Genetics

Modified no. 3

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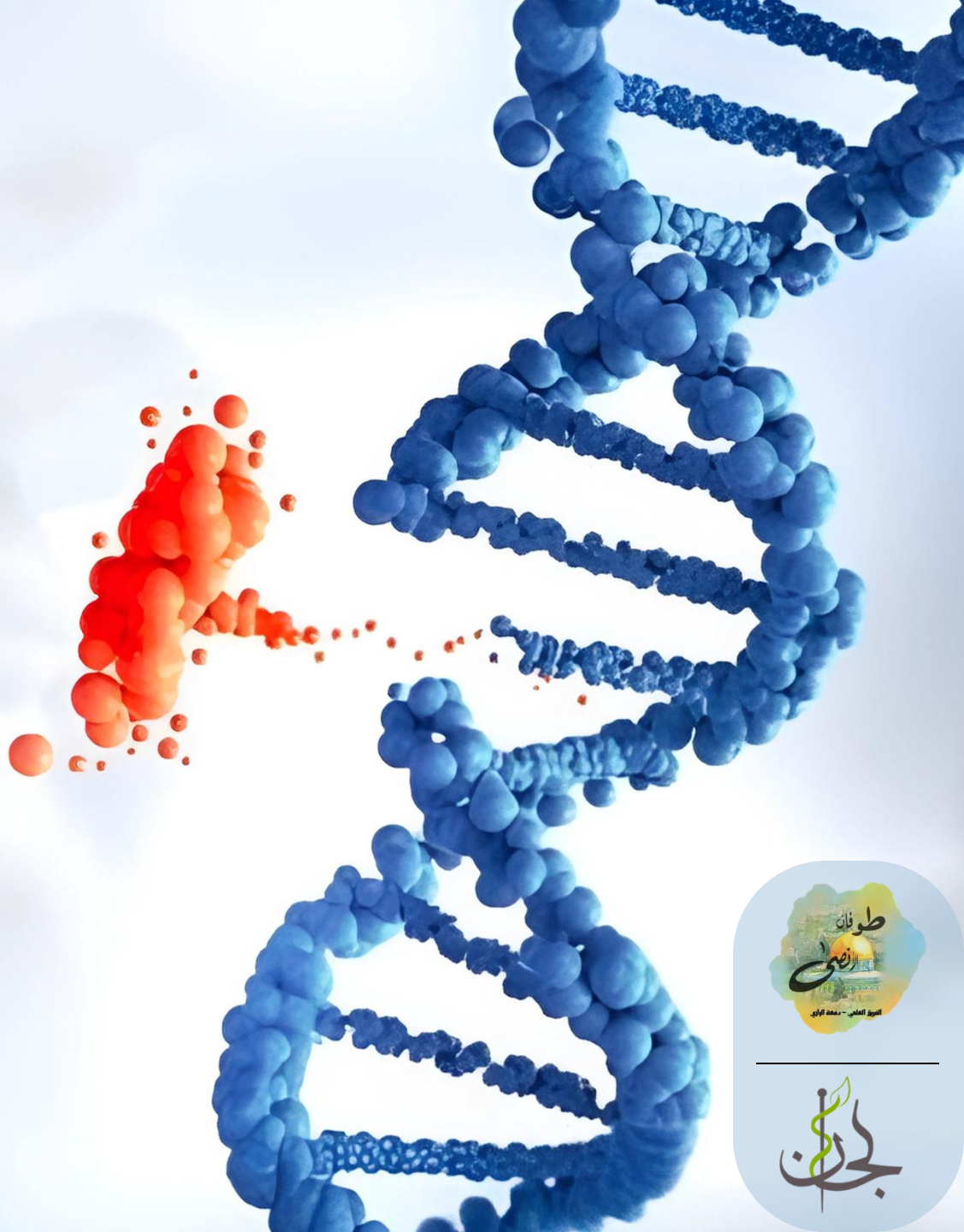

بسم الله الرحمن الرحيم

Introduction to medicmedical genetics

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Check the summaries and tables !!

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- Important

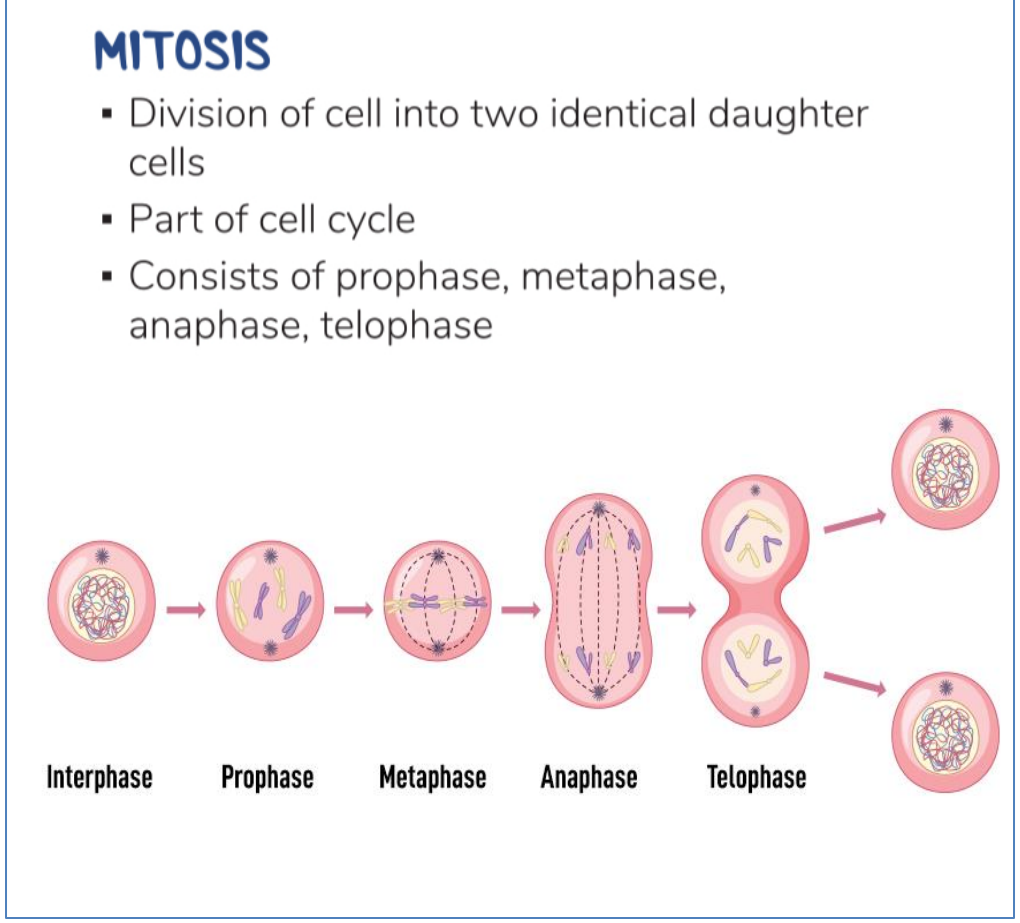
- Our cells undergo **Mitosis** , which is a very slow process . But at the same time, not all cells divide, for example: **Mature cardiac muscle cells and skeletal muscle fibres** in adults are multinucleated and typically **do not undergo mitosis** (very very slow , rarely to devide) . On the other hand, skin cells , elementary tract cells and bone marrow cells , are in continuous cell devision .
- Mitosis is a type of cell division that results in two genetically identical daughter cells, each having the same number of chromosomes as the parent cell. It is essential for growth, tissue repair, regeneration and asexual reproduction in eukaryotic organisms.

- Cell division is the cycle of a cell between interphase and mitosis.

- **Phases of Mitosis :-**

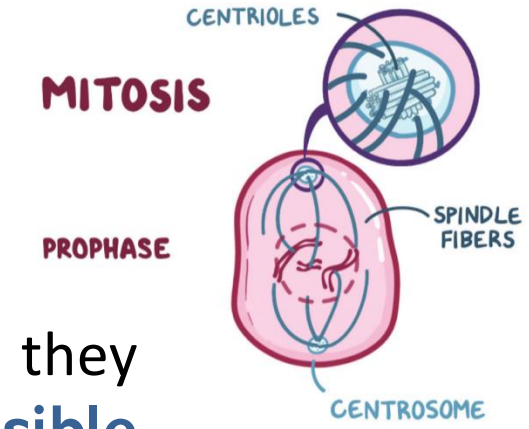
1- Prophase
2- Prometaphase
3- Metaphase
4- Anaphase
5- Telophase

An extra image



A mnemonic to remember mitosis phases:
“Please Meet Ana Today”

Mitosis



Mitosis is divided into several phases.

During **prophase,** the first mitotic stage,

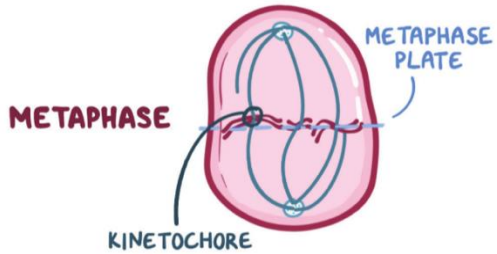
1. The chromosomes become visible[1] under a light microscope as they condense and coil. **(Chromatin condenses into visible chromosomes.)**

2. The two sister[2] chromatids of each chromosome lie together, attached at a point called the centromere. The nuclear membrane, which surrounds the nucleus, disappears during this stage.

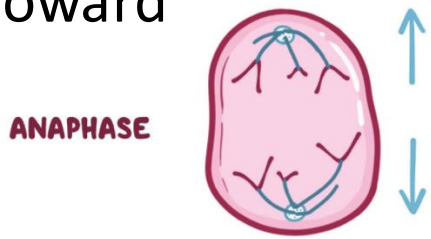
3. [3]**Spindle fibers** begin to form. These radiate from two **centrioles** located on opposite sides of the cell. The spindle fibers become attached to the" centromeres of each chromosome and eventually pull the two sister chromatids in opposite directions.

The chromosomes reach their most highly condensed state during **metaphase**, the next stage of mitosis.
During metaphase the spindle fibers begin to contract and pull the centromeres of the chromosomes, which are now arranged along the middle of the spindle (the **equatorial plane** of the cell). وسط الخلية تمامًا

- **Chromosomes align at the cell's equatorial plane, known as the metaphase plate.**
- **Spindle fibers ensure equal distribution of chromosomes.**



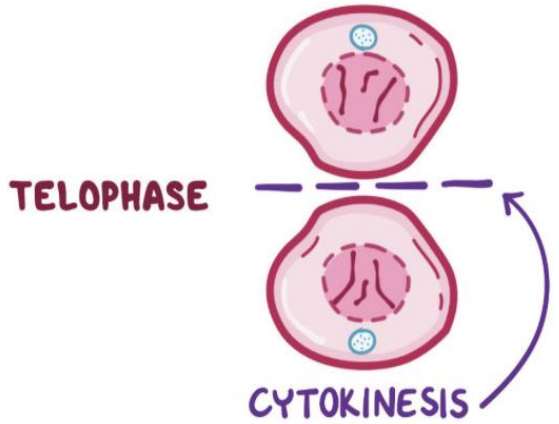
During **anaphase**, the next mitotic stage, the centromeres of each chromosome split, allowing the sister chromatids to separate. The chromatids are then pulled by the spindle fibers, centromere first, toward opposite sides of the cell.



- **Sister chromatids separate and are pulled to opposite poles of the cell by spindle fibers.**
- **This ensures each daughter cell will receive an identical set of chromosomes.**

Telophase, the final stage of mitosis, is characterized by the formation of new nuclear membranes around each of the two sets of 46 chromosomes.

The spindle fibers disappear, and the chromosomes begin to decondense.

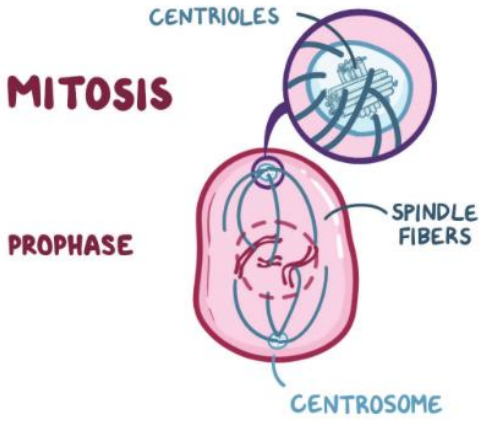


1. The nuclear envelope reforms around each set of chromosomes.
2. Chromosomes begin to decondense into chromatin.
3. The spindle fibers disassemble.

Cytokinesis generally occurs after nuclear division and results in a roughly equal division of the cytoplasm into two parts.

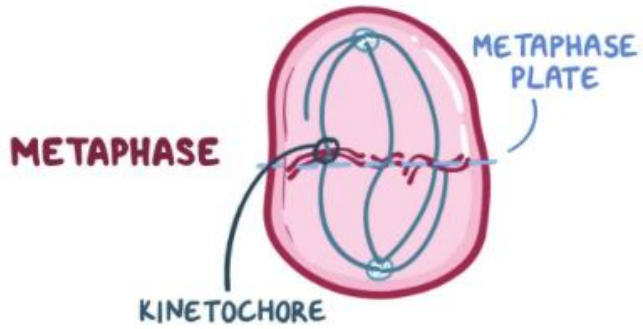
- It is the division of the cytoplasm, leading to the formation of two separate daughter cells.

extra image



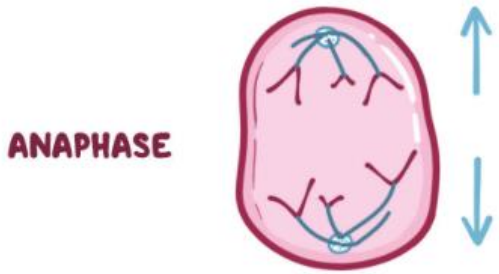
Prophase

- Chromatin fibers condense
- Centrioles align chromosomes between centrosomes



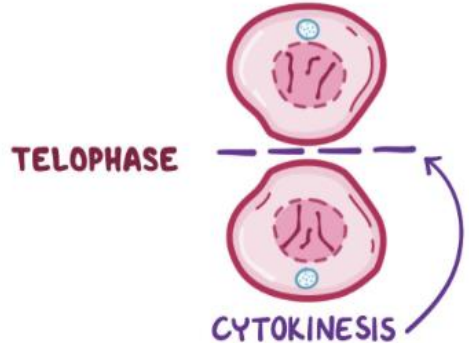
Metaphase

- *Prometaphase:* nuclear membrane, nucleolus disintegrate
- *Metaphase:* chromosomes align along metaphase plate, spindle fibers attach to kinetochores



Anaphase

- Centrosomes pull on spindle fibers to separate chromatids



Telophase

- New nuclear envelopes form

• Summary

- **In interphase,** the DNA replication occurs preparing the cell for mitosis, and any error here will lead to mutations
- **Mitosis** begins with prophase, where chromatin condenses into visible chromosomes, each consisting of two sister chromatids joined at the centromere, while the nuclear envelope starts to break down and spindle fibers begin to form.
- In **prometaphase**, the condensation will be the highest , centrioles will be on the cell poles , the nuclear envelope completely dissolves.
- During **metaphase**, chromosomes align at the metaphase plate, ensuring equal distribution to both daughter cells.
- In **anaphase**, sister chromatids separate and are pulled toward opposite poles of the cell by spindle fibers.
- Finally, in **telophase**, nuclear envelopes reform around each set of chromosomes, which begin to decondense into chromatin, while the spindle fibers disassemble.
  Cytokinesis typically follows, dividing the cytoplasm and completing the formation of two identical daughter cells with equal number of chromosomes to the mother cell , 46 chromosomes .

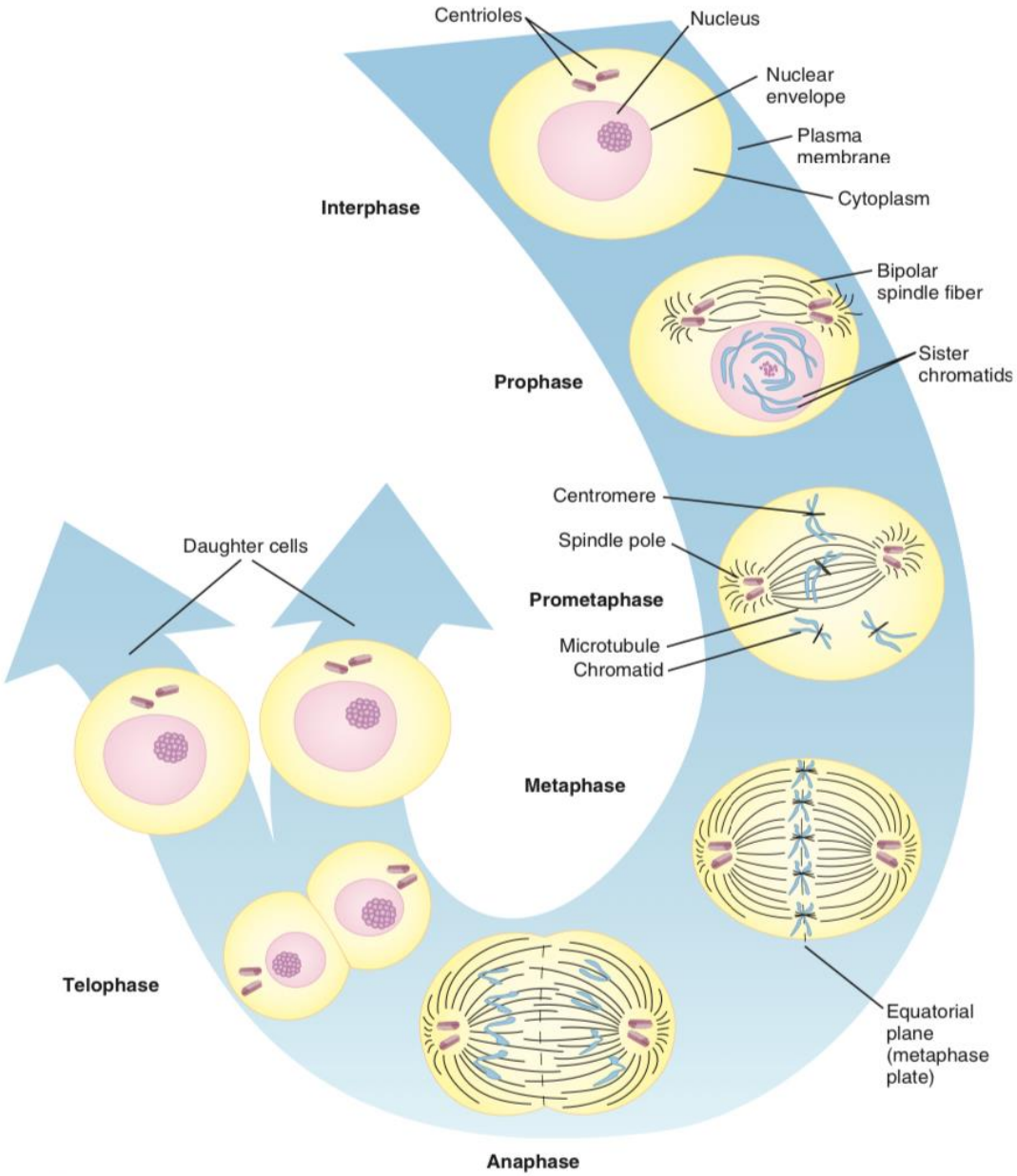


FIG 2-20 The stages of mitosis, during which two identical diploid cells are formed from one original diploid cell.

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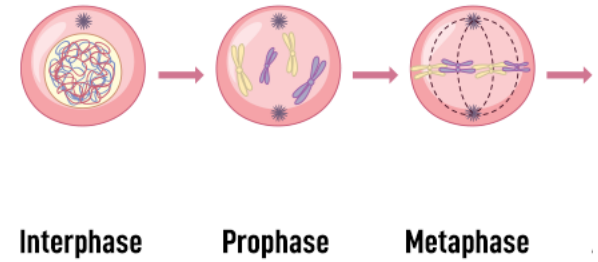
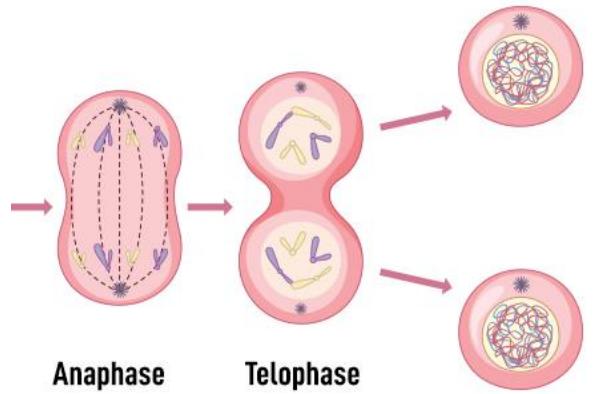
Here's an extra table summarizing the **Stages of Mitosis** along with key events and outcomes:

Stage	Key event	Outcome
Prophase	Chromatin condenses into visible chromosomes, nuclear envelope breaks down, spindle fibers form	Chromosomes become visible, spindle apparatus prepares for attachment
Metaphase	Chromosomes align at the metaphase plate (center of the cell)	Ensures chromosomes are evenly distributed
Anaphase	Sister chromatids separate and move to opposite poles	Equal distribution of chromosomes to daughter cells
Telophase	Nuclear envelope reforms, chromosomes decondense into chromatin, spindle fibers break down	Two nuclei form in one cell
•**Cytokinesis :** Cytoplasm divides, forming two identical daughter cells, Two separate, genetically identical daughter cells are formed		





Meiosis

When an egg cell and sperm cell unite to form a zygote, their chromosomes are combined into a single cell.
Because humans are diploid organisms, there must be a mechanism to reduce the number of chromosomes in gametes to the haploid state.
The primary mechanism by which **haploid gametes** are formed from diploid precursor cells is termed **meiosis.**

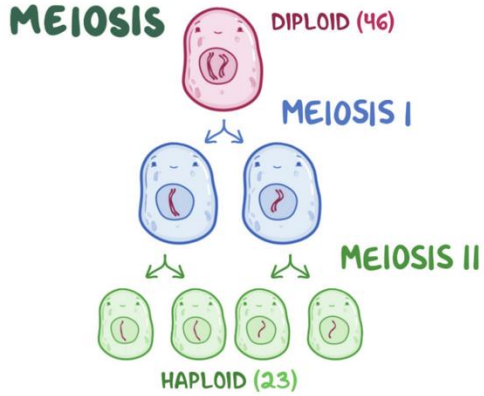


Figure 42.15 Meiosis produces haploid daughter cells with 23 chromosomes each.

- **Meiosis is a type of cell division that produces gametes (sperm and egg cells) , Meiosis reduces the chromosomes number by half (from diploid to haploid), so when sperm and egg combine, the offspring has the correct diploid number.**

- **In males, meiosis is a continuous process that occurs throughout their life after puberty. In females, meiosis begins during fetal development but then it pauses, until puberty, resuming during the menstrual cycle**

- Once the zygot is formed, it then undergoes **mitosis** (growth , baby differentiation)

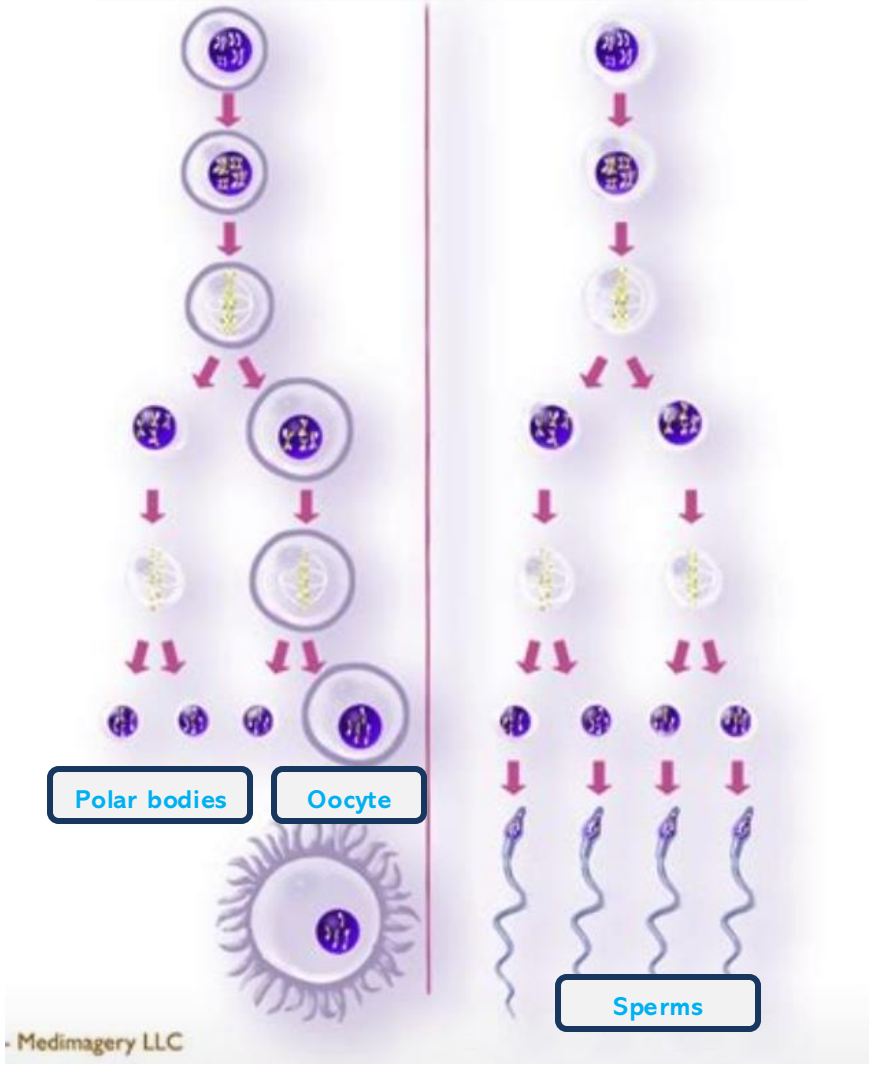
Two cell divisions occur during meiosis.

During **meiosis I**, often called the **reduction division stage,** two haploid cells are formed from a diploid cell. These diploid cells are

- the Oogonia in females (which gives oocytes, Total Cells Produced: 4 cells)
- the spermatogonia in males : (which gives the sperms , Total Cells Produced: 4 cells)

Following meiosis I, a **second meiosis**, the **equational division**, takes place, and each haploid cell is replicated.

Extra image
Oogonia VS Spermatogonia



- **Interphase I**

- The first stage of meiosis is **interphase I**. During this phase, as in mitotic interphase, important processes such as replication of chromosomal DNA take place
- ,

so the genetic material in spermatogonia , oogonia will get replicated (each chromosome will make a copy from itself)

• Prophase I

- The second phase of meiosis I, **prophase I,** begins as the chromatin strands coil and condense, causing them to become visible as chromosomes.
- During a process called **synapsis (crossing-over)** , the homologous chromosomes pair up, side by side, lying together in perfect alignment**. This process doesn't happen in Mitosis .**

Only in meiosis do homologous chromosomes pair; however, when referring to the X and Y chromosomes, they align only at small homologous regions at their tips. Crossing over occurs only in these regions.

- As prophase I continues, the chromatids of the two chromosomes intertwine. Each pair of intertwined homologous chromosomes is called a bivalent (indicating two chromosomes in the unit) or tetrad (indicating four chromatids in the unit).

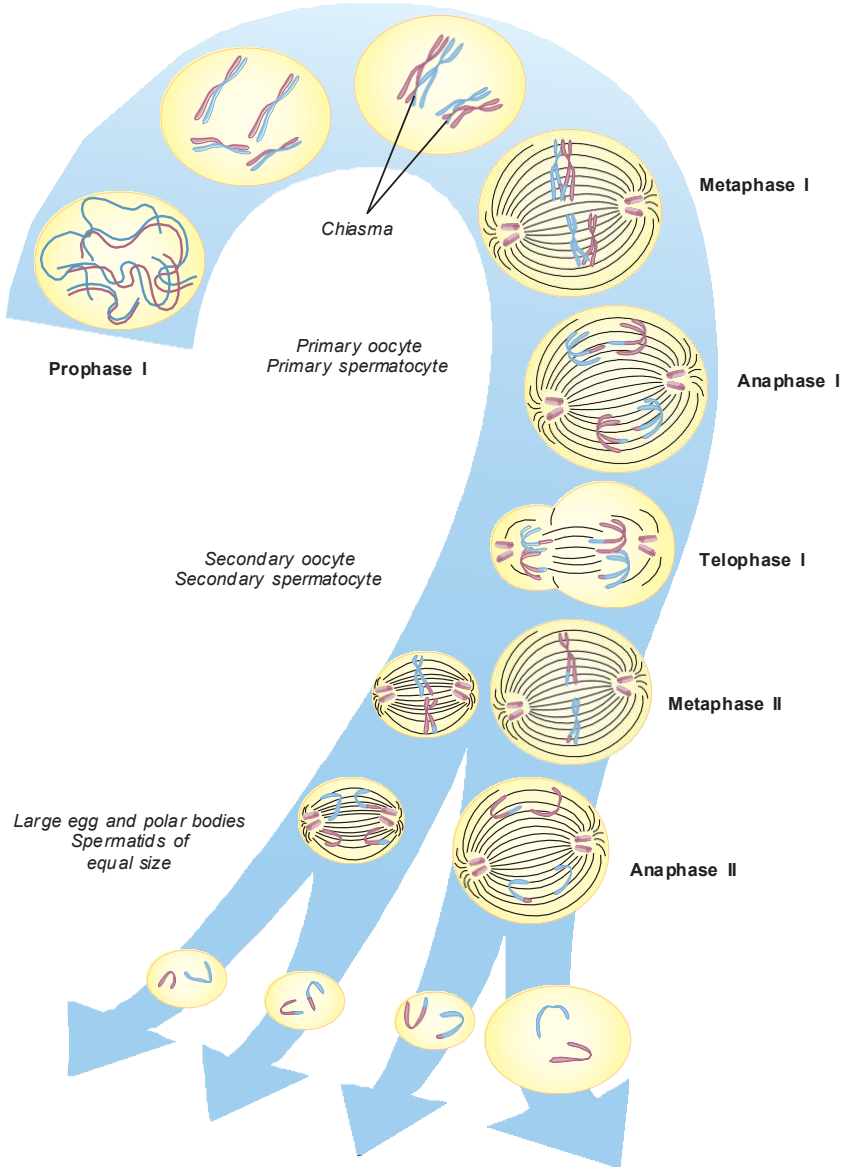


FIG 2-21 The stages of meiosis, during which haploid gametes are formed from a diploid cell. For brevity, prophase II and telophase II are not shown. Note the relationship between meiosis and spermatogenesis and oogenesis.

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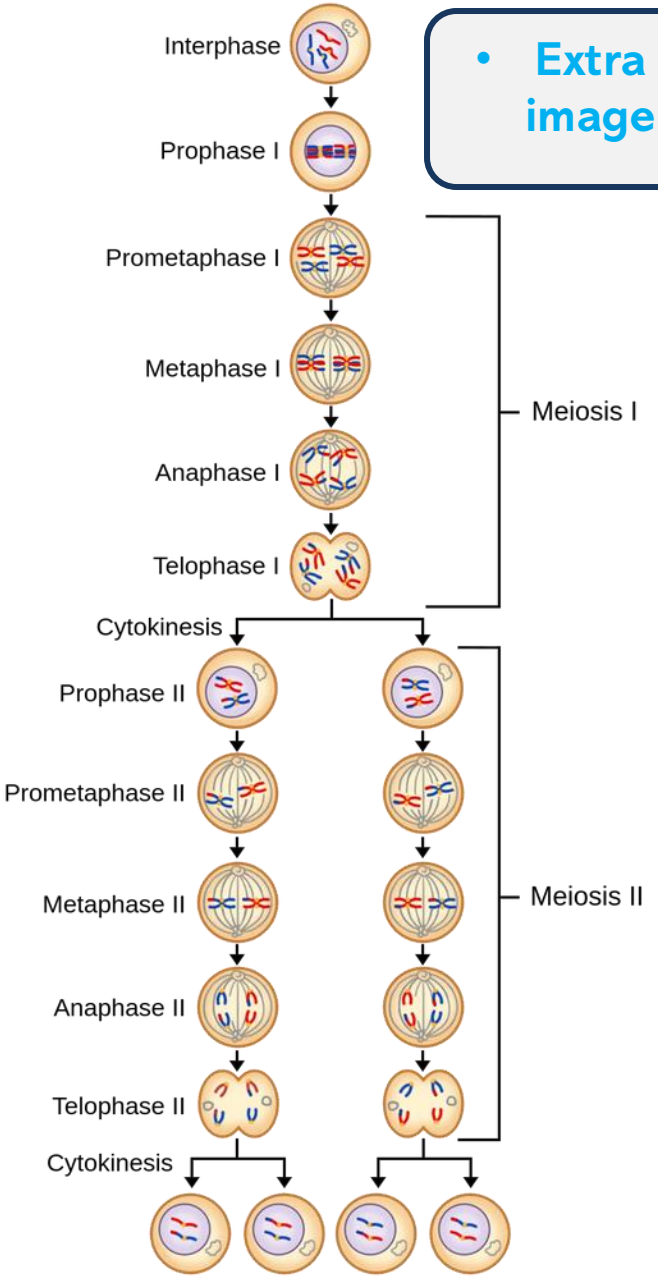
- **Extra image**



- A second key feature of prophase I is the formation of chiasmata(singular of chiasma), cross- shaped structures that mark attachments between the homologous chromosomes.

- This process, called [1]crossing over, produces chromosomes consisting of combinations of parts of the original chromosomes.

- At the end of prophase I, [2] the bivalents begin to move toward the equatorial plane, [3]a spindle apparatus begins to form in the cytoplasm, and [4]the nuclear membrane dissipates.

- During Prophase I of Meiosis I, chiasma formation and crossing over occur, playing a crucial role in genetic variation.
- The process begins with synapsis, where homologous chromosomes (ch 6 with ch 6 , 10 with 10 and so on) pair up, forming a tetrad structure consisting of four chromatids or 2 homologous chromosomes .
- The paired chromosomes align along their length with the help of the synaptonemal complex.
- crossing over takes place as non-sister chromatids exchange genetic material at specific points "Chiasma" .

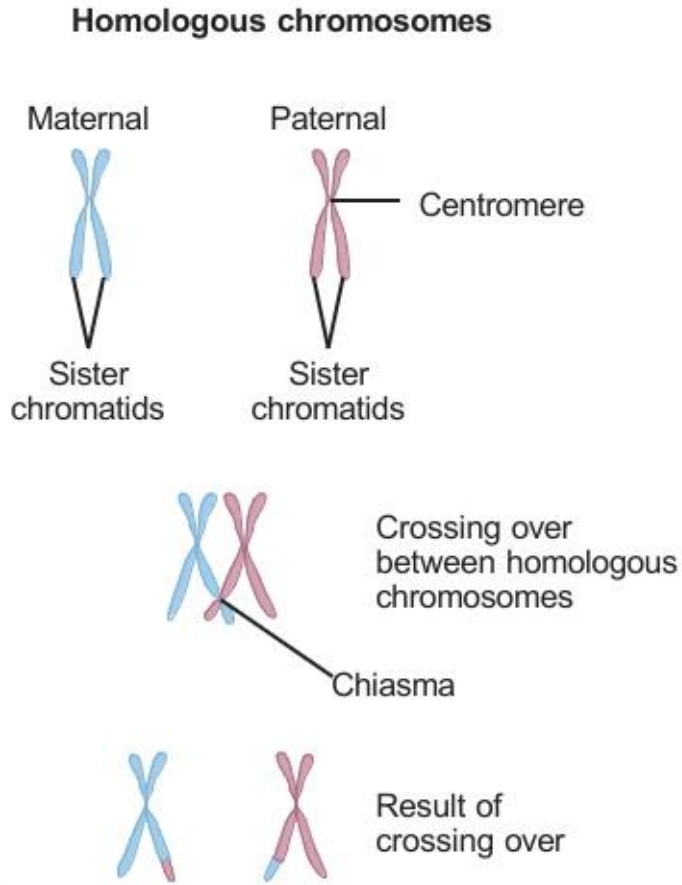
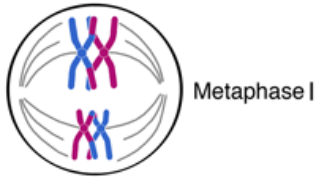


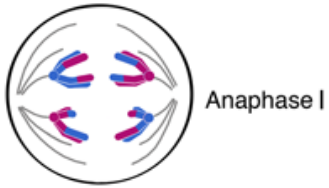
FIG 2-22 The process of chiasma formation and crossing over results in the exchange of genetic material between homologous chromosomes.

• Metaphase I



- Metaphase I is the next phase, this stage is characterized by the completion of spindle formation and the alignment of the bivalents, which are still attached at the chiasmata, in the equatorial plane. The two centromeres of each bivalent now lie on opposite sides of the equatorial plane.

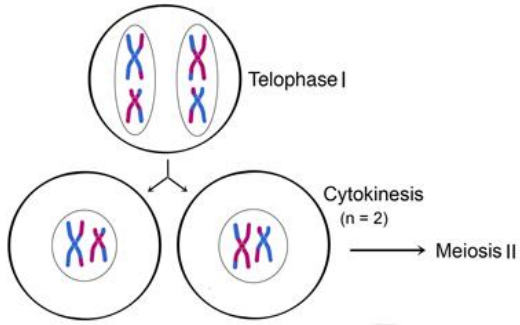
• Anaphase I



- During anaphase I, the next stage, the chiasmata disappear, and **the homologous chromosomes** are pulled by the spindle fibers toward opposite poles of the cell.

- **The key feature of this phase is that, unlike the corresponding phase of mitosis, *the centromeres do not duplicate and divide(don't split)*, so that only half of the original number of chromosomes migrate toward each pole.**

- **Telophase I**

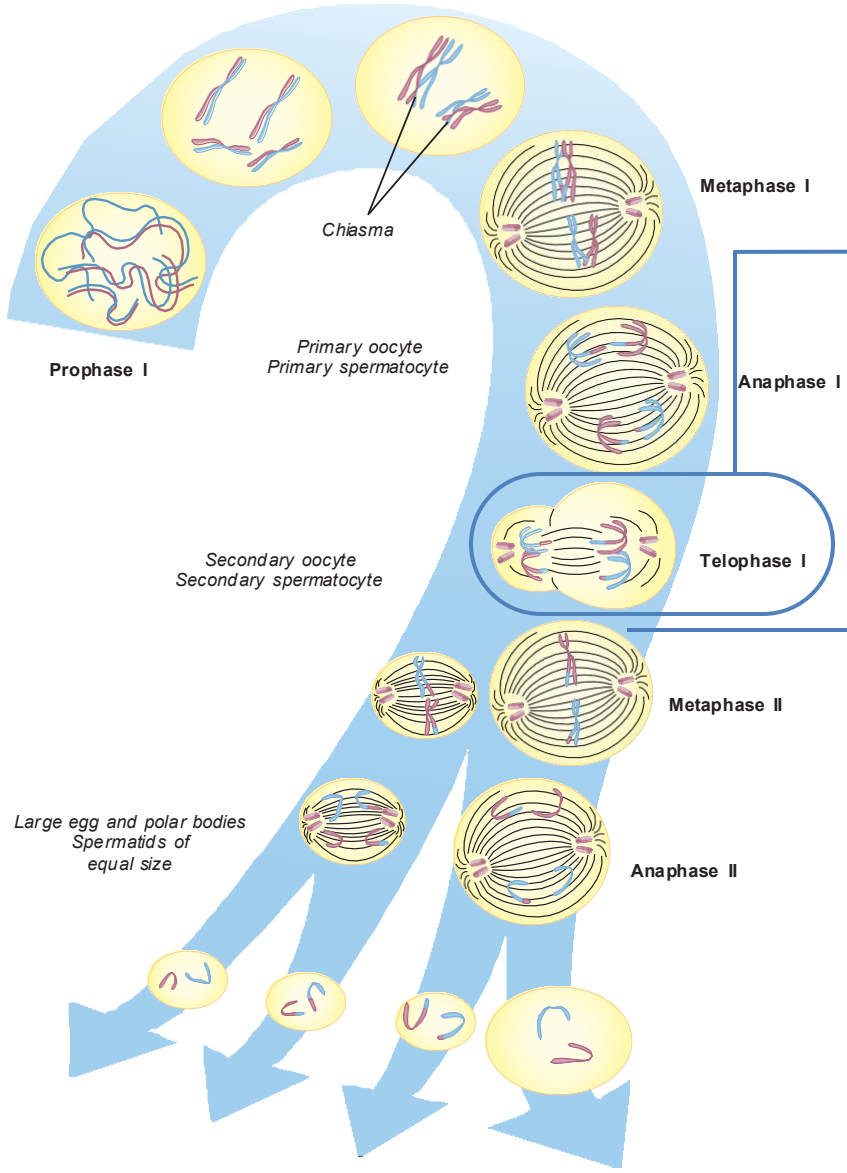


The next stage, **telophase I,** begins when the chromosomes reach opposite sides of the cell. The chromosomes uncoil slightly (returns to their thread-like structure), and a new nuclear membrane begins to form. The two daughter cells each contain the **haploid number of chromosomes (23), each having two sister chromatids.**

In humans, **cytokinesis** also occurs during this phase. The cytoplasm is divided approximately equally between the two daughter cells in the gametes formed in **males.** (Reduction division)

In those formed in **females**, nearly all of the cytoplasm goes into one daughter cell (not equally), which will later form the egg that will be fertilised. The other daughter cell becomes a polar body, a small nonfunctional cell that eventually degenerates.

• Check slide 11



- In spermatogenesis, cell division is symmetrical after telophase, resulting in two equal cells.
- In oogenesis, cell division is asymmetrical, producing one larger cell and a smaller one.

Unlike mitosis, between telophase I and metaphase II there is no DNA replication in prophase.

FIG 2-21 The stages of meiosis, during which haploid gametes are formed from a diploid cell. For brevity, prophase II and telophase II are not shown. Note the relationship between meiosis and spermatogenesis and oogenesis.

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• Meiosis II

1. The equational division, **meiosis II**, then begins with **interphase II.** This is a very brief phase. The important feature of interphase II is that, ***no replication*** *of DNA occurs.*

2. Prophase II, similar to mitotic prophase, except that the cell nucleus contains only the haploid number of chromosomes. During prophase II the chromosomes thicken as they coil, the nuclear membrane disappears, and new spindle fibers are formed.

3. Following this phase is metaphase II, during which the spindle fibers pull the chromosomes into alignment at the equatorial plane.

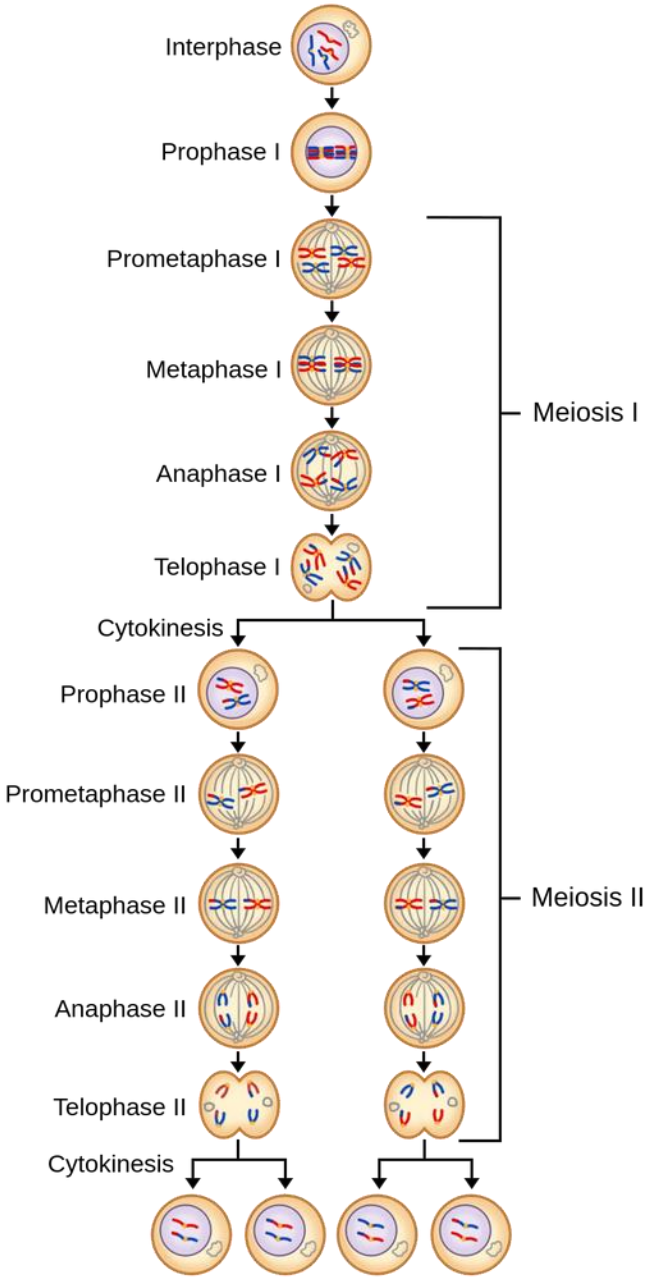
4. Anaphase II then follows. This stage resembles mitotic anaphase in that the centromeres split, each carrying a single chromatid toward a pole of the cell.

- Two new gametes are produced, and since we initially had two, the total number becomes four.

- 5. Telophase II, like telophase I, begins when the chromosomes reach opposite poles of the cell. There they begin to uncoil. New nuclear membranes are formed around each group of chromosomes, and cytokinesis occurs.

- In gametes formed in males, the cytoplasm is again divided **equally** between the two daughter cells. The end result of male meiosis is thus four functional daughter cells, each of which has an equal amount of cytoplasm.

- In female gametes, **unequal** division of the cytoplasm again occurs, forming the egg cell and another polar body.



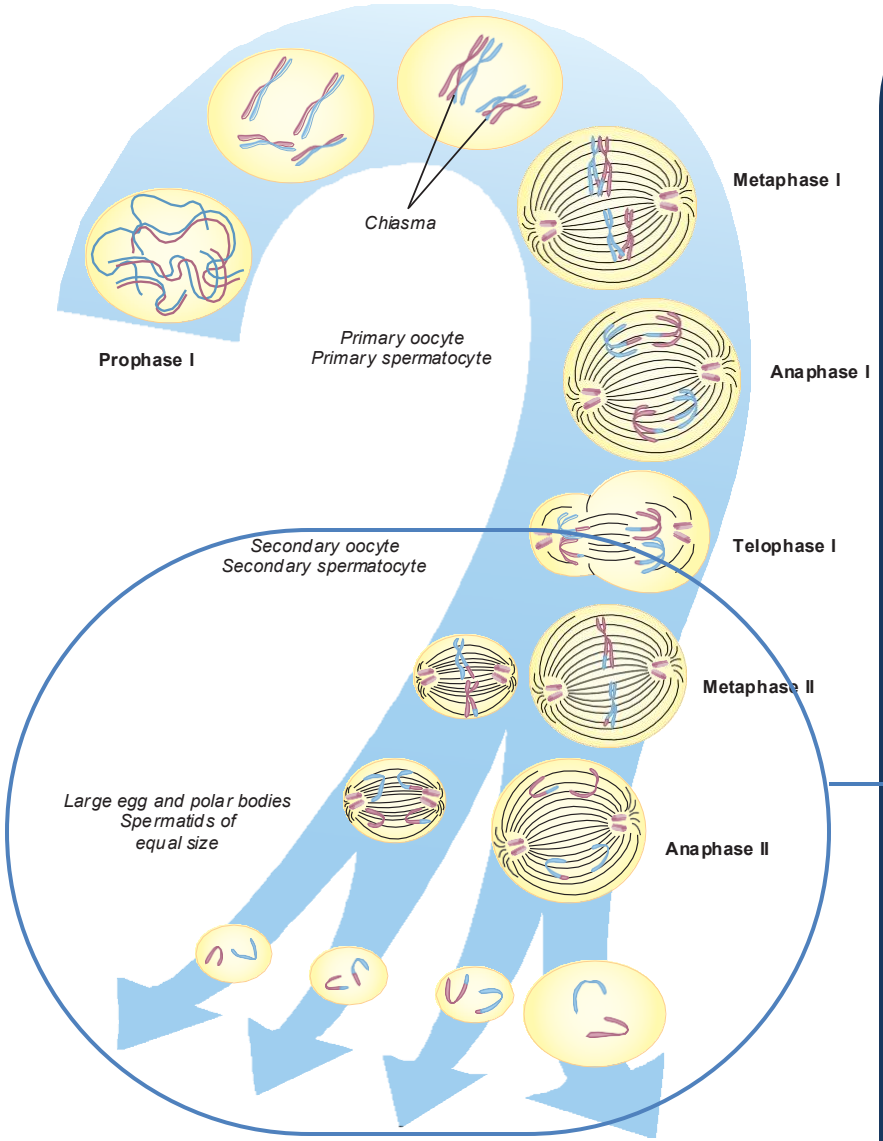


FIG 2-21 The stages of meiosis, during which haploid gametes are formed from a diploid
For brevity, prophase II and telophase II are not shown. Note the relationship between me
and spermatogenesis and oogenesis.

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- **In Metaphase II:The chromosomes align at the center of the cell.**
- **In Anaphase II: The chromosomes separate and move toward opposite poles of the cell.**
- **In Telophase II:**

- In spermatogenesis: the cell divides equally, resulting in four haploid spermatids.

- In oogenesis: the polar body divides into two smaller polar bodies, while the oocyte divides into a secondary oocyte (which matures into an egg) and a polar body. The polar bodies will eventually degenerate, and the one mature egg is released during ovulation.

Extra summary tables

Stage	Description	Outcome
Interphase I	Chromosomal DNA replication occurs in oogonia and spermatogonia, forming identical copies of each chromosome.	Chromosomes duplicate (2n)
Prophase I	Chromosomes condense and become visible. Homologous chromosomes undergo **synapsis** and form **tetrads**. Crossing-over occurs at **chiasmata**, exchanging genetic material.	Genetic variation introduced
Anaphase I	Homologous chromosomes are pulled to opposite poles without centromere division.	Two haploid cells (n) are formed
Metaphase I	Bivalents align at the equatorial plane, with spindle fibers attached to centromeres.	Homologous chromosomes prepare to separate
Telophase I & Cytokinesis	Chromosomes uncoil slightly, nuclear membrane reforms, and cytoplasm divides. In females, most cytoplasm goes into one daughter cell, forming a primary oocyte, while the other becomes a **polar body**.	Two haploid cells (n) with duplicated chromatids

Meiosis II (Equational Division)	**Similar to mitosis, sister chromatids separate without further chromosome duplication.**	**Four haploid daughter cells**
Interphase II	A brief phase where **no DNA replication** occurs, unlike Interphase I.	Preparation for Meiosis II
Prophase II	Chromosomes thicken, nuclear membrane dissolves, and spindle fibers form, similar to mitotic prophase but with the **haploid number of chromosomes**.	Chromosomes prepare for alignment
Metaphase II	Spindle fibers align chromosomes at the equatorial plane.	Chromosomes ready to separate
Anaphase II	The centromeres split, and each centromere carries a single chromatid toward a pole of the cell. This process is similar to mitotic anaphase.	Chromatids are separated and pulled to opposite poles
Telophase II & Cytokinesis	Chromosomes uncoil, nuclear membranes reform, and cytoplasm divides equally in males, producing **four sperm cells**. In females, unequal division produces **one egg cell** and **three polar bodies**.	Two new gametes are produced, and since we initially had two, the total number becomes four.

The Relationship Between Meiosis and Gametogenesis

In mature males, the seminiferous tubules of the testes are populated by spermatogonia (الخلية الأم) which are diploid cells. Like stem cells in the bone marrow or any other tissue, they divide and produce cells.

- After going through several mitotic divisions, the spermatogonia produce primary spermatocytes.
- Each primary spermatocyte, which is also diploid, undergoes meiosis I to produce a pair of secondary spermatocytes, each of which contains 23 double stranded chromosomes.
- These undergo meiosis II, and each produces a pair of spermatids that contain 23 single-stranded chromosomes. 4 spermatids in total from one primary spermatocyte

The spermatids then lose most of their cytoplasm and develop tails for swimming as they become mature sperm cells. This process, known as **spermatogenesis** (formation of sperms), continues throughout the life of the mature male.

Spermatids = immature sperms

We will study abnormalities such as replication errors and new mutations that occur when a man decides to have children after the age of 50, 55, or 60. At this stage, the risk of new mutations in his children increases significantly.Why?

Because sperm cells become "aged," with a defective gene repair mechanism, despite their continuous regeneration. Over time, accumulated replication errors and diminished DNA repair efficiency contribute to a higher likelihood of mutations. We will discuss this in details later.

Oogenesis, the process in which female gametes (haploid) are formed, differs in several important ways from spermatogenesis. Whereas the cycle of spermatogenesis is constantly recurring in males, much of female oogenesis is completed before birth.

Please go to the next slide for a better understanding

- Diploid oogonia divide mitotically to produce primary oocytes by the third month of fetal development.
- More than 2 million primary oocytes are formed during gestation, and these are suspended in prophase I by the time the female is born.
- Meiosis continues only when a mature primary oocyte is ovulated.
- In meiosis I, the primary oocyte produces one secondary oocyte (containing the cytoplasm) and one polar body.
- The secondary oocyte then emerges from the follicle and proceeds down the fallopian tube, with the polar body attached to it.
- **Meiosis II begins only if the secondary oocyte is fertilized by a sperm cell.** If this occurs, one haploid mature ovum, containing the cytoplasm, and another haploid polar body are produced.

Oogenesis begins before female birth and pauses at a specific stage of development. It resumes when the female reaches adulthood and menstrual cycle begins. The completion of meiosis I occurs during each menstrual cycle. If fertilization takes place, meiosis II is completed; if fertilization does not occur, meiosis II does not proceed.
During embryogenesis, oocytes develop, and females are born with a **finite** reserve of approximately 2 million or more oocytes. These oocytes remain suspended throughout the female's life until the female reaches maturity. Upon maturation, oocytes are released and they complete their cell division during the menstrual cycle.

Now, go back to the previous slide :)

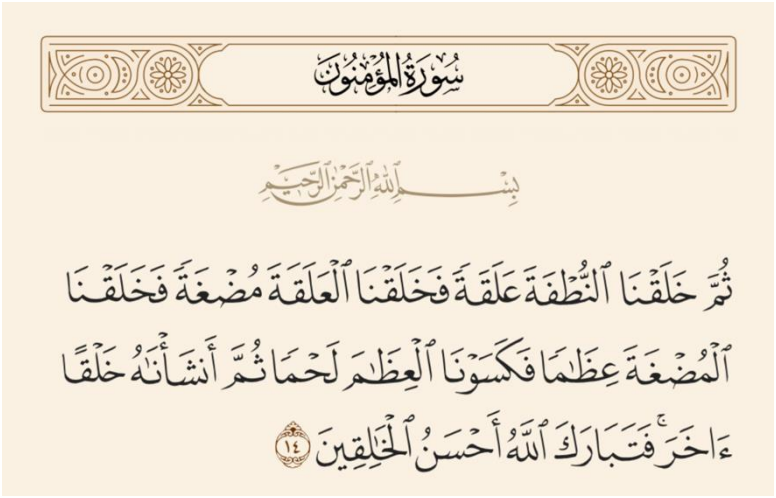
- When studying genetic abnormalities, you will observe that many genetic disorders result from "nondisjunction" This occurs due to one of two main reasons:
- 1.Early maternal age: If a female marries at a very young age (e.g., 14 or 15 years old), her oocytes may not be fully mature or ready for fertilization.
- 2.Advanced maternal age: If a female decides to have a child after the age of 40, her oocytes are considered significantly aged.

Extra summary

	Spermatogonia	Oogonia
Timing	Begins at puberty and continues throughout life . Continuous process, producing new sperms regularly.	Begins during fetal development and pauses until puberty Discontinuous, with long pauses (e.g., primary oocytes are arrested in prophase I until ovulation).
location	Occurs in the seminiferous tubules of the testes.	Occurs in the ovaries
Completion of Meiosis	Meiosis I and II are completed continuously in the testes.	Meiosis I completes at ovulation, while Meiosis II completes only if fertilization occurs.
Cytokinesis	Equal division of cytoplasm, producing four small, motile sperms.	Unequal division, with most cytoplasm retained by the ovum and polar bodies receiving minimal cytoplasm.
Outcome	Each primary spermatocyte (diploid) produces four haploid spermatids, which mature into sperm.	Each primary oocyte (diploid) produces one functional ovum (haploid) and three polar bodies, which degenerate.

Additional sources

1. Book pages
2. Science bites: mitosis
3. Science bites: meiosis
4. Osmosis



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	23	2n -→ 4n	2n the chromosomes are still joined as sister chromatids, so the number of chromosomes doesn't change.
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!