KRISHNAGAR ACADEMY

BIOLOGY -

PRINCIPLE OF INHERITANCE &VARIATION

Class -12

MORGAN AND *DROSOPHILA*

Thomas Hunt Morgan (1866-1945; *Fig. 28*), an American zoologist, carried his experiments of inheritance on fruit fly, *Drosophila melanogaster*. The fruit fly proved eminently suitable for cytogenetic studies because of the following reasons.

Fig. 28. Thomas Hunt Morgan (1866-1945).

(1) Fruit flies breed quickly and prolifically. A pair of flies in a small milk bottle can produce in a single mating a progeny of hundreds. A new generation can be bred every two weeks.

(2) They are simple to breed in the laboratory throughout the year. They are tiny (3 mm long) and feed on rotting fruits.

(3) The female fly is readily distinguished from the male by its larger body size and presence of ovipositor, the egg-laying structure at the rear end of the abdomen.

(4) The complex behaviour of fruit flies, especially their mating dances, provides geneticists with a good system for unraveling the relation between genes and behaviour.

(5) The fruit fly possesses four pairs of chromosomes, which are different in size and easily distinguishable. Three pairs (II, III and IV) are autosomes and the fourth pair (I) sex chromosomes, XX in females and XY in males. The Y-chromosome is characteristically 'J'-shaped *(Fig. 21 A-B)*.

Sex-linked Inheritance in *Drosophila*

In the course of breeding experiments with the normal wild type of *Drosophila* with red eyes, **Morgan** (1910) observed an individual (mutant) in the population with white eyes. A true breeding strain of white-eyed flies was obtained from this individual. When this new white variety was crossed with red-eyed type, the results from the reciprocal cross of white male and red female were different from those obtained from red male with white female. These results were found to depend on the sex of the parent by which the trait was introduced into the cross. For other mendelian characters it makes no difference in F_1 or F_2, whether a given character is brought in by the male or female parent. The details of these experiments are shown in figure 29.

White-eyed male X red-eyed female. From the cross of white-eyed male with red-eyed female *Drosophila*, the first generation (F_1) flies were red-eyed in both sexes. When these were bred together, one-fourth of the F_2 offspring were white-eyed indicating that red and white eye colours

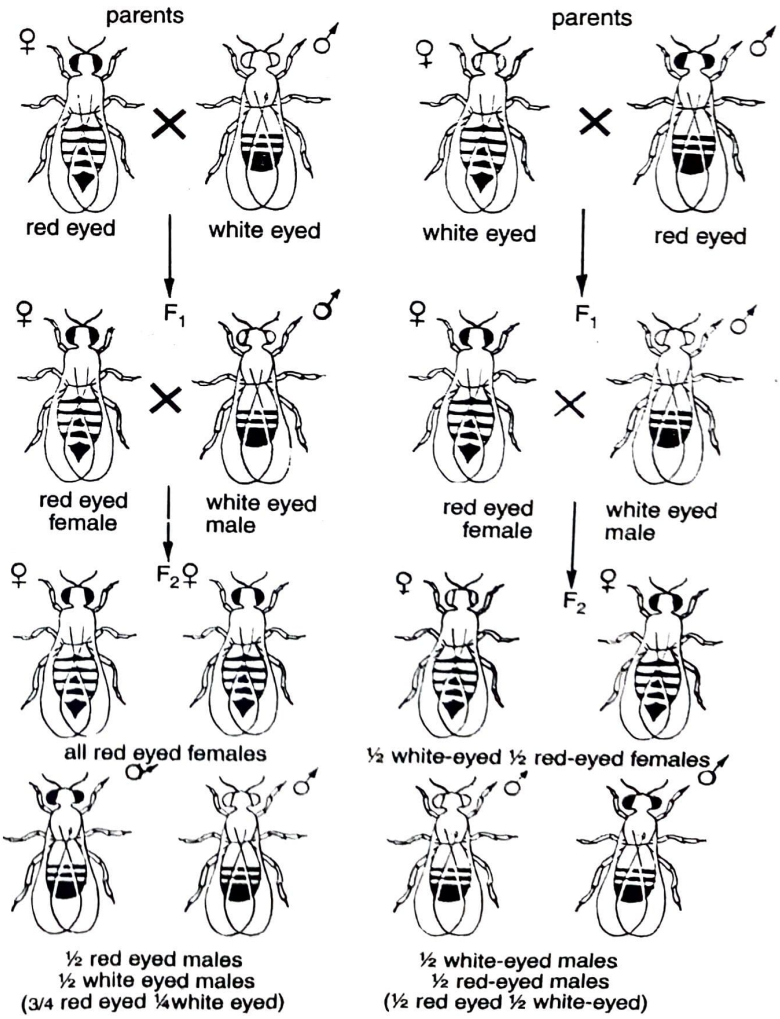


Fig. 29. Sex-linked inheritance in *Drosophila*.

are due to an allelic pair of genes of which red reappears as the dominant. Besides, in F_2 offspring, all the females were red-eyed whereas half the males were red-and half white-eyed.

White-eyed female X red-eyed male. When a red-eyed male was crossed to a white-eyed female, the results were different. In F_1 offspring, females were red-eyed and males were white-eyed. When these were bred together, their offspring (F_2 progeny) consisted of red-eyed and white-eyed flies in equal numbers in both sexes.

The first white mutant observed by **Morgan** was a **male**. This is understandable since the male has only one X-chromosome and there is no gene in the Y-chromosome to mark the expression of white. The white mutant got his X-chromosome from his mother. Sex-linked genes are regularly transmitted from mother to son, and never from father to son.

Wing length in *Drosophila*. Like eye colour, the genes for wing length are also sex-linked in *Drosophila*. Normal wing is dominant to miniature wing. Its inheritance is similar to that of eye colour.

Sex-linked Inheritance in Human Beings

In human beings, 46 chromosomes (23 pairs) are present in each somatic cell. In females, there are 22 pairs of autosomes and one pair of X-chromosomes (22 pairs + XX), whereas in males there are 22 pairs of autosomes and one X and one Y-chromosome (22 pairs + XY). As female produces only one type of gametes, gametes from male determine the sex of the progeny. Sex-linked characters in human beings thus follow the same pattern as in *Drosophila (Fig. 30)*. Colour blindness and haemophilia are two important examples of sex- linked characters in human beings.

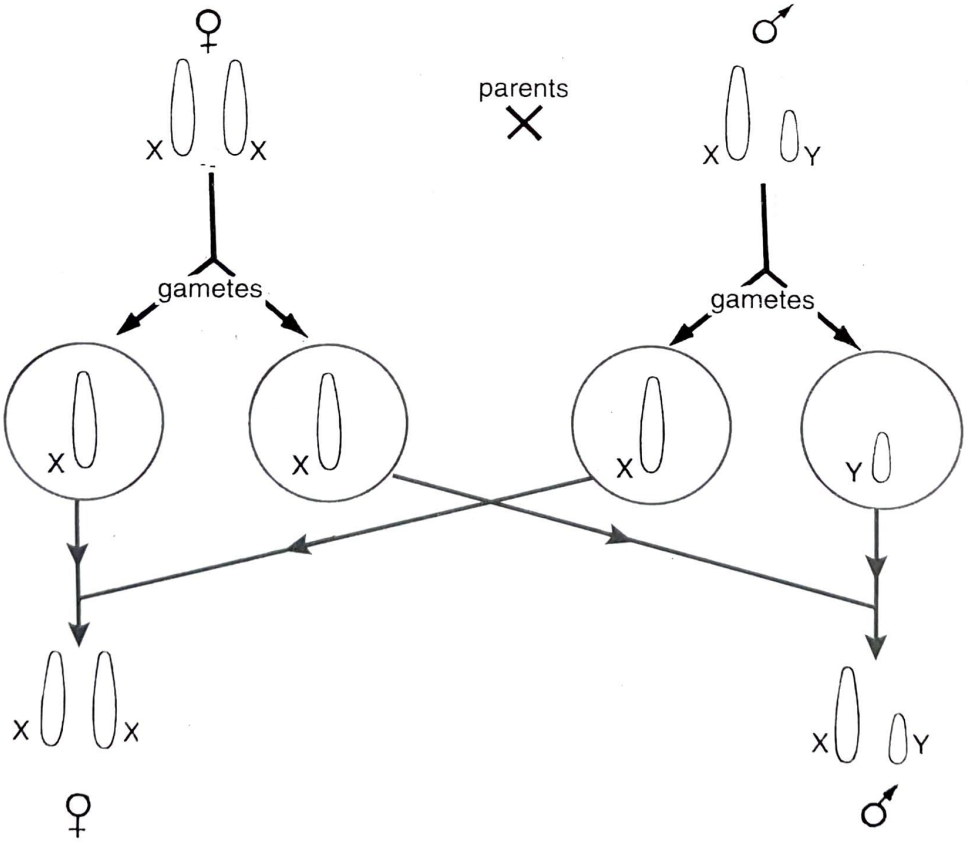


Fig. 30. Determination of sex by Y-chromosome in human beings.

Colour blindness. A particular trait in human beings enables them to differentiate between red and green colours. The gene for this red-green colour blindness is located on X-chromosome.

Colour blindness is recessive to normal vision and is found more often in man. A father transmits his X-chromosome to his daughters but not to his sons, whereas a mother transmits X-chromosomes to both her sons and daughters. Therefore, all the sons of a colour-blind mother are colour-blind regardless of the kind of colour vision her husband may have. But if the husband has normal vision, all his daughters have normal vision. But they, however, carry the gene for colour blindness. Married to man with normal colour vision, they produce all normal girl children, but among the sons about half are normal and the other half colour-blind *(Fig. 31)*.

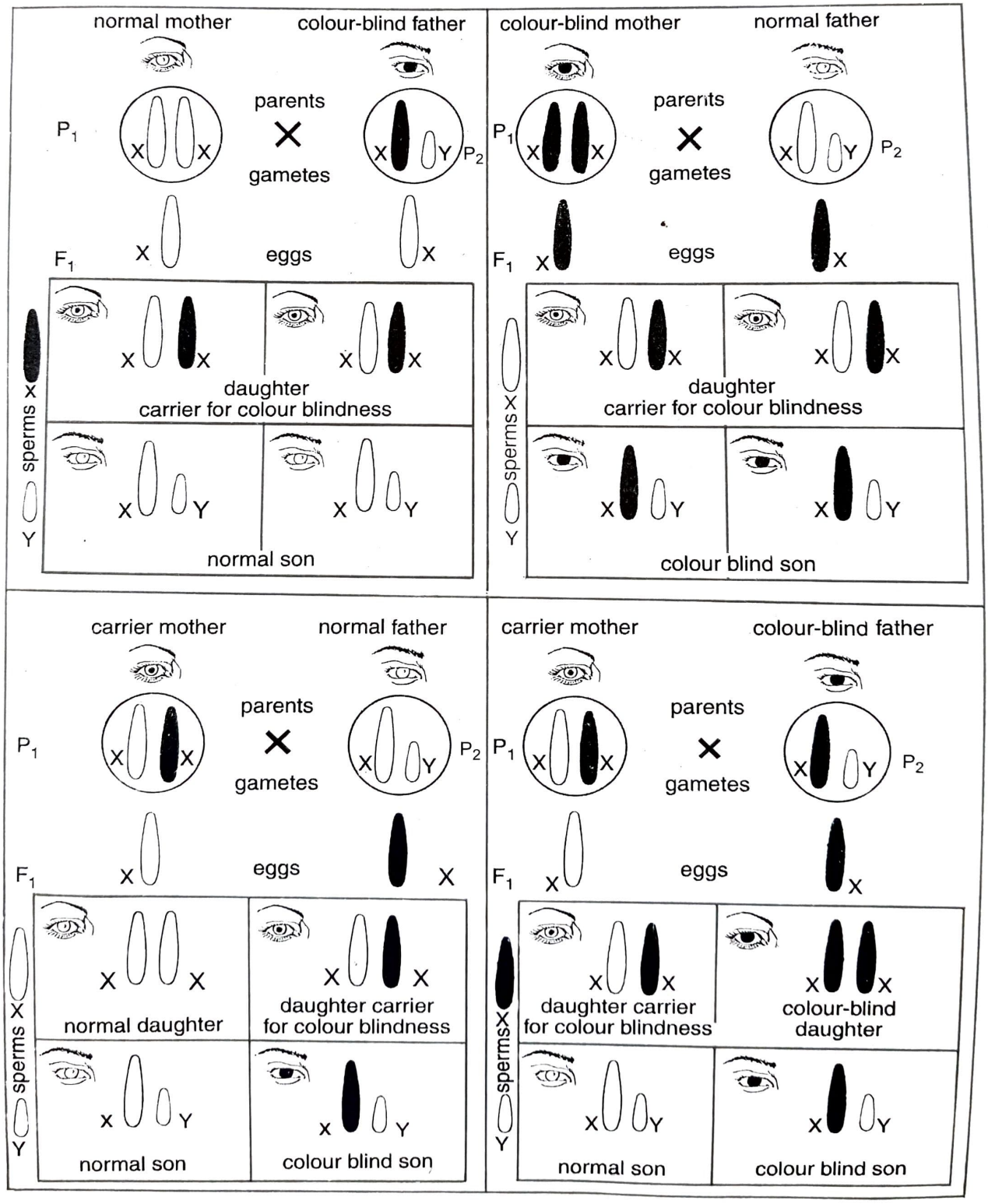


Fig. 31. Inheritance of sex-linked colour blindness in human beings.

A colour-blind daughter is produced only if a colour-blind man happens to marry a carrier or a homozygous colour-blind woman.

Haemophilia. Individuals suffering from haemophilia lack the factor which is responsible for clotting of blood. In such persons even a minor cut may cause prolonged bleeding leading to death. It is also a recessive character and is, therefore, masked in heterozygous condition. Its inheritance is similar to that of colour blindness *(Fig. 32)*.

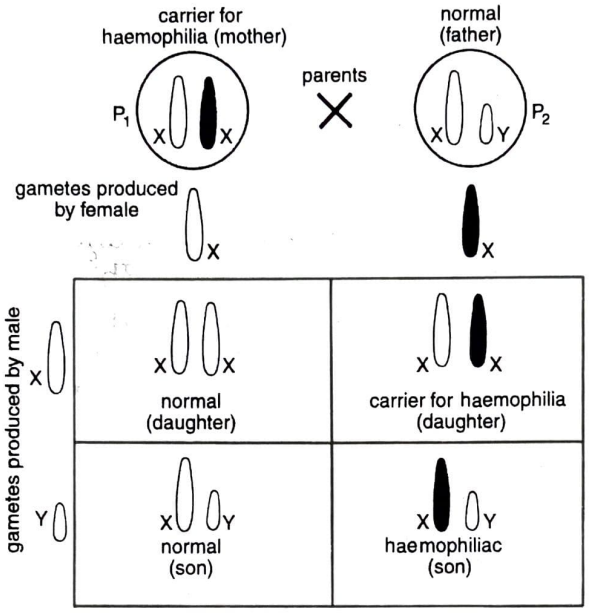


Fig. 32. Inheritance of haemophilia in human beings.

NOTE

If father is haemophilic and mother is normal all children will be normal. This is because the X-chromosome of the male carrying the defective gene is passed on to the daughter who becomes carrier. Draw the Punnett square by yourself and see the result.

HUMAN GENETIC DISORDERS

The diseases which are transferred from generation to generation are called genetic disorders or genetically transmitted diseases. They are **congenital,** i.e., abnormal conditions are present at birth. These disorders may be due to incompatible genes, defective genes or abnormalities in the structure or number of chromosomes. They may be **inherited** or arise a new due to **mutations.**

These disorders may be grouped into two groups, viz., **Mendelian disorders** and **Chromosomal disorders**. **Mendelian disorders** are mainly determined by the alteration in the single gene. These disorders are transmitted to the offspring on the principle of inheritance. The pattern of inheritance of such Mendelian disorders can be traced in a family by the pedigree analysis. On the other hand **chromosomal disorders** are caused due to absence or excess or abnormal arrangement of one or more chromosomes.

Mendelian Disorders in Humans

Most common and prevalent Mendelian disorders are haemophilia, cystic fibrosis, sickle-cell anaemia, colour blindness, phenylketonuria, thalassaemia, etc.

Mendelian disorders may be dominant or recessive and may be linked to both autosomes and sex chromosome. By pedigree analysis one can easily understand whether the trait in question is dominant or recessive.

Haemophilia. Haemophilia is a **sex linked recessive disease**, which shows its transmission from unaffected carrier female to some of the male progeny. In this disease, a protein involved in the clotting of blood is affected. As a result, bleeding does not stop even in a simple cut in an

affected individual. The heterozygous female (carrier) for haemophilia may transmit the disease to sons. The possibility of a female becoming a haemophilic is extremely rare because mother of such a female has to be at least carrier and the father should be haemophilic (unviable in the late stage of life). The family pedigree of Queen Victoria shows a number of haemophilic descendants as she was a carrier of the disease.

Colour Blindness. It is a **sex-linked recessive disorder** due to defect in either red or green cone of eye resulting in failure to discriminate between red and green colour. This defect is due to mutation in certain genes present in the X-chromosome. It occurs in about 8 per cent of males and only about 0.4 per cent of females. This is because the genes that lead to red-green colour blindness are on the X-chromosome.

Sickle-Cell Anaemia. Sickle-cell anaemia is an **autosome linked recessive trait** that can be transmitted from parents to the offspring when both the partners are carrier for the gene (heterozygous). The disease is controlled by a single pair of allele, $\mathbf{Hb^A}$ and $\mathbf{Hb^S}$. Out of the three possible genotypes only homozygous individuals for Hb^S (Hb^S Hb^S) show the disease phenotype. Heterozygous (Hb^A Hb^S) individuals appear apparently unaffected but they are carrier of the disease. The defect is due to the substitution of glutamic acid by valine at the sixth position of the β-globin chain of the haemoglobin molecule. This substitution occurs due to the single base substitution at the sixth codon of the β-globin gene from GAG to GUG. The mutant haemoglobin molecule then undergoes polymerisation causing the change in the shape of the RBC from biconcave disc to sickle like structure *(Fig. 33 A-B)*.

Phenylketonuria. Phenylketonuria is an **inborn error of metabolism, inherited as an autosomal recessive trait**. The affected individual lacks an enzyme that converts the amino acid phenylalanine into tyrosine. As a result, the phenylalanine is accumulated and converted into phenyl pyruvic acid, causing mental retardation.

Thalassaemia. Thalassaemia is an **autosome-linked recessive blood disease** transmitted from parents to the offspring when both the partners are unaffected carrier for the gene (heterozygous). It refers to a group of hereditary hemolytic anaemias associated with deficient synthesis of haemoglobin. The RBCs are small (microcytic), pale, and short-lived. Thalassaemia occurs primarily in populations from countries bordering the Mediterranean sea.

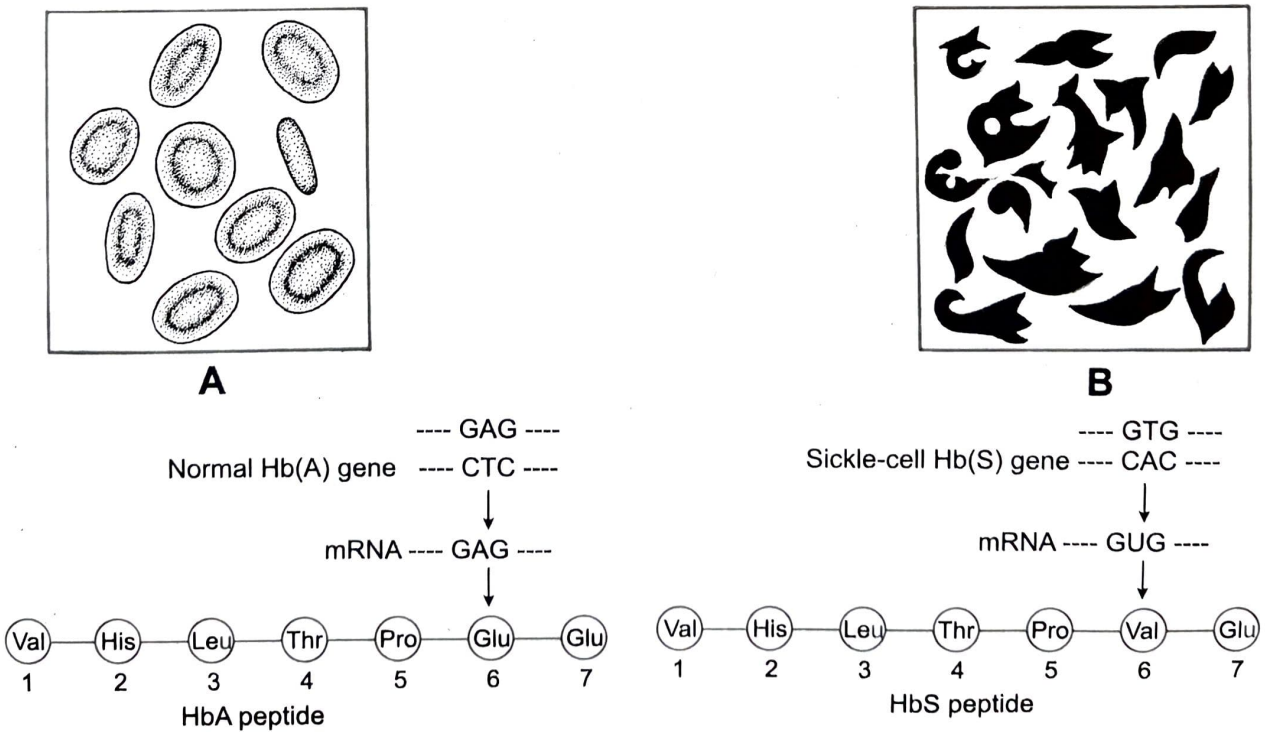


Fig. 33 A-B. Red blood cells and the amino acid composition of the relevant portion of β-chain of haemoglobin : **A.** from a normal person ; **B.** from a person with sickle-cell anaemia.

It is an inherited abnormality in haemoglobin which causes the red blood cells to breakdown too easily. The disease affects both sexes equally.

Thalassaemia differs from sickle-cell anaemia in that the former is a quantitative problem of synthesising too few globin molecules while the latter is a qualitative problem of synthesising an incorrectly functioning globin.

In thalassaemias, absence or reduced synthesis of one of the globin chains results in an excess of the other. As a result, free globin chains, which are insoluble, accumulate inside the red cells and form precipitates which damage the cell, causing cell lysis and resulting in anaemia. Thalassemia can be classified according to which chain of the haemoglobin molecule is affected. In α-thalassemia, production of α-globin chain is affected while in β-thalassemia, production of β-globin chain is affected. α-thalassemia is controlled by two closely linked genes HBA1 and HBA2 on chromosome 16 of each parent. α-thalassaemias result in decreased α-globin production, resulting in an excess of β-chains in adults and excess γ-chains in newborns. The excess β-chains form unstable tetramers (called Haemoglobin H) which have abnormal oxygen dissociation curves. β- thalassemia is controlled by a single gene HBB on chromosome 11 of each parent. In **beta (β) thalassaemias**, formation of β-chains is either prevented (**β^0 or β-thalassaemia major**) or a few β-chain formation occurs (**β^+ or β- thalassaemia intermedia**). In either case there is a relative excess of α-chains, but these do not form tetramers; rather they bind to the red blood cell membranes, causing membrane damage, and at high concentrations they form toxic aggregates.

Albinism. It is the condition where skin and hair of the whole body appear colourless due to total or nearly total absence of pigmentation (melanin pigment). It is an **autosomal recessive disorder** against the normally pigmented skin and hair. An albino is thus always homozygous for the character. Absence of the enzyme **melanocyte tyrosinase** leads to failure of melanin formation from tyrosine, and the person develops albinism. Albinos although lead a normal life, have a strong aversion against exposure to sun.

Disorders Arising from Chromosomal Abnormalities

These disorders are due to abnormal chromosomal numbers and may be **autosomal** or **sex-linked**.

Autosomal Abnormalities

1. **Down's syndrome (Mongolian idiocy).** This is the best example of autosomal abnormalities (first described by **Langdon Down** in 1866). The condition is caused by an abnormality in a baby's chromosomes. Such babies are trisomic for chromosomes 21. Thus, there are 47 chromosomes instead of normal 46 (45 + XX in females and 45 + XY in males). The disease is also called **triplo-21**. Such individuals are developed due to non-disjunction of autosomes during gamete formation. When such a gamete is fertilized by a normal gamete of the opposite sex, a zygote is produced which is trisomic with respect to that autosome. Affected babies suffer from a variable degree of mental retardation and heart defects and are usually recognisable at birth by a number of definite physical characteristics (a short stocky body and characteristic eye folds and lack of muscle tone). Such children are of a happy disposition and have a great sense of humour (*Fig.34*).

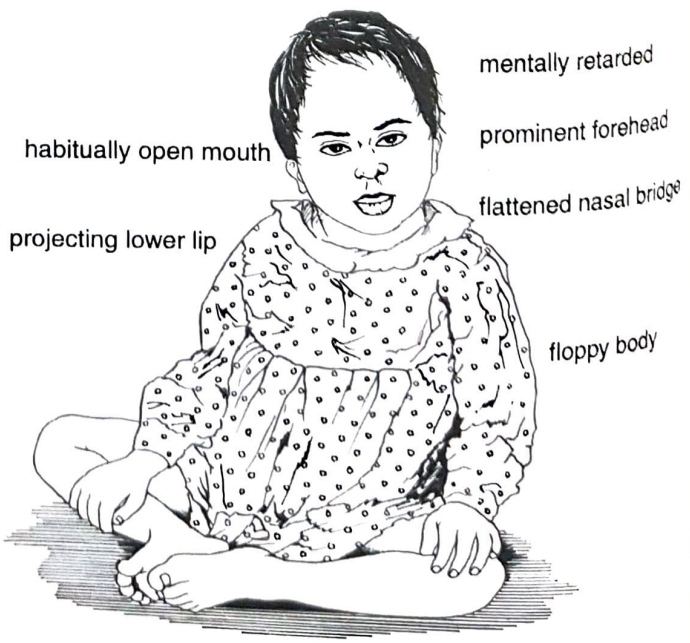


Fig. 34. Signs of Down's syndrome.

Table 4. Disorders of sex development due to sex-chromosome abnormality.

Disorder	Genetic sex	Gonadal sex	Phenotype
1. Klinefelter's syndrome	XXY; genetically female because of the presence of two X- chromosomes.	Testes present, but atrophied, gonadally male; presence of testis is due to Y-chromosome.	Phenotype male, outward appearance male; penis, vas deferens, seminal vesicles present, but small-sized, no spermatogenesis; sterility present.
2. Turner's syndrome	XO; genetically sexless.	No ovary; no testes; no gonadal sex.	Phenotype female, outward appearance female; vulva, vagina and uterus present, but breasts donot develop owing to the absence of estrogens; no menstruation; sterility present.

The afflicted children are mentally retarded having prominent foreheads, flattened nasal bridge, habitually open mouth, projecting lower lips, a large protruding tongue and a characteristic skin fold at the corner of the eye. The baby is usually floppy when handled. The fifth finger is short with only one transverse crease on the palm of the hand. Many Down's babies are also associated with congenital defects in heart and other organs.

Mothers over 35 and those who have had one Down's baby are at the highest risk. The amniocentesis test can detect the condition during the early stages of pregnancy. If positive, this provides legitimate grounds for a parental request for the pregnancy to be terminated. There is no treatment of this disorder. Parental support and maintenance of Down's children at home is the largest contribution that any individual can provide to a Down's baby.

2. Sex chromosome abnormalities. Non-disjunction of sex chromosomes during gamete formation followed by fertilization and development can lead to individuals with abnormal sex chromosome complement. Sometimes the members of a chromosome pair fail to separate at first meiotic division, which results in the formation of one gamete which contains all chromosomes of the pair and other gamete does not contain any chromosome part. This phenomenon is called **non-disjunction**. Klinefelter's syndrome and Turner's syndrome are two main sex chromosome abnormalities found in human beings.

(a) **Klinefelter's syndrome.** Klinefelter's syndrome is characterized by trisomy (XXY). There are 47 chromosomes instead of normal 46 (44 + XXY). Such an individual has overall masculine development. Their genitalia (testis) are under developed and the body hair are sparse. Most cases have some degree of breast development and tend to have longer than normal legs and arms. Such individuals are often mentally defective and are sterile males. It is seen in one out of every 500 male births.

(b) **Turner's syndrome.** Turner's syndrome is characterized by monosomy of XO type. The individuals possess 45 chromosomes instead of normal 46 (44 + XO), and are immature females (sterile). They are characterized by poorly developed ovaries, webbed neck, broad chest with under developed breasts and below average intelligence *(Fig. 35)*. Another interesting sign is the presence of short 4th metacarpal and metatarsal bones. They are short statured. One female in every 2500 births suffers from this syndrome.

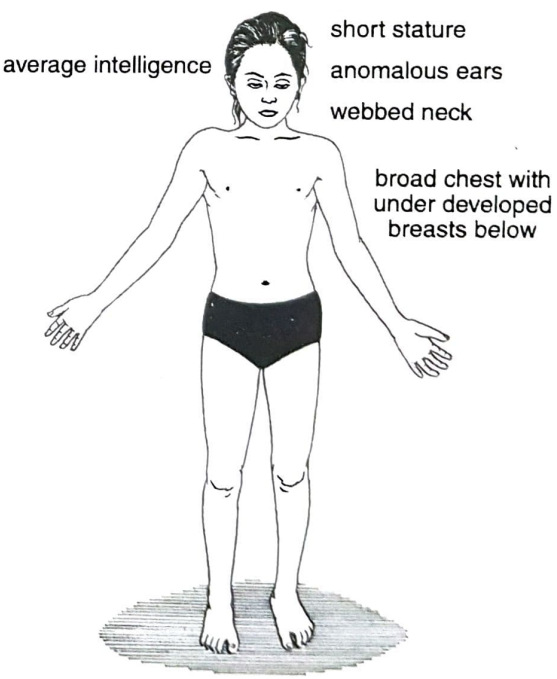


Fig. 35. Signs of Turner's syndrome.

VARIATIONS

Variations may be defined as the process whereby closely related organisms come to differ amongst themselves. Variations are of utmost significance in organic evolution as without variation no change could occur. They may be small, gradual and continuous, but sometimes a sudden change in genetic constitution leads to large variations.

RECOMBINATIONS

The organisms which express characters of both the parents are known as **recombinants** and the phenomenon responsible for mixing maternal and paternal characters in sexually reproducing organisms is said to be **recombination**. Genetic variation in sexually reproducing species arises primarily because parental genes are shuffled into new combinations, i.e., new genotypes in the offspring. The three major sources of such variations are :

(1) Independent assortment of chromosomes during meiosis.

(2) Reciprocal recombination of linked genes on chromosomes by crossing over in prophase-I of meiosis.

(3) Random fertilization of gametes.

MUTATIONS

Mutation is a phenomenon which results in alteration of DNA sequences and consequently results in changes in the genotype and the phenotype of an organism. Mutations in a broad sense include all those heritable changes which alter the phenotype of an individual. While working on evening primrose (*Oenothera lamarckiana*), **Hugo de Vries** (1901, 1903) used the term **mutation** to describe phenotypic changes which were heritable. In addition to recombination, mutation is another phenomenon that leads to variation in DNA.

Mutations may occur **spontaneously** in nature or they may be **artificially induced**. Spontaneous gene mutations are always occurring in nature. In about 10 million specimens of *Drosophila melanogaster*, a few hundred gene mutants were observed. These mutants produce true-breeding stable genotypes varying in characters like eye colour, wing type, etc. from the original wild type. The artificially induced mutations are similar to those produced spontaneously in nature due to the fact that the kinds of changes produced are alike to those created by spontaneous mutations. A comparison between spontaneous and induced mutations is given in Table 5.

Table 5. Comparison between spontaneous and induced mutations.

	Spontaneous mutation	Induced mutation
1.	They originate **spontaneously in nature**.	They are **induced artificially** .
2.	They **continuously arise in nature** automatically.	They are **man-made** and, therefore, occur when man induces them, otherwise never found.
3.	They are produced by **naturally** occurring mutagenic agents such as electric currents, atomic particles and rays, temperature, variations, etc.	They are produced by subjecting organism **artificially** to mutagens such as gamma rays, X-rays, neutrons, ultraviolet rays, etc.
4.	Their frequency of occurrence is **very low**.	Their frequency of occurrence is comparatively **higher**.

The modern theory of mutation as proposed by **Hugo de Vries** has following salient features :

(1) Mutations are observed in all organisms from man to bacteria. It is universal.

(2) They arise all on a sudden (at random).

(3) It results as a change in germplasm of an organism. The mutations which affect germ cells are only heritable.

(4) Mutations may be dominant or recessive, sex linked or autosomal, lethal or non-lethal, and useful or deleterious. But most mutations are recessive and lethal possibly because they disturb genic balance.
(5) Different forms (alleles) of a gene are formed only by mutation.
(6) Mild mutations are more common than severe mutations.
(7) Mutation provides raw material for evolution and it alone does not produce new species.

Types of Mutations

Mutation is a heritable change in the structure of a gene or chromosome, or a change in chromosome number. Accordingly, mutations are of the three principal types : (1) **gene mutations**, (2) **chromosomal mutations** or **aberrations**, and (3) **genomatic mutations** or **polyploidy.**

1. **Gene mutations.** Hereditary characters are due to the effects of genes. In this mutation there are changes in the fine structure of genes. They directly influence the nature and functioning of genes. Since genes are DNA segments, the gene mutations include changes in the arrangement of nucleotides in the genes (**intragenic mutations**). Genes carry genetic information in the form of genetic codes. Any change in the nucleotide sequence and nature can affect the expression of gene adversely. The mutant gene and the original gene are situated at the same fixed point on a particular chromosome. Since, a gene is located at a fixed point on the chromosome, a gene mutation is called **point mutation**. This type of mutation occurs at the molecular level usually at the time of DNA replication when new DNA strands are synthesized. Hence, gene mutations are also said to be **copy-error mutations**. These mutations mostly include alteration in the sequences of nucleotides in the nucleic acids which form the genetic material.

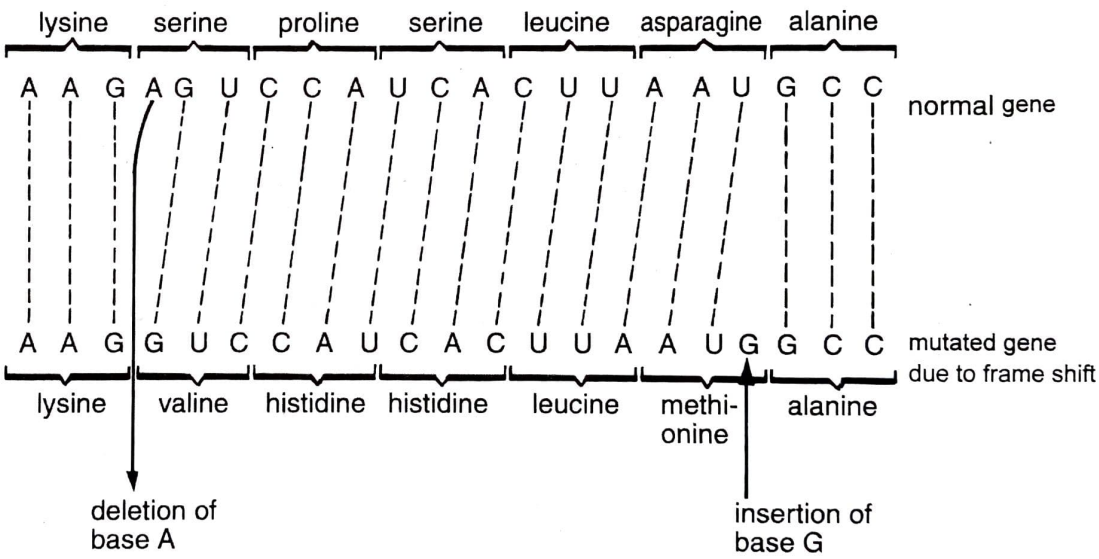


Fig. 36. Shift in the triplet arrangement of the nucleotide sequence by a frame-shift mutation.

Gene mutations are of two types :

(a) **Frame shift mutations.** These are caused by deletion or addition (insertion) of a nucleotide in a DNA segment (gene). Since genetic code is commaless, both addition or deletion of nucleotides shift is reading frame of codons from the site of change onward. Therefore, such mutations are called **frame shift mutations** (*Fig. 36*). They are very harmful mutations as the expression of gene gets completely changed. They change the sequence of amino acids in a protein. For example muscular dystrophy (human hereditary disease) is caused by frame shift mutation which leads to premature termination of translation of protein dystrophism.

Frame shift mutations are of two types :

(i) **Deletion mutation.** In this case one nucleotide is removed off from a gene, so that the frame of genetic information gets changed.

(ii) **Insertion (addition) mutation.** In this case, one nucleotide is added to a gene, so that the frame of genetic information becomes changed.

(b) Substitution (replacement) mutations. In these mutations a particular nucleotide of a DNA segment (gene) is substituted (replaced) by another nucleotide. These are of two types:

(i) Transition mutation. Transitions are those base pair replacements where a purine is replaced by another purine and a pyrimidine is replaced by another pyrimidine. It means that AT is replaced by GC and *vice-versa (Fig. 37 A)*.

(ii) Transversion mutation. Transversions are those base replacements where a purine is replaced by a pyrimidine and *vice-versa*. It means that CG can be replaced by GC and AT is replaced by TA *(Fig. 37 B)*.

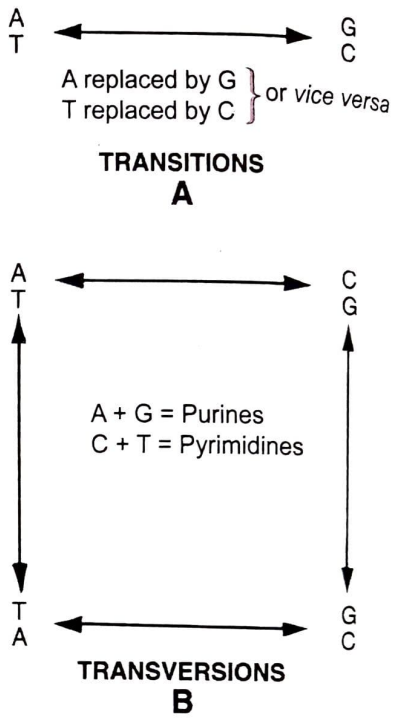


Fig. 37 A-B. Base pair replacements involved in transitions (A) and transversions (B).

Both, transitions and transversions take place due to mistakes in the incorporation of nucleic acid precursors or due to mistakes committed during replication.

Gene mutations occurring during gamete formation are transmitted to all the cells of the offspring and may be significant for the future of the species. Somatic gene mutations which arise in the organism are inherited only by those cells derived from the mutant cells by mitosis. Whilst they may affect that organism, they are lost on the death of the organism. Somatic mutations are probably very common and go unnoticed.

The effects of gene mutation are extremely variable. Most minor gene mutations pass unnoticed in the phenotype since they are recessive, but there are several cases where a change in a single base in the genetic code can have a profound effect on the phenotype. **Sickle cell anaemia** in humans is an example of base substitution mutation affecting a base in one of the genes involved in the production of haemoglobin. The respiratory pigment, haemoglobin, is made up of four polypeptide chains (two α chains and two β chains) attached to the prosthetic group **haem**. The polypeptide chains influence the oxygen-carrying capacity of the haemoglobin molecule. A change in the base sequence of the triplet coding for one particular amino acid out of the 146 in the β chains gives rise to the production of sickle cell haemoglobin (HbS). The amino acid sequences for the normal and abnormal chains differ in the substitution of **valine** for **glutamic acid** at one point in the abnormal polypeptide chains of **haemoglobin S**. Such a minor change causes haemoglobin S to crystallise at low oxygen concentrations. The histological effect of this is to cause haemoglobin-S-containing red blood cells to distort and appear sickle-shaped.

2. Chromosomal mutations or aberrations. The structural changes in chromosomes which appear phenotypically are known as **chromosomal mutations** or **aberrations**. These alterations do not involve changes in the number of chromosomes but result from changes in the number or sequence of genes on chromosomes. These changes were first analysed by **H. J. Muller** (1928) in *Drosophila* and by **Barbara McClintock** (1930) in *Zea*. Some important structural changes in the chromosome are as follows.

(a) Deficiency or deletion. It signifies the loss or absence of a section of a chromosome and may involve one or more genes *(Fig. 38 A)*. Genic balance is usually disturbed due to deletions and this affects the phenotype. Deletions can be recognised by distortions of chromosomes during meiotic pairing of homologous chromosomes. Due to a terminal deletion (from one end), one of the paired chromosomes appears to be much longer than the other, whereas due to an interstitial deletion (between two ends), the normal chromosome forms a loop near the deficient region of its homologue as only identical regions pair with each other.

Inheritance patterns of genes of deleted regions and cytological studies of pairing between normal and deleted chromosomes have helped to find out the relative positions of genes on chromosomes. Thus deletions have helped in constructing and verifying linkage maps of a variety of organisms like maize, *Drosophila*, bacteriophages, etc.

(b) **Duplication. The presence of a part of a chromosome double of the normal complement is known as duplication** *(Fig. 38 B)*. A broken section of a chromosome attaches itself to a normal homologous or non-homologous chromosome or in the presence of a centromere it behaves like an independent chromosome and gets included in an otherwise normal nucleus. Consequently, some genes are present in the cell in more than two doses.

Depending on the mode of joining of the duplicated region to a chromosome or its independent existence, duplications can be of the following five types.

(i) **Extra-chromosomal.** In the presence of a centromere, the duplicated part of the chromosome may behave as an independent chromosome.

(ii) **Tandem.** In this case, the duplicated region is situated just by the side of the normal corresponding section of the chromosome and the sequences of genes are the same in the normal and duplicated regions.

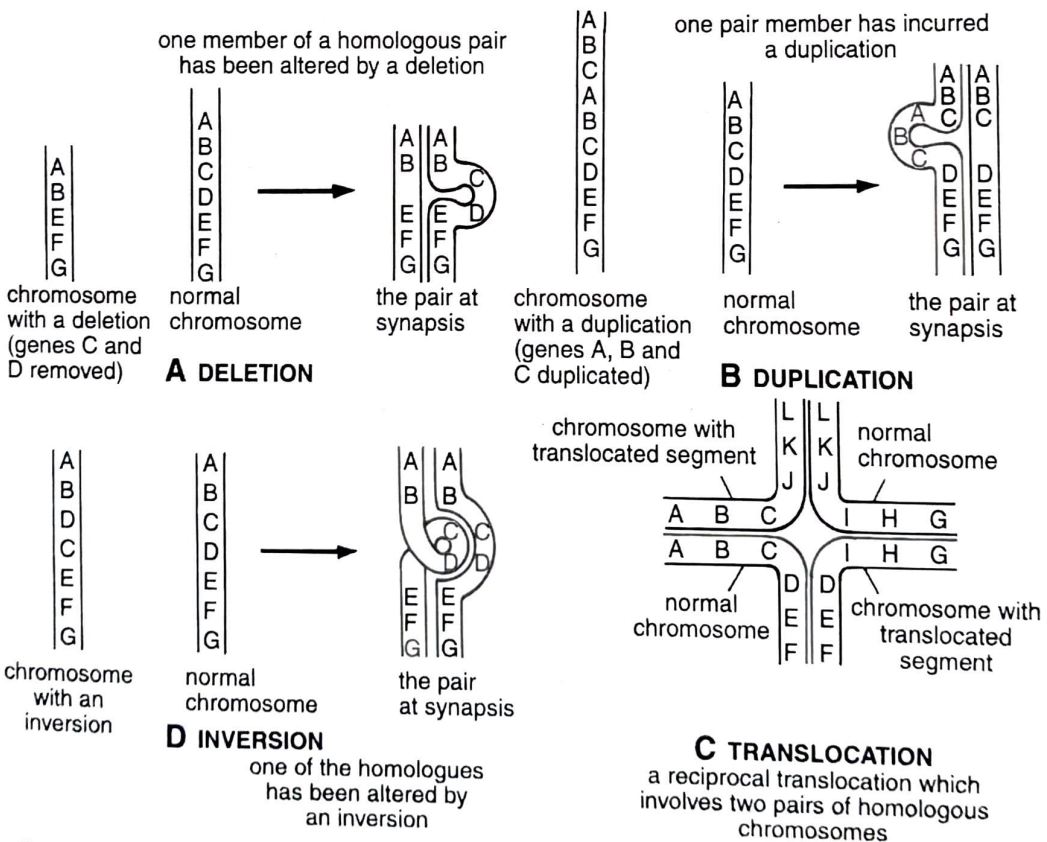


Fig. 38 A-D. Chromosomal mutations : A. deletion; B. duplication; C. translocation; D. inversion.

(iii) **Reverse tandem.** In this case, the sequence of genes in the duplicated section of a chromosome is just the reverse of the normal sequence.

(iv) **Displaced.** Here, the duplicated section is not adjacent to the normal section.

(v) **Transposed.** In this case, the duplicated section is attached to a non-homologous chromosome.

Like deletions, duplications also result into unequal or looped out configurations at the time of pairing of homologous chromosomes.

The effects of duplication on viability are generally less deleterious than those of deficiencies. Individuals carrying duplications show various abnormalities in bodily characters, and these may be used to identify the carriers of the corresponding duplications.

Duplication has played an important role in evolution. It is a means of increasing the number of genes in a cell so that different copies of the same gene may change in different directions without disturbing the normal functions of the organism.

(c) **Translocation. Translocation involves the transfer of a part of a chromosome or a set of genes to a non-homologous chromosome** *(Fig. 38C)*. It results in a change in the sequence and position of genes but not their quantity. For example, if the original chromosomes were A B C D E F and G H I J K L, the new ones may be A B C J K L and G H I D E F. Translocations are of the following three types.

(i) **Simple translocation.** This involves a single break in a chromosome; the broken piece gets attached to one end of a non-homologous chromosome *(Fig. 39 A)*.

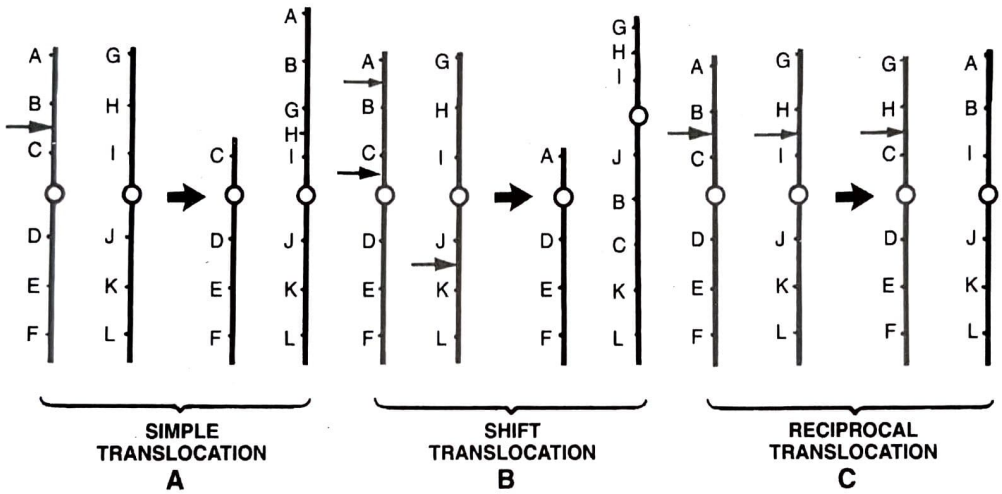


Fig. 39 A-C. Types of translocations : **A.** simple; **B.** shift; **C.** reciprocal. Arrows indicate the points of breaks and letters represent the genes.

(ii) **Shift translocation.** Here, the broken part of a chromosome gets inserted in a non-homologous chromosome *(Fig. 39 B)*.

(iii) **Reciprocal translocation.** In this case, there is an exchange of chromosome part between two non-homologue *(Fig. 39 C)*. This is the most frequent type of translocation.

Due to independent segregation of chromosomes translocations lead to the loss of genes in some of the cells and a reduction in the number of viable gametes, or partial sterility.

(d) **Inversion. Inversion involves a rotation of a part of a chromosome or a set of genes by 180° on its own axis** *(Fig. 38 D)*. Breakage and reunion are essential for inversion. The net result is neither a gain nor a loss in the genetic material but simply a rearrangement of the gene sequence. For example, A B C D E F G gene order may be converted to A B D C E F G. Since, it is extremely unlikely that the homologue of an inverted chromosome would undergo a similar inversion, chromosomes should have to be greatly contorted before proper synapsis can take place. **Inversions** are of the following two types.

(i) **Paracentric inversion.** In this type, centromere is located outside the inversion loop. When a cross over occurs within the loop, one product contains a centromere and the other does not. At anaphase, this results in an abnormal chromosomal 'bridge' and a loss of an entire chromosomal section.

(ii) **Pericentric inversion.** Here, centromere is located inside the inversion loop. When a cross- over between two chromatids occurs within the inversion loop, in the resulting chromatids there are some genes in double number while others are missing. Due to this imbalance, the cell is not viable.

Thus, if the normal sequence of genes in a chromosome is A B C. D E F G, the sequences in para-and peri-centric inversions will be A B C. D G F E and A E D. C B F G, respectively.

Inversions have been useful in establishing and maintaining heterozygous condition, because in inversion heterozygotes crossing-over is suppressed and only parental progeny is produced. Recessive lethals can be of added advantage because heterozygotes for them are viable but homozygotes non-viable.

3. **Genomic mutations or Heteroploidy or Numerical aberrations (changes in chromosomal numbers).** They involve variations in chromosome number of a whole genome. These variations (heteroploidy) are mainly of two types, **aneuploidy,** and **euploidy.**

(a) **Aneuploidy. It is the presence of a chromosome number which is different than the multiple of basic chromosome number. This type of variation involves one or two chromosomes but not the entire set.** It is either due to loss of one or more chromosomes or due to addition of one or more chromosomes to complete chromosome complement. **Aneuploidy** is of the following types.

(1) **Hypoploidy**

(2) **Hyperploidy**

(1) **Hypoploidy.** When one or two individual chromosomes are lost from the normal genome. It is of two types :

(i) **Monosomy. Monosomics** represent the loss of a single chromosome from the diploid set, and they have the chromosome complement $2n - 1$. Since, monosomics lack one complete chromosome, such aberrations create major imbalance and cannot be tolerated in diploids.

(ii) **Nullisomy. Nullisomics** lack a single pair of homologous chromosomes, and have the chromosome complement $2n - 2$.

(2) **Hyperploidy.** When one or more chromosomes (individually) are added to the diploid set of chromosomes. It is of two types :

(i) **Trisomy. Trisomics** are those organisms that have an extra chromosome $(2n + 1)$ which is homologous to one of the chromosomes of the complement. They are specifically useful in locating genes on specific chromosomes.

(ii) **Tetrasomy. Tetrasomics** are those organisms which have an extra pair of homologous chromosomes, and have the chromosome complement $2n + 2$.

(b) **Euploidy. Variations that involve entire sets of chromosomes are known as euploidy.** Some major euploid types are as follows.

(i) **Monoploidy and Haploidy. Monoploids** have a single basic set of chromosomes, e.g., $2n = x = 7$ in barley and $2n = x = 10$ in corn. **Haploids**, on the other hand, represent individuals with half the somatic chromosome number found in normal individual. In haploids each chromosome is represented only once due to which there is no zygotene pairing and all the chromosomes appear as univalents on a metaphase plate at meiosis I. During anaphase I, each chromosome moves independently of the other and goes to either of the two poles. Haploids may originate (i) due to parthenogenetic or androgenic development of gametes, (ii) due to chromosome loss in hybrid embryos, and (iii) by pollen culture. The most important use of haploids is in the production of homozygous diploids.

(ii) **Polyploidy.** In polyploids, each chromosome is represented by more than two homologues. Failure of normal mitotic divisions results into nuclei with increased sets of chromosomes.

Depending on whether polyploids are produced by the multiplication of chromosome sets that are initially derived from a single species or from two different species, they are of two types, **Autopolyploids** and **Allopolyploids.**

(a) **Autopolyploidy. Autopolyploids are those polyploids which have the same basic set of chromosomes multiplied.** For instance, if a diploid species has two similar sets of chromosomes or genomes (AA), an **autotriploid** will have three similar genomes (AAA) and an **autotetraploid** four such genomes (AAAA).

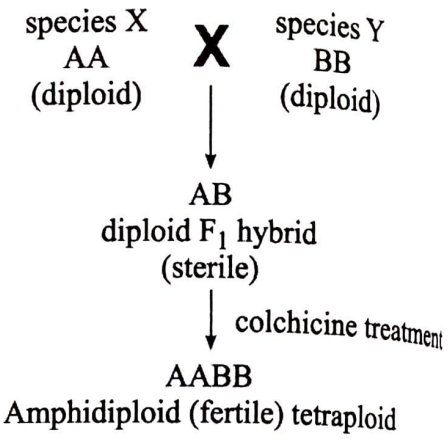
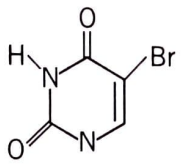
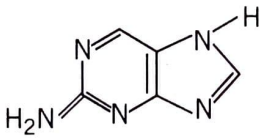
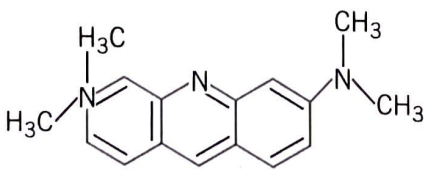


Fig. 40. Derivation of a tetraploid amphidiploid from two diploid species.

(b) **Allopolyploidy. Polyploidy resulting from the doubling of chromosome number in a F_1 hybrid derived from two quite different species is known as allopolyploidy.** Allopolyploidy brings two different sets of chromosomes in F_1 hybrid. Suppose A represents a set of chromosomes (genome) in species X, and B another genome in species Y, the F_1 will then have one A genome and another B genome. The doubling of chromosomes in this F_1 hybrid (AB) will give rise to a tetraploid with two A and two B genomes. Such a polyploid is called **allopolyploid** or **amphidiploid** *(Fig. 40)*.

Induction of gene mutation. Mutation is a random process often occurring spontaneously with a low frequency. Errors during meiosis lead to chromosomal mutations. Besides, they can be induced by several **mutagens. H. J. Muller** (1927) was the first to produce induced mutations. All forms of energy and certain chemicals which disrupt the chemical structure of chromosomes are mutagens (Table 6).

Table 6. Mutagenic agents and their mode of action.

Mutagens	Structure	Mode of action
5-Bromouracil (BU)		replaces thymine by pairing with guanine
2-Aminopurine (AP)		replaces adenine by pairing with cytosine
Nitrous acid	HNO_2	deamination, strand crossing over
Hydroxylamine	NH_2OH	hydroxylation of cytosine
Ethylmethane sulphonate	$CH_2SO_3CH_2CH_3$	alkylation of purines, transitions
Acridine orange		frameshift mutations by intercalation
Ultraviolet rays (UV)	254 nm wavelength	pyrimidine dimers, repair errors
X-rays	5 nm wavelength	breakage of single-and double-stranded DNA

1. **Radiations.** α-, β- and γ- radiations of radioactive substances, X-rays, neutrons and protons induce mutations by ionising the matter. Non-ionising UV- rays also induce mutations but not to the extent as ionising radiations. The natural radiations like cosmic rays, which come from the outer space, are also responsible for spontaneous mutation in living beings. Besides gene mutation, X-rays and other high energy radiations also produce all types of chromosomal aberrations.

2. **Chemicals.** Several chemical substances also induce mutations. These include 5- bromouracil, 2-amino purine, hydroxylamine, mustard gas, nitrous acid, phenol, formaldehyde, ethyl methyl sulphonate, ethyl urethane, ferrous and manganous salts, and acridine dyes like acridine orange and proflavine. Chemical substances can produce both gene mutations and chromosomal alterations. Besides, colchicine induces polyploidy by inhibiting the formation of spindle in cell division.
3. **Temperature.** A rise in temperature may sometimes lead to disturbance in genes which cause mutation.

Implications of Mutations

The effects of chromosome and gene mutations are very variable. In many cases the mutations are lethal and prevent development of the organism, for example in humans about 20% of pregnancies end in natural abortion before 12 weeks and of these about 50% exhibit a chromosome abnormality. Some forms of chromosome mutation may bring certain gene sequences together, and that combined effect may produce a 'beneficial' characteristic. Another significance of bringing certain genes closer together is that they are less likely to be separated by crossing-over and this is an advantage with beneficial genes.

Gene mutation may lead to several alleles occupying a specific locus. This increases both the heterozygosity and size of the gene pool of the population and leads to an increase in variation within the population. Gene reshuffling as a result of crossing-over, independent assortment, random fertilization and mutations, may increase the amount of continuous variation but the evolutionary implications of this are often short-lived, since the changes produced may be rapidly diluted. Certain gene mutations, on the other hand, increase discontinuous variation and this has the more profound effect on changes in the population. Most gene mutations are recessive to the 'normal' allele which has come to form genetic equilibrium with the rest of the genotype and the environment as a result of successfully withstanding selection over many generations. Being recessive, the mutant alleles may remain in the population for many generations until they come together in the homozygous condition and are expressed phenotypically.

Explain the inheritance of haemophilia in the first generation with normal father and carrier mother. Indicate the genotypes and phenotypes of the progeny.

List the three similarities between the behaviour of genes (Mendel's factors) during inheritance and of chromosomes during cell division.

Why does the son of a carrier mother and a normal father suffer from haemophilia whereas the son of a haemophiliac father and normal mother would not?

What are autosomes? How many autosomes would be found in the normal liver cells of a human female?

What are linked genes? How can a pair of linked genes be identified? Diagrammatically represent a cross between a white-eyed female and red-eyed male *Drosophila*.

Write short note on :

(a) Sex linkage (b) Crossing over

(c) Sex chromosomes (d) Karyotype

Show by a series of diagrams only how a cross over between linked genes allows their recombination during meiosis (taking into account two genes A and B with their alleles *a* and *b* located on homologous chromosomes).

Enumerate the advantages of using *Drosophila* for experiments on genetics.

Who proposed the chromosome theory of inheritance ? List the main points of this theory.

What is linkage ? In what way is linkage in opposition to Mendel's law of independent assortment ? Explain.

Name any two syndromes caused due to chromosomal abnormality in humans and mention the abnormality in each case. Describe the physical (body) symptoms related to any one of these syndromes.

How do chromosomal abnormalities due to change in the number of chromosomes arise? Give three examples of the occurrence of such abnormalities in humans.

In humans, males are heterogametic and females are homogametic. Explain. Are there any examples where males are homogametic and females are heterogametic?

What are duplication and translocation in connection with chromosomal mutation?

What are chromosomal mutations? How can they be induced?

Compare the kind of variations introduced within a species that reproduces sexually with another species that reproduces asexually.

What is frame shift mutation? Name the type of mutation that does not affect protein synthesis.

Write an essay on chromosomal aberrations, giving their cytological and genetic effects.

List the different ways by which mutations alter the structure of the chromosomes. Illustrate any one of them by a diagram.

Why is genetic variability essential for a species to survive? Name the main sources of genetic variation. How do these sources work?

How do variations arise in sexually reproducing organisms? Explain very briefly.

Differentiate between chromosomal and gene mutation. How is frame-shift mutation different from point mutation?

Define mutation. List the three ways in which mutations can arise.