CHAPTER – 5

PRINCIPLE OF INHERITANCE& VARIATION

Introduction

- Genetics: is the branch of biology that studies heredity and variation in organisms.
- Gregor Mendel a scientist and the monk was first to study *Pisumsativum*(garden pea) scientifically. He observed that pea plants inherit traits by way of discrete "units of inheritance" and published his work in 1865. The experimental results were described mathematically.

Contrasting characters:

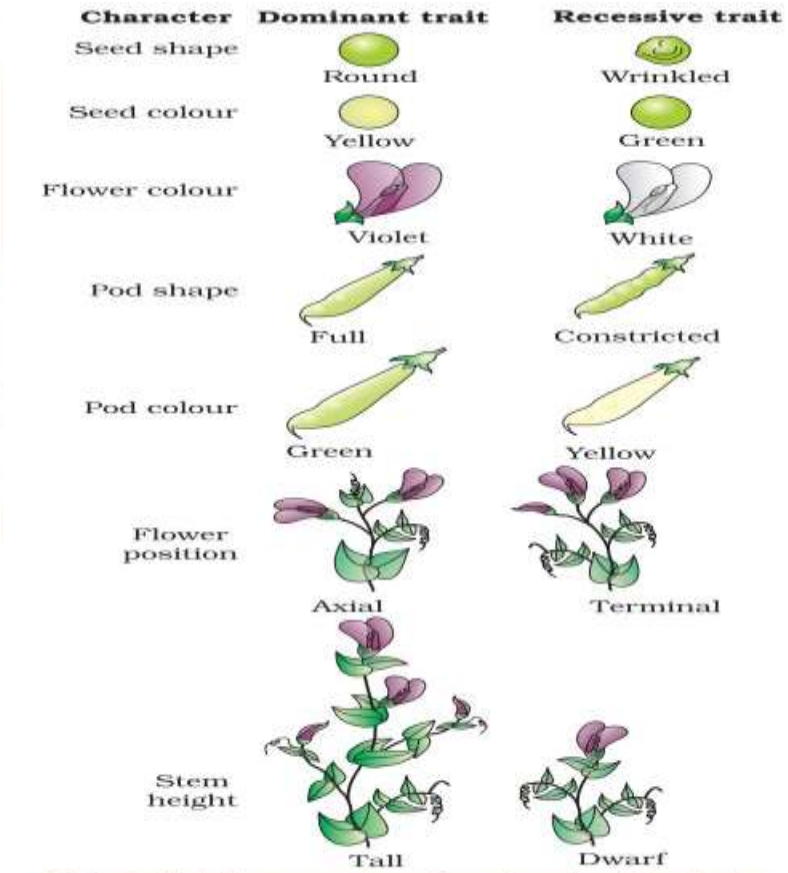


Figure 5.1 Seven pairs of contrasting traits in pea plant studied by Mendel

A singlecharacter that exhibits two opposite different character.

- Contrasting characters of plant height is tall and dwarf.
- Seven pair of contrasting characters is observed in pea plants.

Dominating characters:

- A character that is controlled by a particular allele of a gene and which is displayed when the individual is homozygous or heterozygous for a allele.
- The phenotypic characters that gets expressed in F1 generation.

Recessive characters:

- A character that is controlled by a particular allele of a gene and the gets expressed only when the individual is homozygous for this allele.
- Stem height-dwarf, Flower colour-white, Flower position-terminal, Pod shape-constricted, Pod colour-yellow , Seed shape-wrinkled, Seed colour-green.

Monohybrid cross:

- A cross which determines the allele combination of offspring for a particular gene.
- Tall X Dwarf (**Punnett Square to be drawn**)

(homozygous) (homozygous)

F1 Tall (heterozygous)

Test cross:

- A cross in which breeding of an individual is carried out with phenotypically recessive individual; in order to determine the zygosity of an individual by analyzing the proportions of offspring phenotypes.

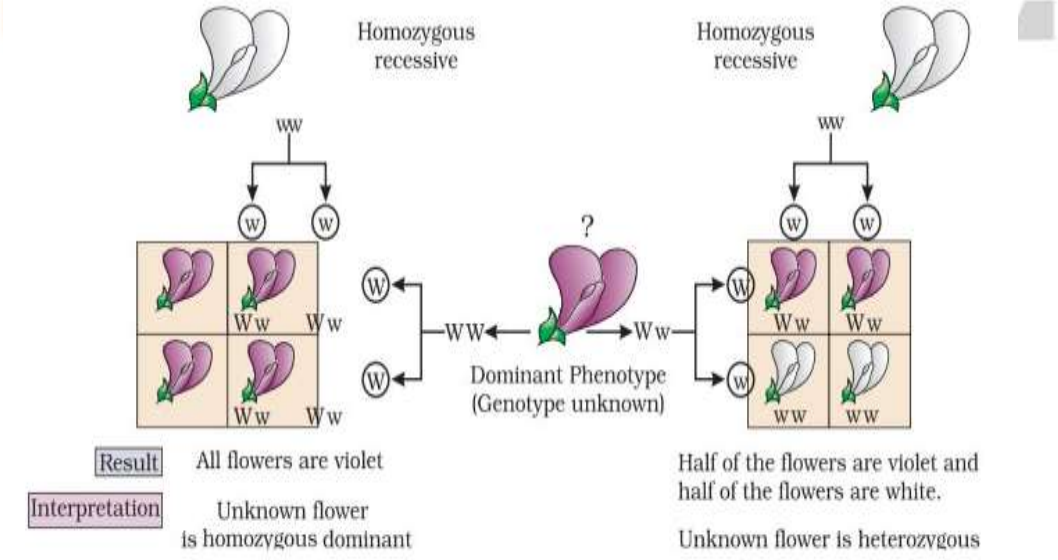


Figure 5.5 Diagrammatic representation of a test cross

The Law of Dominance:

- (i) Characters are controlled by discrete units called factors.

  (ii) Factors occur in pairs.

  (iii) In a dissimilar pair of factors one member of the pair dominates(dominant) the other (recessive).
- The law of dominance is used to explain the expression of only one ofthe parental characters in a monohybrid cross in the F1 and the expressionof both in the F2. It also explains the proportion of 3:1 obtained at the F2.

Law of Segregation:

- The law is based on the fact that the alleles do not show any blendingand that both the characters are recovered as such in the F2 generationthough one of these is not seen at the F1 stage.
- Though the parents containtwo alleles during gamete formation, the factors or alleles of a pair **segregate**from each other such that a gamete receives only one of the two factors.Of course, a homozygous parent produces all gametes that are similarwhile a heterozygous one produces two kinds of gametes each havingone allele with equal proportion.

Inheritance of Two Genes:

- Mendel worked with and crossed pea plants that differed in two characters, as is seen in the cross between a pea plant that has seeds with yellow colour and round shape and one that had seeds of green colour and wrinkled shape.
- RRYY X rryyFig.5.7 (page 79)
- Phenotypic ratio of dihybrid cross is 9:3:3:1

Law of Independent assortment:

law states that 'when two pairs of traits are combined in a hybrid, segregation of one pair of characters is independent of the other pair of characters'.

incomplete dominance:

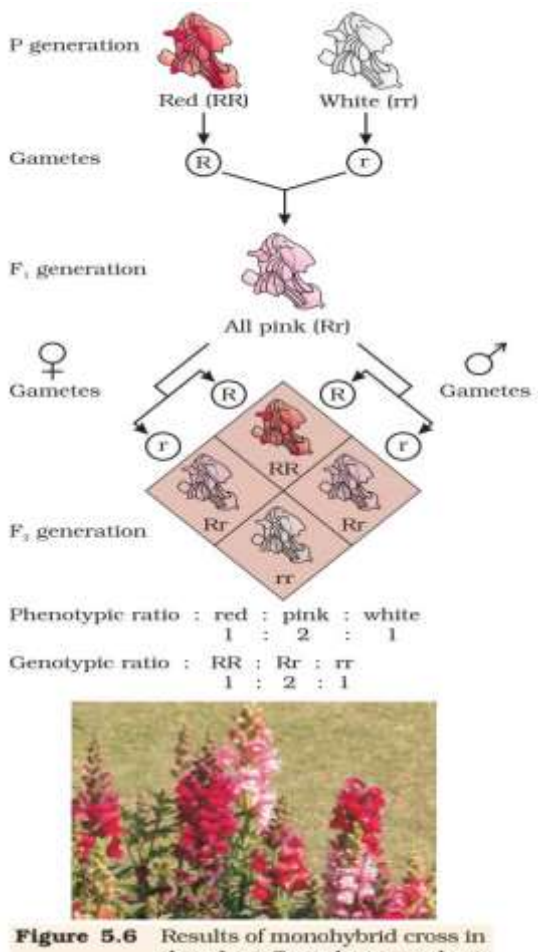


Figure 5.6 Results of monohybrid cross in the plant Snapdragon, where one allele is incompletely dominant over the other allele

Incomplete dominance is a form of **intermediate inheritance** in which one allele for a specific trait is not completely expressed over its paired allele. The phenotypic expression is a combination of both the alleles.

- When experiments on peas were repeated using other traits in other plants, it was found that sometimes the F1 had a phenotype that did not resemble either of the two parents and was in between the two.
- The inheritance of flower colour in the dog flower (***Mirabilis jalapa*** or ***Antirrhinum*** sp.) show **incomplete dominance**.
- In a cross between **true-breeding** red-flowered (RR) and truebreeding white-flowered plants (rr), the **F1** (Rr) was **pink** (Figure 5.6). When the F1 was self-pollinated the F2 resulted in the following ratio 1 (RR) Red: 2 (Rr) Pink: 1 (rr) White.

- Here the genotype ratios wereexactly same as seen inMendelian monohybrid cross, but the phenotype ratios had changed i.e. 1:2:1 (1Red:2 Pink: 1 White).

Co-dominance:

- Co-dominance is a form of inheritance where the pair of alleles of a gene in heterozygous condition are fully expressed. As a result the phenotype of the offspring is a combination of the phenotype of the parents.
- The trait is neither dominant nor recessive.
- In the case of co-dominance the F1 generation resembles both parents.
- A good example is different types of red blood cells that determine ABO blood grouping in human beings. ABO blood groups are controlled by the gene I (isohaemagglutinin).
- The plasma membrane of the red blood cells has sugar polymers that protrude from its surface and the kind of sugar is controlled by the gene. The gene (I) has three alleles I^A, I^B and i (I^o).
- The alleles I^A and I^B produce a slightly different form of the sugar while allele I^o does not produce any sugar. Because humans are diploid organisms, each person possessesany two of the three I gene alleles. I^A and I^B are completely dominant overi, in other words when I^A and i are present only I^Aexpresses (because i does not produce any sugar), and when I^B and i are present I^B expresses.
- But when $\mathbf{I^A}$ and $\mathbf{I^B}$ are present together they both express their own types of sugars: this is because of co-dominance. Hence red blood cells have both A and B types of sugars.
- Since there are three different alleles, thereare six different combinations of these three alleles that are possible, andtherefore, a total of six different genotypes of the human ABO blood types.

Table 5.2: Table Showing the Genetic Basis of Blood Groups in Human Population

Allele from Parent 1	Allele from Parent 2	Genotype of offspring	Blood types of offspring
I^A	I^A	$I^A I^A$	A
I^A	I^B	$I^A I^B$	AB
I^A	i	$I^A i$	A
I^B	I^A	$I^A I^B$	AB
I^B	I^B	$I^B I^B$	B
I^B	i	$I^B i$	B
i	i	$i\,i$	O

Multiple allelism:

- The state of having more than two alternative contrasting characters controlled by multiple alleles at a single genetic locus.
- The ABO blood group in humans is a good example of multiple allelism. Gene I has three alleles **I^A,I^B and I^o.**

Pleiotropy:

- A single gene expressing multiple phenotypic traits.
- Such a gene that exhibits multiple phenotypic expressions is called a pleiotropic gene.
- Examples: i) starch synthesis in pea seeds and shape of the seeds.
  ii) phenylketonuria
- Starch synthesis in pea seeds and shape of the seeds is controlled by one gene. Ithas two alleles (**B and b**). Starch is synthesized effectively by BB**homozygotes** and therefore, **large starch grains** are produced.
- In contrast,**bbhomozygotes** have lesser efficiency in starch synthesis and produce**smaller starch grains**. After maturation of the seeds, **BBseeds** are roundand the **bb** seeds are wrinkled.
- Heterozygotes produce round seeds, andso B seems to be the dominant allele. But, the starch grains produced areof intermediate size in Bb seeds. So if starch grain size is considered asthe phenotype, then from this angle, the alleles show incompletedominance.

Rediscovery of Mendel's Laws:

- In 1900, three Scientists (**de Vries, Correns** and **von Tschermak**) independently rediscovered Mendel's results on the inheritance of characteristics.

Chromosomal Theory of Inheritance

- The advancements in microscopy in early 20th century thatwere taking place, scientists were able to carefully observe cell division.This led to the discovery of structures in the **nucleus** that appeared to**double** and **divide** just before each **cell division**.
- These were called**chromosomes** (colored bodies, as they were visualised by staining). By1902, the chromosome movement during meiosis had been worked out.Walter Sutton and Theodore Boveri noted that the behaviour ofchromosomes was parallel to the behaviour of genes and usedchromosome movement to explain Mendel's laws.

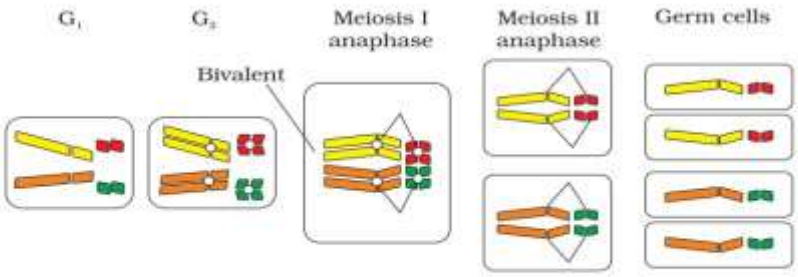


Figure 5.8 Meiosis and germ cell formation in a cell with four chromosomes. Can you see how chromosomes segregate when germ cells are formed?

Table 5.3: A Comparison between the Behaviour of Chromosomes and Genes

A	B
Occur in pairs	*Occur in pairs*
Segregate at the time of gamete formation such that only one of each pair is transmitted to a gamete	*Segregate at gamete formation and only one of each pair is transmitted to a gamete*
Independent pairs segregate independently of each other	*One pair segregates independently of another pair*
Can you tell which of these columns A or B represent the chromosome and which represents the gene? How did you decide?	

The behaviour of chromosomes during mitosis(equational division) and during meiosis (reduction division) is that chromosomes as well as genesoccur in pairs. The two alleles of a gene pair are located on homologoussites on homologous chromosomes.

- During Anaphase of meiosis I, the two chromosome pairs can align at the metaphase plate independently of each other. The pairs of chromosome get segregated independently of the other. As shown in Possibility -I and Possibility-II.

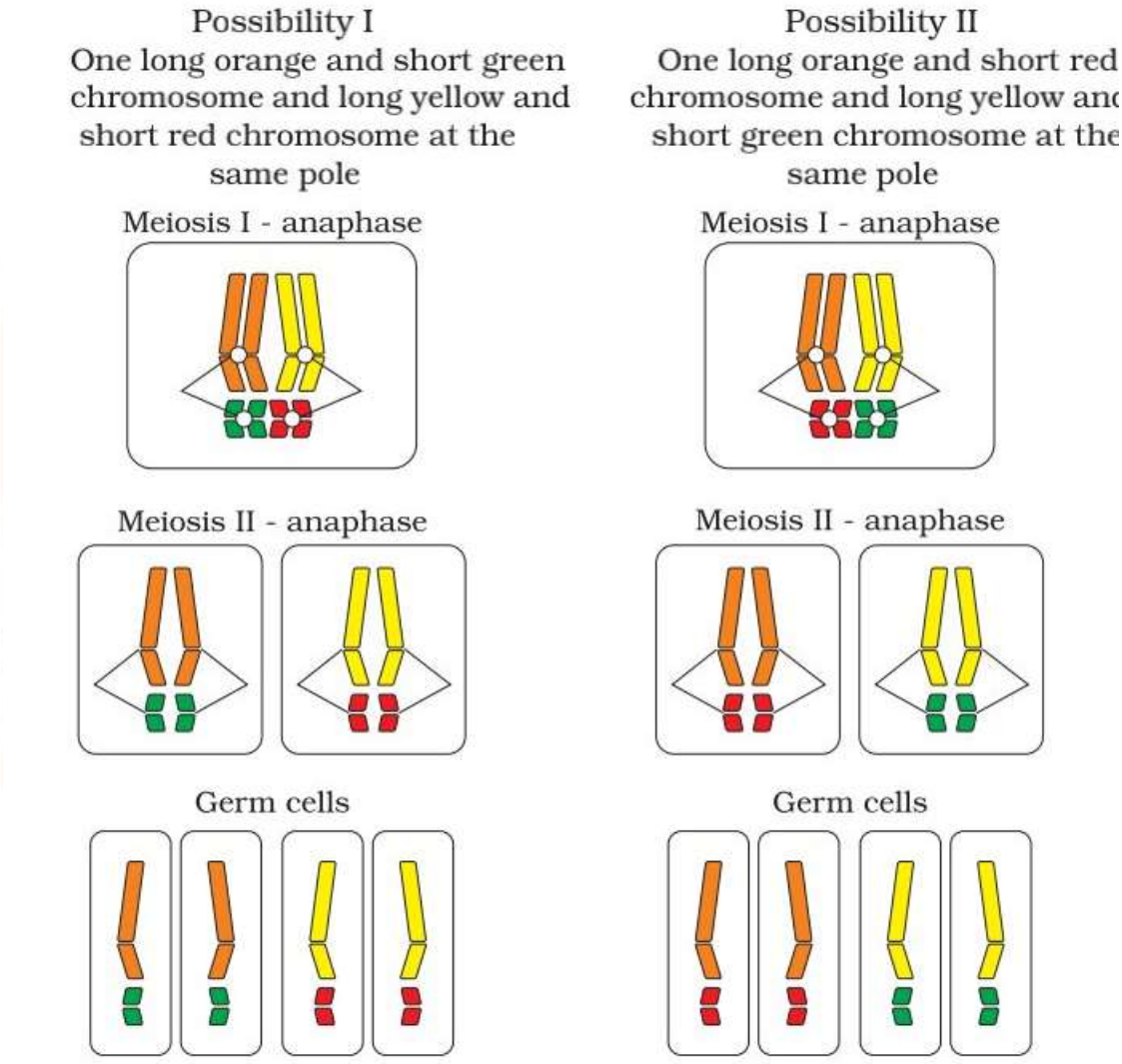


Figure 5.9 Independent assortment of chromosomes

- *Sutton and Boveri* argued that the pairing and separation of apair of chromosomes would lead to the segregation of a pair offactors they carried. Sutton united the knowledge of chromosomalsegregation with Mendelian principles and called it thechromosomal theory of inheritance.

Linkage and Recombination:

- Verification ofthe chromosomal theory of inheritance by **Thomas Hunt Morgan**and his colleagues, led to discovering the basis for the variationthat sexual reproduction produced. Morgan worked with the tinyfruit flies, *Drosophila melanogaster*.
- Fruit flies could be grown onsimple synthetic medium in the laboratory. They complete their lifecycle in about two weeks, and a single mating could produce a largenumber of progeny flies.
- There was a clear differentiation of thesexes –the male and female flies are easily distinguishable. Also, ithas many types of hereditary variations that can be seen with lowpower microscopes.

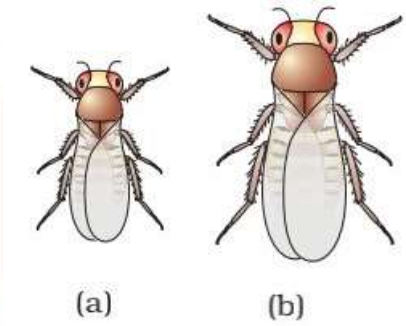


Figure 5.10 *Drosophila melanogaster* (a) Male (b) Female

- Morgan carried out several dihybrid crosses in Drosophila to study genes that were sex-linked. The crosses were similar to the dihybrid crosses carried out by Mendel in peas. Morgan hybridised yellow-bodied, white-eyed females to brown-bodied, red-eyed males and intercrossed their F1 progeny. He observed that the two genes did not segregate independently of each other and the F2 ratio deviated very significantly from the 9:3:3:1 ratio.
- Morgan and his group knew that the genes were located on the X chromosome (Section 5.4) and saw quickly that when the two genes in a dihybrid cross were situated on the same chromosome, the proportion of parental gene combinations were much higher than the non-parental type.
- Morgan attributed this due to the **physical association** or **linkage** of the two genes and coined the term linkage to describe this physical association of genes on a chromosome.
- The term **recombination** todescribe the generation of non-parental gene combinations. Morgan and his group also found that even when genes were groupedon the same chromosome, some genes were very tightly linked (showedvery low recombination)

(Figure 5.11, Cross A) while others were looselylinked (showed higher recombination) **(Figure 5.11, Cross B).**

- He found that the genes white and yellow were very tightly linkedand showed only 1.3 per cent recombination while white and miniaturewing showed 37.2 per cent recombination.

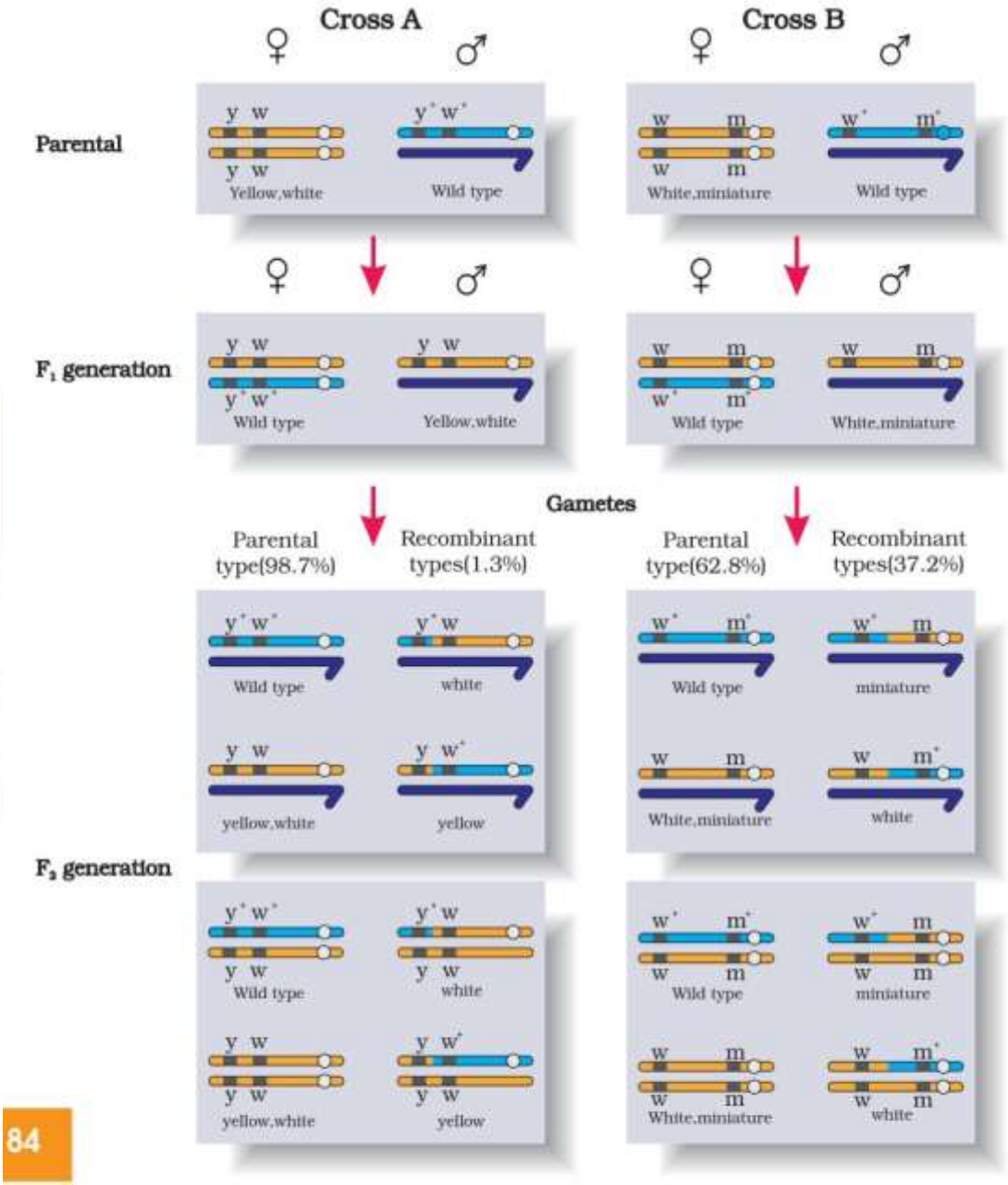


Figure 5.11 Linkage: Results of two dihybrid crosses conducted by Morgan. Cross A shows crossing between gene y and w; Cross B shows crossing between genes w and m. Here dominant wild type alleles are represented with (+) sign in superscript
Note: The strength of linkage between y and w is higher than w and m.

Gene mapping

- Morgan'sstudent AlfredSturtevant used the frequency of recombination between gene pairson the same chromosome as a measure of the distance between genesand 'mapped' their position on the chromosome.

Map distance

- The distance between the positionof two genes on a chromosome.
- A genetic map unit (m.u.) is sometimes referred to as a centimorgan (cM).

Mechanism of Sex Determination:

Chromosomal basis of sex determination:

- Henking's X- body: determination. Henking (1891) could trace a specific nuclearstructure all through spermatogenesis in a few insects, and it was alsoobserved by him that 50 per cent of the sperm received this structureafter spermatogenesis, whereas the other 50 per cent sperm did not receiveit.
- Henking gave a name to this structure as the X body. Further investigations by other scientists led tothe conclusion that the 'X body' of Henking was in fact a chromosomesex chromosomes,that is why it was given the nameX-chromosome.

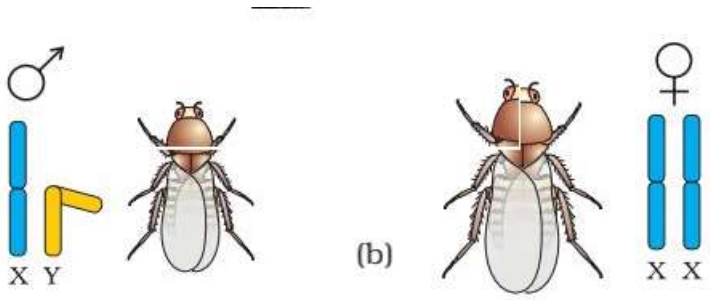
XO-type of sex determination:

- Grasshopper is an example of XO type of sex determination in which the males have only one X-chromosome besides the autosomes, whereas females have a pair of X-chromosomes.
- In Grass hopper it was observed that the females lay eggs bear an additional X-chromosome besides the other chromosomes (autosomes).
- On the other hand, some of the sperms bear the X-chromosome whereas some do not.
- Eggs fertilised by sperm having an X-chromosome become females and, those fertilised by sperms that do not havean X-chromosome become males.
- Due to the involvement of the X-**chromosome** in the determination of sex, it was designated to be the **sex chromosome**, and the rest of the chromosomes were named as autosomes.

Male Heterogamety:

- Males produce two different types of gametes, (a) either with or without X-chromosome or (b) some gametes with X-chromosome and some with Y-chromosome. Such types of sex determination mechanism is designated to male heterogamety.

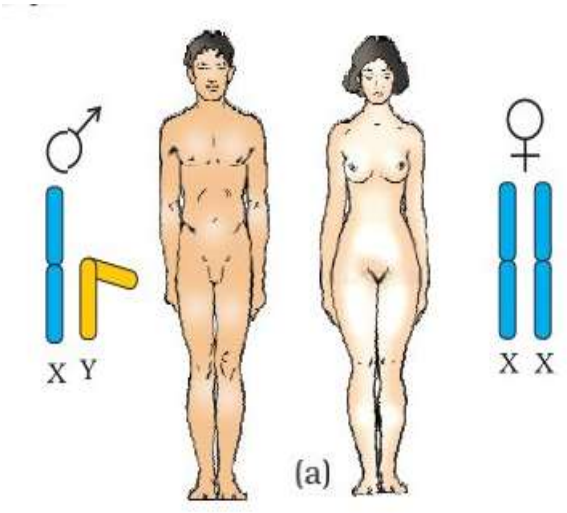
XY-type of sex determination in *Drosophila*fig



In a number of other **insectsand** mammals including man, XY type of sexdetermination is seen where both male andfemale have same number of chromosomes.

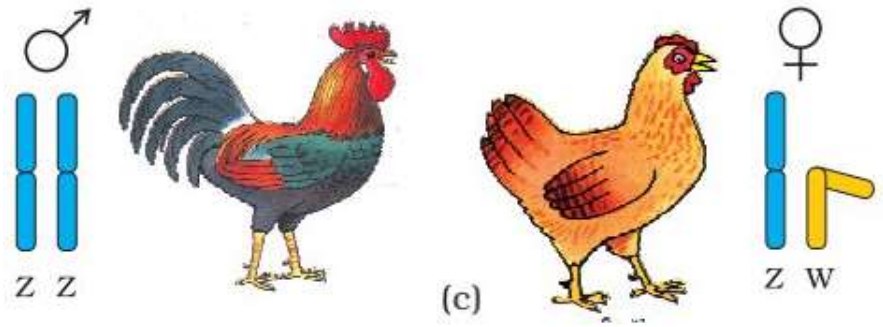
- Among the males an X-chromosome ispresent but its counterpart is distinctlysmaller and called the Y-chromosome.Females, however, have a pair of Xchromosomes.
- Both males and females bearsame number of autosomes. Hence, the males have autosomes plus XY, while female have autosomes plus XX.

XY-type of sex determination in Humanfig



- In human beings males have one X and one Y chromosome, whereas femaleshave a pair of X-chromosomes besides autosomes.In this case the total number of chromosome is same in bothmales and females. But two different types of gametes are produced in terms of the sex.
- Out of 23 pairs of chromosomes present, 22 pairs are exactly same in both males and females; these are the autosomes. A pair of X-chromosomes are present in the female, whereas the presence of an X and Y chromosome are determinant of the male characteristic.
- During spermatogenesis among males, two types of gametes are produced. 50 per cent of the total sperm produced carry the X-chromosome and the rest 50 per cent has Y-chromosome besides the autosomes.
- Females, however, produce only one type of ovum with an X-chromosome. There is an equal probability of fertilisation of theovum with the sperm carrying either X or Y chromosome. In case theovum fertilises with a sperm carrying X-chromosome the zygote developsinto a female (XX) and the fertilisation of ovum with Y-chromosomecarrying sperm results into a male offspring.
- Thus, it is evident that itis the genetic makeup of the sperm that determines the sex of the child.It is also evident that in each pregnancy there is always 50 per centprobability of either a male or a female child.

Female Heterogamety:



- In some organisms two different types of gametes in terms of the sex chromosomes, are produced by females, i.e., female heterogamety.

ZZ-ZW type of sex determination in rooster and hen

- The two different sex chromosomes of a female bird hasbeen designated to be the Z and W chromosomes. In these organisms thefemales have one Z and one W chromosome, whereas males have a pair ofZchromosomes besides the autosomes.

The sex determination in honey bee

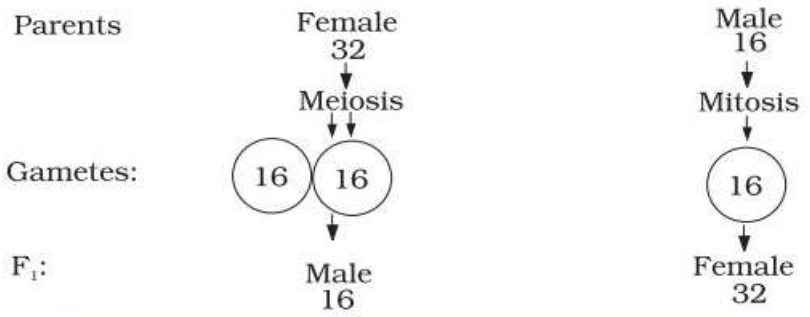


Figure 5.13 Sex determination in honey bee

- The sex determination in honey bee isbased on the number of sets ofchromosomes an individual receives.
- Anoffspring formed from the union of asperm and an egg develops as a female(queen or worker), and an unfertilized egg develops as a male (drone) by meansof parthenogenesis.

- Thus themales have half the number ofchromosomes than that of a female. Thefemales are diploid having 32chromosomes and males are haploid, i.e., having 16 chromosomes.
- This is called as **haplodiploid** sex-determination system has specialcharacteristic features such as the males produce sperms by mitosisthey do not have father and thus cannot have sons, buthave a grandfather and can have grandsons.

Mutation

- Mutation is a phenomenon which results in alteration of DNA sequencesand consequently results in changes in the genotype and the phenotypeof an organism.
- In addition to recombination, mutation is anotherphenomenon that leads to variation in DNA.
- The loss (deletions) or gain (insertion/duplication) of a segment ofDNA, result in alteration in chromosomes. Since genes are known to belocated on chromosomes, alteration in chromosomes results inabnormalities or aberrations.
- Chromosomalaberrations are commonly observed in cancer cells.In addition to the above, mutation also arise dueto change in a single base pair of DNA. This is knownas **point mutation**. A classical example of such amutation is sickle cell anemia.
- Deletions and insertionsof base pairs of DNA, causes frame-shift mutations.
- There aremany chemical and physical factors that inducemutations. These are referred to as mutagens. UVradiations can cause mutations in organisms – it is amutagen.

Pedigree Analysis:

- Study of the family history aboutinheritance of a particular trait in a several of generations of a familyis called the pedigree analysis.
- In the pedigree analysis the inheritanceof a particular trait is represented in the family tree over generations.
- In human genetics, pedigree study provides a strong tool, which isutilised to trace the inheritance of a specific trait, abnormality or disease.
- Some of the important standard symbols used in the pedigree analysishave been shown in the figure.

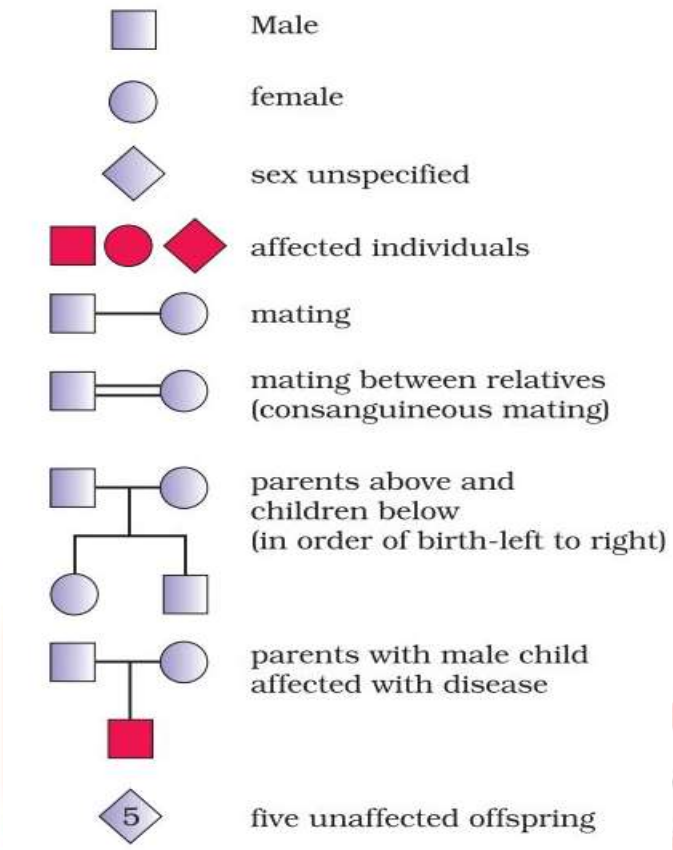


Figure 5.13 Symbols used in the human pedigree analysis

Mendelian disorders:

- Mendelian disorders are mainlydetermined by alteration or mutation in the single gene. These disordersare transmitted to the offspring abiding the principle of inheritance.
- The pattern of inheritance of such Mendeliandisorders can be traced in a family by the pedigree analysis.
- Most commonand prevalent Mendelian disorders are Haemophilia, Cystic fibrosis, Sicklecellanaemia, Colour blindness, Phenylketonuria, Thalassemia, etc.
- Mendelian disorders may bedominant or recessive. By pedigree analysis one can easily understandwhether the trait in question is dominant or recessive.
- The traitmay also be linked to the sex chromosome as in case of haemophilia. It isevident that this X-linked recessive trait shows transmission from carrierfemale to male progeny.
- A representative pedigree is shown in Figure 5.14for dominant and recessive traits.

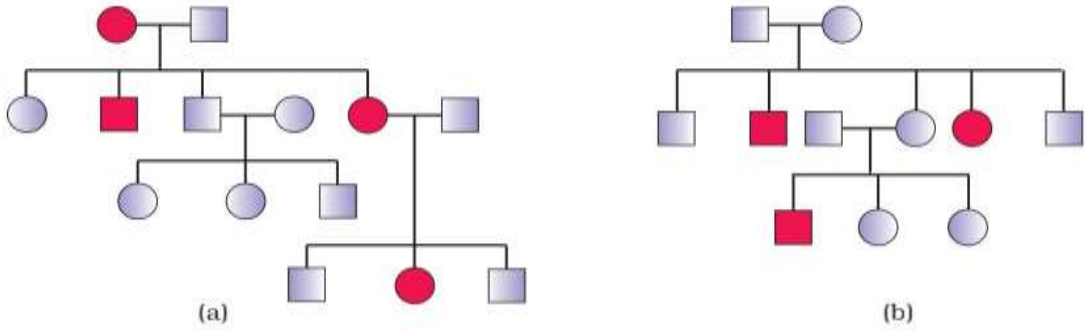


Figure 5.14 Representative pedigree analysis of (a) Autosomal dominant trait (for example: Myotonic dystrophy) (b) Autosomal recessive trait (for example: Sickle-cell anaemia)

colour blindness

- It is a sex-linked recessive disorder due to defect ineither red or green cone of eye resulting in failure to discriminate betweenred and green colour.
- This defect is due to mutation in certain genespresent in the X chromosome. It occurs in about 8 per cent of males andonly about 0.4 per cent of females. This is because the genes that lead tored-green colour blindness are on the X chromosome.
- Males have onlyone X chromosome and females have two.
- The son of a woman who carries the gene has a 50 per cent chance of being colour blind. The mother isnot herself colour blind because the gene is recessive. That means that itseffect is suppressed by her matching dominant normal gene.
- A daughterwill not normally be colour blind, unless her mother is a carrier and herfather is colour blind.

Hemophilia:

- This sex linked recessive disease, which shows itstransmission from unaffected carrier female to some of the male progenyhas been widely studied.
- In this disease, a single protein that is a part ofthe cascade of proteins involved in the clotting of blood is affected.
- Due tothis, in an affected individual a simple cut will result in non-stop bleeding.The heterozygous female (carrier) for haemophilia may transmit the diseaseto sons.
- The possibility of a female becoming a haemophilic is extremelyrare because mother of such a female has to be at least carrier and thefather should be haemophilic (unviable in the later stage of life).

Sickle cell anemia

- This is an autosome linked recessive trait that canbe transmitted from parents to the offspring when both the partners arecarrier for the gene (or heterozygous).

- The disease is controlled by a singlepair of allele, HbA and HbS. Out of the three possible genotypes onlyhomozygous individuals for HbS (HbSHbS) show the diseased phenotype.
- Heterozygous (HbAHbS) individuals appear apparently unaffected but theyare carrier of the disease as there is 50 per cent probability of transmissionof the mutant gene to the progeny, thus exhibiting sickle-cell trait(Figure 5.15).
- The defect is caused by the substitution of Glutamic acid (Glu) by Valine (Val) at the sixth position of the beta globin chain of thehaemoglobin molecule.
- The substitution of amino acid in the globinprotein results due to the single base substitution at the sixth codon ofthe beta globin gene from GAG to GUG.
- The mutant haemoglobin moleculeundergoes polymerisation under low oxygen tension causing the changein the shape of the RBC from biconcave disc to elongated sickle likestructure

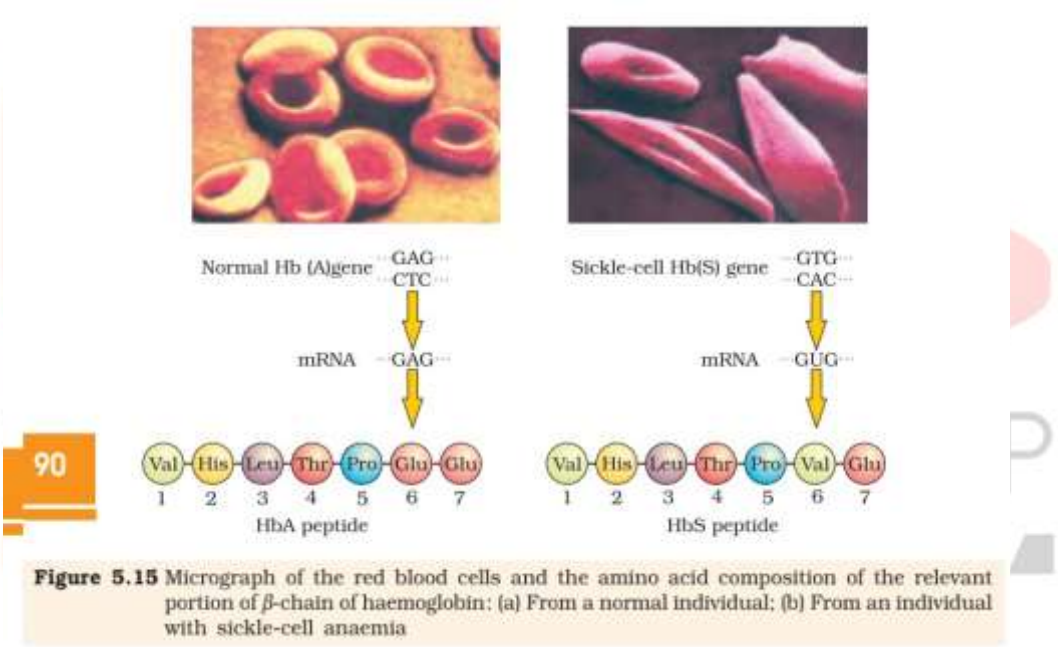


Figure 5.15 Micrograph of the red blood cells and the amino acid composition of the relevant portion of β-chain of haemoglobin: (a) From a normal individual; (b) From an individual with sickle-cell anaemia

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Phenylketonuria

- This inborn error of metabolism is also inherited asthe autosomal recessive trait.
- The affected individual lacks an enzymethat converts the amino acid phenylalanine into tyrosine. As a result ofthis phenylalanine is accumulated and converted into phenylpyruvic acidand other derivatives.
- Accumulation of these molecules in brain results in mentalretardation. These are also excreted through urine because of its poorabsorption by kidney.

Thalassemia :

- This is also an autosome-linked recessive blood diseasetransmitted from parents to the offspring when both the partners areunaffected carrier for the gene (or heterozygous).
- The defect could be dueto either mutation or deletion which ultimately results in reduced rate ofsynthesis of one of the globin chains (a and b chains) that make uphaemoglobin.
- This causes the formation of abnormal haemoglobinmolecules resulting into anaemia which is characteristic of the disease.
- Thalassemia can be classified according to which chain of the haemoglobinmolecule is affected.
- In a Thalassemia, production of a globin chain isaffected while in b Thalassemia, production of b globin chain is affected.
- a Thalassemia is controlled by two closely linked genes HBA1 and HBA2on chromosome 16 of each parent and it is observed due to mutation ordeletion of one or more of the four genes.
- The more genes affected, theless alpha globin molecules produced. While b Thalassemia is controlledby a single gene HBB on chromosome 11 of each parent and occurs dueto mutation of one or both the genes.
- Thalassemia differs from sickle-cellanaemia in that the former is a quantitative problem of synthesising toofew globin molecules while the latter is a qualitative problem ofsynthesising an incorrectly functioning globin.

Chromosomal Disorders

- The chromosomal disorders on the other hand are caused due to absenceor excess or abnormal arrangement of one or more chromosomes.Failure of **segregation** of chromatids during cell division cycle resultsin the gain or loss of a chromosome(s), called **aneuploidy**.
- For example,Down's syndrome results in the gain of extra copy of chromosome 21.
- Similarly, Turner's syndrome results due to loss of an X chromosome inhuman females.
- Failure of cytokinesis after telophase stage of cell divisionresults in an increase in a whole set of chromosomes in an organism and,this phenomenon is known as polyploidy. This condition is often seen inplants.
- The total number of chromosomes in a normal human cell is 46(23 pairs). Out of these 22 pairs are autosomes and one pair ofchromosomes are sex chromosome.
- Sometimes, though rarely, either anadditional copy of a chromosome may be included in an individual or an.individual may lack one of any one pair ofchromosomes.
- These situations are known as trisomyor monosomy of a chromosome, respectively. Such asituation leads to very serious consequences in theindividual. Down's syndrome, Turner's syndrome,Klinefelter's syndrome are common examples ofchromosomal disorders.

Down's Syndrome

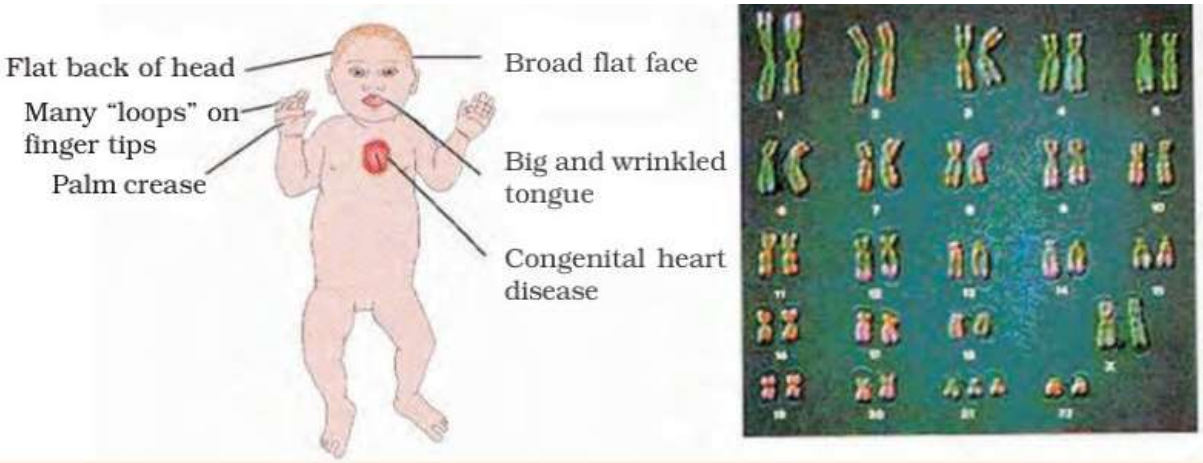

Figure 5.16 *A representative figure showing an individual inflicted with Down's syndrome and the corresponding chromosomes of the individual*

- The cause of this genetic disorderis the presence of an additional copy of thechromosome number 21 (trisomy of 21). This disorderwas first described by Langdon Down (1866).
- Theaffected individual is short statured with small roundhead, furrowed tongue and partially open mouth.
- Palm is broad with characteristic palmcrease. Physical, psychomotor and mentaldevelopment is retarded.

Klinefelter'sSyndrome

(a)
Tall stature
with feminised
character

- This genetic disorder is alsocaused due to the presence of an additional copy of Xchromosomeresulting into a karyotype of 47, XXY.
- Such an individual has overall masculine development,however, the feminine development (developmentof breast, i.e., **Gynaecomastia**) is also expressedSuch individuals are sterile.
- Turner's Syndrome :

(b)

Short stature and
underdeveloped
feminine character

- Such a disorder is caused dueto the absence of one of the X chromosomes, i.e., 45 with X0.
- Such femalesare sterile as ovaries are rudimentary besides other features includinglack of other secondary sexual characters.