Lectures of Ultrastructure of Cell

(Master's Stage)
First Semester 2025-2026

Anatomy and Histology Department

By

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CELL DIVISION

Introduction

A multicellular organism starts its life as a single cell and undergoes repeated division, thus, the growth and development of every living organism depend on the growth and multiplication of its cells. Cell increases in size due to growth and it is the characteristic feature of all living organisms. After the cell attains maximum growth, it begins to divide. The cell division is a continuous and dynamic process, and it involves the following three stages:

1. DNA or genome replication.
2. Nuclear division or karyokinesis.
3. Cytoplasmic division or cytokinesis.

Cell division is of two types based on number of genomes present in the daughter cells in comparison to the dividing parent cell: mitosis and meiosis.

1. Mitosis- it was coined by Fleming in 1882. It is the multiplication of a body cell into two daughter cells of equal size and containing the same number of chromosomes as in the parent cell. It is also called somatic division.

2. Meiosis- it was coined by Farmer and Moore in 1905. It occurs only in germ cells during the formation of gametes (sperm and ovum). Meiosis is a process by means of which double number or 2N or diploid chromosomes is reduced to its half number or 1N or haploid. It is also called reduction process.

Cell Cycle Stages

Every cell having the capacity to divide passes through a regular cycle of changes known as cell cycle which is a regular sequence of events that produce new cells. A cell starts its cycle in diploid condition.

* Phases of Cell Cycle

Cell cycle consists of two stages: A long un-dividing stage called **interphase** or **I-phase** and a short dividing stage called **mitotic** or **M-phase** (Fig. 1).

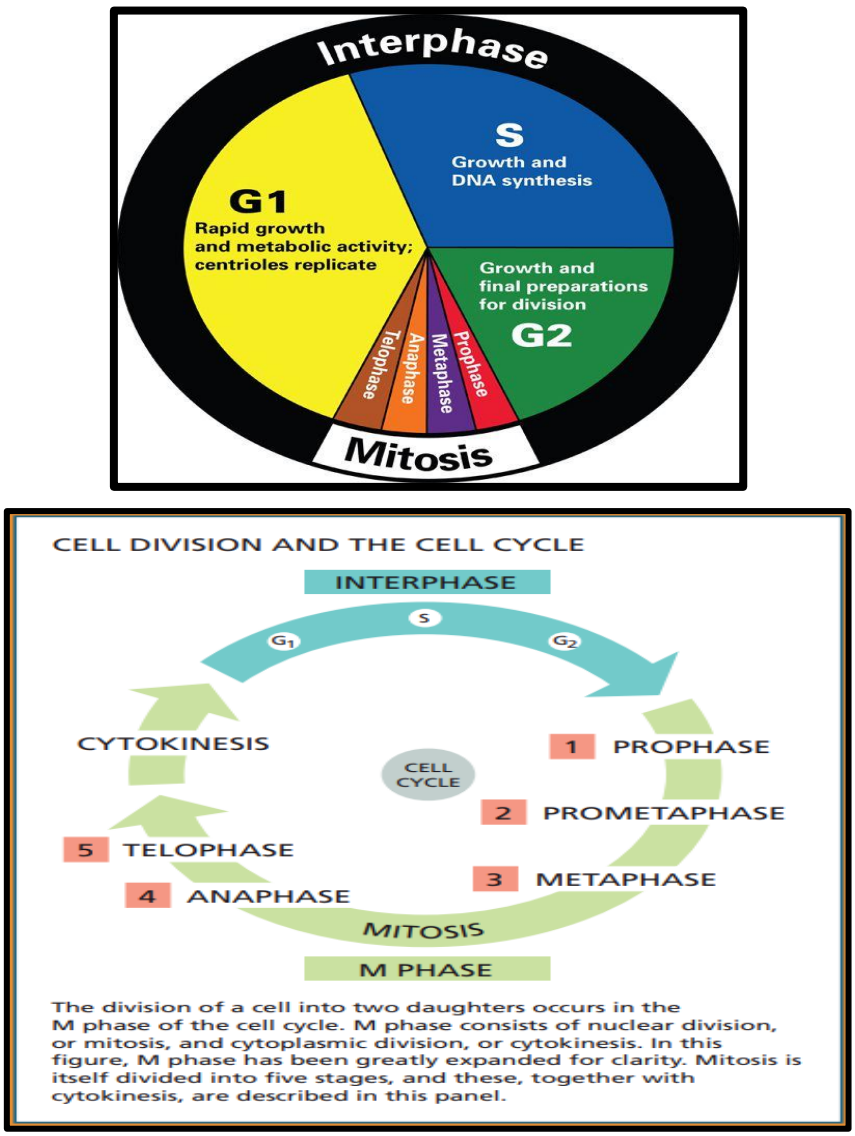


Fig. 1: The Cell Cycle.

1. Interphase: it's the time between the end of telophase and the beginning of the next M-phase. It is a long stage that lasts for (10-30) hours. During this phase the cell grows by synthesizing biological molecules such as lipids, proteins, carbohydrates, nucleic acids (Fig. 2). Interphase is further divided into three subphases or periods: first gap or G1 phase, synthetic or S phase and second gap or G2 phase.

(a) G1 phase- it represents the gap between previous mitosis and beginning of DNA synthesis. In this stage initial growth of a newly formed cell takes place. Various biological molecules (carbohydrates, proteins, lipids, including some non-histones, RNAs) are synthesized in this phase. Normal metabolism is carried out for the preparation for DNA replication that is to take place next to it. DNA synthesis does not occur in this phase.

(b) S Phase- during this phase duplication of each chromosome takes place by replication of new DNA molecule on the template of the existing DNA. Synthesis of histone proteins and some non-histone proteins also occur in S-phase only. In most of the eukaryotes the S-phase lasts for (6-8) hours.

(c) G2 Phase- it is the gap between DNA synthesis and nuclear division. RNA transcription and protein synthesis continues during this phase. Further growth of the cell and preparation for its division also takes place in this stage. During this stage the cytoplasmic organelles such as centrioles, mitochondria and Golgi apparatus are doubled, proteins for spindle and asters are synthesized and active metabolism stores energy for the next mitosis. The G2 phase in most cells lasts for (2-5) hours.

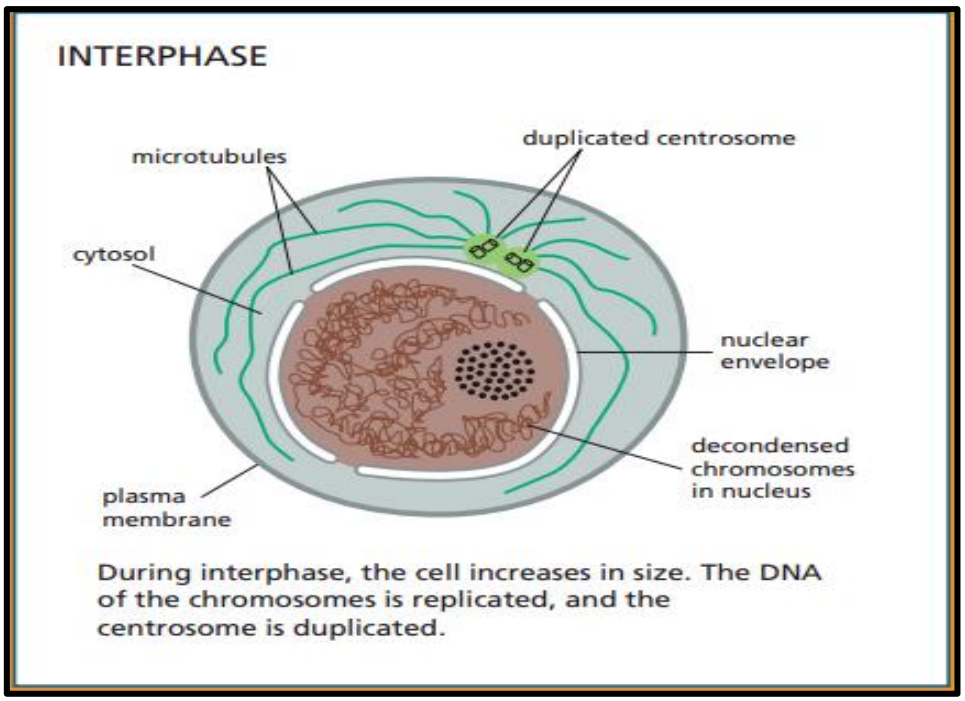


Fig. 2: Interphase.

2. Mitotic Phase: interphase is followed by mitotic phase. During mitotic phase the already duplicated chromosomes are equally distributed to the daughter cells which contain the same hereditary information as the parent cell. Though, the other cell components (organelles and molecules) are also divided approximately equally between the daughter cells, but not as precisely as the DNA. After mitosis is over, the daughter cells enter G1 phase of the next cell cycle.

Control of Cell Cycle

1. Nucleocytoplasmic Ratio: cell division starts when the ratio between the volume of nucleus and the volume of cytoplasm is upset. As the cell grows, the synthesis of proteins, nucleic acids, lipids, and other cellular components takes place. During synthesis of these molecules, the back-and-forth movements of materials through the nuclear and the cell membranes occur. With the growth of the cell, its volume increases more than the surface of the nucleus and the cell, and at a critical point, the surface of the nucleus becomes inadequate for the exchange of materials between the nucleus and cytoplasm required for further growth. The cell divides at this stage and regains the optimum and efficient nucleocytoplasmic ratio that allows the growth. Although the cell division usually occurs after a cell has grown to a certain size, there are important exceptions to this pattern.

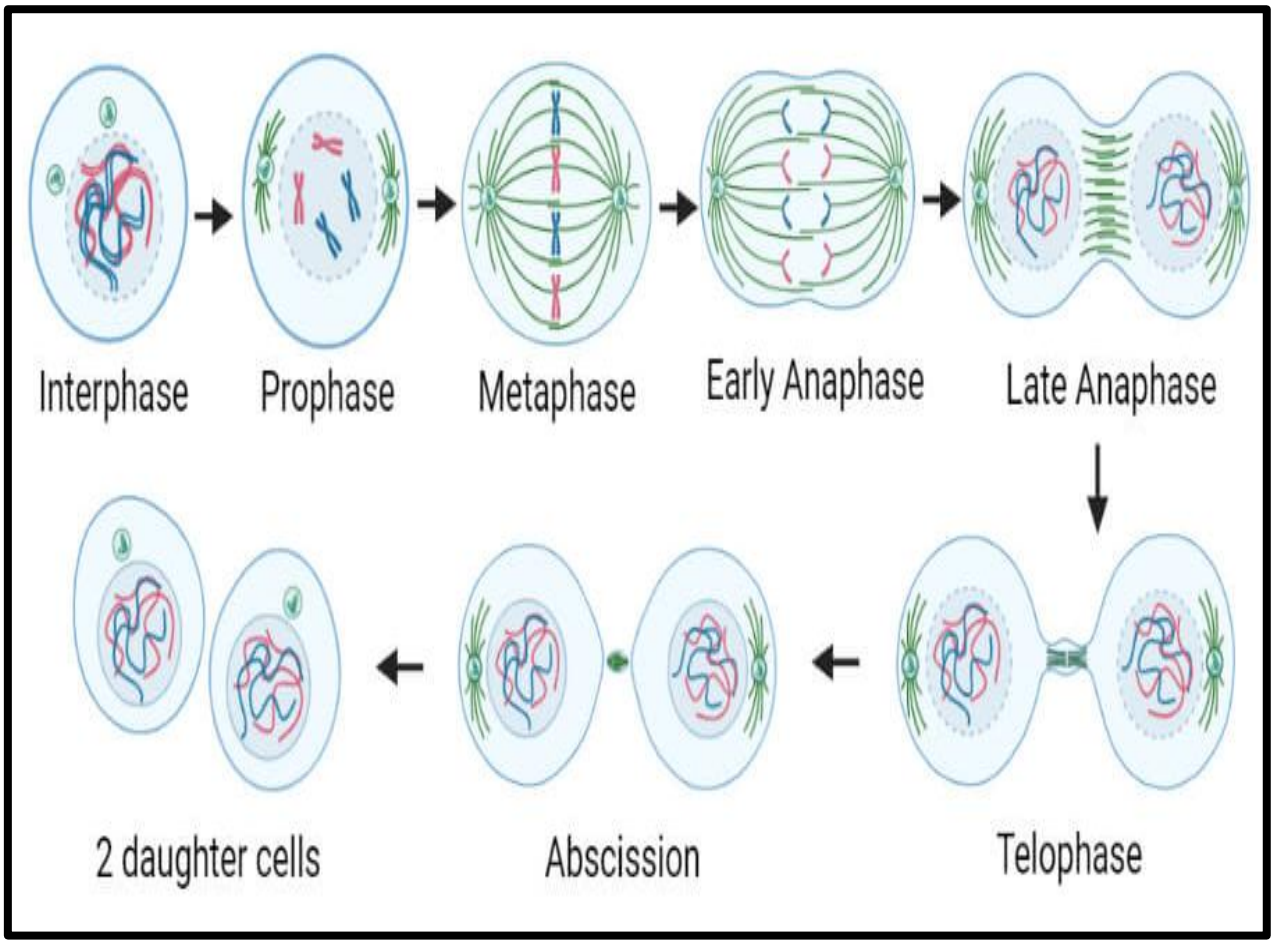
2. Surface-Volume Ratio: with the growth of the cell size, its volume increases more than its surface area. All the materials of the cell required for its maintenance and growth are drawn through its surface. A stage will reach when the surface area is insufficient to supply the large volume of the cell. It is thought that there is a critical point at which the cell division starts, and the division of the cell greatly increases the surface without increasing the volume.

3. Phosphorylation: during cell cycle the phosphate groups are added to the histone groups as the cell enters S phase, increases during M phase, and are removed on the completion of mitosis before G1 starts. Phosphate groups are also added and removed to non-histone proteins during cell cycle. Thus, it is believed that the changes in the histones and non-histones may have a role in the control of cell cycle because these proteins have been found to regulate the activity of genes in RNA transcription during interphase.

4. Cyclin: the concentration of this protein appears to control mitosis as it builds up during interphase and is degraded during mitosis.

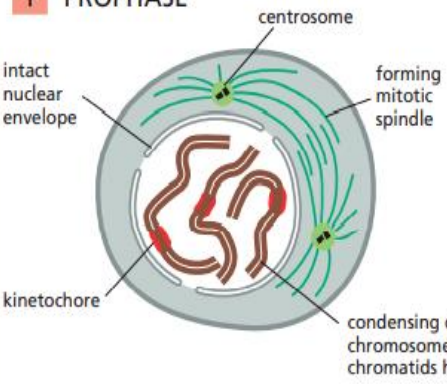
Mitosis Division

It's the most common method of cell division in eukaryotes that takes place in somatic cells of the body (hence it's also called **somatic division**). However, in gonads it occurs in undifferentiated germ cells. In plants it takes place in the cells of meristematic tissues. Duration of mitosis on average is from (30) minutes to (3) hours. Mitosis is defined as the division of a parent cell into two identical daughter cells each with a nucleus having the same amount of DNA, the same number and kind of chromosomes and the same hereditary instructions as parent cell. Therefore, it's also known as **equational division**. There are **two main events** involved in mitosis: **Karyokinesis** (division of nucleus) and **Cytokinesis** (division of cytoplasm) (Fig.3).

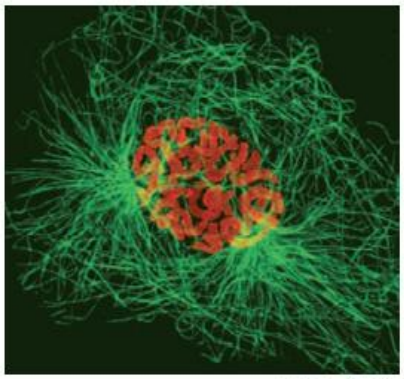


MITOSIS

1 PROPHASE



At prophase, the duplicated chromosomes, each consisting of two closely associated sister chromatids, condense. Outside the nucleus, the mitotic spindle assembles between the two centrosomes, which have begun to move apart. For simplicity, only three chromosomes are drawn.



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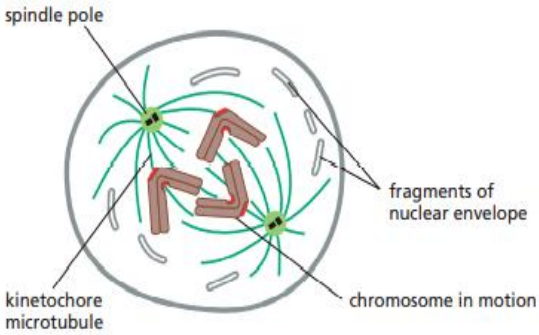
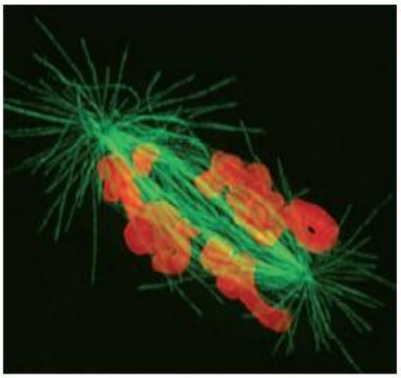
MITOSIS

2 PROMETAPHASE



Prometaphase starts abruptly with the breakdown of the nuclear envelope. Chromosomes can now attach to spindle microtubules via their kinetochores and undergo active movement.



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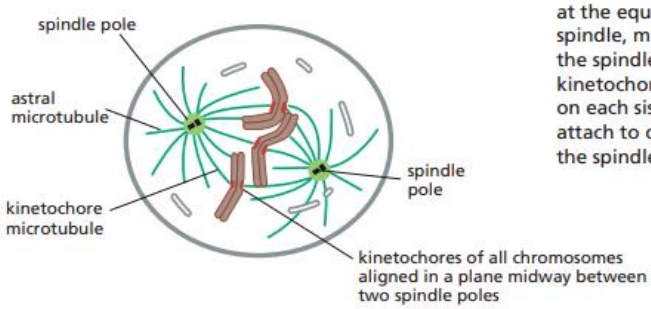
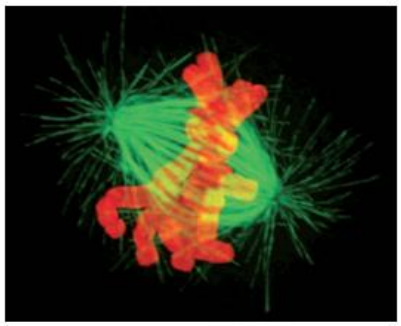
MITOSIS

3 METAPHASE



At metaphase, the chromosomes are aligned at the equator of the spindle, midway between the spindle poles. The kinetochore microtubules on each sister chromatid attach to opposite poles of the spindle.



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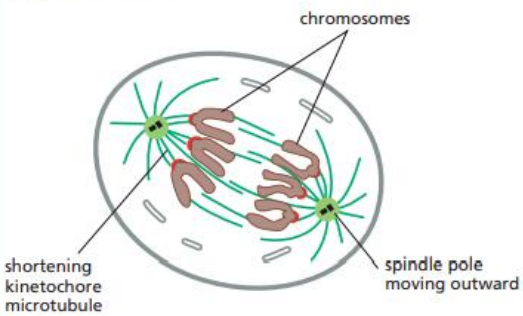
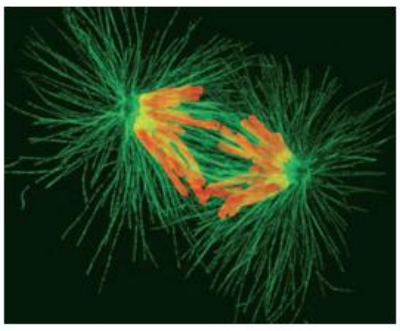
MITOSIS

4 ANAPHASE



At anaphase, the sister chromatids synchronously separate and are pulled slowly toward the spindle pole to which they are attached. The kinetochore microtubules get shorter, and the spindle poles also move apart, both contributing to chromosome segregation.



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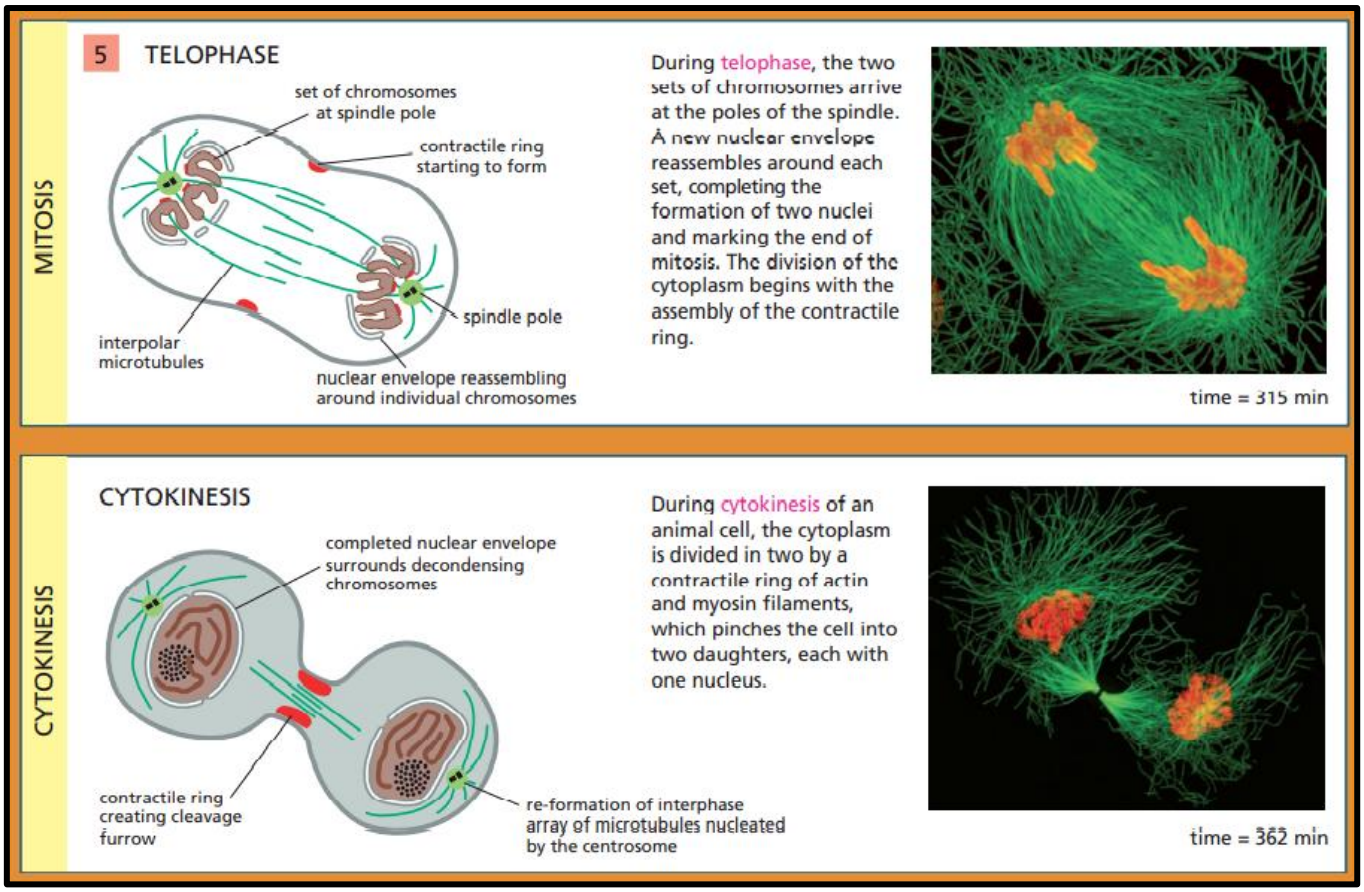


Fig. 3: Mitosis.

Meiosis Division

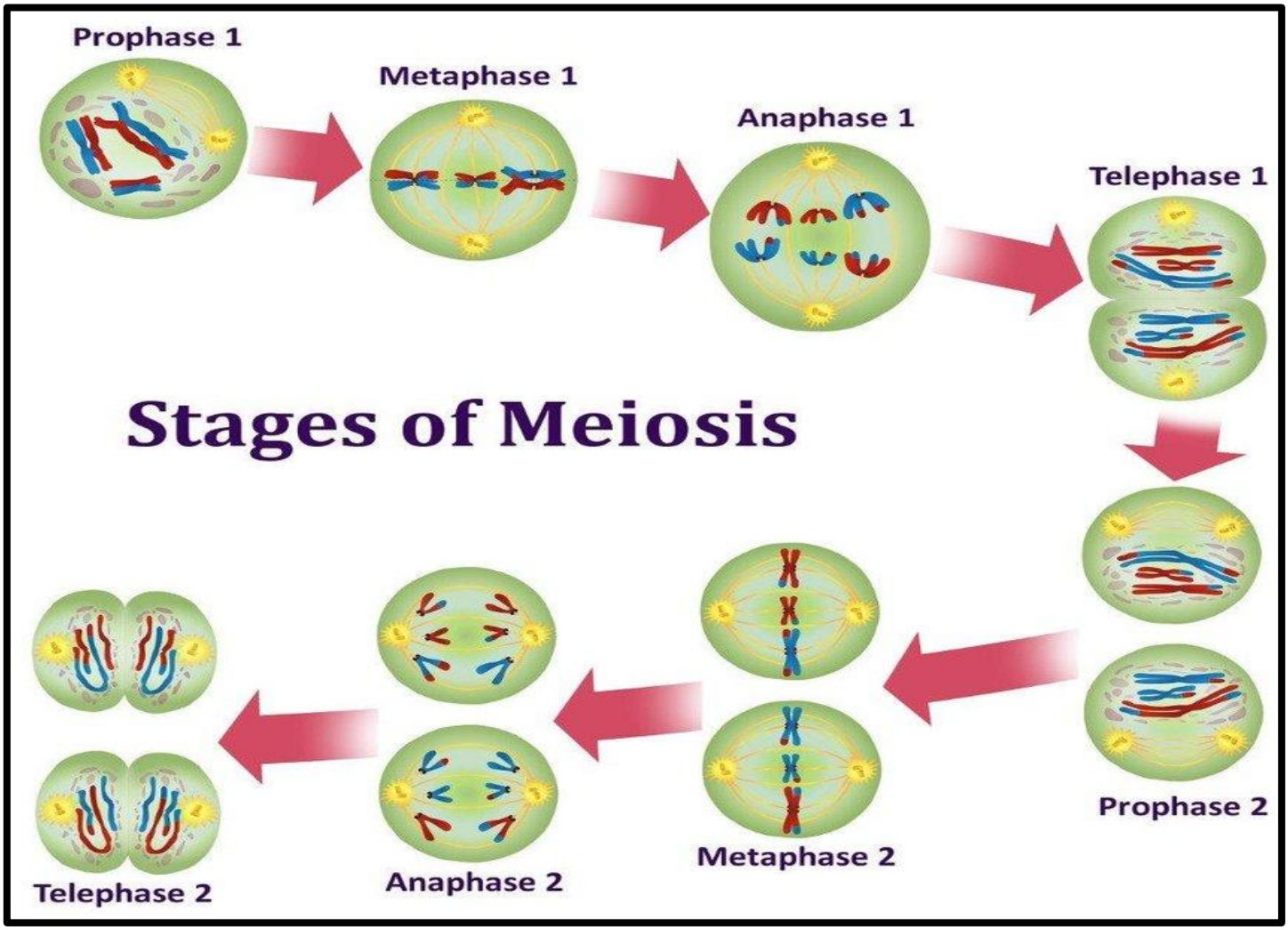
Mitosis occurs in all kinds of eukaryotic cells, while Meiosis is confined to certain cells and takes place at a particular time. Only the cells of sexually reproducing organisms undergo meiosis. Meiosis produces gametes in animals, it consists of two divisions that take place in rapid succession, with the chromosomes replicating only once. Thus, a parent cell produces four daughter cells, each having half the number of chromosomes and half of the nuclear DNA amount present in the parent cell. Meiosis is therefore also known as **reduction division**. The two divisions of meiosis are known as the first and the second meiotic divisions or **meiosis-I** and **meiosis-II** (Fig.4).

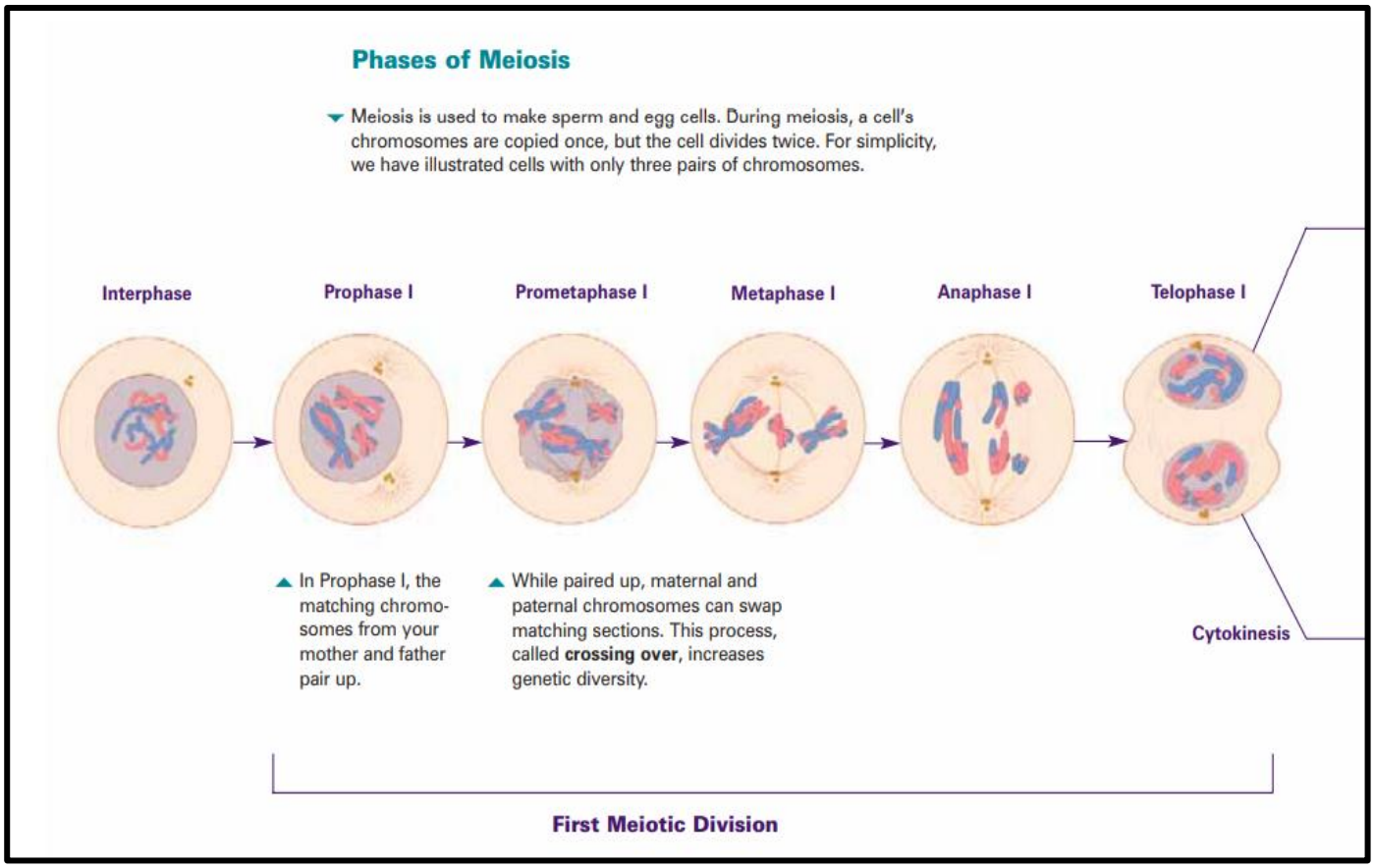
First meiotic division or Meiosis-I

During which, the two homologous chromosomes of each pair separate from each other and go to separate daughter cells. This reduces the number of chromosomes from diploid to haploid condition. The four phases of this division are called prophase-1, metaphase-1, anaphase-1 and telophase-1.

Second meiotic division or Meiosis-II

It is like **Mitosis**, as in this division the two chromatids of each chromosome separate from each other and go to separate daughter cells. As a result, the number of chromosomes remains the same as produced by meiosis-I. The four stages of this division are called prophase-II, metaphase-II, anaphase-II and telophase-II.





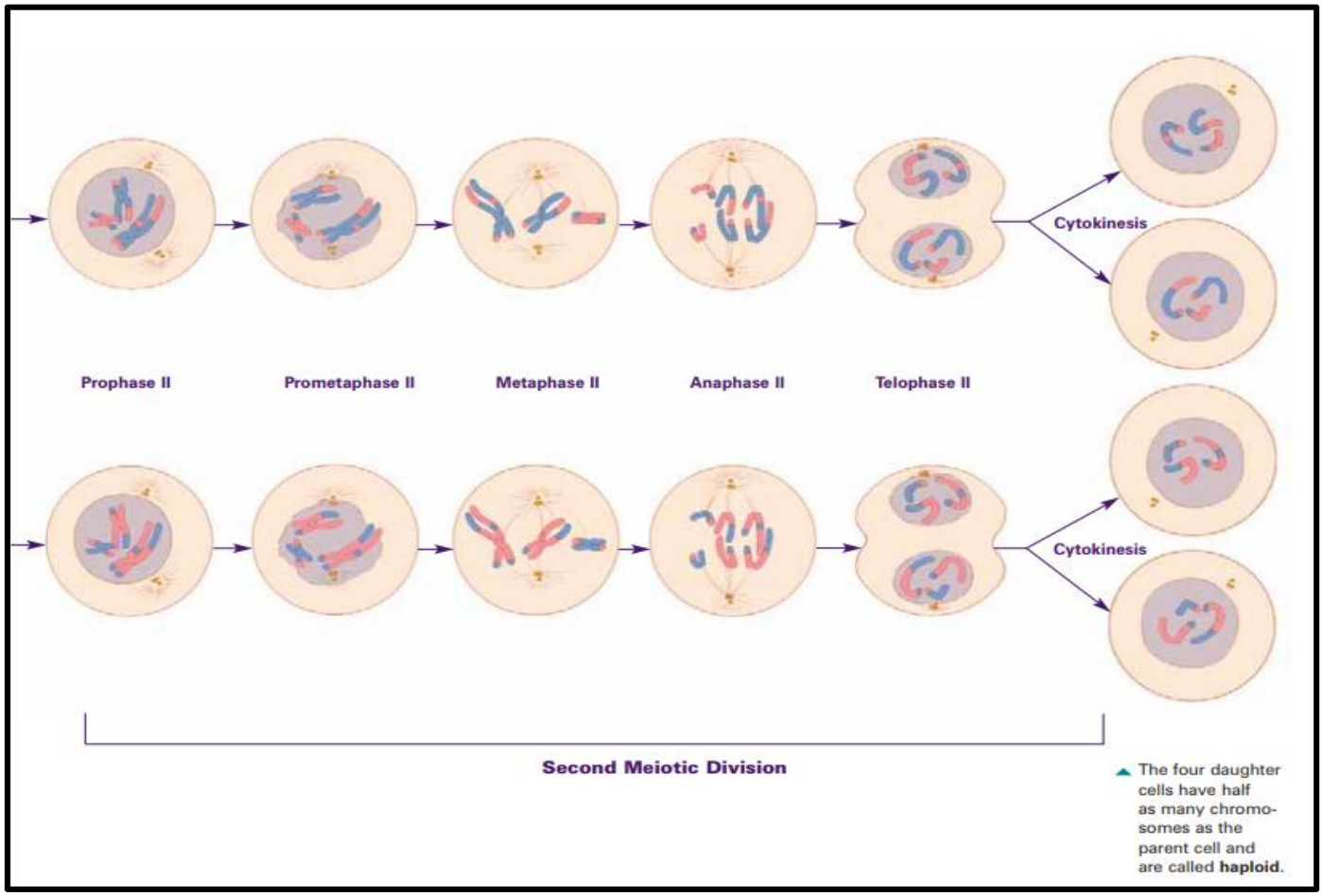


Fig. 4: Meiosis.

Comparison between Mitosis and Meiosis

No.	Mitosis	Meiosis
1	It occurs in all kinds of cells and may continue throughout life.	It occurs only in special cells (gamete mother cells or spore mother cells) and at specific times.
2	It involves a single division, resulting in two daughter cells only.	It involves two successive divisions, resulting in four daughter cells.
3	A cell can repeat mitosis almost indefinitely.	takes place only once in a cell.
4	All mitotic divisions are alike.	Two meiotic divisions are dissimilar, first is reductional and second equational.
5	Each mitotic division is preceded by an interphase.	The second meiotic division is generally not preceded by an interphase.
6	Chromosomes replicate before.	Chromosomes do not replicate before each mitotic division. second meiotic division.
7	Prophase is relatively short and simple.	Prophase-1 is very long and elaborate, comprising 5 sub phases.
8	There is no pairing of homologous chromosomes, hence no chance of crossing over.	Homologous chromosomes pair and often undergo crossing over in prophase-1.
9	No chiasmata are formed.	Chiasmata form temporarily where crossing over occurs.
10	Chromatids are genetically like chromosomes they arise from.	Chromatids may differ genetically from the chromosomes they arise from due to crossing over.
11	The two kinetochores of a chromosome connect to both the poles of the spindle.	The kinetochores of a chromosome connect to the same spindle pole in metaphase-I and to both the poles in metaphase-II.
12	Anaphase involves separation of chromatids of each chromosome.	Anaphase-I involves separation of homologous chromosomes. The chromatids move apart in anaphase-II.
13	Daughter cells have diploid number of chromosomes like the parent cell.	Daughter cells have haploid number of chromosomes unlike the parent cell.
14	Daughter cells divide again after interphase.	Daughter cells, if gametes, do not divide further.
15	Mitosis brings about growth, repair and healing.	Meiosis forms gametes or spores, helps maintain the number of chromosomes constant from generation to generation, and introduces variation.
16	Mitosis is much shorter than meiosis in the same animal.	Meiosis is much longer than mitosis in the same animal.
17	Cytokinesis usually follows karyokinesis.	Cytokinesis often doesn't occur after meiosis-I, but always occur after meiosis-II, forming four cells simultaneously.

Apoptosis

Less evident, but no less important than cell proliferation for body functions, is the process of cell suicide. Apoptosis is a rapid, highly regulated cellular activity that shrinks and eliminates defective and unneeded cells (Fig. 5). It results in small membrane-enclosed apoptotic bodies, which quickly undergo phagocytosis by neighboring cells or cells specialized for debris removal. Apoptotic cells do not rupture and release none of their contents, unlike cells that die because of injury and undergo necrosis. This difference is highly significant because release of cellular components triggers a local inflammatory reaction and immigration of leukocytes. Such a response is avoided when cells are rapidly eliminated by apoptosis following cell cycle arrest or as part of normal organ development.

Apoptosis is controlled by cytoplasmic proteins in the Bcl-2 family, which regulate the release of death-promoting factors from mitochondria. Activated by either external signals or irreversible internal damage, specific Bcl-2 proteins induce a process with the following features:

1. Loss of mitochondrial function and caspase activation: Bcl-2 proteins associated with the outer mitochondrial membrane compromise membrane integrity, stopping normal activity and releasing cytochrome C into the cytoplasm where it activates proteolytic enzymes called caspases, resulting in protein degradation throughout the cell.

2. Fragmentation of DNA: Endonucleases are activated, which cleave DNA into small fragments.

3. Shrinkage of nuclear and cell volumes: Destruction of the cytoskeleton and chromatin causes the cell to shrink quickly, producing small structures with dense, darkly stained pyknotic nuclei that may be identifiable with the light microscope.

4. Cell membrane changes: The plasma membrane of the shrinking cell undergoes dramatic shape changes, such as "blebbing," as membrane proteins are degraded and lipid mobility increases.

5. Formation and phagocytic removal: Membrane-bound remnants of cytoplasm and nucleus separate into very small apoptotic bodies. Newly exposed phospholipids on these bodies induce their phagocytosis by neighboring cells (Fig. 6).

A few examples of apoptosis emphasize its significance. In the ovary, apoptosis is the mechanism for both the monthly loss of luteal cells and the removal of excess oocytes and their follicles. Apoptosis was first discovered as programmed cell death in embryos, where it is important in shaping developing organs or body regions, such as the free spaces between embryonic fingers and toes. In all these examples apoptosis occurs very rapidly, in less time than required for mitosis, and the affected cells are removed without a trace.

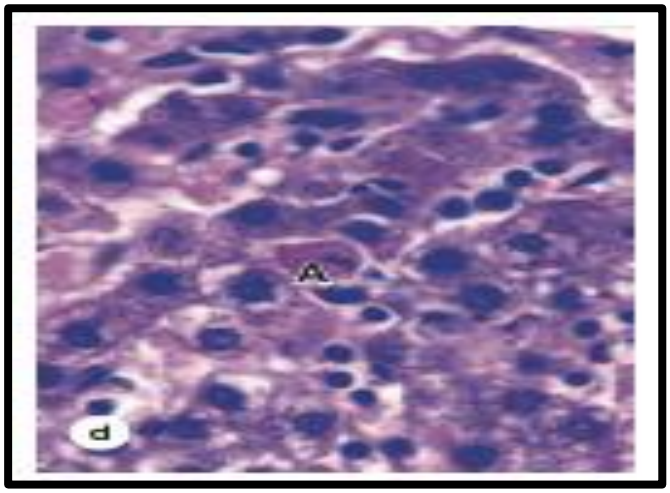


Fig. 5: Apoptotic cells in adult tissues are rare because the process is completed very rapidly. Moreover, with their highly condensed chromatin in pyknotic nuclei and rounded shape, cells early in apoptosis may superficially resemble some mitotic cells. Shown here are apoptotic cells in the liver. (X400; H&E).

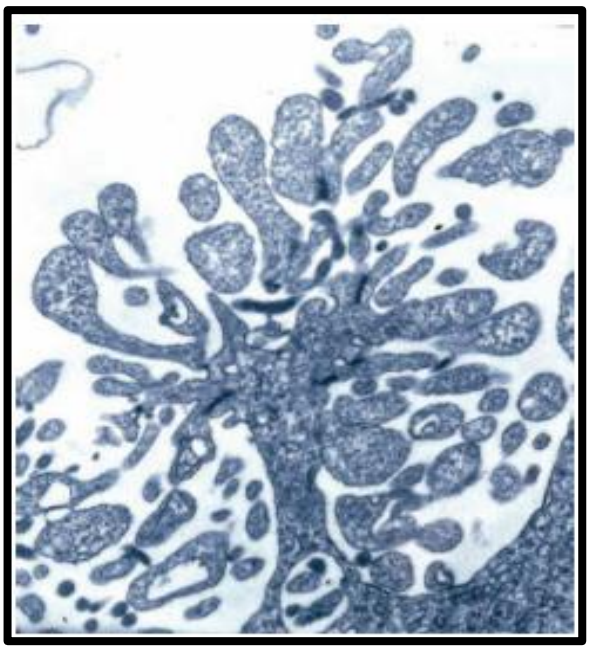


Fig. 6: TEM of a cell in late apoptosis shows radical changes in cell shape, with membrane blebbing and the formation of many membrane-bound cytoplasmic regions. These apoptotic bodies may separate from one another but remain enclosed by plasma membrane so that no contents are released into the extracellular space. The membrane changes are recognized by neigh boring cells, and macrophages and apoptotic bodies are very rapidly phagocytosed. (X10,000).

Note: Cancer cells often deactivate the genes that control the apoptotic process, thus preventing their elimination in this type of cell death and allowing progression toward a more malignant state.