Principles of Inheritance and Variation - Part 4

Objectives

After going through this lesson, the learners will be able to understand the following:

- Linkage and recombination.
- Patterns of sex determination in different animals.
- Brief idea about mutation.
- Pedigree analysis.
- Mendelian disorders and chromosomal disorders.

Content Outline

Introduction

Linkage is the tendency of genes present on a chromosome to inherit together. The Closer the genes are on a chromosome, the less the chance of recombination between them, and the more likely they are to be inherited together.

A sex-determination system is a biological system that determines the development of sexual characteristics in an organism. Most sexually reproducing organisms have two sexes. Occasionally, there are hermaphrodites, characterized by presence of both male and female sex organs in one individual.

In many species, sex determination is genetic: males and females have different alleles or even different genes that specify their sexual morphology. In animals this is often accompanied by chromosomal differences, generally through combinations of XY, ZW, XO, ZO chromosomes.

Mutation is the permanent change in the nucleotide sequence of the genome of an organism, virus, or extra-chromosomal DNA or other genetic elements. Mutations result from errors

during DNA replication or other types of damage to DNA. Mutations may also result from insertion or deletion of segments of DNA due to mobile genetic elements.

A series of symbols are used to represent a pedigree. Pedigree charts are drawn after collecting phenotypic data of several generations. Careful analysis helps us to understand the nature of traits.

A genetic disorder is caused by one or more abnormalities in the genome, especially a condition that is present from birth (congenital). Most genetic disorders are quite rare and affect one person in every several thousands or millions.

Genetic disorders may be hereditary, passed down from the parents' genes. In other genetic disorders, defects may be caused by new mutations or changes to the DNA. In such cases, the defect will only be passed down if it occurs in the germ line. Broadly genetic disorders may be grouped into two categories-Mendelian disorders and chromosomal disorders.

Sex Determination

Sex-determination mechanism determines the development of a particular sex in an organism. Most sexually reproducing organisms have specific sexes. Occasionally, there are hermaphrodites having both the sexes in one individual. There are also some species that are only one sex due which reproduce parthenogenesis, the act of a reproducing without fertilization.

In many species, sex determination is genetic: males and females have different alleles or different genes that specify their sexual morphology.

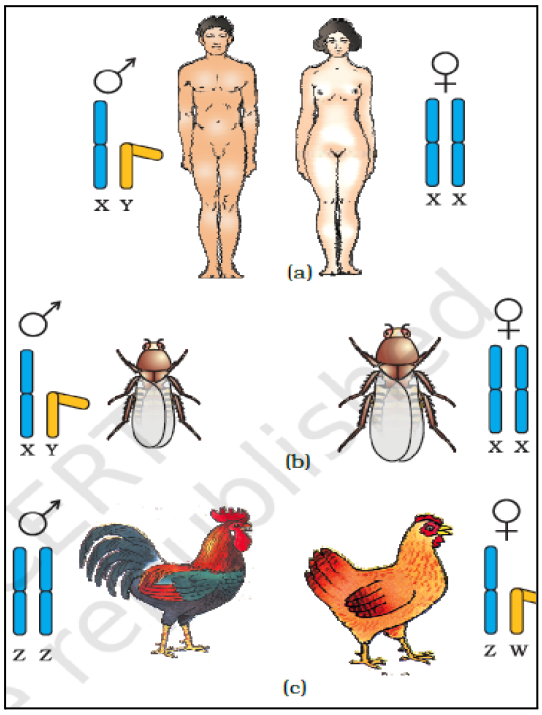
In most of the animals sex is determined by chromosomal differences. There is sex specific difference in the sex chromosomes.

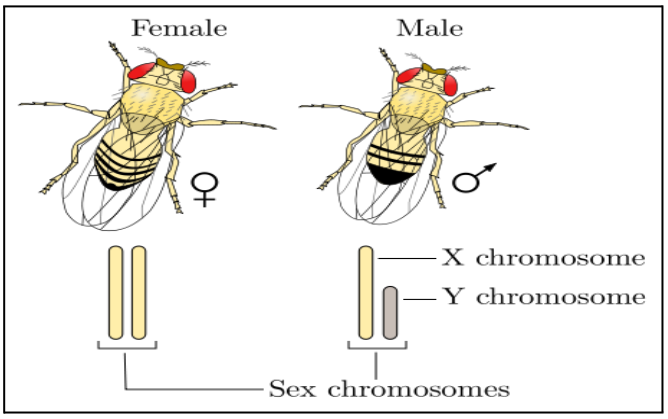
In some of the cases, sex is determined by environmental variables (such as temperature) or social variables (e.g. the size of an organism relative to other members of its population).

Some species do not have a fixed sex, and instead change sex based on certain cues.

Sex Determination in Human

In humans sex is determined by the **XX/XY sex-determination system**. The XX/XY system is found in most other mammals. In this system, the females have two of the same kind of sex chromosome (XX), while males have two distinct sex chromosomes (XY). 22 pairs of the chromosomes in the males and the females are similar. These chromosomes are called autosomes. The 23 pair chromosome differs in the two sexes called sex chromosome. In the females the two chromosomes of the sex chromosome pair are alike called XX chromosomes. In male one of the chromosomes of the sex chromosome pair resembles to the X chromosome of the female and other chromosome is different. This is called XY. The males produce two different types of gametes; some with X-chromosome and some with Y-chromosome. Such type of sex determination.



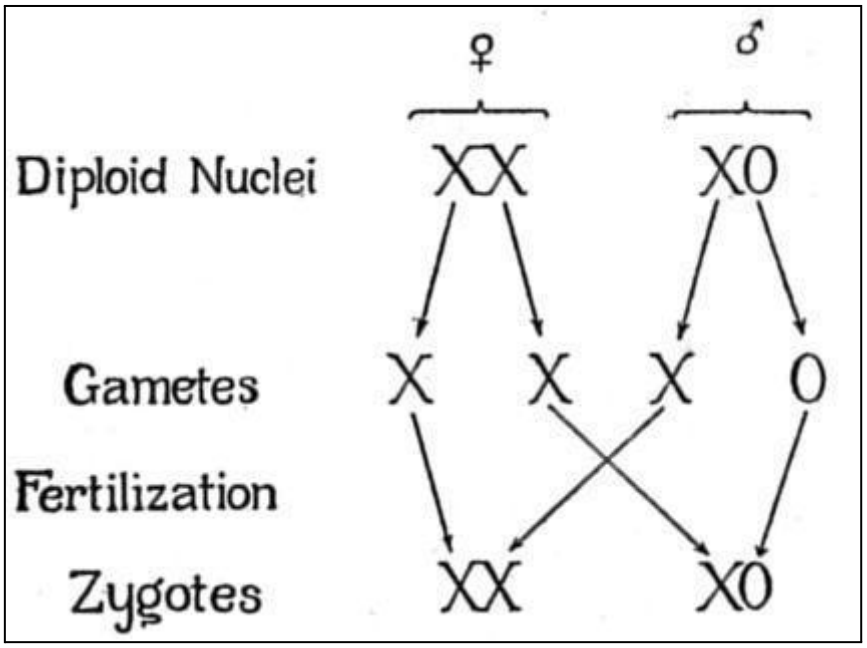


ZW Sex-Determination System

The **ZW sex-determination system** is found in birds, some reptiles, and some insects and other organisms. The ZW sex-determination system is reversed compared to the XY system: females have two different kinds of chromosomes (ZW), and males have two of the same kind of chromosomes (ZZ). Two different types of gametes in terms of the sex chromosomes are produced by females, i.e., **female-heterogamety**.

XO Sex-Determination System

This is a variant of the XY system. In this system the females have two copies of the sex chromosome (XX) but males have only one (XO). The O denotes the absence of a second sex chromosome. This system is observed in a number of insects, including the grasshoppers.



Temperature-Dependent Sex Determination

In some species of reptiles, including alligators and some turtles, sex is determined by the temperature at which the egg is incubated during a temperature-sensitive period. The specific temperatures required to produce each sex are known as the female-promoting temperature and the male-promoting temperature. When the temperature stays near the threshold during the temperature sensitive period, the sex ratio is varied between the two sexes.

All alligators determine the sex of their offspring by the temperature of the nest.

It is unknown how exactly temperature-dependent sex determination evolved. It could have evolved through certain sexes being more suited to certain areas that fit the temperature requirements. For example, a warmer area could be more suitable for nesting, so more females are produced to increase the amount that nest next season.

Environmental sex determination preceded the genetically determined systems of birds and mammals.

Other Systems

There are many other environmental systems. Some species, such as some snails, undergo sex change: adults start life as male which subsequently changed to female.

In tropical clown fish, the dominant individual in a group becomes female while the other ones are male.

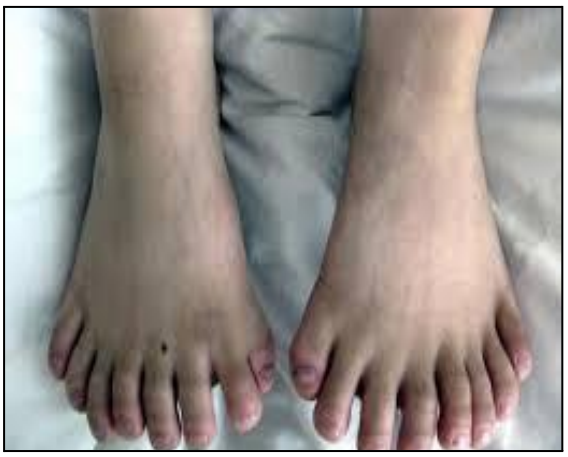
In the marine worm, larvae become males if they are in physical contact with a female, and females if they develop on the bare sea floor.

Some species, however, have no sex-determination system. Hermaphrodite species include the common earthworm and certain species of snails. A few species of fish, reptiles, and insects reproduce by parthenogenesis and are female altogether. There are some reptiles, such as the boa constrictor and Komodo dragon that can reproduce both sexually and parthenogenetic, depending on availability of the mates.

Mutation

Genetic information of an organism can be changed by change in their quantity, arrangement of the genes in the genome, and change in the gene structure. Euploidy is a condition in which the number of sets of chromosomes changes; it can be monoploidy or polyploidy. In aneuploidy number of chromosomes in one set is more or less. There is addition or deletion of the chromosome. Chromosomal aberrations include abnormalities in the structure of chromosomes. Addition, deletion of genes, inversion and translocations are main chromosomal aberrations. Chromosomal aberrations are commonly observed in cancer cells. In evolution, the most important role of such chromosomal rearrangements may be to accelerate the divergence of a population into new species by making populations less likely to interbreed, thereby preserving genetic differences between these populations.

Gene mutation also called point mutation is alteration in DNA base sequence which results in changes in the gene structure and may change the phenotype of an organism. New alleles of a gene are formed by mutation. Gene mutation may arise due to change in a single base pair of DNA. A classical example of such a mutation is **sickle cell anemia**.



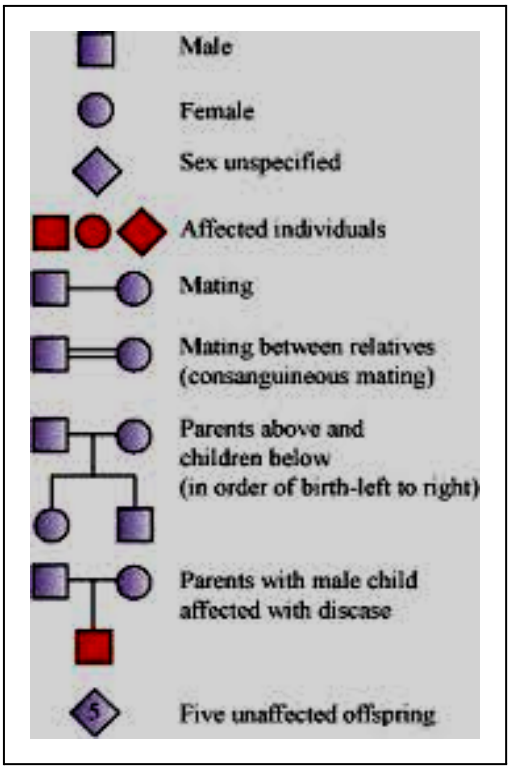
Deletion and insertion of base pairs in DNA cause frame-shift mutations.

There are many chemical and physical factors that induce mutations. These agents are referred to as mutagens. UV radiations can cause mutations in organisms – it is a mutagen**.**

Pedigree Analysis

Natures of alleles of a gene (dominant, recessive, codominant, semidominant) can be assessed by analyzing the results of controlled crosses. In many situations, controlled crosses cannot be performed. In these cases the inheritance of a particular trait is analyzed in the different generations of an existing population. This is always the case when studying human traits. P**edigree analysis** is used to study the inheritance of genes in humans. Pedigree analysis is also useful for the small sized population and for the species with a long generation time.

Pedigree charts are constructed by using standard symbols. Below are the principle symbols used for drawing a pedigree.



Once phenotypic data is collected from several generations and the pedigree is drawn, careful analysis allows determining the nature of the trait.

For a dominant trait

- Affected progeny must have at least one affected parent
- The phenotype generally appears in every generation
- Two unaffected parents will have only unaffected offspring

Genetic Disorders

A genetic disorder is caused by alteration in the genome. These are usually congenital, that is present by birth. Genetic disorders are often hereditary, passed down from the parents to progeny. In some cases the defect is caused by new mutations and inherited if it is present in the germ cells. The same disease, such as some forms of cancer, may be caused by an inherited genetic condition in some people, by new mutations in other people, and mainly by environmental causes in other people. Whether, when and to what extent a person with the genetic defect or abnormality will actually suffer from the disease is almost always affected by the environmental factors.

Some types of recessive gene disorders in heterozygous conditions confer an advantage in certain environmental conditions.

Mendelian Disorders

Mendelian disorders are the genetic disorders in humans that arise from the change or alteration in a single gene. Their inheritance pattern is governed by the Mendelian law of inheritance. Their nature can be predicted from the family history by the help of a pedigree chart. Sickle cell anaemia, Colour blindness, Cystic fibrosis, Haemophilia, Thalassemia and Phenylketonuria are some of the most common Mendelian genetic disorders.

Based on the inheritance pattern these Genetic disorders can be grouped in of four types: Autosomal dominant, Autosomal recessive, Sex-linked dominant and Sex-linked recessive.

Haemophilia

Haemophilia is a disorder of blood clotting mechanism. In this disease, the protein which helps in clotting of blood is affected. As a result, the affected person fails to stop bleeding after a cut. It is a X linked recessive disease Its genetic inheritance pattern shows unaffected carrier mother (heterozygous) passing on the disease to sons. . It is seen more frequently in males than females. Females are rarely affected because for a female to get the disease, father must be haemophilic and the mother should be at least a carrier. The disease is not transmitted from father to sons.

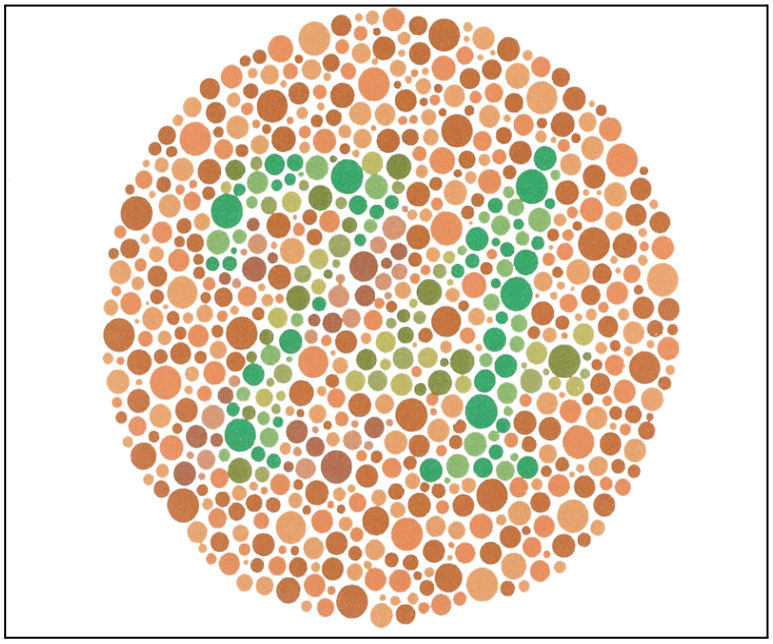
A	B	C
It is the most common type of hemophilia. (Severe)	It is the second most common type of hemophilia. (Moderate)	It is a mild form of hemophilia. (Mild)
It is also known as factor VIII deficiency or classic hemophilia.	It was originally named "Christmas disease". Caused by factor IX deficiency	Deficiency of factor XI.

Types of Hemophilia

Colour Blindness

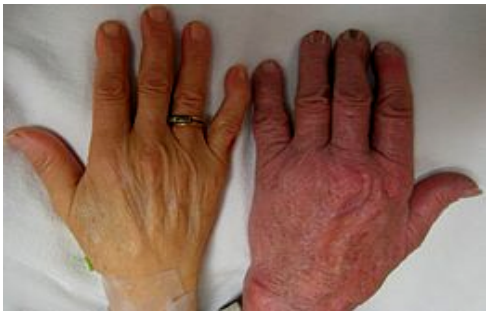
Color blindness, also known as color vision deficiency, is the decreased ability to differentiate the color. Color blindness can make some educational activities difficult. Buying fruit, picking clothing, and reading traffic lights can be more challenging, for example. Problems,

however, are generally minor and most people adapt. People with total color blindness, however, may also have decreased visual acuity and be uncomfortable in bright environments.



The most common cause of color blindness is an inherited fault in the development of one or more of the three sets of color sensing cones in the eye. Males are more likely to be color blind than females as the genes responsible for the most common forms of color blindness are on the X chromosome. As females have two X chromosomes, a defect in one is typically compensated for by the other, while males only have one X chromosome. Diagnosis is typically with the Ishihara color test; however a number of other testing methods also exist.

Thalassemia



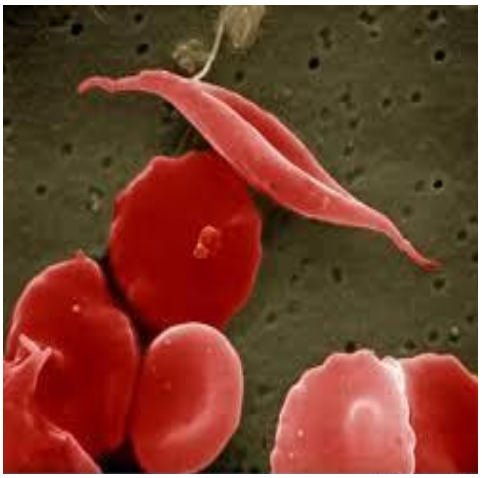
Thalassemias are inherited blood disorders that can result in the abnormal formation of hemoglobin. Symptoms depend on the type and can vary from none to severe. Often there is mild to severe anemia (low red blood cells). There may also be problems in the bones, an enlarged spleen, yellowish skin, dark urine, and among children slow growth.

Thalassemias are genetic disorders inherited from a person's parents. There are two main types, alpha thalassemia and beta thalassemia. The severity of alpha and beta thalassemia depends on how many of the four genes for alpha globin or two genes for beta globin are

missing. Diagnosis is typically by blood tests including a complete blood count, special hemoglobin tests, and genetic tests. Diagnosis may occur before birth through prenatal testing. Both α- and β-thalassemias are often inherited in an autosomal recessive manner.

Sickle Cell Anemia

This is an autosomal recessive trait that can be transmitted from parents to the offspring when both the partners are carriers for the gene (or heterozygous).The disease is controlled by a single pair of allele, HbA and HbS. Out of the three possible genotypes only homozygous individuals for HbS (HbS HbS) show the sickle cell phenotype. Heterozygous (HbA HbS) individuals appear unaffected but they are carriers of the disease. The defect is caused by the substitution of Glutamic acid (Glu) by Valine (Val) at the sixth position of the beta globin chain of the haemoglobin molecule. The substitution of amino acid in the globin protein results due to the single base substitution at the sixth codon of the beta globin gene from GAG to GUG. The mutant haemoglobin molecule undergoes polymerization under low oxygen tension causing the change in the shape of the RBC from biconcave disc to elongated sickle like structure.



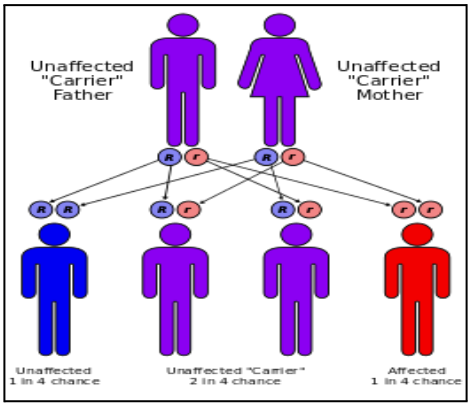
Phenylketonuria

This inborn error of metabolism is also inherited as the autosomal recessive trait. The affected individual lacks an enzyme that converts the amino acid phenylalanine into tyrosine. As a result of this, phenylalanine is accumulated and converted into phenyl pyruvic acid and other derivatives. Accumulation of these in the brain results in mental retardation. These are also excreted through urine because of its poor absorption by the kidney.


Symptoms Of Phenylketonuria (PKU)
Learning disabilities
Mental retardation
Tremors or jerky movements of limbs
Skin rash or eczema
Epilepsy
Hyperactivity
Behavioral issues
For More Information, Visit: www.epainassist.com
ePainAssist.com


Phenylketonuria
RESTRICTIONS
"MEET DIRTY DAN'S NEW ENEMIES"
M Meat
D Dairy Products
D Dry Beans
N Nuts
E Eggs
MILK

Cystic Fibrosis



Cystic fibrosis (CF) is an autosomal recessive genetic disorder. One easily diagnosed symptom of CF is excessively salty sweat. The lungs, pancreas, and liver become clogged with mucus, which results in chronic infections and the eventual malfunction of these vital organs. In addition, mucus often builds up in the digestive tract, causing individuals to be malnourished. Lung infections are recurrent, and patients often die from pneumonia or other infections of the respiratory system. It is caused due to mutations in the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Those with a single working copy are carriers and otherwise mostly normal.

Disorder	Dominant/ Recessive	Autosomal/ Sex linked	Symptom	Effect
Sickle-cell anaemia	Recessive	Autosomal, gene on Chromosome 11	Aggregation of erythrocytes, more rapid destruction of erythrocytes leading to anaemia.	Abnormal haemoglobin in RBC's
Phenylketonuria	Recessive	Autosomal, gene on Chromosome 12	Failure of brain to develop in infancy, mental retardation, idiots	Defective form of enzyme phenylalanine hydroxylase.
Cystic fibrosis (CF)	Recessive	Autosomal, gene on Chromosome 7	Excessive thick mucus clogging in lungs, liver and pancreas anomalies.	Failure of chloride ion transport mechanism through cell membrane.
Huntington's disease (HD)	Dominant	Autosomal, gene on Chromosome 4	Gradual degeneration of brain tissue in middle age, loss of motor control.	Production of an inhibitor of brain cell metabolism.
Haemophilia A/B	Recessive	Sex-linked, gene on X chromosome	Failure of blood to clot	Defective form of blood clotting factor VIII/IX.
Colour blindness	Recessive	Sex-linked, gene on X chromosome	Failure to discriminate between red and green colour.	Defect in either red or / and green cone cells of retina.
Down's Syndrome		Autosomal, Aneuploidy (Trisomy, +21)	Mongolian eyefold (epicanthus), open mouth, protruded tongue, projected lower lip, many loops on finger tips, palm crease	Retarded mental development 1Q below 40
Turner's Syndrome		Sex chromosomal Monosomy 44 + XO	Short stature females (<5'), webbed neck, body hair absent menstrual cycle absent, sparse pubic hair, underdeveloped breasts narrow lips, puffy fingers.	Sterile, hearing problem
Klinefelter's syndrome		Sex chromosomal Aneuploidy (Tri/tetrasomy of X chr) 44 + XXY, 44 + XXXY	These males are tall with long legs, testes small, sparse body hair, barr body present, breast enlargement.	Gynaecomastia, azospermia, sterile

Chromosomal Disorders

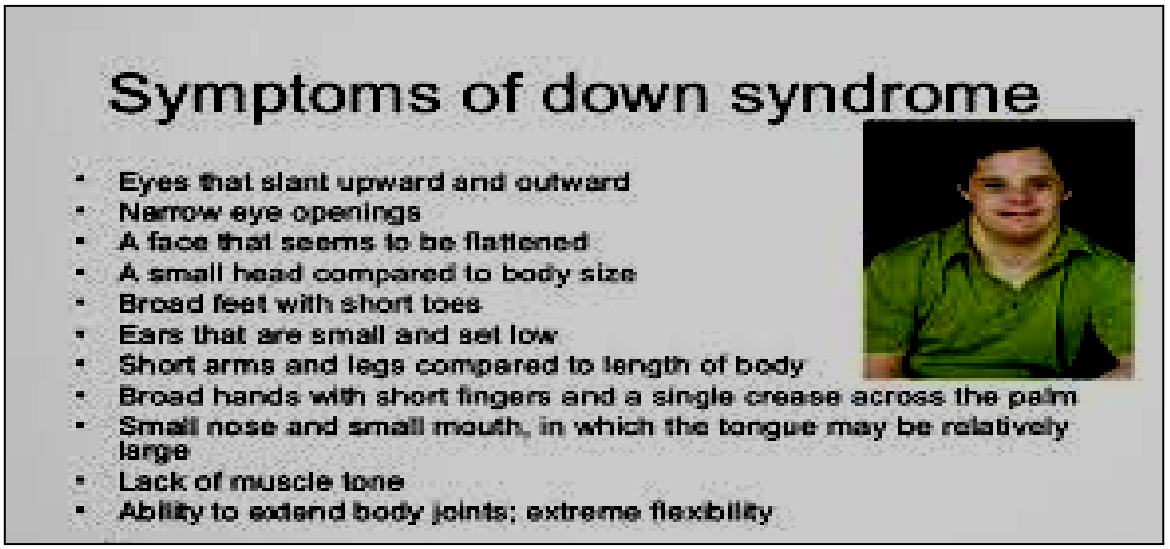
The chromosomal disorders are caused due to addition or deletion of one or more chromosomes. Failure of separation of chromosomes of homologous pair or failure of segregation of chromatids during cell division results in the loss or gain of chromosome(s). This is called aneuploidy.

The total number of chromosomes in a normal human cell is 46 (23 pairs). Out of these 22 pairs are autosomes and one pair of chromosomes are sex chromosome. Sometimes, though rarely, either an additional copy of a chromosome may be included in an individual or an individual may lack one of any one chromosome of the pair. These situations are known as trisomy or monosomy of a chromosome, respectively. Such a situation leads to serious consequences in the individual. Down's syndrome, Turner's syndrome and Klinefelter's syndrome are common examples of chromosomal disorders. Presence of an extra 21 chromosome results in Down's syndrome. Similarly, Turner's syndrome is caused due to loss of an X chromosome in human females.

Failure of cytokinesis after the telophase stage of cell division results in an increase in a whole set of chromosomes in an organism, and this phenomenon is known as polyploidy. This condition is often seen in plants.

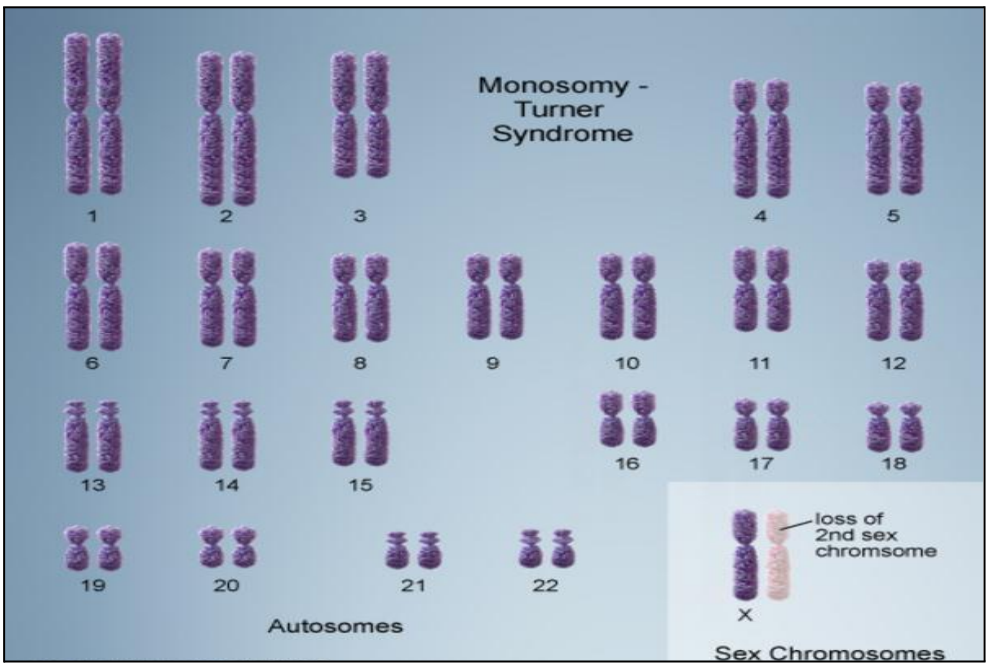
Down's Syndrome

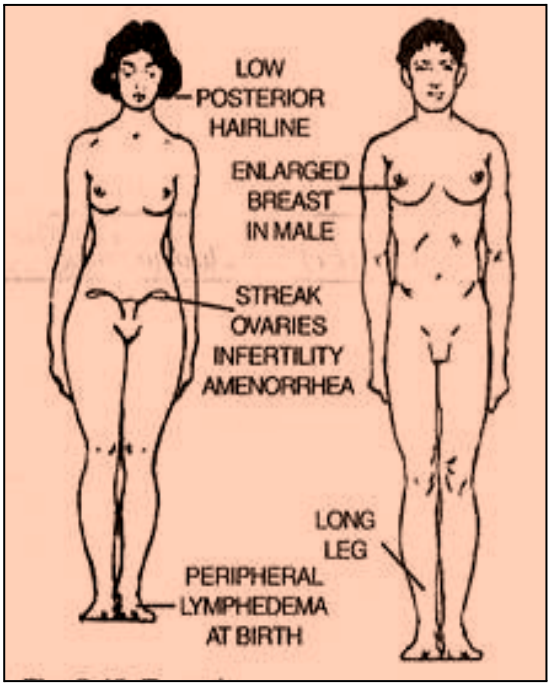
The disorder was first reported in 1866 by Langdon Down. It is an autosomal aneuploidy, caused by the presence of an extra 21 chromosome. During meiosis I of oogenesis due to nondisjunction both the chromosomes of the 21 pair pass into a single egg. Thus the egg possesses 24 chromosomes instead of 23 and the offspring has 47 chromosomes (45 + XY in male, 45 + XX in female) instead of 46. Down's syndrome is also called 21-trisomy. It is characterized by rounded face, broad fore-head, permanently open mouth, protruding tongue, projecting lower lip, short neck, flat hands and stubby (small) fingers, many "loops" on fingertips, coarse and straight hair, furrowed tongue, broad palm with characteristic palmar crease, which runs all the way across the palm and Mongolian type eyelid fold (epicanthus).



Turner's Syndrome

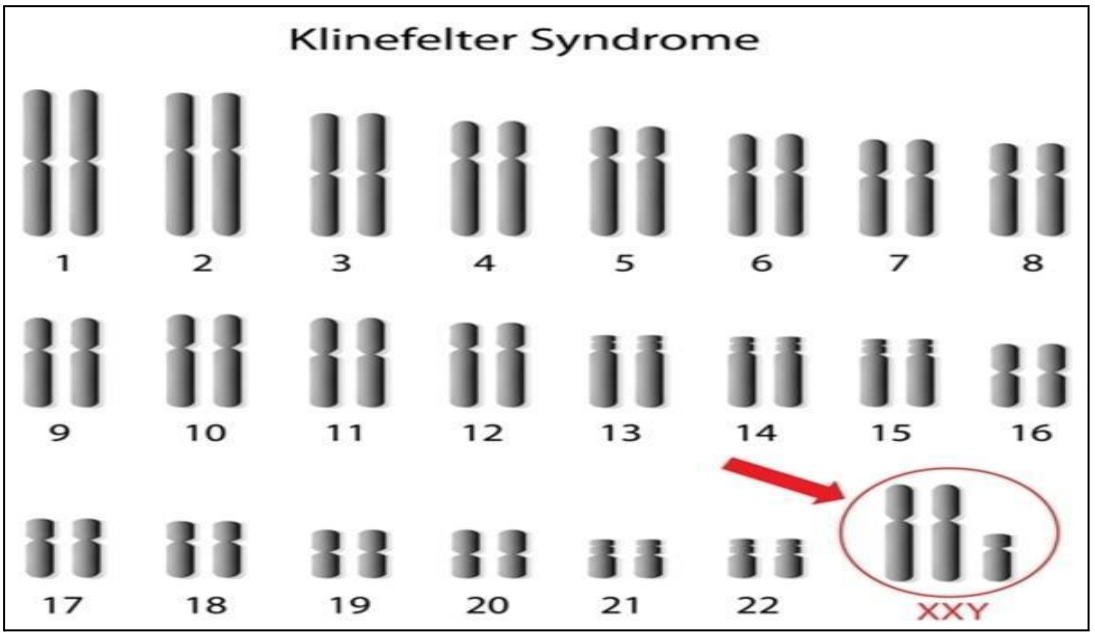
Turner's syndrome (Turner, 1938) is due to lack of one X chromosome in the human females. The females have karyotype (44 +XO). Turner's syndromes are sterile females; they may not menstruate or ovulate. They are characterized by the presence of rudimentary ovaries filled with connective tissue, undeveloped breasts, small uterus, puffy fingers (peripheral lymphoedema). Turner's syndromes are short statured females (less than 5 feet) with webbed necks, abnormal intelligence, cardiovascular abnormalities and hearing impairment. Frequency of Turner's syndrome is 1 in every 3000 female births.





Klinefelter's Syndrome

Klinefelter's syndrome (Klinefelter, 1942) is due to the presence of at least one extra X chromosome in males. It is formed by the union of an abnormal XX egg and a normal Y sperm.



The individual has 47 chromosomes (44+XXY). Such persons are sterile males (also called feminized male). Klinefelter's syndrome is characterized by presence of undeveloped testes, mental retardation, female-like sparse body hair, knock knees, long limbs and with some

female characteristics such as feminine pitched voice and enlarged breasts (gynaecomastia). It is considered that the more the number of X chromosomes, the greater the mental defect. Frequency of Klinefelter's syndrome is 1 in every 500 male births.

Summary

Mendel's laws were extended in the form of 'Chromosomal Theory of Inheritance'. Later, it was found that Mendel's law of independent assortment does not hold true for the genes that were located on the same chromosomes. These genes were called 'linked genes'. Closely located genes assorted together, and distantly located genes, due to crossing over, exhibit varied degree of recombination. Linkage maps corresponded to arrangement of genes on a chromosome.

Genes present on sex chromosomes shows sex specific difference in their inheritance pattern, such genes are called sex-linked genes. All except one pair of the chromosome in the males and the females are similar. The chromosomes which were different in two sexes were named as sex chromosomes. The remaining set was named as autosomes. In humans, a normal female has 22 pairs of autosomes and a pair of sex chromosomes (XX). A male has 22 pairs of autosomes and a pair of sex chromosome as XY. In chicken, sex chromosomes in male are ZZ, and in females are ZW.

Mutation is defined as change in the genetic material. A point mutation is a change in gene structure. Sickle-cell anemia is caused due to change of one base in the gene coding for beta-chain of hemoglobin. Inheritable mutations can be studied by making a pedigree chart of a family. Genome of an organism can be altered by change in the whole set of chromosomes (euploidy) or change in the number of chromosomes in a set (aneuploidy). Different genetic disorders involving aneuploidy have been reported in human beings. Down's syndrome is due to trisomy of chromosome 21. In Turner's syndrome, one X chromosome is missing and the sex chromosome is as XO, and in Klinefelter's syndrome, the condition is XXY.