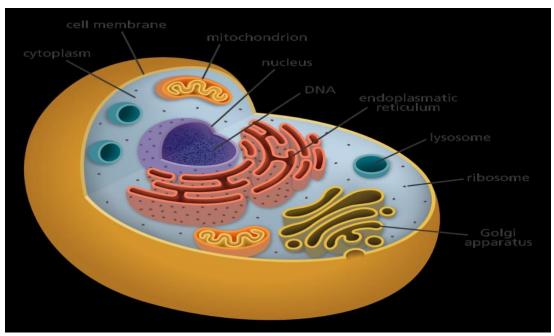
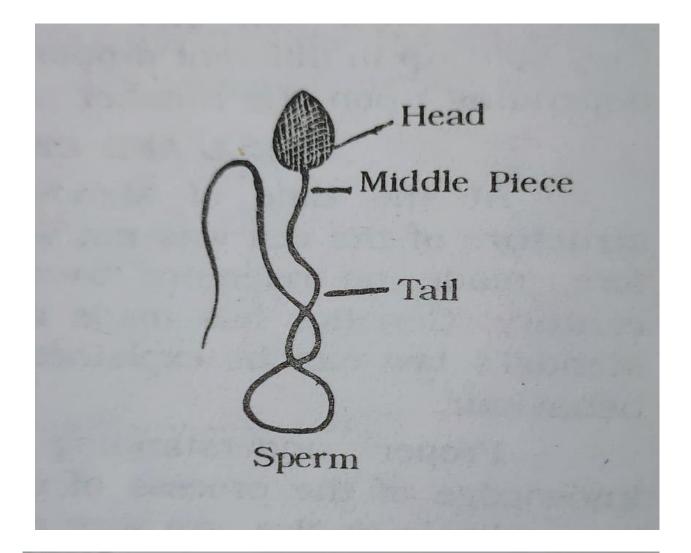
The **cell** (from <u>Latin</u> *cella*, meaning "small room") is the basic structural, functional, and biological unit of all known organisms. A cell is the smallest unit of life. Cells are often called the "building blocks of life". The study of cells is called <u>cell biology</u>, cellular biology, or cytology.

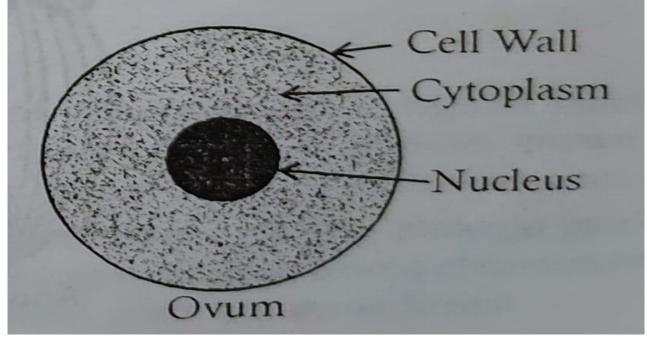


Cell Structure: The wall that surrounds each cell is termed as the cell wall. Inside the cell lies a semifluid, jellylike, hyaline substance protoplasm which is made up of complex chemical substances. Protoplasm is said to be the "material basis of life". The cytoplasm and the nucleus are two important parts of the cell protoplasm. The cytoplasm consists of various substances. The nucleus is somewhat denser than the rest of the cell, it is spherical in shape, and surrounded by a thin membrane, called the nuclear membrane. The nuclear cavity is filled up by a dense, clear protoplasmic substance, known as the nucleoplasm. Numerous fine, thread-like structures, known as the nuclear reticulum or chromatic network, are seen suspending in the nucleoplasm. The threads are readily stainable, and are made up of a substance known as chromatin. Besides these, a very minute body much denser than the nucleoplasm, is seen to occur in nucleus. This is called nucleolus.

Types of Human Cell: Human cell is mainly divided in to two types that is Somatic or body cell and Germ or reproductive cell. Somatic cells comprise of muscle cells, nerve cells and others. Germ cells comprise of male sex cell (sperm) and female sex cell (ovum).

Human sperm: In its immature stage a human sperm resembles a typical cell consisting of a nucleus and a mass of cytoplasm. But a mature human sperm, instead of being spherical, is long and thread-like with an enlarged head formed by the nucleus, a long slender tail and a conical middle piece.



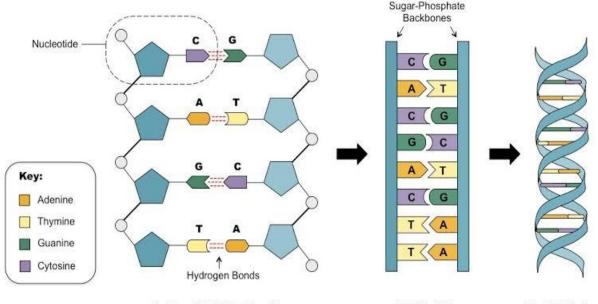


Human Ovum or Egg : The human egg or ovum is spherical cell and about 1/7 of a millimetre (or about 1/175 of an inch) in diameter. Though the egg is small, but it is the largest cell of the human body. The egg contains large amount of nutrient substances, commonly known as yolk material.

Fertilization : Fertilization is the union of a sperm cell and an ovum. After the egg and the sperm have fused, the head and the middle piece of the sperm sink into the egg, while the tail is left outside. The head of the sperm assumes the appearance of a normal nucleus by absorbing fluid from the cytoplasm of the ovum. The two nuclei then approach one another and finally fuse. Thus nuclear fusion completes the process of fertilization.

DNA STRUCTURE

DNA (Deoxyribonucleic acid) is a molecule composed of two polynucleotide chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth and reproduction of all known organisms. DNA is a large compound made of three smaller molecules bounded together. The basic unit of each of these three molecules is called a nucleotide. The three kinds of molecules are : sugar, phosphate and organic base or nitrogenous base. This specific sugar is known as deoxyribose. This sugar contains only five carbon atoms as against six in common glucose. This is one of the main differences between these two kinds of sugar. All the nucleotides of a DNA are identical in respect of their phosphate group (phosphoric acid) and sugar contents, but they differ in their organic base, the molecular compounds of which are made of varying amounts of oxygen, hydrogen, nitrogen and carbon. The organic base can be of two main categories, purine base and pyrimidine base. The two kinds of purine bases are adenine (A) and guanine (G); and the pyrimidine bases are cytosine (C) and thymine (T).



Antiparallel DNA Strands

DNA Ladder

Double Helix

Watson – Crick Model of DNA : At present molecular biology is regarded as a separate discipline. It may be said that the beginning of this new discipline was made by James D. Watson and Francis Crick, when they announced their model of DNA, known as Watson – Crick Model. According to them a DNA molecule is composed of two long chains or strands. Each chain contains thousands and thousands of nucleotides linked together. In each chain the phosphate group is linked to one sugar molecule and the base of each nucleotide (a purine or a pyrimidine) is linked to a sugar, not to a phosphate. Through the phosphate group each nucleotide is attached to its neighbour in the chain. Since one chain is composed of one nucleotide after another attached through the sugar and

phosphate components, a DNA chain may be called a polynucleotide. The two complementary polynucleotide chains are twisted around each other in a helical or spiral form. The bases of the two chains are always bound together in a specific way. Adenine (A) always pairs with thymine (T) and the other purine base guanine (G) always pairs with the other pyrimidine base cytosine (C). Thus, the sequence of nucleotides in one determines the sequence of nucleotides in the other, and hence the two chains of each DNA molecule must be complementary.

The Watson – Crick model and the genetic components of DNA clearly imply that each gene is a segment of DNA along the molecule.

DNA Replication

DNA Replication can be defined as "formation of new DNA molecules from the parent DNA which are exactly similar to it (*i.e. its replica*).

Mechanism of DNA Replication:

Watson and Crick suggested a very simple mechanism of DNA Replication based on their double stranded helical model of DNA. It was described by them as **Semi Conservative** Replication of DNA. The mechanism of DNA replication is very complex. It took several years to understand the actual mechanism of formation of new daughter DNA molecules from the parent DNA even after the semi conservative mode of replication of DNA was experimentally demonstrated by Messelson and Stahl.

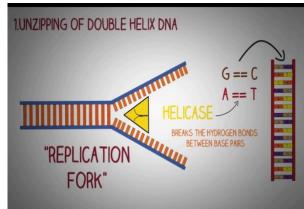
DNA replication involves series of enzymes and other protein factors. The whole process can be explained by the following steps –

- 1. Activation of deoxyribonucleotides : The raw materials for DNA synthesis remain floating in the nucleoplasm in the form of 4 nucleotides viz. AMP, GMP, CMP and TMP. These are activated by ATP to form deoxyribonucleotide triphosphates called ATP, GTP, CTP and TTP.
- 2. **Recognition of Initiation Point :** Replication of DNA begins at a particular point on DNA called **initiation point.** Specific **initiator protein** is required to recognize the initiation

point in DNA. In eukaryotes there may be several points of origin. The initiator protein along with the DNA directed RNApolymerase initiates the synthesis of RNA primer (a short segment of RNA formed at DNA template) for the formation of new DNA strand.

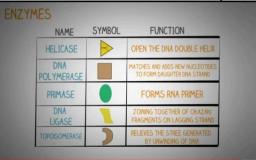
3. Unwinding or unzipping of DNA molecule : The two strands of DNA

separate in presence of enzymes called as **helicase.** It involves the breakage of the weak hydrogen bonds present between the nitrogenous bases of the polynucleotide strands of



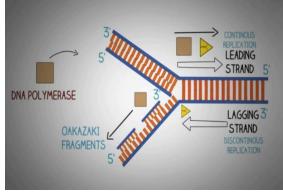
DNA. The energy required for the process is derived from ATP molecule. The enzyme

topoisomerase, cut and reseal one strand of DNA thus helping in separation of interwined strand of long DNA molecule. It is like separating two interwined ropes by pulling them apart with force. But when the force is released, the two ropes come together and automatically interwine



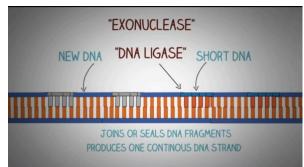
with each other. At the same time, if a partially separated strand is cut, the tension is relieved and the two strands will not come back together.

- 4. **Formation of RNA primer :** Primer is a short RNA segment that is formed on the DNA template before replication begins. The enzyme which polymerises RNA building blocks (A,G,C,U) into a primer is known as **primase.** Without a primer, new DNA strand formation is not possible.
- 5. Synthesis of New DNA strand : In this step, the building blocks nucleotides available in the nucleoplasm are added to the primer in a definite sequence as directed by the DNA template. It is possible in presence of an enzyme called DNA polymerase. When the double stranded DNA is unwind up to a point,



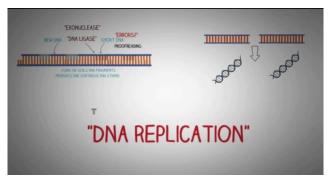
it will give rise to a Y shaped structure referred to as **replication fork.** The replication proceeds from 5' - 3' direction only in the new DNA strand. The two strands of DNA are in opposite direction i.e. they are anti-parallel (one is in 5' - 3' direction while the other is in 3' - 5' direction). Hence, DNA polymerase produces continuous stretch in one of the two strands only. This is called **leading strand.** In the other strand of DNA, DNA

polymerase produces short section of DNA molecules. These short segments are called **Okazaki fragments** and the strand is called **lagging strand.** Later, these short strands are joined by another enzyme called **DNA ligase.**



6. Proof reading and DNA repair : The base pairing in DNA is highly specific i.e, cytosine

always pairs with **guanine** and **adenine** pair with **thymine.** Somehow, it is possible that wrong entries of bases may be introduced as a rare occurrence at a frequency of one in 10,000. These wrong entries are removed by **DNA polymerase** in bacterial cells. Thus,



DNA polymerase can do proof reading. These repairs enzymes, cut off the wrong segment of DNA and introduce and join the normal correct segment.

Helicase : An enzyme that helps in breaking the weak hydrogen bonds between two strands of DNA. (Unzipping the DNA double helix structure).

Topoisomerase : An enzyme that can break and reseal one strand of DNA.

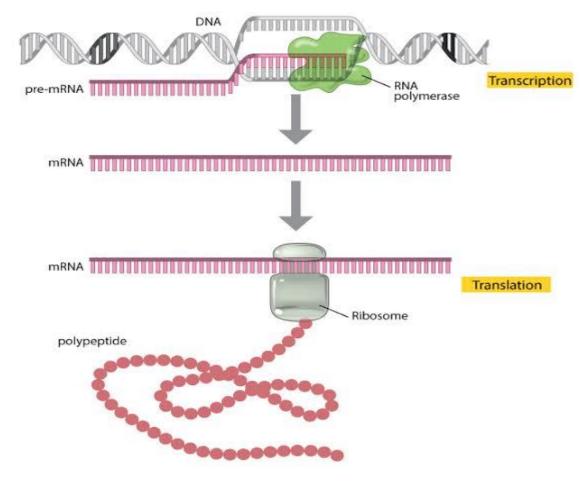
DNA polymerase : "The builder" – this enzyme replicates DNA molecules that actually build a new strand of DNA.

Primase : An enzyme that helps in the formation of a **primer.** "The initializer" – primase makes the primers of that DNA polymerase can figure out where to go to start the work. Primers are actually made of RNA.

DNA ligase : An enzyme that can join the short segments of newly synthesized polynucleotide chain. (Gluer).

Protein Synthesis:

Protein synthesis consists of two processes — <u>transcription</u> and translation. In eukaryotic <u>cells</u>, transcription takes place in the <u>nucleus</u>. During transcription, <u>DNA</u> is used as a template to make a molecule of messenger <u>RNA</u> (mRNA). The molecule of mRNA then leaves the nucleus and goes to a <u>ribosome</u> in the cytoplasm, where translation occurs. During translation, the <u>genetic code</u> in mRNA is read and used to make a <u>protein</u>. These two processes are summed up by the <u>central</u> <u>dogma</u> of molecular biology: <u>DNA</u> \rightarrow **RNA** \rightarrow <u>**Protein**</u>.



Transcription

Transcription is the first part of the <u>central dogma</u> of molecular biology: $\underline{DNA} \rightarrow \underline{RNA}$. It is the transfer of genetic instructions in DNA to mRNA. During transcription, a strand of mRNA is made to complement a strand of DNA.

Transcription takes place in three steps: initiation, elongation, and termination. The steps are illustrated in the figure <u>below</u>.

- 1. **Initiation** is the beginning of transcription. It occurs when the <u>enzyme RNA</u> polymerase binds to a region of a gene called the **promoter**. This signals the DNA to unwind so the <u>enzyme</u> can "read" the bases in one of the DNA strands. The enzyme is ready to make a strand of mRNA with a complementary sequence of bases.
- 2. Elongation is the addition of nucleotides to the mRNA strand.
- 3. **Termination** is the ending of transcription. The mRNA strand is complete, and it detaches from DNA.

Translation

The process by which the genetic information present in the mRNA molecule is converted into protein with specific amino acid sequence, taking help of tRNA molecules in ribosomes is known as translation.

Once the mRNA is released from the DNA, it travels out of the cell nucleus and into the body of the cell. There it attaches to a structure in the cell called a *ribosome*, which uses the information on the mRNA to make proteins. The ribosome essentially "reads" the chemical bases on the mRNA in commands that tell the ribosome the specific amino acids to join together to form a protein. For example, the mRNA sequence adenine, adenine, guanine (AAG) tells the ribosome to place the amino acid *lysine* in that location, whereas the sequence adenine, adenine, cytosine (AAC) calls for amino acid *lysine*. There are also mRNA commands that tell the ribosome when to begin and when to stop constructing a protein. Thus, the DNA code copied into mRNA provides all the information necessary for ribosomes to build the proteins that make up the structures of organisms and drive the processes of life.

Gene

The basic unit of inheritance is commonly known as gene. A part of DNA molecule that directs synthesis of a polypeptide chain or RNA molecule. It consists of many codons. Though the concept of gene was first used by Johannsen in 1909. Earlier it was referred to as Mendelian factor or determinor. The concept of gene was later on developed by other scholars like Morgan (1913), Bridges (1923), Muller (1913). The word Gene has been derived from a Greek word gennom, means to produce.

Genes are located in the chromosomes, where these are arranged in a single linear order. Genes are ordinarily transmitted from one generation to the next one. Genes determine the biological characteristics in a living system. Each gene has a specific position in a specific chromosome. This position is called locus. However, the positions may be changed because of various reasons. Genes are capable of duplicating themselves. Duplication takes place very accurately. This phenomenon is called replication. Mutation, a spontaneous change in the composition of a Gene, may produce mutant gene. The expression of the mutant gene will be different from that of the original gene. Gene of one chromosome may move to another chromosome by crossing over or by translocation. An allele is an alternative form of a gene has a specific locus. These forms are said to be alleles. When three or more gene forms are associated with a specific locus, the phenomenon is called multiple allelism.

From the second half of the present century remarkable changes have occurred in the concept of gene. Many discoveries have been made in the field of molecular biology. Now gene is not regarded as a single entity as the basic unit of inheritance, but is defined as a segment of DNA molecule. It is the carrier of coded information connected with a specific function. There are three kinds of genetic units in the segment. These are : cistron, recon and muton. The cistron is the functional unit. The recon is that smallest unit of DNA which recombined during crossing over. The muton is the smallest unit of genetic material that mutates. Thus, genes can be recognized for function, recombination and mutation.

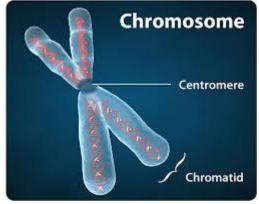
Chromosome

In 1988, W.Waldare coined the term chromosome. In 1902, Walter S. Sutton and T. Boveri proposed the "chromosome theory of heredity". Sutton claimed that the newly discovered Mendel's hereditary factors were physically located on chromosomes.

A chromosome is a long DNA molecule with part or all of the genetic material of an organism. In eukaryotes, Chromosomes reside in the nucleus. An interphase nucleus has chromosomes in coiled and extended portions. Coiled portion stains darker and appears in clumps, called *heterochromatin* while the extended portion is pale staining and it forms *euchromatin*. The chief constituent of

chromatin is deoxyribonucleic acid.

Chromosome number in a particular species is fixed. The human chromosome complement consists of 46 chromosomes (23 pairs). This number 46 is called *diploid*, often designated as 2n. An *haploid* number 'n' is 23 and it is encountered only in gametes. Of the total 46, 44 are autosomes (in 22 pairs) and 2 are sex



chromosomes. The latter in females are XX, and in males X and Y. In females, of the two X chromosomes, one is rendered inactive to form Barr body.

The word chromosome is derived as follows: *Chroma* means colour, and *soma* means body. As they appear like coloured (stained) rod-shaped structures, they are called chromosomes. Each chromosome (in metaphase) consists of two *chromatids* joined together at centromere. Depending upon the placement of centromere, chromosomes are classified into various types. Chromosomes have small units of heredity, called *genes* which have specific positions on the chromosome. This is called gene *locus*. Chromosomes are usually studied in *metaphase of mitosis*.

Classification of Chromosomes:

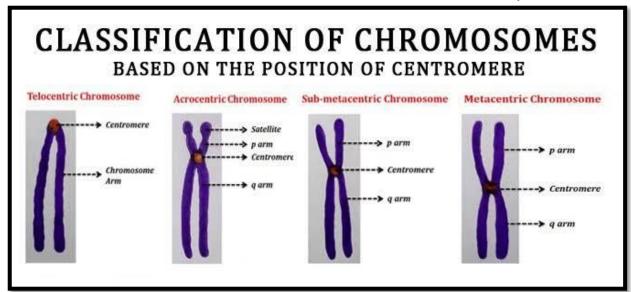
For identification of chromosomes the following classifications are used.

1. Classification based on position of centromere;

Metacentric: In this type of chromosomes the centromere is located near the centre and two arms are almost equal in length.

Sub-metacentric: Here the centromere is slightly away from the centre so that two arms of unequal length.

Acrocentric: The position of centromere is very close to one end so that one arm is very short and other is long.



Telocentric: These chromosomes have centromere at one end and thus have only one arm.

2. Standard Classification (Denver classification):

In this classification the chromosomes are classified in seven groups as per their descending length. These groups are designated as A to G. Female sex chromosome (X) is included in group C and male chromosome (Y) in group G.

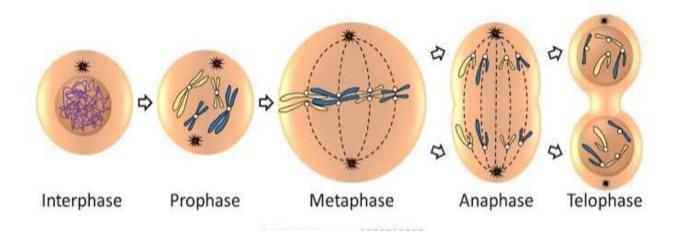
3. Paris Classification:

After the invention of banding techniques more accurate methods for identification of chromosomes came into existence. According to this method, the long and short arms of a chromosome are divided into 1, 2 and 3 region starting from centromere. These region are further subdivided into bands. With the help of banding not only individual chromosome is identified precisely. This method has helped to determine structural abnormalities within a chromosome.

Mitosis

In 1882, Flaming has given the word mitosis in which chromosomes divided and move towards North and South pole in the cell and it divides as two separate cells. There are four phases of *mitosis* are mentioned below:

- (1) **Prophase** : As an indicative that the cell is preparing to divide, the chromosomes which are long, slender and loosely packed in the resting stage, gradually contract and thicken owing to coiling and the apposition of material. Each chromosome is seen to be made up of two identical strands or chromatids lying against each other throughout their length. A chromosome bears a constriction, a region of attachment which is called *centromere*. As prophase advances the chromatids become closely coiled and thus the double nature of the chromosomes disappear.
- (2) **Metaphase :** In this stage, the nucleolus and nuclear membrane disappear, and a spindleshaped body known as *spindle fiber* is formed. The spindle extends into the nuclear area and occupies the centre of the cell. The chromosomes move to the equatorial plane of the spindle and become attached to it by the centromeres.



(3) **Anaphase :** The chromosomes begin to separate. Each centromere divides equally. First the two centromeres and later on the chromatids are pulled apart. The two halves or the identical sets of chromatids move to two opposite poles of the spindle fiber. The movement of the chromatids is autonomous. Thus chromatids become separated from each other.

(4) Telophase : The two groups of chromatids, now known as *chromosomes* pass towards opposite poles of the spindle. There the chromosomes uncoil and again become thin and long. The polar caps of the spindle disappear; and nuclear membrane encircling the chromosome develops : nucleoli reappear.

Cytokinesis : Mitosis accomplishes not only the segregation of duplicated chromosomes into daughter nuclei (*karyokinesis*), but the cell itself is divided into two daughter cells by a separate process called *cytokinesis* at the end of which cell division will be completed.

Meiosis

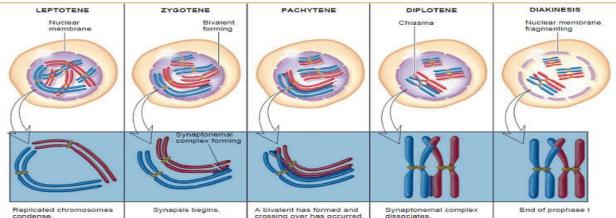
Meiosis is a very complicated process of nuclear division and by this process the chromosome number is reduced to half. That's why meiosis is also known as *reduction division*. Meiosis was first described by **J.B. Farmer** in 1905. In higher animal, meiosis takes place shortly before the germ cells are formed.

In fact, in meiosis there are always two successive divisions. During the first division the chromosome number is reduced to half, while the second division is mitotic in nature. The process of meiosis is briefly as follows :

Usually meiosis I and meiosis II have a common *interphase*, which occurs prior to meiosis II. Sometimes there may be resting phase in between meiosis I and meiosis II. However, DNA duplication occurs only once at the beginning.

Meiosis I

Prophase I : After interphase the meiocyte enters into Prophase I, which is typically longer and more complex when compared to prophase of mitosis. Because of the complexity of these genetic events, prophase I is further divided into five sub-stages: Leptotene, Zygotene, Pachytene, Diplotene and Diakinesis.



a) Leptotene or Leptonema (*lepto: thin, nema: thread*) : In this stage the chromosome in the form of slender thread in diploid number appears in the nucleus. Each chromosome bears a definite number of granules known as *chromomeres*, and as such the chromosomes look like chains of beads of various sizes.

- b) Zygotene or Zygonema (zygo: pair, nema: thread): The identical chromosomes come close to each other and they undergo pairing throughout the whole length. The phenomenon is called *synapsis*. The paired chromosomes are said to be in *bivalent* condition. The pairing, however, does not mean fusion.
- c) **Pachytene or Pachynema** (*pachy: thick, nema: thread*): The bivalent chromosomes coil around one another and become short and thick. At this stage the chromosomes are present in haploid number.
- d) **Diplotene or Diplonema** (*diplo: two, nema: thread*) : The chromosomes split longitudinally and as a result each chromosome produces two chromatids. The chromosome threads begin to separate. The separation is, howev er not always complete, as they remain attached to one or several points. At this stage one paternal and one maternal chromatid exchange parts by breakage at corresponding places of the two chromatids. This process is known as *crossing over*. At certain stage the point of breakage and rejoining come to lie at right angle forming a cross-like structure, which is called a *chiasma*. The chromosomes further shorten and thicken through coiling.
- e) **Diakinesis** : The chromosomes further coil and become very short. They remain sparsely distributed throughout the nucleus.

Metaphase I

With the disappearance of the nuclear membrane and the nucleus the nuclear spindle develops and the bivalent chromosomes move towards the equatorial plane. Each pair of chromosomes has one centromere on each side by which it is attached to the spindle fibers.

Anaphase I

Disjunction of chromosomes occur and chromosome numbers become half. Chromosomes are separated from each other and starts moving towards opposite poles. Chromosomal fibers pull it towards opposite poles.

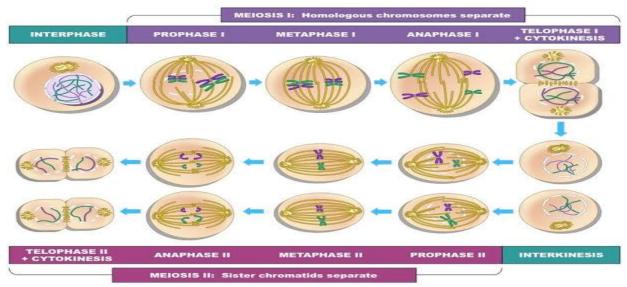
Telophase I

Nuclear membrane and nucleolus reappears. Spindle fibers disappear. Chromosomes recoil to form chromatin material.

Cytokinesis I

Two daughter cells appear.

Each nucleus then may rest for a while (interphase) or it may not, after which it passes on to the second division; which is mitotic in nature.



Prophase II

The nuclear membrane disappears by the end of prophase II. The chromosomes again become compact. Pair of sister chromatids attached by a common centromere. The centromere of each chromosome attach to the recently formed spindle fibers from the centriole.

Metaphase II

At this stage the chromosomes align at the equator and the microtubules from opposite poles of the spindle get attached to the kinetochores of chromatids.

Anaphase II

It begins with the simultaneous splitting of the centromere of each chromosome, allowing them to move towards opposite poles of the cell.

Telophase II

Meiosis ends with Telophase II, in which the two groups of chromatids once again get enclosed by a *nuclear envelope; cytokinesis* follows resulting in the formation of four haploid daughter cells.