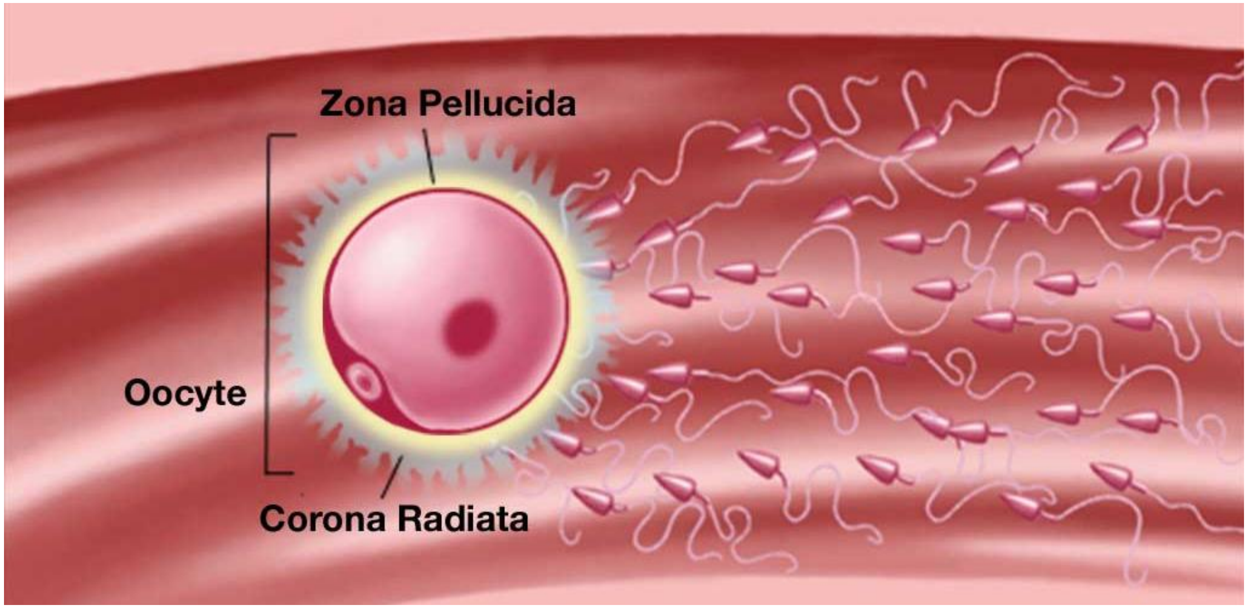
Gametogenesis
Spermatogenesis vs. Oogenesis



Gametogenesis

- The process whereby haploid gametes (reproductive sex cells) are created.
  - Spermatogenesis in males
  - Oogenesis in females

SOME TERMS

Gamete: egg or sperm
Gametogenesis: production of eggs or sperm
Oogenesis: production of eggs
Spermatogenesis: production of sperm
Spermiogenesis: differentiation of sperm morphology
Follicle: where eggs mature in the ovary
Ovulation: release of egg from follicle
Polar body: nonfunctional product of meiotic
divisions in oogenesis
Zygote: Fertilized egg

Mammalian gametes

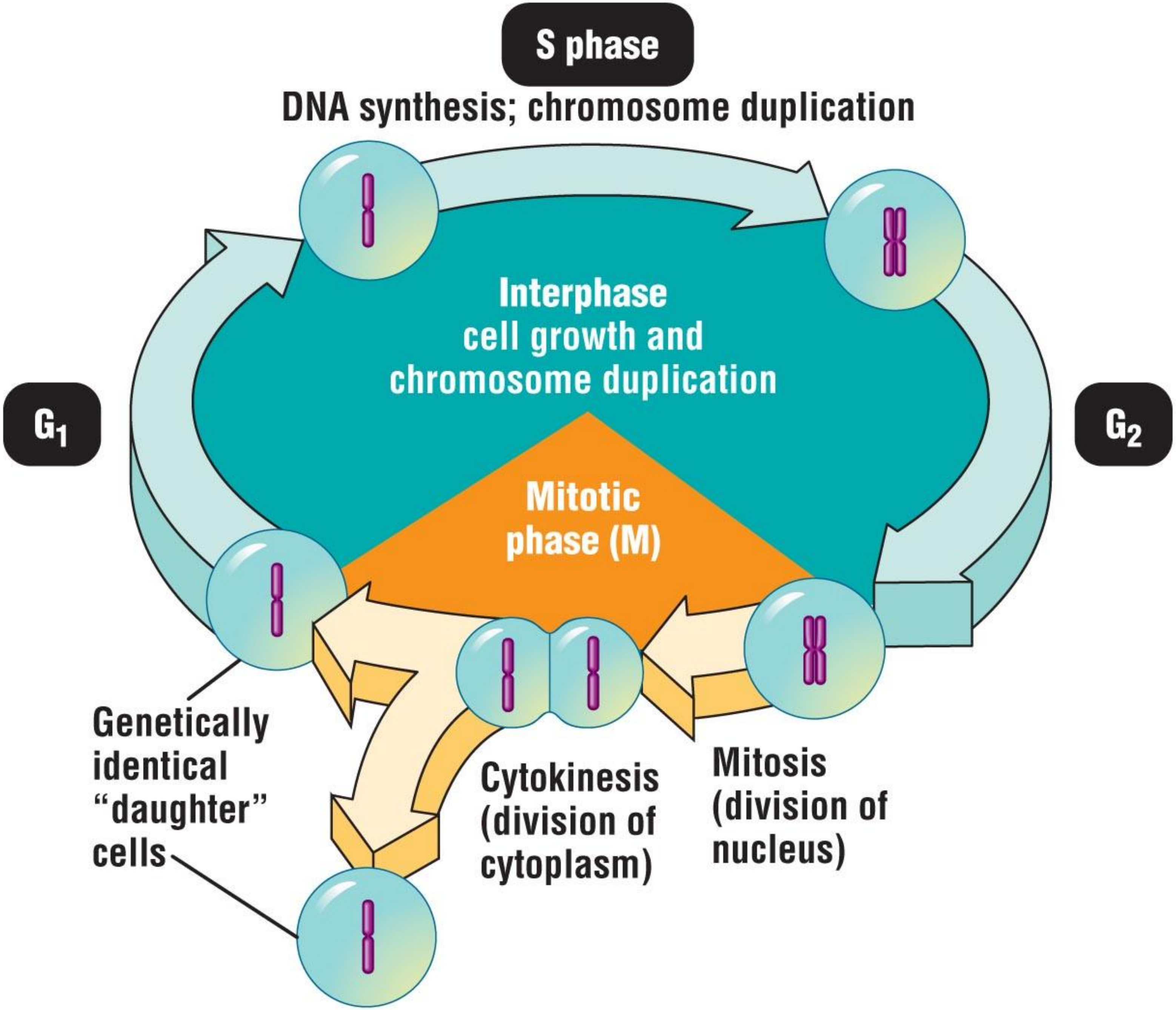
- Both mitosis and meiosis play a role in gametogenesis.
- Mitosis provides the precursor cells. Meiosis brings about the reduction divisions that result in gametes

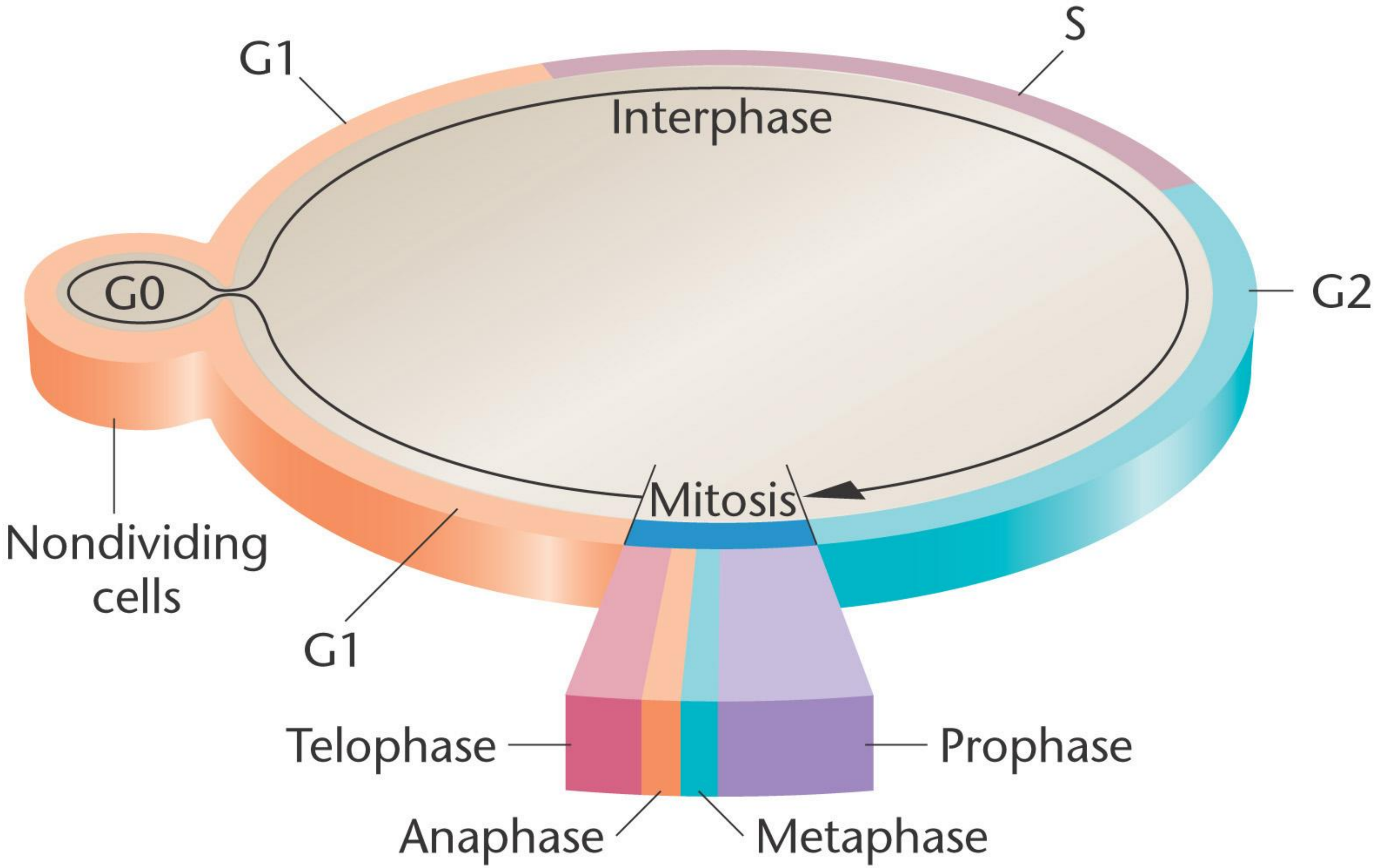
- Special cells, primordial germ cells, in the gonads divide, grow, divide again and then differentiate into the gametes.

- Sperm produced in testes, Ova produced in the ovaries

Mammalian gametes

- In human males gametogenesis continues constantly from puberty.
- In females the mitotic divisions take place before birth.
- The meiotic divisions take place in a few oocytes each monthly cycle from puberty to menopause


S phase
DNA synthesis; chromosome duplication
Interphase
cell growth and
chromosome duplication
G1
G2
Mitotic
phase (M)
Genetically
identical
“daughter”
cells
Cytokinesis
(division of
cytoplasm)
Mitosis
(division of
nucleus)



The phases of the cell cycle. Following mitosis (M), cells enter the G1 stage of interphase, initiating a new cycle. Cells may become nondividing (G0) or continue through G1, where they become committed to begin DNA synthesis (S) and complete the cycle (G2 and M). Following mitosis, two daughter cells are produced and the cycle begins anew for each cell.

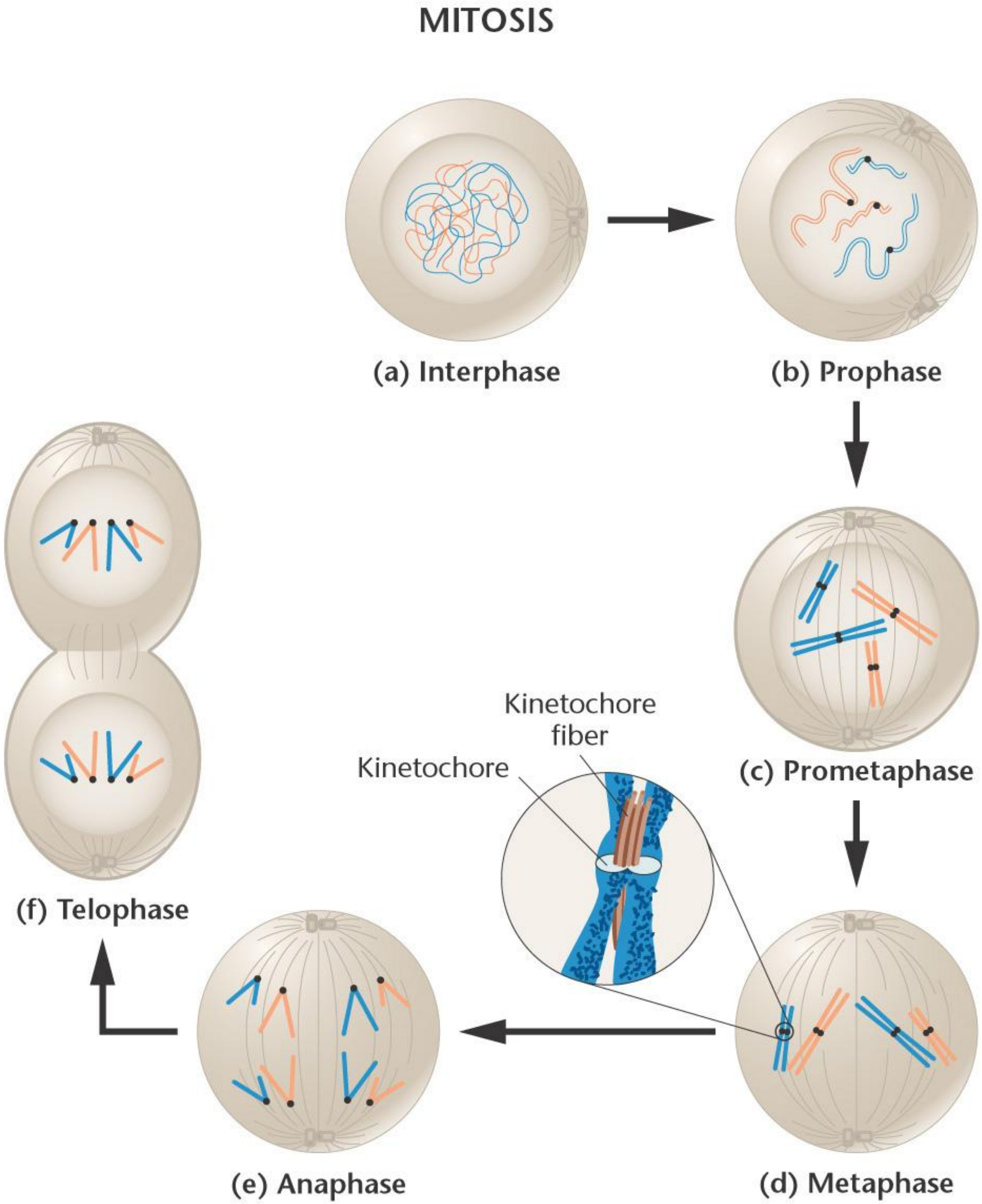
Interphase			Mitosis
G1	S	G2	M
5	7	3	1

Hours

Pro	Met	Ana	Tel
36	3	3	18

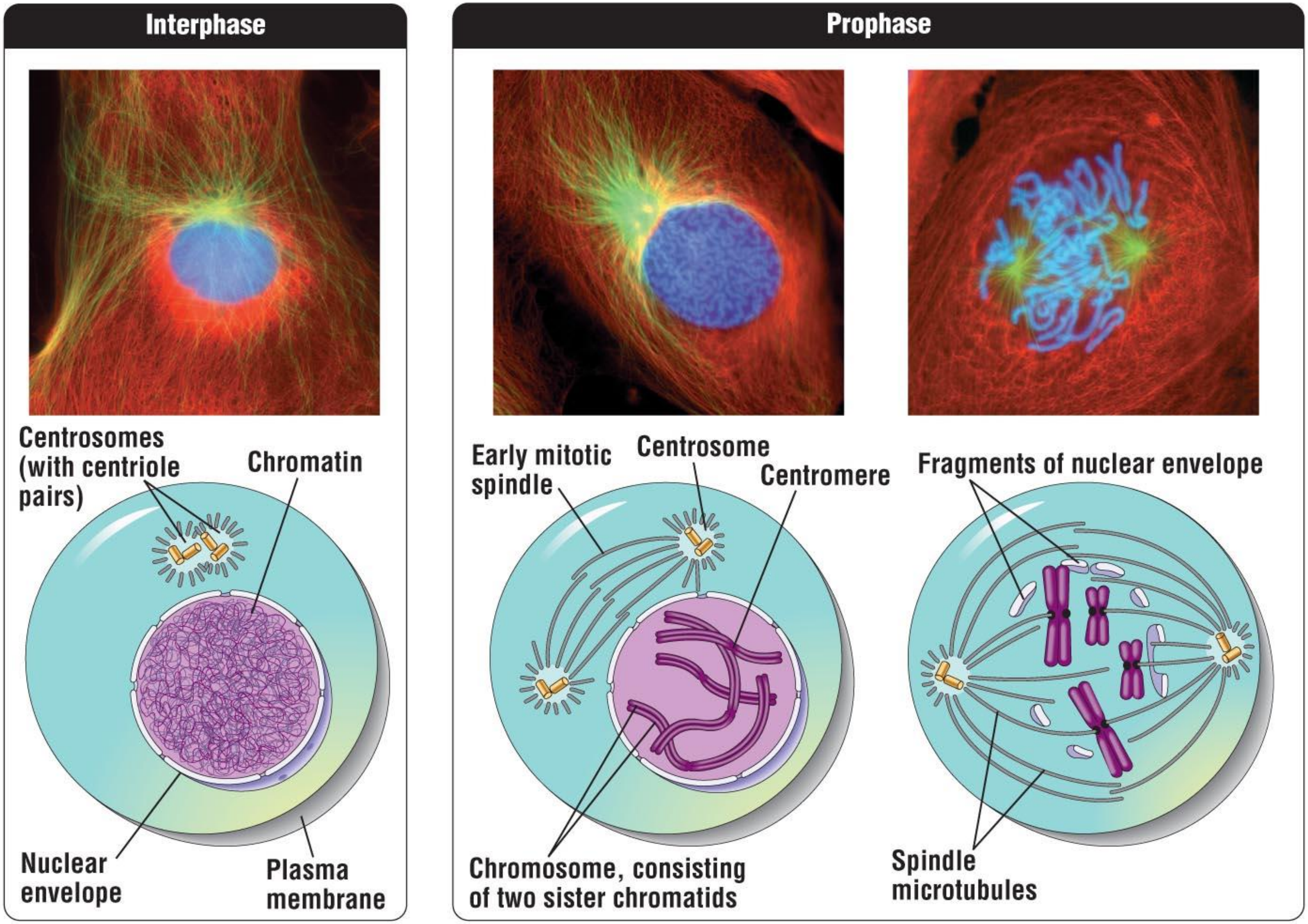
Minutes

The length of time spent in each phase of one complete cell cycle of a human cell in culture. Actual times vary according to cell types and conditions.



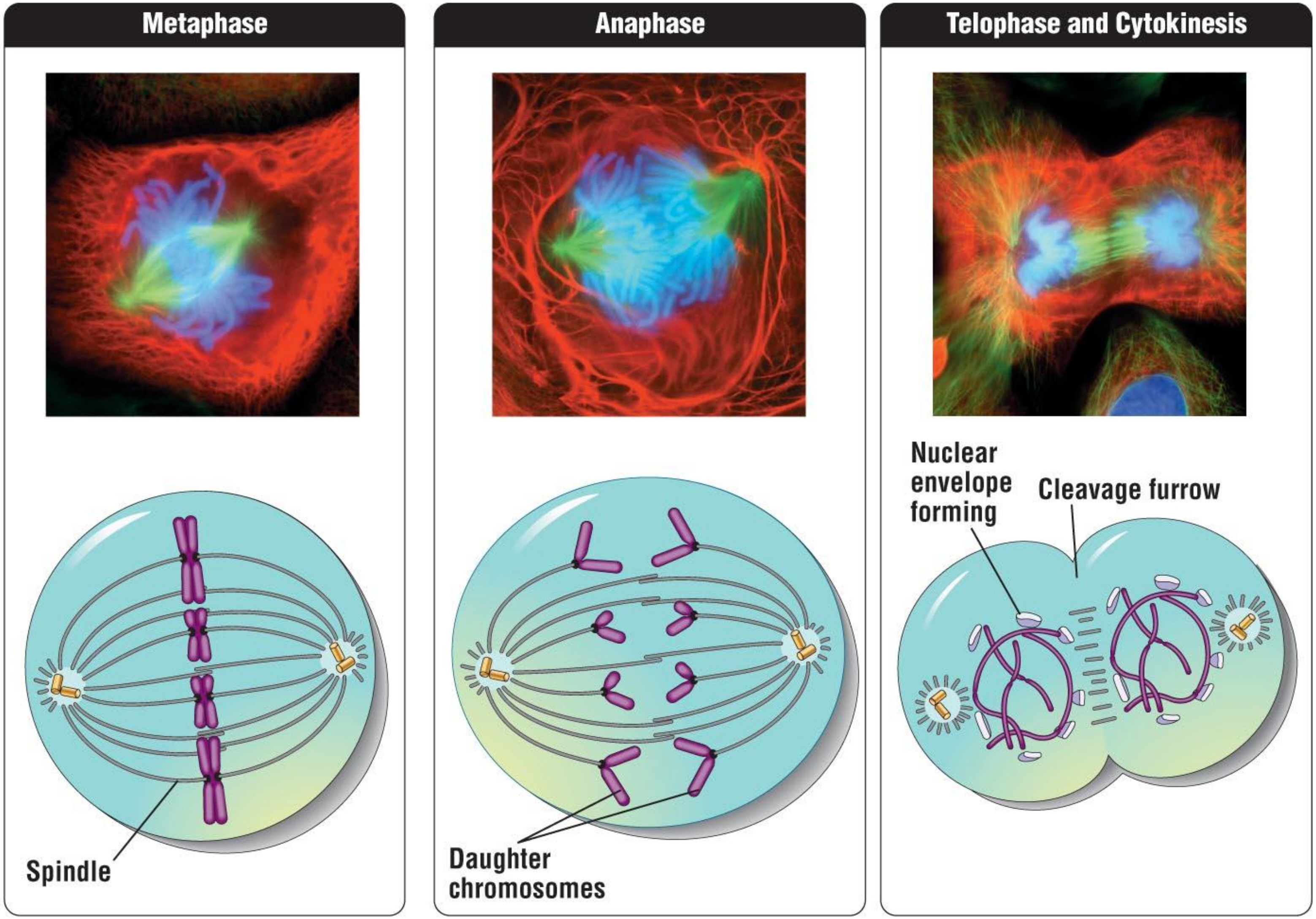
Of the two homologous pairs of chromosomes, one contains longer, metacentric arms and the other, shorter, submetacentric arms. The maternal chromosome and paternal chromosome of each pair are shown in different colors.

Prophase: The DNA recoils, and the chromosomes condense; the nuclear membrane disappears, and the mitotic spindles begin to form.



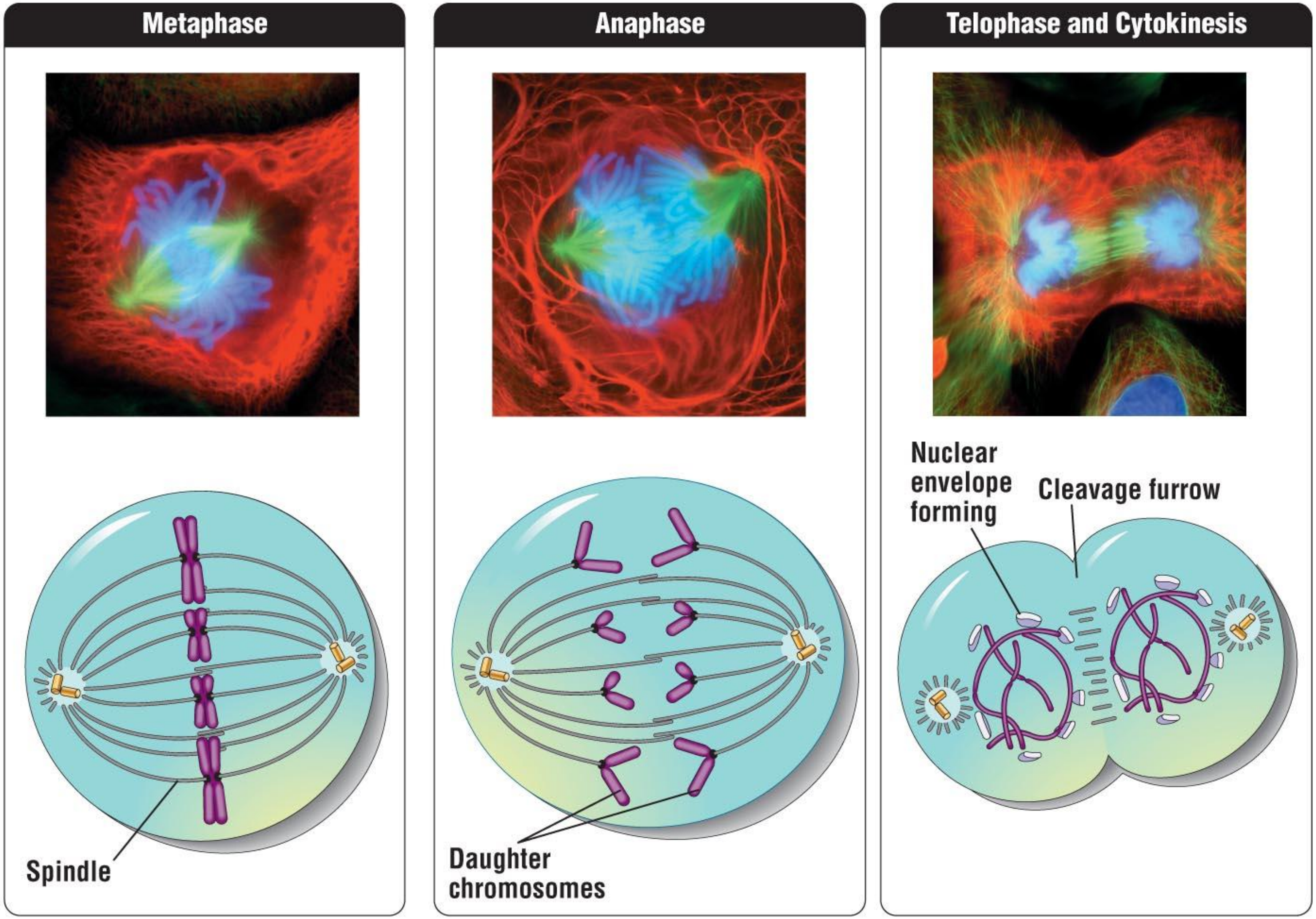
MITOSIS steps 0-1 – Interphase and Prophase

Metaphase: The chromosomes line up the middle of the cell with the help of spindle fibers attached to the centromere of each replicated chromosome.



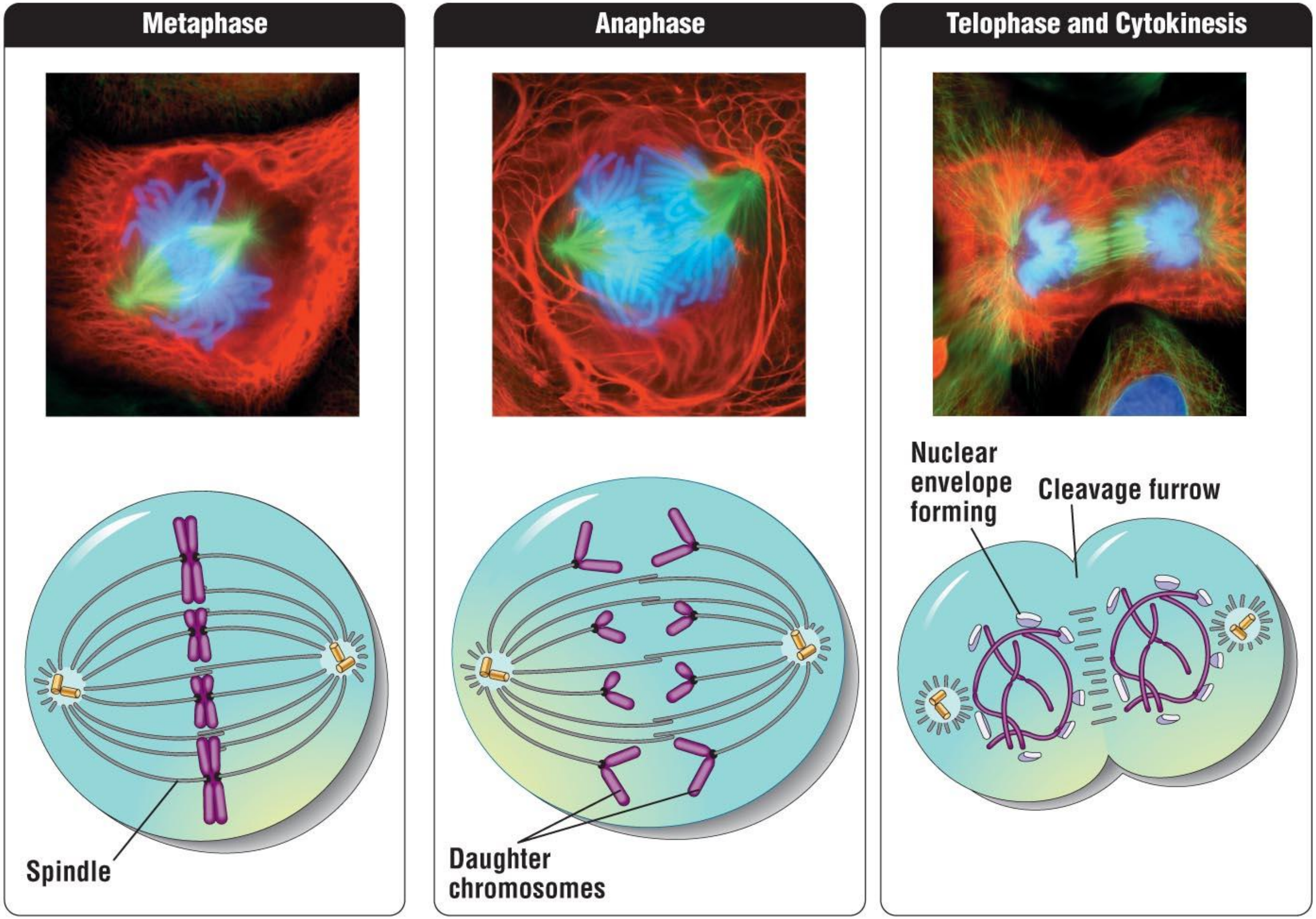
MITOSIS steps 2-4– Metaphase, Anaphase, Telophase

Anaphase: The chromosomes split in the middle and the sister chromatids are pulled by the spindle fibers to opposite poles of the cell. .



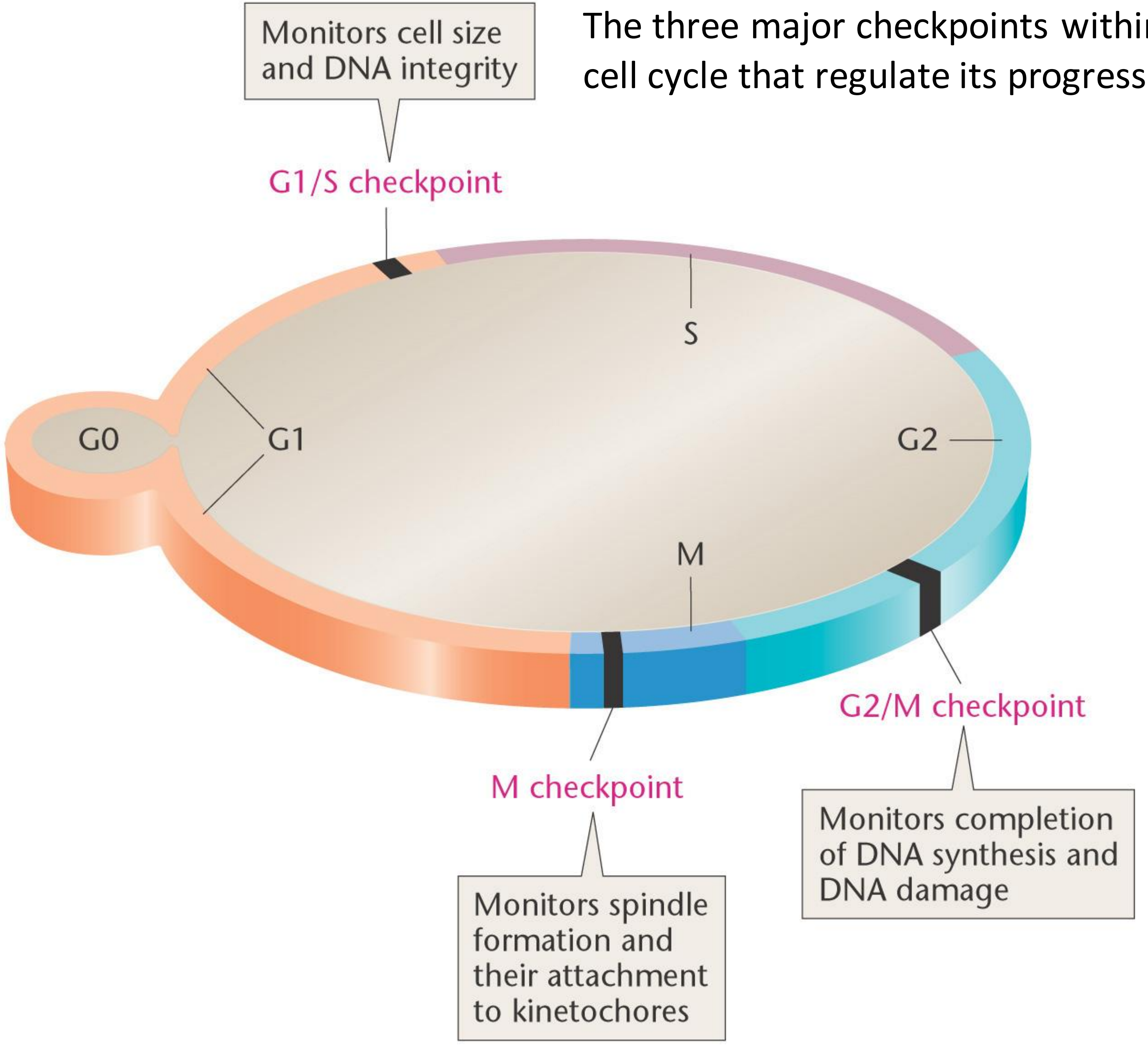
MITOSIS steps 2-4– Metaphase, Anaphase, Telophase

Telophase: The chromosomes, along with the cytoplasm and its organelles and membranes are divided into 2 portions. This diagram shows the end of telophase. The actual splitting of the daughter cells into two separate cells is called <u>cytokinesis.</u>



MITOSIS steps 2-4– Metaphase, Anaphase, Telophase

The three major checkpoints within the cell cycle that regulate its progress.

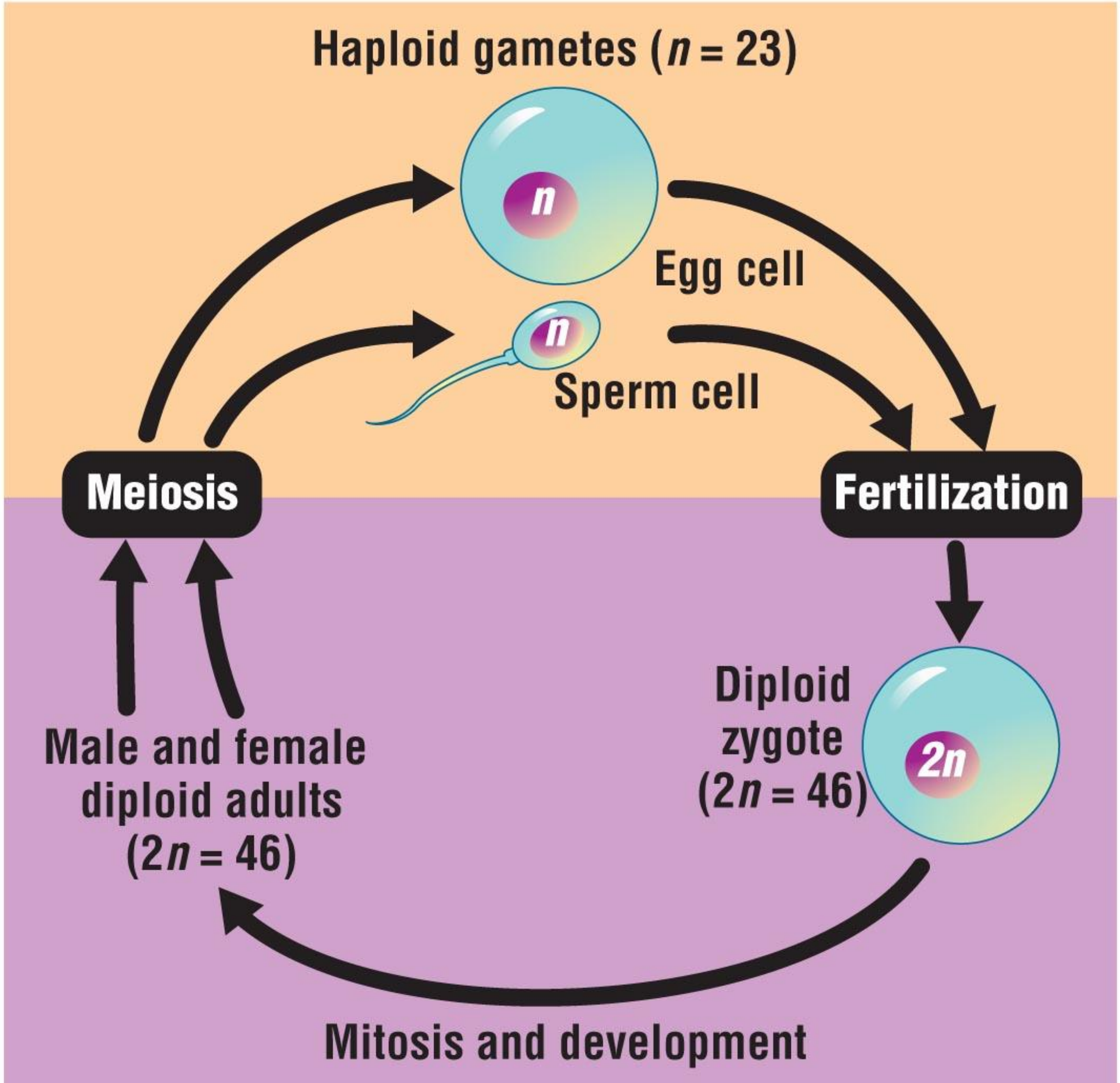


MEIOSIS

- MAKING REPRODUCTIVE CELLS (SPERM AND EGG) in reproductive organs (testis, ovary)
- SIMILAR TO MEIOSIS BUT TWO STEPS, the idea is to reduce a double set to single –

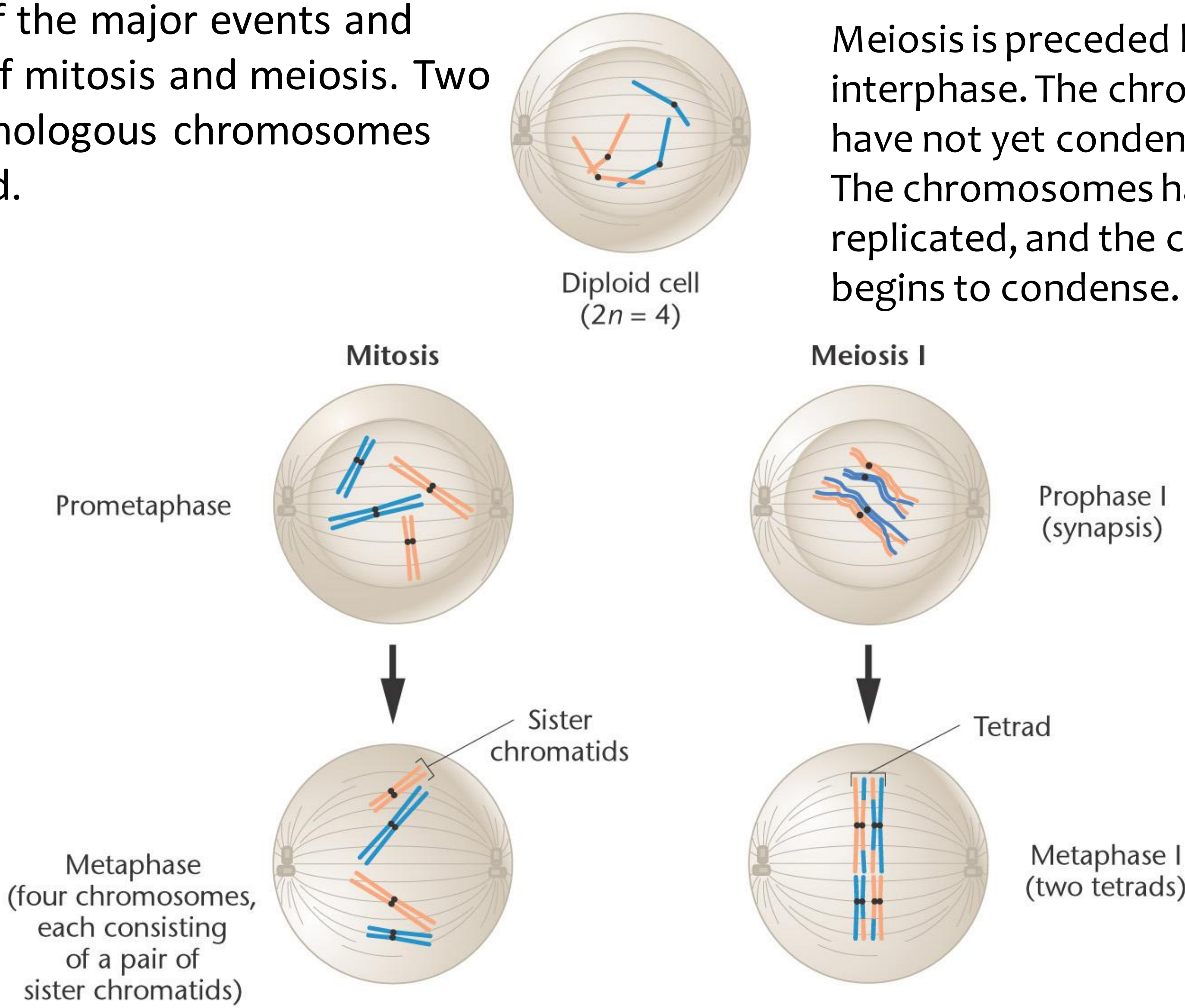
so single sets from two parents can join in fertilization to produce baby's double set

Human Life Cycle



Overview of the major events and outcomes of mitosis and meiosis. Two pairs of homologous chromosomes are followed.

Meiosis is preceded by interphase. The chromosomes have not yet condensed. The chromosomes have replicated, and the chromatin begins to condense.



Prophase I: The chromosomes are completely condensed. In meiosis (unlike mitosis), the homologous chromosomes pair with one another

Metaphase I: The nuclear membrane dissolves and the homologous chromosomes attach to the spindle fibers. They are preparing to go to opposite poles.

The substages of meiotic prophase I

Leptotene

Chromosomes start to condense, dyads (replicated chromosomes) of homologous pairs first become visible as linear strings of DNA

Zygotene

Chromosomes condense further. Dyads of homologous pairs of chromosomes pair-up and their chromatids start to undergo synapsis.

Pachytene

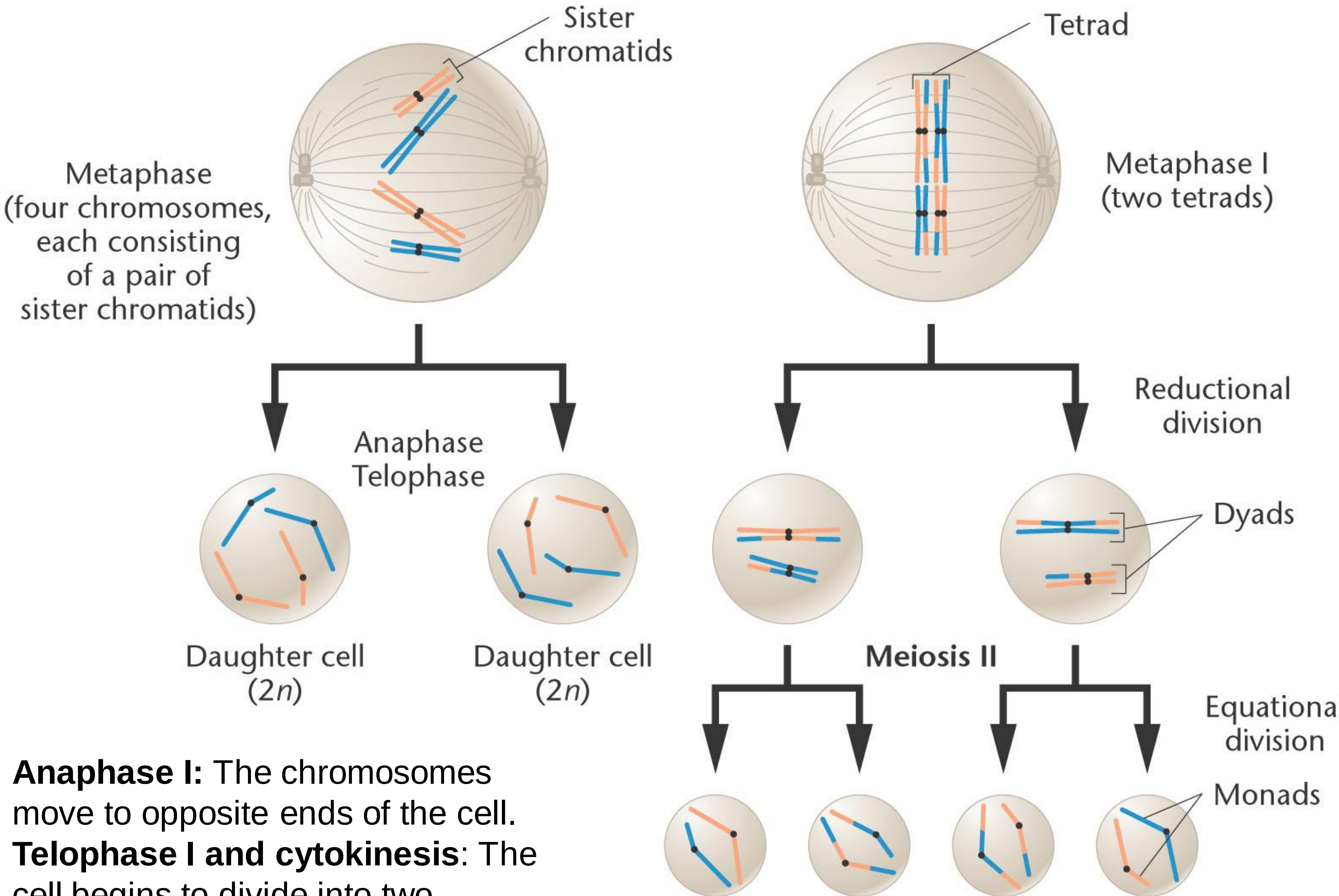
Synapsis is completed with synapsed chromosomes forming tetrads. Cross-over takes place. Synapsed chromosomes thicken up (pachy - thick).

Diplotene

Chromosomes condense further, Desynapsis begins. Chromatids of homologous pairs of chromosomes remain connected at chiasmata where cross-over may have occurred.

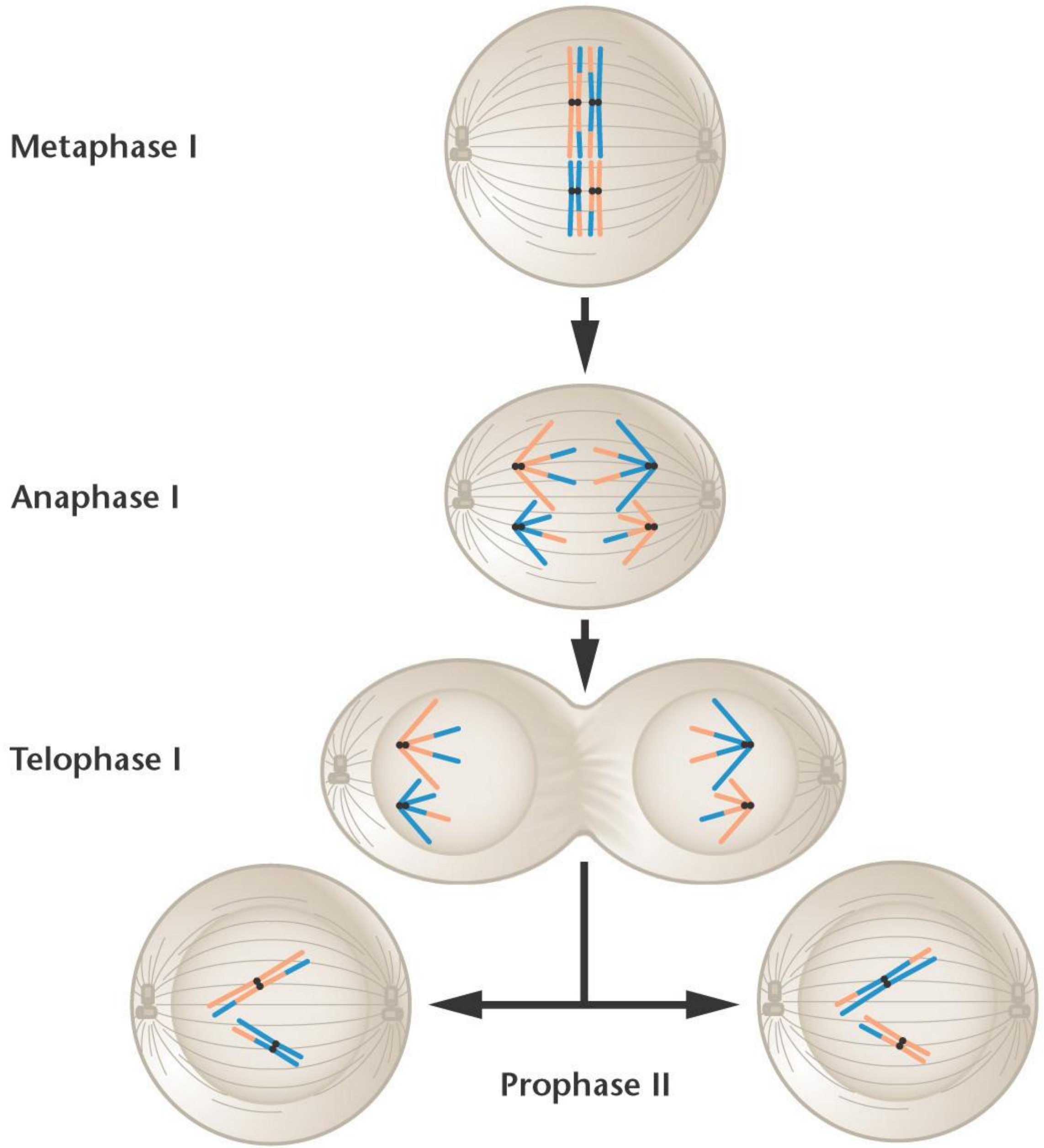
Diakinesis

Chromosomes condense even further. Separating tetrads form strange shapes like crosses, fish, infinity signs as chiasmata move toward the ends of the paired chromatids of the homologous chromosomes (called terminalization). Eventually desynapsis is completed and the homologues separate from one and other completely and metaphase begins.



Anaphase I: The chromosomes move to opposite ends of the cell. **Telophase I and cytokinesis**: The cell begins to divide into two daughter cells.

The major events during meiosis in an animal with a diploid number of 2n = 4 beginning with metaphase I. The combination of chromosomes in the cells produced following telophase II depends on the random alignment of each tetrad and dyad on the metaphase plate during metaphase I and metaphase II. Several other combinations (not shown) can also be formed.

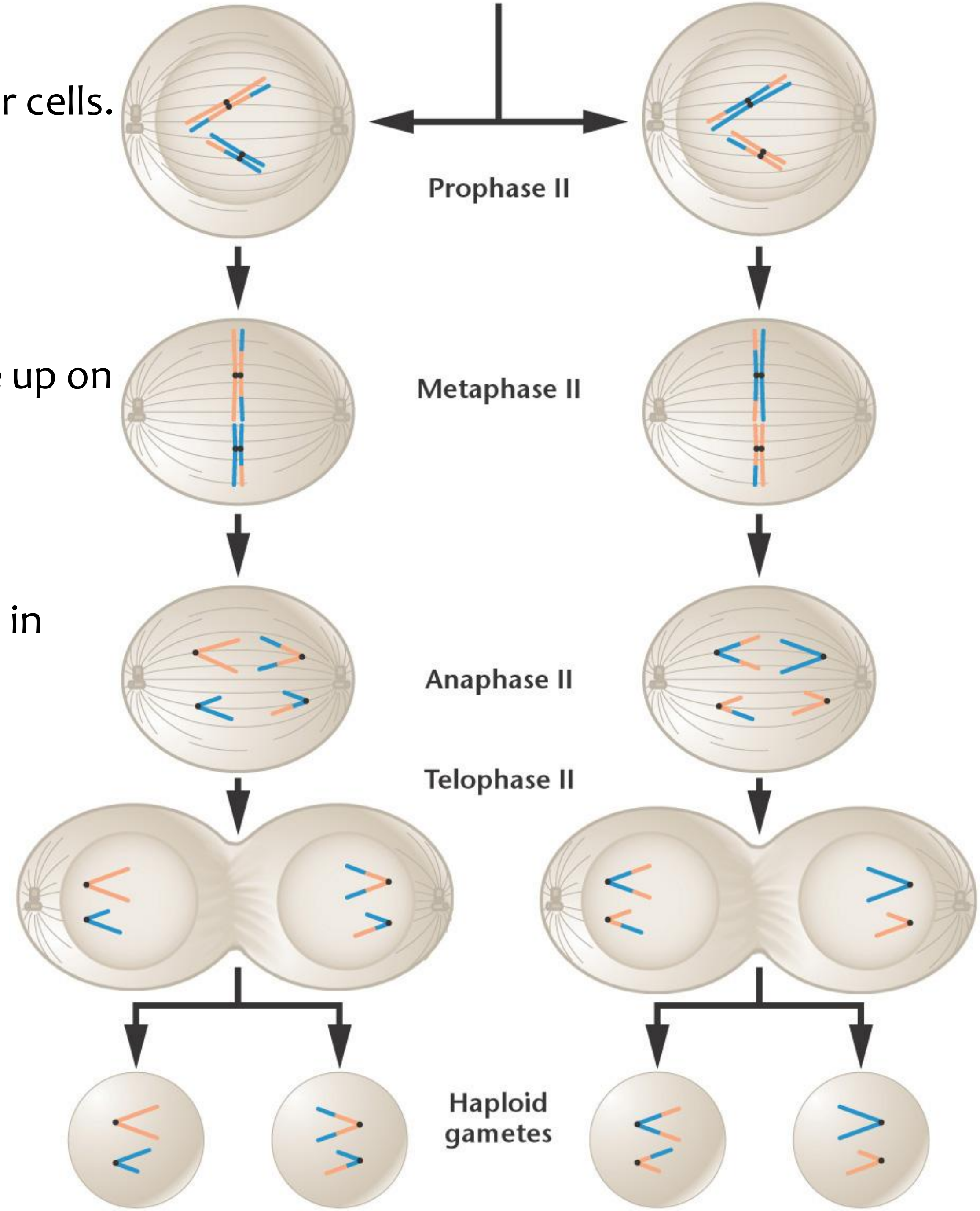


The cell has divided into two daughter cells.

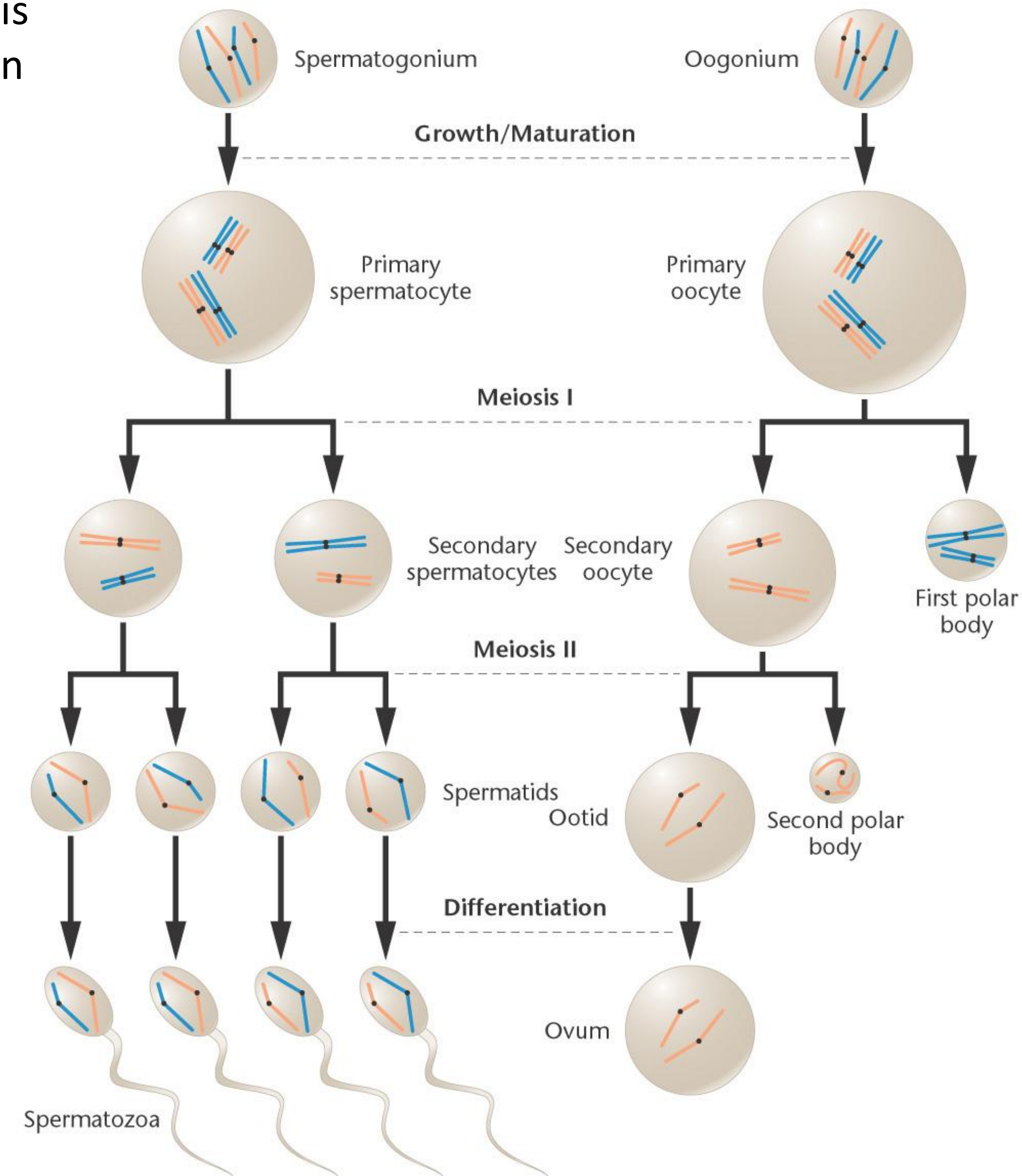
As in Meiosis I, the chromosomes line up on the spindle fibers.

The two cells each begin to divide. As in Meiosis I, the chromosomes move to opposite ends of each cell.

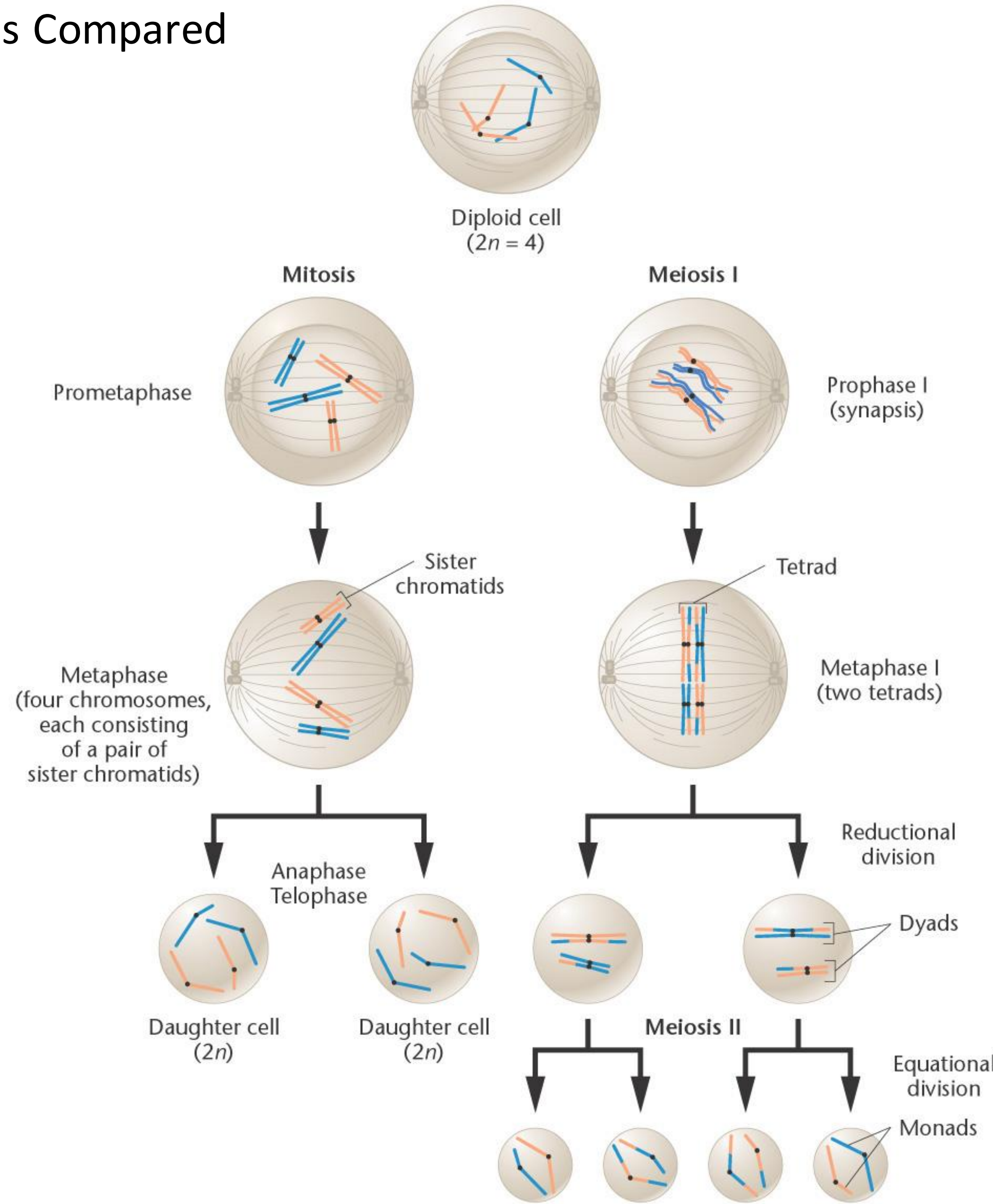
With the formation of four cells, meiosis is over. Each of these prospective germ cells carries half the number of chromosomes of somatic cells.



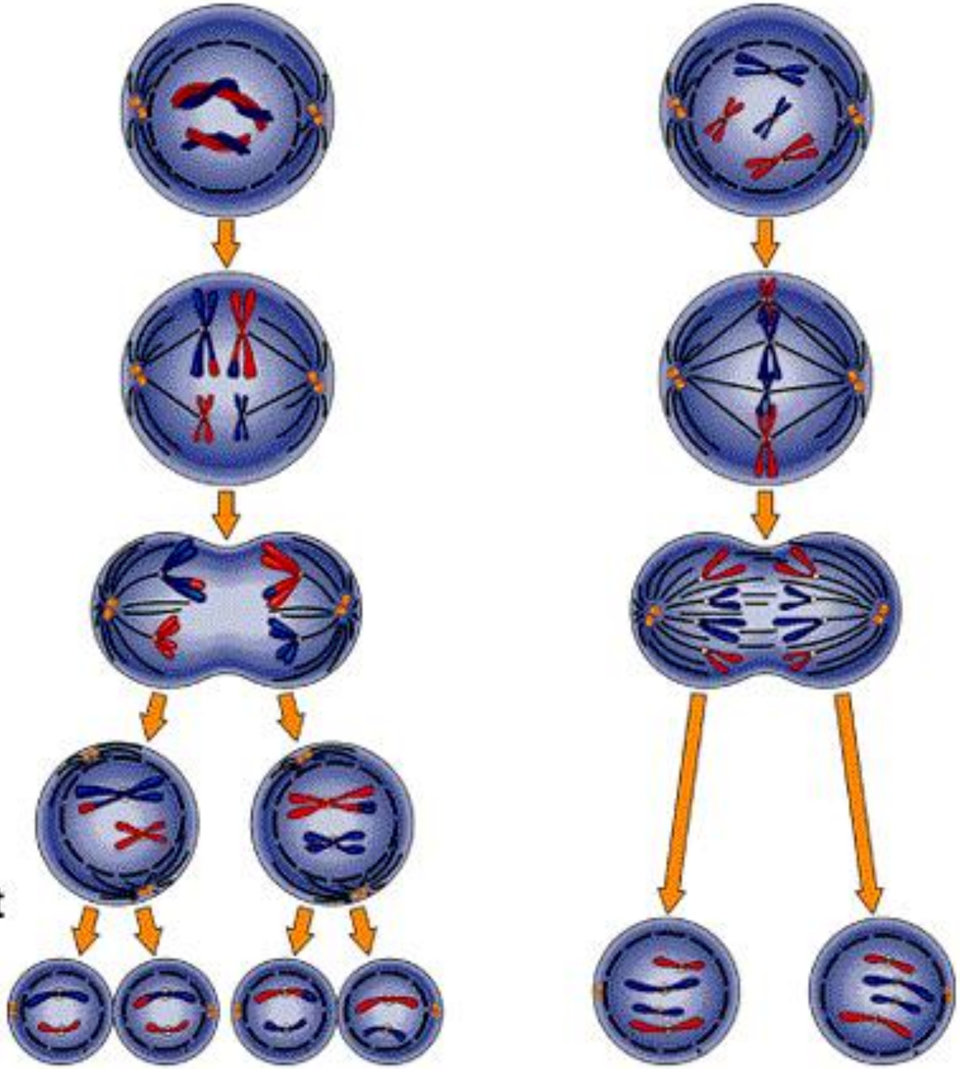
Spermatogenesis and oogenesis in animal cells.



Mitosis and Meiosis Compared



Comparison of Meiosis and Mitosis



Meiosis

daughter nuclei are not genetically identical to parent cell

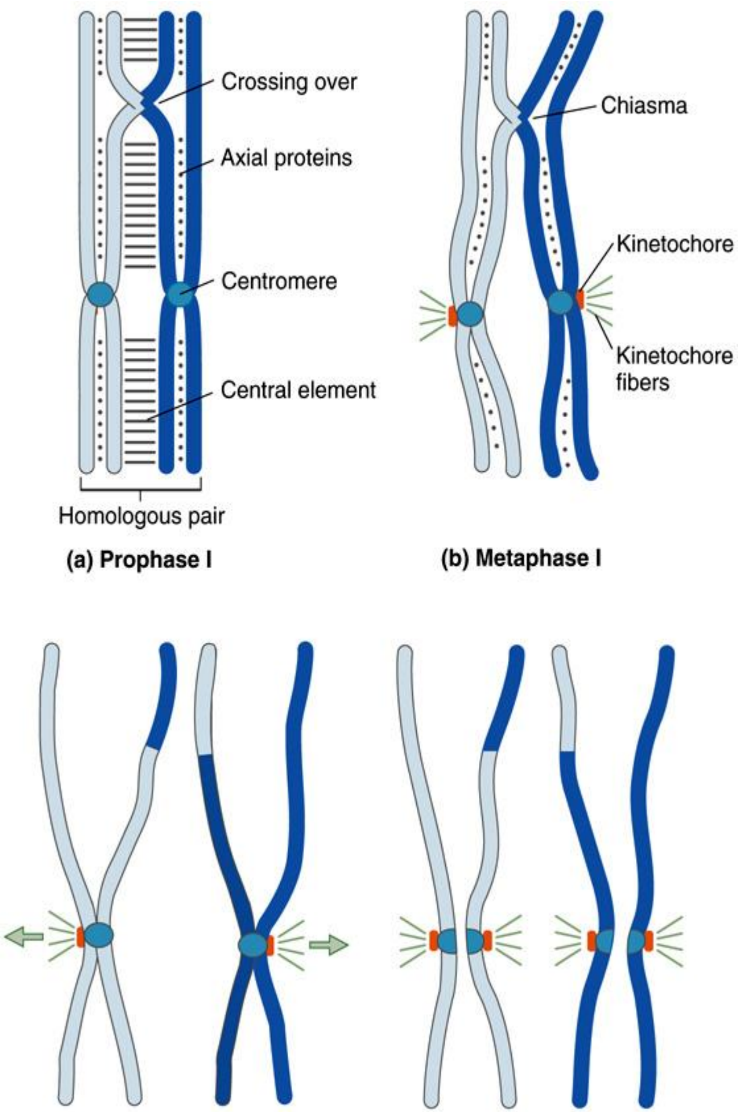
Mitosis

daughter nuclei are genetically identical to parent cell

Meiosis I	**Mitosis**
Prophase I	Prophase
Pairing of chromosomes	No pairing
Metaphase I	Metaphase
Homologous chromosomes at Metaphase plate	Duplicated chromosomes at metaphase plate
Anaphase I	Anaphase
Homologous chromosomes separate	Sister chromatids separate, becoming Daughter chromosomes
Telophase I	Telophase
Daughter cells are haploid	Daughter cells are diploid

Meiosis II	**Mitosis**
Prophase II	Prophase
No pairing of chromosomes	No pairing
Metaphase II	Metaphase
Haploid # of chromosomes at metaphase chromosomes at plate	Diploid # of duplicated metaphase plate
Anaphase II	Anaphase
Sister chromatids separate, becoming daughter chromosomes	Sister chromatids separate, becoming daughter chromosomes
Telophase I	Telophase
4 haploid daughter cells	Daughter cells are diploid

In older women, failure of the synaptonemal complex to separate properly can cause genetic disease



(a) Prophase I
(b) Metaphase I
(c) Anaphase I
(d) Metaphase II

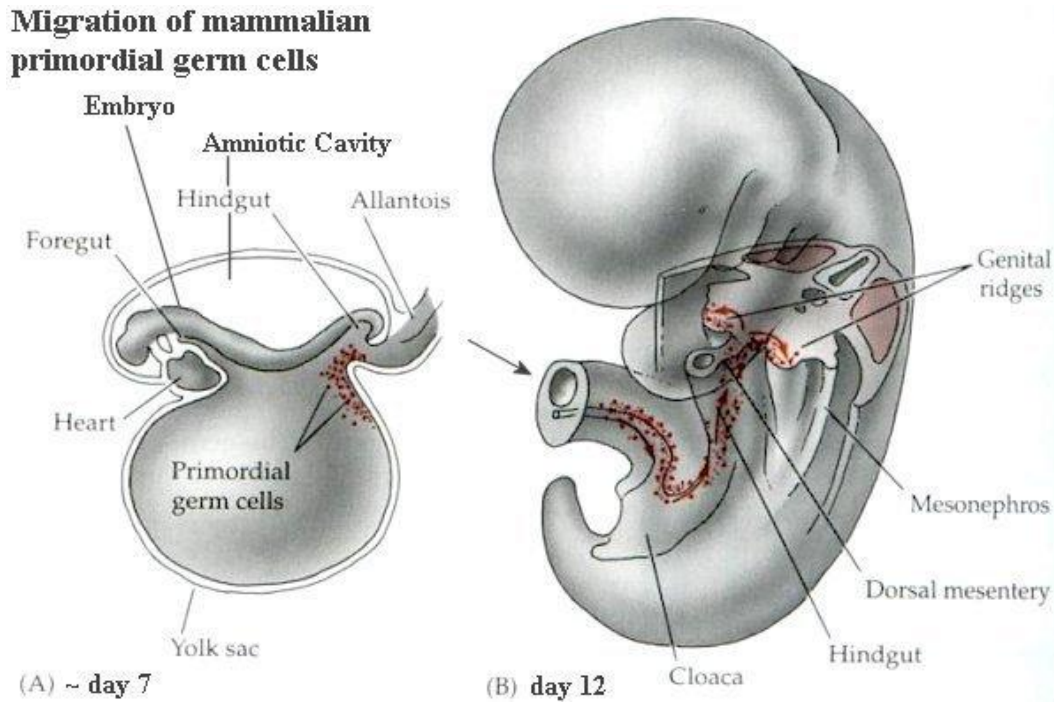
Down syndrome is trisomy 21. **It results in short stature, round face and mild to severe mental retardation.**

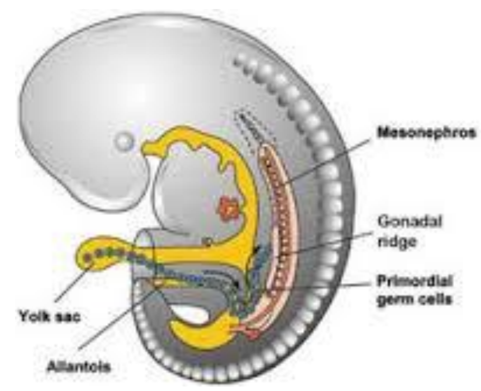
This is the failure of the 2 chromatids to separate during meiosis 2. It results in one oocyte receiving 2 instead of 1 chromatid. In older women, long term association of chromatids (i.e., over 50 years) results in the axial proteins failure to separate.

Down syndrome occurs with a frequency of 0.2% in women under 30 but at 3% in those over 45 years of age.

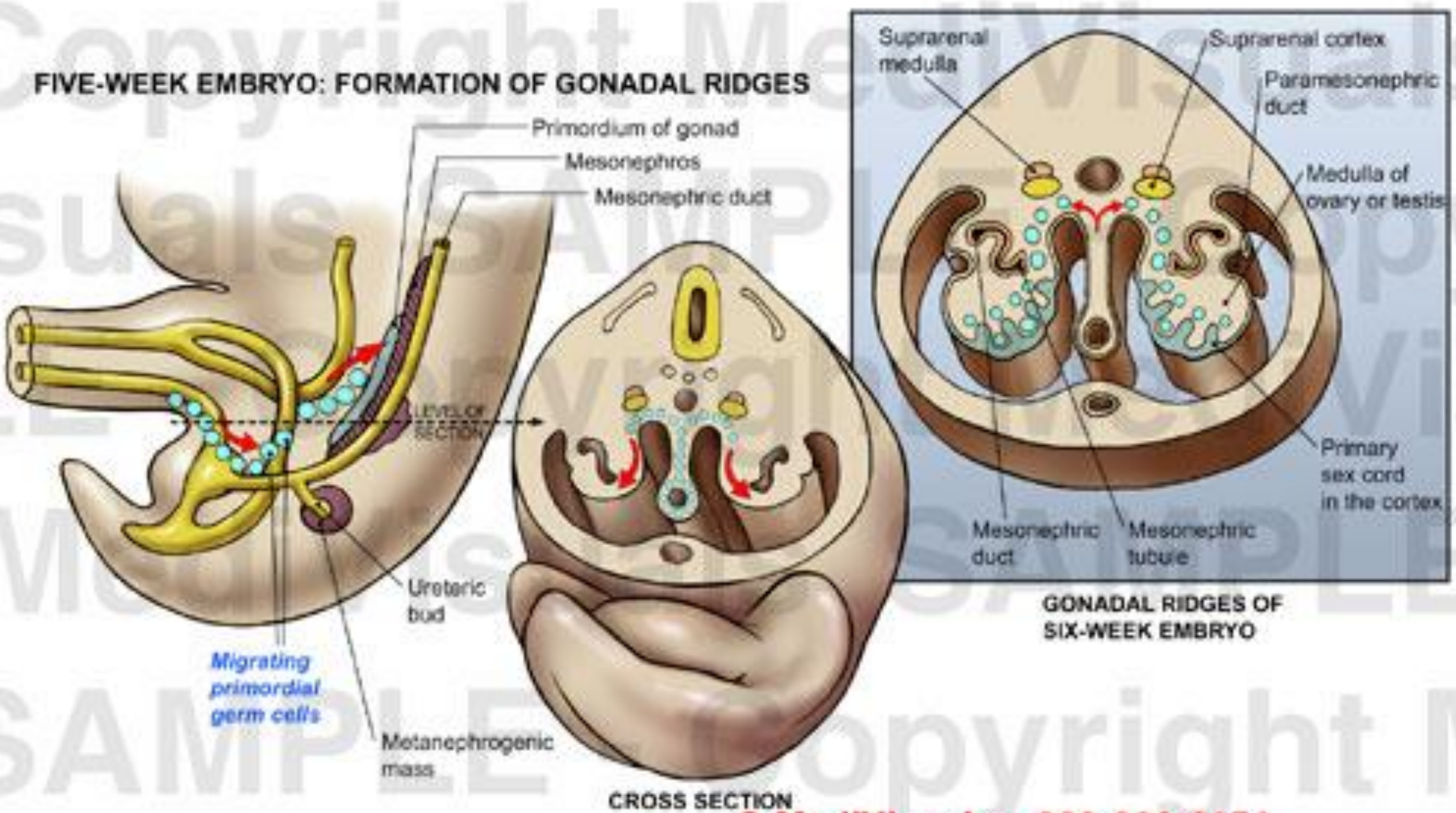
PRIMORDIAL GERM CELLS

- Gametes are derived from PGCs.
- Formed in the epiblast during 2nd week and then move to the wall of yolk sac, begin to migrate from the yolk sac in the 4th week and arrive in the gonads by end of 5th week.





Primordial Germ Cells Migrate to Gonadal Ridges of Embryo



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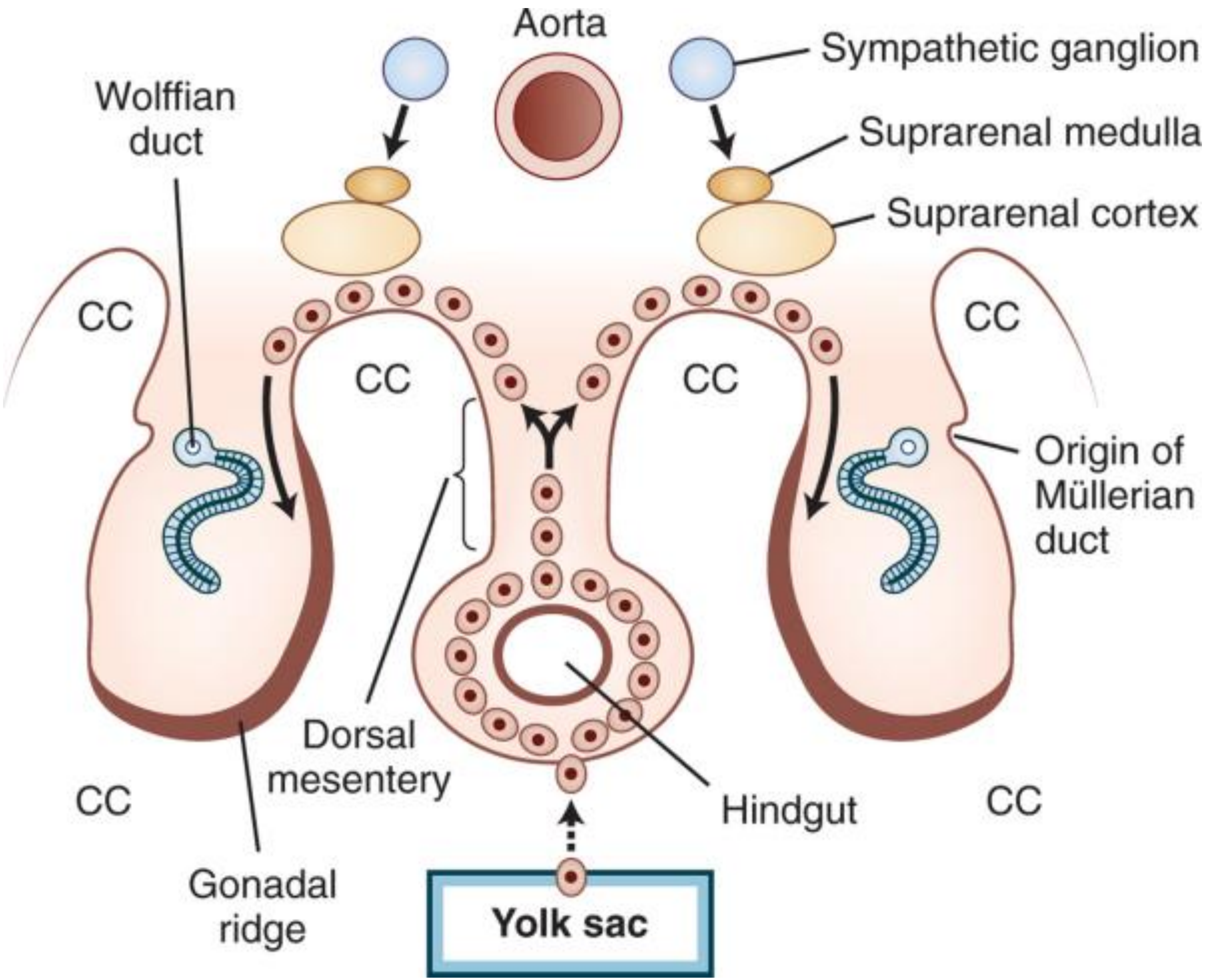

Aorta
Sympathetic ganglion
Wolffian duct
Suprarenal medulla
Suprarenal cortex
CC
CC
CC
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Origin of Müllerian duct
Dorsal mesentery
Hindgut
CC
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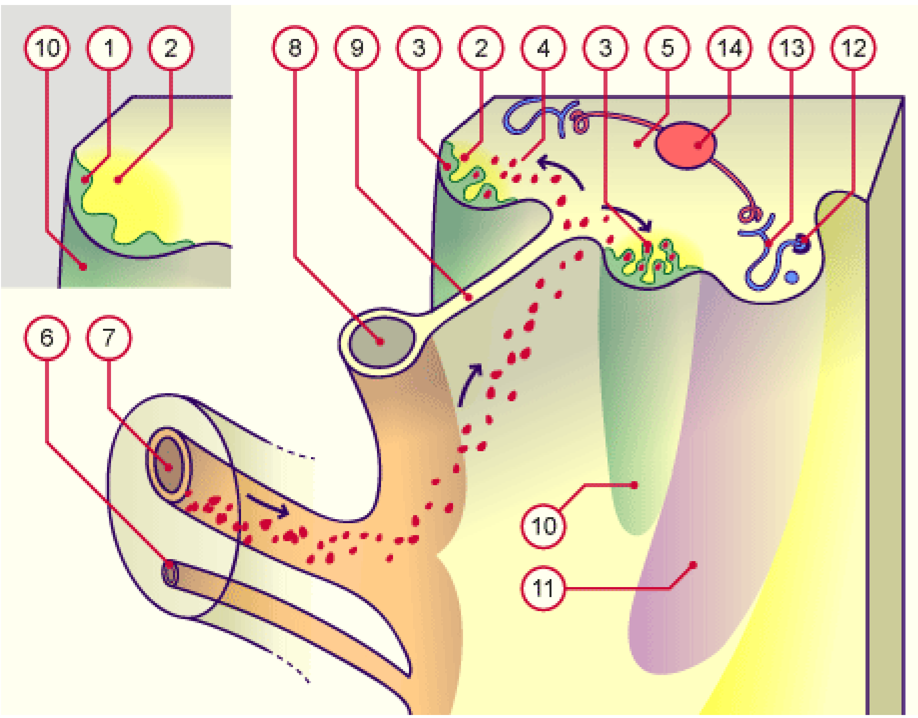
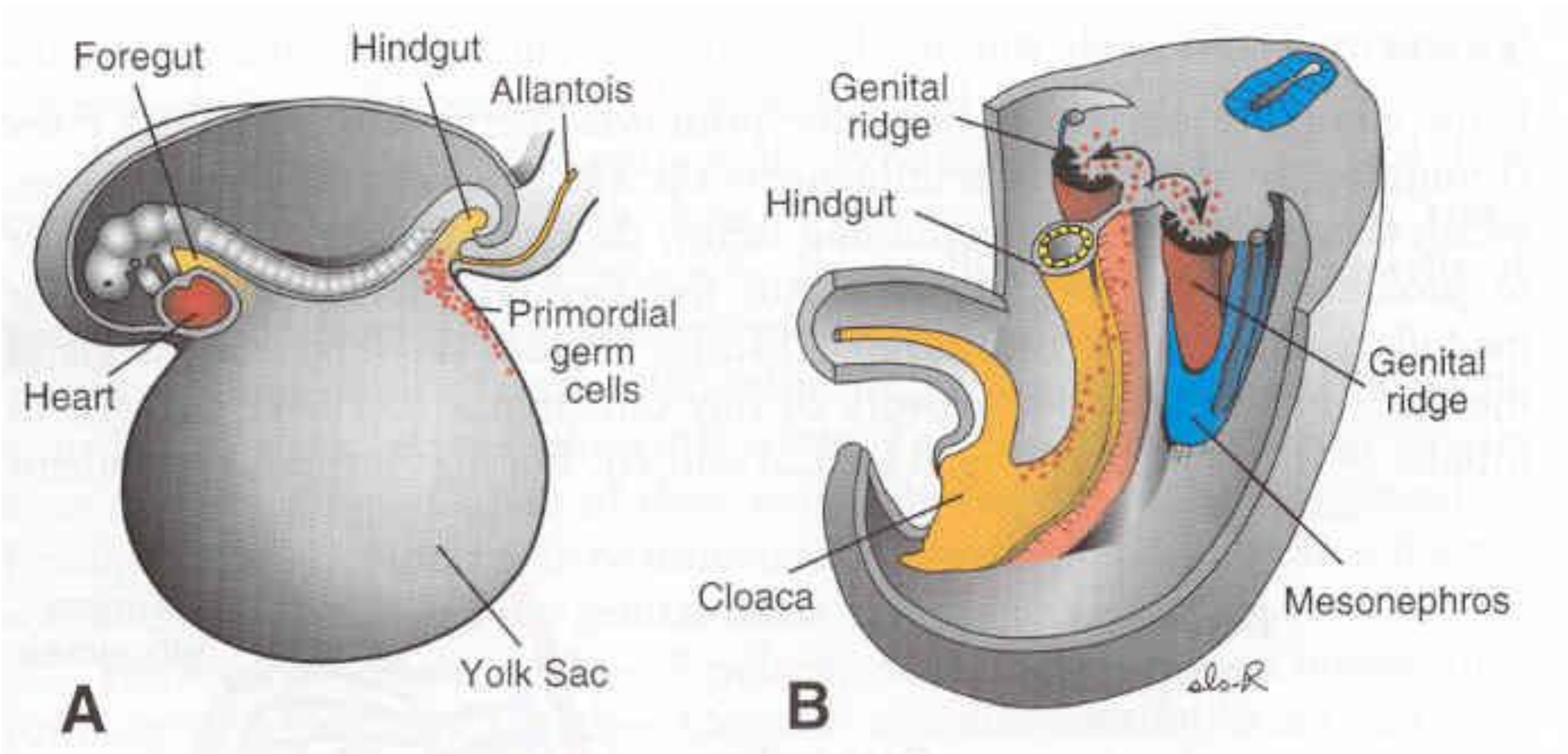
Gonadal ridge
Yolk sac

Undifferentiated Gonad

- Primordial Germ Cells



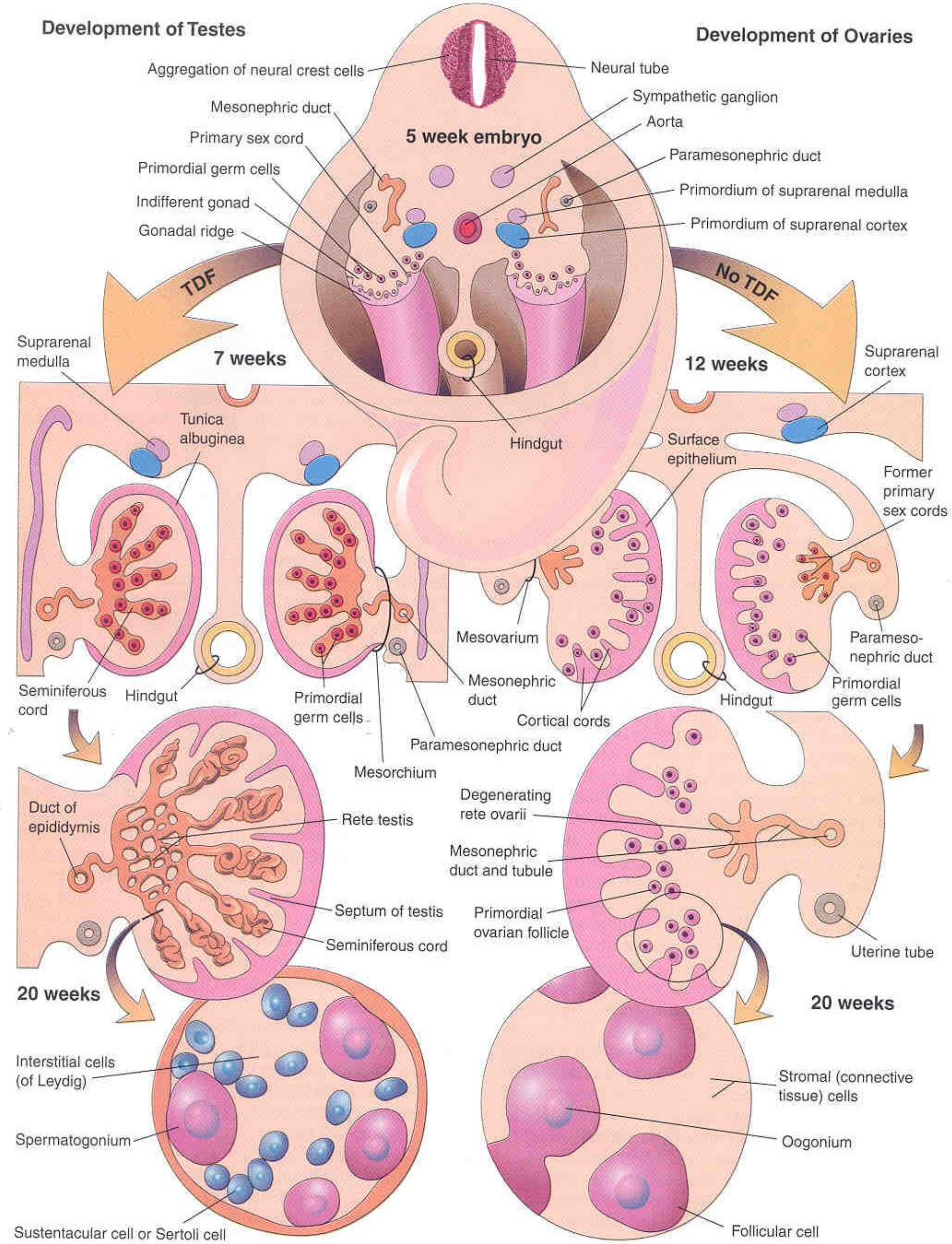
1	Coelomic epithelium	**8**	Intestine
2	Local mesenchyma (in proliferation)	**9**	Dorsal mesentery
3	Gonadal cord	**10**	Genital ridge
4	Primordial germ cells (PGC)	**11**	Nephrogenic cord
5	Mesenchyma	**12**	Mesonephric duct (Wolff)
6	Allantois	**13**	Mesonephric tubule
7	Omphalomesenteric duct	**14**	Aorta



- Epithelium of genital ridge proliferate and grow into the underlying mesenchyme of the Medullary region

7. Weeks

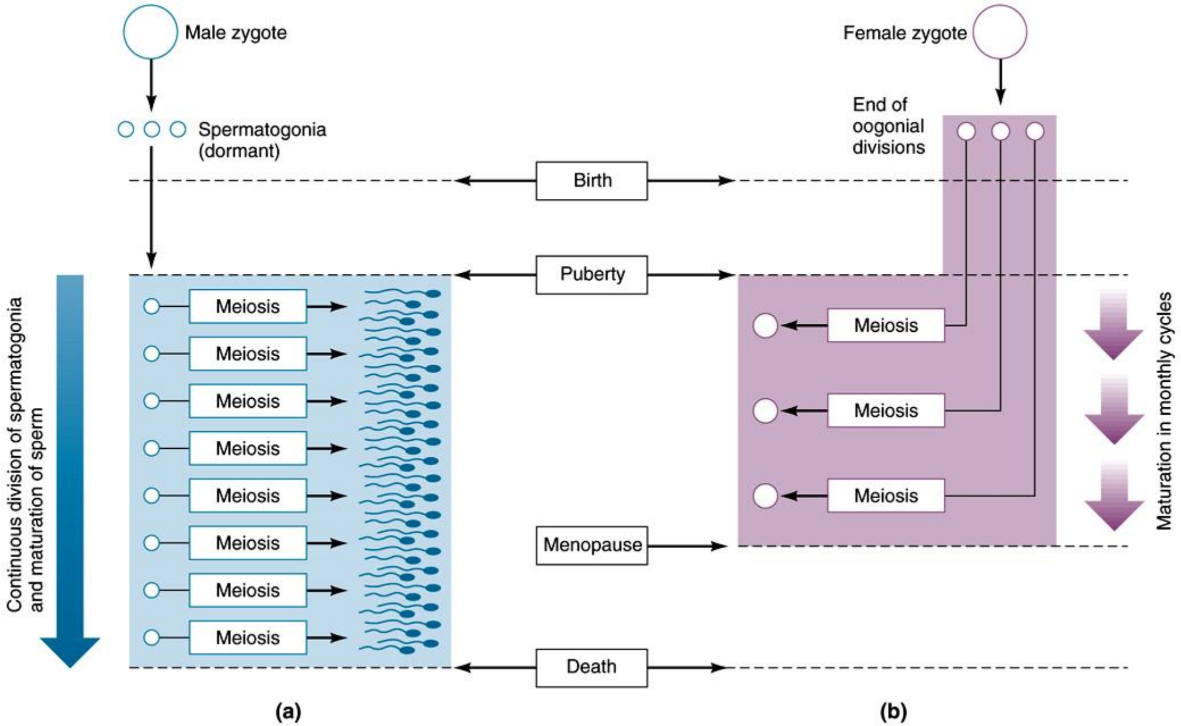
- **Testis Determining Factor (TDF)**
- Required to form the testis; the female phenotype is baseline and will always form in the absence of male genes.



The timing of meiosis differs in females and males

In males, the spermatogonia enter meiosis and produce sperm from puberty until death. The process of sperm production takes only a few weeks. Each ejaculation has 100 to 500 million sperm.

In females, this process is more complex. The first meiotic division starts before birth but fails to proceed. It is eventually completed about one month before ovulation in humans. In humans, the second meiotic division occurs just before the actual process of fertilization occurs.



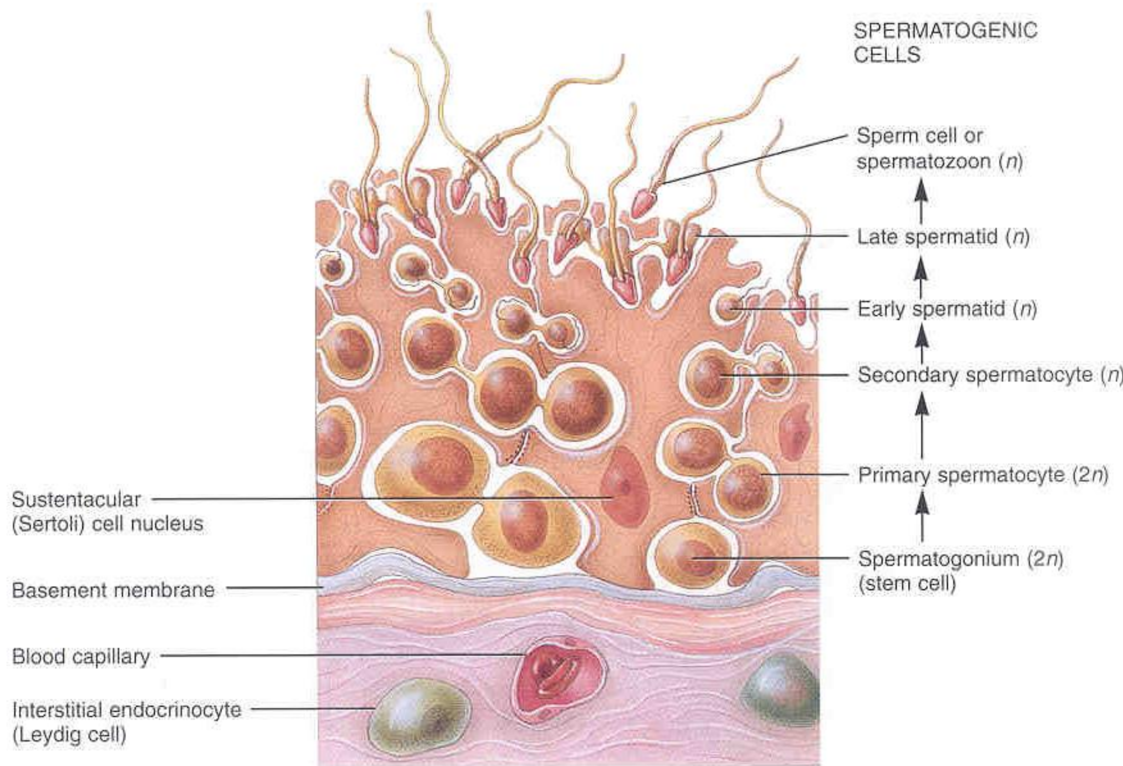
Thus, in females, the completion of meiosis can be delayed for over 50 years. This is not always good.

Only I egg produced

In addition, all meiosis is ended in females at menopause.

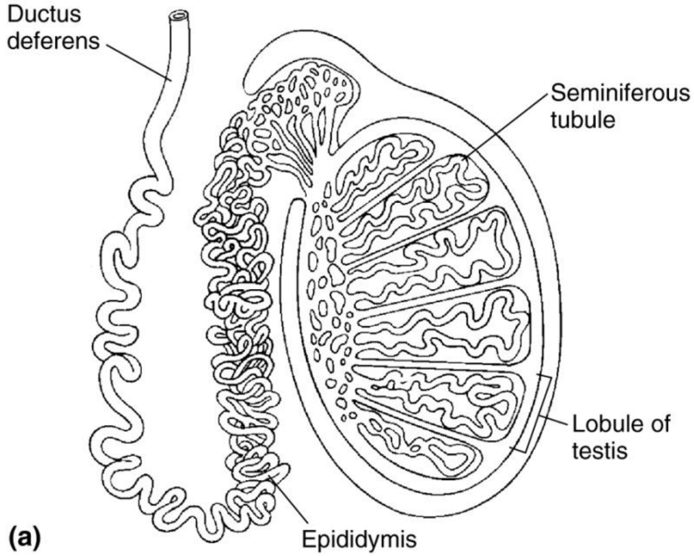
Spermatogenesis

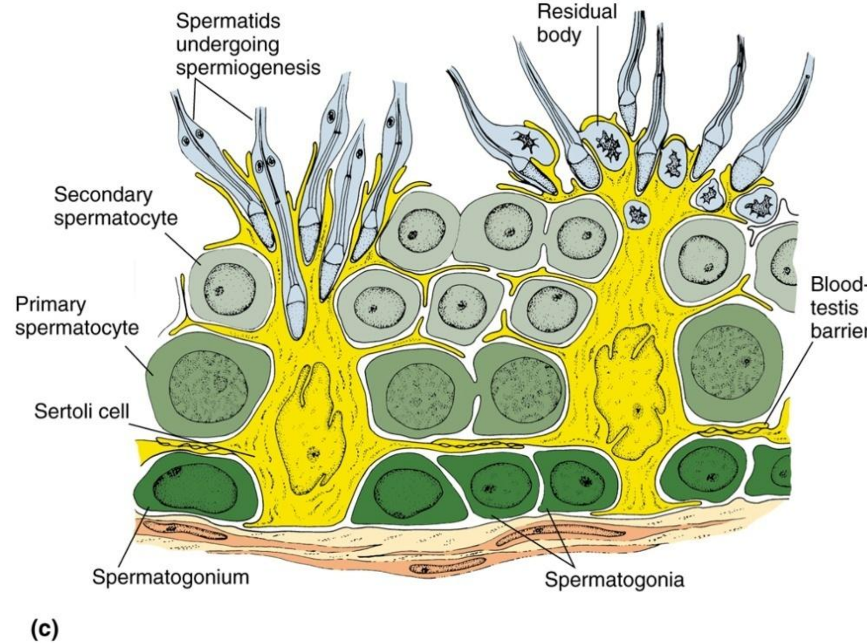
- Spermatogenesis: The production of sperm using meiosis
- Occur in the seminiferous tubules in the testes in males



<u>Spermatogenesis</u> occurs in the seminiferous tubules

The mammalian testes are divided into many lobules, and each lobule contains many tiny seminiferous tubules. Sperm develop in an ordered fashion in these tubules. Cells start to mature on the outside and move inward (towards the lumen) as the become mature sperm.



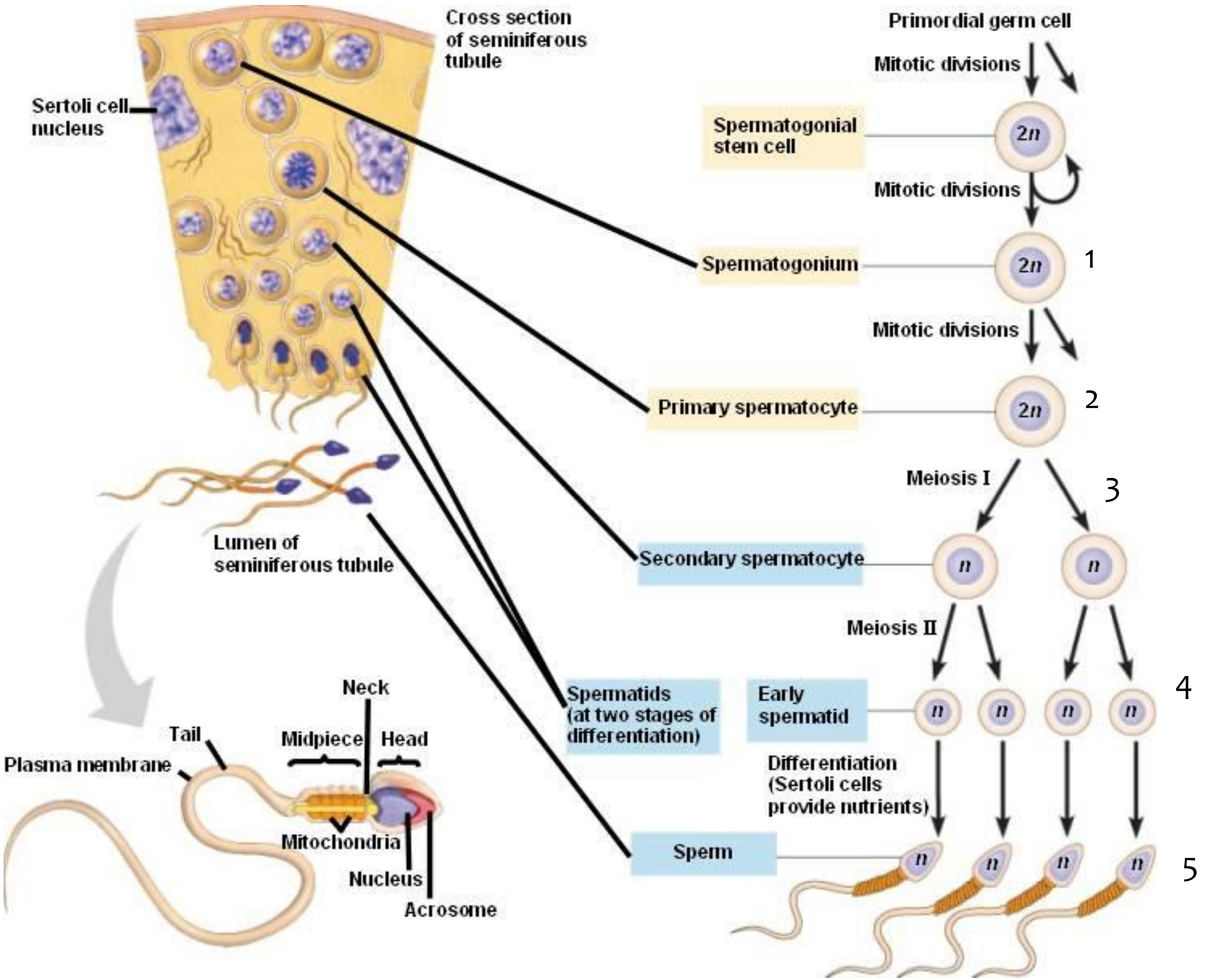


Spermatogonia are the most primative cells. They differentiate as primary spermatocyte → secondary → spermatid → sperm are released into lumen.

Sertoli cells are supporting cells that stretch from the lumen to the edge of the tubule. They nourish the developing sperm. They form a blood-testis barrier to control spermatogenesis (similar to the blood-brain barrier). These cells also inhibit spermatogenesis before puberty and stimulate the process after puberty.

Spermatogenesis

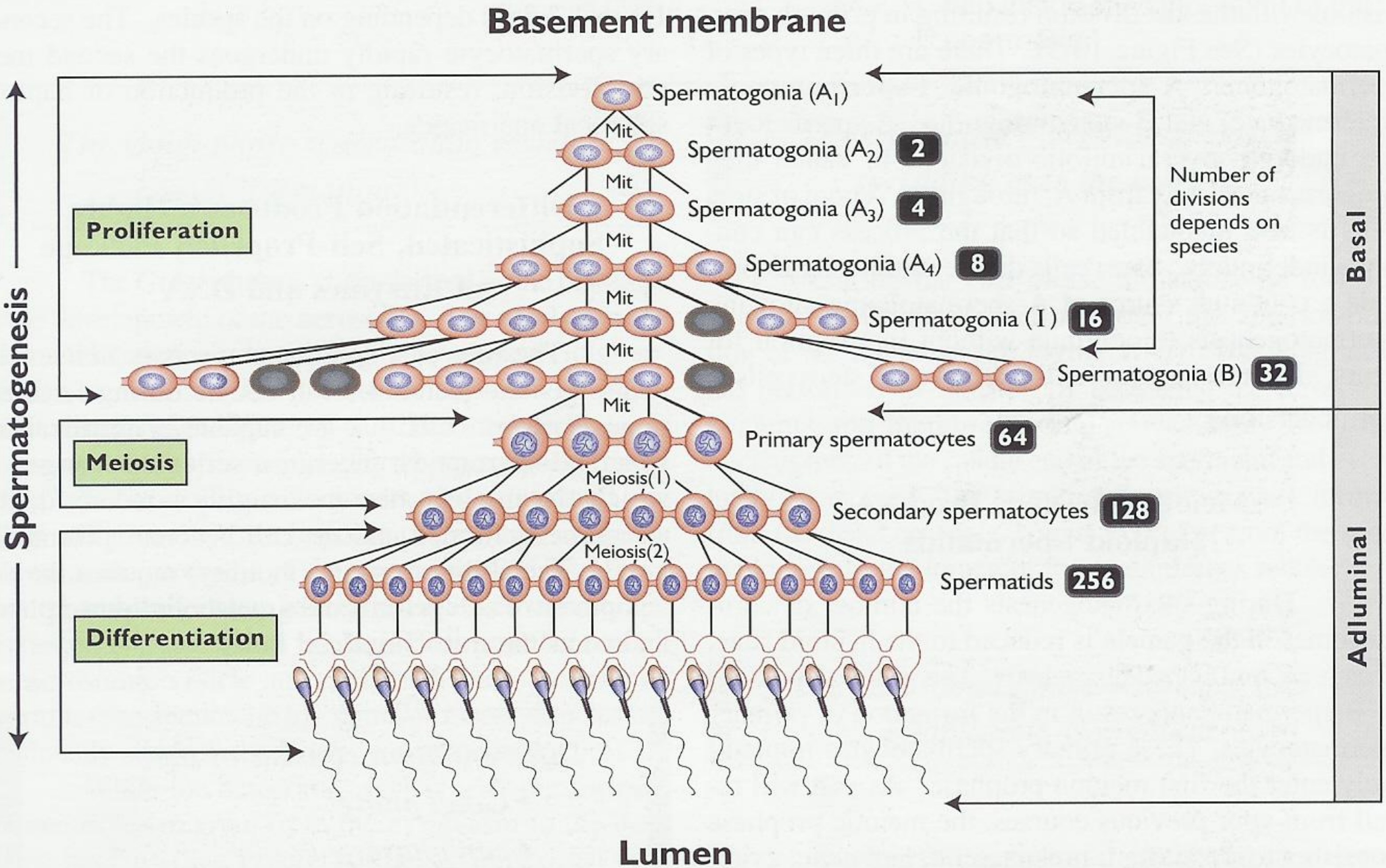
- **(1) Spermatogonia** are the Germ-Line cells. They are diploid (2n). They undergo mitosis to reproduce themselves.
- (2) One of these spermatogonia undergoes meiosis, and it is called a **primary spermatocyte**. It is diploid (2n).
- (3) The primary spermatocyte undergoes MEIOSIS I to produce two **secondary spermatocytes.** These are now haploid (n) but still contain two chromatids per chromosome
- (4) Each of these secondary spermatocytes undergoes MEIOSIS II to each produce two **spermatids.** Spermatids are haploid (n) and each contain 1 chromosome that was previously a chromatid. The result is 4 total spermatids.
- (5) Spermatids mature into the sperm we know, and these sperm cells are called **spermatozoa.** They are then ready to leave the body and fertilize an egg.



Cross section of seminiferous tubule
Sertoli cell nucleus
Lumen of seminiferous tubule
Primordial germ cell
Mitotic divisions
Spermatogonial stem cell
2n
Mitotic divisions
Spermatogonium
2n
1
Mitotic divisions
Primary spermatocyte
2n
2
Meiosis I
3
Secondary spermatocyte
n
n
Meiosis II
Spermatids (at two stages of differentiation)
Early spermatid
n
n
n
n
4
Differentiation (Sertoli cells provide nutrients)
Sperm
n
n
n
n
5
Neck
Tail
Midpiece
Head
Plasma membrane
Mitochondria
Nucleus
Acrosome

Figure 10-5. Typical Sequence of Spermatogenesis in Mammals

Spermatogonia (A_1-A_4, I and B) undergo a series of mitotic divisions (Mit) and the last mitotic division gives rise to primary spermatocytes that enter meiosis. This series of mitotic divisions allows for continual proliferation of spermatogonia and replacement of A_1 spermatogonia.



After meiosis, haploid spherical spermatids differentiate into spermatozoa. Meiosis and differentiation take place in the adluminal compartment. Notice that each generation of cells is attached by intercellular cytoplasmic bridges. Thus, each generation divides synchronously in cohorts. Some cells (black) degenerate during the process. Numbers indicate the theoretical number of cells generated by each division.

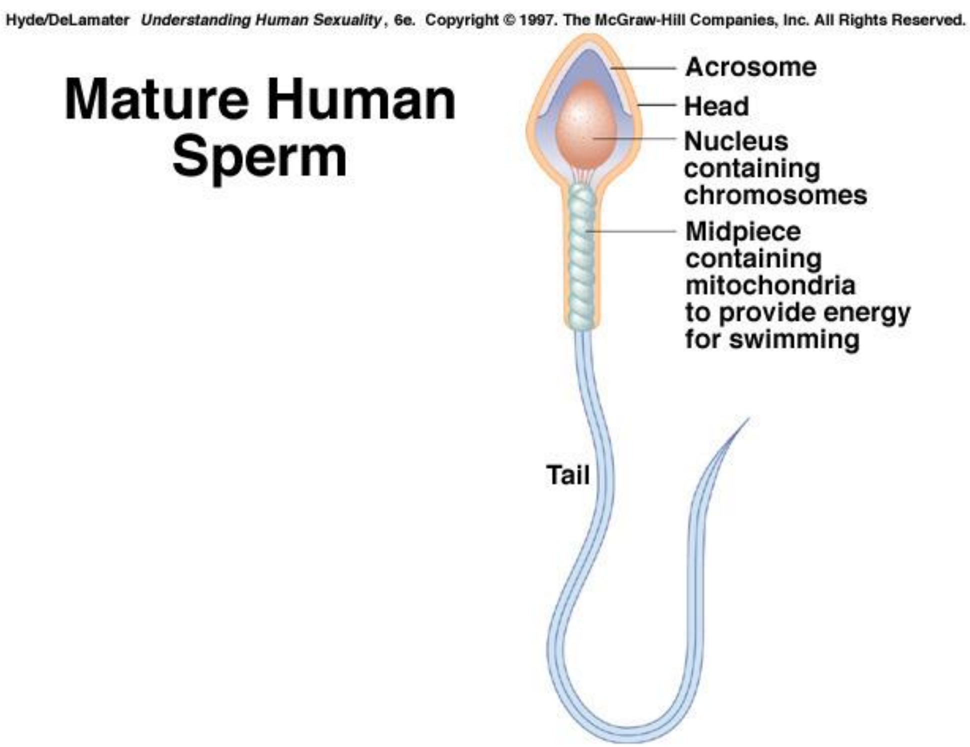
Spermatogenesis

- Also, **Sertoli cells** are in the seminiferous tubules and help the process of spermatogenesis. They engulf (take in) extra cytoplasm from the spermatids.

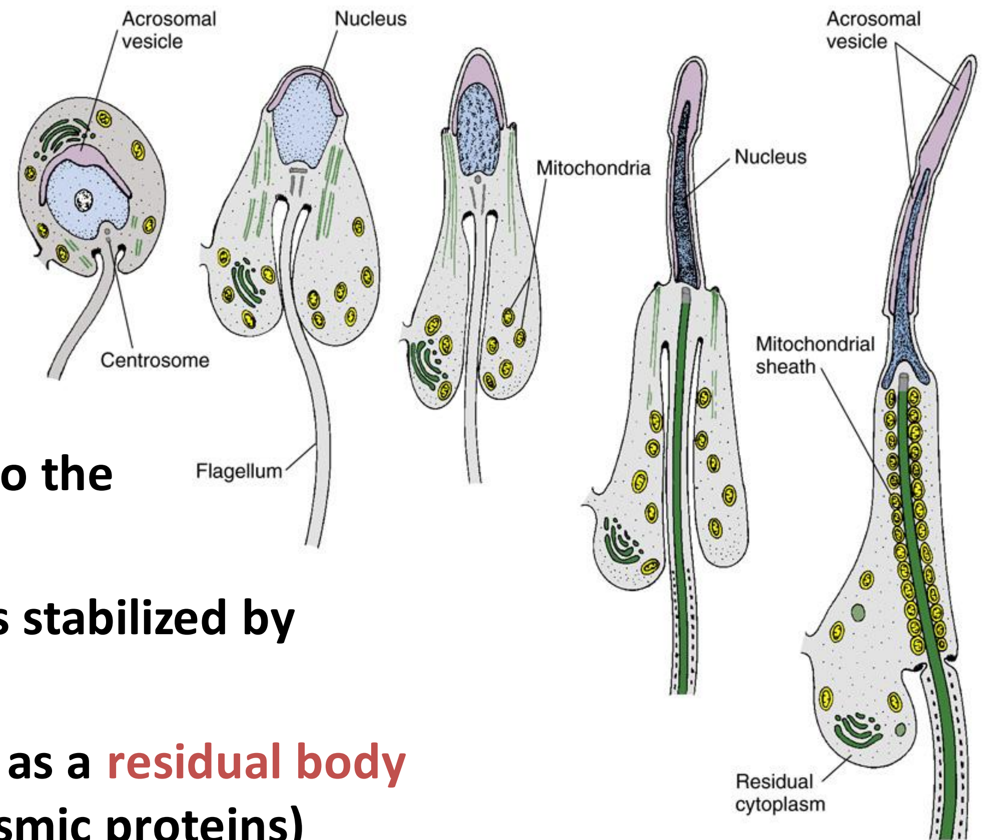
- SUMMARY of SPERMATOGENESIS:
  - 4 haploid spermatozoa (mature sperm) are created via meiosis from an original diploid spermatogonium (germ line cell)
  - Occurs in the testes in the seminiferous tubules
  - The production of sperm is an ongoing process in the seminiferous tubules

Spermiogenesis

- Structure of a mature sperm (spermatozoa)



Spermiogenesis is the maturation process into sperm



The golgi vesicles combine to form an acrosomal vesicle that lies over the nucleus. Its full of enzymes

Centosomes start to organize microtubules into long flagella

Mitochondria start to localize next to the flagella to provide ready energy

The nucleus condenses in size and is stabilized by special proteins called protamines

The excess cytoplasm is pinched off as a residual body (no need for organelles and cytoplasmic proteins)

Sperm are tiny, but highly specialized missiles for delivering the male genome:

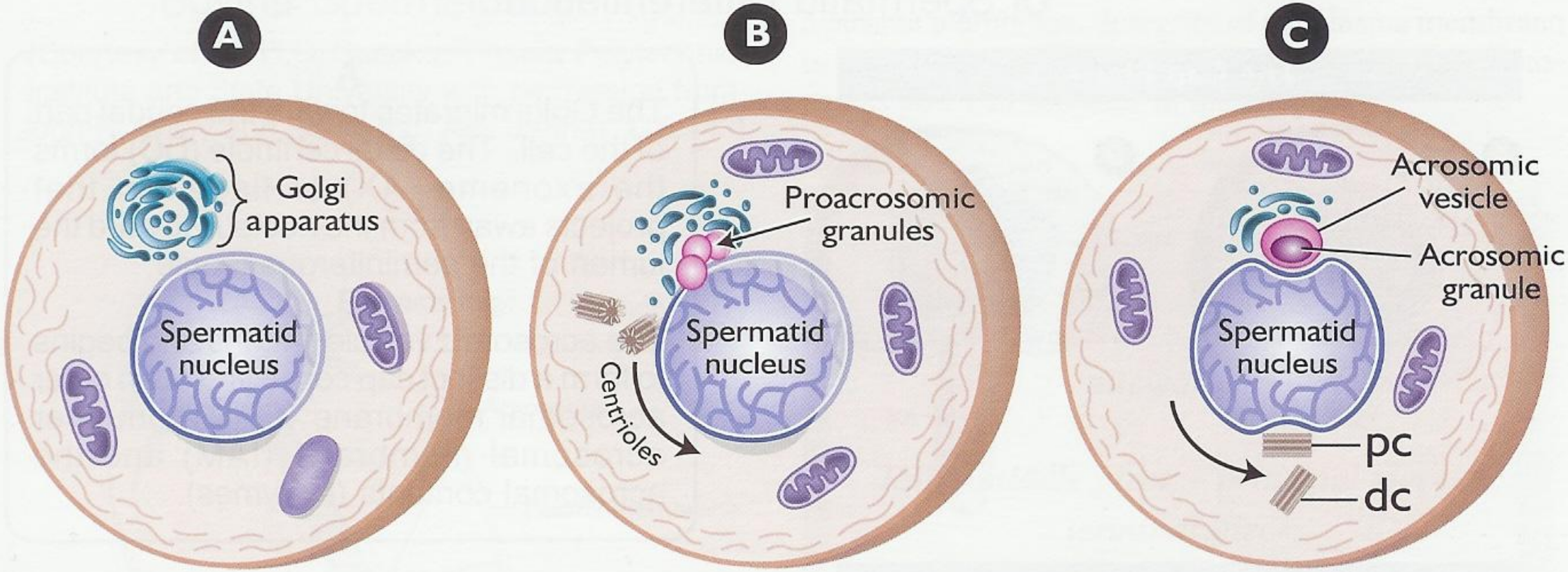
Microfilaments shoot the acrosome into the egg to 'harpoon it' and pull it in.

The acrosome has enzymes for breaking into the egg.

The midpiece has large numbers of mitochondria for horsepower.

The tail has a powerful flagellum for driving the sperm into the proximity of the egg (in humans, through the uterus and up into the oviduct.

Figure 10-6. The Golgi Phase of Spermatid Differentiation

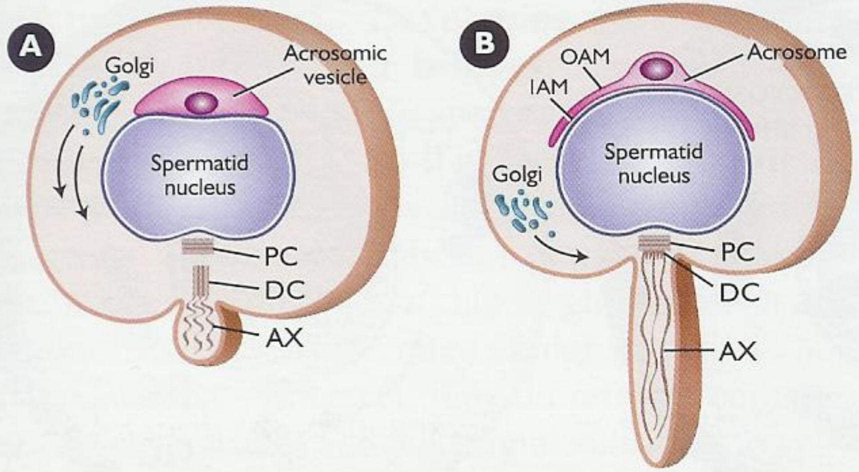


A The newly formed spermatid is almost perfectly spherical and has a well developed Golgi apparatus.

B Small vesicles of the Golgi fuse, giving rise to larger secretory granules called pro-acrosomic granules. The centrioles start to migrate to a position beneath the nucleus that is opposite the acrosomic vesicle.

C Vesicle fusion continues until a large acrosomic vesicle is formed that contains a dense acrosomic granule. The proximal centriole (PC) will give rise to the attachment point of the tail. The distal centriole (DC) will give rise to the developing axoneme (central portion of the tail) inside the cytoplasm of the spermatid.

The Cap Phase



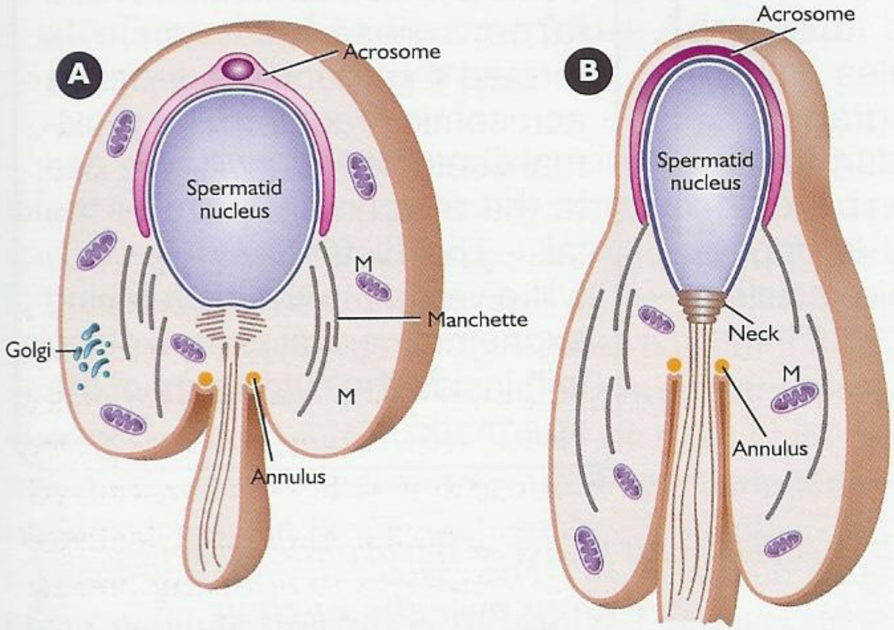
A

The Golgi migrates toward the caudal part of the cell. The distal centriole (DC) forms the axoneme (AX) or flagellum that projects away from the nucleus toward the lumen of the seminiferous tubule.

B

The acrosomic vesicle flattens and begins to form a distinct cap consisting of an outer acrosomal membrane (OAM), an inner acrosomal membrane (IAM) and the acrosomal contents (enzymes).

The Acrosomal Phase

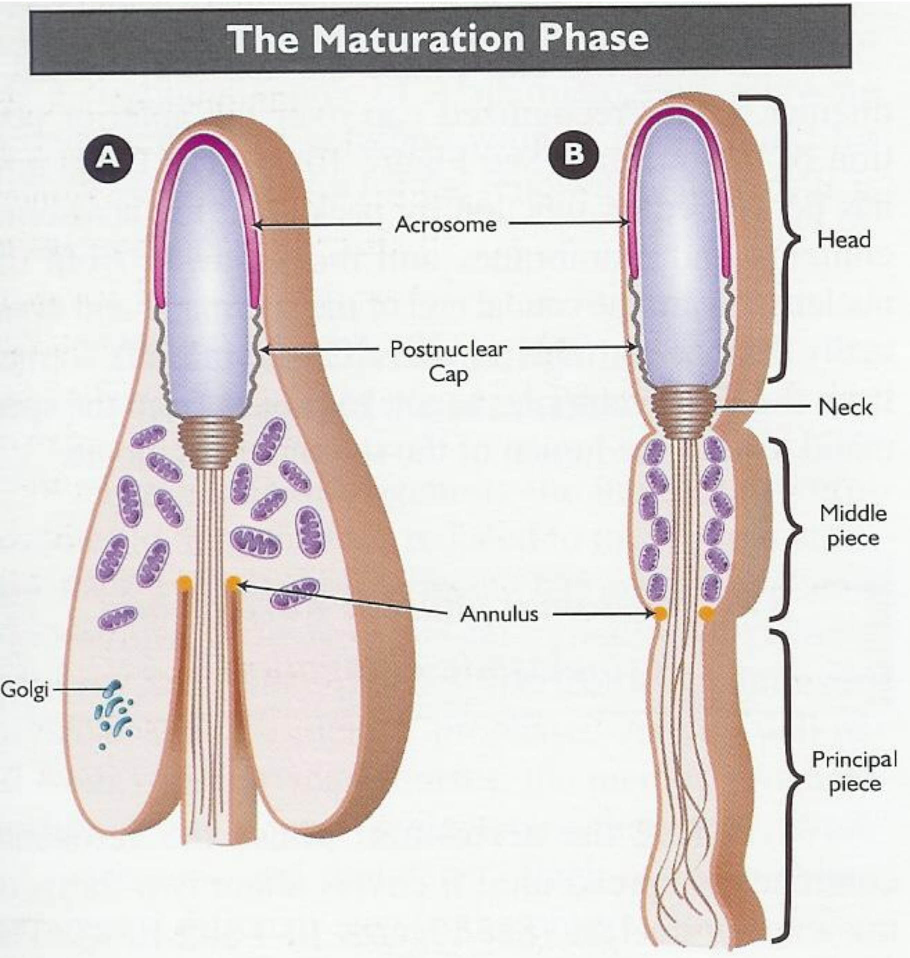


A

The spermatid nucleus begins to elongate and the acrosome eventually covers the majority of the anterior nucleus. The manchette forms in the region of the caudal half of the nucleus and extends down toward the developing flagellum.

B

The neck and the annulus are formed and the later will become the juncture between the middle piece and the principal piece. Notice that all components of the developing spermatid are completely surrounded by a plasma membrane. M = mitochondria.



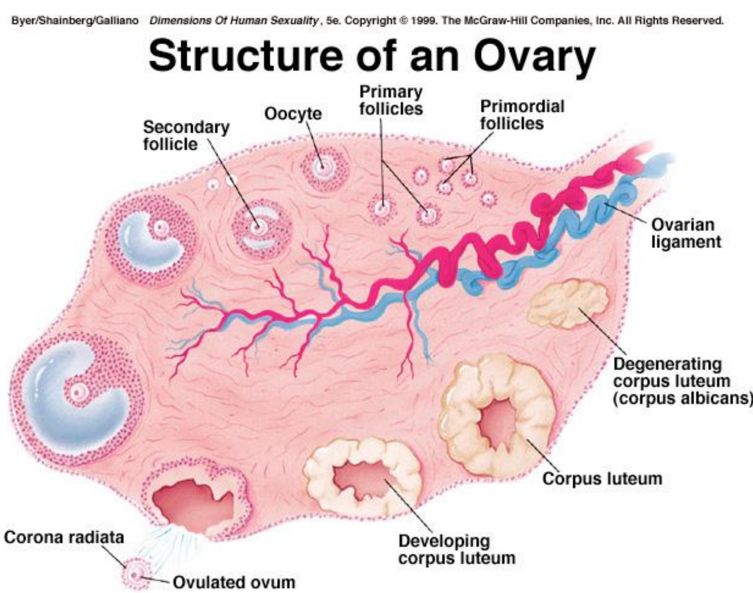
A and B

Mitochondria form a spiral assembly around the flagellum that defines the middle piece. The postnuclear cap is formed from the manchette microtubules. The annulus forms the juncture between the middle piece and the principal piece.

- https://www.youtube.com/watch?v=eddh-AGV-6c

Oogenesis

- Oogenesis: creation of haploid egg cells using meiosis
- Occurs in the ovaries of females



Oogenesis

- Oogonia: mitotically dividing cells in the ovary, will become Oocytes
- Primary oocyte: decision has been made to undergo meiosis, cell has grown. Cells are arrested at this stage until puberty.
- Secondary oocyte: has completed first meiotic division the division was unequal in terms of cytoplasm
- Ovum: Ovulated egg, ready to be fertilized. If fertilized, the second meitoic division will occur, another polar body will be given off.

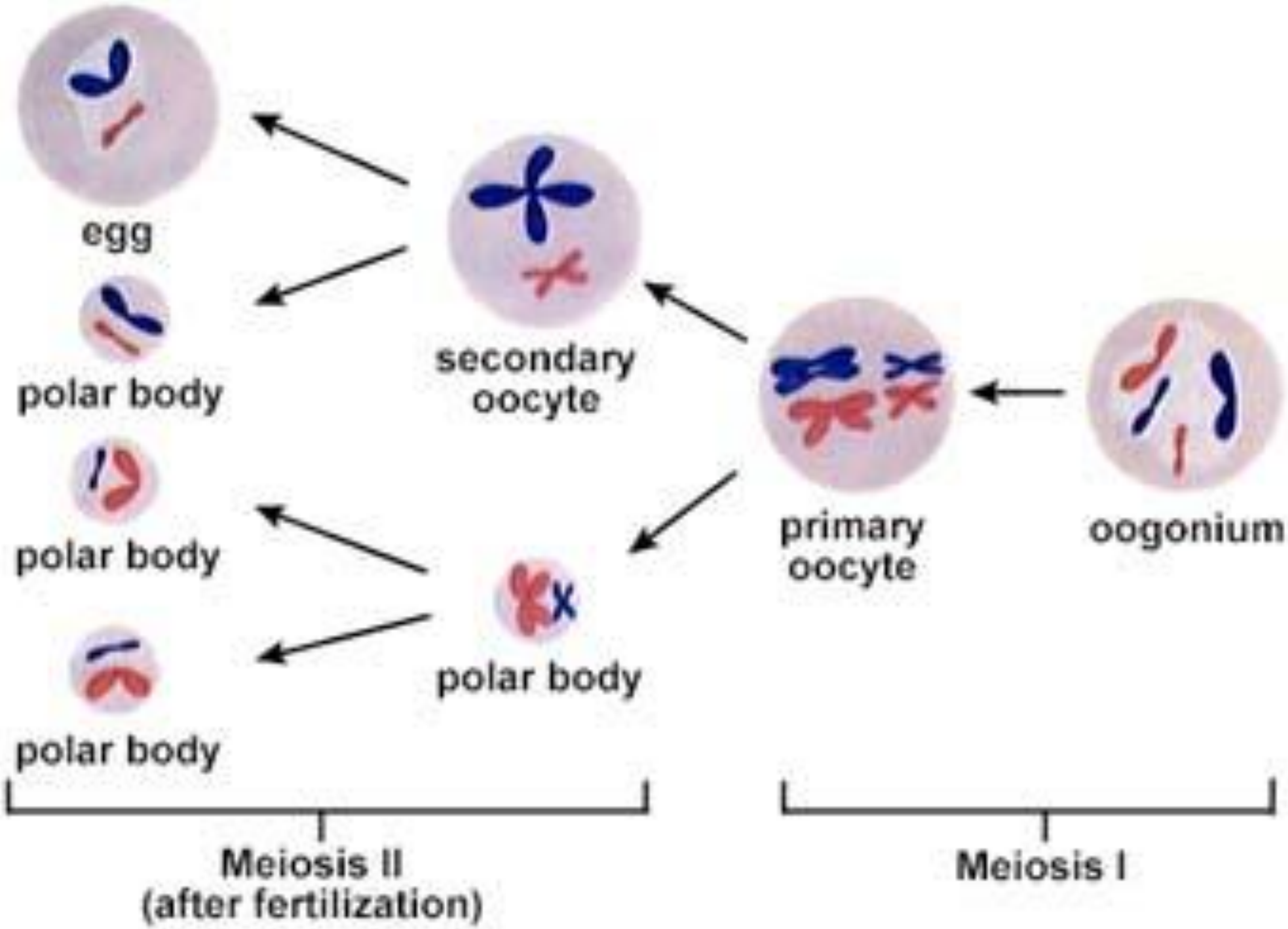
Oogenesis

- **Follicles** in the ovaries are structures that contain primary oocytes. The germ line cells, **oogonia**, produced all of the primary oocytes while the fetus was developing. Therefore, when a baby female is born all of her follicles contain primary oocytes! They stay this way unless they undergo ovulation.
- Females are born with 1 million follicles in their ovaries.

Oogenesis

- The primary oocytes that are diploid (2n) are arrested (paused) at Prophase I of Meiosis I.
- When a female undergoes **ovulation** once a month, one of these follicles with the primary oocyte matures. It fully undergoes Meiosis I and results in two different structures:
  - ONE haploid (n) **secondary oocyte.** It contains half the number of chromosomes but still has sister chromatids.
  - ONE haploid (n) structure called a **polar body!**
- The **polar body** does not go on to become an egg. Through **UNEQUAL CYTOKINESIS**, the secondary oocyte gets most of the cytoplasm and the polar body is left with little cytoplasm.

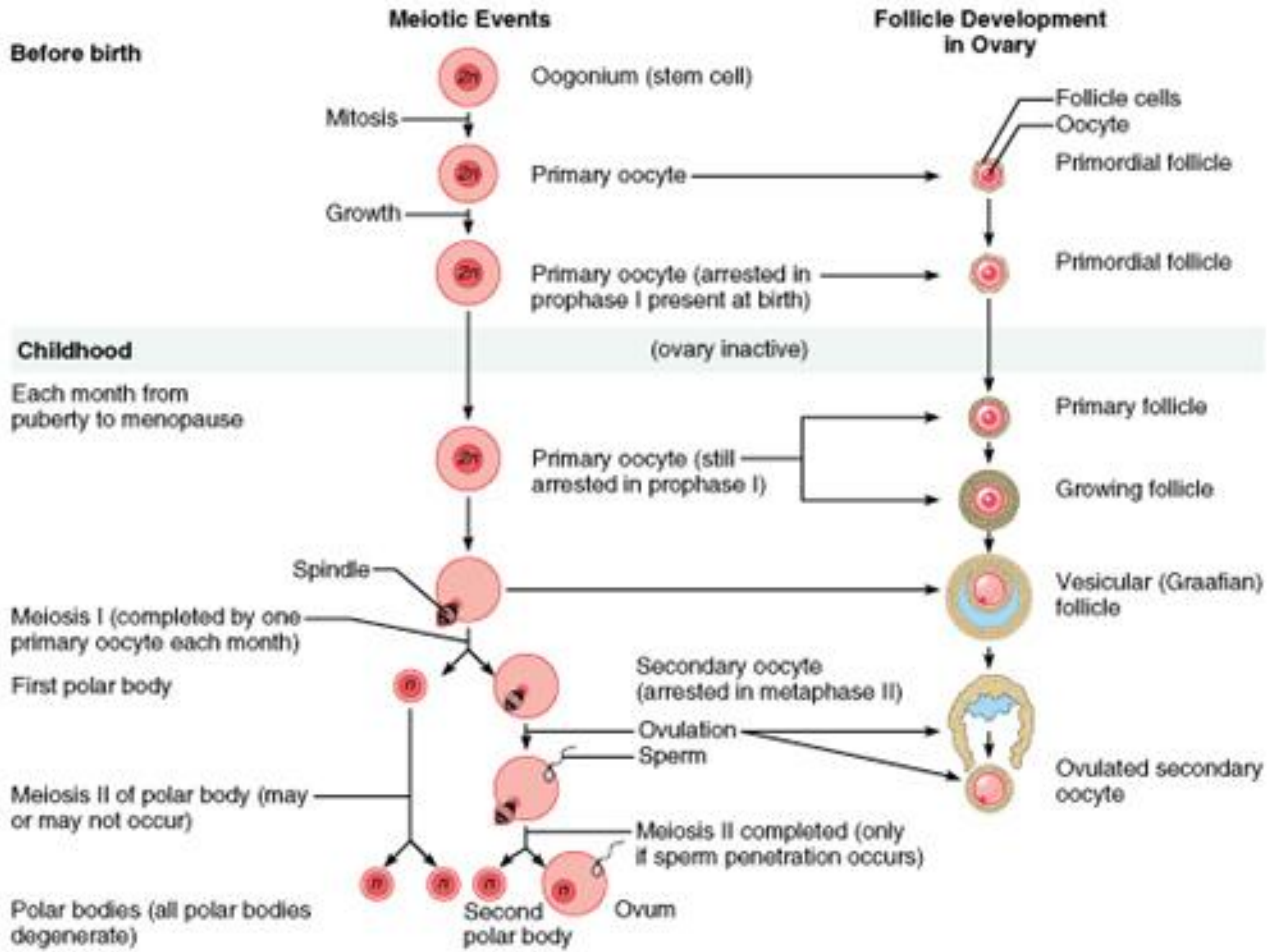
Oogenesis


egg
polar body
polar body
polar body
secondary oocyte
polar body
primary oocyte
oogonium
Meiosis II
(after fertilization)
Meiosis I

Oogenesis

- After Meiosis I occurs, the secondary oocyte that is haploid (n) is arrested (paused) at Metaphase II of Meiosis II. It stays in this state until FERTILIZATION.
- Once fertilization occurs, the secondary oocyte undergoes Meiosis II and the result again is two separate structure:
  - ONE haploid **ovum** (egg)
  - ONE polar body
- The other polar body from the previous step contained chromatids, so it also undergoes Meiosis II and produces TWO polar bodies.

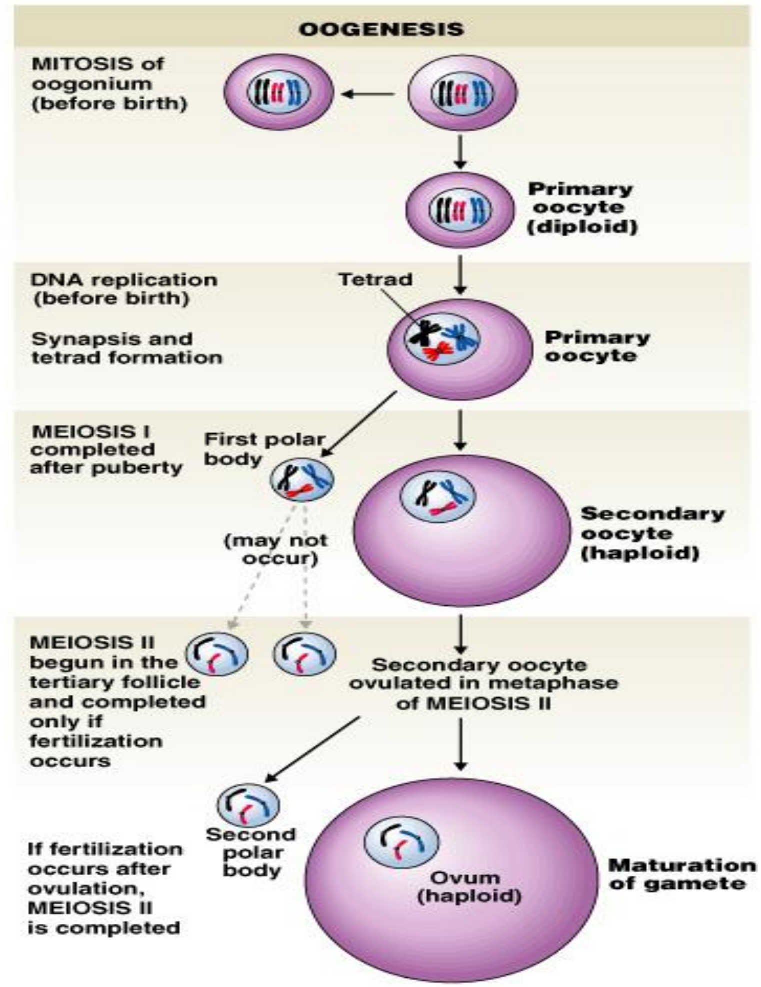
Oogenesis



Meiotic Events
Follicle Development in Ovary
Before birth
2n
Oogonium (stem cell)
Mitosis
Follicle cells
Oocyte
Primordial follicle
Primary oocyte
Growth
Primordial follicle
Primary oocyte (arrested in prophase I present at birth)
Childhood
(ovary inactive)
Each month from puberty to menopause
Primary follicle
Primary oocyte (still arrested in prophase I)
Growing follicle
Spindle
Vesicular (Graafian) follicle
Meiosis I (completed by one primary oocyte each month)
First polar body
n
Secondary oocyte (arrested in metaphase II)
Ovulation
Sperm
Ovulated secondary oocyte
Meiosis II of polar body (may or may not occur)
Meiosis II completed (only if sperm penetration occurs)
Polar bodies (all polar bodies degenerate)
Second polar body
Ovum

OOGENESIS

- Is the sequence of events by which germ cells oogonia differentiate into mature oocytes.



OOGENESIS

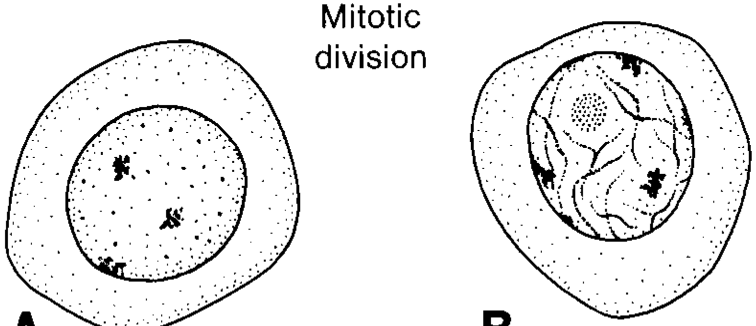
- Maturation of oocytes begins **before birth.**
- Accelerates at **puberty.**
- Ends at **menopause.**

Morphological changes during maturation of gametes

<u>Maturation of oocytes begin before birth</u>

<u>End of 3rd month</u>

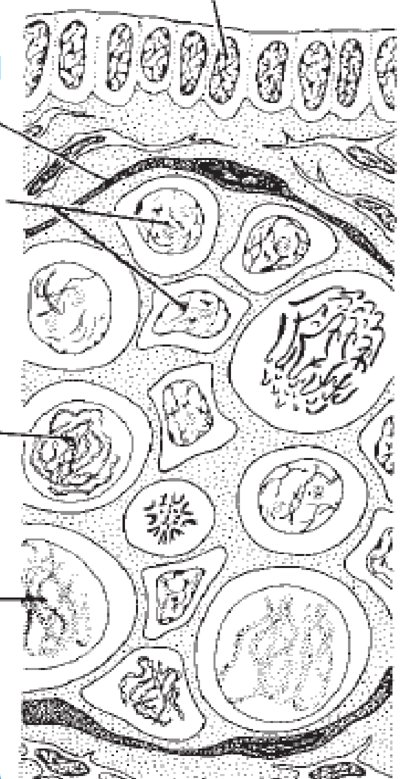
Mitotic division



A Primordial germ cell

B Oogonium

Mitotic division

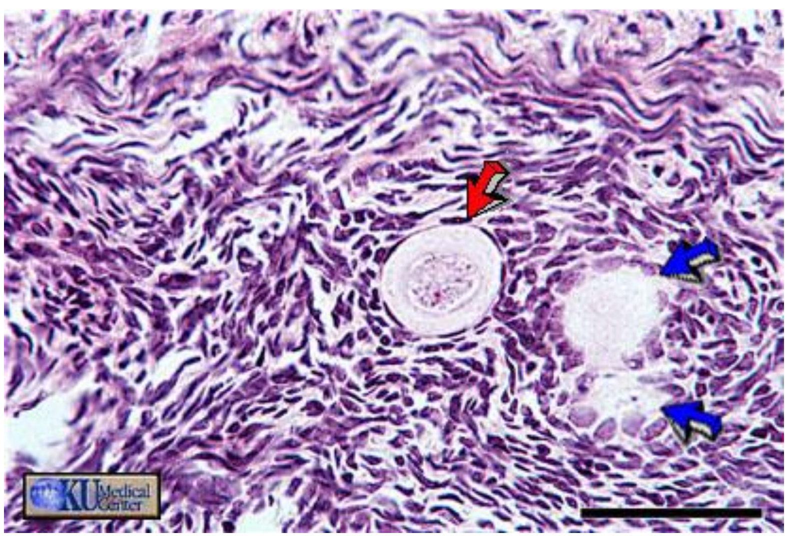


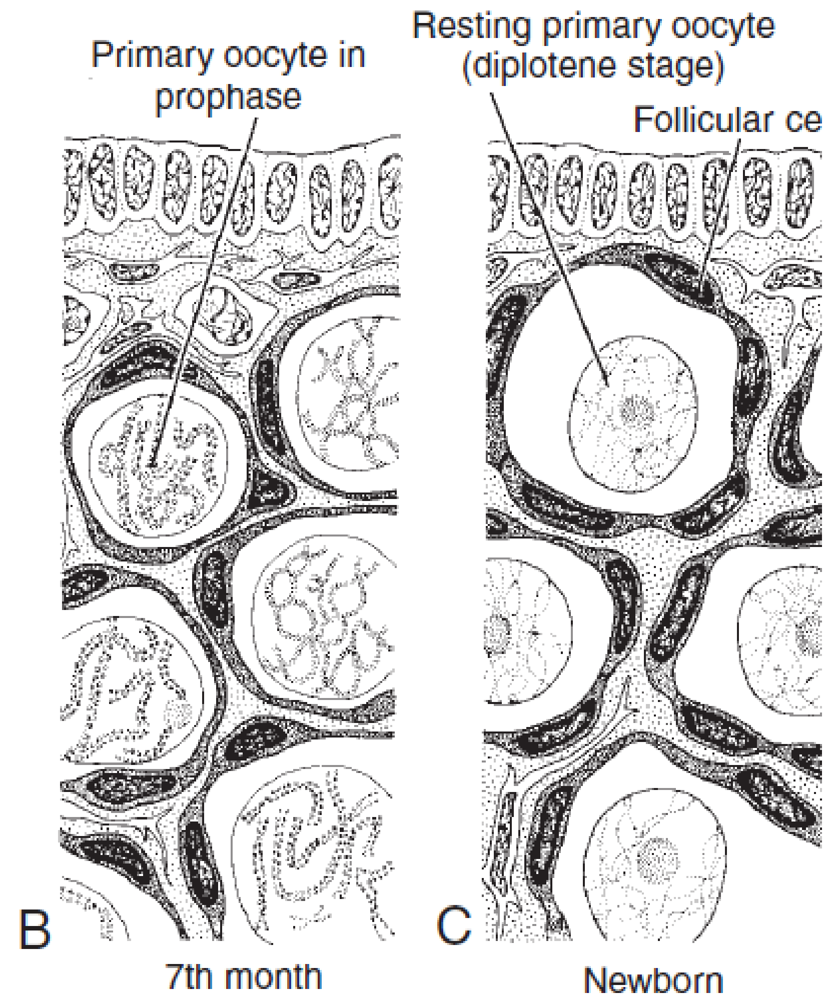
A

4th month

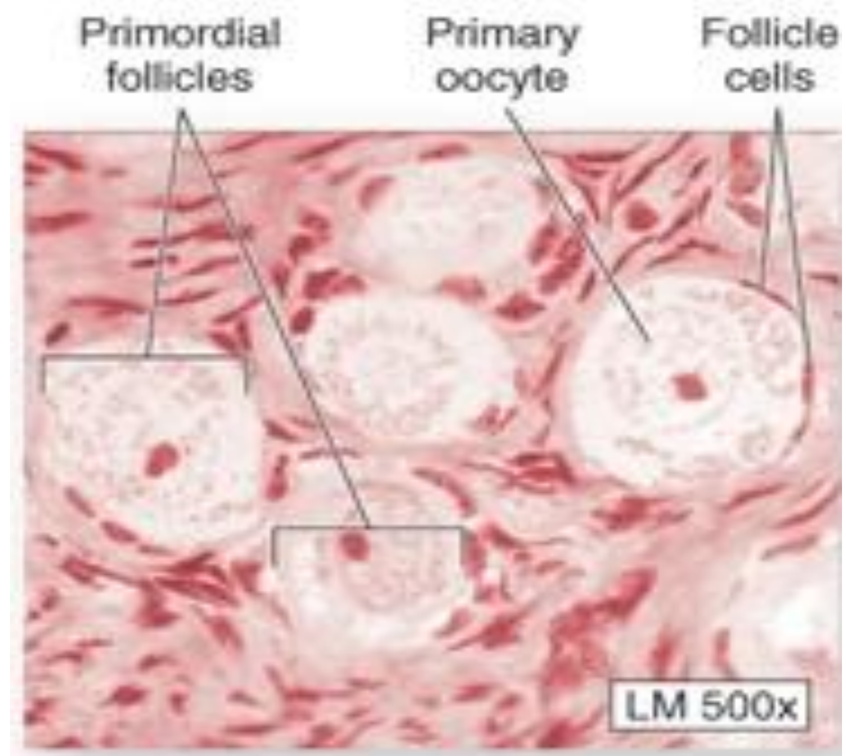
Segment of ovary showing different stages of development

- Majority of oogonia continue to divide by mitosis but some arrest their cell division in prophase of meosis I and form **primary oocytes**
- By 5th month number of germ cells reaches 7 million in the ovaries.
- Cell death (atresia) begins
- By 7th month majority of oogonia and primary oocyte degenerate.





- All surviving primary oocytes have entered the prophase of meiosis I, and most are individually surrounded by flat epithelial cells to form **primordial follicle.**



(b) Primordial follicles

Maturation of oocytes continue at puberty

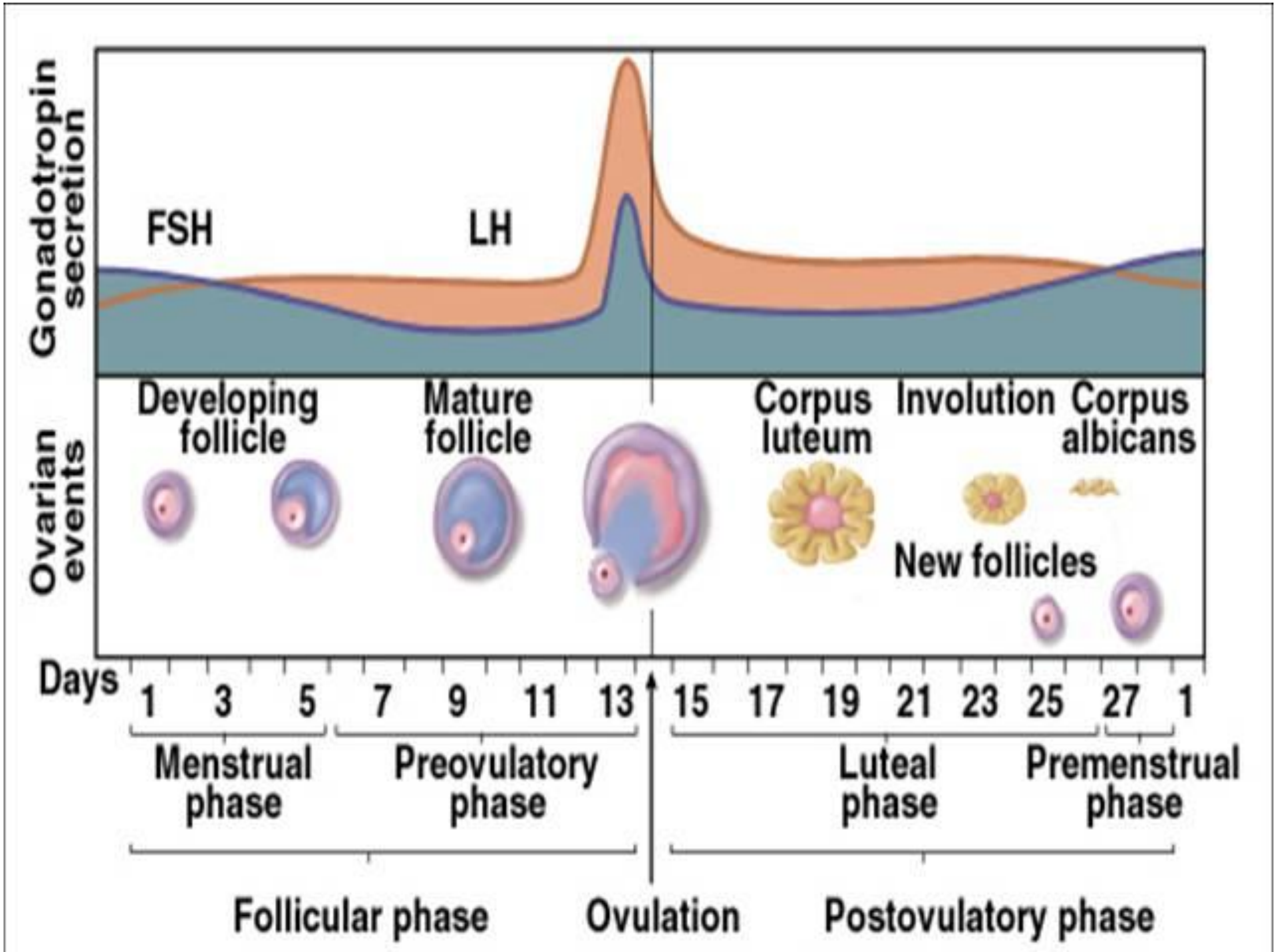
- **At birth: The total number of primary oocytes at birth is 600,000 – 800,000**

  All Primary oocytes are arrested in the **Diplotene stage** (resting stage during prophase, characterized by lacy network of chromatin) till puberty.

  This arrested stage is due to OMI secreted by follicular cells.

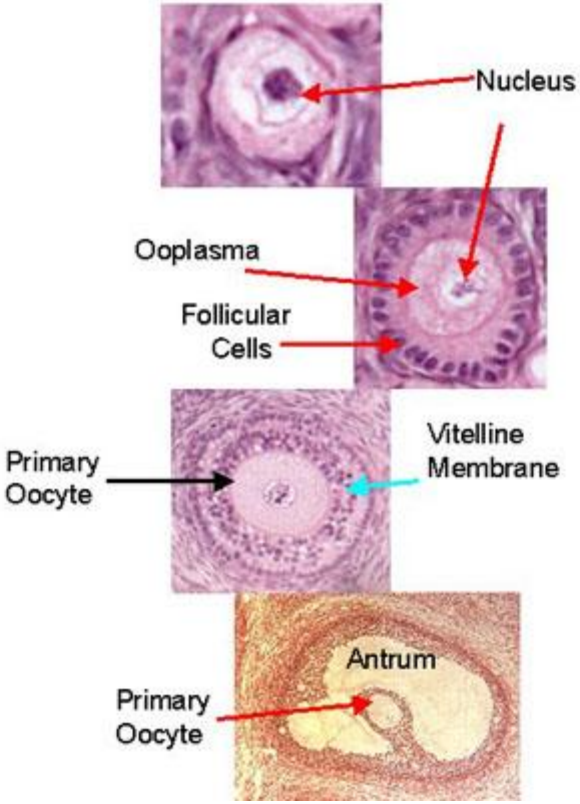
- **By puberty:** Number drops to about 40,000 by the beginning of puberty. Rising FSH triggers start of ovarian cycle
- **Ovarian cycle:** Fewer than 500 ovulate in the reproductive life of a female

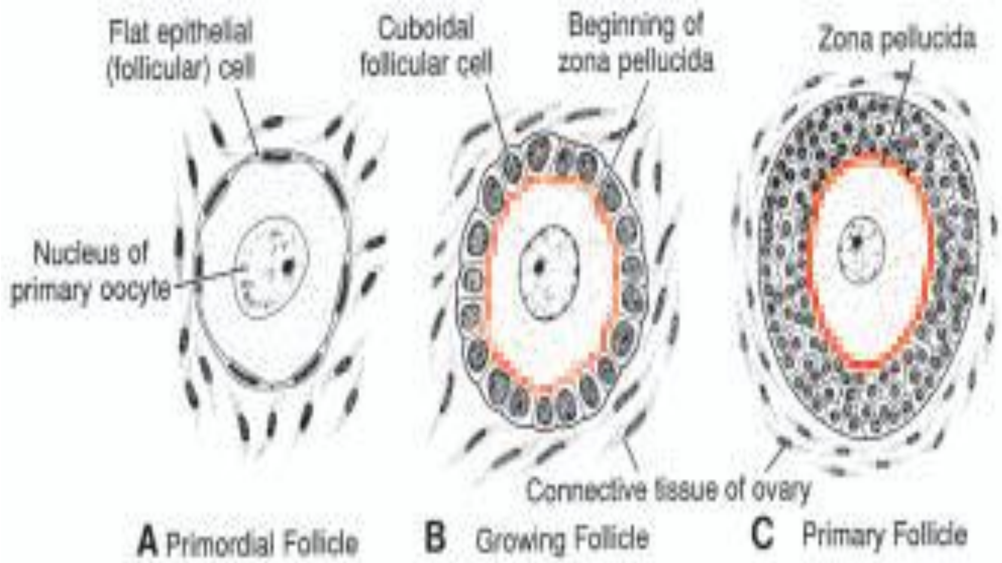
Ovarian Cycle

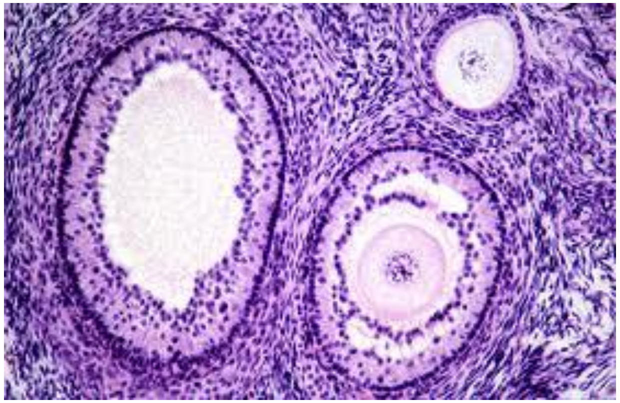


At puberty a pool of growing follicles is maintained from primordial follicles

Each month 15-20 follicles begin to mature and pass through 3 stages:





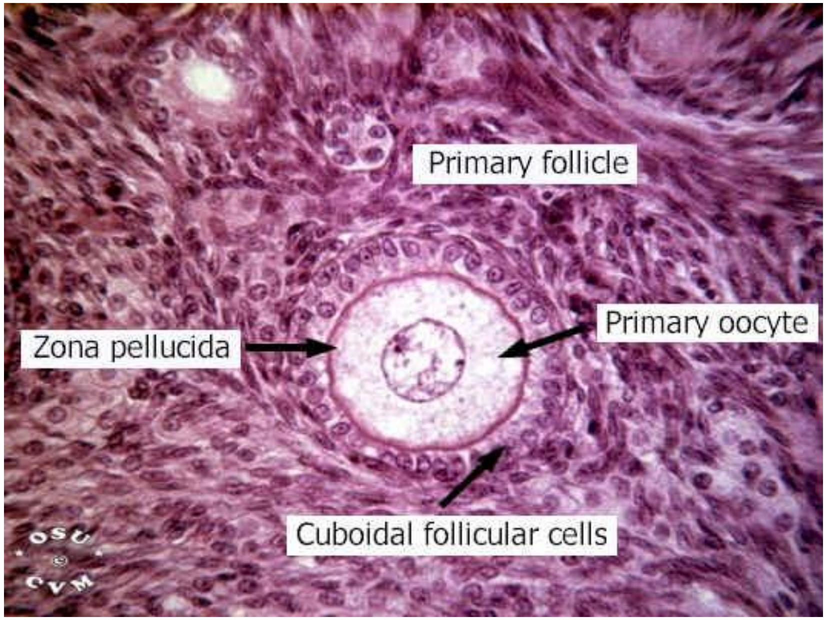


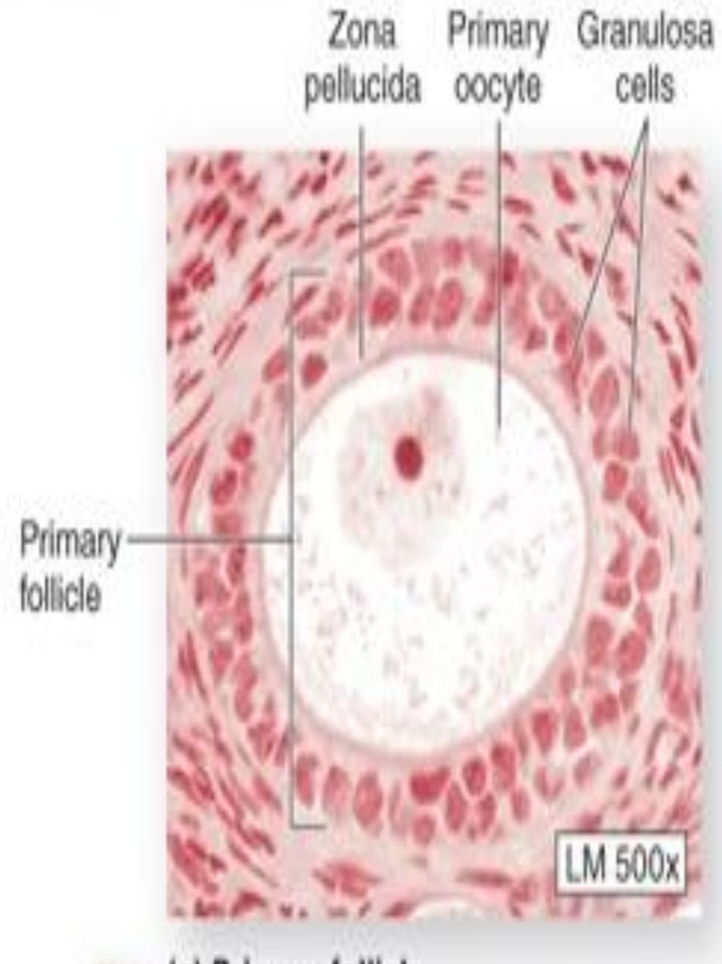
<u>Primary Follicle</u> (Preantral stage)

- Follicular cells will form a stratified epithelium/granulosa cells around the primary oocyte

- Granulosa cells rest on a basement membrane that separates them from ovarian connective tissue (stromal cells) that form theca folliculi.

- Zona pellucida- a layer of glycoprotein secreted by granulosa cells and oocyte

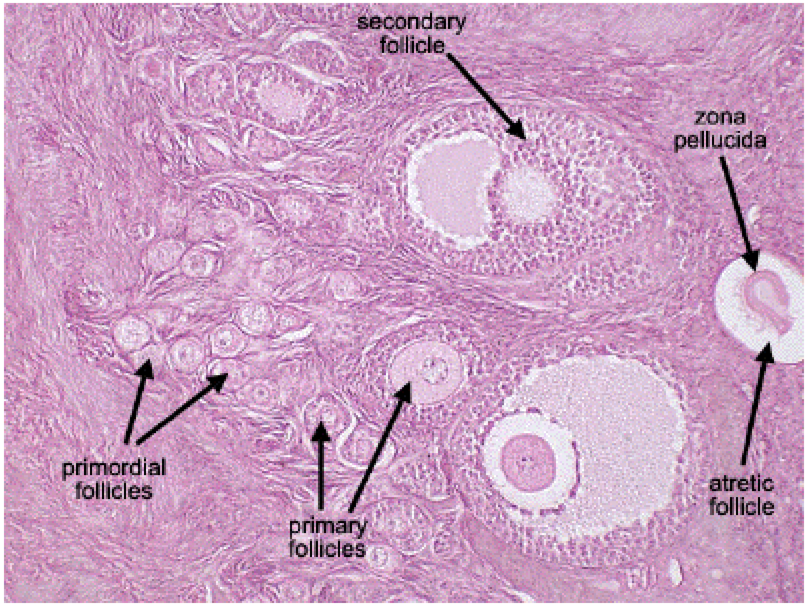




(c) Primary follicle

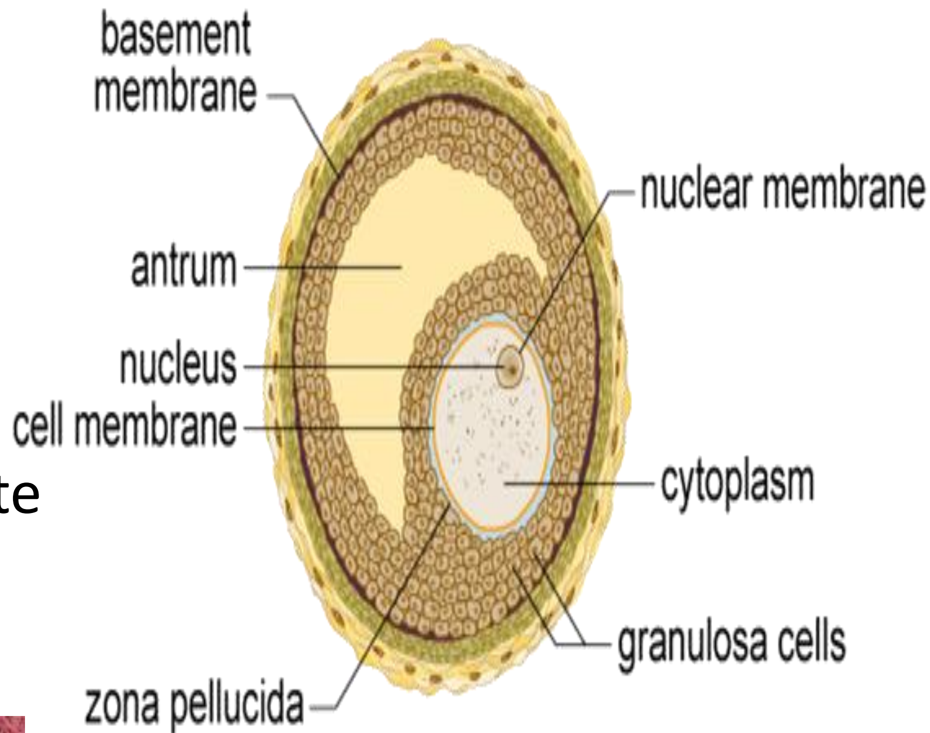
Growing follicles

- As the follicles continue to grow cells , cells of theca folliculi organize into layers.
- Finger like processes of follicular cells interdigitates with microvilli of plasma membrane of oocyte



Secondary/Antral/Vesicular Follicle At maturity size reaches(25mm)

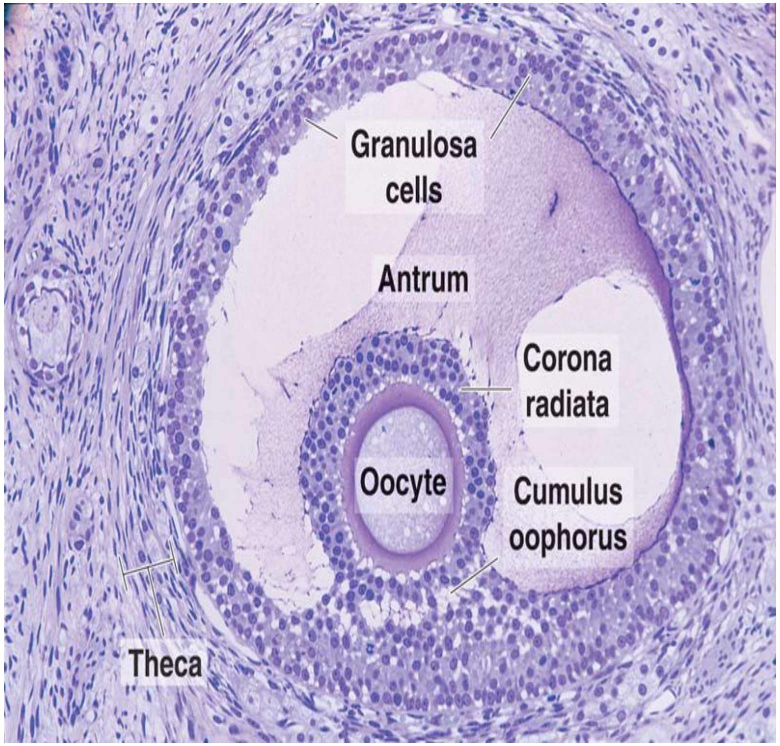
- Longest stage
- Stratum granulosum 6-12 cell layers
- Liquor folliculi (hyaluronic acid)
- **Formation of Antrum**
- Granulosa cells surrounding the oocyte remains intact and oocyte is off center.
- Well defined **Theca interna & externa**



Secondary or Antral Follicle

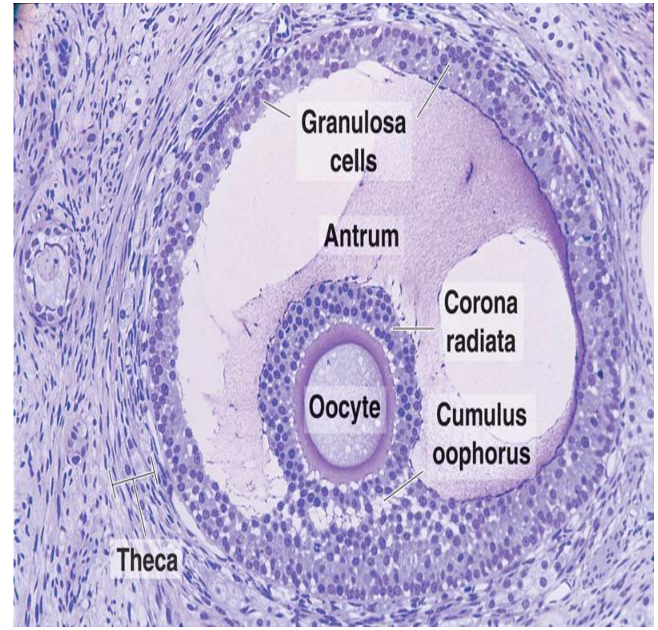
Tertiary or Graafian Follicle (Preovulatory stage lasts for 37 hrs)

- Spans entire width of cortex & produces a bulge on the surface of ovary
- St. granulosum appears to be thinner
- One large antral cavity
- Cumulus oophorus & corona radiata (loose connection)
- A surge in LH, First meiotic division being completed: Primary oocyte divides into a Secondary oocyte and a polar body



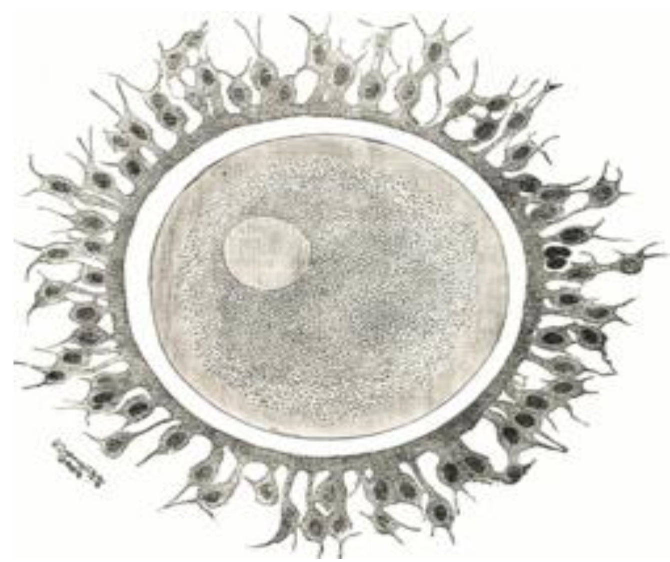
Cumulus oophorus

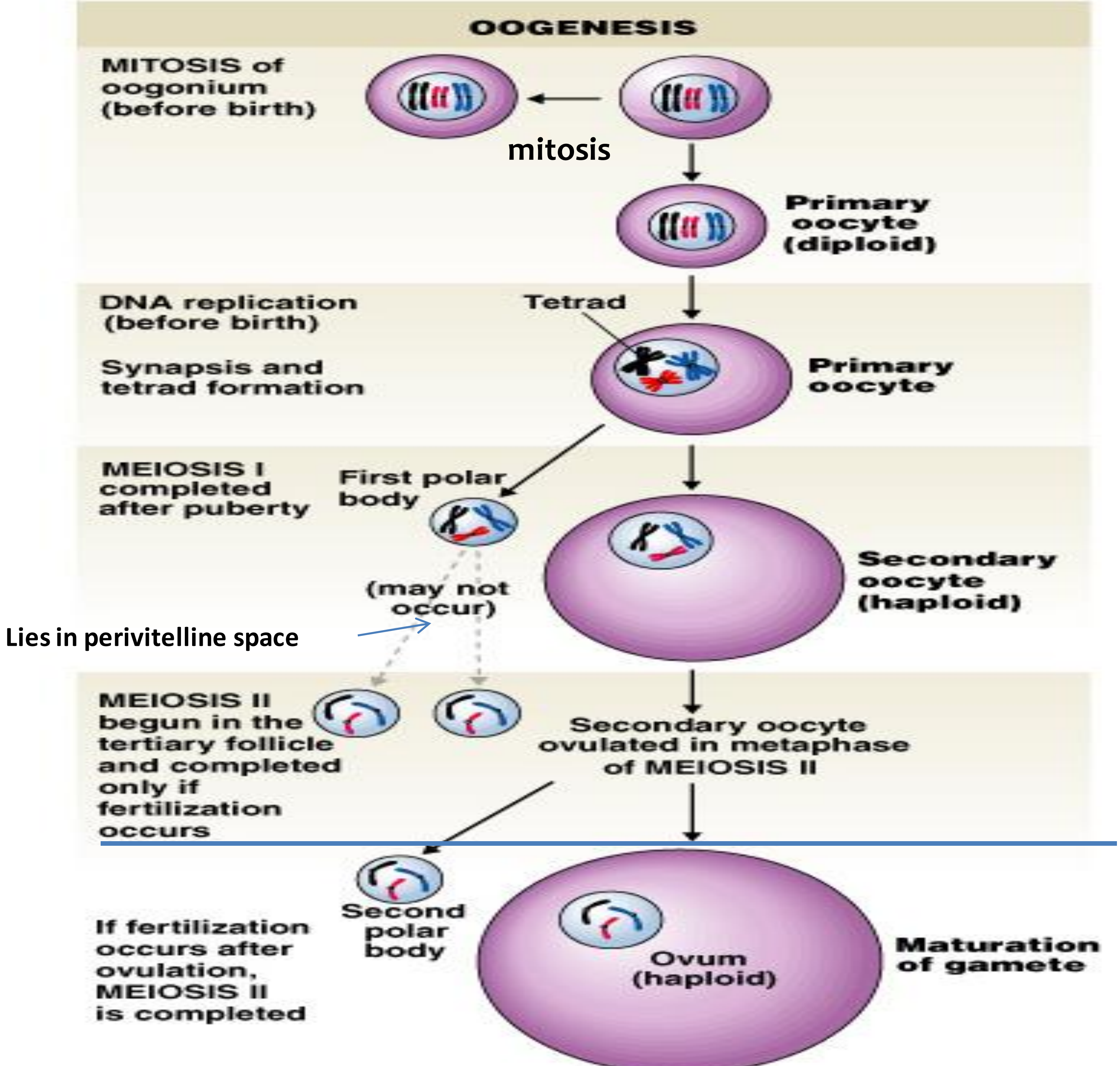
- Is a column/mound of granulosa cells that attaches the oocyte to the follicle wall. At ovulation, this column of cells is broken or separates to release the oocyte from its follicle attachment.



Corona radiata

- Is composed of cumulus/granulosa cells that immediately surround the oocyte & send microvilli through ZP that communicate with microvilli of oocyte




OOGENESIS
MITOSIS of oogonium (before birth)
mitosis
Primary oocyte (diploid)
DNA replication (before birth)
Synapsis and tetrad formation
Tetrad
Primary oocyte
MEIOSIS I completed after puberty
First polar body
Secondary oocyte (haploid)
(may not occur)
Lies in perivitelline space
MEIOSIS II begun in the tertiary follicle and completed only if fertilization occurs
Secondary oocyte ovulated in metaphase of MEIOSIS II
Second polar body
If fertilization occurs after ovulation, MEIOSIS II is completed
Ovum (haploid)
Maturation of gamete

Maternal Contributions to the Oocyte

As the oocyte is a product of female gametogenesis, the maternal contribution to the oocyte and consequently the newly fertilized egg is enormous. There are many types of molecules that are maternally supplied to the oocyte which will direct various activities within the growing zygote.

- Half of zygotic genome
- Maternal Mitochondria
- Maternal Nucleolus
- Maternal Ribosomes

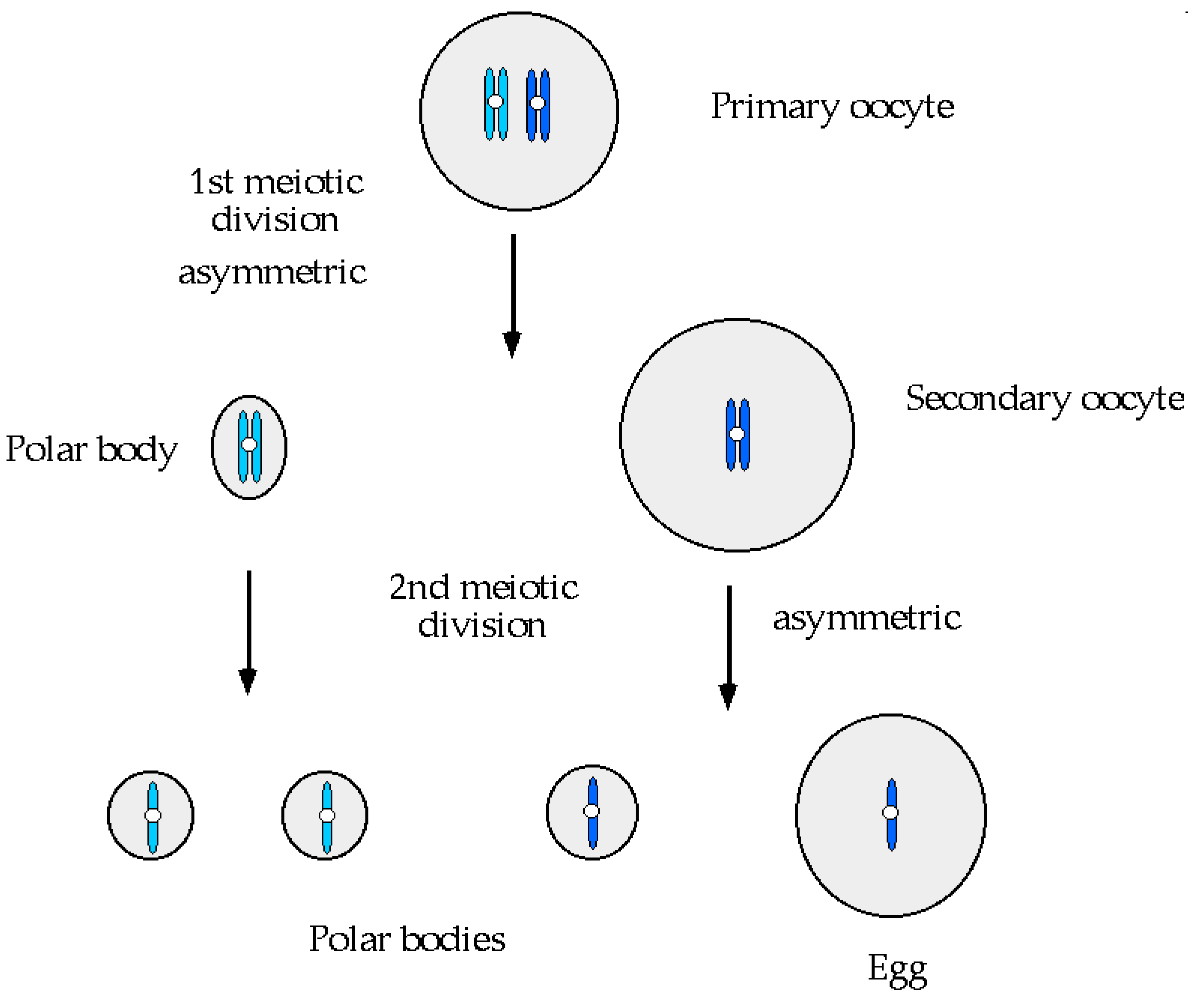
Paternal Contributions to the Oocyte

- Half of zygotic genome
- Centriole

Oogenesis

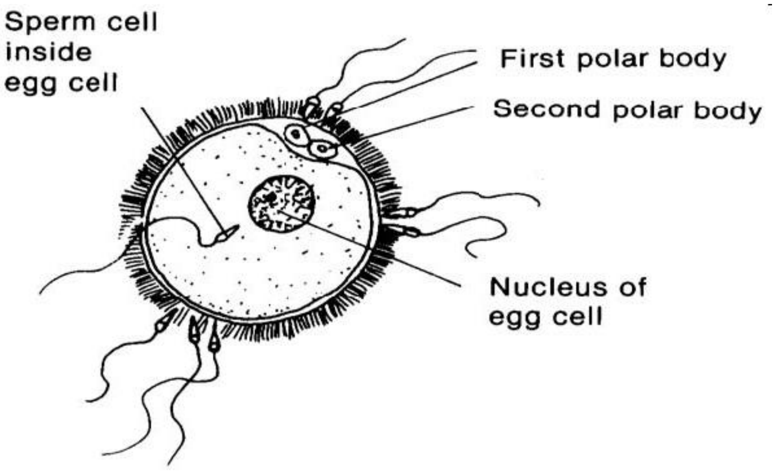
- SUMMARY of OOGENESIS:
  - Results in three POLAR BODIES and one OVUM (egg) that has extra cytoplasm
  - Meiosis I occurs during ovulation
  - Meiosis II occurs after fertilization
  - Occurs in the ovaries (and fallopian tubes for meiosis II) in females

Oogenesis



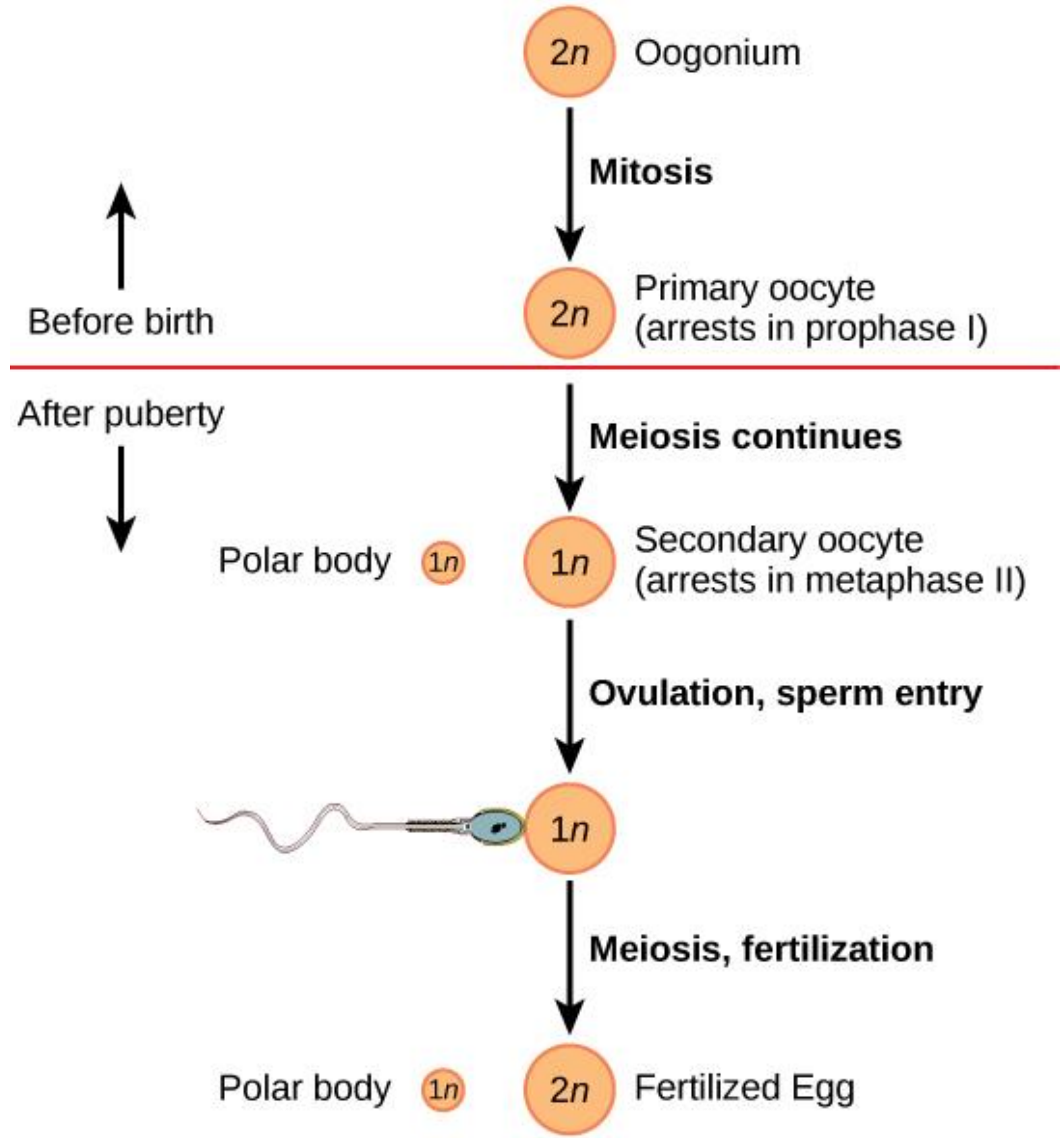
Primary oocyte
1st meiotic division
asymmetric
Polar body
Secondary oocyte
2nd meiotic division
asymmetric
Polar bodies
Egg

- **Oogenesis** is the creation of an ovum (an egg cell).
- It is the female process of gametogenesis.
- It involves the various stages of immature ova.



- Oogenesis is the process of meiosis in female organisms from an oogonium to a primary oocyte, to a secondary oocyte, and then to an ovum.
- Oogenesis begins soon after fertilization, as primordial germ cells travel from the yolk sac to the gonads, where they begin to proliferate mitotically.

- The germ cells multiply from only a few thousand to almost 7 million. They become oocytes once they enter the stages of meiosis several months after birth.
- Now called primordial follicles, they are made up of oogenic cells from the primordial germ cells surrounded by follicle cells from the somatic line.
- The oocyte is then arrested in the first meiotic prophase until puberty.

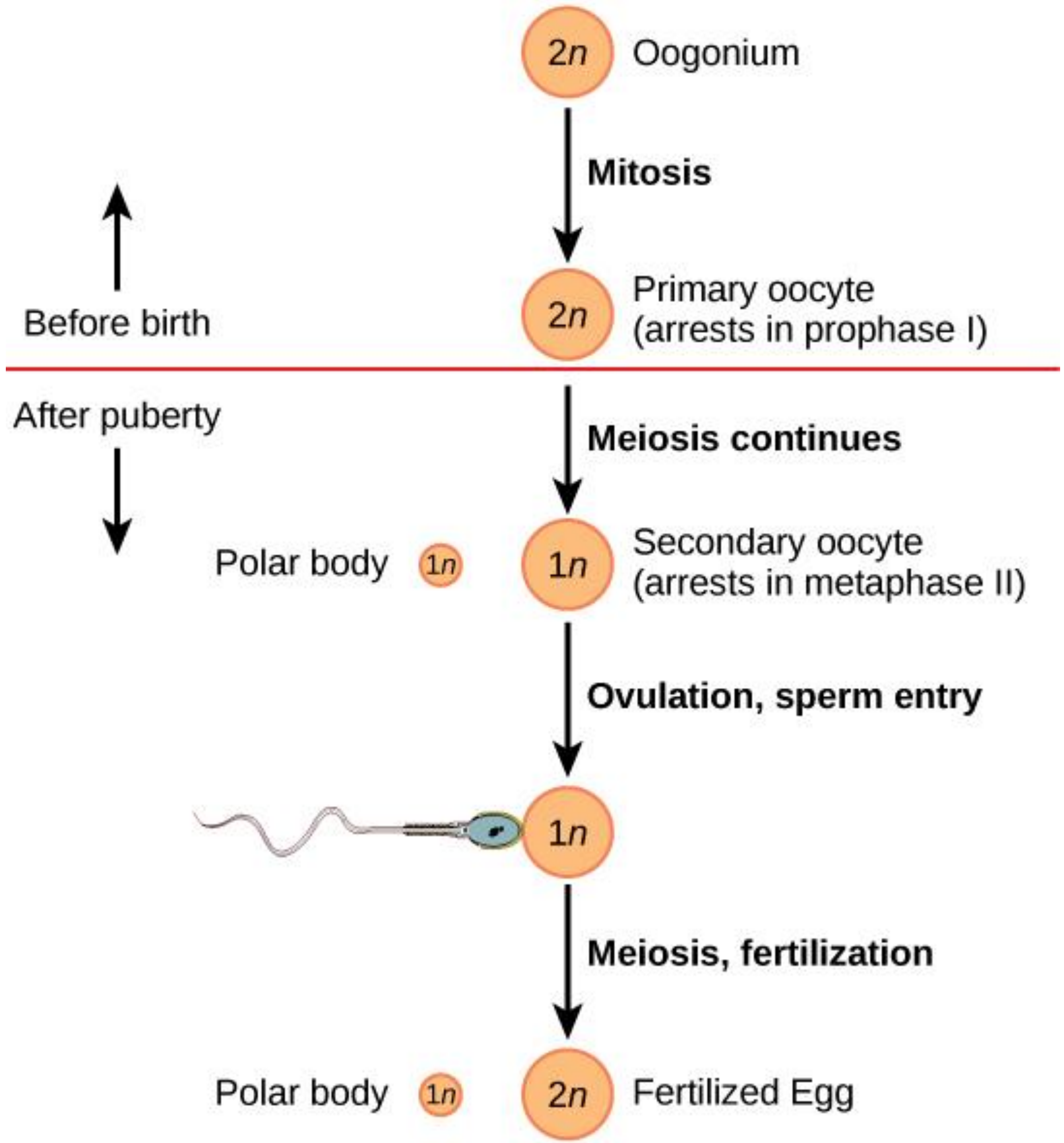


- At puberty, between 4 to 10 follicles begin to develop, although only 1-2 are actually released.

- Surrounding each oocyte is a zona pellucida, membrana granulosa, and theca cell layer. Each oocyte finishes its first meiotic division, creating a secondary oocyte and polar body, which serves no further function.

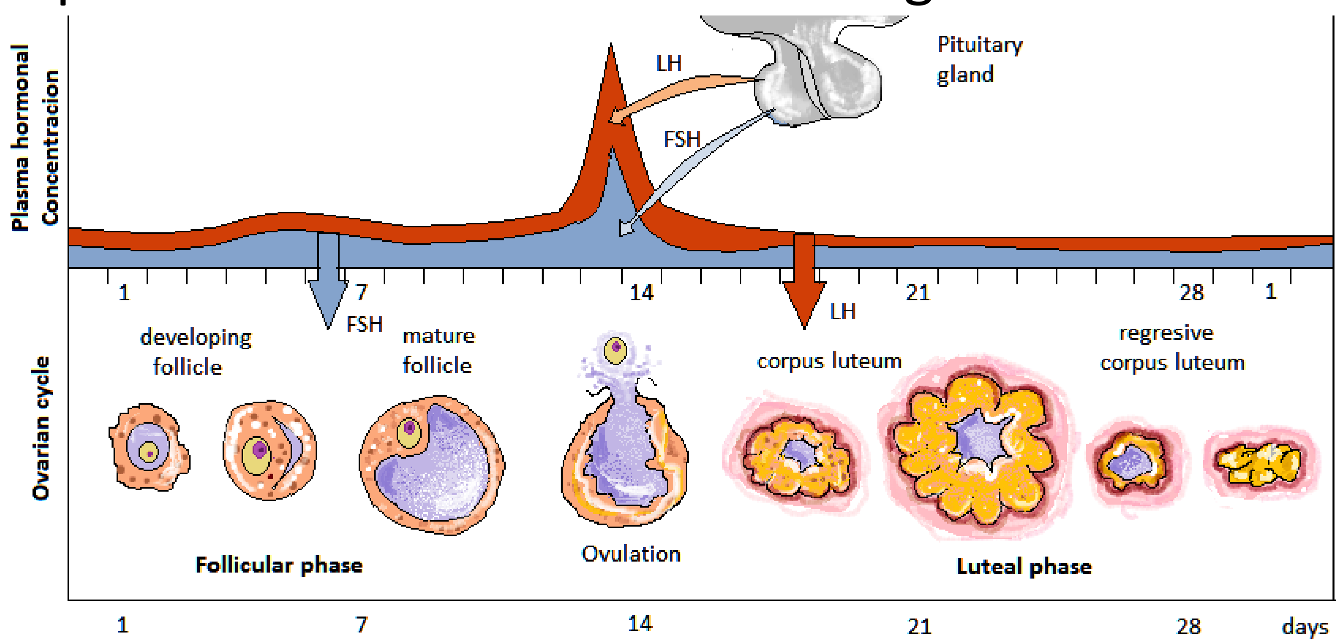
- It begins the next meiosis cycle and is arrested in its second metaphase, at which point it is released from the ovary in ovulation.

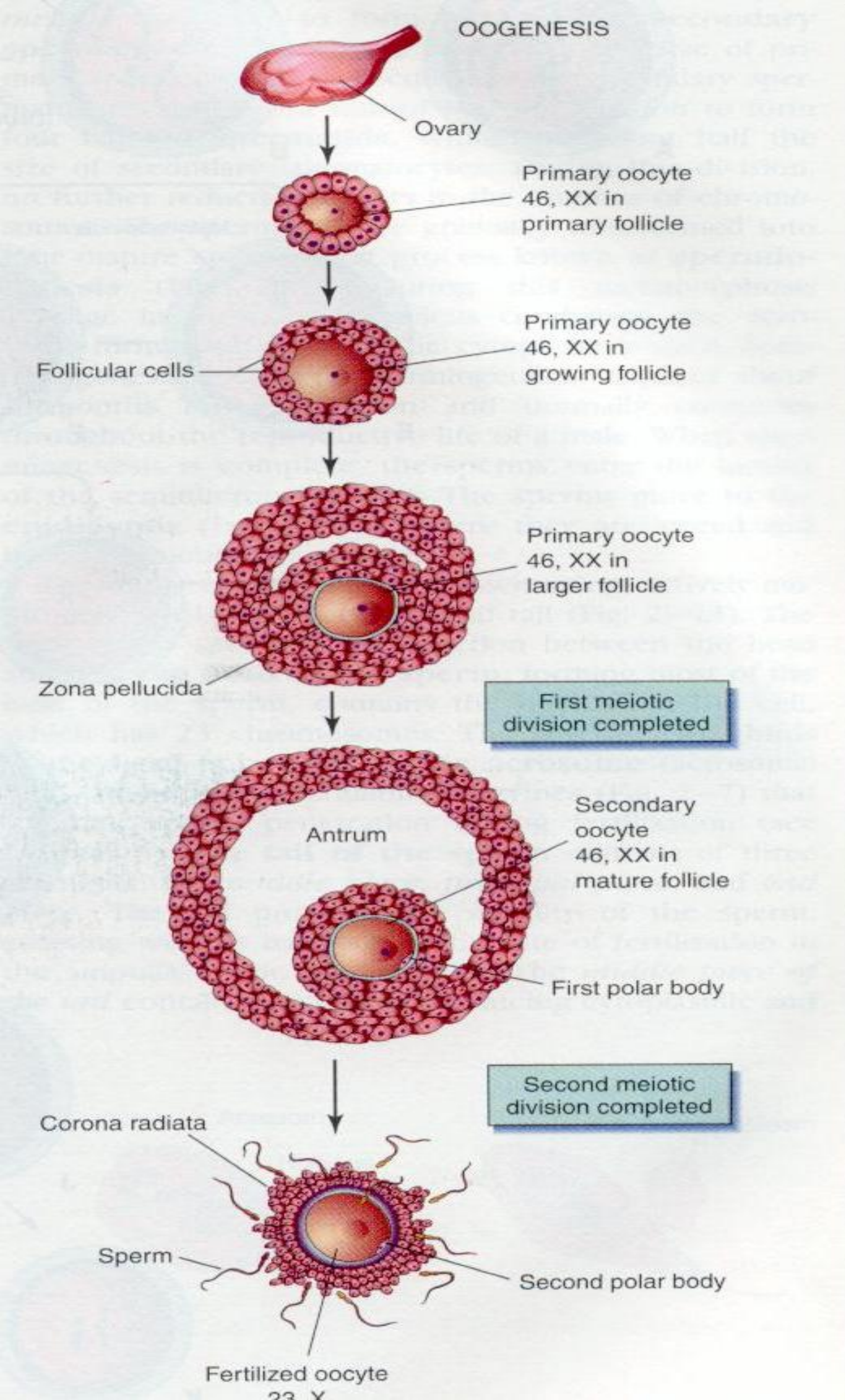
- It will not finish the meiosis cycle until it encounters the stimuli of a sperm.



Process of Human Oogenesis

- At the start of the menstrual cycle some 12 to 20 primary follicles begin to develop under the influence of elevated FSH to form secondary follicles.
- By around day 9 of the cycle only one healthy secondary follicle is remaining, with the rest having undergone atresia.
- The remaining follicle is called the dominant follicle and is responsible for producing large amounts of oestradiol during the late follicular phase. Oestradiol production depends on co-operation between the theca and granulosa cells.

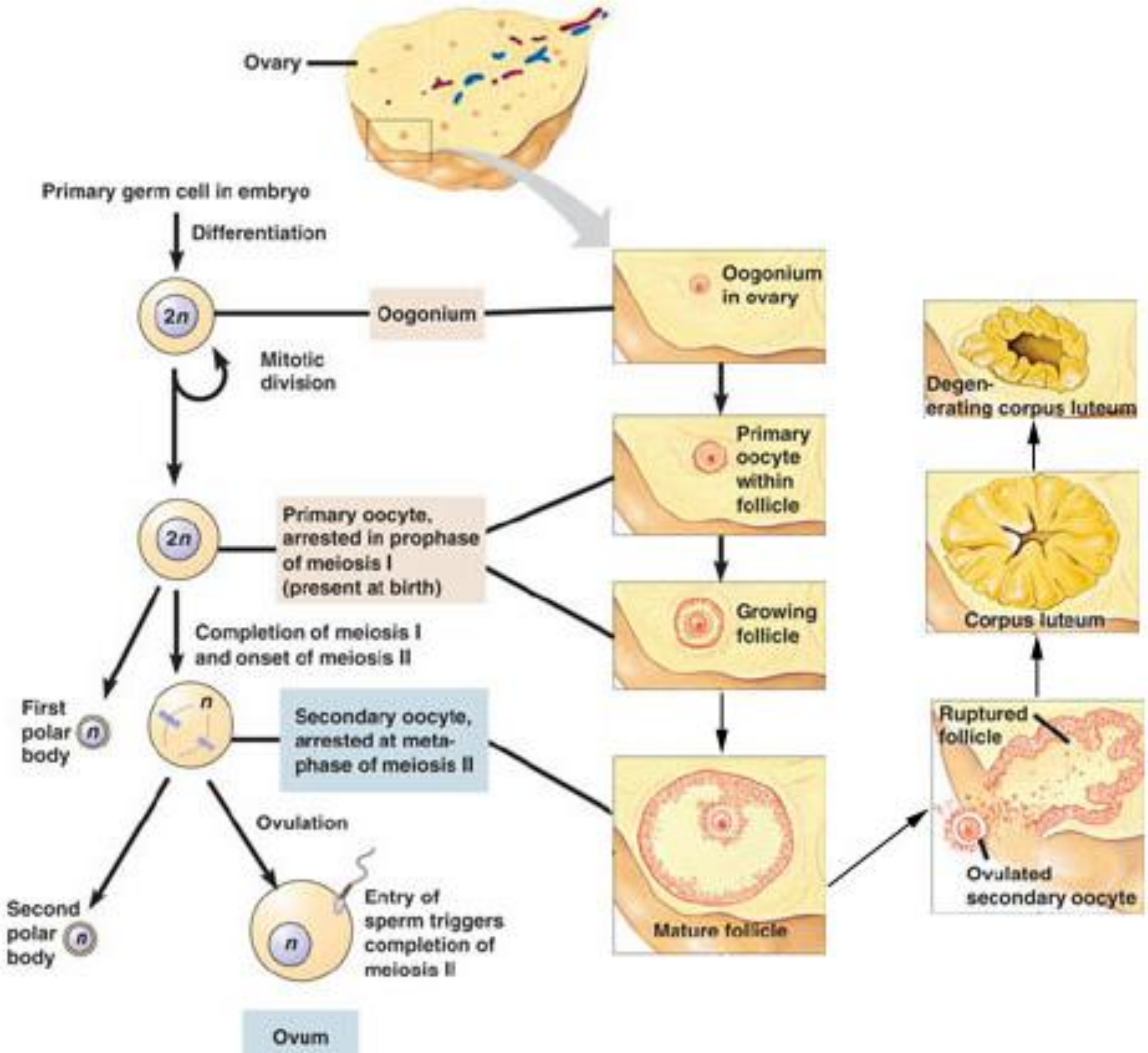




On day 14 of the cycle an LH surge occurs which is triggered by positive feedback of oestradiol. This causes the secondary follicle to turn into a tertiary follicle which ovulates some 24–36 hours later.

An important event in the tertiary follicle is that the primary oocyte completes the first meiotic division with formation of a polar body and a secondary oocyte.

The empty follicle then forms a corpus luteum (The **corpus luteum** (plural **corpora lutea**) is a temporary endocrine structure in mammals, involved in production of progestogen, which is needed to maintain the endometrium.).


Ovary
Primary germ cell in embryo
Differentiation
2n
Oogonium
Oogonium in ovary
Mitotic division
2n
Primary oocyte, arrested in prophase of meiosis I (present at birth)
Primary oocyte within follicle
Growing follicle
Completion of meiosis I and onset of meiosis II
First polar body
n
n
Secondary oocyte, arrested at meta-phase of meiosis II
Ovulation
Mature follicle
Second polar body
n
n
Entry of sperm triggers completion of meiosis II
Ovum
Ruptured follicle
Ovulated secondary oocyte
Corpus luteum
Degen-erating corpus luteum

Maturation processes prepare the oocyte for ovulation and fertilization

Most oocytes of different species are arrested in the first meiotic division.

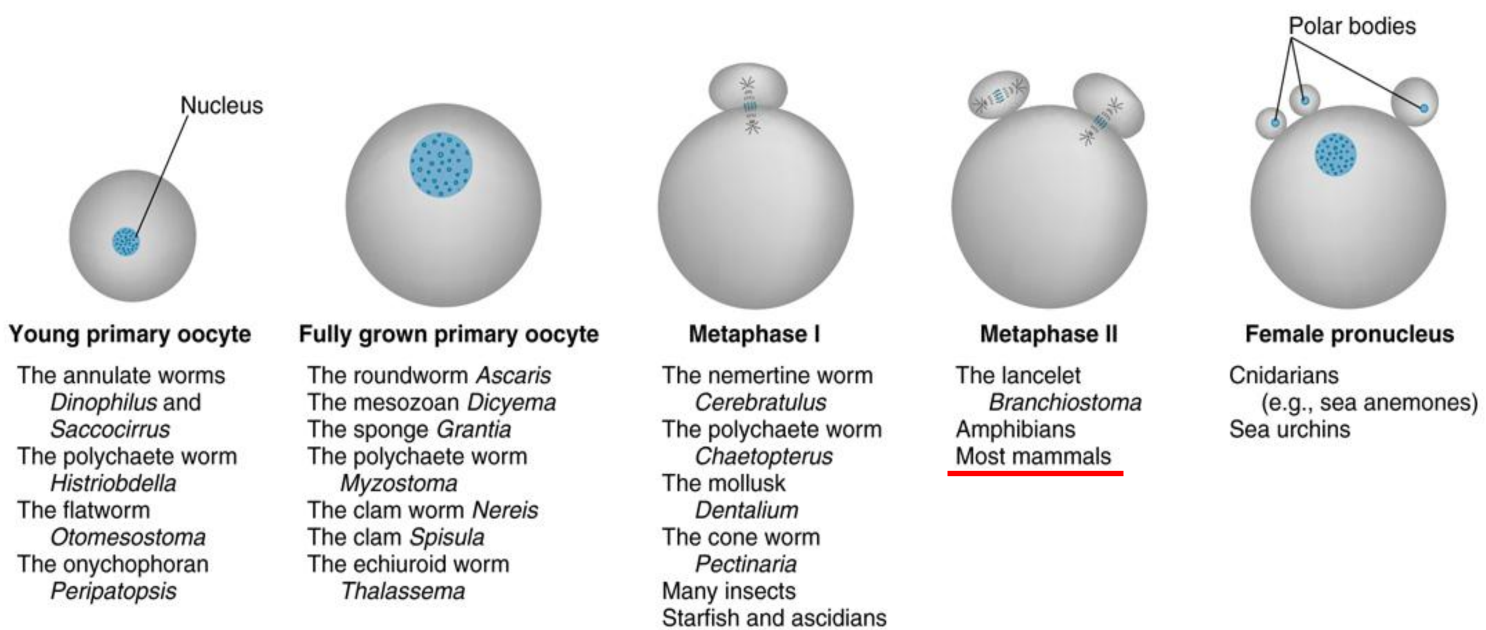
Oocyte maturation begins officially when this block is removed and meiosis starts once again.

1. The nuclear membrane breaks down and DNA starts to condense into chromosomes

2. The permeability of the oocyte plasma membrane changes so it can function outside of the ovary.

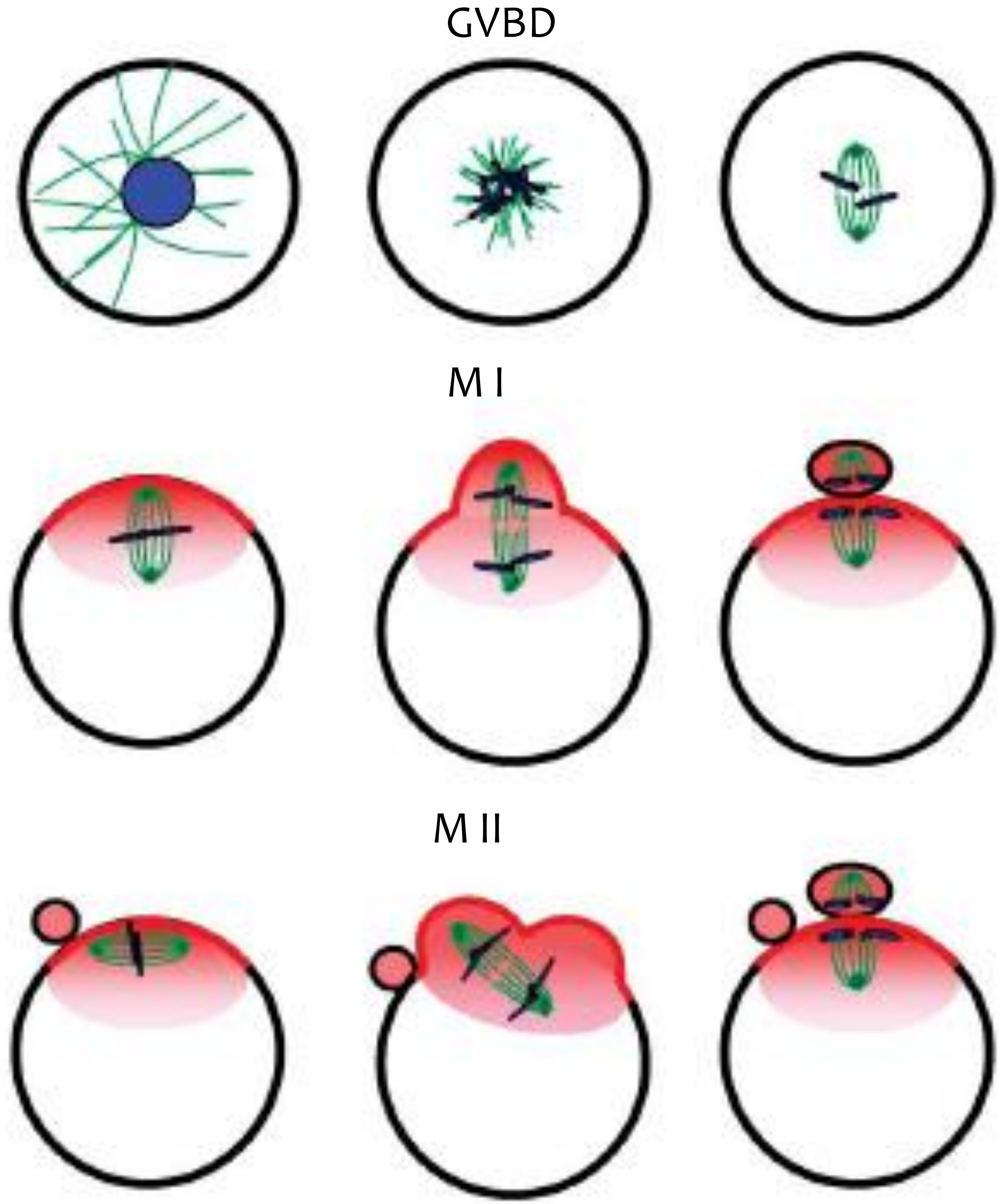
3. The plasma membrane develops receptors to interact with the sperm

<u>Fertilization occurs at different stages of oocyte maturation</u>:

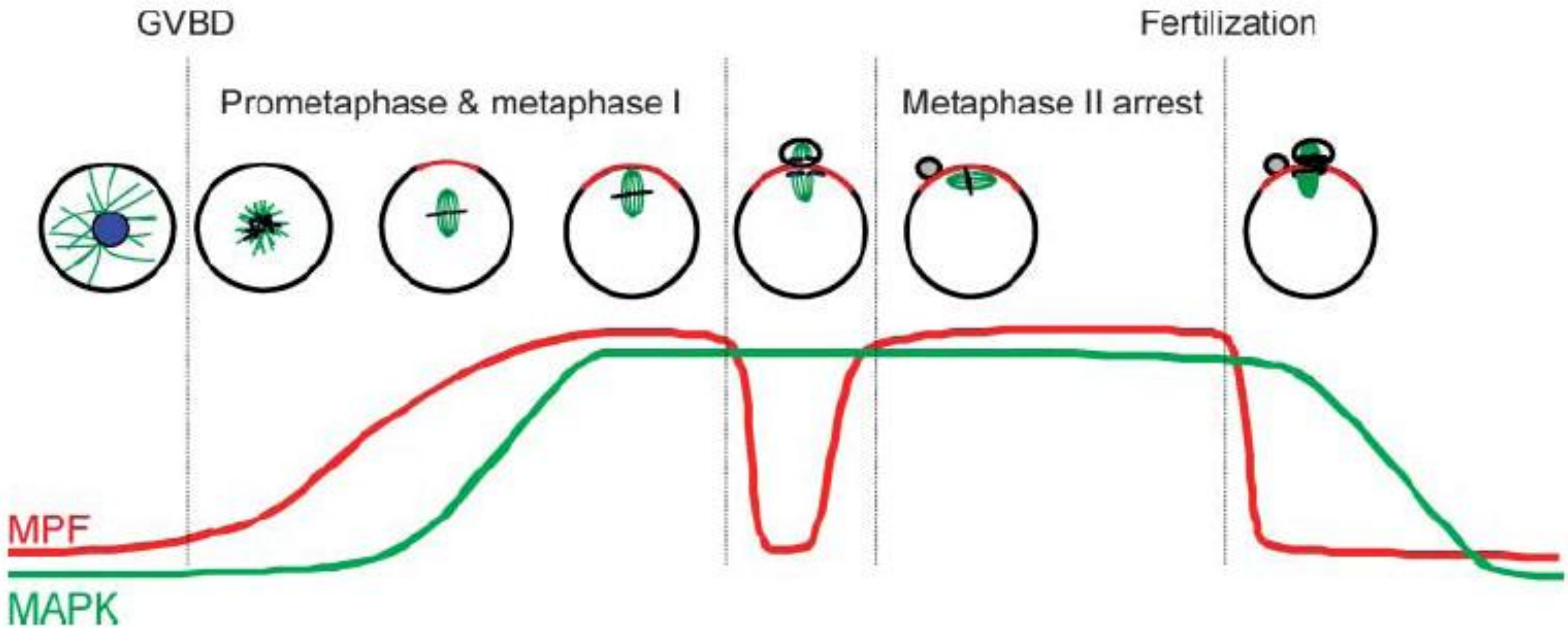


Maturation processes prepare the oocyte for ovulation and fertilization

- At GVBD (first row), microtubules (in green) polymerize radially around the mass of chromosomes and organize progressively into a bipolar spindle. At the end of MI (second row), the bipolar spindle migrates toward the oocyte cortex. Spindle migration induces the local reorganization of the cortex of the oocyte (red and pink area). The first polar body is extruded in the axis of spindle migration. During MII arrest (third row), the metaphase spindle is anchored under the plasma membrane. The cortex reorganization is maintained in the vicinity of the spindle. Fertilization or experimental activation of the oocyte triggers a 90° spindle rotation and the extrusion of the second polar body.



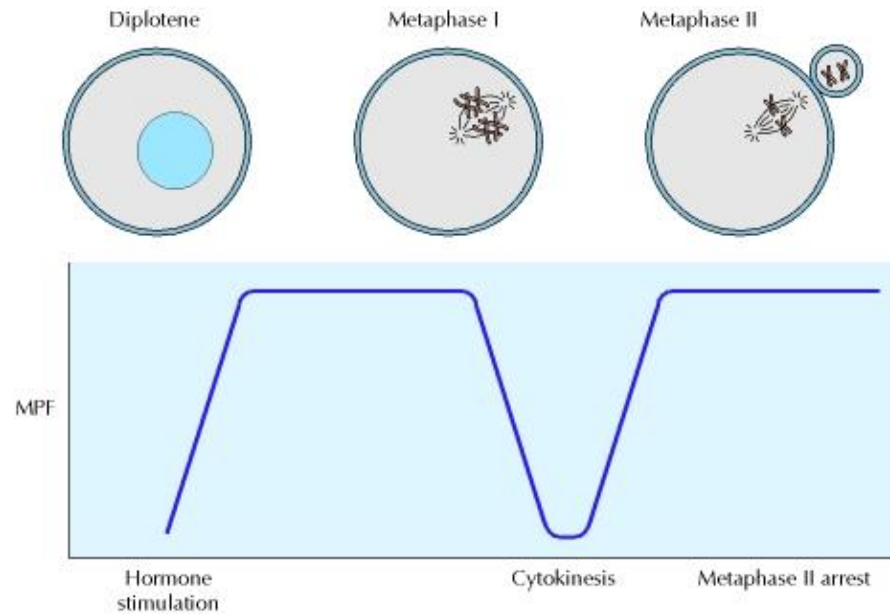
The different steps of meiotic maturation



- MPF (Maturation Promoting Factor)
- MAPK (Mitogen-Activated Protein Kinases)
- MPF and MAPK activities during meiotic maturation in mouse oocytes.
- MPF activity appears as a red line and MAPK as a green line.

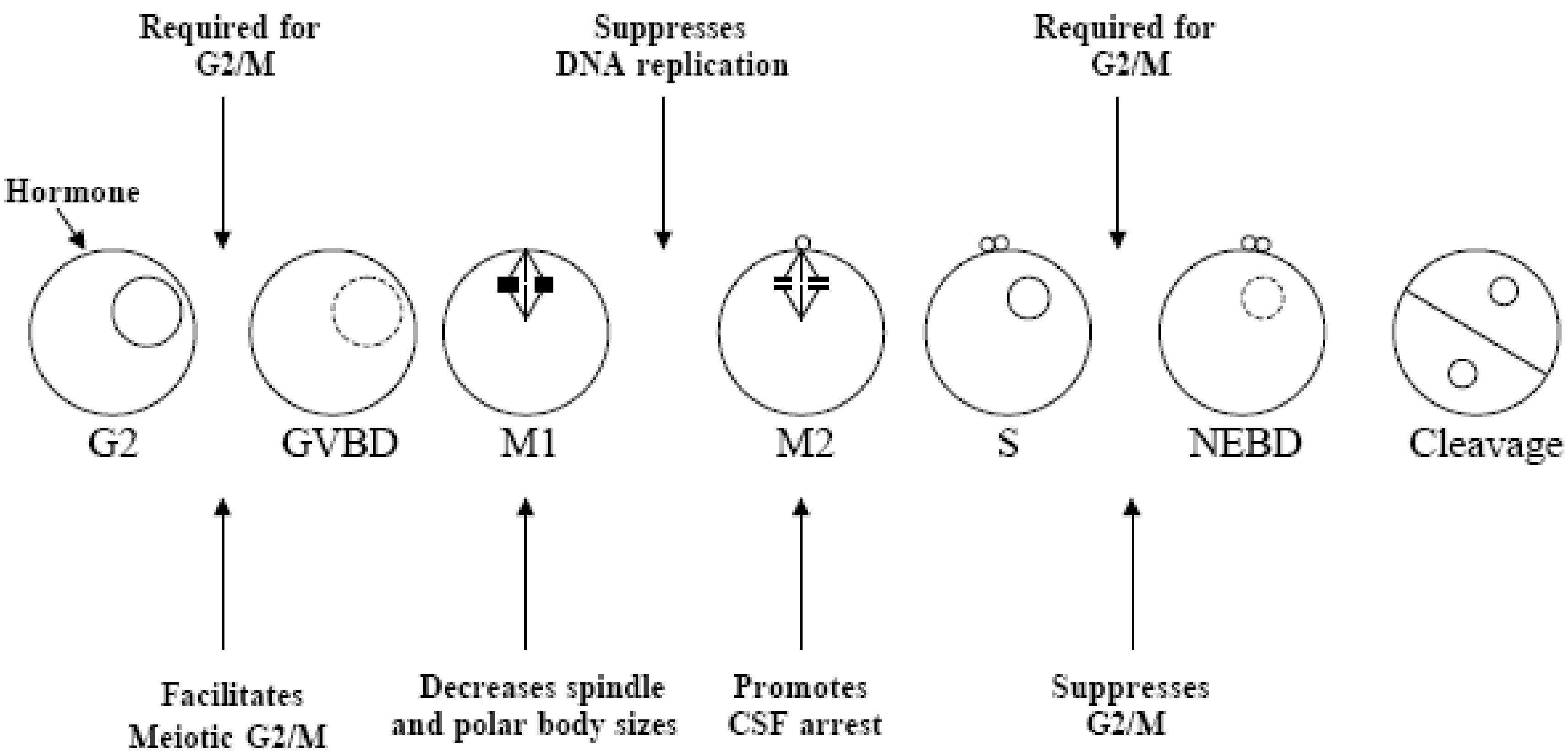
MPF (Cdk1/CyclinB)

- Like the M phase of somatic cells, the meiosis of oocytes is controlled by MPF.
- The regulation of MPF during oocyte meiosis, however, displays unique features that are responsible for metaphase II arrest.
- Hormonal stimulation of diplotene-arrested oocytes initially triggers the resumption of meiosis by activating MPF, as at the G_2 to M transition of somatic cells.
- As in mitosis, MPF then induces chromosome condensation, nuclear envelope breakdown, and formation of the spindle. Activation of the anaphase-promoting complex B then leads to the metaphase to anaphase transition of meiosis I, accompanied by a decrease in the activity of MPF.



Following cytokinesis, however, MPF activity again rises and remains high while the egg is arrested at metaphase II. A regulatory mechanism unique to oocytes thus acts to maintain MPF activity during metaphase II arrest, preventing the metaphase to anaphase transition of meiosis II and the inactivation of MPF that would result from cyclin B proteolysis during a normal M phase.

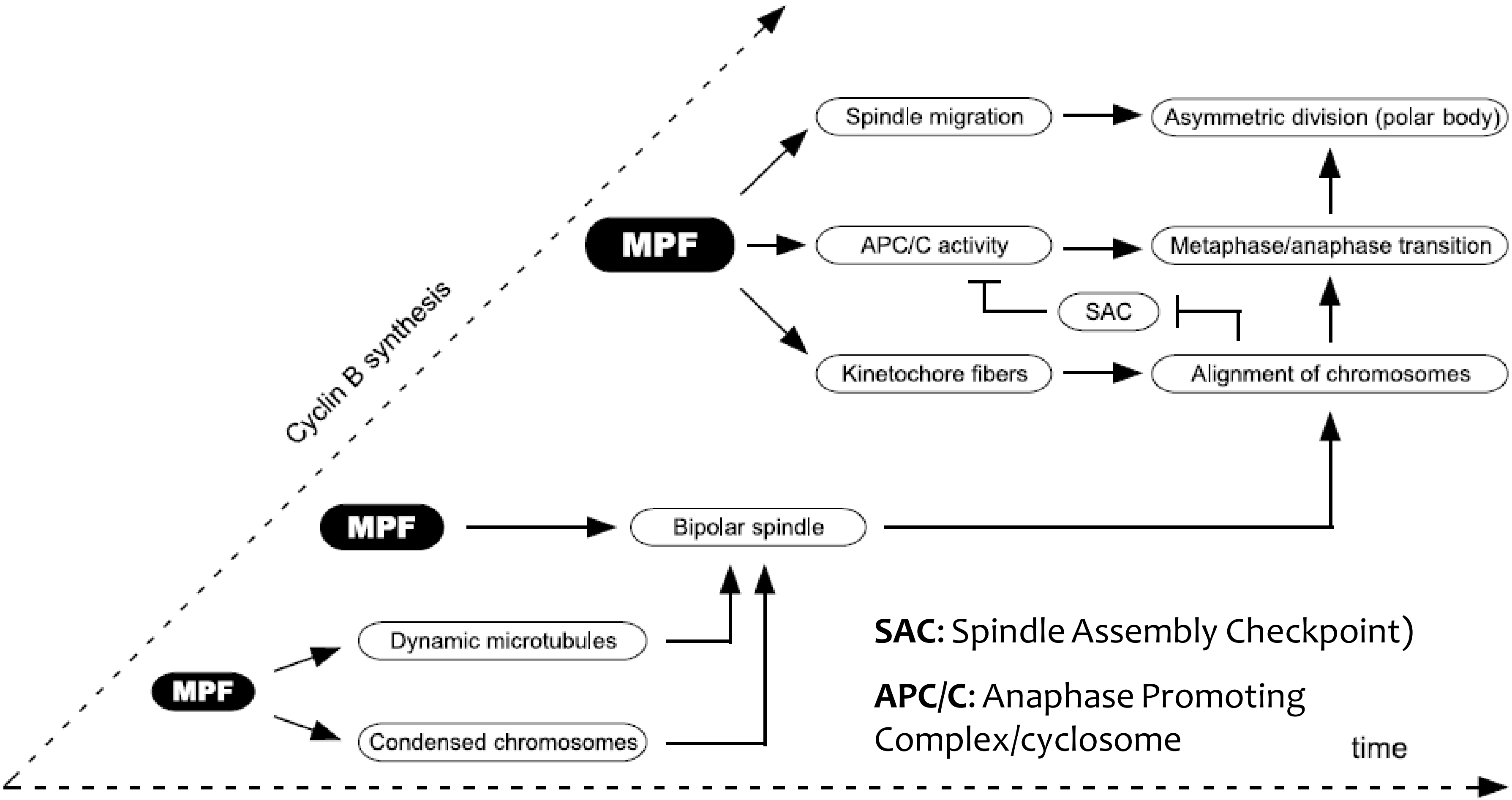
MPF



MAP kinases

Correlation of MPF ve Cyclin B Synthesis

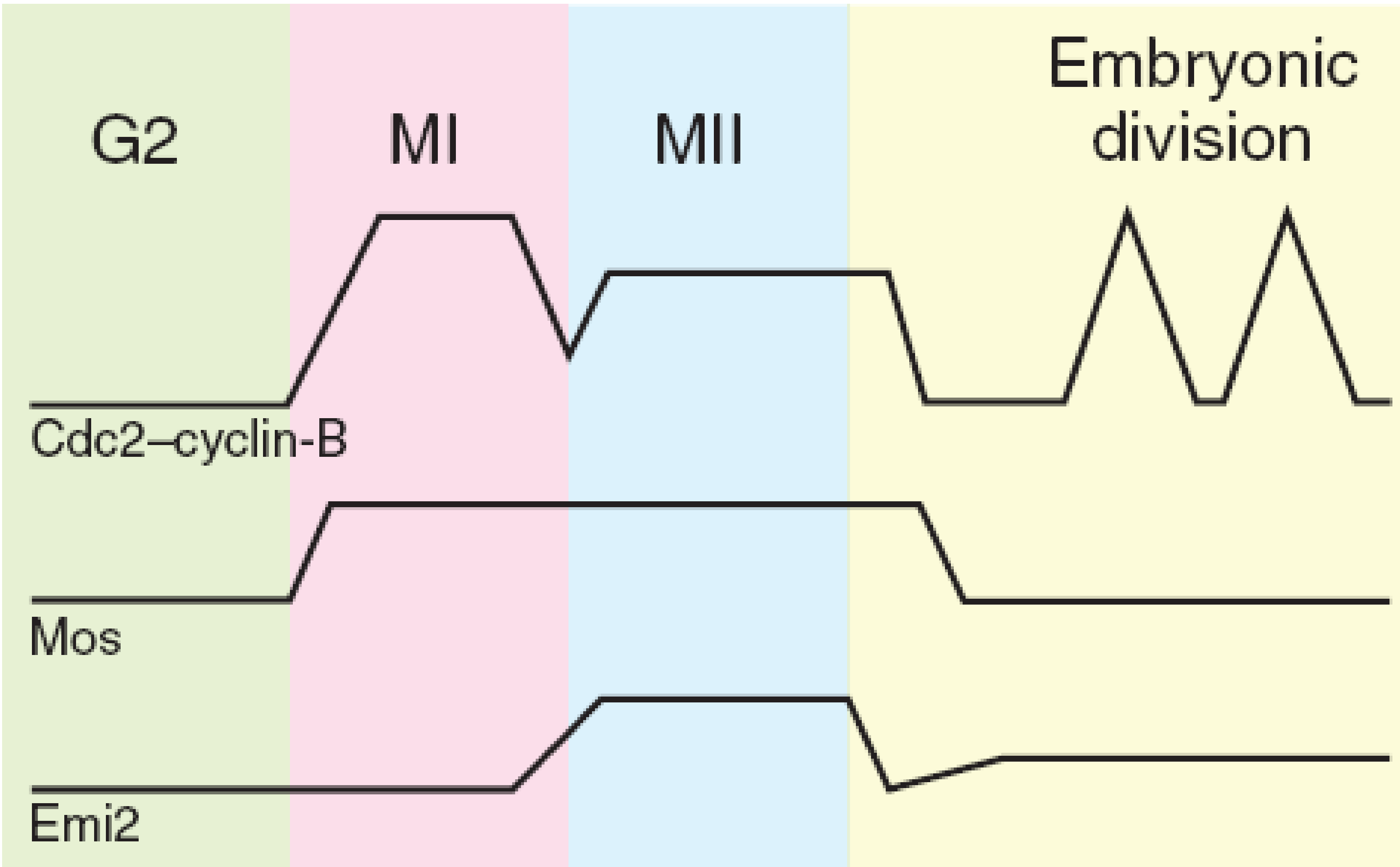
Cyclin B synthesis controls the timing of meiotic maturation through the level of MPF activity.



SAC: Spindle Assembly Checkpoint)

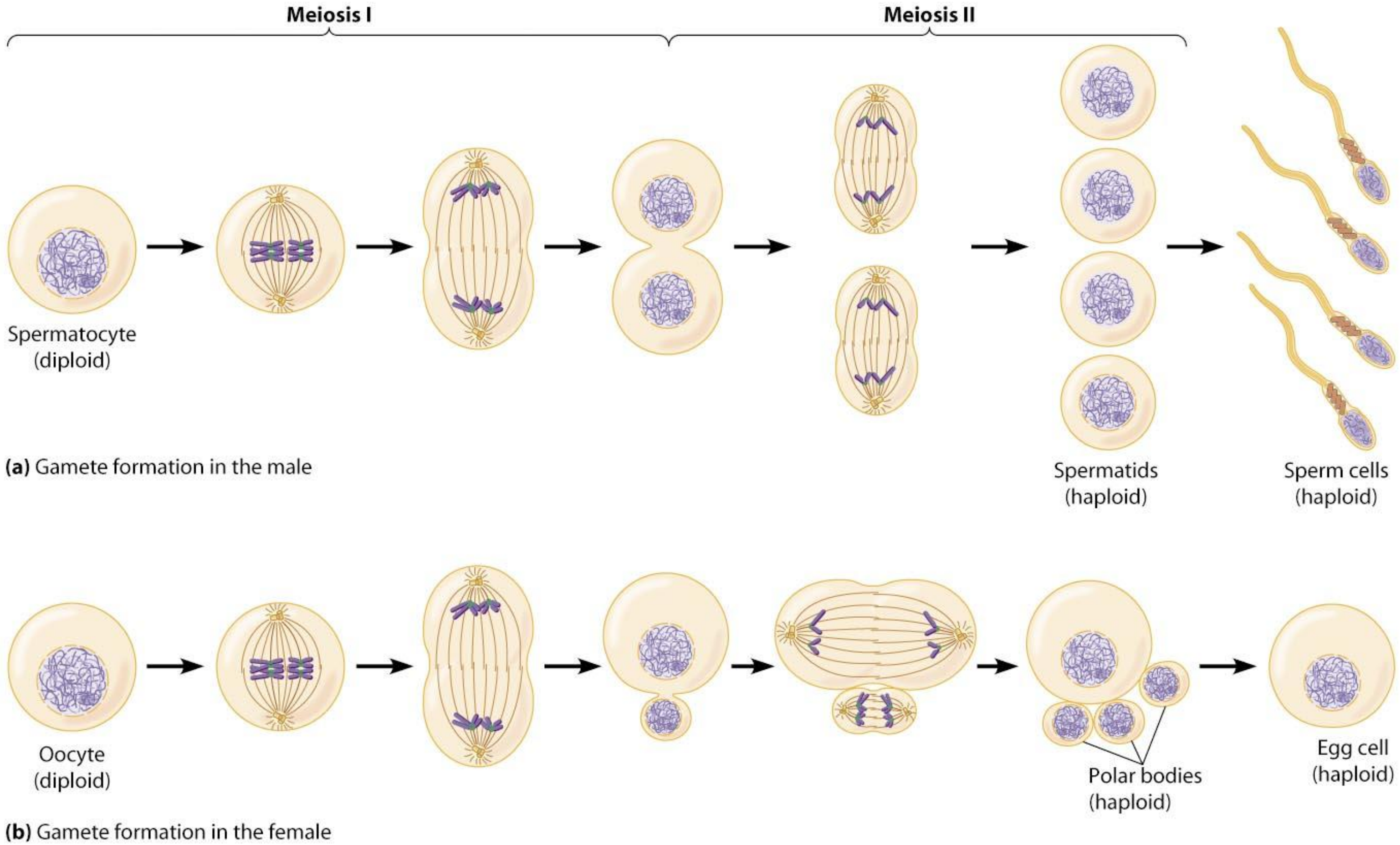
APC/C: Anaphase Promoting Complex/cyclosome

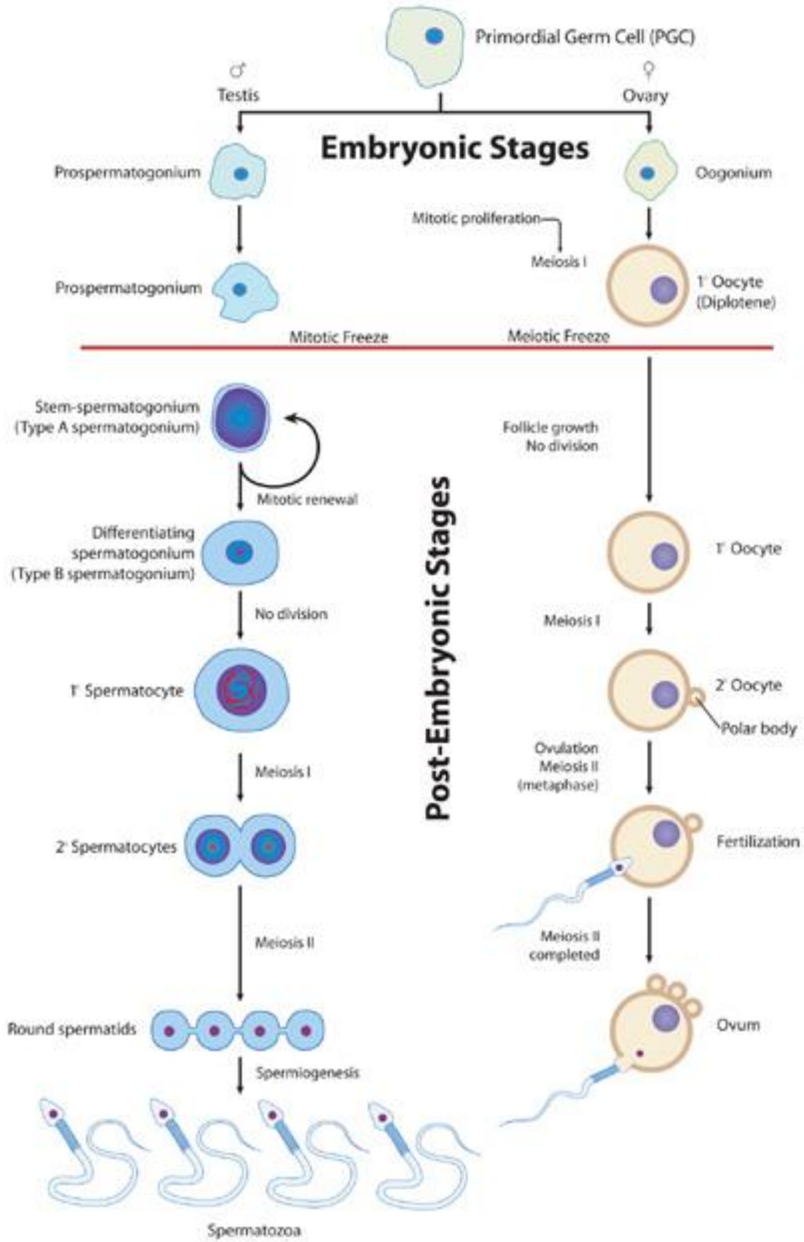
MPF/Mos/Emi2



- https://www.youtube.com/watch?v=eddh-AGV-6c

Spermatogenesis vs. Oogenesis





Primordial Germ Cell (PGC)
♂
Testis
♀
Ovary
Embryonic Stages
Prospermatogonium
Oogonium
Mitotic proliferation
Meiosis I
Prospermatogonium
1' Oocyte
(Diplotene)
Mitotic Freeze
Meiotic Freeze
Stem-spermatogonium
(Type A spermatogonium)
Follicle growth
No division
Mitotic renewal
Post-Embryonic Stages
Differentiating
spermatogonium
(Type B spermatogonium)
1' Oocyte
No division
Meiosis I
1' Spermatocyte
2' Oocyte
Polar body
Ovulation
Meiosis II
(metaphase)
Meiosis I
2' Spermatocytes
Fertilization
Meiosis II
Meiosis II
completed
Round spermatids
Ovum
Spermiogenesis
Spermatozoa

Meiosis is the first step in gametogenesis: separation of homologous chromosomes into haploid daughter cells

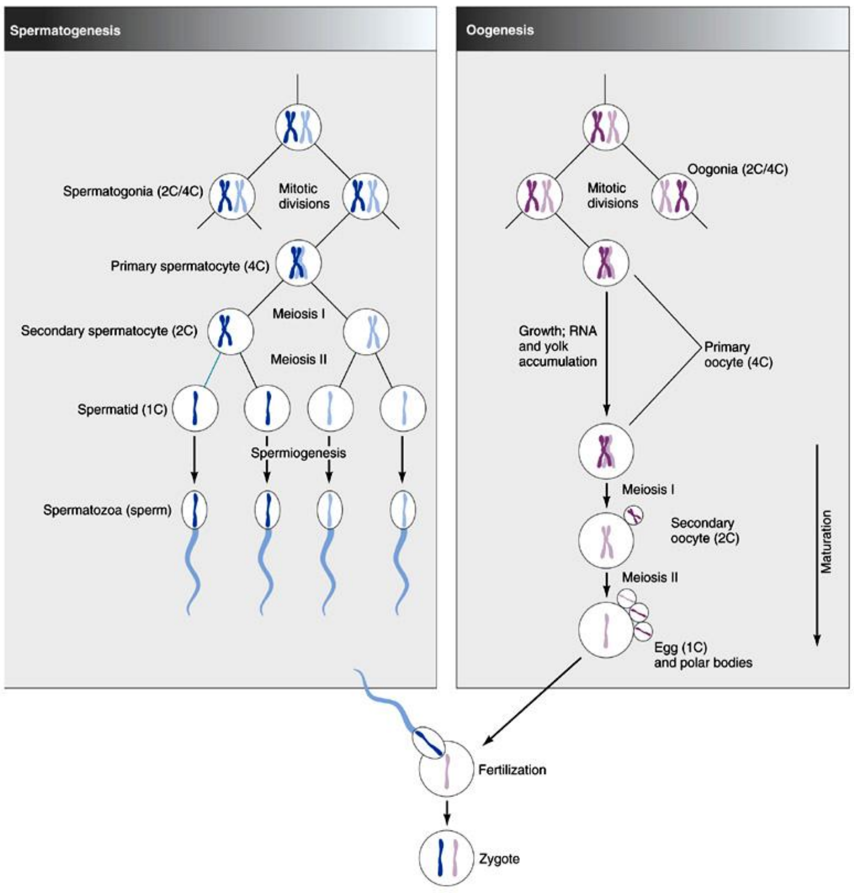
Spermatogonia and oogonia are the germ cells that will eventually develop into the mature sperm or egg

Primary spermatocyte or oocyte: the first step in this development is the duplication of homologous chromosomes to get ready for meiosis

Secondary spermatocyte or oocyte: the first meiotic division separates the homologous chromosomes from each parent

Spermatids or eggs: the second meiotic division separates the 2 chromatids and creates 4 haploid cells

In males, this eventually produces 4 sperm cells by the process of spermiogenesis. In females, it produces 1 egg and 3 polar bodies. This allows the egg to retain more cytoplasm to support early stages of development



Spermatogonia and oogonia are stem cells

What is a stem cell?

Stem cells have 3 properties:

1. **They are <u>undifferentiated</u> cells**
2. **They have potential for <u>self renewal</u>**
3. **They are able to undergo <u>differentiation</u> to form committed progenitor cells (a fancy word for all types of differentiated adult cells such as muscle, bone, skin, etc)**