L1.A.B.
University of Médéa 2023/2024
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GAMETOGENESIS

General informations : Gametogenesis is the process of **gamete formation** in both male and female sexes, occurring within the reproductive glands (gonads): the testes in males and the ovaries in females. Gametes (**spermatozoa** and **ovum**) are haploid cells, meaning their nucleus contains n chromosomes. Gametogenesis involves two processes: oogenesis (production of **ovum**) and spermatogenesis (production of **spermatozoa**).

1.Female Gametes:

Oocytes are female gametes capable of fertilization, arrested in metaphase II, produced from the germline stem cells (**oogonia**).

1.1. Female Reproductive System: From an anatomical perspective, the internal female reproductive system comprises:

- An ovary attached to the uterus by ligaments on each side, responsible for the production of gametes and sex hormones**.**
- The uterine tubes (or Fallopian tubes or oviducts) are conduits that extend from the uterus to the ovary on each side of the reproductive system. This is the site of fertilization and comprises several segments:

- The infundibulum: at the free end, with a fringed funnel-like shape.
- The ampulla: a swollen portion, with a diameter of 7 to 8 mm, located in the upper third of the tube.
- The isthmus: the interstitial segment.

- The uterus, where embryonic development occurs, consists of the body, which receives the two uterine tubes at its upper edge.
- The cervix opens into the vagina.

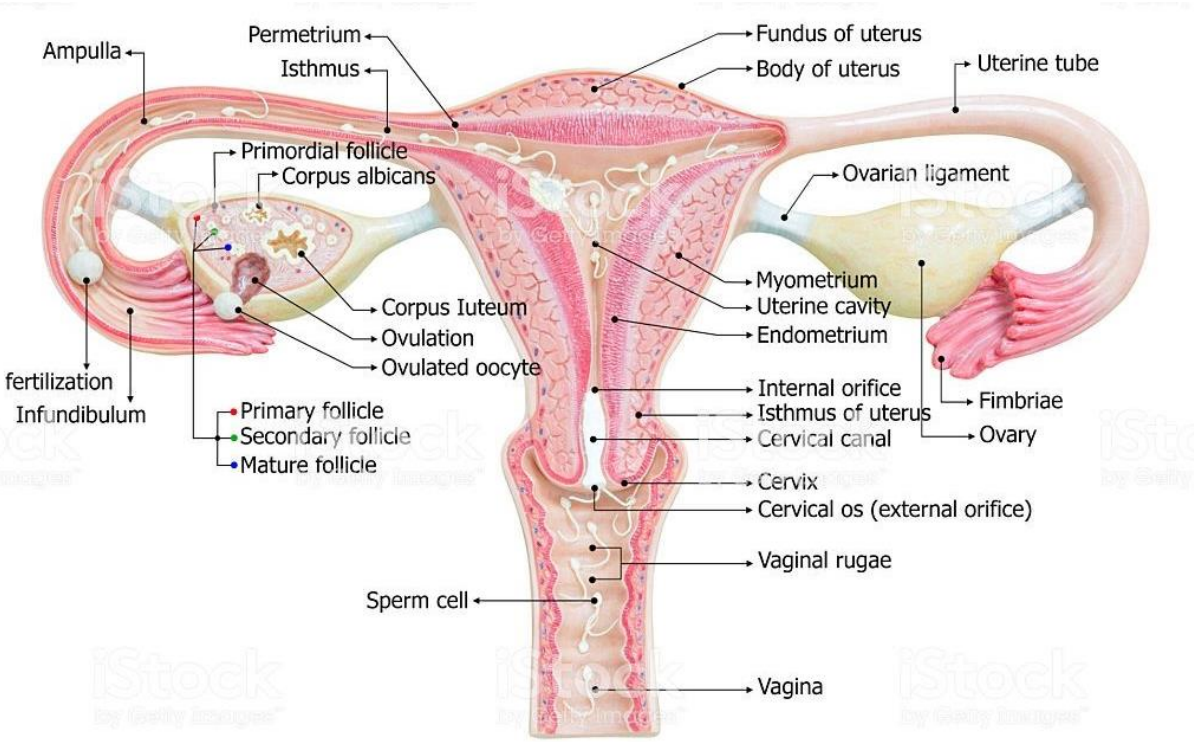


Figure 1 : Female reproductive system

1.2.Female Gonads: Ovaries:

The ovary is an oval-shaped organ, which serves as the site for the production and storage of oocytes, as well as the process of folliculogenesis. The entire ovary is surrounded by a superficial lining epithelium: ovarian epithelium (simple cuboidal). Two regions are described in a histological section of the ovary:

1.2.1. The cortical region: It includes, from outermost to innermost:

- **A simple cuboidal epithelium:** the ovarian epithelium (lining tissue).
- **The ovarian albuginea:** connective tissue poor in cells and rich in ground substance.
- **A cortical stroma:** consisting of fibroblast-like cells and very few fibers. The stroma contains the following structures: follicles (oocyte + surrounding cells with endocrine gland function), corpora lutea, and atretic bodies (resulting from degeneration of follicles or corpora lutea).

1.2.2. The medullary region:

The deep central region contains two zones:

- **A hilar zone (hilum):** fibrous appearance
- **A parenchymal zone:** continuous with the cortical region, containing loose connective tissue traversed by numerous blood vessels that distribute to or originate from the cortical region in a spiral pattern.

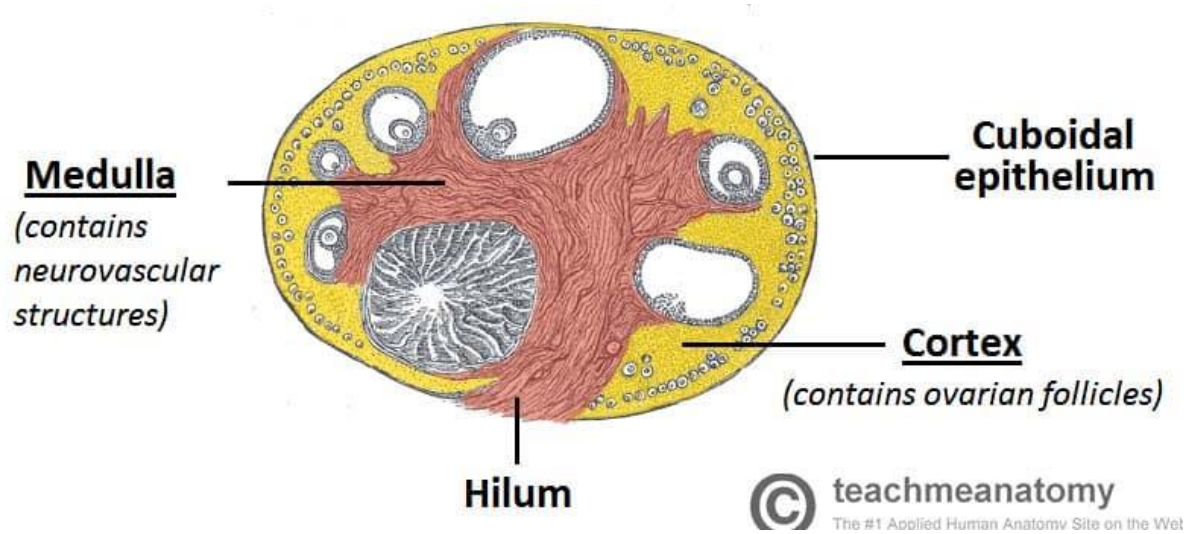


Figure 2 : Histological structure of the ovary

1.3. Oogenesis:

Oogenesis is the process of producing female gametes (**oocytes**). This process is discontinuous: from fetal life until menopause, it occurs at the level of the fetal ovary through the multiplication of oogonia. It is completed between **puberty** and **menopause**, by producing, **once every 28 days**, a fertilizable gamete, the secondary oocyte arrested in metaphase of the second meiotic division (oocyte II in metaphase II).

Oogenesis includes phases of multiplication, growth, and maturation

1.3.1. Multiplication Phase:

This phase involves **oogonia** (**diploid stem cells**) and is characterized by a series of **mitotic** divisions that result in the formation of **oocytes I** (primary oocytes), which are also diploid. This phase occurs in women during **embryonic** and **fetal life**.

Oogonia become **primary oocytes** blocked at the end of **prophase I** and are contained within primordial follicles. These follicles constitute a reserve that will not be replenished but will instead diminish until menopause. Their number is approximately **7 million** at the end of the **7th month of gestation**, **one million** at **birth**, **400,000 at puberty**; around the age of forty, degeneration accelerates until the total disappearance of oocytes at menopause.

1.3.2. Growth Phase:

A very long phase characterized by:

- A significant increase in the size of the oocyte I, which increases from 20 to 120 µm in diameter during follicular development (from primary follicle to mature follicle).
- Synthesis activities of RNA, proteins.
- Accumulation of various exogenous materials.
- Accumulation of reserves (yolk).
- Formation of cortical granules.

1.3.3. Maturation Phase:

Each month, at the time of ovulation, the oocyte I (2n chromosomes) completes the first meiotic division and yields an oocyte II (n chromosomes) with the emission of the first polar body. Immediately after, the second meiotic division begins. However, the process once again halts (in metaphase of the second meiotic division) and is conditioned by whether fertilization occurs or not:

- In the absence of fertilization, the oocyte remains at this stage of meiosis and degenerates after 24 hours.
- If fertilization occurs, the oocyte II will complete its maturation and transform into a mature ovum (oocyte) with the emission of the second polar body.

The maturation phase is associated with folliculogenesis.

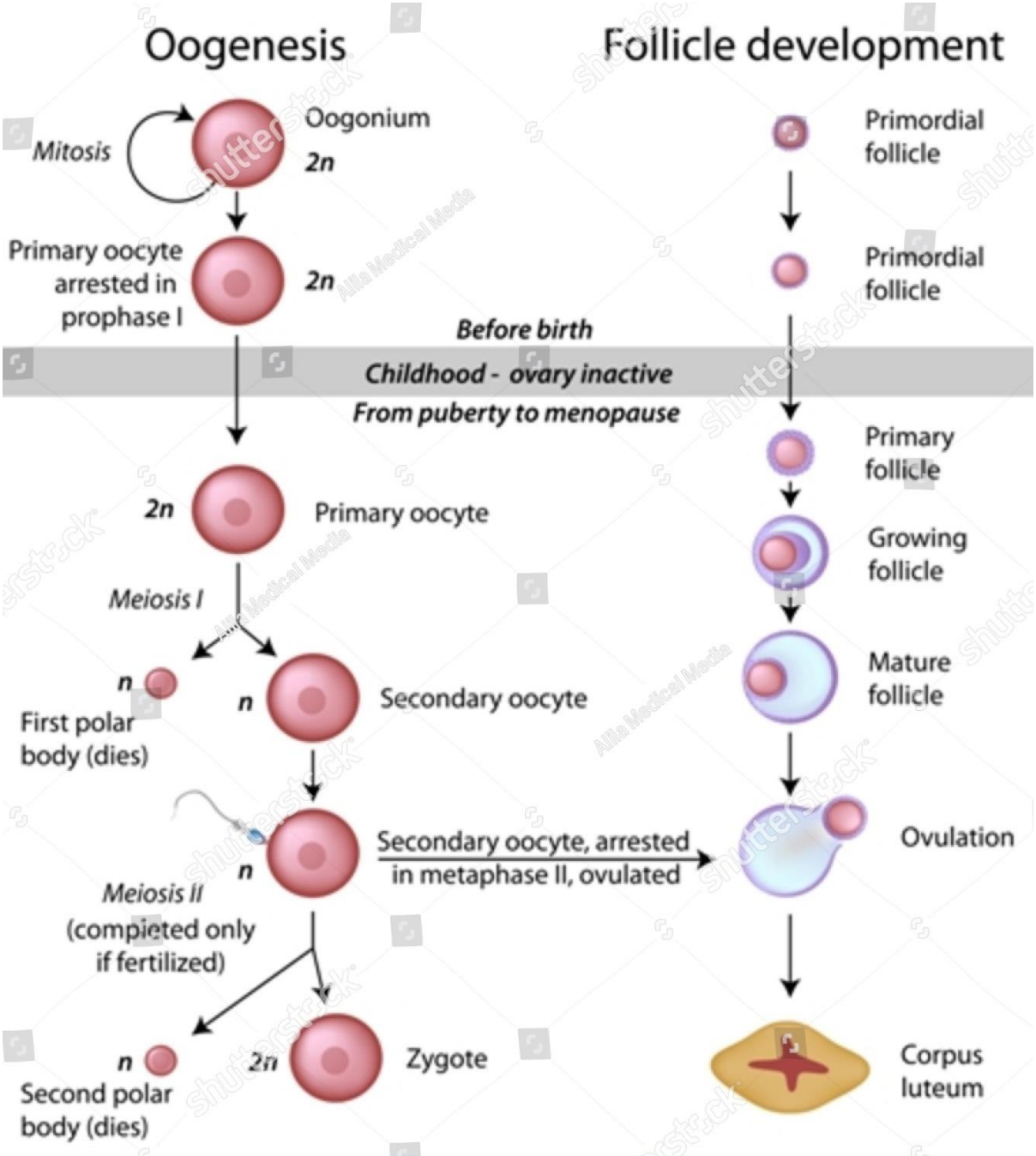


Figure 3 : Stages of oogenesis

Folliculogenesis: It's the set of stages of development of a primordial ovarian follicle that, upon ovulation, gives rise to a mature haploid (with 23 chromosomes) secondary oocyte, arrested in metaphase of the second meiotic division; this is the female gamete (or ovum) ready to be fertilized by a spermatozoon.

1. **Primordial Follicle:**

This is the cellular structure in which each primary oocyte (oocyte I) is kept in a state of rest since intrauterine life. It is a first-order oocyte arrested in prophase of the first meiotic division; it is surrounded by a single layer of flattened follicular cells. The primordial follicle measures approximately 50 µm, with a first-order oocyte of 20 µm in diameter. It is separated from the ovarian stroma by the Slavjanski membrane.

2. **Primary Follicle:**

Its diameter increases from 50 to 100 µm (due to oocyte growth and an increase in the number of follicular cells, which then form 4 or 5 layers around the oocyte). They are now roughly spherical and of small size (10 µm).

3. **Secondary Follicle:**

Its diameter increases from 100 to 200 µm, due to the proliferation of follicular cells, reaching a number of 1 million, arranged in about twenty compact layers (full follicle). Additionally, outside the Slavjanski membrane, stromal cells organize into a theca.

4. **Tertiary Follicle (Cavitary, with Antrum):**

Its diameter increases from 200 µm to 12 mm due to the proliferation of follicular cells (5 to 10 million), and the oocyte has a diameter of 90 µm. It is characterized by the appearance of spaces between the cells, filled with a fluid they secrete, called follicular fluid. These spaces fuse into a single cavity, the follicular cavity or antrum. Additionally, the theca differentiates into 2 layers, the inner and outer theca, with different histological structures.

5. Mature Follicle (Graafian, Preovulatory):

Its diameter reaches 12 to 25 mm in women. Swollen with follicular fluid, it takes on a cystic appearance and protrudes from the surface of the ovary. This growth is due to the proliferation of follicular cells (50 million) and, above all, to the increase in the volume of the follicular cavity, which reaches 3 to 5 ml. Its structure is as follows:

- It is limited by the external theca, made of connective tissue.
- The internal theca has a structure resembling an endocrine gland, with cellular cords separated by sinusoidal capillaries; these cells are steroidogenic.
- The Slavjanski membrane separates the internal theca from the follicular cells.
- Several layers of follicular cells surround the follicular cavity.
- The follicular cavity is filled with an opalescent fluid of complex composition: proteins, lipids, carbohydrates, prostaglandins, various growth factors and interleukins, and especially steroids at very high concentrations.
- At one pole of this cavity, the follicular cells remain more numerous and form a sort of protrusion into the cavity called the cumulus oophorus, inside of which the oocyte is located.
- The regular layer surrounding the oocyte is called the corona radiata, in contrast to the rest of the follicular cells grouped under the term granulosa.
- The oocyte is surrounded by an envelope of 10 to 20 µm in thickness, the zona pellucida, penetrated by extensions of the corona radiata cells coming into contact with the oocyte membrane, to which they are connected by junction systems, particularly gap junctions.
- The zona pellucida is separated from the oocyte by a perivitelline space, approximately 5 µm in thickness.
- The primary oocyte, which now has a diameter of about 110 µm, is still arrested in prophase of the first meiotic division.

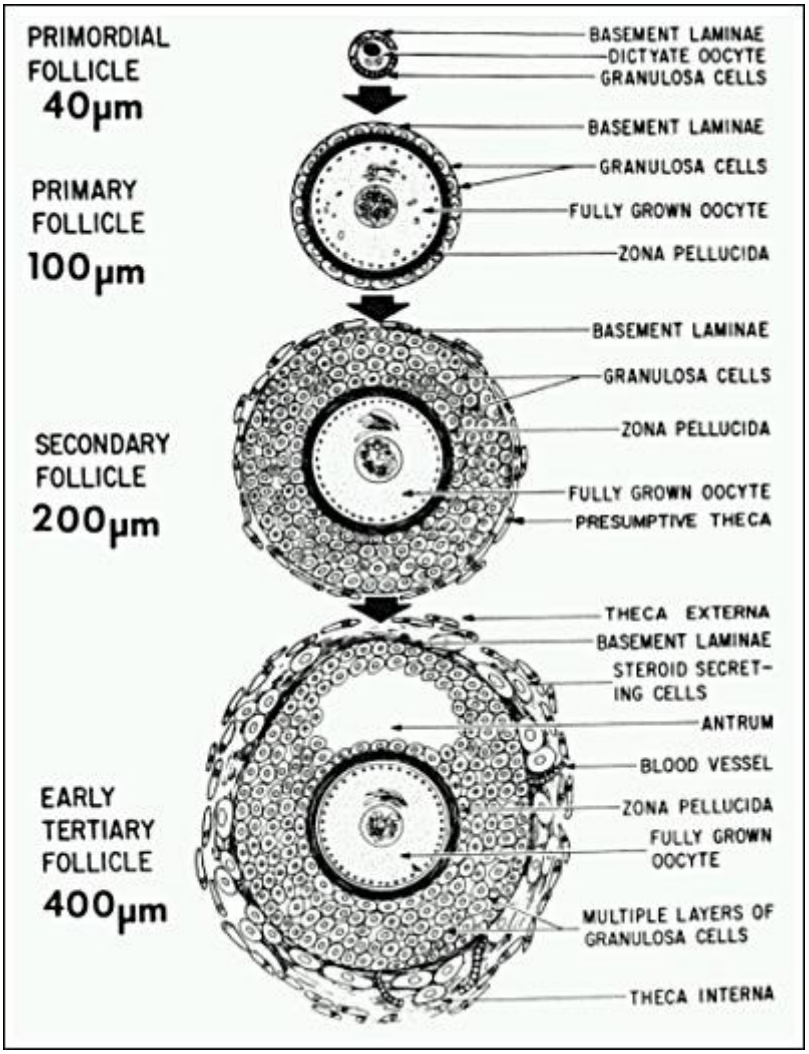


Figure 4 : Folliculogenesis

The luteal phase : is the second phase of the menstrual cycle in women. It begins after ovulation, when the empty ovarian follicle transforms into a structure called the corpus luteum, or luteal body. This phase is characterized by an increased production of progesterone by the corpus luteum, which prepares the uterus for the possible implantation of a fertilized egg. If fertilization does not occur, the corpus luteum degrades, leading to a decrease in progesterone levels and the onset of menstruation. The luteal phase typically lasts about 12 to 14 days, but its length can vary from woman to woman**.**

1.4. Different Types of Eggs: The presence or absence of yolk allows distinguishing:

- **Alecithal eggs:** devoid of yolk, as in Placental Mammals.
- **Oligolecithal eggs:** have little yolk, ex : Sea Urchin.
- **Mesolecithal eggs:** have a moderate amount of yolk, ex :Amphibians.
- **Megalecithal or telolecithal eggs:** eggs with a very large amount of yolk distributed throughout most of the cytoplasm, ex :Reptiles, Birds.
- **Centrolecithal eggs:** eggs with a large yolk mass occupying the center, ex : Insects.

2. Spermatogenesis:

It is the process of producing male gametes (spermatozoa) from diploid stem cells called spermatogonia. This process occurs in the male reproductive system, specifically in the seminiferous tubules of the testicle.

2.1. Male Reproductive System:

2.1.1. General Appearance: The male reproductive system comprises, on each side:

- **A testicle:** capped by the epididymis and housed in the scrotum.
- **A vas deferens :** which extends from the epididymis.
- An **ejaculatory duct** that follows the vas deferens.
- In the terminal part of the apparatus, the organs are singular:
- The **urogenital canal** or **urethra**, originating from the bladder.
- **The prostate.**

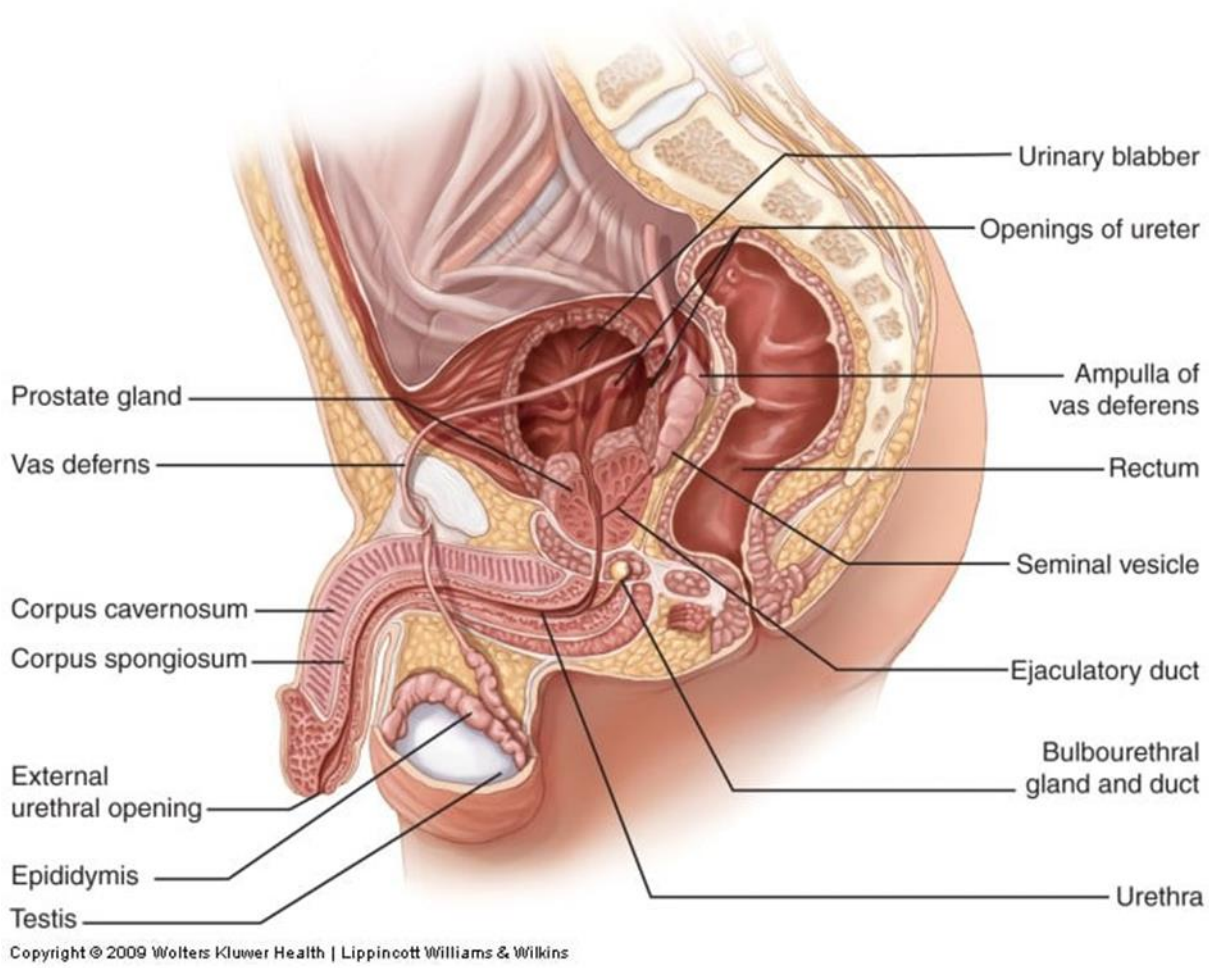


Figure 5 : Anatomy of the male reproductive system

a- Testicle and Epididymis:

Testicle: Ovoid organ (4.5 x 3 x 2 cm), it is housed in an external cutaneous sac: the scrotum. The testicle, in sagittal section, presents the following appearance:

- It is surrounded by the **tunica albuginea**, a fibrous connective tissue capsule, inextensible, a thickened portion of which at the upper pole forms the **corpus of Highmore.**
- Radiating from the latter and extending towards the periphery, thin connective tissue partitions (testicular septa) delineate testicular lobules (200 to 300 per testicle).
- Each lobule contains, within an interstitial tissue, a bundle of **seminiferous tubules** (1 to 4 per lobule).

- The seminiferous tubules of each lobule converge into a **straight tubule**, 1 mm long, which continues into the **rete testis** (a tight network of canaliculi with irregular diameters) connected to the epididymis.
- The straight tubules and **rete testis** are embedded in the corpus of Highmore.

Epididymis: It consists of three parts:

- A thick "head" caps the upper pole of the testicle.
- A "body" follows its external shape.
- A "tail" terminates directly into the vas deferens.

The epididymis contains two types of ducts:

• **Efférent ductules:** They refer to 12 to 15 tubes arising from the rete testis and emerging from the hilum of the testicle to join the epididymal duct at a right angle.

• **Epididymal duct:** A long duct (6m) coiled upon itself and continuing as the vas deferens.

b- **Seminiferous Tubules:**

In cross-section, a seminiferous tubule appears to be composed of a thin external connective tissue membrane, called the tunica propria, containing contractile myoid cells and separated from the epithelium by a basal membrane. They are made up of germ line cells (spermatogonia, spermatocytes I, spermatocytes II, spermatids, and spermatozoa) and somatic cells, Sertoli cells. In the loose connective tissue surrounding the seminiferous tubules, islands of interstitial cells, or Leydig cells, are found, arranged in cords around capillaries. They are responsible for androgen secretion.

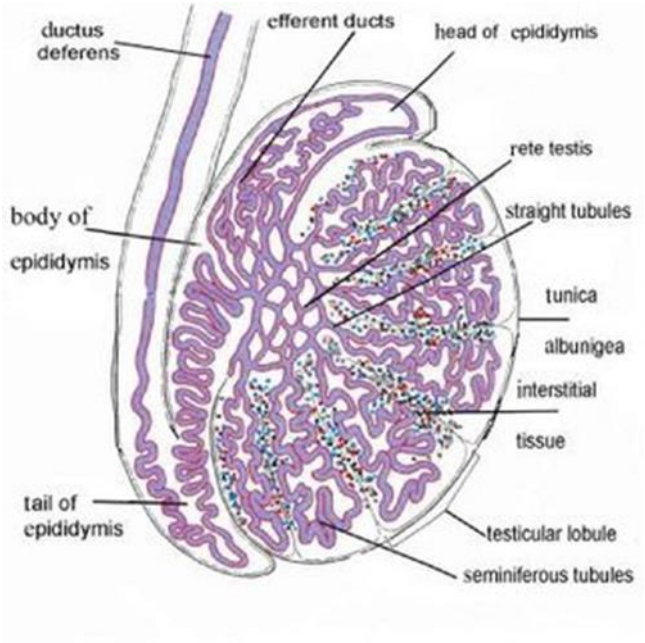


Figure 6: Histological section of a testicle

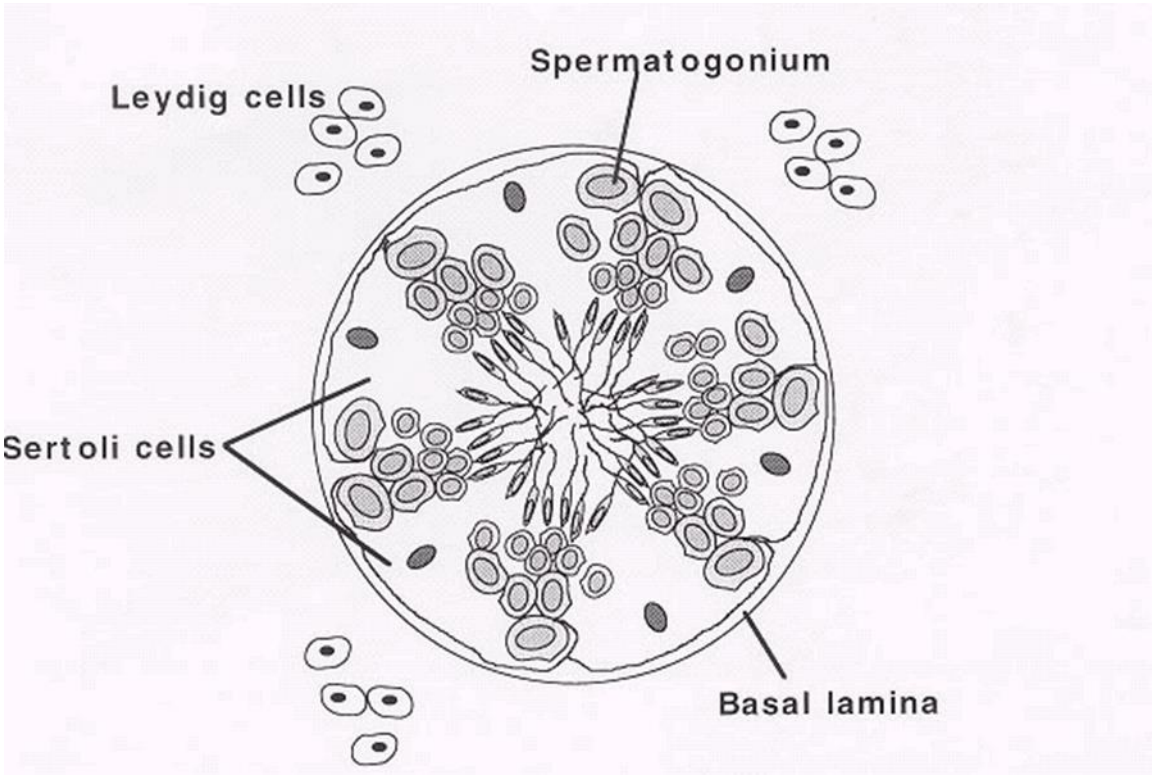


Figure 7: Transverse section of a seminiferous tubule

2.1.2. Stages of Spermatogenesis:

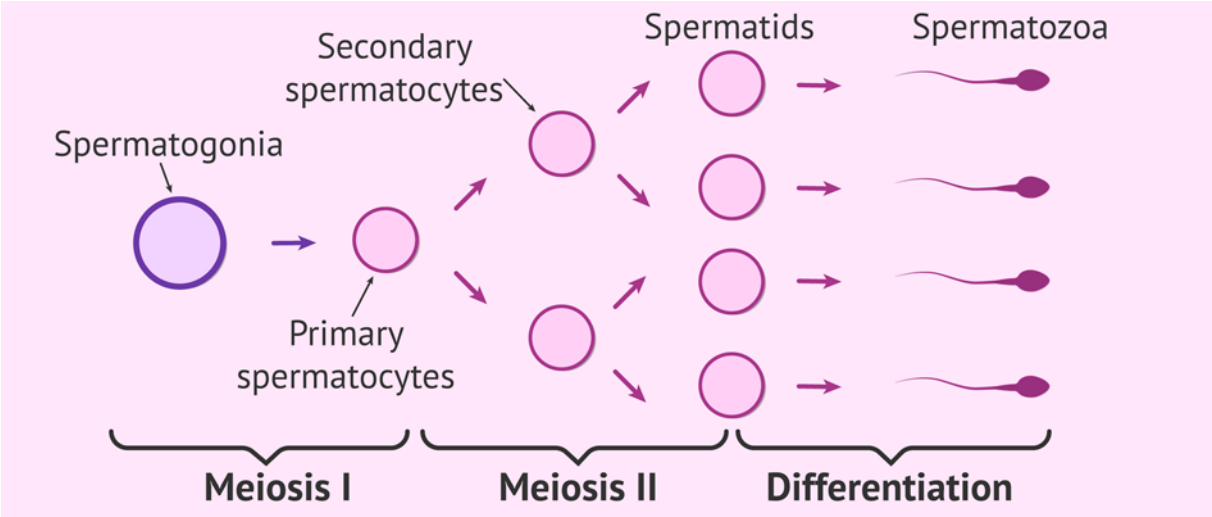
It occurs in the seminiferous tubules and consists of 4 stages:

a- Multiplication phase: It involves spermatogonia, diploid stem cells located at the periphery of the tubule with dark nuclei. These cells undergo a series of mitoses, with the final one resulting in the formation of pale dusty spermatogonia which will divide by mitosis into crusty spermatogonia.

b- Growth phase: Cytoplasmic growth is observed in crusty spermatogonia, which become spermatocytes I with 2n chromosomes.

c- Maturation phase: It corresponds to meiosis and involves the two generations of spermatocytes (primary I or secondary II). A spermatocyte I with 2n chromosomes undergoes the first meiotic division, resulting in 2 spermatocytes II with n chromosomes each. Each spermatocyte II undergoes the second meiotic division, resulting in 2 spermatids with n chromosomes each.

d- Differentiation phase: Also called spermiogenesis, this phase does not involve division but rather the differentiation of spermatids into spermatozoa (formation of the acrosome, flagellum), which will be released into the lumen of the seminiferous tubule.



2.1.3. Structure of Spermatozoa: The spermatozoon is a highly elongated cell composed of 3 visible parts under the optical microscope: the head, the flagellum, and the neck, a narrow portion connecting the flagellum to the head.

- **The head:** It is roughly ovoid but slightly flattened and tapered towards the front, thus showing a flame-like appearance in sagittal section. It consists of a nucleus and an acrosome, enveloped by a thin layer of hyaloplasm and the plasma membrane.
- **The neck:** It is the junction zone between the head and the flagellum, in which two components can be distinguished: a centriolar apparatus and a connecting piece, surrounded by a thin layer of hyaloplasm and the plasma membrane.
- The flagellum: Starting from the neck, three parts of decreasing diameters can be distinguished along its length: the intermediate piece, the principal piece, and the terminal piece. They all share a common axial structure, the axoneme, and differ in their concentric structures. The axoneme has the classical structure found in motile cilia, with 9 peripheral doublets of microtubules and a central doublet.

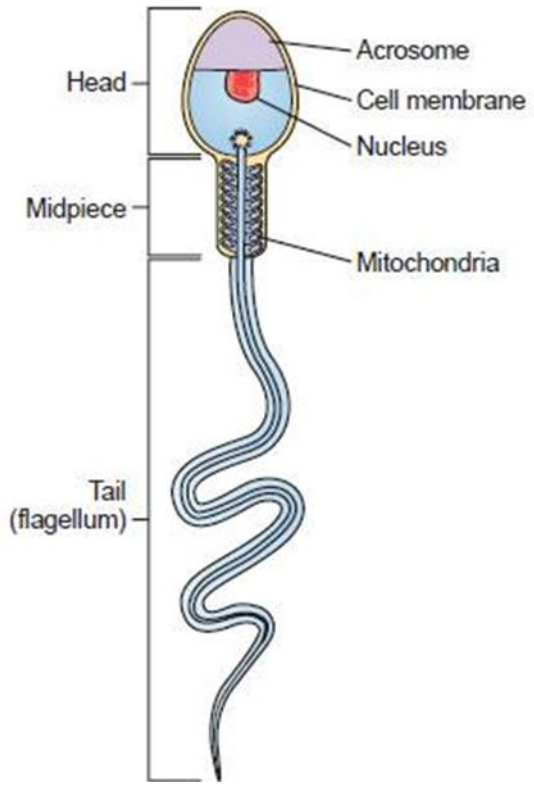


Figure 9: Spermatozoa Structure

Differences between spermatogenesis and oogenesis

	spermatogénèse	**ovogénèse**
Organe	**testicules**	**Ovaires**
Nombre des gamètes produits	**4 spermatozoides**	**1 ovule et 3 globules polaires qui dégénèrent**
Type de chromosome	**Moitié de spz → X** **Moitié de spz → Y**	**Tous les ovules → X**

Mobilité	+	-
Longévité du gamète	4 jours environ	24h environ
Taille	Petite cellule	Grosse cellule
Rythme de production	Journalier (des millions /j) de spz	Mensuel (1 ovule /mois)
Durée de production des gamètes	De la puberté jusqu'à un age avancé. Les spermatogonies se renouvellent par mitose	puberté → ménopause (50 cms env). Les ovogonies ne se renouvellent pas. La fillette naît avec son capital (700 000 env

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