Gametogenesis

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- ***Reproduction*** is the process of formation of a new living organism
- Purpose of reproduction is maintenance & propagation of species
- *gametes* or *germ cells* are produced in the gonads (testis in males and ovary in females)
- male gametes are called *spermatozoa* and female gametes the *ova*

- **Gametogenesis**
- process of formation & development of specialized generative cells, **gametes**
- conversion of germ cell to male & female Gametes
- Gametes are derived from the primordial germ cells
- formed in the epiblast during the second week of development
- move to the wall of the York sac
- 4th week migrate to the developing gonads
- Prepares sex cells for fertilization

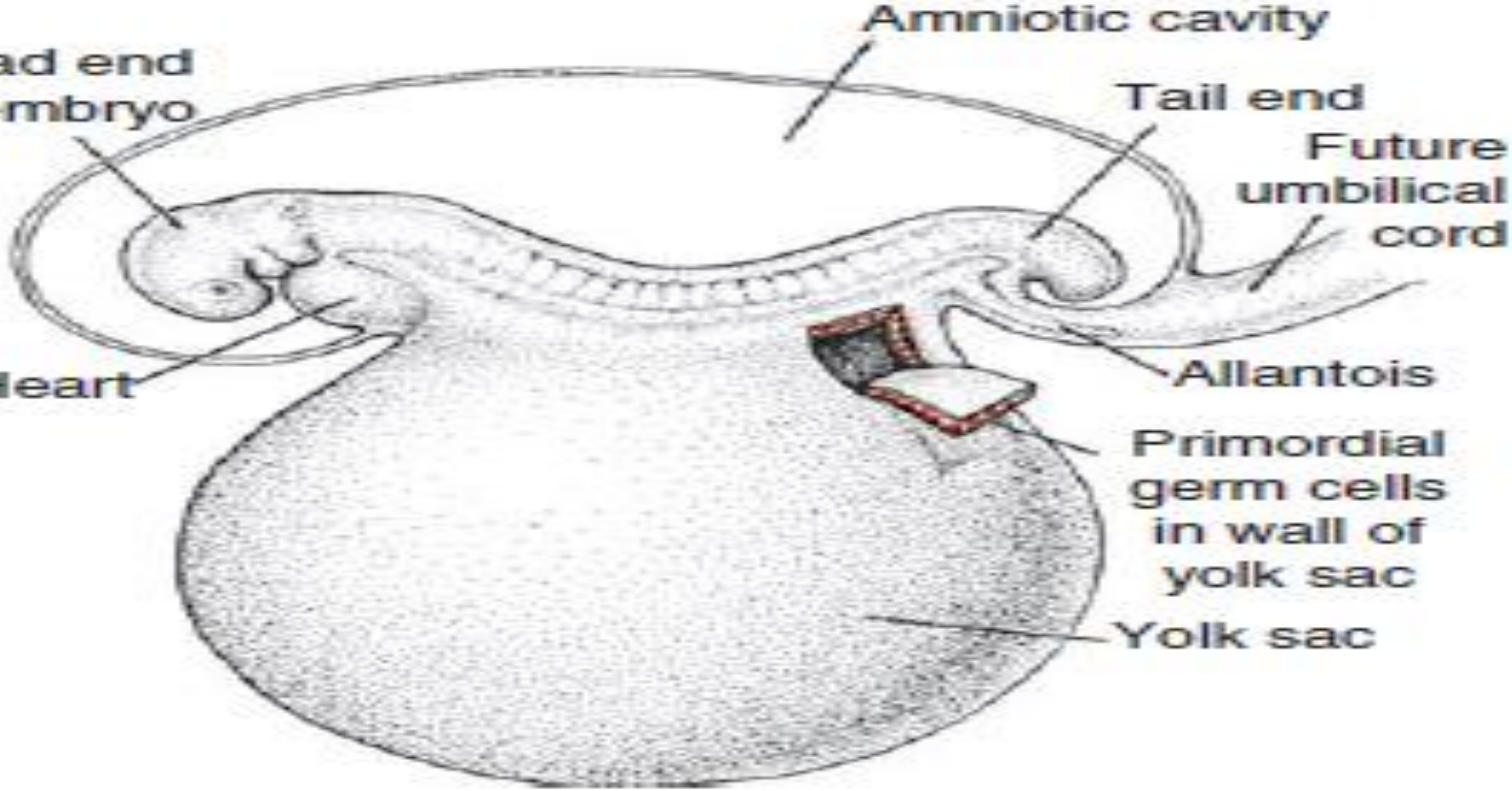
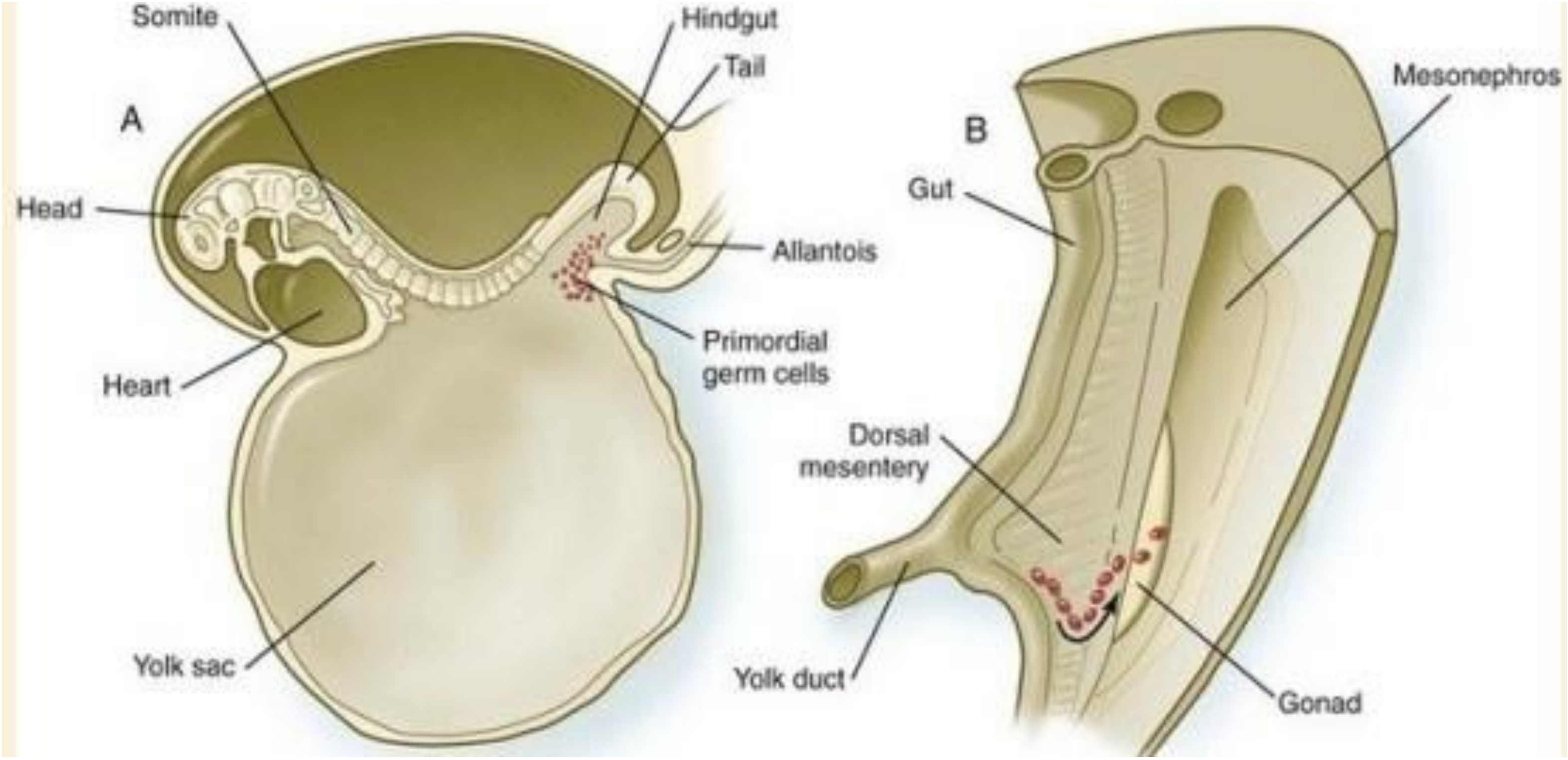
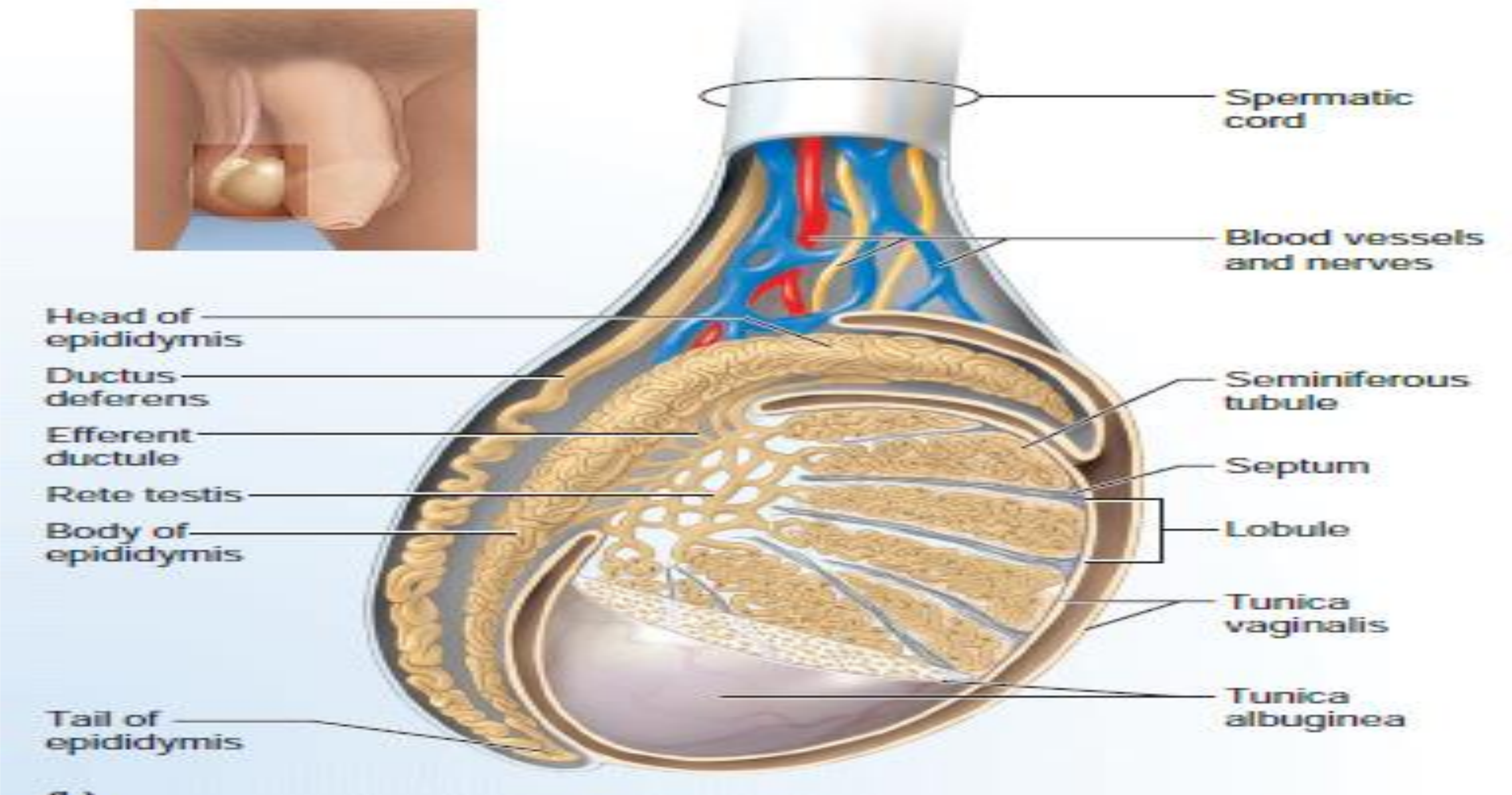


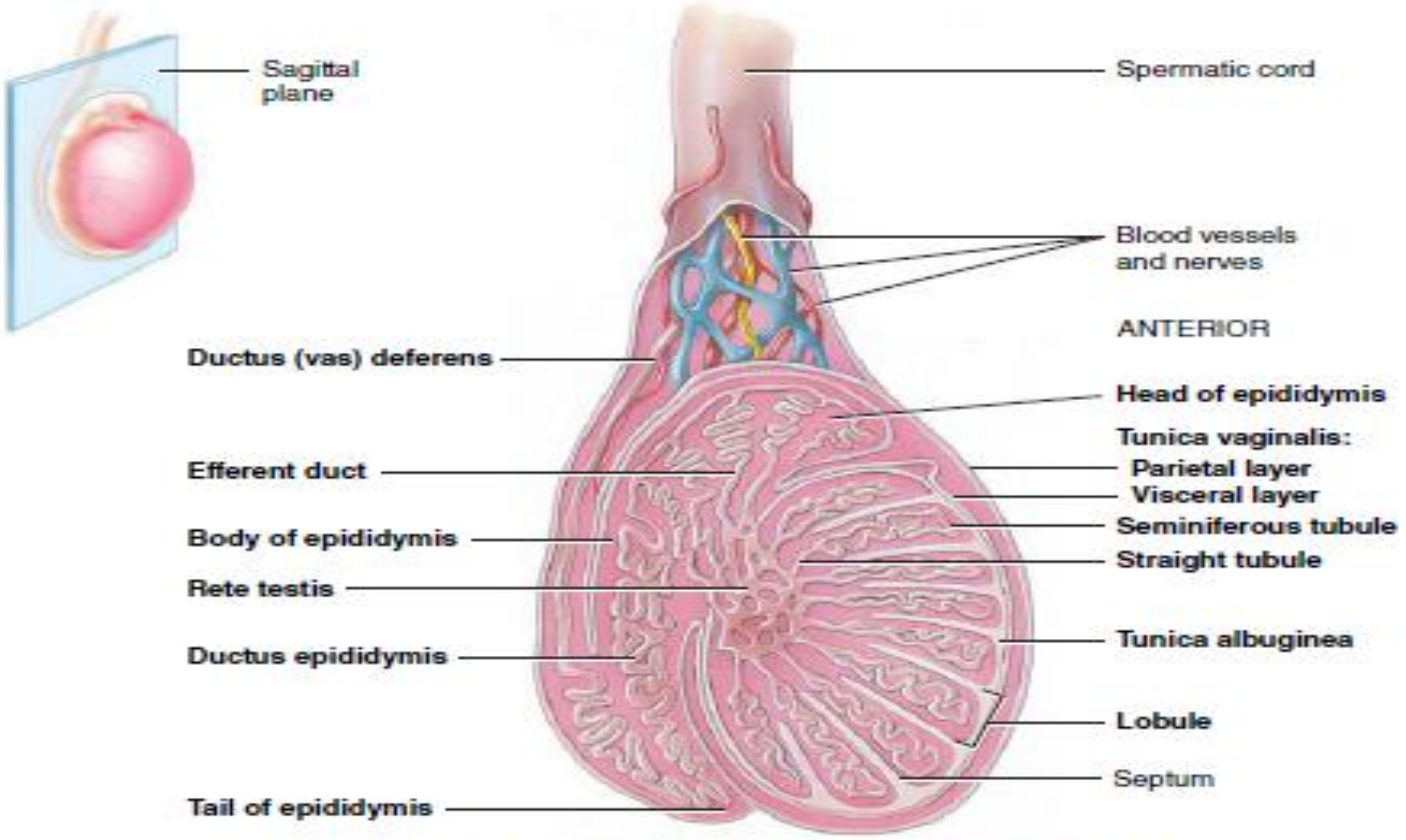
Figure 2.1 An embryo at the end of the third week, showing the position of PGCs in the wall of the yolk sac, close to the attachment of the future umbilical cord. From this location, these cells migrate to the developing gonad.

- **Primordial Germ Cells**
- Origin of gametes
- Divide by mitosis to increase in number
- Divide by meiosis to produce gametocytes & reduce the number of chromosomes
- Cytodifferentiation to complete their maturation



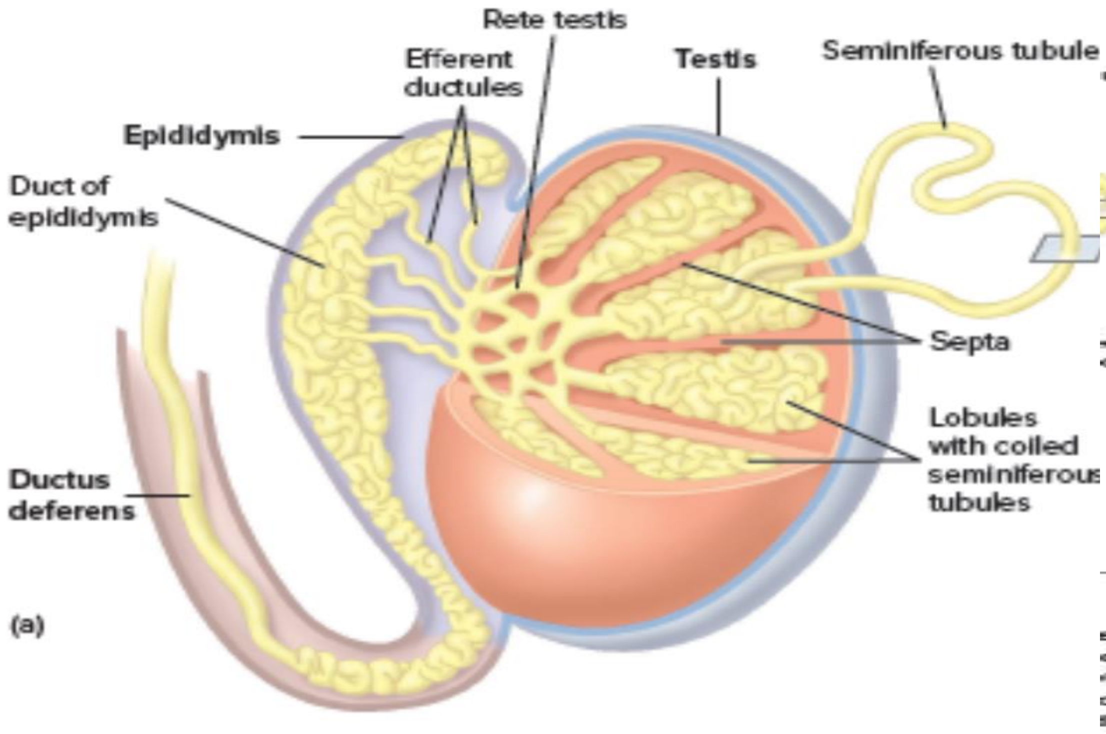
- **Testes(** ***testicles)***
- are paired oval glands in the scrotum measuring about 5 cm long and 2.5 cm in diameter
- covered laterally and anteriorly by a serous membrane called the **tunica vaginalis**
- it has a visceral layer and a parietal layer
- Internal to the visceral layer of the tunica vaginalis, the testis is surrounded by a white fibrous capsule composed of dense irregular connective tissue, the **tunica albuginea**
- it extends inward, forming septa that divide each testis into a series of internal compartments called **lobules**

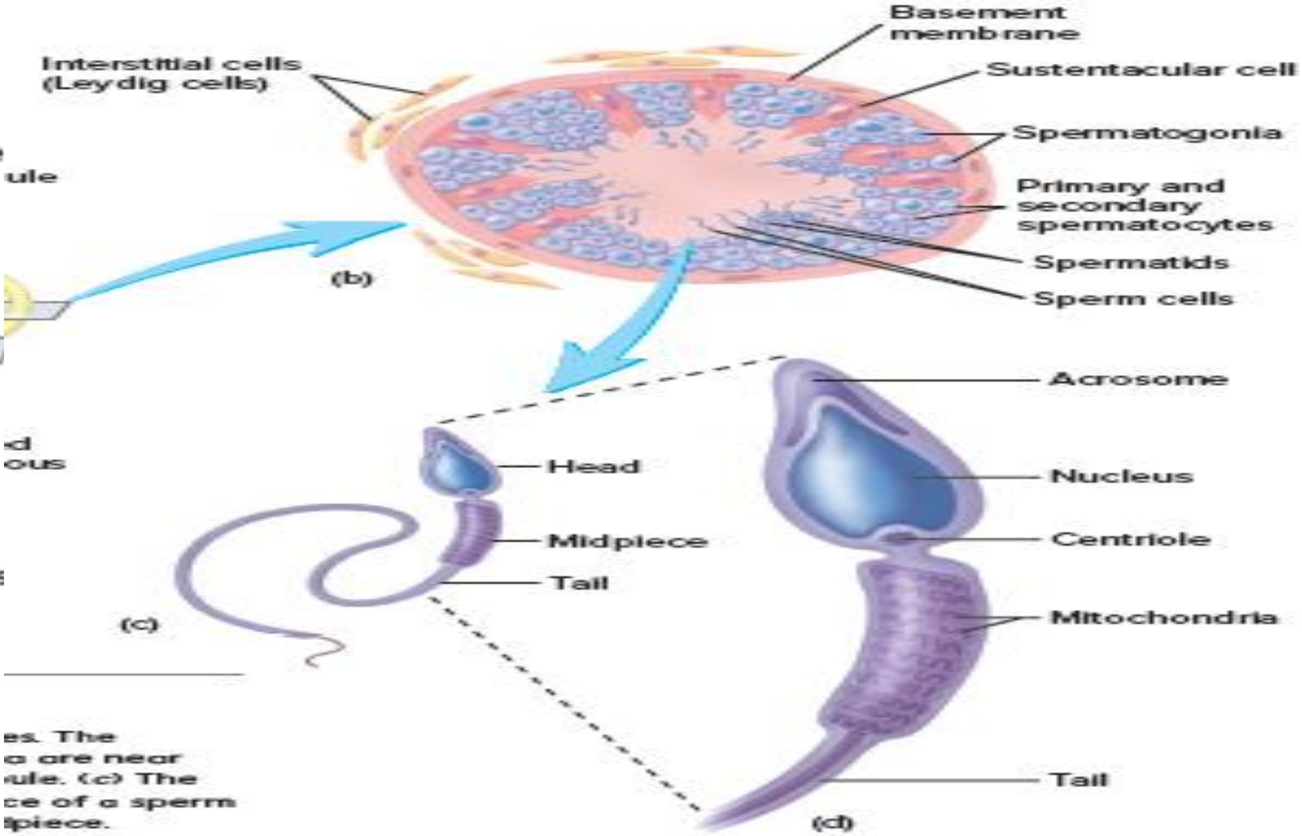


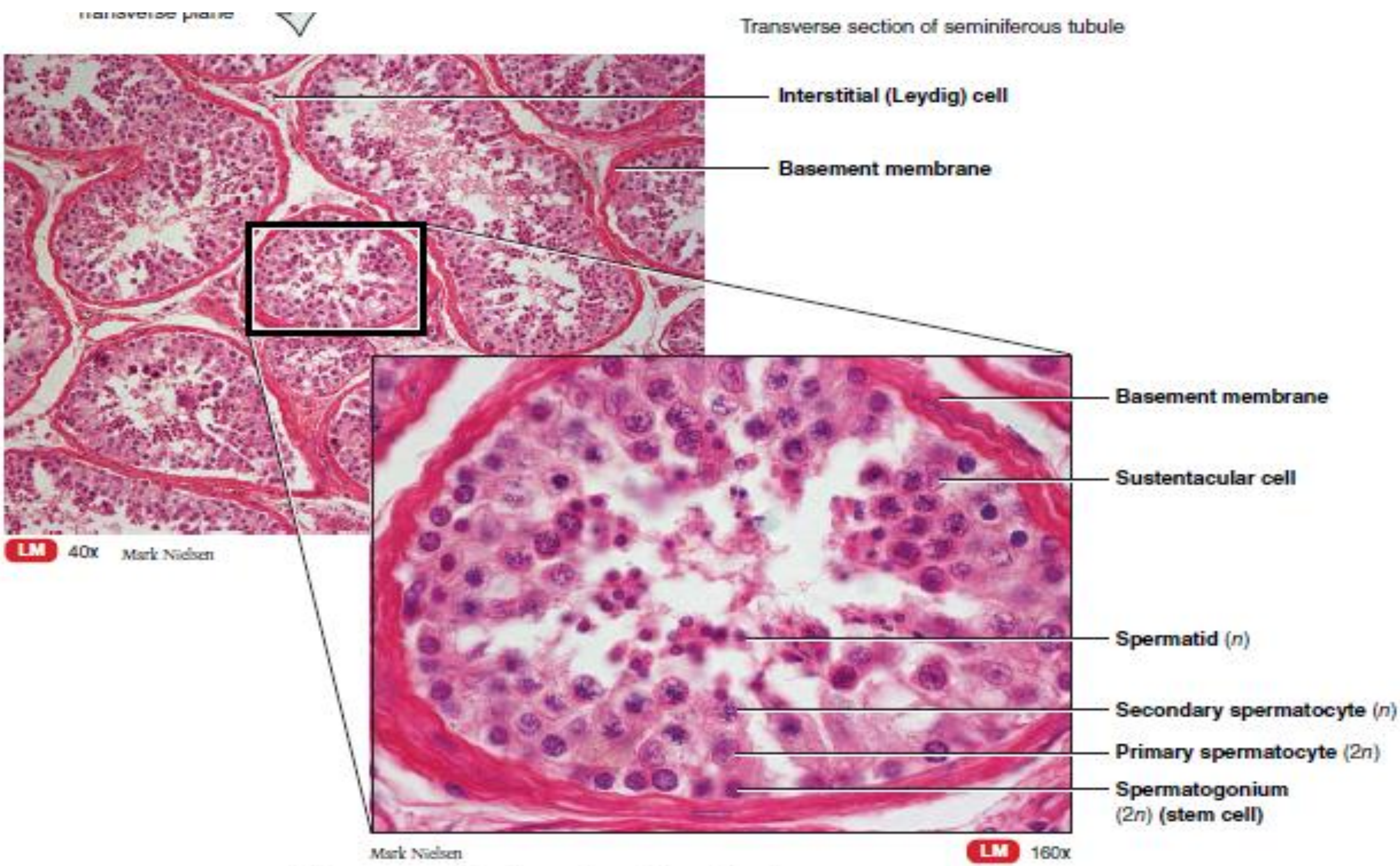


(a) Sagittal section of a testis showing seminiferous tubules

- Each of the 200–300 lobules contains 1 to 3 tightly coiled tubules, **seminiferous tubules** where sperm are produced
- process by which the seminiferous tubules of the testes produce sperm is called **spermatogenesis**
- walls of the seminiferous tubules contain 2 types of cells:
- **spermatogenic cells** the sperm-forming cells & **sustentacular cells** or ***Sertoli cells***
- Starting at puberty, sperm production begins at the periphery of the seminiferous tubules in stem cells called **spermatogonia**







(a) Transverse section of several seminiferous tubules

- Sustentacular cells support and protect developing spermatogenic cells in several ways:-

❖ They nourish spermatocytes, spermatids & sperm

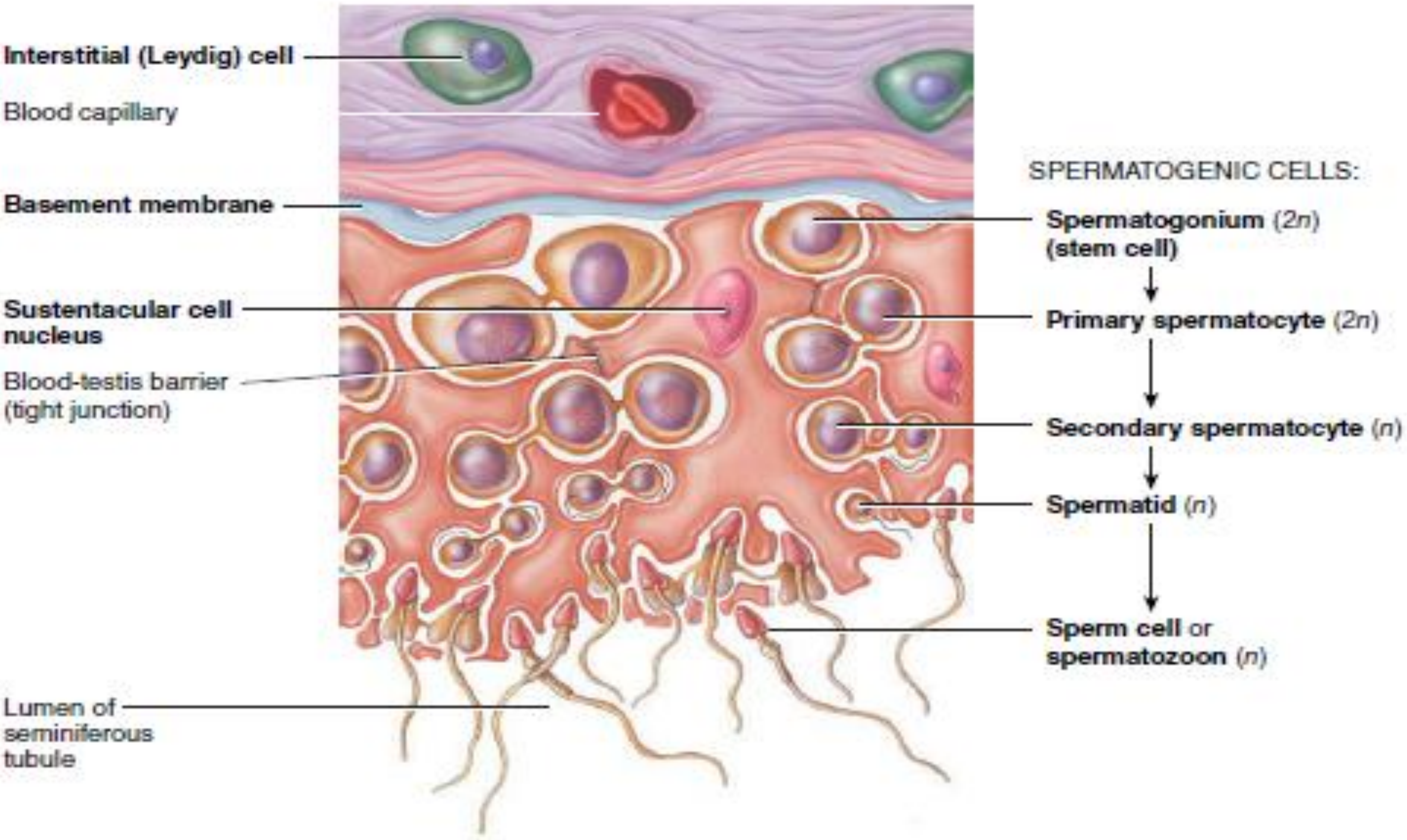
❖ phagocytize excess spermatid cytoplasm as development proceeds

❖ control movements of spermatogenic cells & the release of sperm into the lumen of the seminiferous tubule

❖ They produce fluid for sperm transport

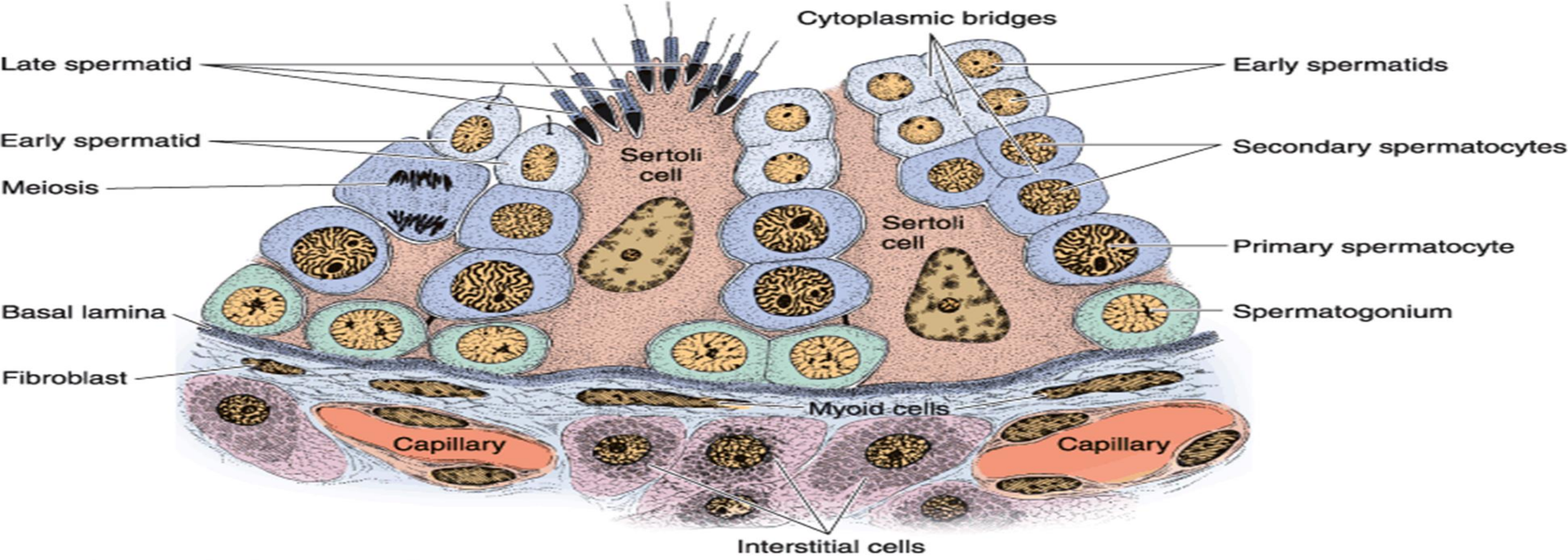
❖ secrete the hormones:

- **Inhibin** decreases the rate of spermatogenesis & regulate the effects of testosterone and FSH
- **Androgen-binding protein** (**ABP**) to maintain the concentration of testosterone in the seminiferous tubules, thereby promoting spermatogenesis
- **Anti-Müllerian hormone** prevent oviducts from developing from the Mullerian duct in the early stages of the male embryo



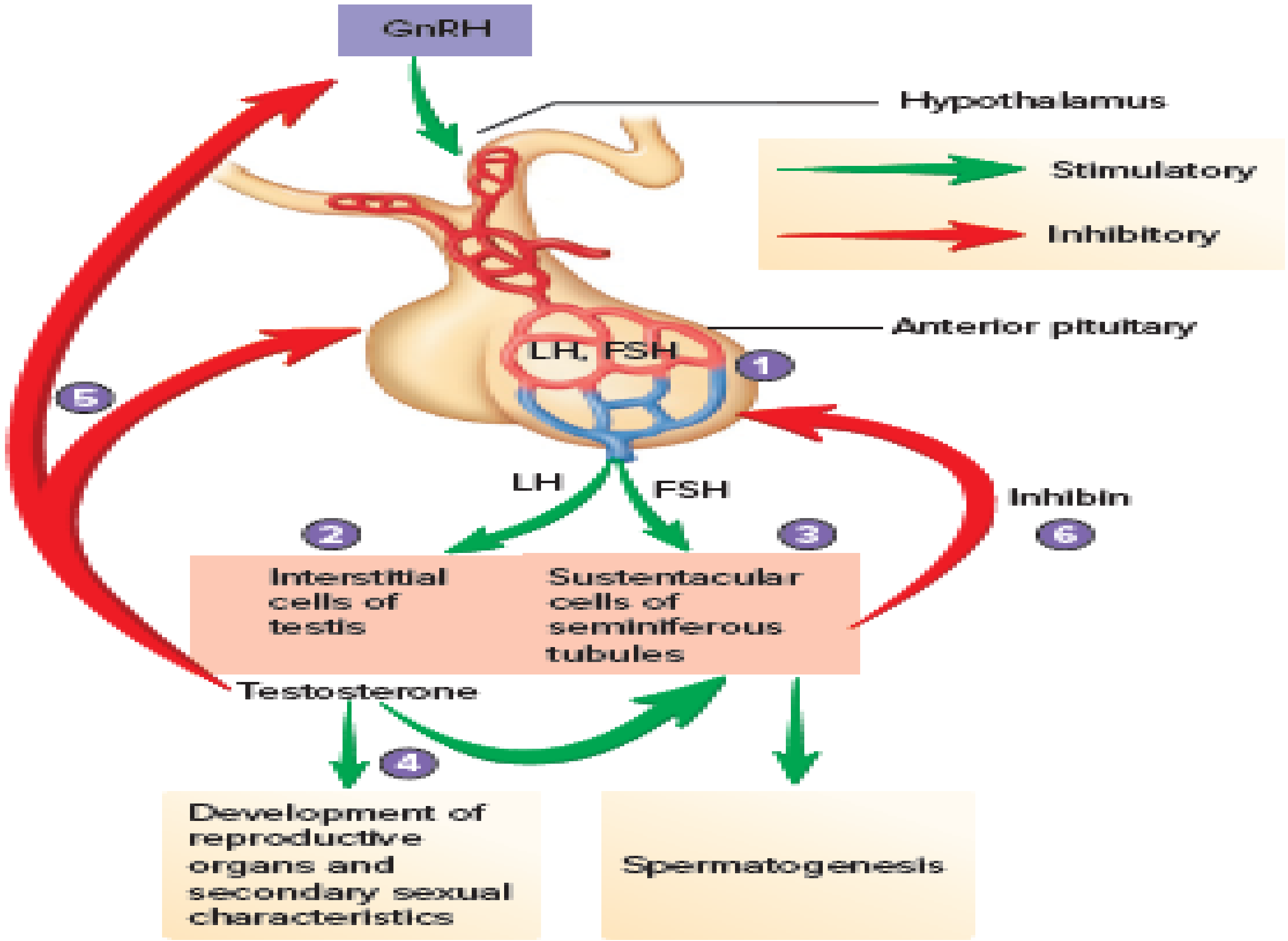
(b) Transverse section of a part of a seminiferous tubule

- In the spaces between adjacent seminiferous tubules are clusters of cells called **interstitial cells** or *Leydig cell*
- These cells secrete testosterone, the most important androgen.
- (An **androgen**) is a hormone that promotes the development of masculine characteristics
- Testosterone also promotes a man's *libido* (sex drive)



- LH binds to the interstitial cells in the testes & causes them to secrete testosterone
- FSH binds primarily to sustentacular cells in the seminiferous tubules & promotes sperm cell development
- also increases the secretion of a hormone called **inhibin**

1. Gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary.
2. LH stimulates testosterone secretion from the interstitial cells.
3. FSH stimulates sustentacular cells of the seminiferous tubules to increase spermatogenesis and to secrete inhibin.
4. Testosterone has a stimulatory effect on the sustentacular cells of the seminiferous tubules, as well as on the development of reproductive organs and secondary sexual characteristics.
5. Testosterone has a negative-feedback effect on the hypothalamus and pituitary to reduce GnRH, LH, and FSH secretion.
6. Inhibin has a negative-feedback effect on the anterior pituitary to reduce FSH secretion.

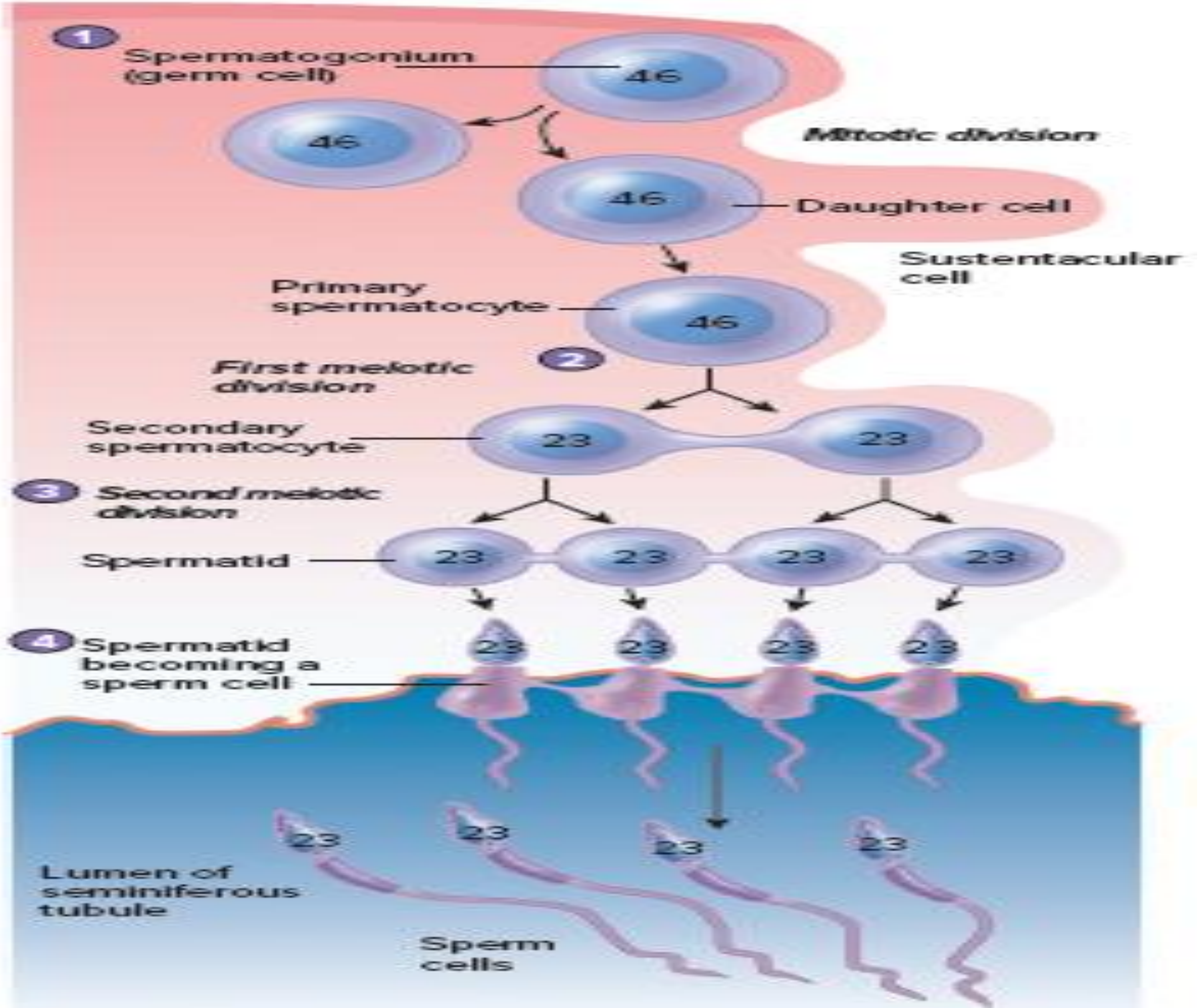


- **SPERMATOGENESIS**
- Sequence of events by which spermatogonia are transformed into mature spermatozoa
- Begins at puberty 13-16 years and continues into old age
- Divided into 3 phases

A. SPERMACYTOGENESIS

- **Primordial germ** cells(46,2N) arise from the yolk sac to the testis during the 4th week of development
- In the embryonic testes, the primordial germ cells differentiate into spermatogonia, which remain dormant during childhood and become active at puberty
- At puberty differentiates into Type A spermatogonia(46,2N) which contain the diploid (2*n*) chromosome number
- Type A spermatogonia undergoes mitosis for continuous supply of stem cells throughout males life

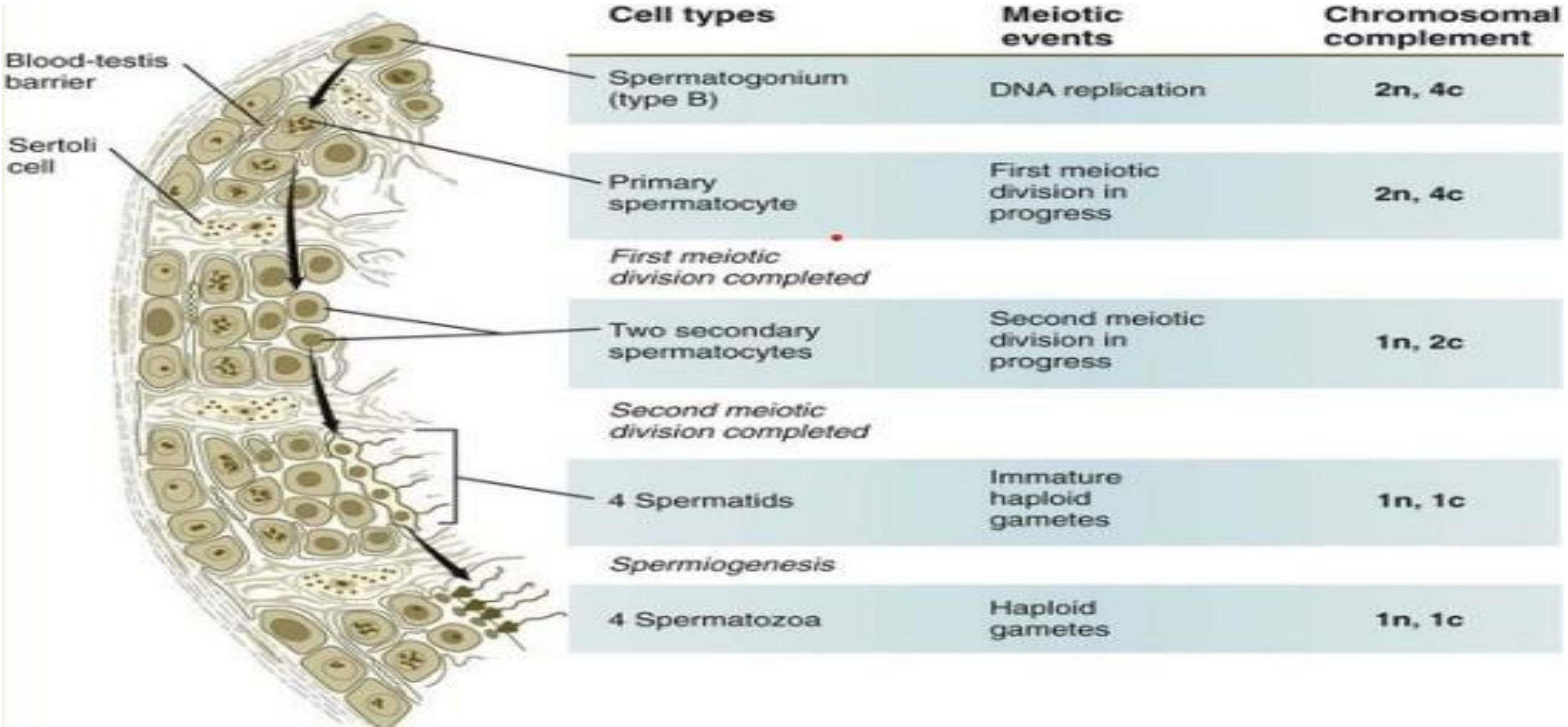
1. Spermatogonia are the cells from which sperm cells arise. The spermatogonia divide by mitosis. One daughter cell remains a spermatogonium that can divide again by mitosis. One daughter cell becomes a primary spermatocyte.
2. The primary spermatocyte divides by meiosis to form secondary spermatocytes.
3. The secondary spermatocytes divide by meiosis to form spermatids.
4. The spermatids differentiate to form sperm cells.

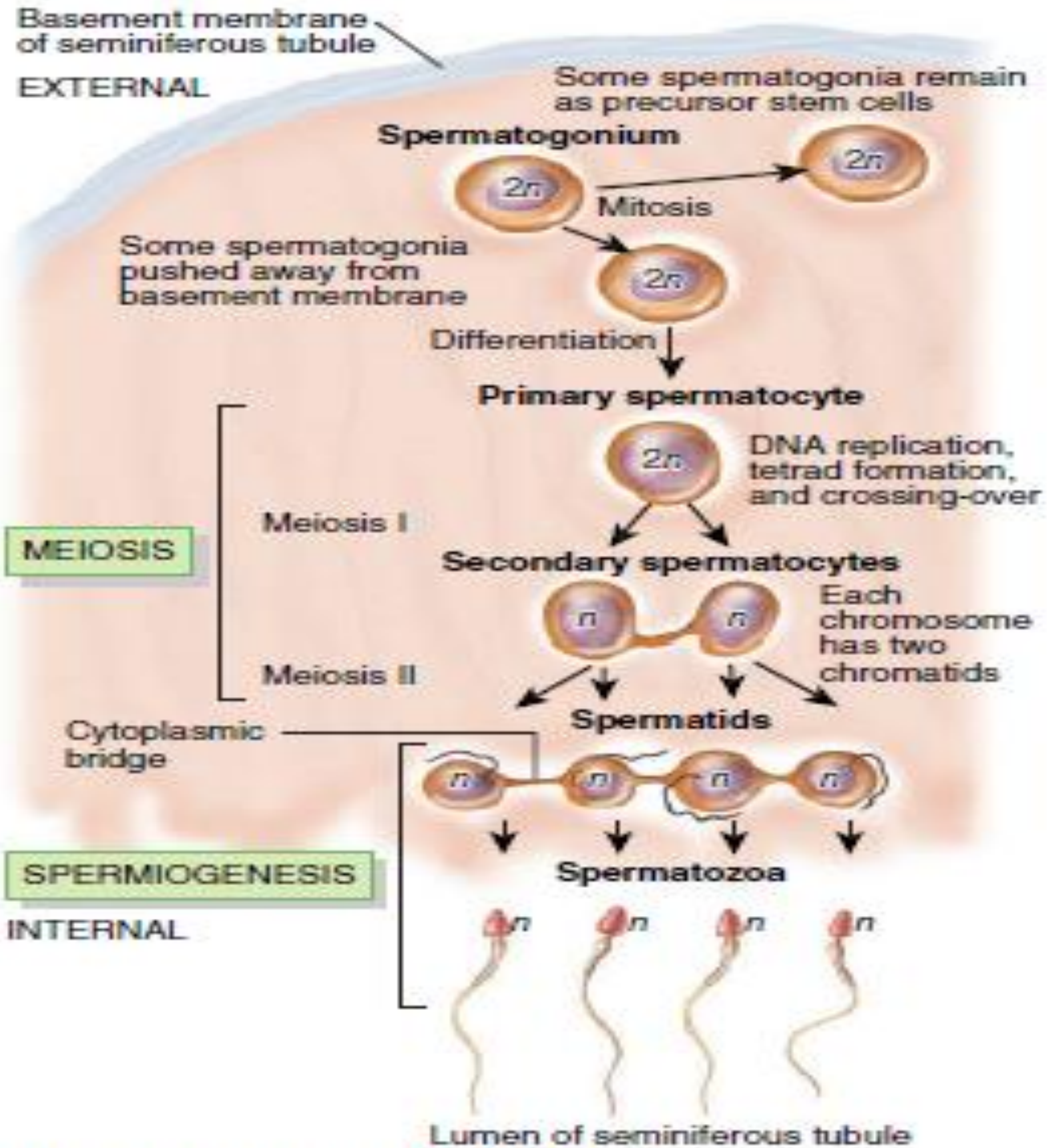


- some cells remain near the basement membrane of the seminiferous tubule in an undifferentiated state to serve as a reservoir of cells for future cell division & subsequent sperm production
- Type A Spermatogonia differentiates to Type B spermatogonia(46,2N)
- Type A spermatogonia are dark & type B are pale in color
- Spermatogonia (type B) (44 +X + Y) enlarge, or undergo mitosis , to form primary spermatocytes.
- Primary spermatocytes, like spermatogonia, are diploid (2*n*); that is, they have 46 chromosomes
- It takes 16 days

B.MEIOSIS

- Shortly after it forms, each primary spermatocyte replicates its DNA, & then meiosis begins
- In meiosis I, homologous pairs of chromosomes line up at the metaphase plate, and crossing-over occurs
- the meiotic spindle pulls one (duplicated) chromosome of each pair to an opposite pole of the dividing cell
- Primary spermatocytes completes 1st meiosis to form 2 cells the **secondary spermatocytes(23,2N)**

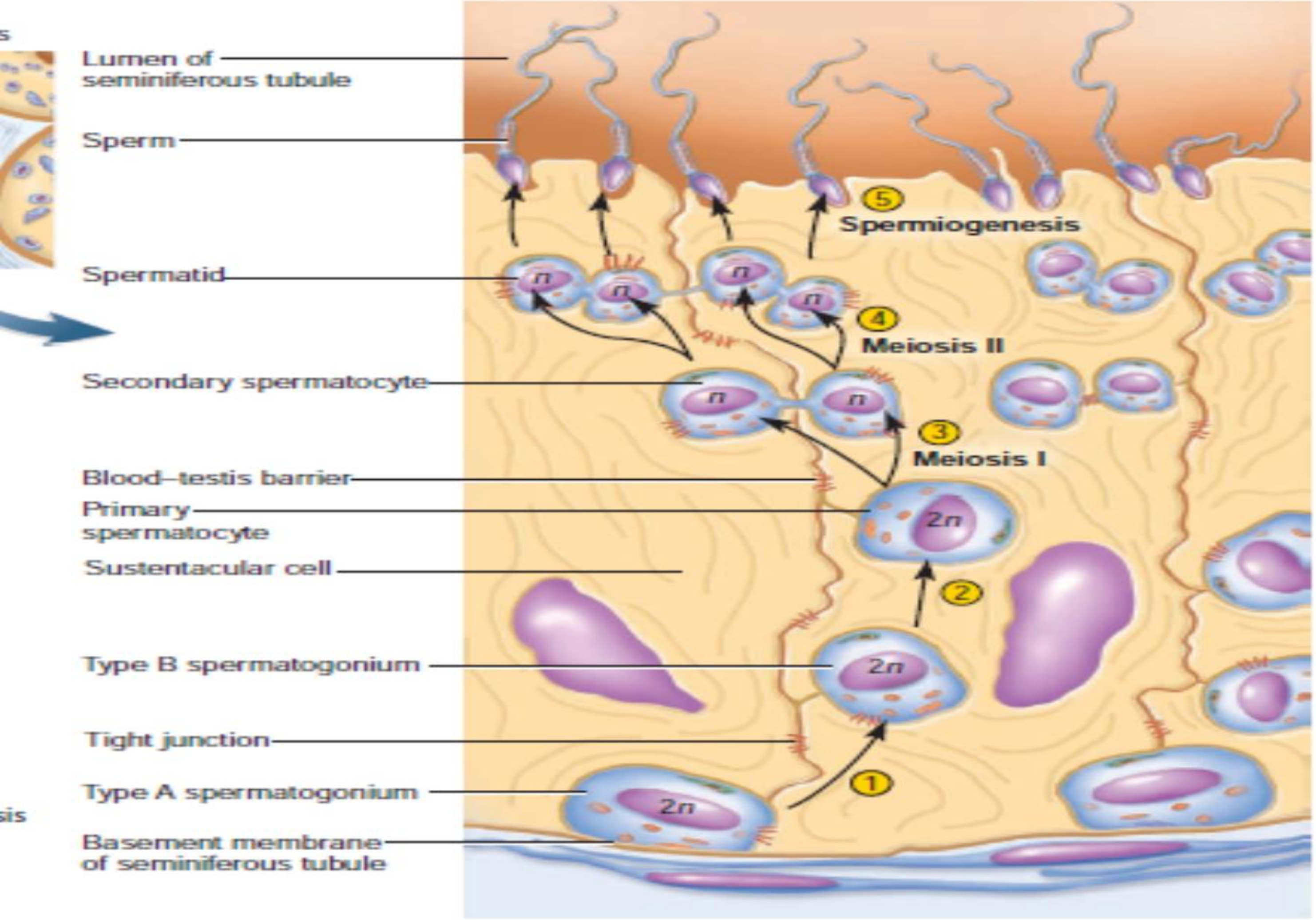


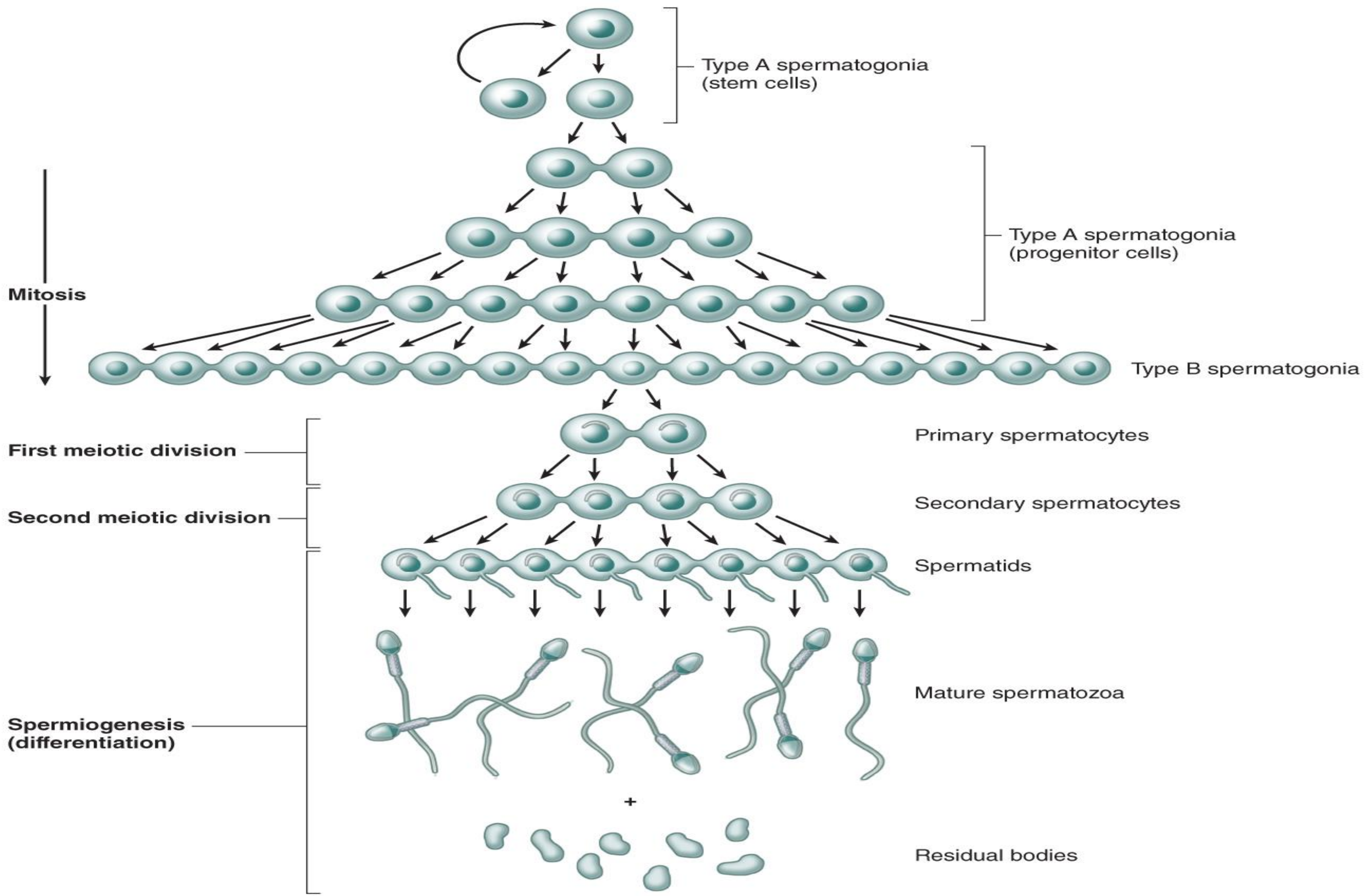


What is the outcome of meiosis I?

- Each secondary spermatocyte has 23 chromosomes, the haploid number (*n*).
- Each chromosome within a secondary spermatocyte, is made up of 2 chromatids (two copies of the DNA) still attached by a centromere
- No replication of DNA occurs in the secondary spermatocytes
- meiosis II, no replication of DNA occurs
- chromosomes line up in single file along the metaphase plate, and 2 chromatids of each chromosome separate
- Secondary spermatocyte goes into 2^{nd} meiosis to form 4 Spermatids (23, 1N)
- All the 4 spermatid mature into sperms
- *Duration*: 64–74 days.

- A unique process occurs during spermatogenesis
- As the sperm cells proliferate following their production by spermatogonia, they fail to complete cytoplasmic separation (cytokinesis)
- The cells remain in contact by cytoplasmic bridges through their entire development

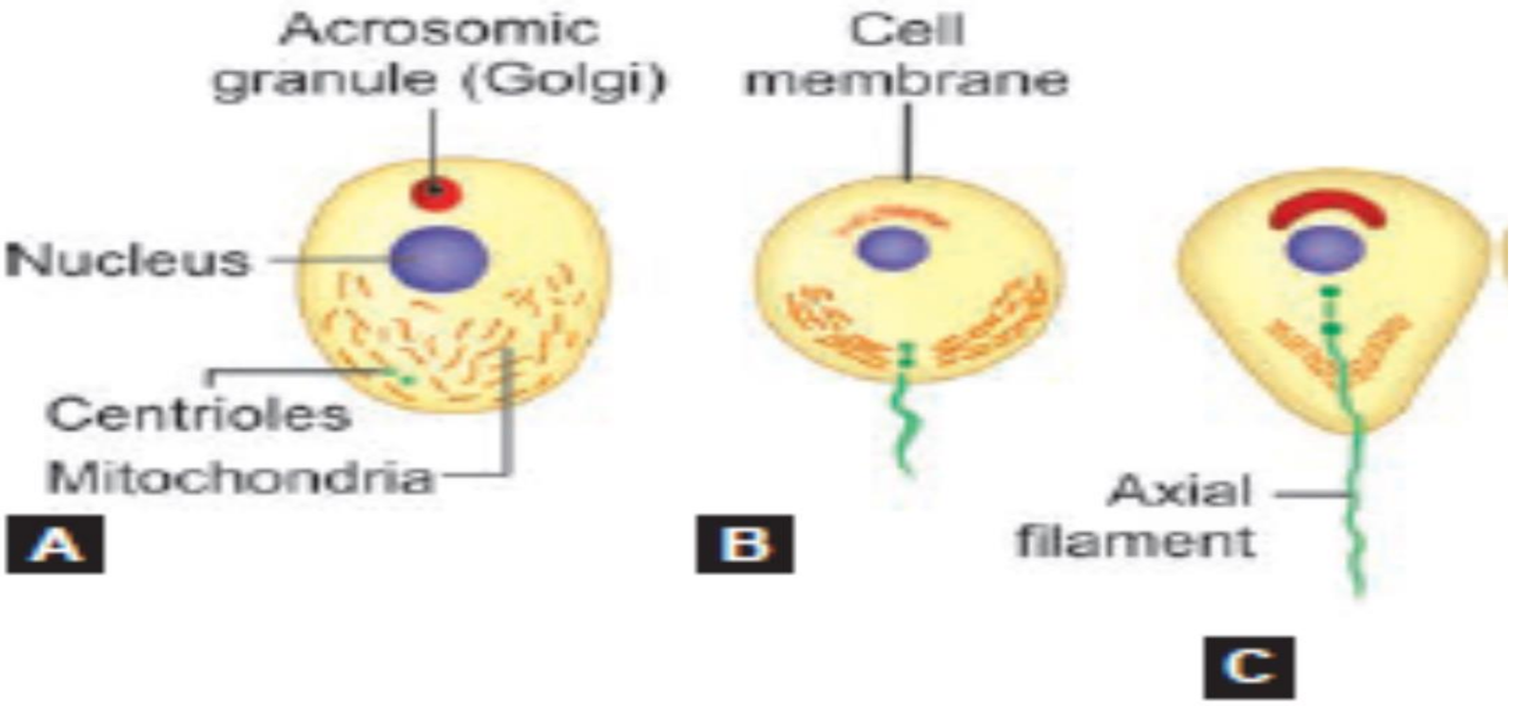



Type A spermatogonia
(stem cells)
Type A spermatogonia
(progenitor cells)
Mitosis
Type B spermatogonia
First meiotic division
Primary spermatocytes
Second meiotic division
Secondary spermatocytes
Spermatids
Mature spermatozoa
Spermiogenesis
(differentiation)
+
Residual bodies

C. Spermiogenesis

Process by which spermatid undergoes changes in shape & in orientation of its organelles to form a spermatozoon.

- takes 24 days ,spermatid become mature spermatozoa in the seminiferous tubule
- It is the final stage in the maturation of spermatids into mature, motile spermatozoa
- spermatid is a more or less circular cell containing a nucleus, Golgi apparatus, centriole and mitochondria



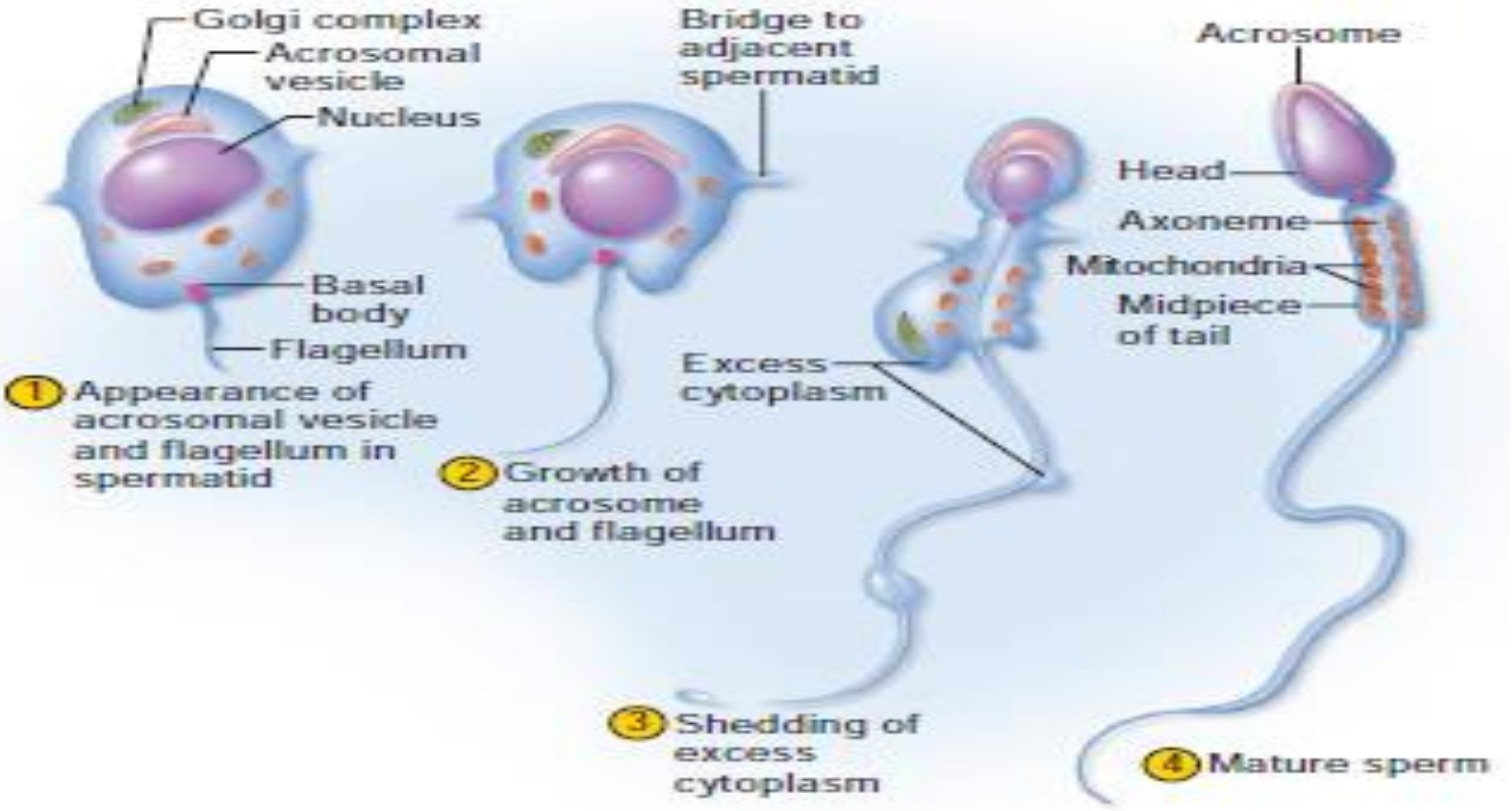
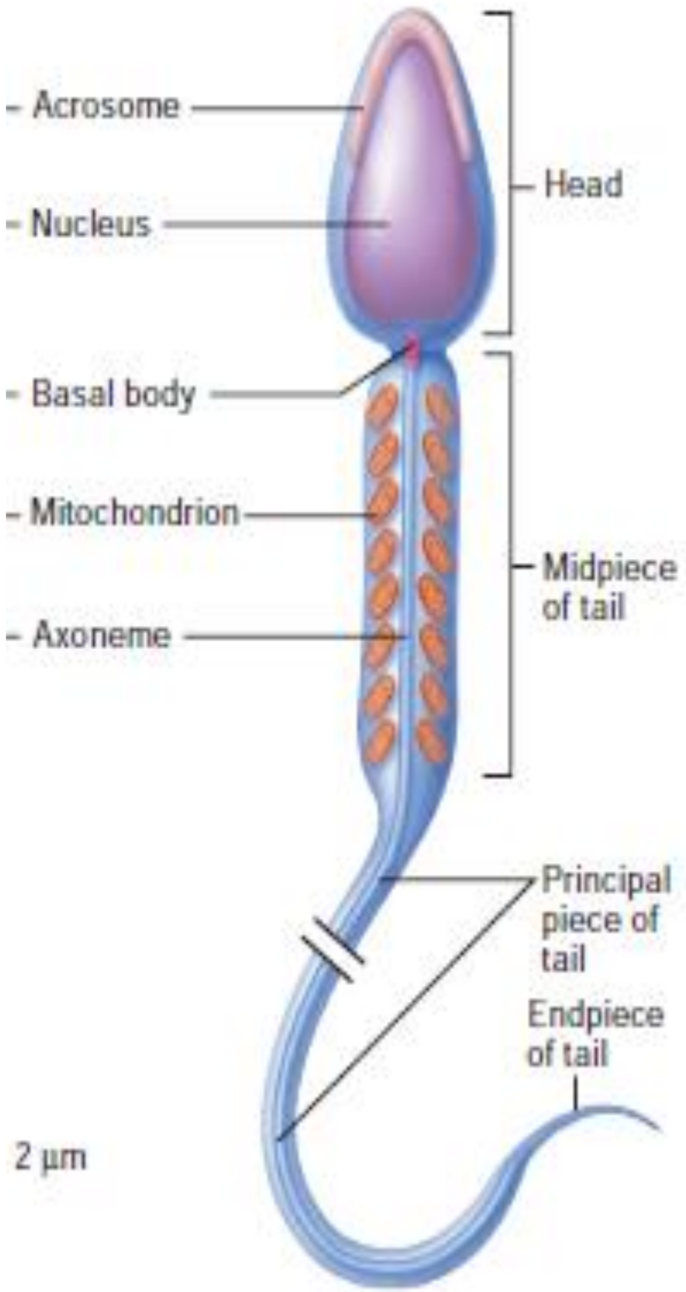
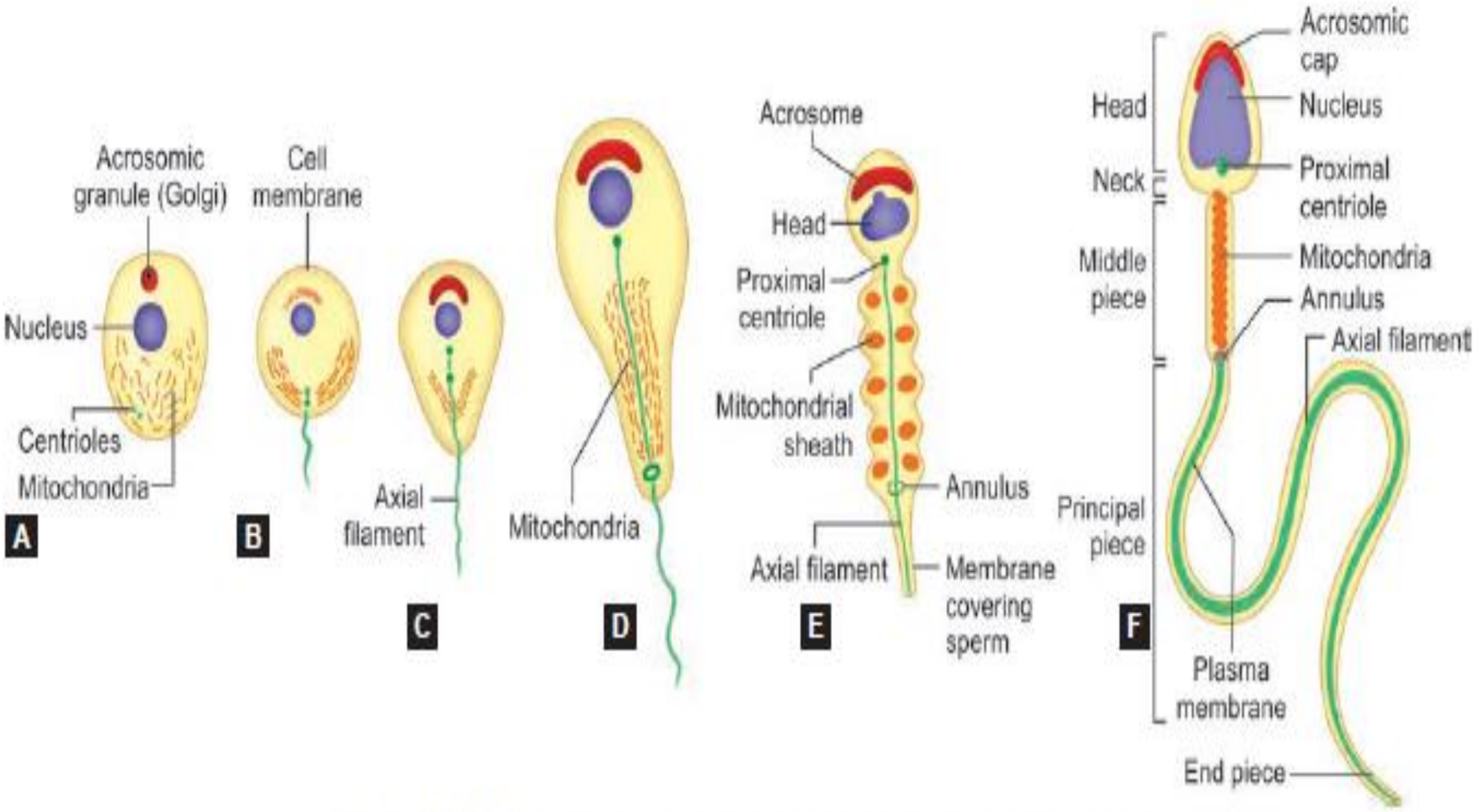


Figure 26.7 Spermiogenesis. In this process, the spermatids discard excess cytoplasm, grow tails, and become spermatozoa.

- ***Major events in spermiogenesis***
- Nuclear morphogenesis and condensation
- Formation of tail
- Formation of acrosome
- Rearrangement of organelles (Mitochondria, centrioles)
- Shedding of excess cytoplasm
- Spermatocyte elongates





Figs 3.11A to F: Stages in spermiogenesis and parts of a spermatozoon

- ***Various processes in spermiogenesis***
- **Nucleus**: condensation of nucleus & its movement to one pole forms the *head*
- **Golgi apparatus:** transformed into the *acrosomic cap* Acrosomal cap covers two third of nucleus
- caplike vesicle filled with enzymes that help a sperm to penetrate a secondary oocyte to bring about fertilization
- Among the enzymes are hyaluronidase and proteases

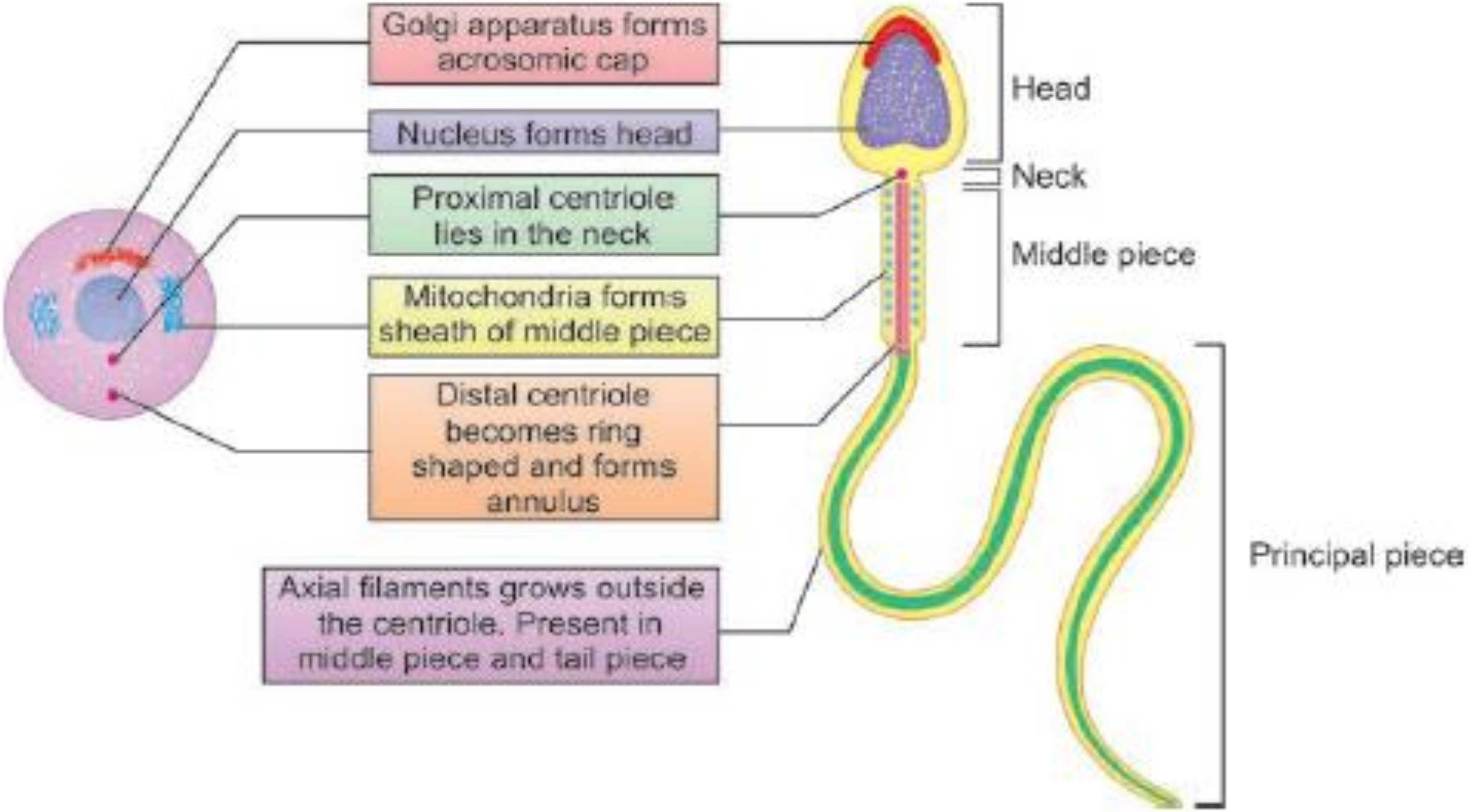


Fig. 3.10: Parts of a spermatozoon and their derivation

- ***Mitochondria***: Form a spiral sheath around middle piece
- The part of the axial filament between the neck and the annulus becomes surrounded by mitochondria, forms the middle piece
- Mitochondria provide the energy (ATP) for locomotion of sperm to the site of fertilization and for sperm metabolism
- The remaining part of the axial filament elongates to form the principal piece and tail

- ***Cytoplasm***: most of it is shed as residual bodies of Renaud and are engulfed by Sertoli cells

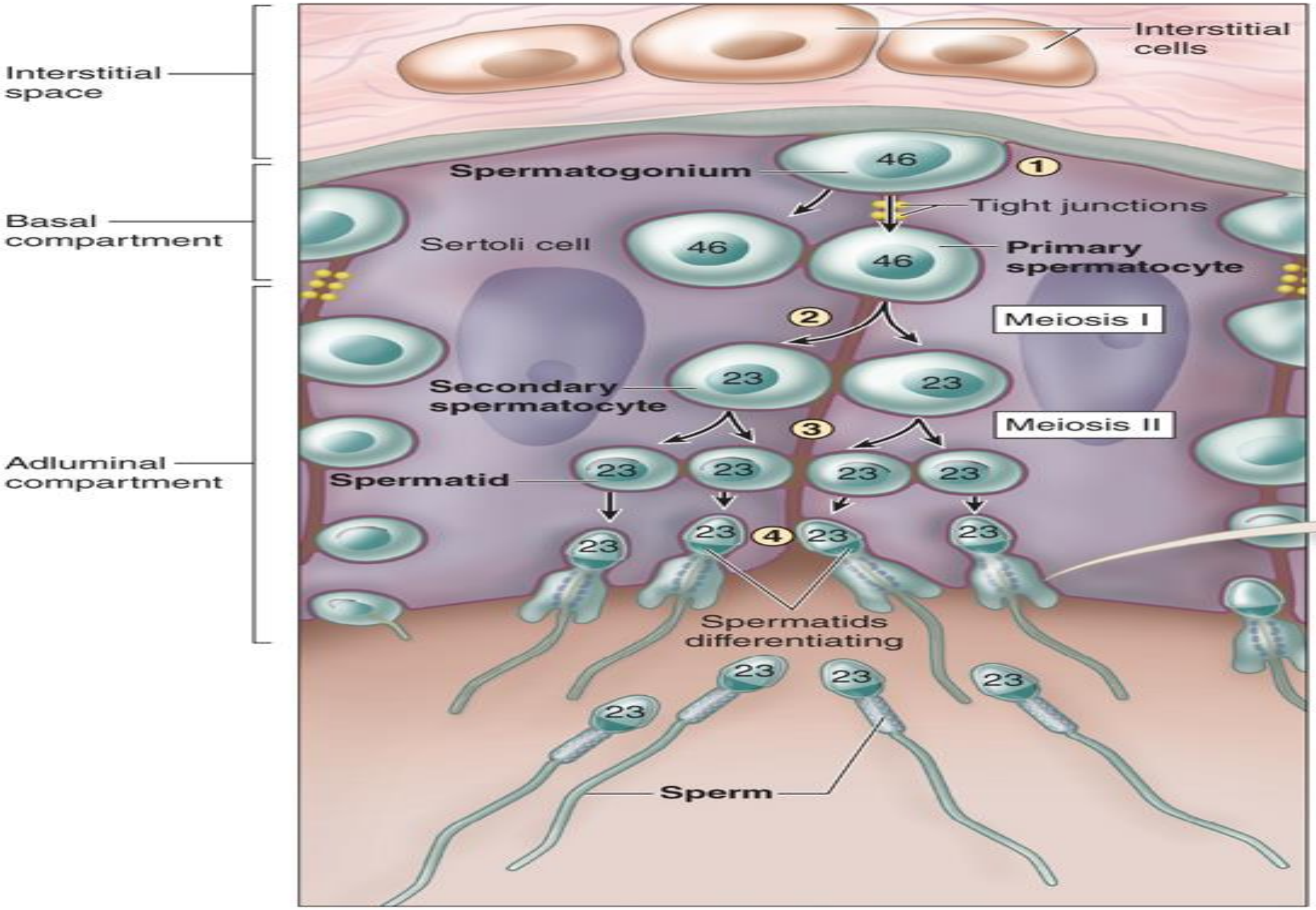
- ***Cell membrane:*** Persists as a covering for the spermatozoon
- Presents specialization for fertilization that includes:

-- Sperm-egg recognition

-- Sperm-egg binding

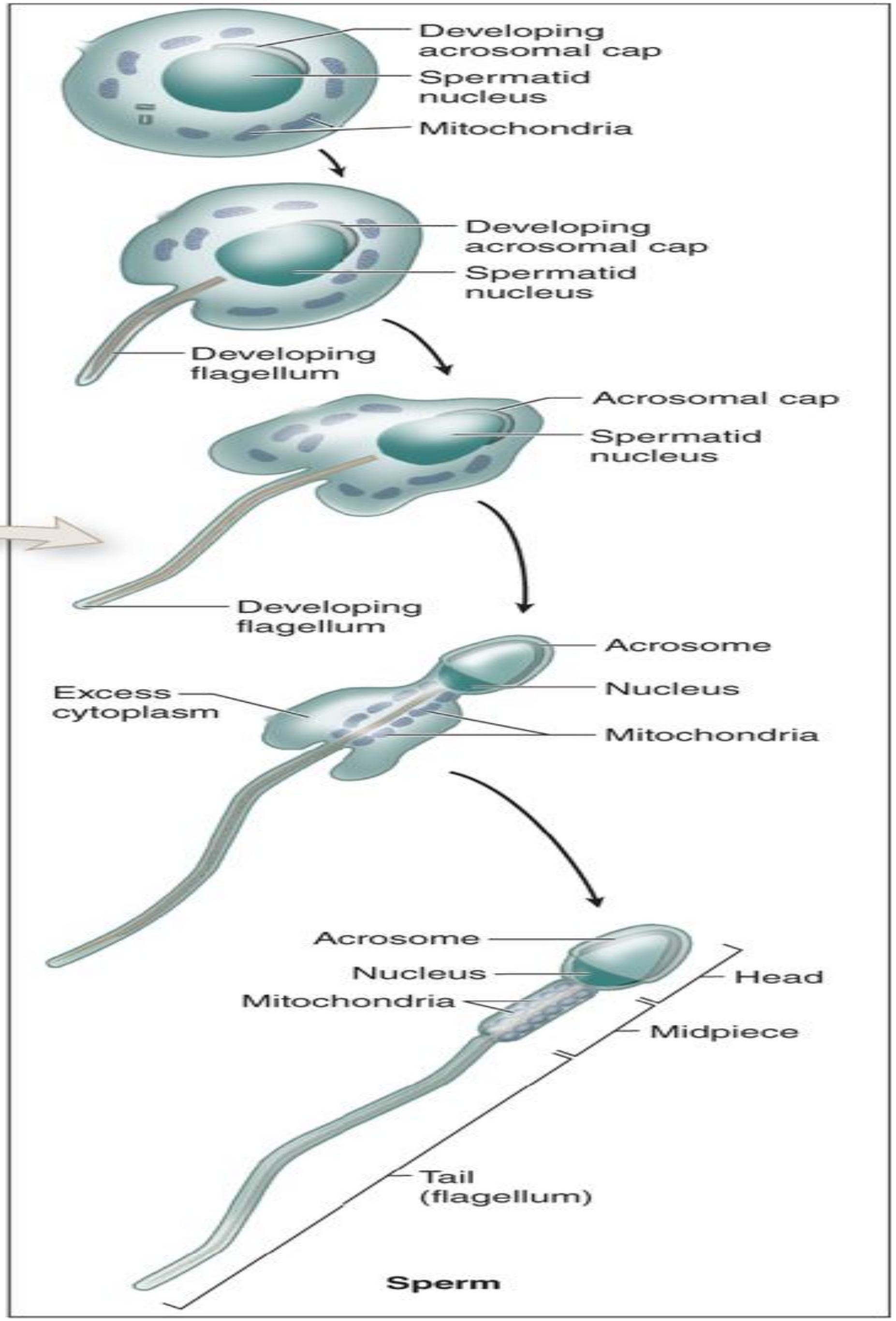
-- Sperm-egg fusion.

- ***Centrosome***: centriole divides into 2 parts that are at first close together
- *proximal centriole* becomes spherical & comes to lie in the neck
- The *axial filament* appears to grow out of it
- distal centriole forms the distal end of the middle piece i.e. the annulus



(a) Spermatogenesis

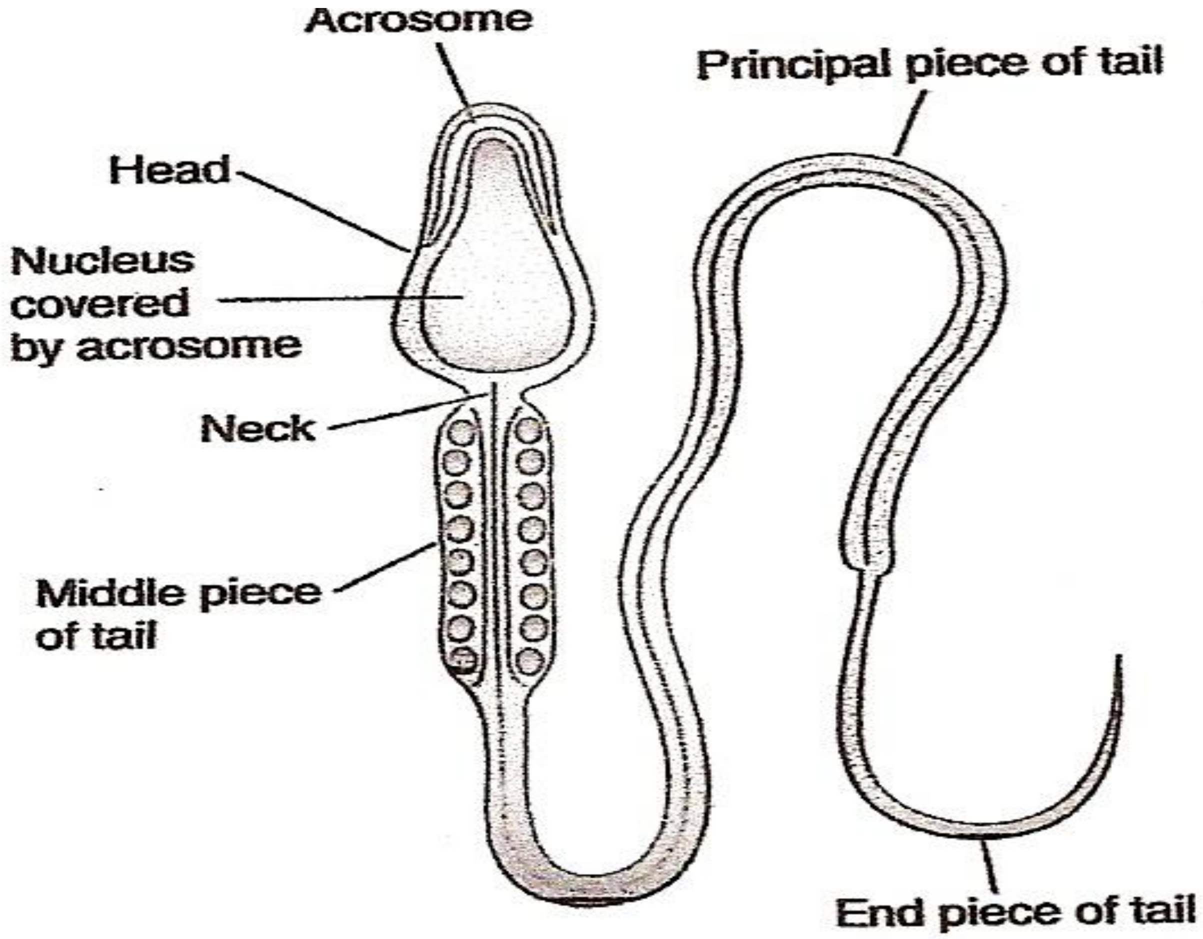
1. The spermatogenic progenitor cells, called spermatogonia, are diploid cells containing 46 chromosomes (23 pairs). Mitotic divisions of these cells each produce a new spermatogonium and a cell called a primary spermatocyte committed to meiosis.
2. Each new primary spermatocyte transiently disassembles the tight junctions of the blood-testis barrier and moves from the tubule's basal compartment to the adluminal compartment. At the same time these cells replicate their DNA, enter meiosis I, and undergo synapsis. The first meiotic division produces two haploid secondary spermatocytes each with 23 chromosomes.
3. Meiosis II is rapid as chromatids in the secondary spermatocyte chromosomes separate into two smaller haploid cells, the spermatids.
4. Near the lumen but still embedded in Sertoli cells, the spermatids differentiate and undergo the morphological changes required to become motile and capable of fertilization.



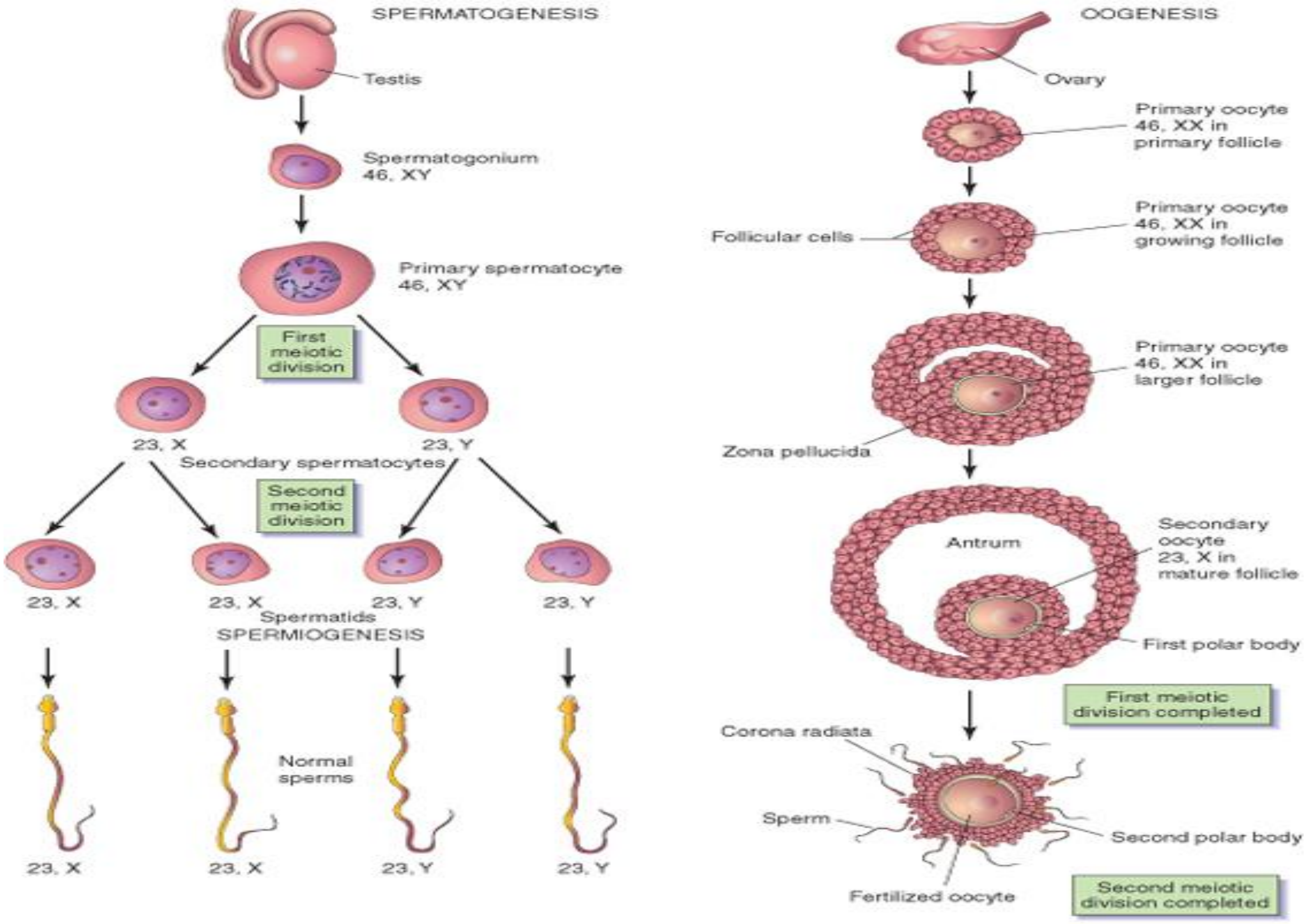
(b) Spermiogenesis

Structure of spermatozoa

- Head
- Tail
- Neck
- Middle piece

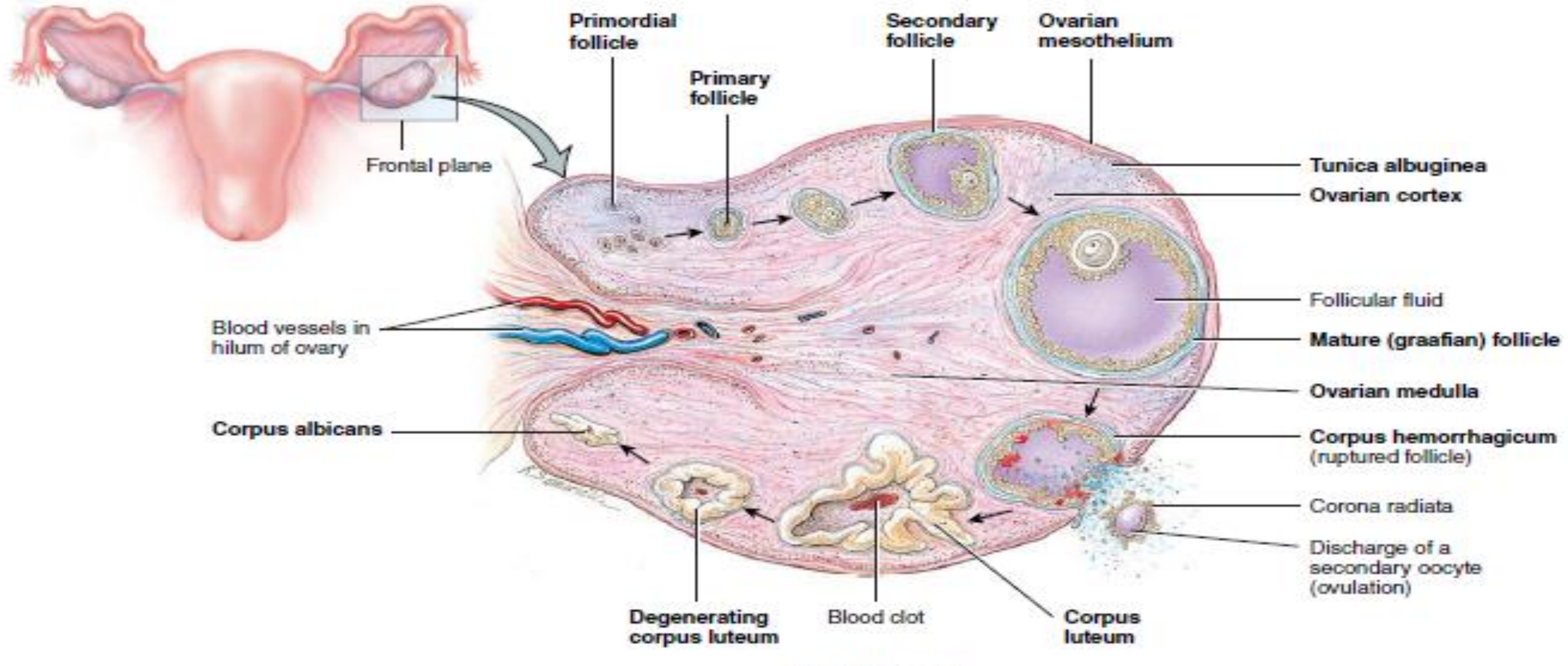


NORMAL GAMETOGENESIS



OOGENESIS

The ovaries are the female gonads; they produce haploid oocytes.



(a) Frontal section

- **Oogenesis**
- Also known as ovogenesis
- The process of maturation and differentiation of PGC to oogonia, primary oocytes, secondary oocytes and to mature ova in the female genital tract
- Starts before birth
- Completed after puberty (12-15yrs)
- Continues to menopause
- No primary oocytes form after birth

- **PRENATAL MATURATION OF OOCYTES**
- Primodial germ cells migrate from the wall of the yolk sac to developing gonads(ovaries)
- Primodial germ cells differentiates into oogonia proliferate by mitosis
- Are arranged in clusters surrounded by a layer of flat epithelial cells(follicular cells)
- Oogonia with replicated DNA enter into meiosis 1 & form to **primary oocytes**

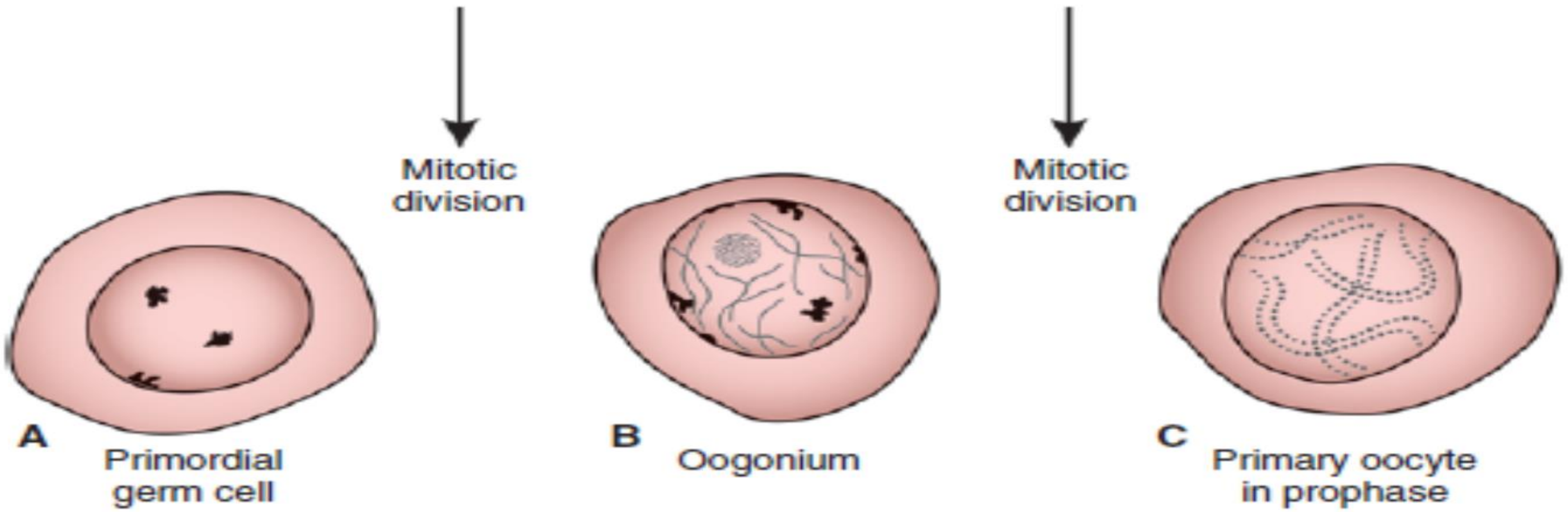
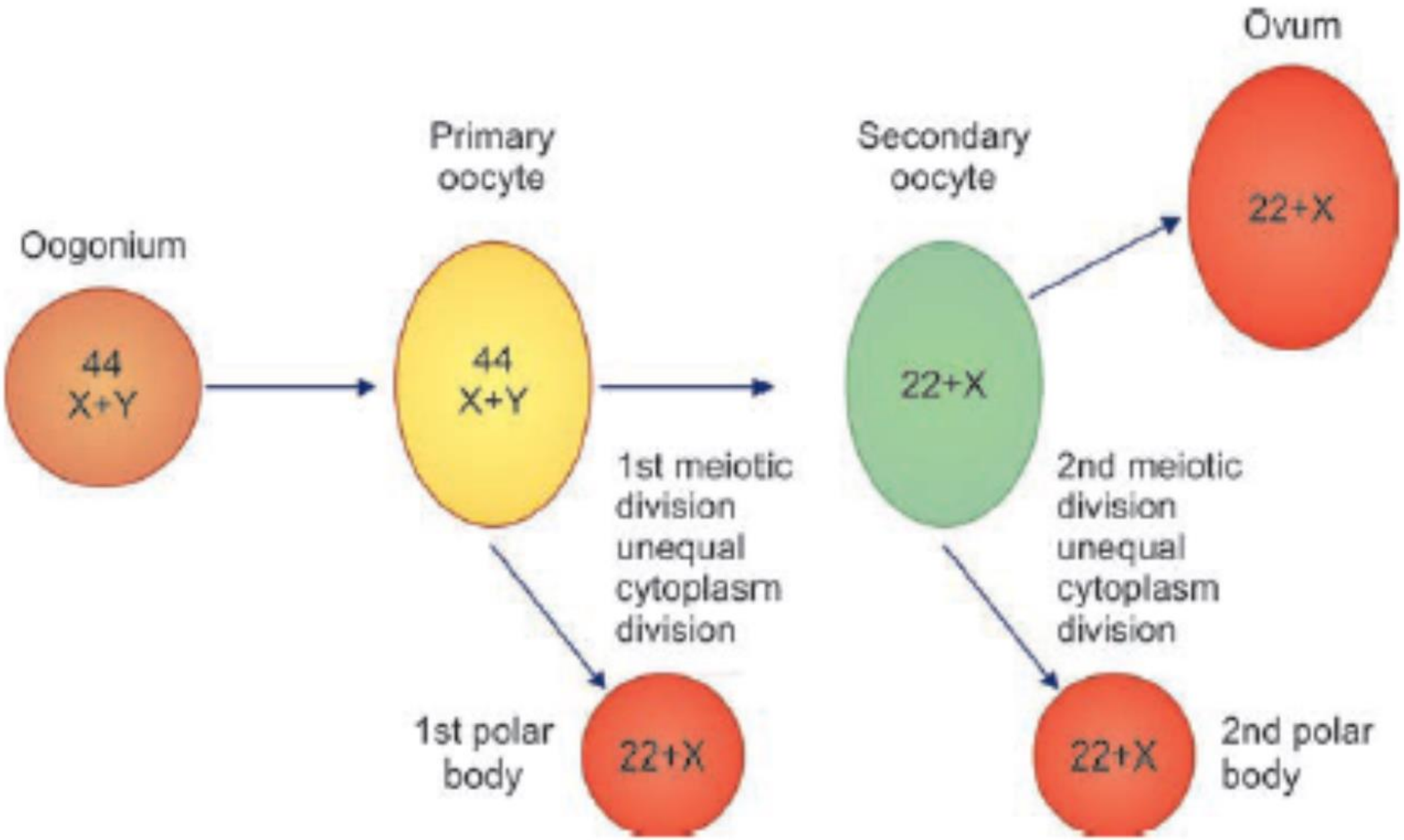


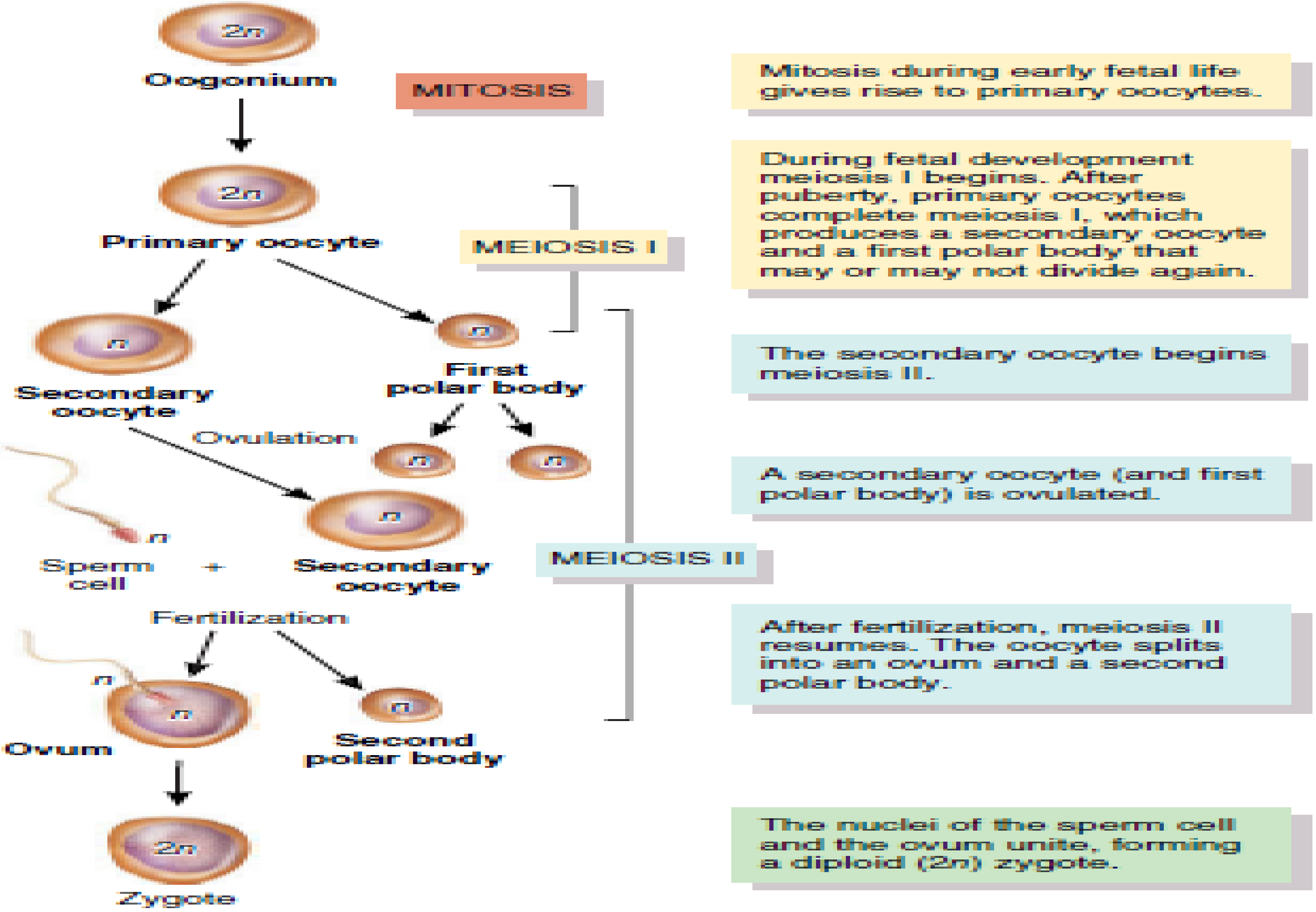
Figure 2.16 Differentiation of PGCs into oogonia begins shortly after their arrival in the ovary. By the third month of development, some oogonia give rise to primary oocytes that enter prophase of the first meiotic division. This prophase may last 40 or more years and finishes only when the cell begins its final maturation. During this period, it carries 46 double-structured chromosomes.

Age	Follicular histology		Meiotic events in ovum	Chromosomal complement
Fetal period	No follicle		Oogonium	2n, 2c
			Mitosis	
Before or at birth	Primordial follicle		Primary oocyte	2n, 4c
			Meiosis in progress	
After birth	Primary follicle		Primary oocyte	2n, 4c
			Arrested in diplotene stage of first meiotic division	
After puberty	Secondary follicle		Primary oocyte	2n, 4c
			First meiotic division completed, start of second meiotic division	
	Tertiary follicle		Secondary oocyte + Polar body I	1n, 2c
			Ovulation	
	Ovulated ovum		Secondary oocyte + Polar body I	1n, 2c
			Arrested at metaphase II	
	Fertilized ovum		Fertilized ovum + Polar body II	1n, 1c + sperm
			Fertilization—second meiotic division completed	

- By 5^{th} month all primary oocytes have been formed and no oogonia
- **Primodial follicles** (primary oocyte surrounded by flat follicular cells)
- Primary oocytes start 1^{st} meiotic division before birth
- Rest in **prophase I** (diplotene) is arrested by oocyte maturation inhibitor (OMI) factor till puberty
- **Primary oocytes remain in prophase (diplotene)**and **do not finish their first meiotic division before puberty is reached**
- Even before birth, most of these germ cells degenerate in a process known as **atresia**

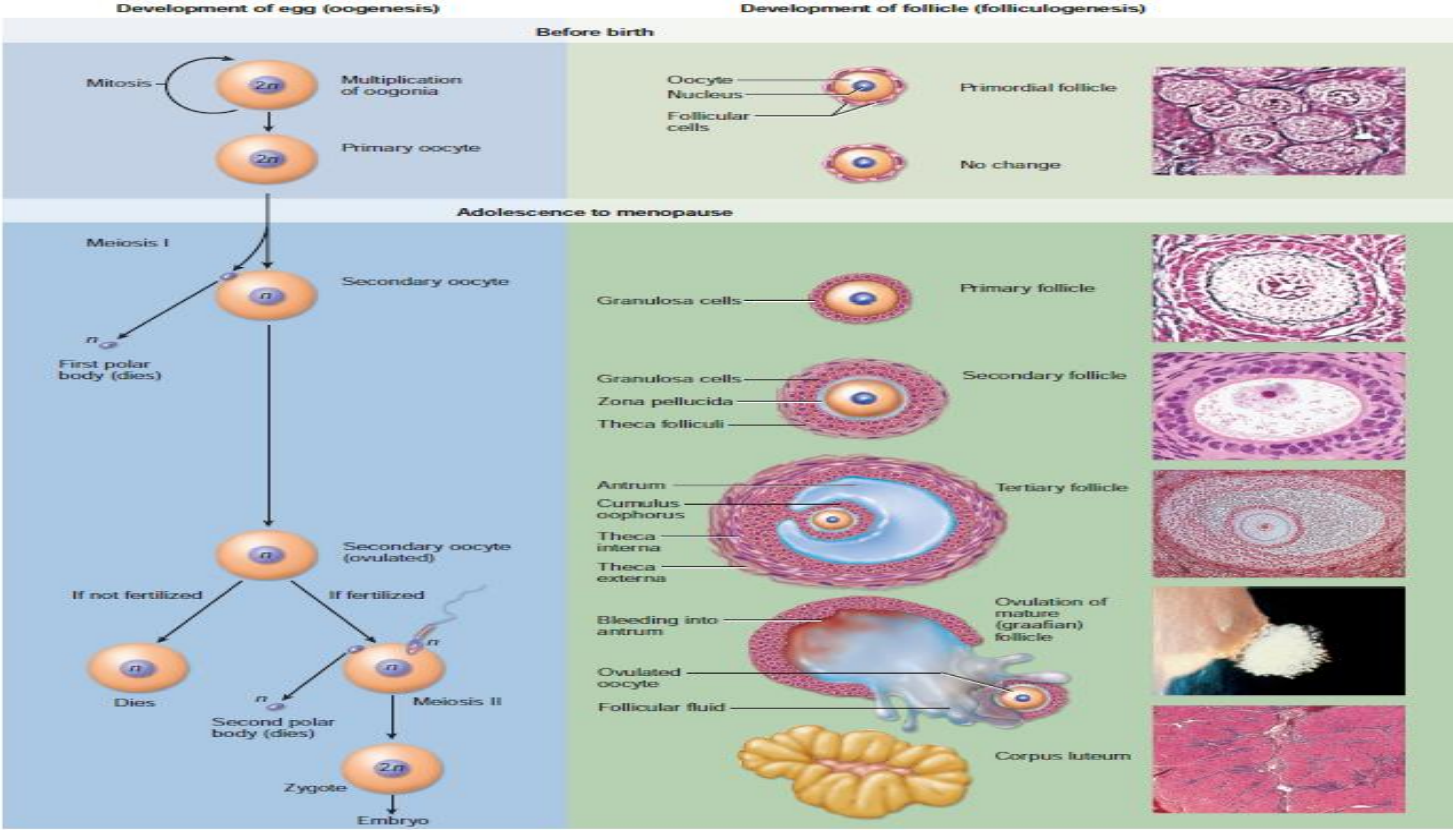
- After puberty the primary oocyte resumes its 1st meiotic division
- It produces 2 daughter cells
- The secondary oocyte and the 1st polar body





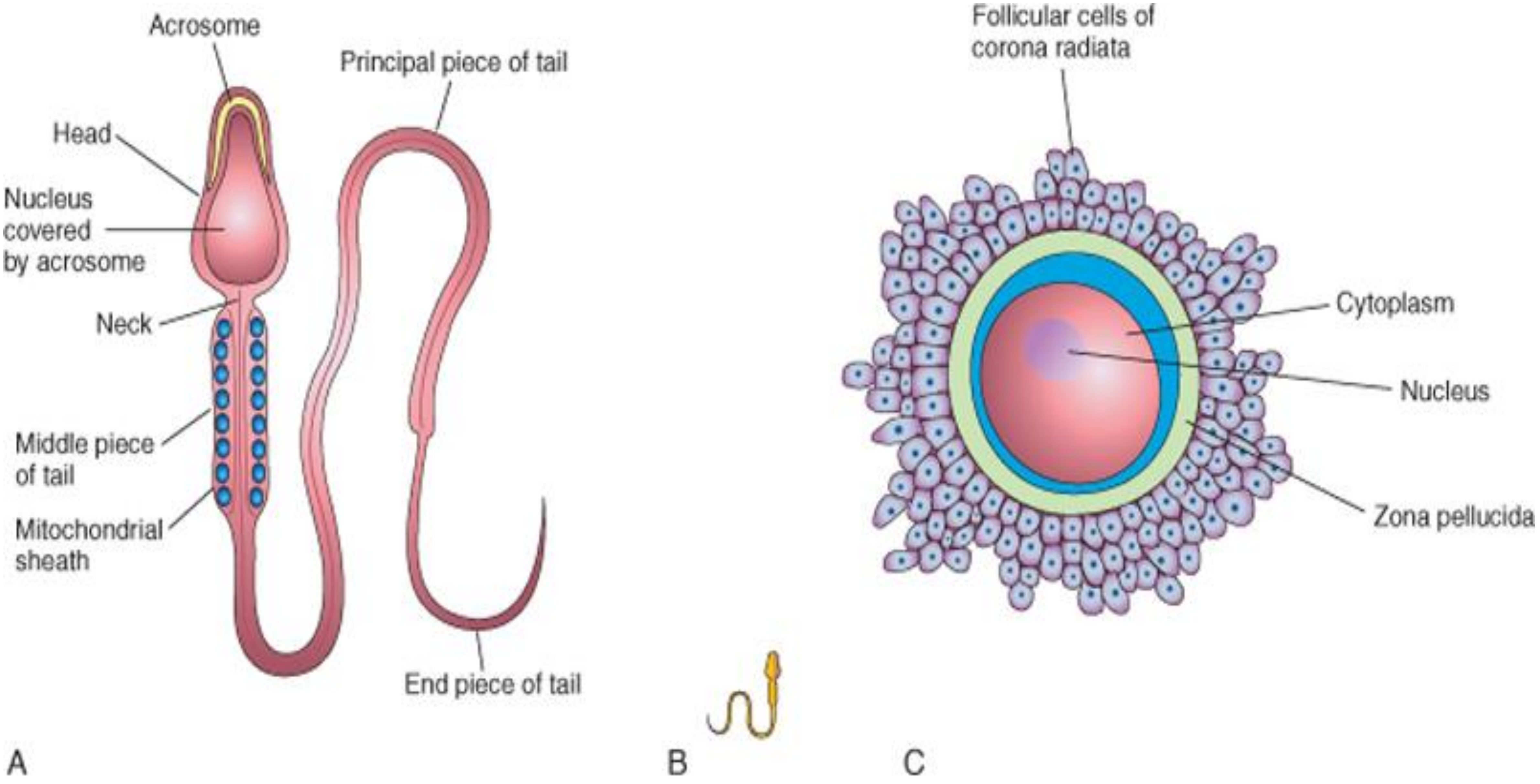
2n
Oogonium
MITOSIS
Mitosis during early fetal life gives rise to primary oocytes.
2n
Primary oocyte
MEIOSIS I
During fetal development meiosis I begins. After puberty, primary oocytes complete meiosis I, which produces a secondary oocyte and a first polar body that may or may not divide again.
n
Secondary oocyte
n
First polar body
The secondary oocyte begins meiosis II.
Ovulation
n
n
A secondary oocyte (and first polar body) is ovulated.
n
n
Sperm cell
+
Secondary oocyte
MEIOSIS II
Fertilization
After fertilization, meiosis II resumes. The oocyte splits into an ovum and a second polar body.
n
n
Ovum
n
Second polar body
2n
Zygote
The nuclei of the sperm cell and the ovum unite, forming a diploid (2n) zygote.

- The secondary oocyte immediately enters the second meiotic cell division
- Ovulation takes place while the oocyte is in metaphase
- secondary oocyte remains arrested in metaphase till fertilization occurs
- second meiotic division is completed only if fertilization occurs
- This division results in 2 **unequal daughter cells**
- larger cell is called *ovum*.
- The smaller daughter cell is called the second polar body
- If fertilization does not occur, the secondary oocyte fails to complete the second meiotic division and degenerates about 24 hours after ovulation



Development of egg (oogenesis)
Development of follicle (folliculogenesis)
Before birth
Mitosis
2n
Multiplication of oogonia
Primary oocyte
Oocyte
Nucleus
Follicular cells
Primordial follicle
No change
Adolescence to menopause
Meiosis I
n
Secondary oocyte
First polar body (dies)
Granulosa cells
Primary follicle
Granulosa cells
Zona pellucida
Theca folliculi
Secondary follicle
Antrum
Cumulus oophorus
Theca interna
Theca externa
Tertiary follicle
Secondary oocyte (ovulated)
If not fertilized
If fertilized
Dies
Meiosis II
Second polar body (dies)
Zygote
Embryo
Bleeding into antrum
Ovulated oocyte
Follicular fluid
Ovulation of mature (graafian) follicle
Corpus luteum

- About 2million primary oocytes in new born
- By adolescent only no more than 40 thousand remain
- Only about 4 hundred become secondary oocytes and are expelled by ovulation
- Few of these oocytes, if any become mature
- About 12 ovulated per year
- Up to about 480 over entire reproductive life


Acrosome
Principal piece of tail
Head
Nucleus covered by acrosome
Neck
Middle piece of tail
Mitochondrial sheath
End piece of tail
Follicular cells of corona radiata
Cytoplasm
Nucleus
Zona pellucida
A
B
C

- ***Clinical Application***
- **Male Infertility**
- common cause of infertility in males is a low sperm cell count.
- If the sperm cell count drops to below 20 million sperm cells per millilitre, the male is usually sterile
- sperm cell count can decrease because of damage to the testes as a result of trauma, radiation, cryptorchidism
- or infections, such as mumps, which block the ducts in the epididymis. Reduced sperm cell counts can also result from inadequate secretion of LH and FSH, which can be caused by hypothyroidism, trauma to the hypothalamus, infarctions of the hypothalamus or anterior pituitary gland, or tumors. Decreased testosterone secretion reduces the sperm cell count as well

- infertility *is* may as a result of insufficient numbers of sperm or poor motility
- Normally, the ejaculate has a volume of 3 to 4 ml, with approximately 100 million sperm per ml
- Severe male infertility, in which the ejaculate contains very few live sperm
- **(oligozoospermia)** or even no live sperm **(azoospermia)**
- Even when the sperm cell count is normal, fertility can be reduced if sperm cell structure is abnormal, as occurs due to chromosomal abnormalities caused by genetic factors.

- Infertility in a woman may be due to a number of causes, including :-
- occluded oviducts (most commonly caused by pelvic inflammatory disease)
- hostile cervical mucus
- immunity to spermatozoa
- reduced hormone secretion from the pituitary gland or the ovaries
- interruption of implantation
- Absence of ovulation, and others

- Misdirected primordial germ cells that lodge in extragonadal sites usually die but if they survive they may develop into teratomas
- Teratomas are bizarre growths contain scrambled mixtures of highly differentiated mixtures such as skin, hair, cartilage, and even teeth
- They are found in the mediastinum, sacrococcygeal region and oral region.

Fig. 1.2 **A,** Sacrococcygeal teratoma in a fetus. **B,** Massive oropharyngeal teratoma.

- Quiz
- 1. In a routine chest x-ray examination a the radiologists sees what appears to be teeth in the mediastinal mass. What is the likely diagnosis and what is the probable embryological explanation for its appearance?
- 2. When does meiosis begin in the female and the male?
- 3. At what stages of oogenesis is meiosis arrested in the female ?
- 5. What is the difference between spermatogenesis and spermiogenesis?
- 6. The actions of what hormones are responsible for the changes in the endometrium during the menstrual cycle ?
- 7. Sertoli cells in the testis are stimulated by what two major reproductive hormones?
- 8. What are the components of the blood-testis barrier and what is its significance?