and B antigens, the RBC's of humans contain a special type of antigen called Rh antigen/Rh factors. Erythroblastosis foetalis, also called haemolytic disease of the newborn, in which the red blood cells of a foetus are destroyed due to maternal immune reaction

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resulting from a blood group incompatibility between the foetus and the mother.

The mechanism of determination of male and female individuals in a species is called sex determination. The chromosomes are different in two sexes and referred to as allosomes; the remaining chromosomes are named autosomes. In human beings a normal female has 22 pairs of autosomes and a pair of sex chromosomes (44A + XX) and a male has 22 pairs of autosomes and a pair of sex chromosomes (44A + XY). In birds, reptiles and some fishes, sex chromosomes are ZZ in males and ZW in females. In moths and butterflies, sex chromosomes are represented as ZZ in males and ZO in females. Sex in *Drosophila* is determined polygenically. The sex of an individual depends upon the ratio of X chromosomes to autosome sets. The inheritance of a trait that is determined by a gene located on one of the sex chromosomes is called sex linked inheritance. Haemophilia, colourblindness, muscular dystrophy are some examples for X linked inheritance in human beings.

Pedigree analysis is the study of traits as they have appeared in a given family line for several generations. The genetic disorders are of two types- Mendelian and chromosomal. Alternations or mutation in single gene causes Mendelian disorders like, thalassemia, albinism, phenylketonuria, and Huntington's chorea. Chromosomal abnormalities arise due to chromosomal non-disjunction, translocation, deletion, duplication and inversion. Downs syndrome, Klinefelter's syndrome, Turner's syndrome and Patau's syndrome are some of the chromosomal disorders. Downs syndrome is due to trisomy of chromosome 21. Presence of trisomic condition of chromosome 13 results in Patau's syndrome. In Turner's syndrome the sex chromosome is XO and in Klinefelter's syndrome the condition is XXY. An idiogram refers to a diagrammatic representation of chromosomes.

The cytoplasmic extra nuclear genes have a characteristic pattern of inheritance which does not resemble genes of nuclear chromosomes and are known as Extrachromosomal/ Cytoplasmic inheritance. The betterment of human race can be achieved by methods like Eugenics, Euthenics and Euphenics.

Evaluation

D4VMH6

1. Haemophilia is more common in males because it is a
   a) Recessive character carried by Y-chromosome
   b) Dominant character carried by Y-chromosome
   c) Dominant trait carried by X-chromosome
   d) **Recessive trait carried by X-chromosome**

2. ABO blood group in man is controlled by
   a) Multiple alleles
   b) Lethal genes
   c) Sex linked genes
   d) Y-linked genes

3. Three children of a family have blood groups A, AB and B. What could be the genotypes of their parents?
   a) $I^A I^B$ and ii
   b) **$I^A I^o$ and $I^B I^o$**
   c) $I^B I^B$ and $I^A I^A$
   d) $I^A I^A$ and ii

4. Which of the following is not correct?
   a) Three or more alleles of a trait in the population are called multiple alleles.
   b) A normal gene undergoes mutations to form many alleles
   c) **Multiple alleles map at different loci of a chromosome**
   d) A diploid organism has only two alleles out of many in the population

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5. Which of the following phenotypes in the progeny are possible from the parental combination AxB?

a) A and B only
b) A,B and AB only
c) AB only
d) **A,B,AB and O**

6. Which of the following phenotypes is not possible in the progeny of the parental genotypic combination I^AI^O x I^AI^B?

a) AB **b) O**
c) A d) B

7. Which of the following is true about Rh factor in the offspring of a parental combination DdXDd (both Rh positive)?

a) All will be Rh-positive
b) Half will be Rh positive
c) About ¾ will be Rh negative
d) About one fourth will be Rh negative

8. What can be the blood group of offspring when both parents have AB blood group?

a) AB only **b) A, B and AB**
c) A, B, AB and O d) A and B only

9. If the childs blood group is 'O' and fathers blood group is 'A' and mother's blood group is 'B' the genotype of the parents will be

a) $I^A I^A$ and $I^B I^o$ b) **$I^A I^o$ and $I^B I^o$**
c) $I^A I^o$ and $I^o I^o$ d) $I^o I^o$ and $I^B I^B$

10. XO type of sex determination and XY type of sex determination are examples of

a) **Male heterogamety**
b) Female heterogamety
c) Male homogamety
d) Both (b) and (c)

11. In an accident there is great loss of blood and there is no time to analyse the blood group which blood can be safely transferred?

a) 'O' and Rh negative
b) 'O' and Rh positive
c)'B' and Rh negative
d) 'AB' and Rh positive

12. Father of a child is colourblind and mother is carrier for colourblindness, the probability of the child being colourblind is

a) 25% **b) 50%**
c) 100% d) 75%

13. A marriage between a colourblind man and a normal woman produces

a) **All carrier daughters and normal sons**
b) 50% carrier daughters, 50% normal daughters
c) 50% colourblind sons, 50% normal sons
d) All carrier offsprings

14. Mangolism is a genetic disorder which is caused by the presence of an extra chromosome number

a) 20 **b) 21**
c) 4 d) 23

15. Klinefelters' syndrome is characterized by a karyotype of

a) XYY b) XO
c) XXX **d) XXY**

16. Females with Turners' syndrome have

a) Small uterus
b) Rudimentary ovaries
c) Underdeveloped breasts
d) All of these

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17. Pataus' syndrome is also referred to as

a) **13-Trisomy** b) 18-Trisormy
c) 21-Trisormy d) None of these

18. Who is the founder of Modern Eugenics movement?

a) Mendel b) Darwin
c) Francis Galton d) Karl pearson

19. Improvement of human race by encouraging the healthy persons to marry early and produce large number of children is called

a) Positive eugenics
b) Negative eugenics
c) Positive euthenics
d) Positive euphenics

20. The _____deals with the control of several inherited human diseases especially inborn errors of metabolism

a) **Euphenics** b) Eugenics
c) Euthenics d) All of these

21. "Universal Donor" and "Universal Recipients" blood group are _____ and_____respectively

a) AB, O **b) O, AB**
c) A, B d) B, A

22. ZW-ZZ system of sex determination occurs in

a) Fishes b) Reptiles
c) Birds **d) All of these**

23. Co-dominant blood group is

a) A **b) AB**
c) B d) O

24. Which of the following is incorrect regarding ZW-ZZ type of sex determination?

a) It occurs in birds and some reptiles
b) **Females are homogametic and males are heterogametic**
c) Male produce two types of gametes
d) It occurs in gypsy moth

25. What is haplodiploidy?

26. Distinguish between heterogametic and homogametic sex determination systems.

27. What is Lyonisation?

28. What is criss-cross inheritance?

29. Why are sex linked recessive characters more common in the male human beings?

30. What are holandric genes?

31. Mention the symptoms of Phenylketonuria.

32. Mention the symptoms of Downs syndrome.

33. Differentiate Intersexes from Supersexes.

34. Explain the genetic basis of ABO blood grouping man.

35. How is sex determined in human beings?

36. Explain male heterogamety.

37. Brief about female heterogamety.

38. Give an account of genetic control of Rh factor.

39. Explain the mode of sex determination in honeybees.

40. Discuss the genic balance mechanism of sex determination with reference to *Drosophila*.

41. What are the applications of Karyotyping?

42. Explain the inheritance of sex linked characters in human being.

43. What is extra chromosomal inheritance? Explain with an example.

44. Comment on the methods of Eugenics.

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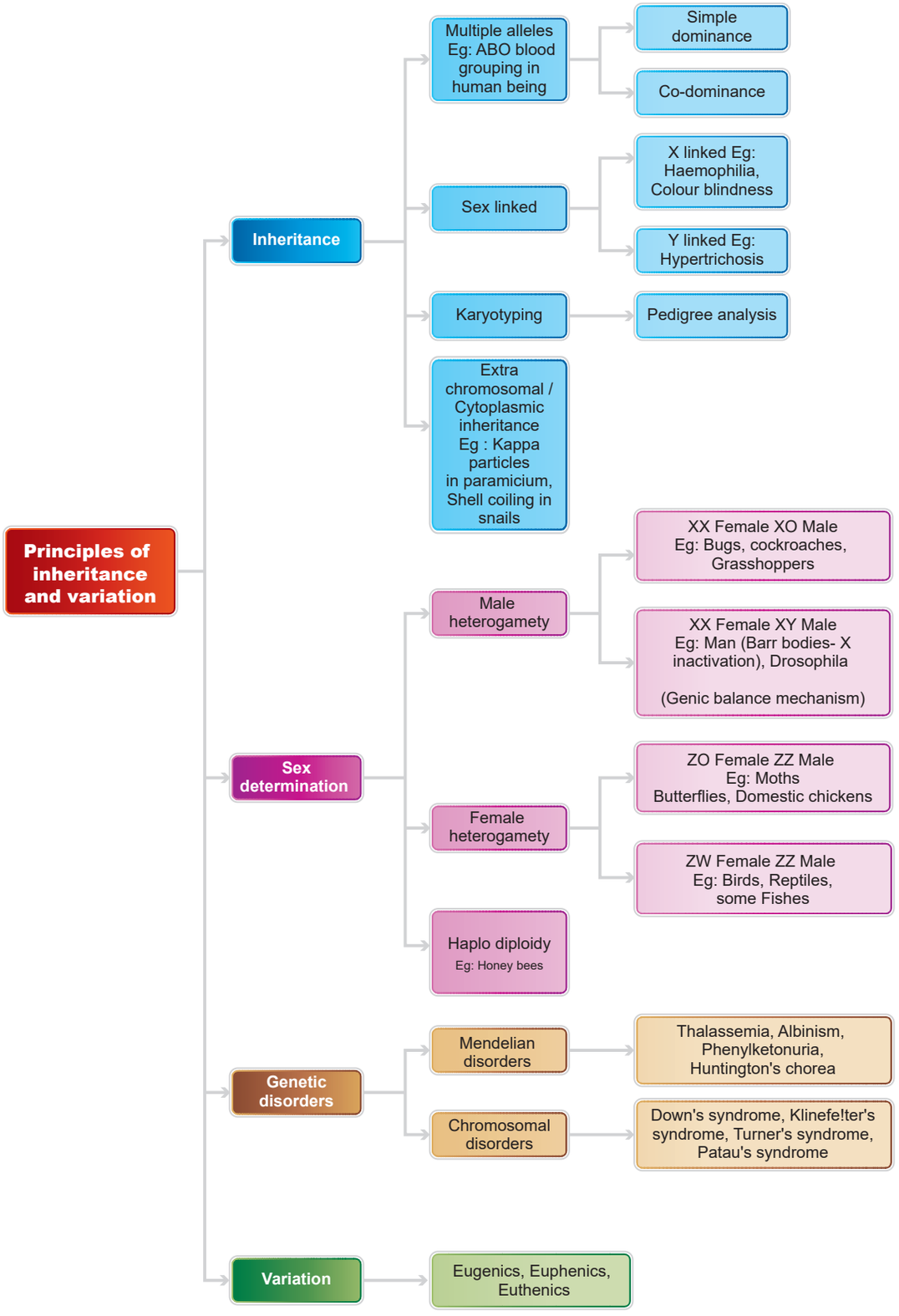
Concept Map



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ICT CORNER

PRINCIPLES OF INHERITANCE AND VARIATION

Shall we can investigate on DNA?

Procedure:

Step -1: Type the **URL** or scan the **QR** code to open the activity page.

Step -2 :Click **"Timeline"** to know the history of **DNA** identification and the work of scientists. On the right top of the window, find hexagons revealing about other tabs to click.

Step -3 :Click **"Genome"** to go through "**FLYOVER", " Chromosome Close Up"** and in **" Genome Fishing"**, click on the tabs such as **"Centromere"**, etc., to know the shape. And Click "Genome Spots" to know the various responsible Spots respective to their activities.

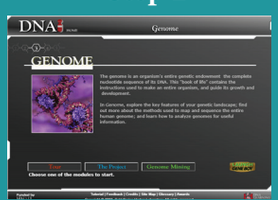
Step – 4 : Find **"Launch Gene Body"** on the right bottom of the window, and Click it to analyse and understand about the cloning.

Step -5 :Click on **"Applications (Hexagon 4)"** to know the uses behind. And click **"Chronicle (Hexagon 5)"** to know the documentations.

Step 1

Step 2

Step 3



Step 4

PRINCIPLES OF INHERITANCE AND VARIATION URL:

http://www.dnai.org/

*Pictures are indicative only

*Allow flash player

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