Genes and chromosomes

Genes :→ Term 'Gene' was given by Johannsen (1909) for any particle to which properties of Mendelian factor or determiner can be given.

⇒ Genes act by producing enzymes, i.e. each gene in an organism produces a specific enzyme, which controls a specific metabolic activity.

⇒ Gene is chemically DNA, but the length of DNA which constitutes a gene, is controversial. Three terms, i.e. Cistron, Muton and Recon were given by Seymour Benzer to explain the relation between DNA length and Gene.

(i) **Cistron** is that particular length of DNA which is capable of producing protein molecule or polypeptide chain or enzyme molecule.

(ii) **Muton** is that length of DNA which is capable of undergoing mutation. Muton is having one or part of nucleotide.

(iii) **Recon** is that length of DNA, which is capable of undergoing crossing over or capable of recombination. Recon is having one or two pairs of nucleotides.

Types of Genes :→

I. **Transposons or Jumping genes :→** Transposons or Jumping genes (Mc Clintock 1951 in maize) are DNA segments which can pass from one place to other in the Genome. At their ends, transposons have similar or inverted repetitive DNA sequences. The sequences can be cleaved by an enzyme transposase.

II. **Retroposons :→** The term retroposon was given by Rogers (1983) for DNA segments which are formed from RNA (RNA origin) or which are formed by reverse transcription under the influence of reverse transcriptase enzyme or RNA dependent DNA polymerase enzyme i.e.

RNA $\xrightarrow{\text{Reverse transcription}}$ DNA (Retroposon).

III. **Split genes or interrupted gene :-** R.J. Robert and P.A. Sharp (1977) discovered split genes (gene with introns) in eukaryotes for which they were awarded Noble Prize in 1993.

⇒ Split Genes, present in eukaryotes have coding gene which are not continuous but are

interrupted by non-coding sequence. There are two kinds of alternating segments in the split genes — Exon and Intron.

Exon contains coding nucleotides sequence which are ultimately translated into poly peptides. They carry genetic information.

Intron contains non-coding nucleotide sequence which are not translated into poly peptide. Eukaryote genes without introns are called exonic genes (non split gene) e.g. histone gene, inter feron genes.

⇒ Certain eukaryotic exonic genes are called processed genes which lack both intron and promotors. Therefore they are non-functional. Non-functional or inactive DNA present in eukaryotes is known as repititive DNA or excess DNA. Gene splicing was developed by Cohen and Boyer (1973).

Splicing involves:→ Removal of intron portion and fusion of exon to produce continuous gene or mRNA.

⇒ Uniting foreign gene with bacterial genome for producing specific substances (e.g. insulin). Functional eukaryotic mRNA transcribed by exon formed by splicing.

IV. Pseudogenes (false gene) and Multiple Genes:→

Pseudogenes are non-functional genes. They unable to produce functional products due to inactivation of promotor region, presence intervening nonsense codons insertion or deletions. e.g. several snRNA genes.

⇒ Pseudogenes are useless to the organisms and considered to be defective copies of functional genes (cistrons). These are reported in Drosophila, mouse and human beings.

Multigenes or multiple gene family is a group of nea similar genes which produces tissues and time specific products. e.g. globin gene family. In a cell hardly 10% of the gene are active and 90% being inactive.

V. Inducible genes and Repressible genes:→ Non constitutive genes are those genes which can be switched on or off as per requirements. They are of two kinds:- Inducible (remain repressed but are switched on in the presence of an inducer chemical) and repressible (remains active till switched off by a chemical).

two called diploid (2n), three called triploid (3n) and more than three called polyploid.

⇒ Gametes (sperm and unfertilized eggs) and gametophytes possess half the number of genomes present in the somatic cells. The two conditions are respectively called haploid (1X) and diploid (2X). In diploid cells there are two chromosomes of each type or also called homologous chromosomes.

Physical Structure :→

⇒ The shape of the chromosome is changeable from phase to phase in the continuous process of cell growth and cell division. In the resting phase or interphase stage of the cell, the chromosomes occur in the form of thin, coiled, elastic and contractile thread like stainable structure, the chromatin threads.

⇒ In the metaphase and the anaphase stage the chromosomes become thick and filamentous. A metaphase chromosome consists of two identical components: the chromatids and the centromere.

Chromatids :→ Chromatid lie side by side along their (chromosome) length and are held together at one point, the centromere.

⇒ The chromatids become separated at the beginning of anaphase, when the sister chromatids of a chromosome migrate to the opposite pole.

⇒ The parts of the chromatids on the two sides of the centromere are known as arms. The arms may be equal (isobrachial) or unequal (heterobrachial), depending upon the position of the centromere.

Centromere :→ Centromere, also called primary constriction, is a non stainable area. At this region, each chromatid has a trilaminar plate like kinetochore where spindle microtubules join the chromosome during cell division.

⇒ Kinetochore plays an important role in chromosome movement. It is through these specialized structure (kinetochores) that the chromosomes get attached to microtubules and help in their movement during anaphase.

⇒ The chromosomes are classified on the basis of the position and number of centromeres, and size of the arms.

Chromosome on the basis of position and number of centromere!-

I. Position!-

(A) **Metacentric!-** Centromere lies at the centre of chromosome dividing the latter in two equal arms. These appear V shaped during anaphasic movement. e.g. Amphibians, man, In Trillium and Tradescantia all the chromosomes are meta centric.

(B) **Submetacentric!-** Centromere lies 'off the centre' i.e. some distance away from the midpoint, dividing the chromosome in the two unequal arms. During anaphasic movement these appear L or J shaped. e.g. Man.

(C) **Acrocentric!-** The centromere lies towards one end of chromosome dividing it in two grossly unequal arms. They appear J shaped during anaphasic movement.
e.g. Locust, Man.

(D) **Telocentric!-** The centromere lies just at the tip of the chromosome and only telomeric part lies on its other end giving an appearance of I-shape, during anaphasic movement. The chromatids in a telocentric chromosome are not divided in arms. The chromosome remain rod shaped.

II Number!-

(A) **Acentric!-** It is an unusual chromosome without any centromere. Such a chromosome can neither orient itself on the spindle apparatus nor can it participate in anaphasic movement. Factually the Kinetochore does not attach itself to the chromosome and hence microtubular insertion can not take place.
⇒ Such a chromosome is often 'lost' during cell division and may result in severe problematic condition in the progeny cell or causes lethality.
⇒ Also called holocentric as the entire surface functions as a centromere.

(B) **Dicentric!-** A chromosome with two centromeres is formed due to translocation. Such dicentric chromosomes are often seen during meiotic anaphase, forming anaphase bridge.
e.g. maize chromosome.

(C) **Polycentric!-** Contain many centromeres. It is also called 'diffused centromeric chromosomes'. Chromosomes of hemipteran insects, Ascaris etc. are diffused centromeric chromosome. (Polycentric chromosomes are with more than two centromeres, but diffused chromosomes are with indistinct centromere).

(D) **Monocentric!-** A chromosome with single centromere. It is the most common.

VI. House Keeping genes! → These are the genes which are always expressed and are also called Constitutive genes. Their common functions are required in all types of cells e.g. RNA - polymerase determining genes such as tRNA and rRNA.

Parallelism Between Mendelian Factors (Genes) and chromosomes! →

⇒ In 1900 the significance of Mendel's work was realised almost simultaneously by three Scientists de Vries, Correns and Tschermark.

⇒ In fact, it was Correns who summarised Mendel's conclusions in the familiar form of two principles and coined the term 'factor'. Mendel has used the term 'elements' to describe the hereditary unit.

⇒ It was an American, W. Sutton however, who noticed the striking similarities between the behaviour of chromosomes during gamete formation and fertilization, and the transmission of Mendel's hereditary factors.

⇒ The similarities between Mendel's hereditary factors and the behaviour of chromosomes are given in the following table! -

Behaviour of chromosomes and genes during meiosis and fertilization	Behaviour of Mendel's factors / genes.
⇒ Chromosomes occurs in pairs in a diploid cell and in organisms. The paired chromosomes are called as homologous chromosomes	⇒ Mendel's factors occurs in pairs as each trait is controlled by a pair of factors.
⇒ Homologous chromosomes separate out or segregate during meiosis at the time of gamete formation.	⇒ A pair of factors separate / segregate during gamete formation.
⇒ only one chromosome of a homologous pair passes into a gamete.	⇒ only one factor is present in a gamete.
⇒ During fertilization, gamete unite restoring the chromosomes number, Each homologous pair has one paternal and one maternal chromosome.	⇒ During fertilization, gametes unite Each organism contain
⇒ Chromosomes retain their individuality during segregation. Each pair segregates independently of every other pair.	⇒ Factors remain unchanged from generation to generation. Each factors segregates independently of every other factor.

⇒ The above similarities led Walter Sutton and Theodore Boveri (1902) to postulate the "Chromosomal Theory of inheritance". According to this theory, each pair of factor is carried by a pair of homologous chromosomes, with each chromosome carrying one of the factors.

⇒ Since the number of characteristics of any organism vastly outnumber the chromosomes, as revealed by microscopy, each chromosome must carry many factors.

⇒ The term factor as the basic unit of heredity was replaced by Johannsen in 1909 with the term Gene.

⇒ whilst gene is used to describe the unit of heredity, it is the alternative form of the gene or alleles which influence phenotypic expression.

⇒ Alleles are the alternative forms in which a gene may exist and they occupy the same loci in homologous chromosomes.

Salient features of chromosomal theory of inheritance:→

⇒ Bridge between one generation and the next is through sperm and ovum. The two must carry all the hereditary characters.

⇒ Both the sperm and egg contribute equally in the heredity of the offspring. The sperm provides only the nuclear part of the egg. As such hereditary characters are governed by nuclear material. There is fusion of the sperm and egg nuclei during fertilization.

⇒ Nucleus contains chromosomes. Therefore, chromosomes must carry the hereditary traits.

⇒ Every chromosome or chromosome pair has a definite role in the development of an individual. Loss of a complete or part of the chromosome produces structural and functional deficiency in the organism.

⇒ Like the hereditary traits the chromosomes retain their number, structure and individuality throughout the life of an organism and from generation to generation. The two neither get lost nor mixed up. They behave as units.

⇒ Both chromosome as well as genes occur in pairs in the somatic or diploid cells.

⇒ A gamete contains only one chromosomes of a type and only one of the two alleles of a trait.

⇒ The paired condition of both chromosomes as well as Mendelian factors is restored during fertilization.
⇒ Genetic homogeneity and heterogeneity, dominance and recessiveness can be suggested by chromosomal type and behaviour.
⇒ Homologous chromosomes synapse during meiosis and then separate or segregate independently into different cells which establishes the quantitative basis for segregation and independent assortment of hereditary factors.
⇒ In many organisms, sex of an individual is determined by specific chromosomes called sex chromosomes or allosomes

Chromosomes:→ E. Strasburger (1875) discovered thread like structures in the cell during cell division. These thread like structures are called chromosomes due to their affinity for basic dyes.
⇒ W. waldeyer (1888) coined the term chromosomes. In Viruses and prokaryotes hereditary material is not associated with histone proteins. It forms a single complex and is, therefore considered to be equivalent to a single chromosome but simpler than it and hence called prochromosome.
⇒ In eukaryotic organisms at the interphase stage of the cell cycle, chromosomes within the nucleus remain in the form of long, loosely coiled irregular strands called chromatin reticulum
⇒ At the S-phase, they replicate and the two chromatids remain attached. with the onset of mitosis or meiosis I, the long replicated chromosomes condense. At the metaphase stage, they become distinct.
⇒ Connected together at the centromere, individual chromosomes can be distinguished by their shape, size and position of centromere and patterns of banding.
⇒ Chemically chromosomes are made up of DNA (Deoxyribonucleic acid) and proteins. The presence of DNA enables the chromosomes to reproduce with a high degree of fidelity.
⇒ The chromosomes are called the vehicles of heredity since they carry the genes and the genes are located in the DNA molecule.

Functions of chromosomes :→

⇒ Chromosomes contain genes. All the hereditary information is located in the genes.
⇒ Chromosomes control the synthesis of structural proteins and thus help in cell division and cell growth.
⇒ They control cellular differentiation.
⇒ By directing the synthesis of particular enzymes, chromosomes control cell metabolism.
⇒ Chromosomes can replicate themselves or produce their carbon copies for passage to daughter cells and next generation.

Viral chromosomes :→ Virus are small obligate intracellular parasites which by definition contain either RNA or DNA genome surrounded by a protective virus coded protein coat.

⇒ For propagation, Virus depend on specialized host cells supplying the complex metabolic and biosynthetic machinery of eukaryotic or prokaryote cells.
⇒ A complete virus particle is called a virion. The viruses infecting plant cells usually have their chromosome formed of a linear RNA molecule.
⇒ The viruses infecting animal and bacterial cells may have RNA or DNA molecule of linear or circular form composing their chromosome.
⇒ The viral DNA is generally double-stranded but is single-stranded in some forms, viral RNA is usually single-stranded but may be double-stranded in certain cases.

Bacterial chromosome (Prokaryotic chromosomes):→

⇒ In bacteria there is no organized nucleus. The entire hereditary material is packed in a single chromosome. The latter is irregularly folded into a compact mass, the nucleoid or genophore of indefinite form.
⇒ The bacterial chromosome is a single, double stranded DNA (circular) forming a closed circle with no free ends attached permanently to an infolding of the plasma membrane called mesosome.
⇒ DNA lacks histone proteins, however polyamines have been associated with it. A small amount of protein, the RNA polymerase enzyme is, however, associated with it.

⇒ Generally, the circular molecule is present in a highly folded and supercoiled state. This is expected because the diameter of a bacterial cell (e.g. Escheriachia coli) is about 1-2 microns while the total length of the circular DNA is about 1000 microns.

⇒ The circular molecule has 40-50 folds or looped domains. These folds are held in position by RNA molecules (RNA connectors) and some non-histone proteins associated with the bacterial chromosome. (Histones are absent in bacteria).

⇒ The bacterial chromosome is attached to mesosome by two closely placed replicating Y-forks.

⇒ Bacterial chromosome replicates while attached to mesosome.

⇒ In addition to the normal DNA chromosome, extra chromosomal genetic elements are often found in the cytoplasm of most bacterial species and in some species of eukaryotes. These elements are called plasmids.

⇒ These are capable of autonomous replication in the cytoplasm of the bacterial cell. Therefore, plasmids are also described as autonomously replicating. ("mini chromosomes"). A bacterial cell can have one to many copies of a plasmid. Plasmids represent extra genes.

⇒ Some plasmids are called episomes. An episome is a plasmid with a dual ability to replicate, i.e. it can replicate autonomously in the cytoplasm like other plasmids or it can also integrate itself into the DNA of the bacterial chromosome and behave as part of the chromosome.

⇒ The plasmids are known to move around freely in the bacterial world and may pick up genes from one bacterium and transfer them to another. This may be one method of providing variability to the asexually multiplying bacteria.

⇒ The plasmids mainly carry genes for fertility, antibiotic resistance, and bacteriocin (colicin) production. The plasmid with such genes are called F plasmid, R plasmid and Col plasmid respectively.

⇒ The plasmids do not have genes for any vital function. They are non-essential and a bacterium can survive without its plasmids.

Differences between prokaryotic and eukaryotic chromosomes :→

Prokaryotic chromosome (Prochromosome)	Eukaryotic chromosome (Chromosome).
⇒ It is a primitive structure, also called prochromosome.	⇒ Eukaryotic chromosome is the typical chromosome.
⇒ A prokaryotic cell has a single chromosome equivalent.	⇒ A eukaryotic cell possesses two to several chromosome.
⇒ The chromosome is attached to a replicating structure like mesosome.	⇒ A mesosome like structure is absent.
⇒ DNA is circular.	⇒ DNA is linear.
⇒ DNA is not ~~attached~~ associated with histone proteins, It is therefore called naked.	⇒ DNA is associated with histones.
⇒ Coiling is caused by bands of RNA or polyamines.	⇒ Coiling is due to scaffolding and histone protein.
⇒ It is in contact with plasma membrane through mesosome.	⇒ The chromosomes are seldom in contact with plasmalemma.
⇒ Prokaryotic chromosome is embedded directly in the cytoplasm.	⇒ Eukaryotic chromosomes do not lie in direct contact with cytoplasm.
⇒ A nuclear envelope is absent around the chromosome.	⇒ A nuclear envelope surrounds the chromosome complex.
⇒ Chromosomes are compact in the metabolic cell.	⇒ Chromosomes occur in the form of chromatin fibres in the metabolic cell.
⇒ There is a single replicon.	⇒ A eukaryotic cell has several replicons.

Eukaryotic chromosome :→

Tradescantia.

⇒ Eukaryotic chromosomes were discovered by Hofmeister (1848) in the pollen mother cell of ↑

⇒ Eukaryotic chromosome is DNA-histone complex having a distinct number and morphology, becoming distinct only during nuclear division, otherwise forming chromatin fibres inside the nucleus.

⇒ Eukaryotes also possess DNA inside mitochondria and plastids. It is known as organelle pro-chromosome and is similar to prokaryotic prochromosomes.

⇒ The size of chromosome is normally measured at mitotic metaphase and may be as short as 0.25 mm in fungi and birds, or as long as 30 mm in some plants such as

⇒ A complete set of chromosomes found in an organism is called genome, where each chromosome is represented only once. The condition of having single genome is called monoploid (1n), two

Secondary Constriction :- These are narrow areas other than the primary constriction. Secondary constrictions are of two types :- one type (Secondary constriction II) is produced by breaking and subsequent fusion of chromosome segments and the other type of secondary constriction are metabolically active and are the sites for the formation of nucleoli during interphase.

⇒ These are termed nucleolar organizers (called Secondary Constriction I).

⇒ These are so called because they are necessary for the formation of nucleolus (which is formed in the post mitotic reconstruction phase). It consists of euchromatin. They possess rDNA.

⇒ The chromosomes having nucleolar organizers are called nucleolar chromosomes.

⇒ The location of secondary constriction II is constant for a particular chromosomes and is therefore useful for identification of chromosome.

⇒ In Man it is found on the long arm of chromosomes 1, 10, 13, 16 and Y. In human beings 5 chromosomes (13, 14, 15, 21, 22) have nucleolar organizer regions (secondary constriction II).

Satellite :→ The area of a chromosome distal to the nucleolar organiser is called satellite or trabant. The presence or formation of satellite is called Satellitism. Satellite may be small and knob like. The chromosome bearing it is called SAT- chromosome.

⇒ The word 'SAT' is not derived from satellite but from poor staining ability of the nucleolar organizer region as its DNA content is low. The prefix SAT stands for 'Sine Acid Thymo-nucleinico' (without thymo nucleic acid or DNA), since the chromosome on staining shows relative deficiency of DNA in the nucleolar organiser region.

Telomere :→ The telomere seems to be functionally different from the rest of the chromosome. It is the terminal end of a chromosome formed of a moderately repetitive DNA.

⇒ A chromosome may break up and its pieces may rejoin but no segment connects to the telomere. Thus, the telomere has a polarity and it "seals" the end. It, however, attaches to the nuclear envelope.

Chromomeres :→ The surface of a chromosome or chromatid bears a number of small swellings or dense areas called chromomeres. Chromomeres are arranged in linear fashion.

⇒ Chromomeres are regions of tightly folded DNA and have great interest for the cell biologists.

⇒ They are believed to correspond to the units of genetic function in the chromosomes.

Chromatin:→ The material of the chromosome is the chromatin which may be distinguished in the interphase nucleus depending on their staining properties.

⇒ The term chromatin was coined by Flemming (1879).

Types of chromatin:-

⇒ Chromosomes area which never show condensed form or stain lightly are called euchromatin and the reverse of this called hetero chromatin.

(i) **Euchromatin:→** Euchromatin contains structural genes which replicate and transcribe during G_1 and S phase of interphase.

⇒ The euchromatin is considered genetically active chromatin since it has a role in the phenotype expression of the genes.

(ii) **Heterochromatin:-** A chromosome may possess some heterochromatic areas which have replication (during early stage of S-phase) and coiling phases different from rest of the chromosome.

⇒ Heterochromatin is more labile than euchromatin and is affected by temperature, sex, age of parents, proximity to the centromere and presence of an additional Y- chromosomes. Types of heterochromatin are:→

(a) **Constitutive heterochromatin:→** Heterochromatin is constitutive if it occurs in the all cell types. It was originally called satellite DNA (S-DNA) or repetitive DNA because upon ultracentrifugation, it separates from the main component of DNA.

⇒ It occurs in the region of telomeres, satellites and around centromeres. Constitutive hetero-chromatin is highly polymorphic.

⇒ Probably because of the instability of the satellite DNA constitutive heterochromatin is strongly stained by the C-band technique.

(b) **Facultative heterochromatin:→** Heterochromatin is called facultative if it is present in specific cells at particular stages of development.

⇒ It is characterised by the presence of line-type repeated sequences. It is reversible. Its heterochromatic state depending on the stage of development or the cell type examined. It becomes the sex chromatin body or Barr body in early embryo genesis. It is the hetero-chromatin which results from inactivation of one of the two X-chromosomes in females.

⇒ It is not particularly rich in satellite DNA, and is therefore not polymorphic. It is never stained by the C-band technique.

Ultrastructure of chromosome:→ Structurally a chromosome is differentiated into the following parts:- (i) pellicle (ii) Matrix (iii) chromonemata (iv) Primary Constriction (v) Secondary Constrictions (vi) Satellite (vii) Telomere.

(i) **Pellicle:→** It is the outer thin but doubtful covering or sheath of the chromosome.

(ii) **Matrix:-** Matrix or ground substance of the chromosome is made up of proteins, small quantities of RNA and lipid.

⇒ It has one or two chromonemata (singular- chromonema) depending upon the state of chromosome.

⇒ Both matrix and pellicle are non-genetic materials and appear only at metaphase when the nucleolus disappears.

(iii) **Chromonemata:-** The chromonemata form the gene bearing portions of the chromosomes. Basically chromonema is made up of nucleosome chains.

⇒ It would be necessary here to make a distinction between Chromonema and chromatid. While a Chromatid is a half chromosome, two chromatids being connected at the centromere, the Chromonema is a structure which is of a sub-chromatid nature and there can be more than one chromonemata in a chromatid.

⇒ In interphase chromosomes changes into long, thin chromatin fibres. Electron microscope shows a Chromatin fibre as a chain of similar subunits called nucleosomes.

⇒ Nucleosomes are usually packed together, with the aid of a histone to form a 30nm large fibre. As a 30 nm fibre, the typical human chromosome would be about 0.1 cm in length and would span the nucleus 100 times. This suggests higher order of packaging, to give a chromosome the compact structure seen in a typical karyotype (metaphase) cell.

⇒ Nucleosome is the fundamental packaging unit in eukaryotes. It consists of a Core particle and DNA linker.

⇒ Core particle of nucleosome is wrapped by DNA strand (comprise of 146 loose base pairs). The core particle is an octamer of 8 histone molecules, two each of H2A, H2B, H_3 and H_4.

⇒ Each nucleosome is connected to the next by a short DNA linker (~70 -75 base pairs). A nucleosome and a linker are together referred to as a Chromatosome.

⇒ A molecule of histone protein H1 is associated with each linker and it serves to pack nucleosomes together. There is no pellicle around the chromatid. The octamer of nu body or core of nucleosome is most conserved proteins being similar in different species.

⇒ Their charged ends (positively) are towards outside. DNA is wrapped over nu body almost twice to form nucleosome (100 Å diameter). It is not conserved but is quite specific for different tissues.

⇒ Nucleosome chain gives a beads on string appearance under electron microscope. The bead string is coiled to form cylindrical coil or solenoid having 6 nucleosomes per turn.

⇒ Actually the nucleosomal organisation has approximately 11 nm thickness, which gets further condensed and coiled to produce a solenoid of a 30 nm diameter.

⇒ This solenoid structure undergoes further coiling to produce a chromatin fibre of 300 nm and then a chromatid of 700 nm.

DNA (2nm diameter) → nucleosome (10 nm dia^{n}) → Solenoid (30 nm dia^{n}) → chromatin fibre (300 nm dia^{n}) → Chromatid (700 nm diameter)

Chromosome (1400 nm diameter)

Chemical Composition:- The eukaryotic chromosomes are composed of DNA, proteins, RNA, metal ions and enzymes.

DNA:- There is a single long, double-stranded, linear DNA molecule in a chromosome. The DNA contains biological and genetic information.

⇒ Its amount in all somatic cells of an organism is the same, the gametes have half of this amount.

Proteins:- They are of two types:- Simple basic histones (most abundant) and acidic or neutral non-histones.

⇒ Histones are low-molecular weight proteins rich in the basic amino acids lysine and arginine but completely lack tryptophan.

⇒ The mass of histone in a chromosome is about equal to the mass of the DNA.

⇒ The DNA and histones are loosely bound together in about 1:1 ratio to form deoxyribonucleo-proteins (DNP), also called chromatin.

⇒ The positively charged R groups of these amino acids bind strongly to the negatively charged phosphate group of DNA. This linkage maintains the helical form of the DNA molecule without disturbing its structure. The histones prevent RNA transcription.

⇒ There are five principal classes of histones:- H1, (H5), H2A, H2B, H3 and H4. The bulk of the histones are synthesized during the S phase of the cell cycle.

⇒ The eukaryotic DNA contains repetitive genes coding for histones. Histones are translated from 7-12 S m RNA. Histones probably mask DNA in a non-specific manner.

⇒ Histones also appear to have a structural role in packing of DNA molecules so as to render them more compact. In humans chromosomes the packing ratio of DNA is about 10^4. The ratio is however varies during the cell cycle.

⇒ Chromosomes are highly packed greatly during the metaphase and are highly dispersed in interphase.

Non-histone chromosomal proteins (NHC) are high molecular weight proteins having amino acids tyrosine and tryptophan. Non histone proteins are synthesized throughout the cell cycle.

RNA :→ The RNA is transcribed by DNA. Most of it passes into the cytoplasm. Some RNA remains associated with DNA along with proteins.

Metal ions :→ The metal ions found in the chromosomes include Mg^{++}, Ca^{++} and Fe^{++}. They keep the organization of chromosomes intact.

Enzymes :→ The enzymes of the chromosomes are DNA polymerase, RNA polymerase, nucleoside triphosphatase.

Giant Chromosomes :→ In some special types of cells of certain animals, at specific stages of their life cycle, the chromosomes are of unusually large size.

⇒ These are 200 or even more times larger than the size of corresponding ordinary somatic chromosomes. Therefore, these chromosomes are called as giant chromosomes. These chromosomes are extremely useful in cytogenetic studies.

⇒ Giant chromosomes are the polytene chromosomes and lampbrush chromosomes.

Polytene chromosomes :- Polytene chromosomes were first reported by E.G. Balbiani (1881) in the salivary glands of chironomous and was named so by Kollar.

⇒ These are found in salivary glands of dipterans such as Drosophila.

⇒ Polytene chromosomes are visible during interphase and prophase of mitosis. Their 2 mm length is much longer than metaphase chromosomes.

⇒ In polytene chromosomes, 100 or more copies of DNA are arranged side by side. The DNA is duplicated.

⇒ Alternating bands and interbands (i.e. highly and moderately dense regions) can be seen, when these chromosomes are examined (by Feulgen staining) under light microscope.
⇒ These chromosomes bear conspicuous swellings called chromosomal puffs. In certain developmental stages larger swellings are called Balbiani rings.
⇒ In the puff region, DNA strands uncoil, become active and produce mRNA.

Lampbrush Chromosomes :-

⇒ Lampbrush chromosomes were first observed by Flemming (1882), but these were first described by R. Ruckert (1892).
⇒ These chromosomes occurs at the diplotene stage of meiosis prophase I during oogenesis in amphibian oocytes.
⇒ The chromosome is a diplotene bivalent (i.e. 2 pairs of sister chromatids held together by chiasmata).
⇒ These chromosomes are larger than even polytene chromosomes.
⇒ In lampbrush chromosome, the strands of chromosome (consisting of 2 double strands of DNA) are dotted without 5000 chromomeres (dark staining irregular structures).
⇒ Twin loops emerge from chromomeres. These loops are identical on both pairs of sister chromatids.

Sex determination :-

⇒ Sex is an aggregate of those morphological, physiological and behavioural qualities that differentiate the organisms producing eggs from those organisms producing sperms.
⇒ The organisms producing eggs are known as female and those producing sperms are known as males.
⇒ Establishment of sex through differential development in an individual at an early stage of life is called sex determination.
⇒ It is determined at the time of fertilisation and is also called as Syngametic sex determination.
There are various mechanisms of determination and differentiation of sex, which are as follows :-
(i) Genetic or chromosomal sex determination (ii) Non-chromosomal or cytoplasmic sex determination
(iii) Environmental determination of sex (iv) Genic balance mechanism of sex determination.
(v) Effect of single gene in sex determination.

(1) Genetic or chromosomal sex determination:- Wilson and Stevens (1905) put forward the chromosome theory of sex.

⇒ They named the X and Y chromosome as sex-chromosome or allosomes and other chromosome of the cell as autosomes.

⇒ In most mammals, the sex is genetically determined and nearly 50% individuals are males and 50% females. Chromosomal sex determination is based on heterogamesis i.e. formation of two kinds of gametes in one sex.

⇒ There are five main genetic mechanism of sex determination:-

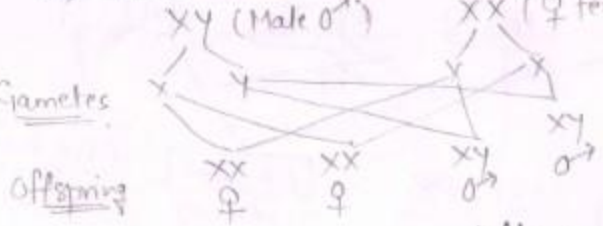
(A) XY-method:- (mammals, some insects):- XX-♀, XY-♂ (Lygaeus type) → first of all studied in milk weed bug, Lygaeus turcicus)

⇒ In this type the female is homomorphic (= isomorphic) possessing ~~one XX~~ two similar sex chromosomes XX, and the male is heteromorphic possessing one X-chromosome similar to that of female and one shorter and morphologically different Y-chromosome (humans), however morphology may vary in different organisms

⇒ The female is said to be homogametic (produces similar eggs) and the male is heterogametic (produces two types of sperms).

⇒ The Y-containing sperms and X-containing sperms are respectively called androsperms and gynosperms and the condition is called male digamy.

⇒ Sex is determined at the time of fertilization by the kind of sperm that fuses with the ovum.



XX-XY type is found in mammals and some insects such as Drosophila. It is also found in many bryophytes. Examples of plants showing XY sex determination method are Melandrium, Coccinia, Salix, Elodea etc.

The sex (X and Y) chromosomes have two regions each:- homologous and non-homologous or differential. The differential regions carry completely sex-linked genes as they do not undergo crossing over.

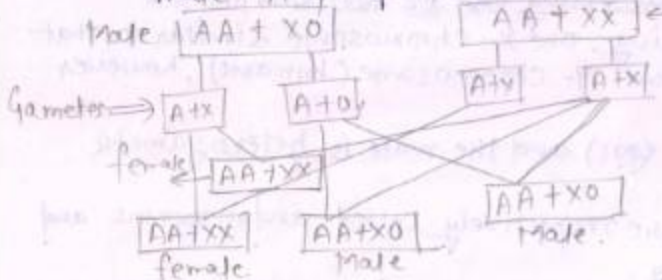
⇒ The homologous regions are incompletely sex-linked genes because they undergo crossing over. These regions help in pairing.

⇒ The genes present in the differential region of the Y-chromosome are called holandric genes.

⇒ Example of XY-linked genes are genes for Xeroderma pigmentosum, epidermolysis bullosa and of Y-linked genes or holandric genes are SRY, hypertrichosis of pinna, porcupine skin, TDF or testes determining factor.

(B) XX-XO type :- In this type the female has two homomorphic sex chromosomes (XX) (homogametic) and produces similar eggs while the male has one chromosome only (heterogametic) and produces two types of sperms :- gynosperm with X and androsperm without X.

⇒ Fertilization of an egg by X-bearing sperm yields female offspring, and by no X sperm yields male offspring. This mechanism is seen in grasshoppers, cockroaches etc.



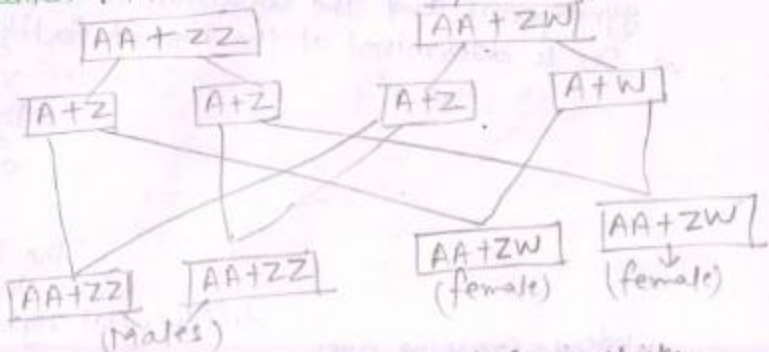
XX-♀, XO-♂ (roundworm, insects).

(C) ZW-ZZ method (birds, reptiles, fishes) :- ZW-♀, ZZ-♂

In this type the male has two homomorphic sex chromosomes (ZZ) and is homogametic and the female has two heteromorphic sex chromosomes (ZW) and is heterogametic. Thus there are two types of eggs :- with Z and with W, and only one type of sperm i.e. each with Z.

⇒ Fertilization of an egg with Z chromosome by a sperm with Z chromosome gives a Zygote with ZZ chromosomes (male), Fertilization of an egg with W chromosome by a sperm with Z chromosome yields a Zygote with ZW chromosome (female).

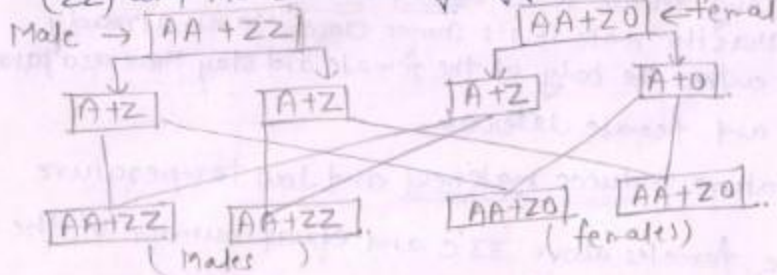
⇒ This mechanism operates in certain insects (butterflies and moths) and in Vertebrates (Fishes, reptiles and birds).



ZW-ZZ determination of sex in chicken.

(D) ZO-ZZ type (moths, butterfly) :- ZO-♀, ZZ-♂ :- In this type the female is heterogametic, while the male is homogametic.

⇒ Fertilization by a sperm with Z chromosome, the Z-containing egg gives rise to a male offspring (ZZ) and the Z-lacking egg produces a female offspring (ZO).



This mechanism occur in certain butterflies and moths.

(E) Haploid-diploid mechanism or haplodiploidy

⇒ It is a unique phenomenon in which an unfertilized egg develops into a male and a fertilized egg develops into a female. Therefore, the female is diploid (2n), and the male is haploid(n).

⇒ Eggs are formed by meiosis and sperms by mitosis. Fertilization restores the diploid number of chromosomes in the zygote which gives rise to the female.

⇒ If the egg is not fertilized, it will still develop but into a male (arrhenotoky or arrhenotokus parthenogenesis).

⇒ Thus, the sex is determined by the number of chromosomes and is seen in hymenopterous insects, such as bees, wasps, saw flies and ants.

(ii) Non-chromosomal / Non-allosomic / Cytoplasmic Sex determination :-

⇒ In bacteria Cytoplasmic factors or F-factor or Fertility factor located in plasmid determine the sex. Male or donor cells fertility factor is designated as F^+ cells, while that of female or recipient is designated as F^- cells.

⇒ In Chlamydomonas the genes controlling (+) and (-) behaviour are present over autosomes.

⇒ In maize sex chromosomes are absent. It possess separate genes for development of tassel (male inflorescence) and cob (female inflorescence).

(iii) Environmental determination of sex :→ It is non-genetic determination of sex which is based purely on environmental conditions.

⇒ The organisms are potentially hermaphrodite and capable of expressing any of the two sexes.

⇒ Marine mollusc Crepidula becomes female if reared alone. In company of a female, it develops into male (Coe, 1943).

⇒ Marine worm Bonellia develops into 3 cm long female if its larva settels down in an isolated place. It grows into small (0.3 cm long) parasitic male if its comes closer to an already established female (Baltzer, 1935). The male enters the body of the female and stay there as a parasite.

⇒ Ophryotocha is male in the young state and female later on.

⇒ In crocodiles and some lizards high temperature induces maleness and low temperature femaleness.

⇒ In turtles, males are predominant below 28°c, females above 33°c and equal number of the two sexes between 28-33°c.

(iv) Genic balance mechanism of sex determination :→

⇒ Sex determination in Drosophila is the same as that of human, however Bridges (1916) found that in these XXY genotype forms female fly while in human it produces phenotypically male individual. (Klinefelter's syndrome).

⇒ After studying a number of abnormal genotypes, Bridges (1926) put forward this theory of sex determination. According to this theory X : A autosomes ratio of 1.0 produces fertile female, (ii) more than one an infertile female (iii) 0.5 the fertile male provided. Y is also present below 0.5 infertile metamales and between 0.5 to 1.0 intersexes.

⇒ Female determining gene known as Sxl has been discovered in X chromosomes of Drosophila. Another transformer gene (tra) is present on an autosome which in the homozygous state transforms a genetic female fly into sterile male.

Single Gene Effect:→ In some organisms like Neurospora, yeast, Asparagus, Drosophila and several fishes, single gene is responsible for the expression of sex.

⇒ In Asparagus maleness is dominant over femaleness and male plants are ordinarily heterozygous.

⇒ In Maize the gene for tassel seed (ts) converts the male inflorescence (tassel) into seed-bearing inflorescence and the gene for silkless (sk) causes the absence of silk (female inflorescence). Therefore, a plant sk/sk is found to be male plant and a plant ts/ts a female plant. By using these genes it is possible to convert maize from a monoecious to a dioecious form.

⇒ In Drosophila a transformer gene (tra) when present in homozygous condition (tra/tra) converts a female into a sterile male, but has no influence on normal male. Thus XX female with tra/tra genotype is a sterile male while a XY male with tra/tra genes is a normal male.

Chromosomal Staining:→ Chromosomes are stained with special flourescent dyes that have differential affinity for different parts of the chromosomes.

⇒ Bands are segments of stained chromosomes that appear lighter or darker stained as compared to adjacent parts.

⇒ Chromosome banding was discovered by Caspersson and others in 1970. With one particular dye, the chromomes show a particular unique banding pattern, i.e. the banding pattern is constant with a particular treatment.

Types of staining technique:→ There are many types of staining techniques which show different banding patterns:→

C-Banding:→ It stains region having constitutive heterochromatin (e.g. pericentromeric regions). The chromosomes are first treated with strong alkali.

⇒ DNA is then denatured with tricodium citrate. It is followed by staining with Giemsa.

Q-Banding:→ Treatment with quinacrine mustard and observation with fluorescent microscope bring out AT rich regions.

⇒ It was the first fluorescent staining technique developed by Caspersson et al. Q-banding technique stains Y-chromatin in the interphase nucleus of human males.

G-Banding (Giemsa staining):→ Chromosomes incubated in saline solution are stained with Giemsa.
⇒ It brings out sulphur-rich protein parts. Ordinary light microscope can be used.
G-Banding is absent in plant chromosomes.

R-Banding:→ chromosomes incubated in buffer at high temperature are treated with Giemsa to produce bands in sulphur deficient regions (hence reverse Giemsa).

∴ Importance of banding techniques:-

⇒ Banding technique of chromosome staining is highly useful in knowing various types of chromosomal aberrations or abnormalities like additions, deletions and inversions.
⇒ The aberrations or chromosomal abnormalities produce abnormalities in organisms. The abnormalities are quite common even in human beings — 4 to 5 for every 1000 births. Some examples are:-

Cat-Cry Syndrome:- due to deficiency of short arm of chromosome 5.
Chronic granulytic leukemia:- due to deficiency of long arm of chromosome 22.
Down's Syndrome:- (mongolism):→ with an extra chromosome number 21.
Patau's Syndrome:- with an extra chromosome number 13.
Klinefelter's Syndrome:→ with an extra X-chromosome in female and super male with extra-Y-chromosome in male.

20% of all spontaneous abortions are due to chromosomal abnormalities.

** Karyotype:→ Karyotype is chromosome complement of a cell/organism providing description of number, types and characteristics of chromosomes.

Idiogram is a karyotype consisting of photograph or diagram of all the metaphasic chromosomes arranged in homologous pairs according to decreasing length, thickness, position of centromere, shape etc. with sex chromosomes placed at the end (but at position I in Drosophila).

⇒ Cultured cells growing under aseptic conditions are generally used for karyotyping.

⇒ The cells are administered colchicine to arrest division of cells at the metaphase. In case of human beings white blood and skin cells are usually cultured. The colchicine treated cells are killed, fixed and stained.

Human Karyotype:→ Tjio and Levan (1956) of sweden found that human cells have 23 pairs or 46 chromosomes.

⇒ 22 pairs of 44 chromosomes are autosomes are autosomes and the last 23rd pair is that of sex chromosomes. XX in females and XY in males.

⇒ Human autosomes are numbered and distinguished morphologically on the basis of their relative size, shape and positions of centromere.

⇒ According 'Denver System' of classification, the 22 pairs of human chromosomes are placed in seven groups, A to G as described in the given table:-

∴ Karyotype or Idiogram of man:-

	Group	Size	Position of centromere	Idiogram number.
I	(A)	Large.	Metacentric	1, 2, 3.
II	(B)	Large (Medium large)	submetacentric	4, 5.
III	(C)	Medium	Submetacentric	6, 7, 8, 9, 10, 11, 12 and X
IV	(D)	Large.	Submetacentric, Acrocentric, Sat (Subterminal)	13, 14 and 15.
V	(E)	Small (medium Short)	Metacentric or Submetacentric	16, 17, 18.
VI	K(F)	Small	Metacentric	19, 20.
VII	(G)	Small	Metacentric	21, 22 and Y. (have no sat)

BARR BODY (Sex chromatin):→ Barr and Bertram reported a deeply stained (with orcein) chromatin body (i.e. a chromocentre) in the nerve cells of female cat which was absent in the male. This chromatin body is called Sex chromatin or Barr body after the name of its discoverer.

⇒ Such Barr body has also been observed in most of the body cells (e.g. skin, oral epithelium and blood cells) of man and other mammals.

⇒ Human females have the Barr body in the nuclei of their body cells in higher proportion than males and are, therefore, referred to as sex chromatin positive. The human males are called sex chromatin negative.

⇒ In the human embryo X chromosome inactivation begins in the late blastocyst stage (roughly 16th day of embryonic life) with germ cell developing inactivation towards the last.

⇒ Barr body formation does not affect the integrity of the chromosomes. The inactivation is completely a consequence of the way the DNA is packaged.

⇒ The X-chromosome is reactivated in meiotic prophase. The small arm of heterochromatic X-chromosome continues to bear active genes throughout.

⇒ In embryo, placental cells show inactivation of paternal X-chromosome. ~~Continues to bear active genes~~ In rest of the body, it is random either paternal or maternal.

⇒ The best known example of nuclear expansion is that of the neutrophil leucocyte of female in which the sex chromatin (Barr body) appears as a small rod called the drumstick (Davidson and Smith 1954).

⇒ Barr body is produced due to partial inactivation of one X-chromosome and development of facultative heterochromatin in it. Any of the two X-chromosomes can become heterochromatic. The other X-chromosome behaves like an autosome and is not heteropycnotic at interphase.

⇒ Later Lyon (1972) confirmed the existence of Barr body in normal females, meta females or superfemales (XXX) or in Klinefelter's male (XXY).

⇒ The inactivation of X-chromosome is a random phenomenon. This fact has been demonstrated in human diseases linked to X-chromosome.

⇒ The Lesch Nyhan Syndrome in which a deficiency of one enzyme of the purine metabolism (i.e. hypoxanthine guanine phosphoribosyl transferase) produces mental retardation and increased uric acid levels results, from a recessive mutation in the X-chromosome.

⇒ Mammalian X-chromosome inactivation is initiated from the X-inactivation centre or Xic, usually found near the centromere. The centre contains 12 genes, 7 of which code for proteins, five for untranslated RNAs, of which only 12 are known to play an active role in the X inactivation process Xist and Tsix.

Sex Linkage or Sex linked Inheritance :-

⇒ Sex linkage or Sex-linked inheritance is the transmission of characters and their determining genes alongwith sex determining genes which are borne on the sex chromosomes and therefore are inherited together from one generation to the next.

⇒ Most Sex-linked genes are located on the X-chromosome, forming X-linkage. A few genes occur on the Y-chromosome, forming Y-linkage. The Y-linked traits are transmitted only through the male, for example gene for Sex determination in mammals.

⇒ The Sex linkage was discovered by Morgan (1910) when he studied the inheritance of red-white eye colour trait (locating genes on chromosomes). Two important sex-linked human diseases are haemophilia and colour blindness.

⇒ Sex linked traits are those traits the determining genes of which are found on the Sex chromosomes.

⇒ Sex limited traits are those traits which are expressed in a particular sex. There are certain autosomal genes which are expressed in one sex, not in the other due to hormonal

differences or anatomical dissimilarities between male and female sexes. Since the expression of such genes are limited to one sex, therefore they are known as sex-limited genes and the traits controlled by them are called sex-limited traits.

⇒ Certain autosomal and sex-linked genes have sex-influenced inheritance. when they come in heterozygous condition they may be expressed in one sex not in other E.g. baldness in man. The gene for baldness behaves as autosomal dominant in males and autosomal recessive in females.

Sex-linkage and the Y-chromosome!→ In case of Drosophila and many other organisms Y chromosome is said to be genetically empty while the X-chromosome carries thousand of genes.

⇒ Besides X-linked trait sometime Y-linked genes are also called sex-linked trait. The Y-linked type sex-linked inheritance is performed by those genes which are localized in non homologous section of Y-chromosome and that no corresponding alleles in X chromosome.

⇒ The Y-linked gene are commonly known as holandric genes Though hypertrichous is the common example of holandric gene but recently certain other holandric genes have been reported in human e.g. genes for H-Y antigen, histo compatibility antigen, spermatogenesis, height (stature) and slower maturation of individual.

⇒ The Y-linked gene of H-Y antigen is located on short arm of Y chromosome, while genes controlling spermatogenesis occur on the long arm of Y chromosome.

⇒ In case of man Y-chromosome controls the differentiation of testis, and influences the male characteristics.

⇒ Some of the diseases which are carried on only from fathers to sons, for example hairy ears, or baldness are supposed to be due to genes present on the Y chromosome. Y chromosome of Drosophila too contain Y-linked gene for male fertility.

Characteristics of sex-linked inheritance:→ These are the following:-

→ It is criss-cross inheritance. Father does not pass the sex-linked allele of a trait to his son. The same is passed to the daughter, from where it reaches the grandson i.e. diagynic inheritance.

⇒ Mother passes the alleles of a sex-linked traits to both sons and daughters.

⇒ Majority of the sex-linked traits are recessive.

⇒ Sex-linked traits are more apparent in males than in females.

⇒ As many sex-linked traits are harmful, males suffer more from sex-linked disorders.

⇒ females generally function as carriers of sex-linked disorders because recessive genes can express themselves in females only in the homozygous state.

⇒ Most of the sex-linked traits are recessive and some of them are dominant also.

⇒ Traits governed by sex-linked recessive genes:→

* Produce disorders in males more often than in females. They express themselves in males even when represented by a single allele because y-chromosome does not carry any corresponding alleles.
* Traits seldom appear in both father and son.
* Traits fails to appear in females unless their father also possesses the same and the mother is carrier.
* Females heterozygous for the trait function as carriers.
* Females homozygous for the recessive trait, tranfer the trait to all the sons.

⇒ Traits governed by sex-linked dominant genes:-

* Produce disorders in females more often than in males.
* All the female offsprings will exhibit them if father possesses the same.
* These traits do not get transmitted to son if mother does not exhibit them.

Criss-Cross inheritance:→

⇒ It is a type of sex-linked inheritance where a parent passes the traits to the grand child of the same sex through off-spring of the opposite sex, that is, father passes the traits to grandson through his daughter (diagynic) while the mother transfers traits to her grand daughter through her son (dia-andric).

⇒ It was first studied by Morgan (1910) in case of eye colour in Drosophila. criss-cross inheritance is applicable to most sex-linked disorders in humans. e.g. green colour blindness, haemophilia.

⇒ Any trait that shows criss-cross inheritance is located on the sex chromosome. Knowledge of criss-cross inheritance is useful in knowing the past, present and future transmission of sex-linked disorders.

⇒ Discovery of criss-cross inheritance proved that genes are located in the chromosomes. Besides criss-cross inheritance sex-linked inheritance can be holandric (from father to Son e.g. hypertrichy, maleness). and hologynic (from mother to daughter).

Non-Disjunction:→

Non-disjunction is an abnormal meiotic division that results in abnormal segregation of chromosomes in the gametes. As a result one gamete may have n+1 chromosomes and other may have n-1 chromosomes.

⇒ Normal chromosome number in the gametes should be n, but sometimes a change in the number of chromosomes occurs due to an error during meiosis.

⇒ Non-disjunction is due to failure of the two X chromosomes to separate during anaphase I of meiosis. As a result one of the eggs gets both the X chromosomes (total chromosom number n+1) while the other egg is without X chromosome (total chromosome n-1).

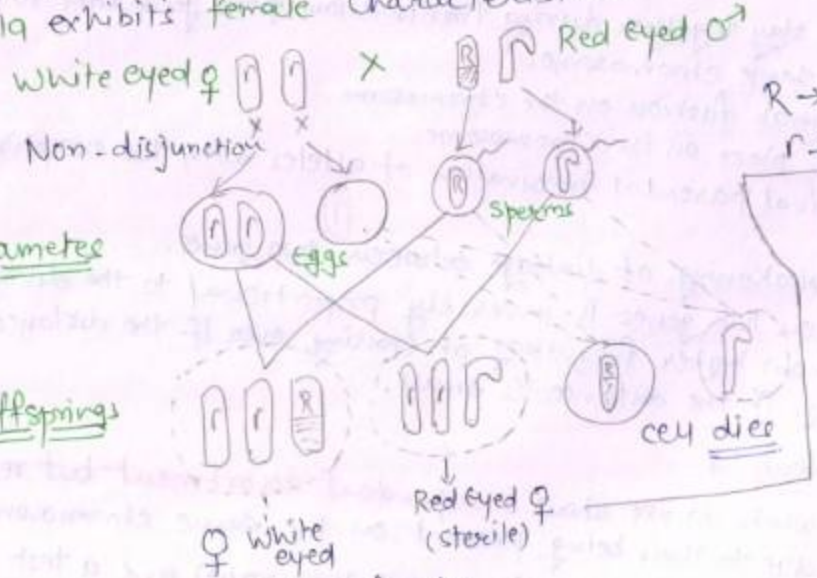
⇒ When both kinds of abnormal eggs are fertilised by normal sperms, four kinds of offsprings would be produced.

⇒ Non-disjunction was observed by Bridges while working on eye colour in Drosophila.

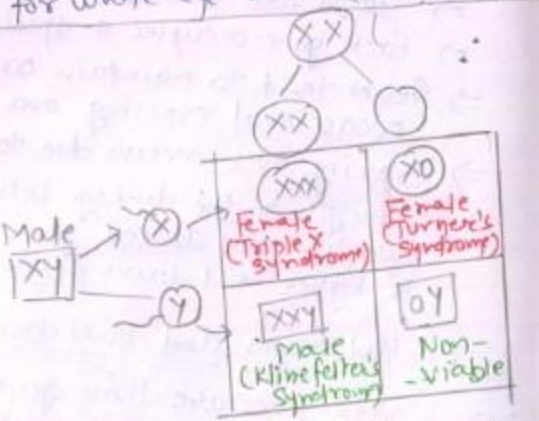
⇒ When he mated white eyed female with red eyed male, the result should have been only red eyed female as one X chromosome from the male was for red colour. To his surprise he found a white eyed female.

⇒ It was due to the presence of two X chromosomes, both containing allele for white colour. It was found due to the fusion of an egg containing XX chromosomes fusing with sperm containing Y chromosome resulting in an XXY offspring.

⇒ This XXY offspring had only white eye allele and so was white eyed. In such a genotype Drosophila exhibits female characteristics.



R → for red eye colour (dominant)
r → for white eye colour (recessive).



⇒ In case of humans, the Klinefelter's syndrome (XXY), triple X syndrome (XXX), and Turner's Syndrome (XO) are the results of non-disjunction.

LINKAGE:→ Linkage is the phenomenon of certain genes staying together and their en block inheritance from generation to generation without any separation or change due to their being present on the same chromosome.

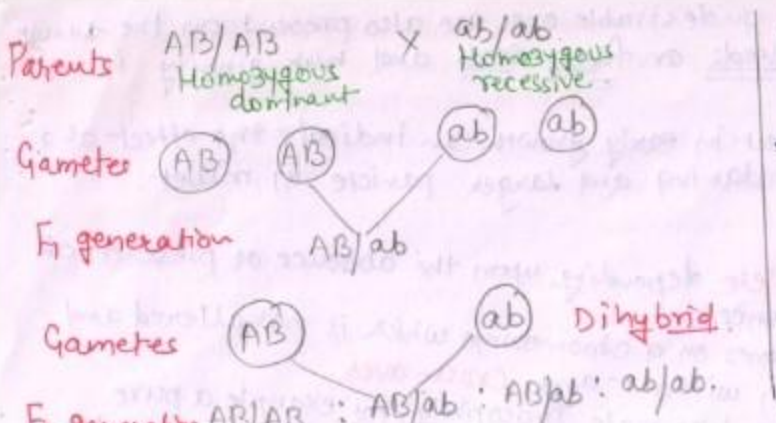
Sutton and Boveri (1902) first of all suggested this phenomenon and Bateson and Punnett (1906) also noted the presence of linkage and absence of independent assortment in a number of characters.

It was T. H. Morgan (1910) who clearly proved and defined linkage on the basis of his breeding experiments in fruitfly Drosophila melanogaster. He also proposed chromosome theory of linkage which states that:-

⇒ Linked genes are genes which stay together during transmission from generation to generation.
⇒ Linked genes occur on the same chromosome.
⇒ Genes are arranged in a linear fashion on the chromosome.
⇒ Each gene occupies a specific place on the chromosome.
⇒ Genes tend to maintain original parental combination of alleles with the exception of an occassional crossing over.
⇒ Crossing over occurs due to weakening of linkage between two genes.
⇒ Strength of the linkage between two genes is inversely proportional to the distance between the two, i.e. two linked genes show higher frequency of crossing over if the distance between them is higher and lower frequency if the distance is small.

Linked Genes and Unlinked Genes:→

⇒ Linked genes are those genes which do not show independent assortment but remain together and are inherited en block due to their being present on the same chromosome.
⇒ Linked genes show a dihybrid ratio of 3:1 (like monohybrid ratio) and a test cross ratio of (1:1) (like monohybrid test cross). Progeny consists of only parental types. Recombination are absent.



Unlinked genes are those genes which occur on different chromosomes and are thus free to undergo independent assortment.

⇒ Dihybrid ratio is 9:3:3:1 while the dihybrid test cross ratio is 1:1:1:1. In both the crosses, 50% are parental types while 50% are recombinants.

Arrangement of linked genes:-

⇒ Two linked genes of a heterozygous individual can have two types of arrangement **cis** and **trans**.

⇒ In **cis-arrangement** dominant alleles of both the genes are present on one chromosome while their recessive alleles occur over its homologous chromosome.

⇒ In **trans-arrangement** a chromosome contains dominant allele of one gene and recessive allele of the other. Reverse arrangement is present over its homologue.

Linkage Group:- All those genes which are located on the single chromosome, constitutes a **linkage group**.

⇒ The number of linkage groups in a species corresponds to its **haploid number of chromosomes**. This principle is known as the **limitation of linkage groups**. For example, there are **four** linkage groups in Drosophila, 23 in man, 7 in sweet pea, 10 in maize. and only 1 in *E. coli*.

⇒ Linkage group has following **importance**:-

⇒ The number of linkage group being equivalent to number of chromosomes proves that genes are present on the chromosome.

⇒ It prevents or reduces the incidence of recombination so that specific varietal or racial characters are retained over the generations.

⇒ It is highly useful for maintaining the good characters of the newly developed variety.

⇒ It is the biggest headache for breeders because it does not allow them to freely bring all the desirable traits in one variety.

⇒ It dilutes the use of desirable traits if ~~under~~ undesirable ones are also present on the same linkage group e.g. low ginning and naked seeds or fuzzy seeds and high ginning in American cotton.

⇒ Marker genes or genes which express their effect in early growth can indicate the effect of a linked gene which is to express late, e.g. wavy leaving and larger panicle in millet.

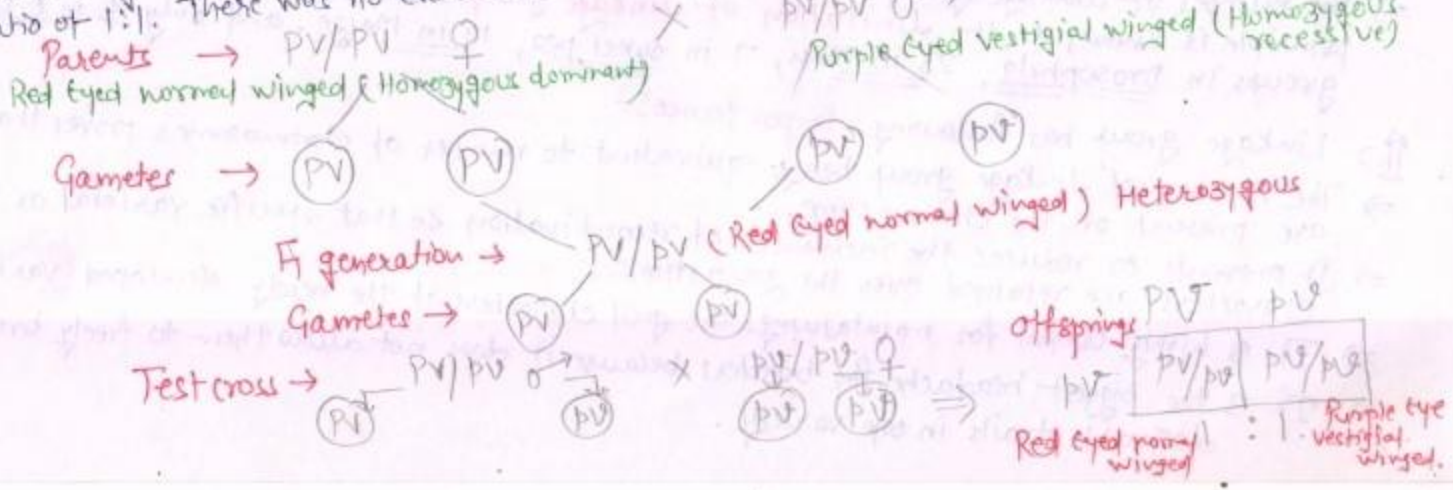
Types of linkage :→

⇒ Linkage has been found to be Complete or Incomplete depending upon the absence or presence of non parental or new combinations of linked genes.

⇒ Complete linkage is a linkage or grouping of genes on a chromosome which is not altered and is inherited as such form generation to generation without any cross-over.

⇒ It is rare but has been reported in certain cases like male Drosophila. For example a pure breeding red eyed and normal winged female Drosophila (PV/PV) is crossed with pure breeding purple eyed and vestigial winged male fly (pv/pv). F1 generation is red eyed and normal winged showing that both the traits are dominant.

⇒ F1 hybrid males are test crossed with purple eyed and vestigial winged females. The offspring were only of two types, red eyed normal winged and purple eyed vestigial winged in the ratio of 1:1. There was no cross over indicating that linkage in male Drosophila was complete.



⇒ **Incomplete linkage** is the phenomenon of an occasional crossing over between two homologous chromosomes so that one or more alleles present in a linkage group are replaced by other alleles.

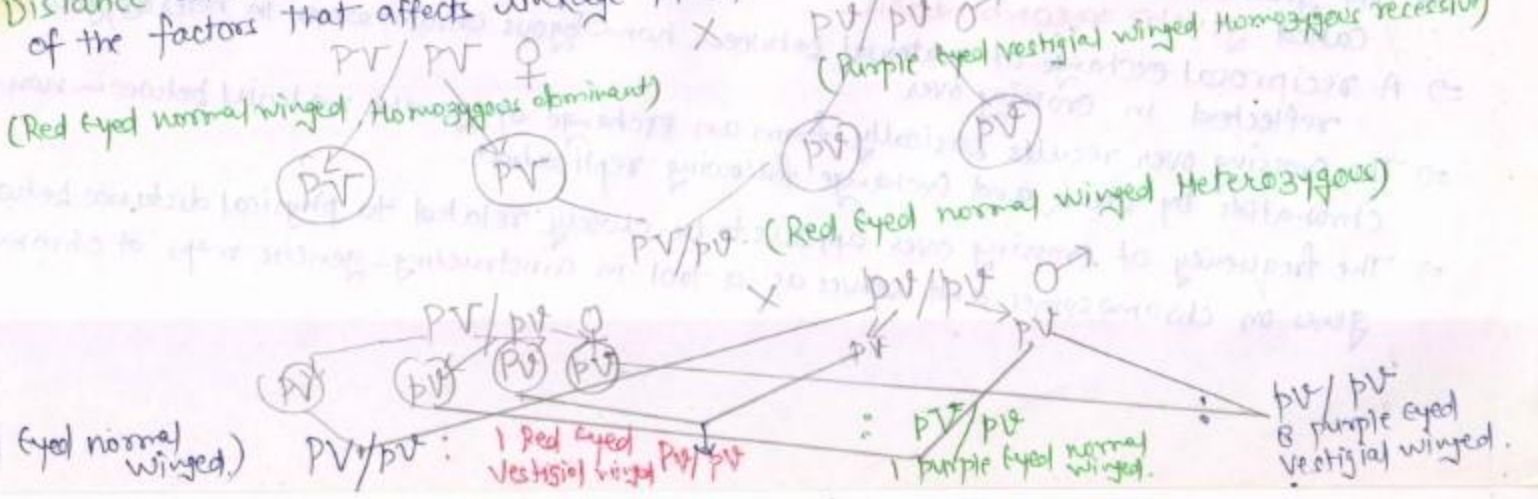
⇒ It produces both parental and recombirant individuals. The percentage of each parental type is more than 25%. while that of each recombirant type is less than 25%., i.e. parental types are more than 50% of population while recombirant types are less than 50%.

⇒ Fore example, homologous pure breeding red eyed normal winged female Drosophila (PV/PV) is crossed to homozygous pure breeding purple eyed eyed and vestigial winged (double recessive) male Drosophila (pv/pv). F_1 flies are hybrid red eyed and normal winged.

⇒ A Female hybrid of F_1 fly (PV/pv) is crossed with double recessive purple eyed and vestigial winged male fly. The ratio comes to be 9:1:1:8 while it should have been 1:1:1:1 in case of independent assortment and 1:1 in case of complete linkage.

→ This shows that the two genes did not segregate independently of each other.

⇒ Distance between two genes, Age and Sex of animals, temperature and X-rays are some of the factors that affects linkage in one or the other way.



CROSSING OVER :→ Janssens (1909) was the first person to discover chiasma formation and related process of crossing over.

⇒ Morgan (1910) found phenomena of linkage and recombination. The recombination or new combination of genes is possible only due to exchange of genetic material between homologous chromosomes. Linkage is incomplete in such cases.

⇒ Crossing over is a recombination of genes due to exchange of ~~genes~~ genetic material between two synapsed homologous chromosomes.

⇒ It is the mutual exchange of segments of genetic materials between non-sister chromatids of two homologous chromosomes, so as to produce recombination of new combinations of genes.

⇒ The non-sister chromatids in which exchange of segments has occured are called recombinants or cross-overs while the other chromatids in which crossing over has not taken place are known as parental chromatids or non-cross overs.

Characteristics of crossing over :→

⇒ Crossing over or recombination occurs at two levels :–

⇒ At gross chromosomal level, called chromosomal crossing over, and at DNA level called genetic recombination.

⇒ A reciprocal exchange of material between homologous chromosomes in heterozygous reflected in crossing over.

⇒ The crossing over results basically from an exchange of genetic material between non-sister chromatids by break and exchange following replication.

⇒ The frequency of crossing over appears to be closely related to physical distance between genes on chromosomes and serves as a tool in constructing genetic maps of chromosomes.

Mechanism of crossing over :→ Chromosomes get replicated in S-phase of interphase. The chromosomes which tend to undergo recombination due to meiotic crossing over necessarily complete two functions :→

(i) 99.7% replication of DNA and 75% Synthesis of Histones both of which take place prior to onset of prophase I and

(ii) attachment of each chromosomes by its both ends (telomeres) to the nuclear envelope (i.e. to nuclear lamina) via the specialized structure called attachment plaques. This event occurs during the leptotene stage of prophase I and though each chromosome at this stage is visually long and thin thread, but contains material of two sister chromatids (i.e. two DNA molecules plus almost duplicated amount of histones).

⇒ Therefore, the leptotene chromosomes are double stranded though the two strands are not visible due to presence of nucleoprotein complex in between the chromatids.

⇒ The process of crossing over comprises four steps :→

(A) **Synapsis :→** Replicated but apparently single homologous chromosomes come to lie side by side with similar gene loci of the two chromosomes exactly opposite. It occurs in the zygotene stage of prophase I. The phenomenon is called Synapsis. The synapsed pairs of homologous chromosomes are called bivalents. The small amount of unreplicated chromosomes (0.3%), if present also undergoes replication. The two homologous chromosomes are held together by a Synaptonemal Complex.

(B) **Tetrad formation :→** The chromatids of each synapsed chromosome slightly separate and become visible in the pachytene stage of prophase I. A group of four homologous chromatids is called a tetrad and the cell proceeds to diplotene stage of prophase I.

(C) **Exchange of chromatids :→** At this time breakage of chromatid segments, exchange of non-sister chromatid segments and later their fusion in new places occur. The Synaptonemal Complex begins to dissolve except in the region of crossing over. The synaptonemal attachment points between the homologous chromosomes are called Chiasmata. The crossing

over thus includes the breaking of chromatid segments, their transposition and fusion.

D) Disjunction :→ After the completion of crossing over, the synaptic forces end and the homologous chromosomes moves apart by shifting chiasmata to the sides. The phenomenon is called terminalization. Many of them disappear before metaphase I.

Types of crossing over :→

⇒ According to the number of chiasma, crossing over may be of following types :-

(A) Single Crossing over :→ Crossing over occurs at one point between two non-sister chromatids so that two cross-over or recombinant chromatids and two parental chromatids are produced.

(B) Double Crossing over :→ Crossing over is found at two points in the same tetrad. It is of two types :→

(i) Reciprocal :→ Crossing over takes place at two points between the same two non-sister chromatids so that two parental and two double recombinant chromatids are produced. Recombinant chromatids have new segments at two places.

(ii) Complementary :→ Here three or all the four chromatids are involved in the double cross-over. If three chromatids are involved, one chromatid remains parental, one recombinant with double crossing over while the remaining two recombinant chromatids have single crossing over. If four chromatids are involved, a parental type is absent.

(C) Multiple crossing over :→ When crossing over takes place at more than two places in the same chromosomes pair then such crossing over is known as multiple crossing over.

⇒ There are three (triple), four (quadruple) or many (multiple) points at which crossing over is found in the same tetrad.

⇒ According to the occurrence it may be :→

(A) Somatic :→ or mitotic crossing over :→ It is rare but can occur between homologous chromosomes even without meiosis. It produces chromosomes with unequal chromatids. Somatic or mitotic crossing over occurs at a four strand stage and during this process there occurs pairing of chromosomes.

(5) **Germinal or meiotic crossing over:→** Usually the crossing over occurs in germinal cells during the gametogenesis in which the meiotic cell division takes place. This type of crossing over is known as germinal or meiotic crossing over. The meiotic crossing over is universal in its occurrence and is of great genetic significance.

Factors influencing crossing over:→ Crossing over occurs when linkage becomes weak. The factors affecting linkage also influence crossing over, though in reverse. Some of the factors influencing crossing over are:→

(i) Increases in distance between two genes increases the frequency of crossing over. Close-ness of the genes reduces the chances of crossing over.
(ii) Drastic changes in temperature increase the frequency of crossing over.
(iii) X-rays bring about crossing over even in male Drosophila which normally shows perfect linkage.
(iv) There is decrease in frequency of crossing overe with increase in age.
(v) Sex with heteromorphic sex chromosomes has lesser number of cross-overs, e.g. male Drosophila.
(vi) The genes present near heterochromatic areas have reduced rate of crossing over.
(vii) Most Mutagens affect crossing over even in very dilute concentration. Ca^{2+}, Mg^{2+} and other metallic ions also affect frequency of crossing over.
(viii) Interference i.e. occurrence of one cross-over reduces the chances of another cross - over nearby.

**** Significance of crossing over:→** Crossing over is a wide-spread phenomenon among living organisms occurring in practically all higher plants and animals and has a great significance in genetics.

⇒ It brings new combination of genes which are different from parents thus introducing variations. The variations are helpful in struggle for existence and adaptability to changes in environment.

⇒ Variation form a platform for natural selection to act.
⇒ It is established that genes occur in a linear fashion over the chromosomes.
⇒ The phenomenon has helped in understanding the effect of different genes over themselves as wey as over the organism.
⇒ The rarity or abundance of a particular combination of genes is known from frequency of crossing over.
⇒ Useful recombinations are picked up by breeders for development of improved varieties.
⇒ The frequency of crossing over is used for building linkage maps or chromosome maps.

Genetic Variations :- Genetic mapping is highly important in studying the architecture of the chromosomes and the architecture of entire genome. Its maximum importance is in genetic engineering and gene therapy.

⇒ The phenotype of an individual is determined by its genotype. Except identical twins, genotypes of any two human beings are never identical.
⇒ In contrast the asexually reproducing organisms hardly show any variations and even if they do so it is clear it must be due to the environmental changes since their genetic make up is same in all sexually reproducing organisms.
⇒ The genetic variations exist due to reshuffling of genes caused by recombinations or by mutations.

Recombination :- The recombinations are produced by the routine reshuffling of genes during following processes :-

(i) Independent assortment of chromosomes :- During gamete formation in the metaphase I of meiosis, homologous chromosomes come together in pairs and then segregate into daughter cells independent of each other.
⇒ It is their random alignment on the equatorial plate which gives rise to large number of possibilities. for example if only 2 pairs of chromosomes are present, possible recombination are $2^2 = 4$ i.e. 4 kinds of gametes would be formed. Similarly 3 pairs of chromosomes means $2^3 = 8$ types of gametes. Man has 23 pairs of chromosomes, hence the number of possible combinations are 2^{23} = about 8·6 million.

(ii) Reciprocal crossing ~~ete~~ of genes during crossing over :→ During crossing over chromatids of homologous chromosomes break and recombine and produce new linkage groups, As a result new genetic varieties or recombinants are produced.

(iii) Random fertilization of gametes :→ The fusion of a male gamete and female gamete occurs by random fertilization.

⇒ As stated above there are 8·6 million kinds of gametes possible. It means 8·6 million kind of sperms and the same number of egg. By random fusion $(8{\cdot}6 \times 10^6) \times (8{\cdot}6 \times 10^6) = 74 \times 10^{12}$ kinds of zygotes are possible. This number is much more than the total human population on earth.

MUTATION :→ Mutation is the sudden inheritable discontinuous variation which appears in an organism due to permanent changes in their genotypes.

⇒ The term mutation was coined by ~~H~~ Hugo de Vries (1901). Darwin called these ~~mutiny~~ mutation as 'sports'.

⇒ First scientific study of mutation was made by T. H. Morgan (1910 in Drosophila). The micro-organism which have been used since last 25 years for studies of mutation are Neurospora (red mould), E. Coli and bacteriophages.

⇒ Range of mutations is from very small to large e.g. in Neurospora there is no structural change and only modification of nutritional requirement occurs, whereas in ancon sheep, mutation is large.

⇒ Mutation can occur at any stage during the development e.g. before formation of gametes → all the organisms resulting from these gametes will be affected; in gametes or zygote – only one organism will be affected and in zygote, when it has undergone some divisions, only organs will be affected.

⇒ Mutation is permanent change in the DNA molecule of an organism that occurs randomly and spontaneously. Mutation are heritable changes, that is, if they appear in somatic cells they are inherited to daughter cells by mitosis but if they appear in gamete cells they are inherited to the offsprings.

⇒ The former are known as somatic mutations and latter as germ mutations. They bring about a change in the genetic message.

⇒ Mutation generally result in a loss of a function for e.g. normal flower colour is purple, mutant form may result in colourless or white flowers.

Chromosomal mutations :→

(I) **Chromosomal mutations due to structural changes :-** The structural changes may occur during prophase I of meiosis when the homologous chromosomes undergo crossing over.

⇒ The sequence of genes may be altered and genes in new locations may cause alteration of the expression. These are also called **chromosomal aberrations**. They are categorised in two main kinds :- intrachromosomal and interchromosomal.

(A) **Intrachromosomal aberrations :-** (In a single chromosome) may occur by following means :→

(i) **Deficiency :→** It is the loss of a terminal segment of a chromosome and is produced by a single break in the chromosome. e.g. abd / abcd (segment c is missing).

(ii) **Deletion :→** It is the loss of an intercalary segment of a chromosome which is produced by a double break in the chromosomes followed by the union of remaining parts, e.g. abcfgh / abcdefgh (segment de missing).

⇒ Deficiency or deletion in a single chromosome can be known during synapsis of homologous chromosomes when certain segment of one chromosome remains unpaired or forms a loop. Notched wing margin in Drosophila is formed by deletion of a segment in X-chromosome.

(iii) **Inversion :→** It is a type of chromosome aberration in which part of chromosome segment gets inverted by 180°. For example, chromosome abcde develops inversion in the part cde to form abedc.

Inversion involving centromere is called pericentric. Inversion occuring beyond a centromere is termed as paracentric.

⇒ Inversion inhibits the chromosomal synapsis in the region of change.

(3) Inter-Chromosomal aberration (between two chromosomes) :→

(i) Duplication :→ It is the phenomenon of having an extra chromosome segment attached to its normal homologous chromosome so that a gene or set of genes is represented twice in the same chromosome e.g. abcdcdefgh / abcdefgh (segment cd duplicated). Sometimes duplication of a gene has a deleterious affect.
For example, in Drosophila when the B gene for normal eye located on X-chromosome becomes duplicate, the eyes become smaller (Bar Eye).

(ii) Translocation :→ It is the separation of a chromosome segment and its union to a non-homologous chromosome. Translocation is of two types :→

(a) Simple translocation :→ one chromosome shows deletion or deficiency while a non-homologous comes to have an additional segment.

(b) Reciprocal translocation :→ Two non-homologous chromosomes exchange segments between themselves to create new linkage groups in both the chromosomes.

Reciprocal translocation is also called illegitimate crossing over.

Chromosomal mutations due to change in number (Genomic mutation) :→

⇒ Mutations are also caused by the variation in chromosome number which is of two types :-
(A) Euploidy and (B) Aneuploidy.

(A) Euploidy :→ In euploidy there is a variation of entire sets of chromosomes. Variations from the normal diploid number (2n) may either be monoploids (haploids) or polyploids (3n, 4n, 5n, 6n, etc.)

(i) Monoploidy (Haploidy) :→ A haploid organism contains only one set of chromosomes, and is said to be hemizygous. Each chromosome is represented only once.
Haploidy may be normal in particular species, or may arise as an abnormality.

(ii) Polyploidy :→ Polyploidy is due to increase in the entire haploid sets of chromosomes. When there are three sets of haploid numbers or 3n condition it is called a triploid, when 4 sets or 4n it is called tetraploid and so on. Polyploidy is rare in

animals but common in plants where it is associated with increased size, greater hardness and increased resistance to diseases.

⇒ Polyploidy is of three types:- (i) autopolyploidy (ii) allopolyploidy (iii) autoallopolyploidy.

(i) Autopolyploidy :- It is a type of polyploidy in which there is a numerical increase of the same genome e.g. autotriploid (AAA), autotetraploid (AAAA). some of the crop and garden plants are autopolyploide. e.g. maize, rice, gram, Autopolyploidy induces gigas effect.

Natural autopolyploids are found in apple, banana, doob grass (Cynodon dactylon), grapes, tomato, watermelons, oenothera, maize etc.

⇒ Polyploidy can be induced artificially by colchicine treatment in 0.01 - 0.5% concentration. colchicine is a alkaloid obtained from seeds and corms of Colchicum autumnale a plant belonging to family Liliaceae (first obtained by Houde, 1807 and was first used for inducing polyploidy by Dustin 1934).

⇒ Colchicine has no effect on its parent plant (Colchicum) because of presence of anticolchicine in it.

(ii) Allopolyploidy :- It has developed through hybridization between two species followed by doubling of chromosomes (e.g. AABB). Allotetraploid is the common types, Allo polyploids function as new species e.g. Wheat, American cotton, Nicotiana tabaccum.

Parents — AA (Species A) × BB (Species B)

Gametes → A B

F1 hybrid → AB

Colchicine treatment | Doubling of chromosome no.

AABB (Allotetraploid)

:- Raphanobrassica :- This allopolyploid was produced by G.D. Karpechenko (1927) by doubling the chromosome no. of F1 hybrid produced by crossing radish (Raphanus sativus) and cabbage (Brassica oleracea). This cross was made to produce a new plant with roots like radish and upper portion like cabbage. i.e.

Raphanus sativus (2n=18) 18R × Brassica oleracea (2n=18) 18B

9R 9B

9R+9B → Doubling of chromosome no.

Raphanobrassica → 18R + 18B (allotetraploid)

2n = 36.

(iii) Autoallopolyploidy :→ It is a type of allopolyploidy in which one genome is in more than diploid state. Commonly autoallopolyploids are hexaploids (AAAABB)

e.g. Helianthus tuberosus.

(13) Aneuploidy :→ Aneuploidy is a condition that arises due to abnormal number of chromosomes in the zygote. It is a condition of having fewer or extra chromosomes than the normal genome number of the species.

⇒ The organisms showing aneuploidy are known as aneuploids or heteroploids. They are denoted by the number of affected chromosomes with the suffix — somic, e.g. nullisomic, monosomic, trisomic etc.

⇒ The errors occur during meiosis when non-disjunction results in half of the gametes containing n+1 chromosomes and half n-1 chromosomes.

⇒ During fertilization with normal gamete, the n+1 gamete will result in zygote with a 2n+1, condition where a particular chromosome is present in three copies called trisomy. Down's syndrome in human is due to trisomy of 21st chromosome.

⇒ The n-1 gamete on fertilization with normal gamete will produce a zygote with 2n-1 condition where a particular chromosome will be present in a single copy called monosomy.

⇒ Aneuploidy is of two types :- hyperploidy (or addition of chromosomes) and hypoploidy (or loss of chromosome).

Hyperploidy are of following types :→

(i) Trisomic (2n+1) :- It has one chromosome in triplicate. Double trisomic has two different chromosomes in triplicate (2n+1+1). Trisomics show a number of changes some of which are lethal. Down's Syndrom is trisomic in origin where chromosome number 21 is triplicate. Patau's Syndrom is trisomy of 13th chromosome. Kline felter's Syndrom has an extra X-chromosome

(ii) Tetrasomic (2n+2) :- It is aneuploid having one chromosome represented four times. Tetrasomics show more variability than trisomics. Both trisomics and tetrasomics are believed to have given rise to new hypoploid species through secondary polyploidy e.g. apple, pear

(iii) Pentasomic :→ A hyperploid with one chromosome represented five times (2n+3). e.g. a rare super female in human beings (44 + XXXXX)

Hypoploidy are of following types :→

(i) Monosomic (2n-1) :→ It is an aneuploid in which one chromosome is devoid of its homologue. Monosomic is generally weaker than the normal form. Turner's Syndrome is a sex monosomic in human being (44 + X).

(ii) Nullisomic (2n-2) :→ The aneuploid is deficient in a complete pair of homologous chromosomes. Nullisomics do not survive except amongst poly ploids.

Mixed aneuploids :- They are aneuploids with both hypoploidy and hyperploidy e.g. 2n+1A-1B

Gene Mutations (Point mutations) :→

⇒ The sudden stable change in the structure of gene or cistron due to change in nucleotide type or nucleotide sequence is called gene mutation. The first scientific study of gene mutations started with the discovery of white eye trait in Drosophila by Morgan in 1910.

⇒ Mutations can occur in somatic or germinal cells. They may be lethal, harmful, neutral or advantageous. Most of the mutations are recessive and involves loss of functions. A few are dominant ones.

⇒ Gene mutations may occur naturally and automatically due to internal reasons. They are termed as spontaneous mutations. Others are produced by external factors or chemicals. They are known as induced mutations.

Types of mutations :→

⇒ Mutation from wild to new type is forward mutation and mutated gene to its wild form is reverse or back mutation.

⇒ Mutation which affects vegetative cells are called Somatic mutation and those that affect germinal cells are called germinal mutation.

⇒ Somatic mutation are not inheritable while germinal mutation inheritable.

⇒ Recessive mutation show their effect after many generation when they become homozygous.

⇒ Pleiotrophic mutation is the result of single mutation changing more than one character.

⇒ The gene mutation which involve more than one base pairs or entire gene are called gross mutation.

⇒ The smallest part of gene that can mutate is called muton. The smallest muton in a gene is a single base pair of DNA.

⇒ In morphological mutations change occurs in external form like - shape, size and colour etc. e.g. Albino ascospores in Neurospora, Kernel colour in corn, curly wings in Drosophila and dwarfism in pea.

⇒ Lethal mutations involves genotypic changes leading to death of an individual.

⇒ Biochemical mutations are identified by a deficiency, so that the defect can be overcome by supplying the nutrient or any other chemical compound.

⇒ Resistant mutations are those which are identified by their ability to grow in the presence of an antibiotic (e.g. streptomycin, ampicillin, Cycloheximide) or a pathogen.

⇒ Conditional mutation are those which allow the mutant phenotype (include lethality) to be expressed only under certain condition (e.g. high temperature) called restrictive condition.

⇒ Spontaneous mutations :- They are mutations which occur randomly, naturally and automatically due to internal reasons without any relation to any external factor. Rate of spontaneous mutations varies from 1 in 2000 to 1 in several million divisions. The possible reasons are :-

(i) Background radiations :- They occur naturally from various sources. e.g. sun, radioactive minerals.

(ii) Tautomers :- All the four nitrogen bases also occur in their tautomeric or isomeric states, forming either imino group (-NH, e.g. cytosine, adenine) instead of amino group ($-NH_2$) or enol group (-COH, e.g. thymine, guanine) instead of keto group (=CO). Tautomers pair with different bases so as to cause a change in the sequence like AT to CG.

(iii) Deamination of cytosine :- Cytosine slowly deaminates to produce uracil which pairs with adenine resulting in change in base pairing.

iv) Copy error :→ There are a number of steps involved in replication, transcription and translation. Any wrong choice or entry of different group will cause mutation. Most of the copy errors are corrected during proof reading but a few do escape correction.

Induced mutations :→ They are mutations that are produced in response to specific factors and chemicals. Muller (1927) was the first to produce induced mutations in Drosophila by exposing them to X-rays. The specific factors and chemicals of the environment that induce mutations are called mutagens.

Mechanisms of gene mutations :→ Gene mutations occur by three methods :- inversion, substitution (of two types - transition and transversion) and frameshift (of two types - insertion and deletion).

Inversion :→ A distortion of DNA by mutagen can change the base sequence of a cistron in the reverse order. The process is called inversion. The new sequence naturally have different codons.

Substitution (Replacement) :→ This type of mutation involves the substitution of N-base (nitrogen base) of DNA either by another N-base or by some derivative of the N-base changing the genetic code.

-) The altered codon may code for a different amino acid thus producing a protein molecule with a substituted amino acid.

=) The substitution mutations may involve the replacement of a purine in a DNA strand with the other purine and the replacement of a pyrimidine in the complementary strand with the other pyrimidine i.e. a transition.

=) or it may involve the substitution of a purine for a pyrimidine and vice versa i.e. a transversion.

Frame-shift mutation :→ They are those mutations in which the reading of the frame of base sequence shifts laterally either in the forward direction due to insertion (addition) of one or more nucleotides or in the backward direction due to deletion of one or more nucleotide.

The genetic disease muscular dystrophy is caused by frame-shift mutation which leads