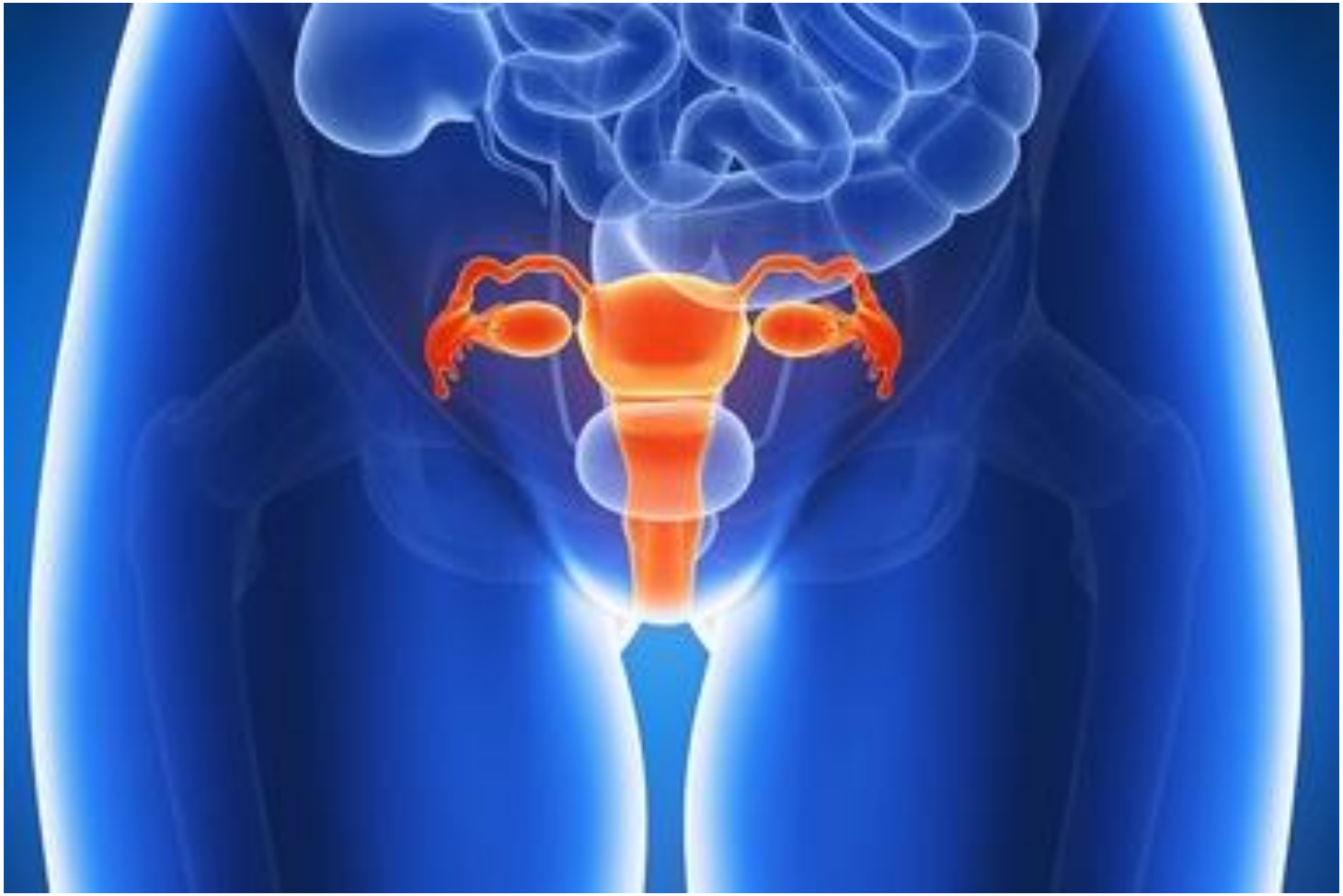
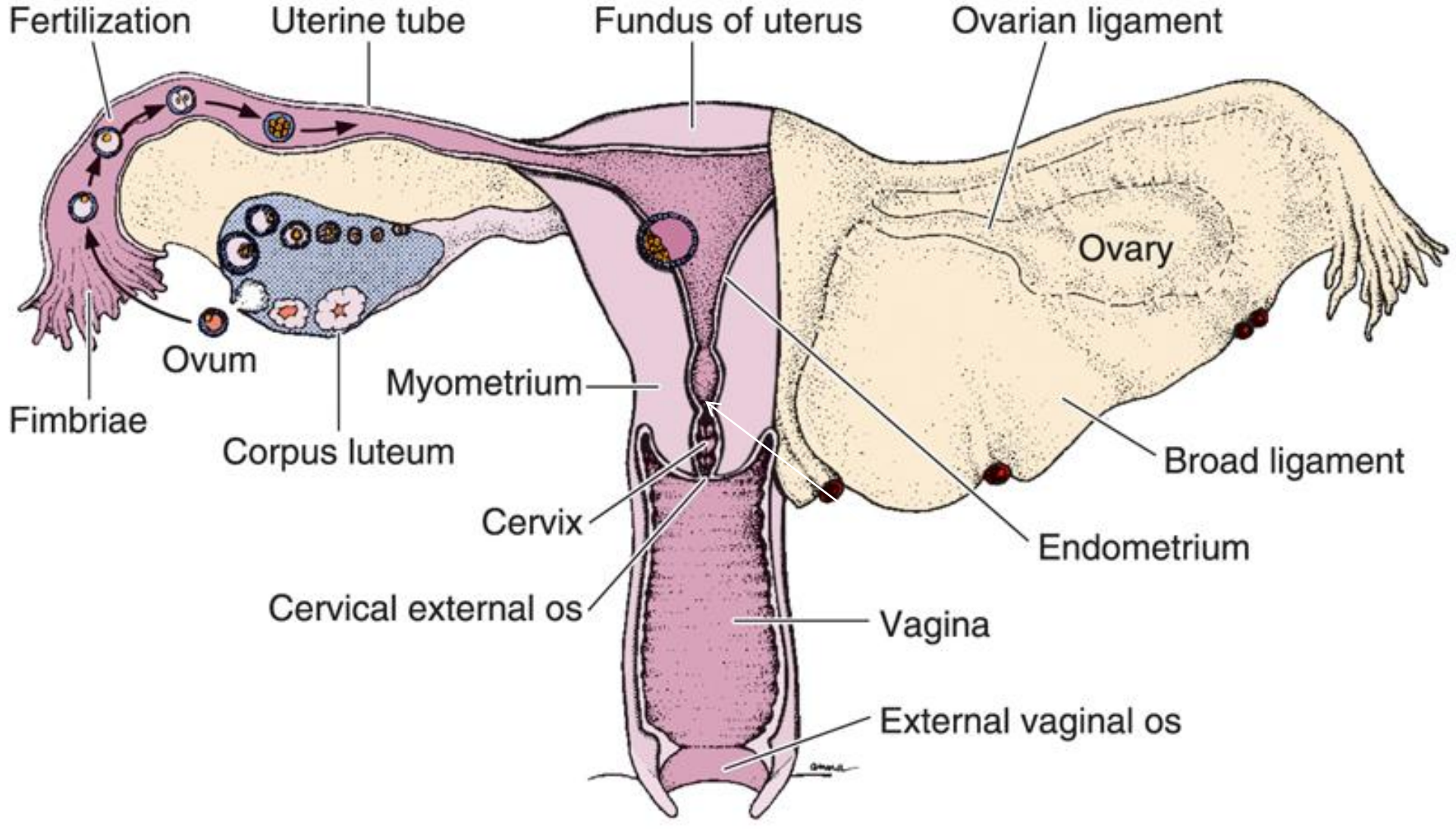
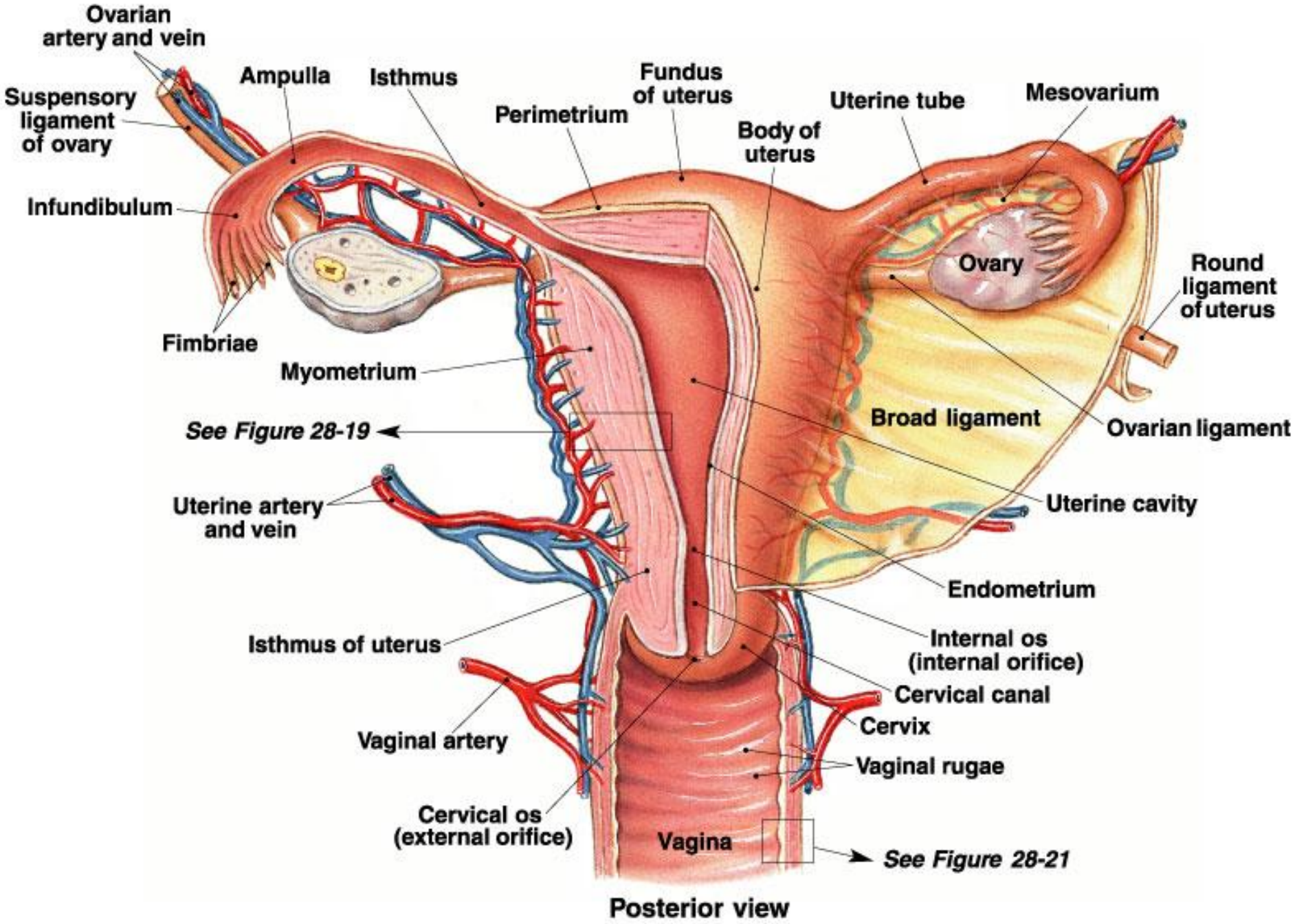
Female reproductive system

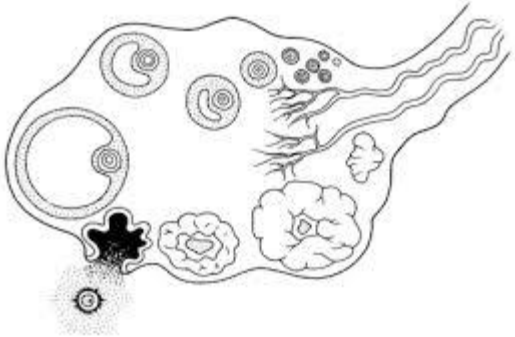


General outlook



The **female reproductive system** consists of the internal reproductive organs (the paired ovaries and oviducts, the uterus, and the vagina) and the external genitalia (the clitoris, the labia minora and the labia majora).


Ovarian artery and vein
Suspensory ligament of ovary
Ampulla
Isthmus
Fundus of uterus
Perimetrium
Body of uterus
Uterine tube
Mesovarium
Infundibulum
Ovary
Round ligament of uterus
Fimbriae
Myometrium
See Figure 28-19
Broad ligament
Ovarian ligament
Uterine artery and vein
Uterine cavity
Endometrium
Isthmus of uterus
Internal os (internal orifice)
Cervical canal
Cervix
Vaginal artery
Vaginal rugae
Cervical os (external orifice)
Vagina
See Figure 28-21
Posterior view



ovary

cortex

medulla

Stroma

Connective tissue framework

Ovarian follicles

Primordial follicles

Primary follicles

Secondary follicles

Graafian follicles

Corpus luteum

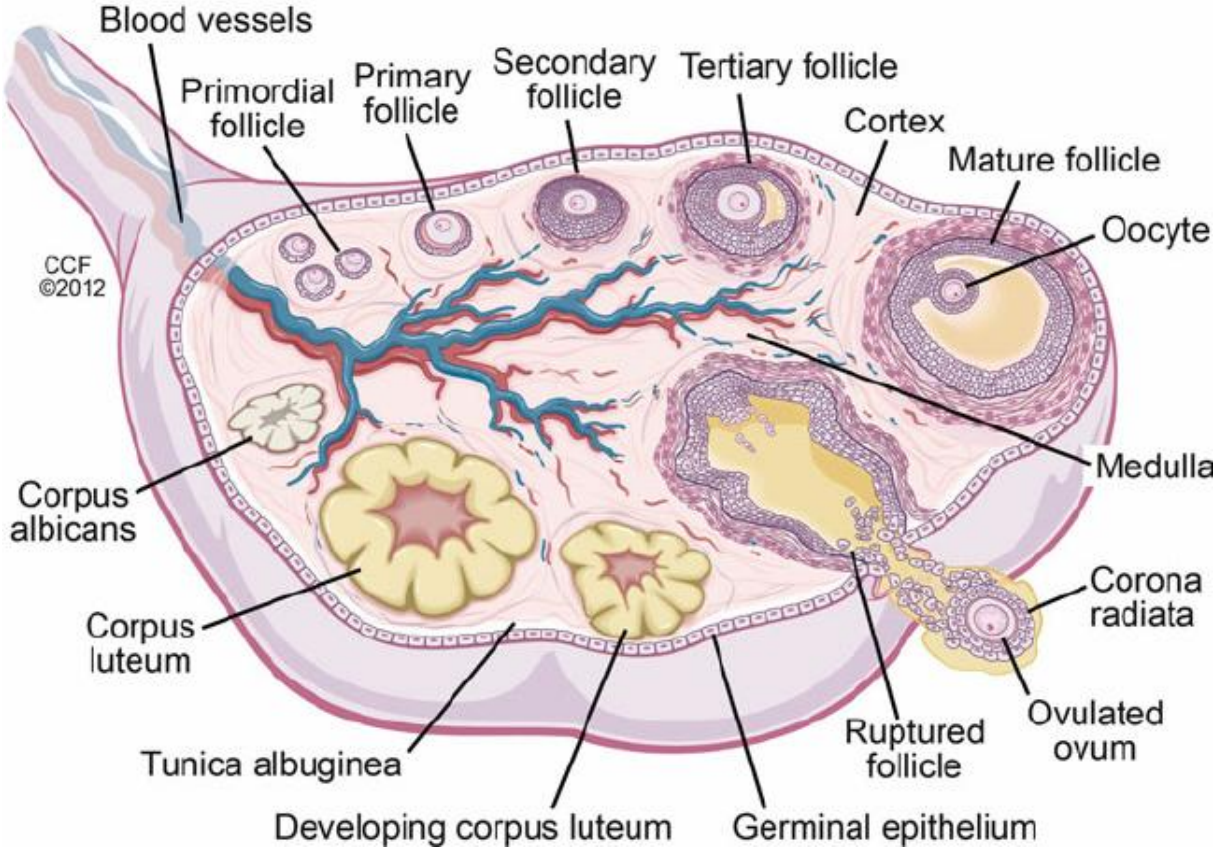
Corpus albicans

Large blood vessels

Lymph vessels

Nerve fibers

Ovary – schematic presentation of structure

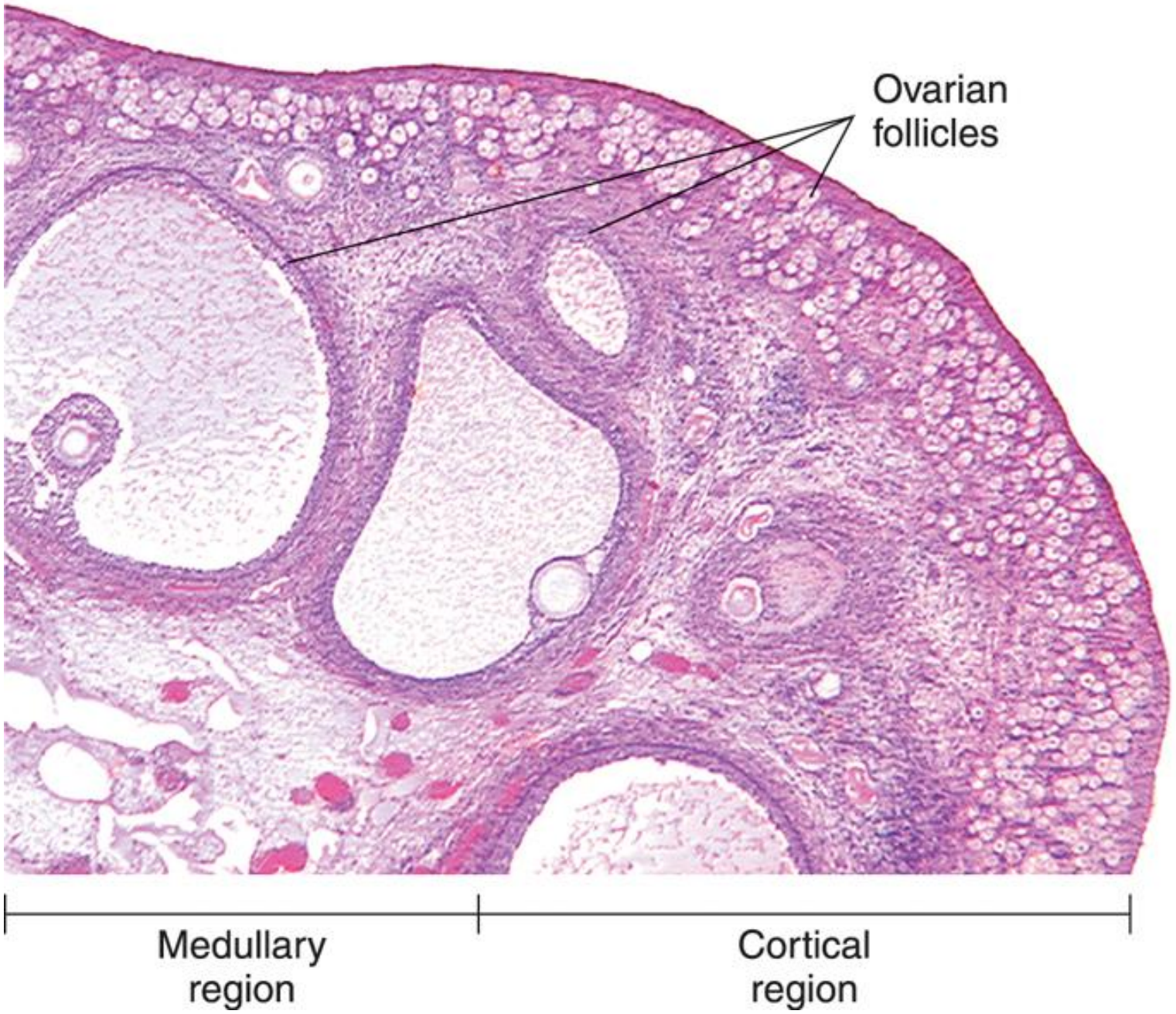


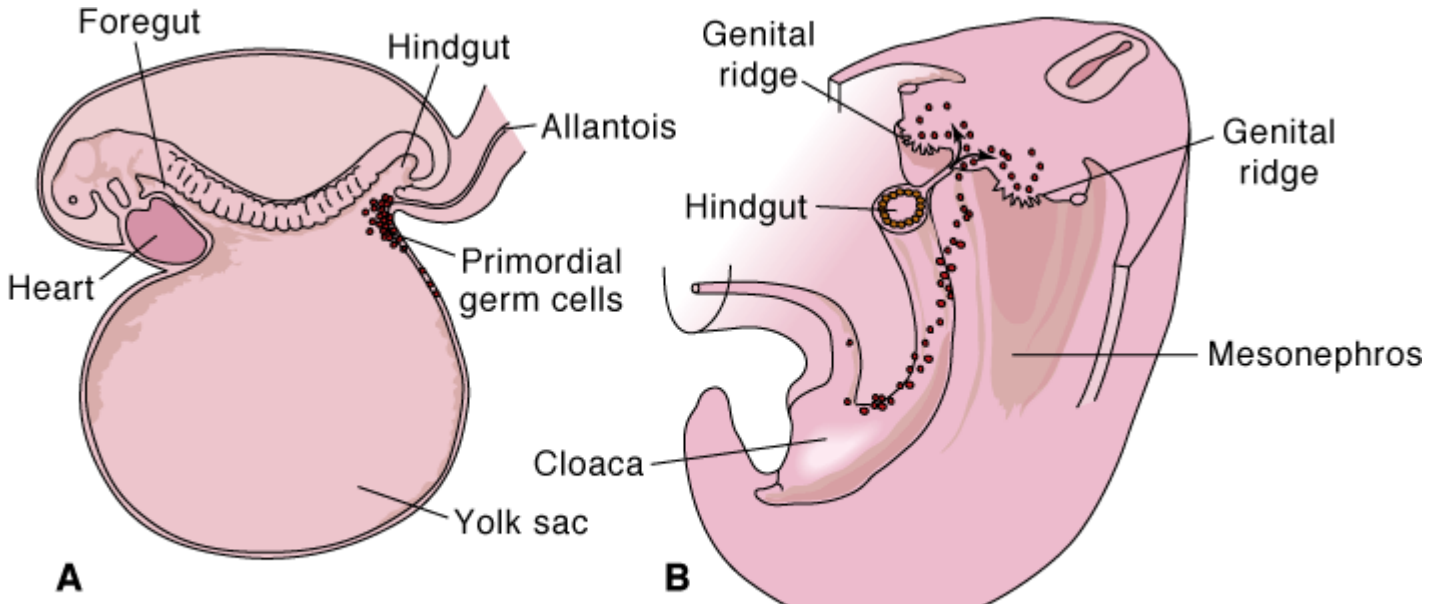
Tunica albuginea - dense irregular connective tissue. Each ovary is subdivided into cortex and medulla.

Germinal epithelium – simple squamous to cuboidal epithelium.

Cortex - connective tissue framework (stroma) and ovarian follicles.

Medulla – richly vascularized fibroelastic connective tissue, large blood vessels, lymph vessels, nerve fibers and 2 types of epithelioid cells – interstitial cells secreting estrogens (involute during 1 menstrual cycle) and hilus cells secreting androgens.


Ovarian follicles
Medullary region
Cortical region



Source: Gardner DG, Shoback D: *Greenspan's Basic & Clinical Endocrinology, 9th Edition:* www.accessmedicine.com
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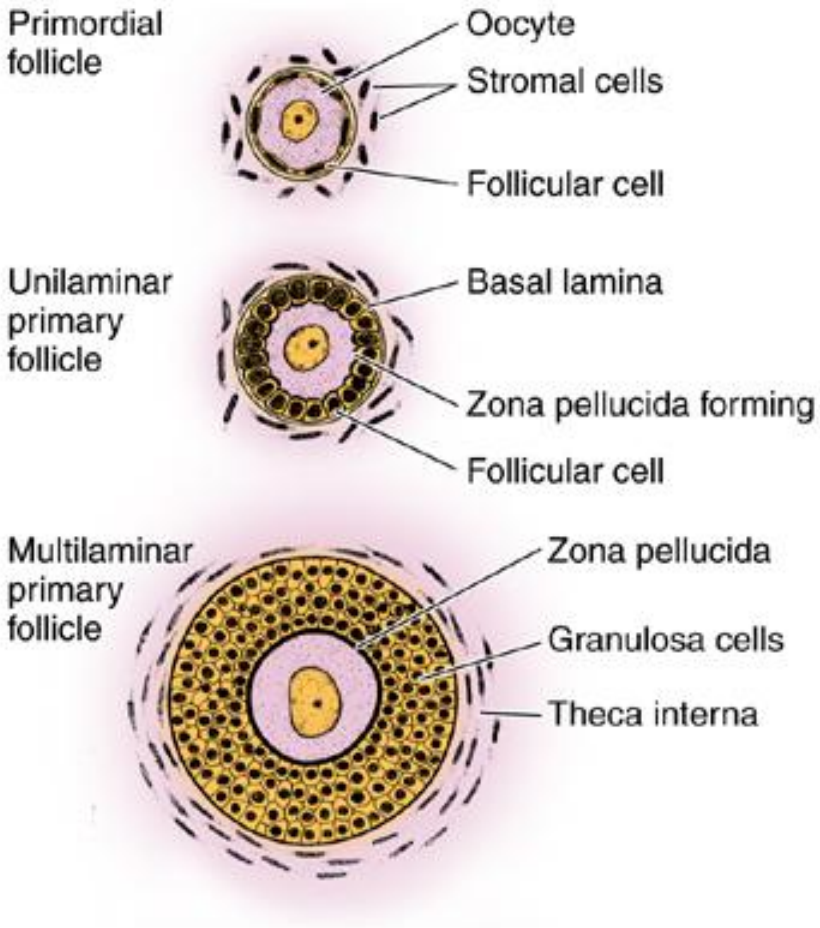
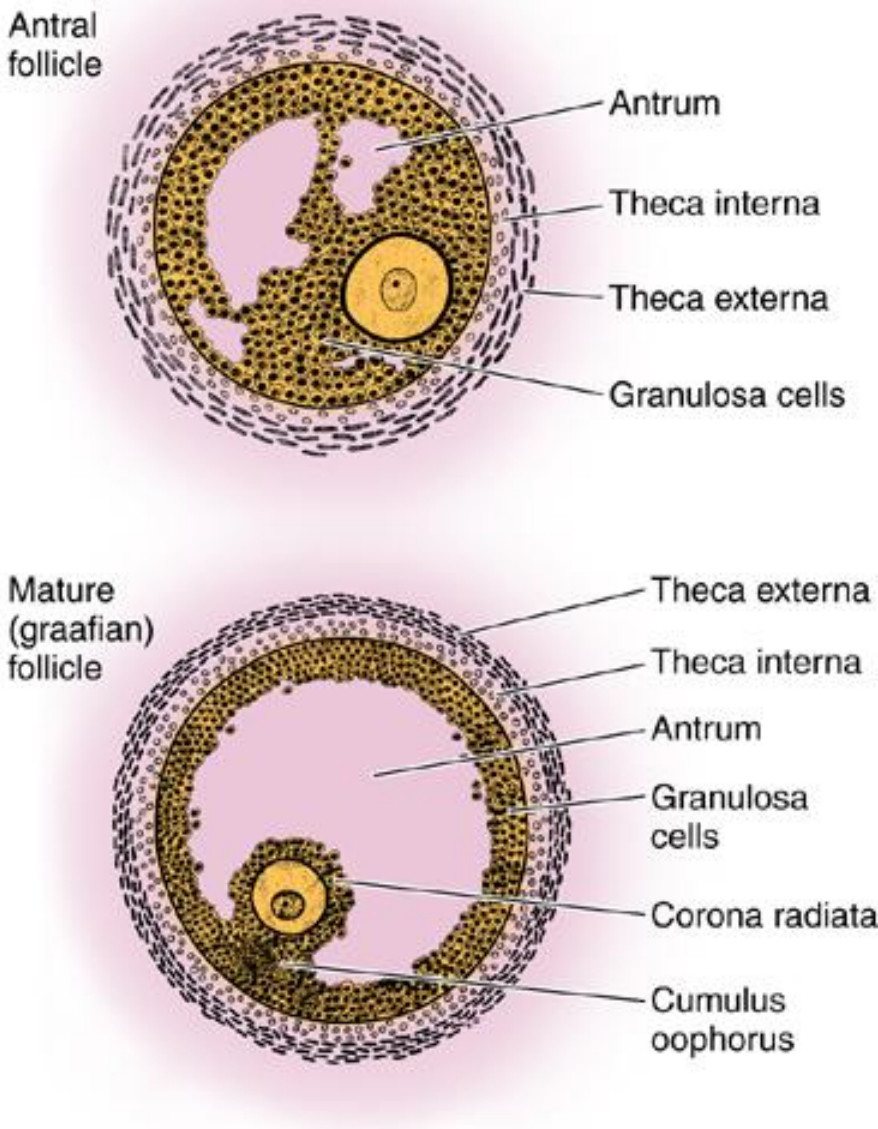
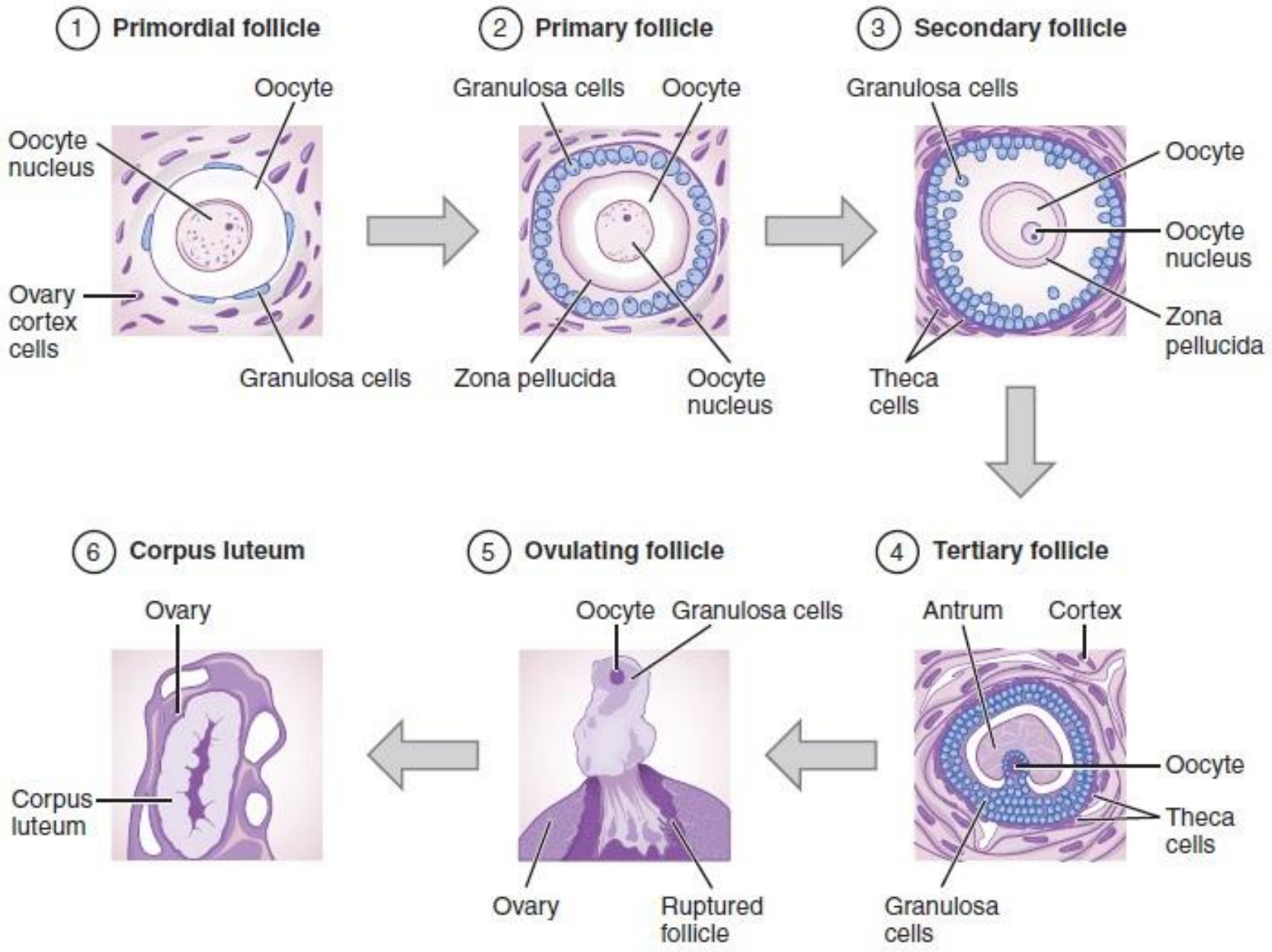
Primordial germ cells (**oogonia**) appear in the endodermal yolk sac at the end of first month of pregnancy. They populate the cortex of the future ovary and divide up to fifth month of pregnancy. Each ovary has about 5-7 million of oogonia. About 1 milion of them become surrounded by follicular cells and survive to the time of birth. The remaining undergo **atresia**.

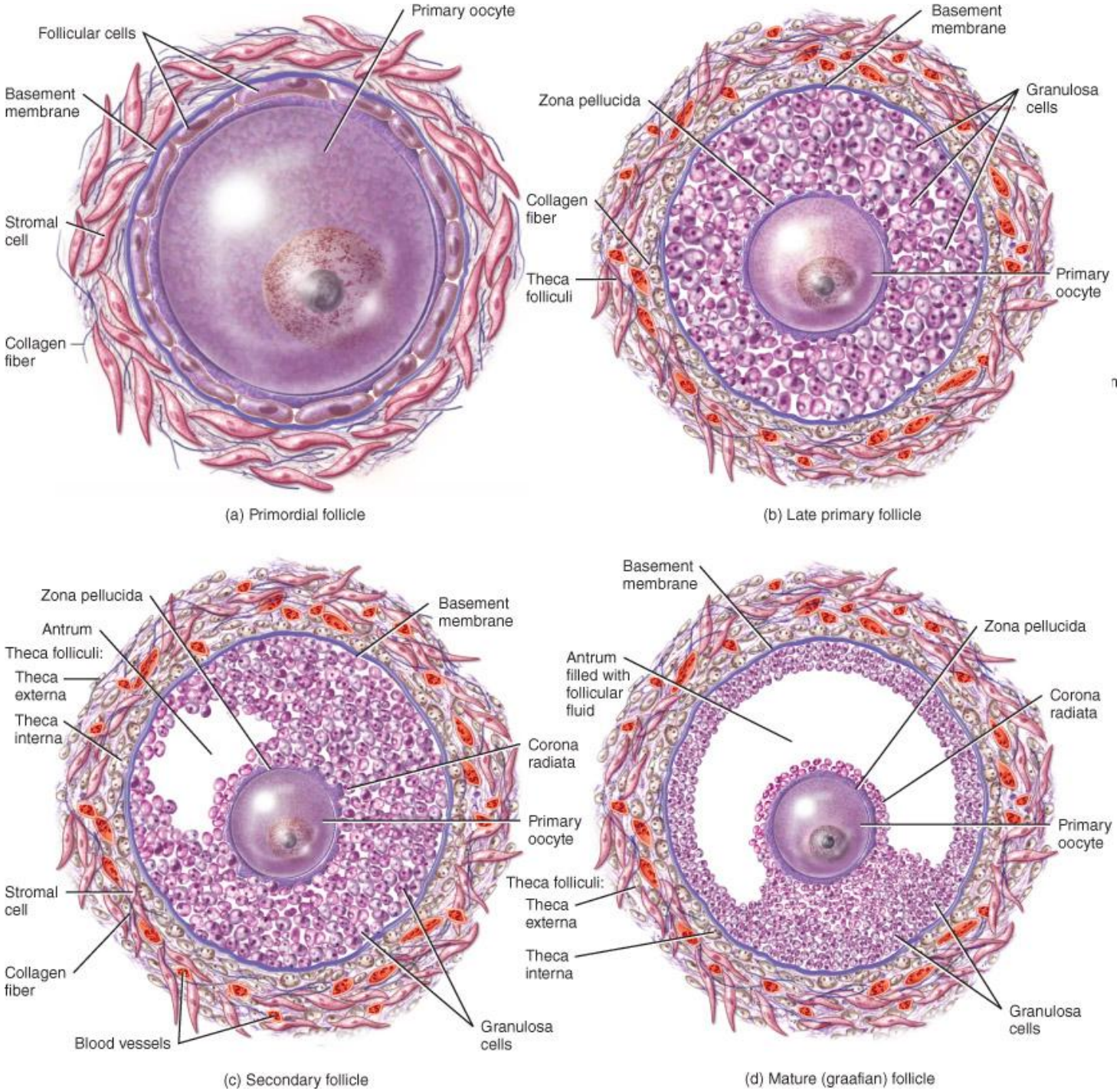
Types of ovarian follicles, from primordial to mature



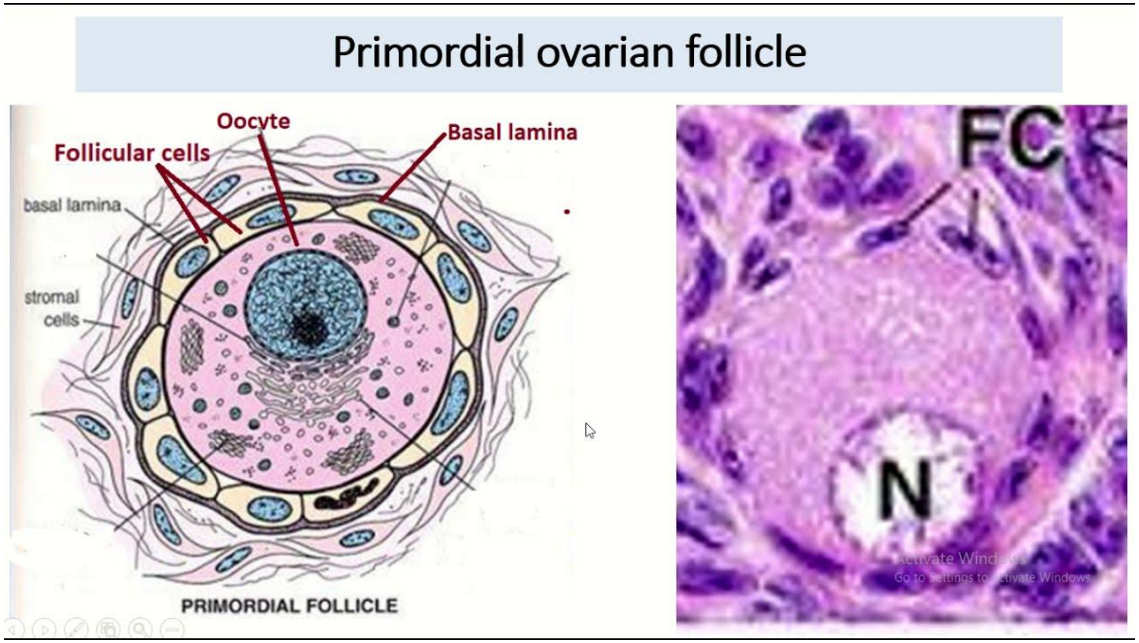


(a) Stages of Folliculogenesis



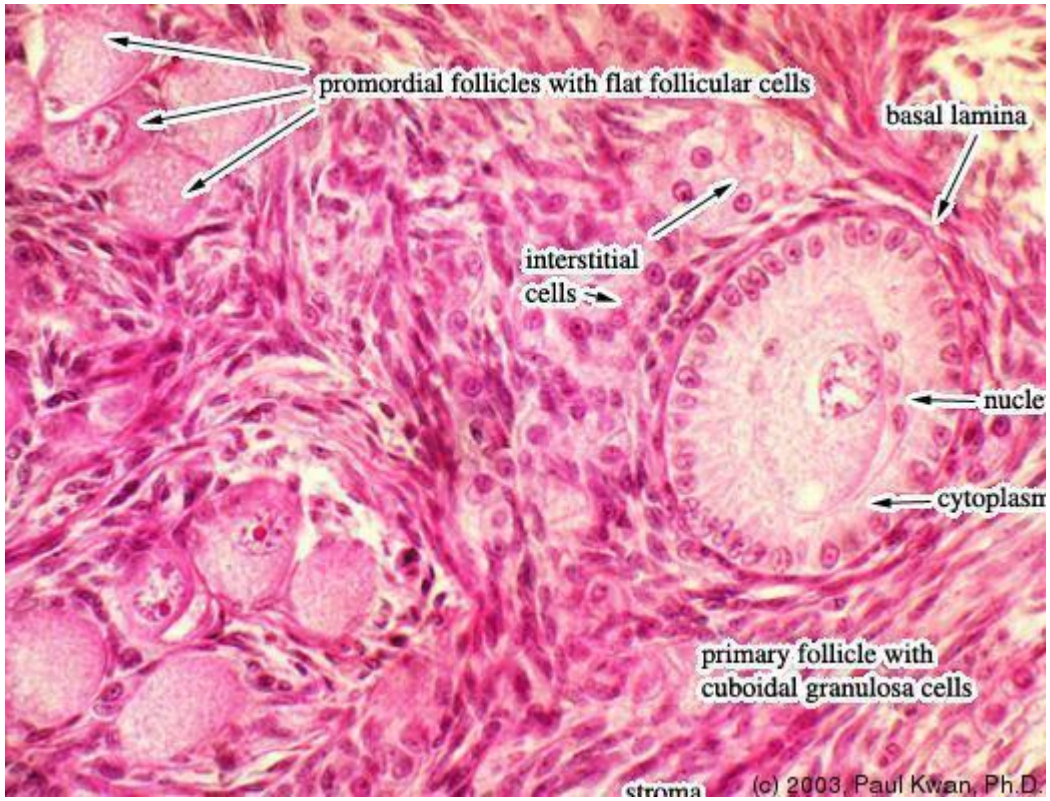

Follicular cells
Primary oocyte
Basement membrane
Stromal cell
Collagen fiber
(a) Primordial follicle
Basement membrane
Zona pellucida
Granulosa cells
Collagen fiber
Theca folliculi
Primary oocyte
(b) Late primary follicle
Zona pellucida
Basement membrane
Antrum
Theca folliculi:
Theca externa
Theca interna
Corona radiata
Primary oocyte
Stromal cell
Collagen fiber
Blood vessels
Granulosa cells
(c) Secondary follicle
Basement membrane
Zona pellucida
Antrum filled with follicular fluid
Corona radiata
Primary oocyte
Theca folliculi:
Theca externa
Theca interna
Granulosa cells
(d) Mature (graafian) follicle

Primordial follicles



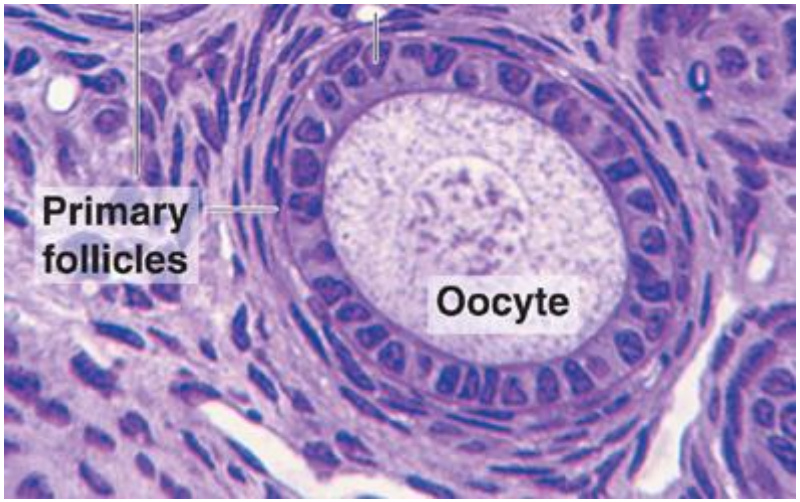
Primordial follicle is composed of primary oocyte (25 µm in diameter cell, arrested in **prophase stage of meiosis I-diplotene**)and flattened follicular cells joined by desmosomes. They are separated from stroma by a basal lamina.

Primordial follicles



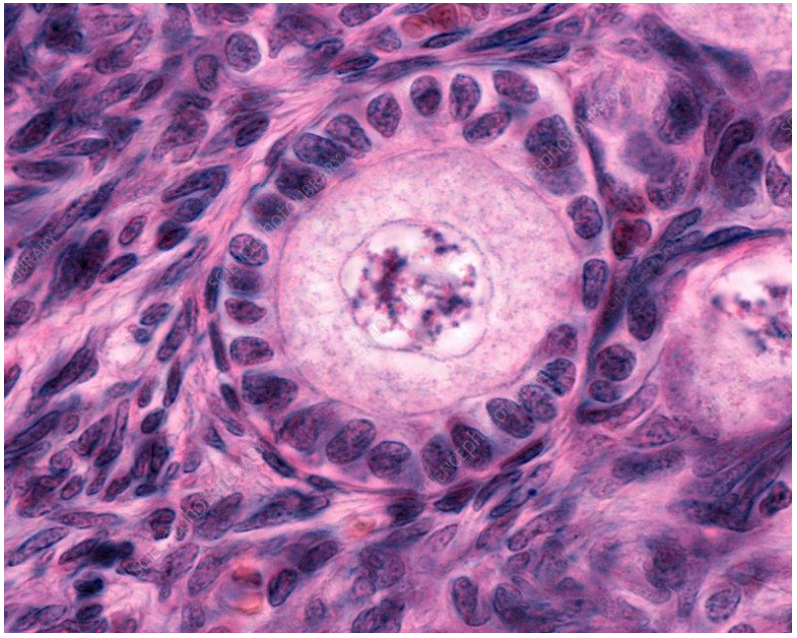
The pulsatile release of **GnRH** (**LHRH**) from the hypothalamus results in a similar, pulsatile (90 min), release of gonadotropins - follicle-stimulating hormone [**FSH**], and luteinizing hormone [**LH**] from the basophils of the anterior pituitary that culminates in the commencement of follicular development and the onset of the ovulatory cycle.

Unilaminar primary follicle

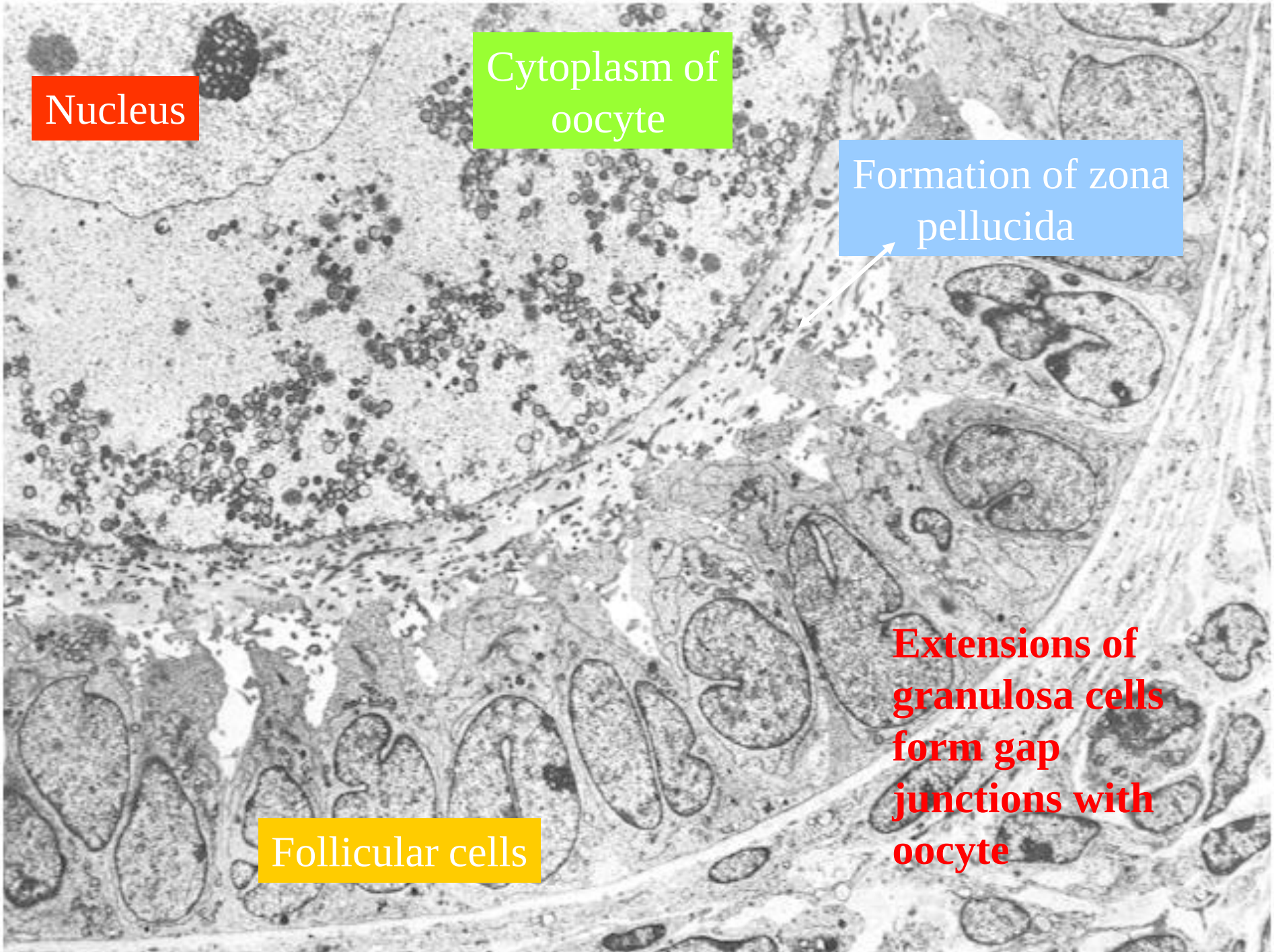


Primary oocyte grows 100-150 μm and possesses enlarged nucleus – germinal vesicle. Follicular cells became cuboidal.

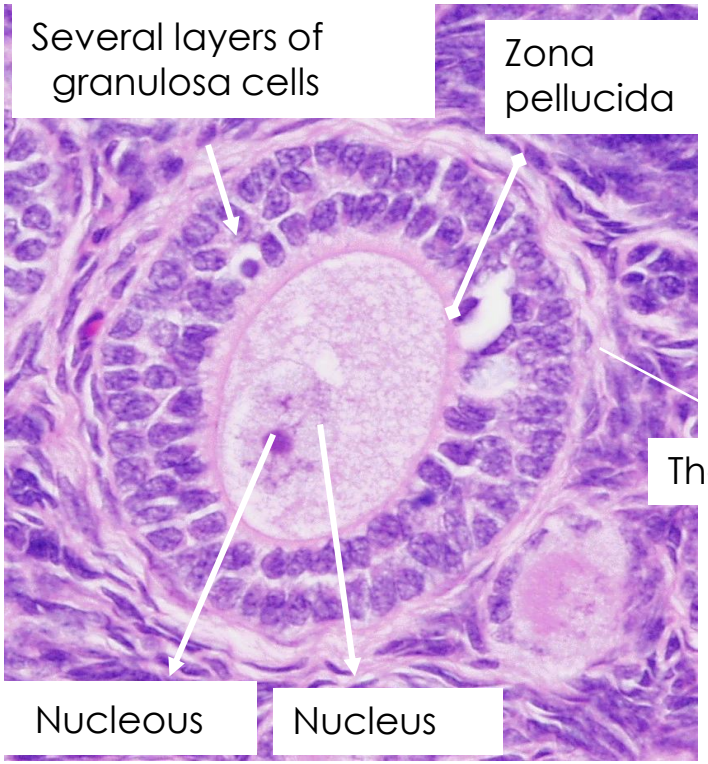
The **zona pellucida** – amorphous substance (4 glycoproteins - ZP1, ZP2, ZP3 and ZP4) produced by the oocyte appears. It separates the oocyte from follicular cells. Filopodia of follicular cells form gap junctions with the oocyte.



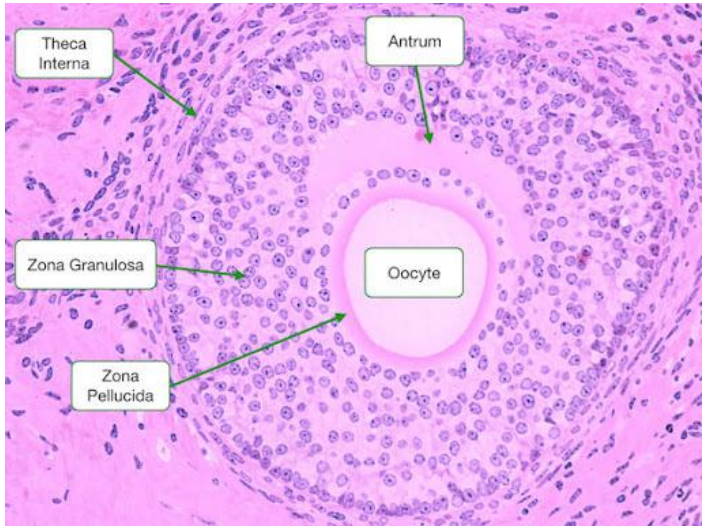
The development of primary follicles is **independent on FSH**, but the proliferation and differentiation of follicular cells depends on local factors produced in ovary.


Nucleus
Cytoplasm of oocyte
Formation of zona pellucida
Extensions of granulosa cells form gap junctions with oocyte
Follicular cells

Multilaminar primary follicle



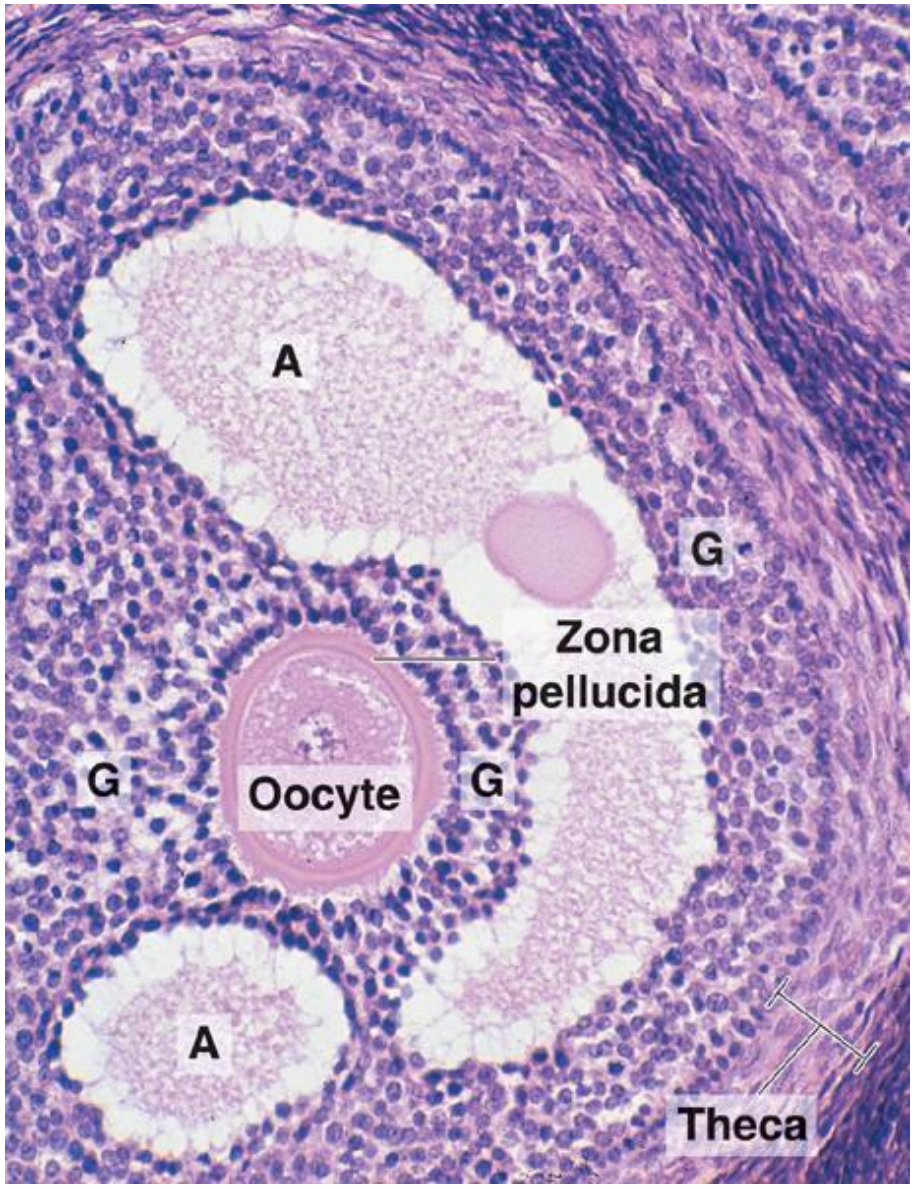
Follicular cells proliferate and stratify, and they are now called **granulosa cells**. The proliferative activity of these cells is stimulated by **activin** produced by the oocyte. **Stromal cells** form an **inner theca interna** and **outer theca externa** around this type of follicle.



Theca interna - richly vascularized cellular layer surrounded by basal lamina. The cells of theca interna possess LH receptors and produce male sex hormone – androstenedione, which enters the granulsa cells and is converted by aromatase into estradiol.

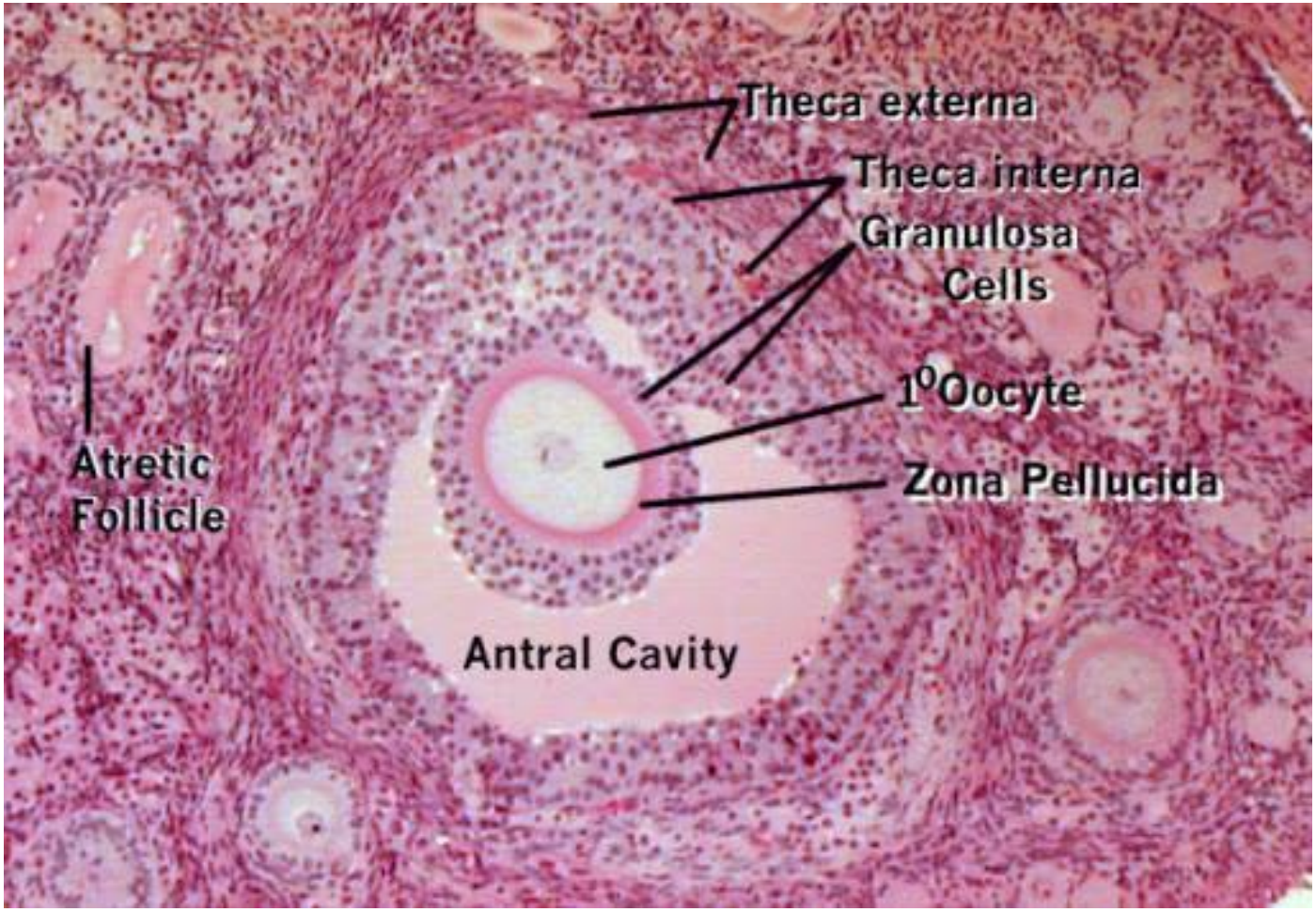
Theca externa – composed of fibrous connective tissue.

Secondary (antral) follicle



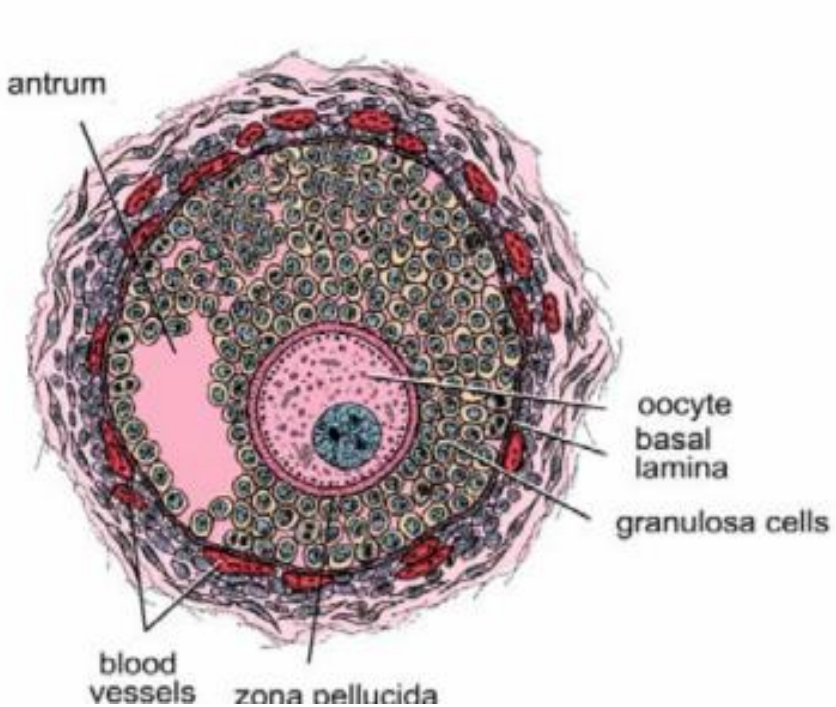
Several spaces develop between granulosa cells and become filled with liquor folliculi - exudate of plasma, containing GAGs, PGs and steroid-binding proteins produced by granulosa cells. This fluid contains also progesterone, estradiol, inhibin, follistatin and activin, which regulate release of FSH. FSH and estrogens induce the granulosa cells to produce LH receptors. **The droplets of fluid coalesce and form the antrum**.

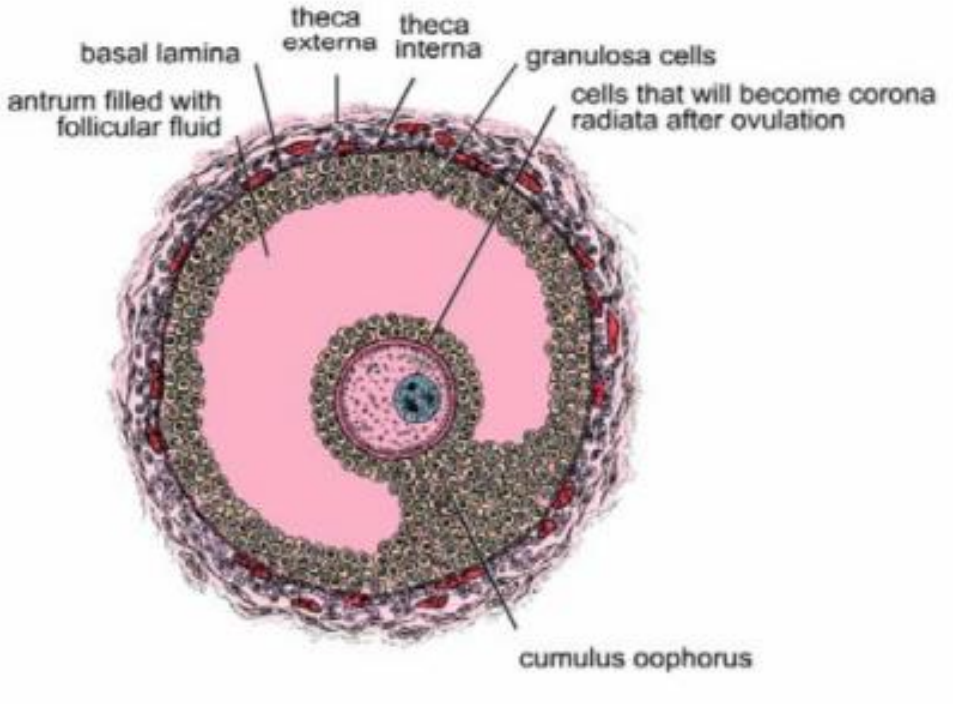
Secondary (antral) follicle



The primary oocyte is surrounded by small group of granulosa cells – **cumulus oophorus**. The single layer of these cells that directly surrounds the oocyte – **corona radiata**.

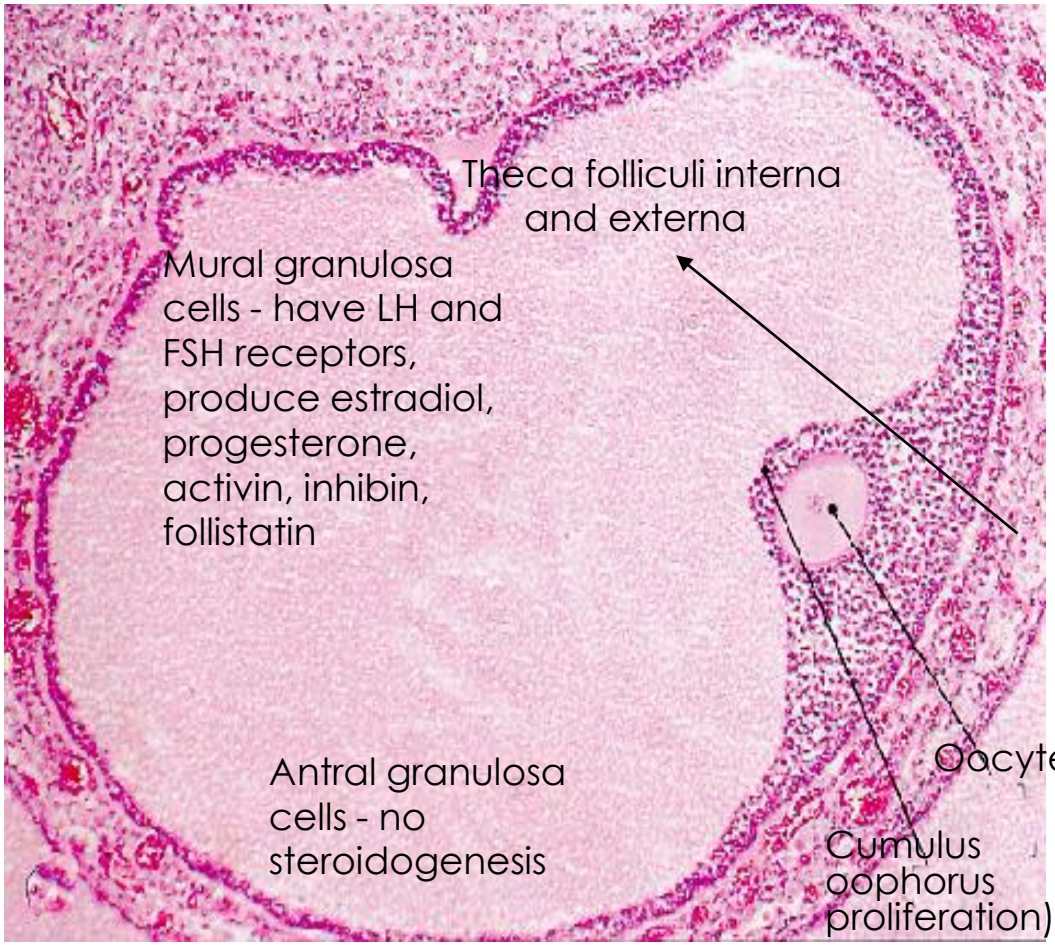
SECONDARY FOLLICLES



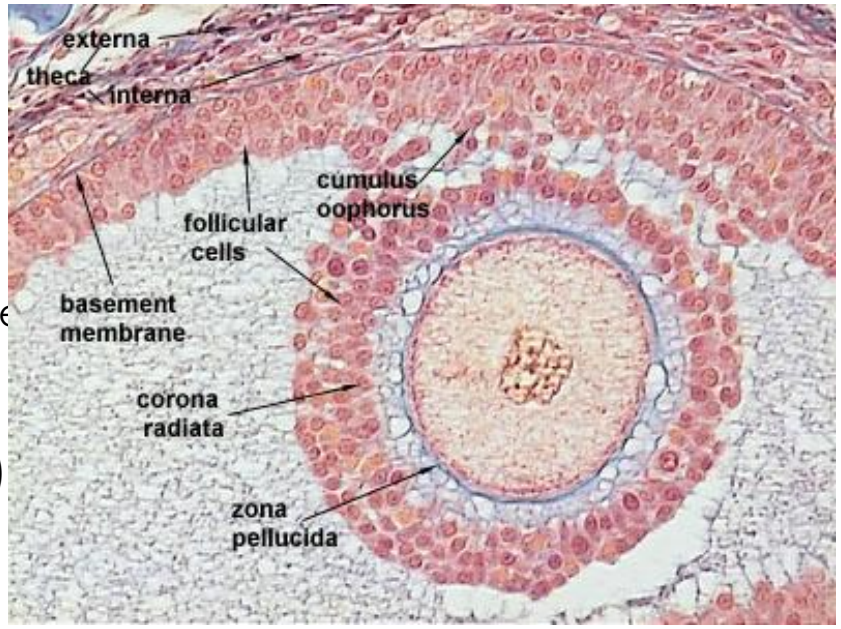


Two types of granulosa cells – **membrana granulosa** and **cumulus oophorus** cells.

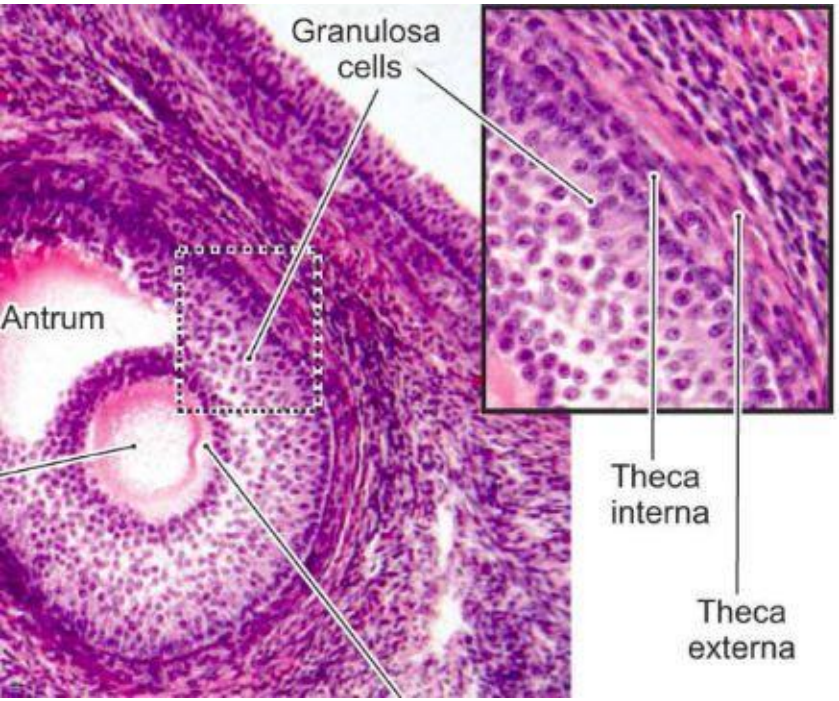
Mature (graafian) follicle

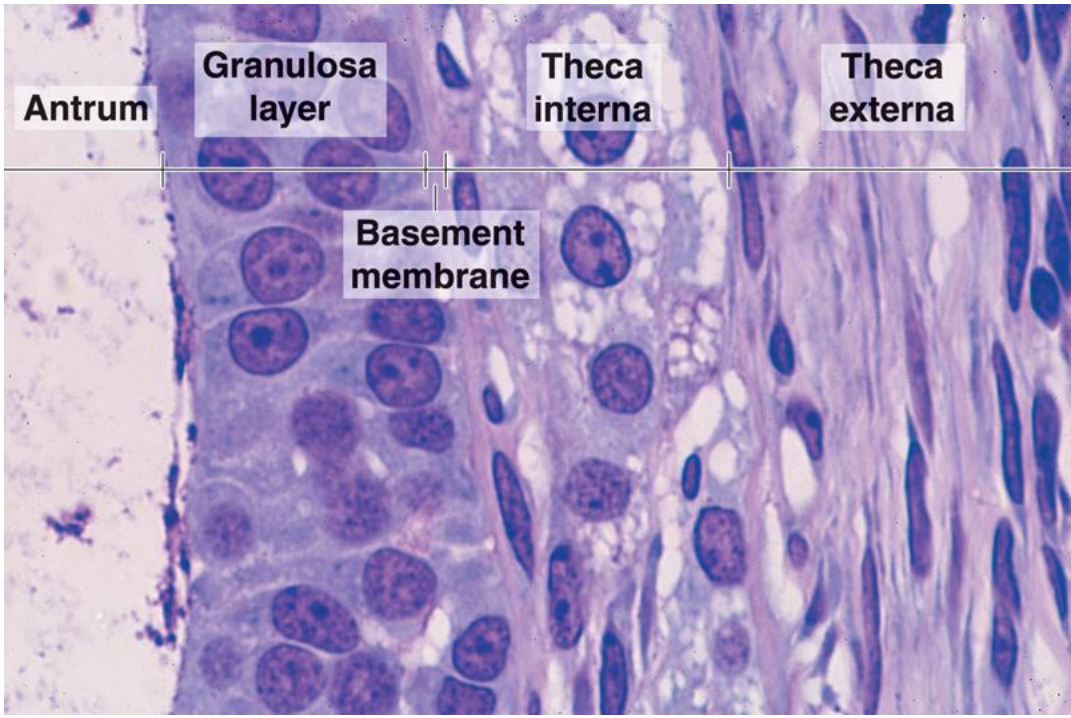


Proliferation of the granulosa cells and formation of liquor folliculi result in the formation of a Graafian follicle.



THECA FOLLICULI

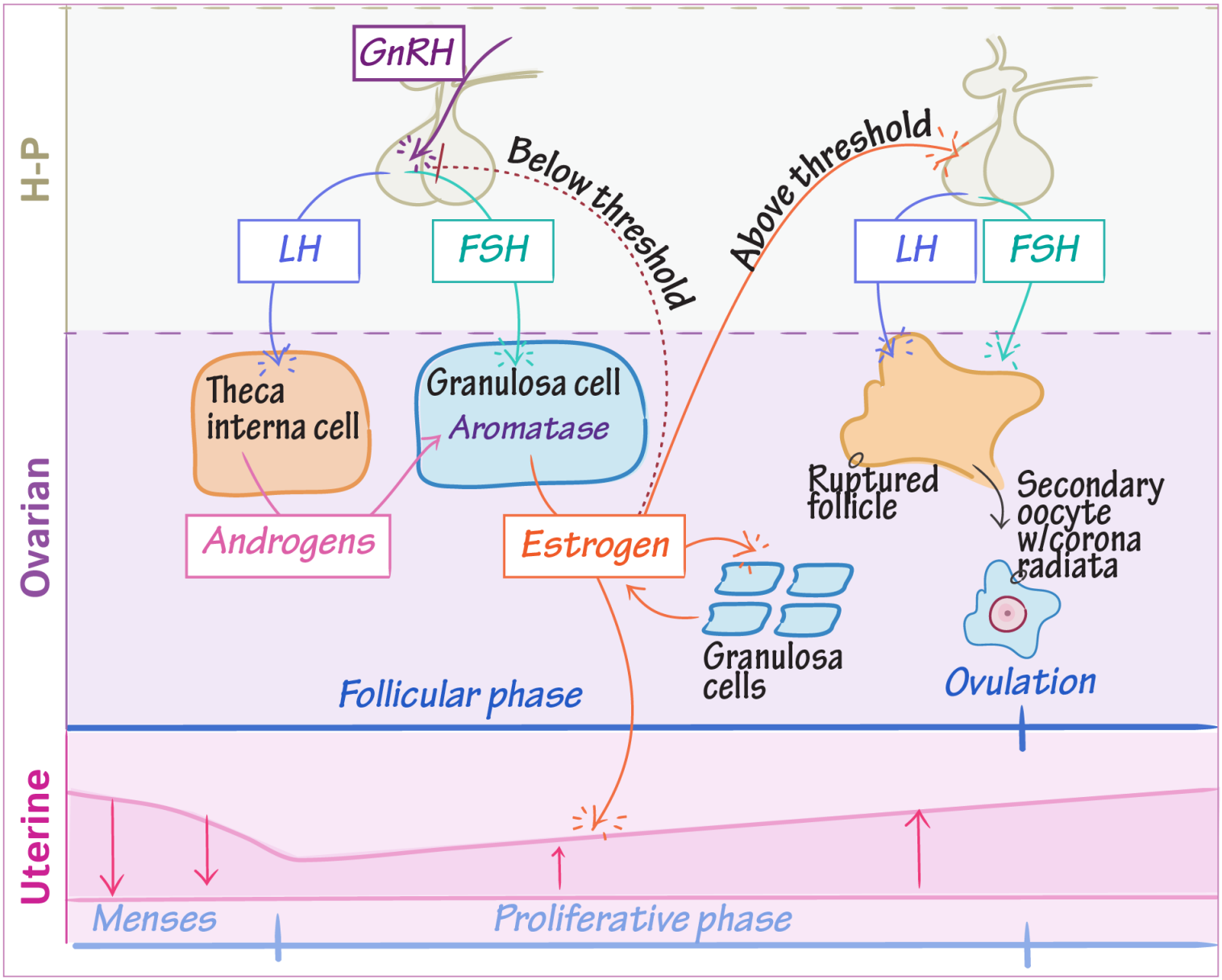


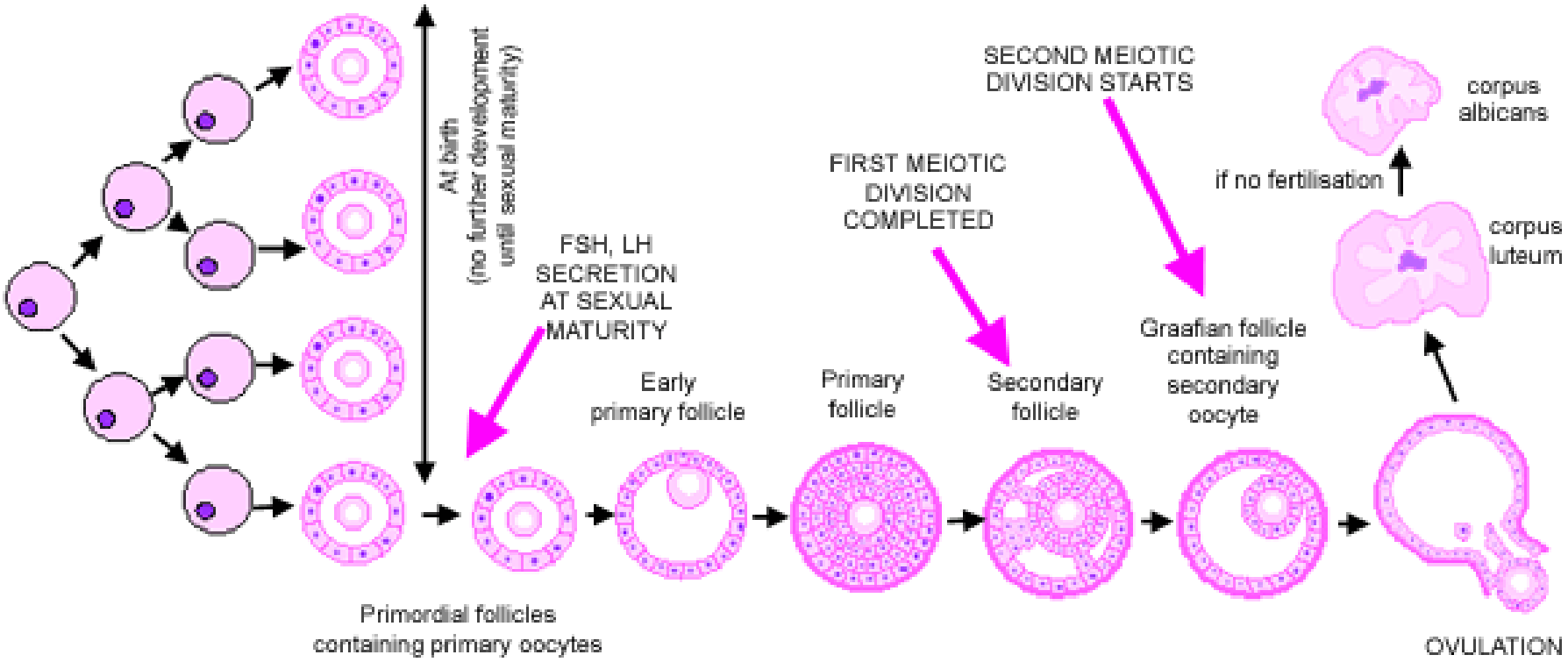


Theca folliculi interna participate in hormone production and its blood vessels nourish avascular granulosa cells.

Theca folliculi externa offers mechanical support to maturing follicles.

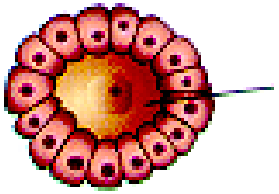
Menses to Ovulation



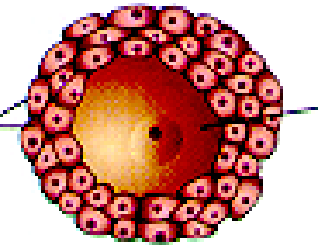


Estrogen produced by the **graafian follicle and secondary follicles** causes elevation of blood **estrogen** to levels high enough to shut off of **FSH** release and a surge in **LH** release. The high blood levels of **LH** causes the completion of the first meiotic division resulting in the formation of the secondary oocyte and the first polar body. The secondary oocyte is arrested in the metaphase stage of meiosis II and is released from the graafian follicle during ovulation with cumulus oophorus.

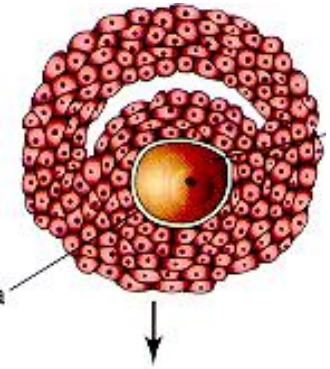
Meiotic divisions of ova



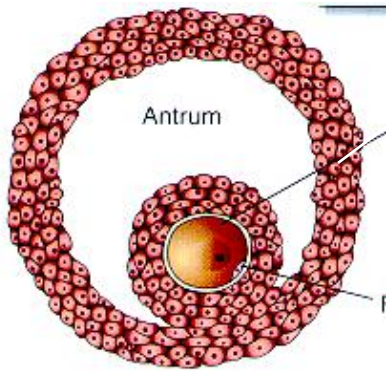
Unilaminar primary follicle - oocyte – 46, XX arrested in prophase of meiosis I



Multilaminar primary follicle – oocyte – 46, XX



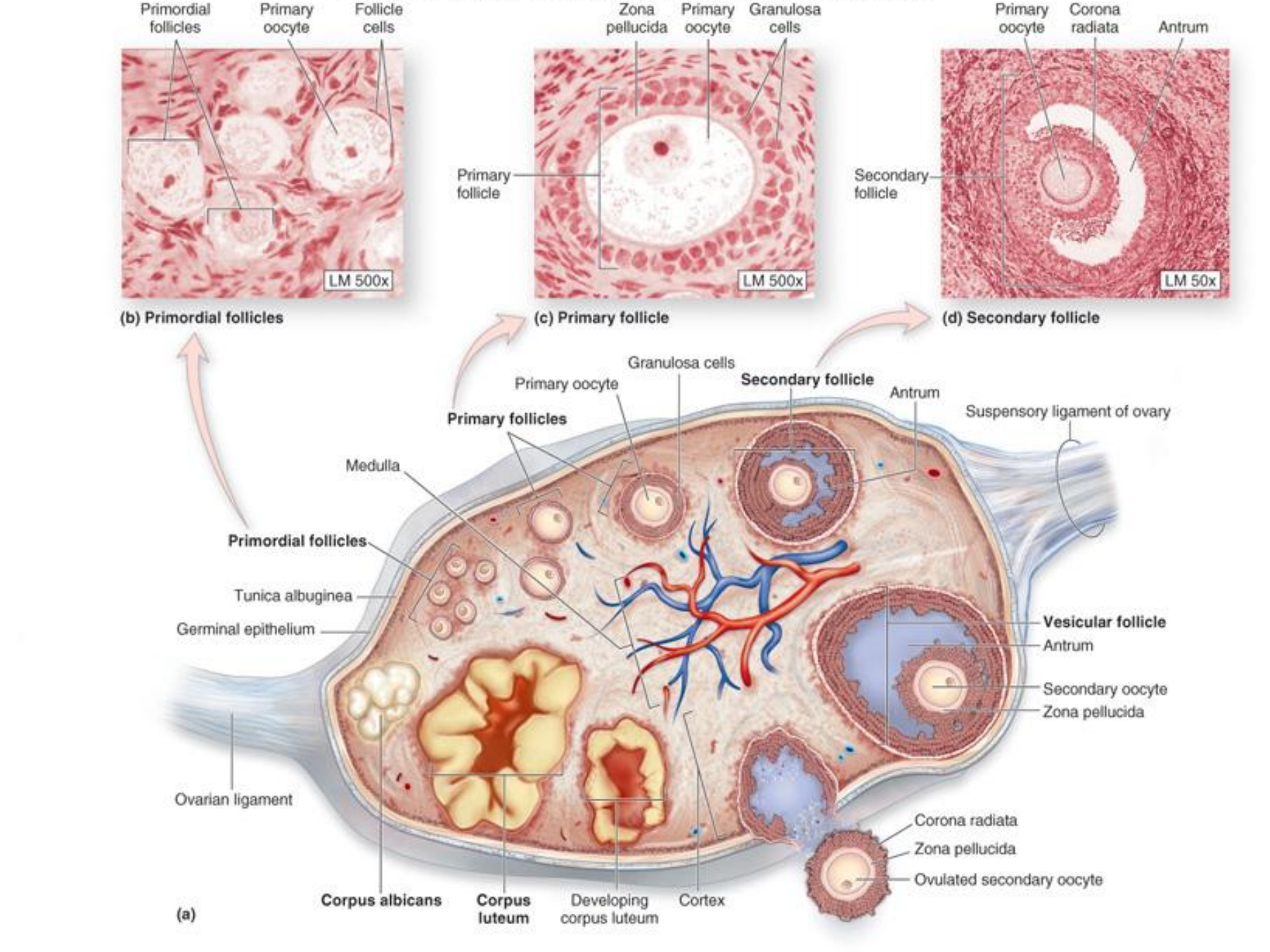
Secondary (antral) follicle oocyte – 46, XX



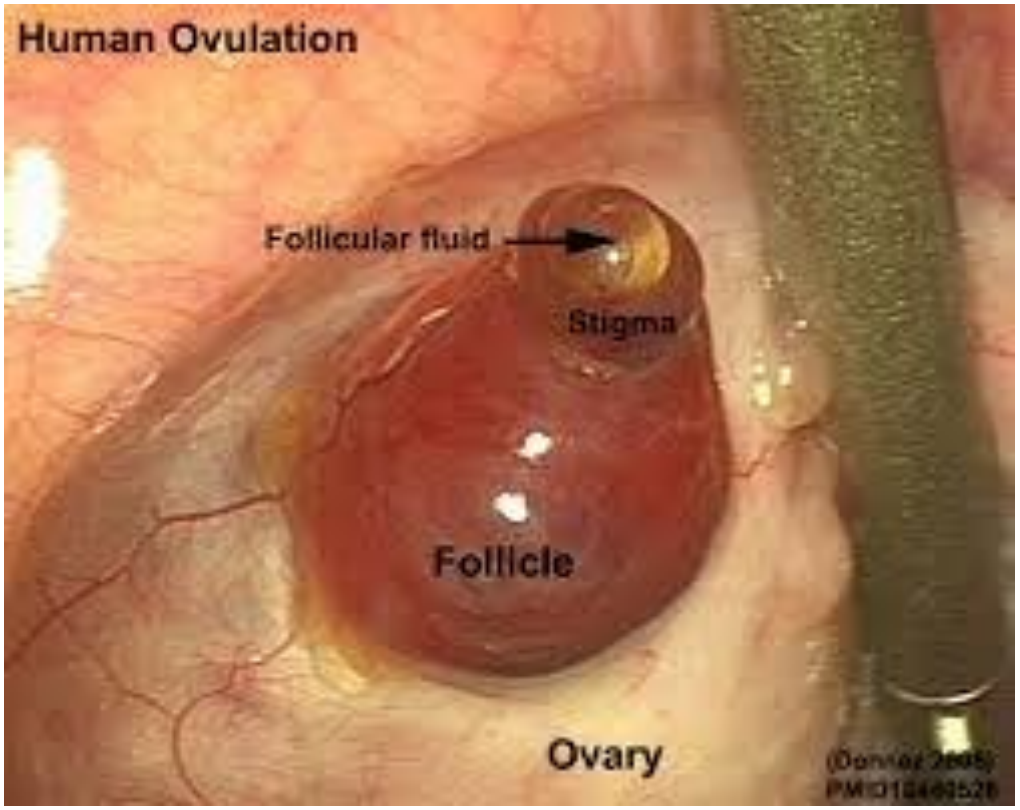
First polar body

Graafian (mature) follicle - secondary oocyte 23, X.

Under the influence of **meiosis-inducing factor** primary oocyte completes the I meiotc division – secondary oocyte and first polar body. Soon before ovulation secondary oocyte enters second meiotic division and halts it in metaphase. (**Division is completed after fertilization**.)Just before the ovulation oocyte with cumulus oophorus cells is detached from its base and floats freely.


Primordial follicles
Primary oocyte
Follicle cells
LM 500x
(b) Primordial follicles
Zona pellucida
Primary oocyte
Granulosa cells
Primary follicle
LM 500x
(c) Primary follicle
Primary oocyte
Corona radiata
Antrum
Secondary follicle
LM 50x
(d) Secondary follicle
Granulosa cells
Primary oocyte
Secondary follicle
Antrum
Suspensory ligament of ovary
Primary follicles
Medulla
Primordial follicles
Tunica albuginea
Germinal epithelium
Vesicular follicle
Antrum
Secondary oocyte
Zona pellucida
Ovarian ligament
Corona radiata
Zona pellucida
Ovulated secondary oocyte
Corpus albicans
Corpus luteum
Developing corpus luteum
Cortex
(a)

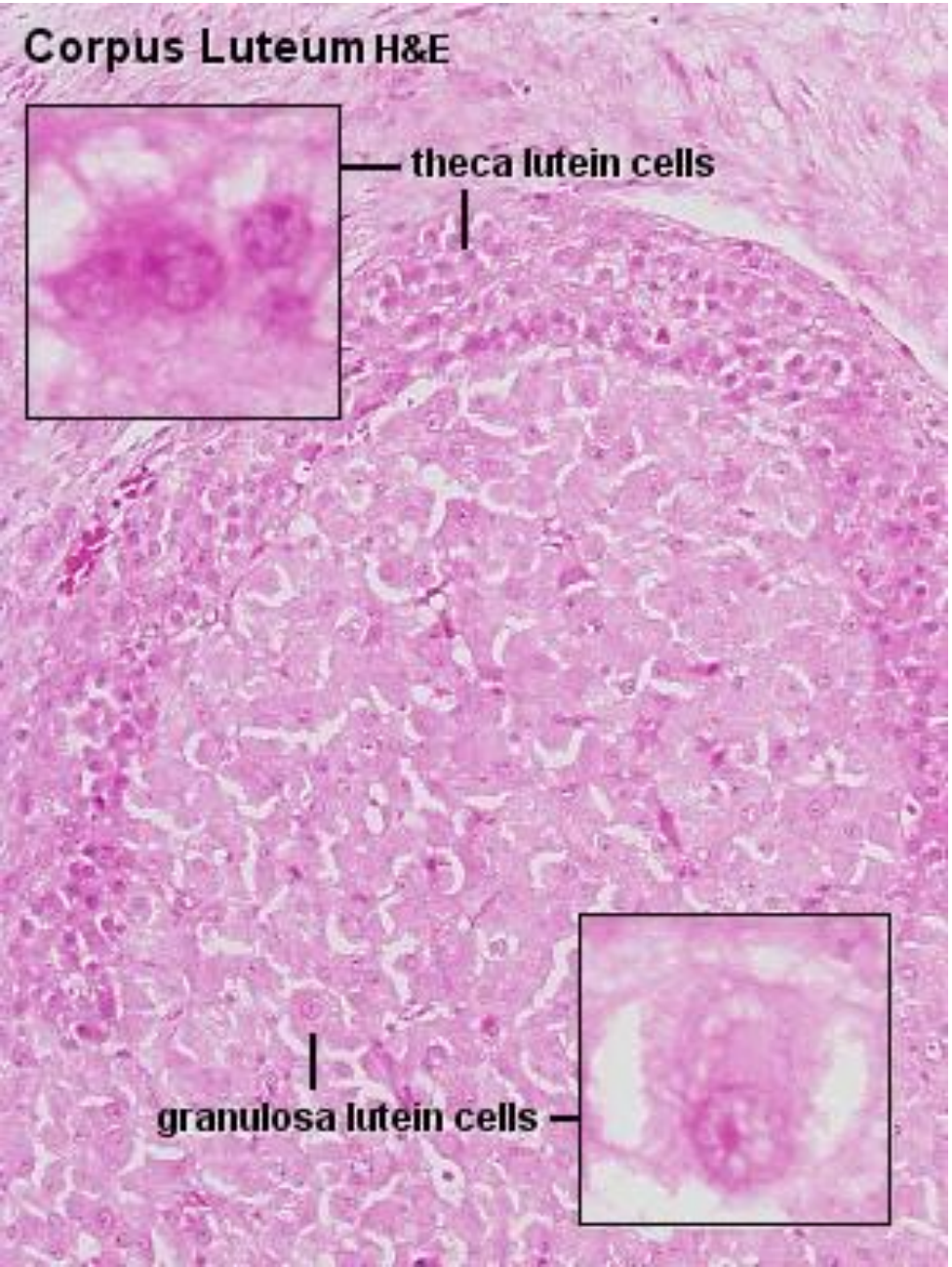
OVULATION



The PGs and HA formed by granulosa cells attract water. The surface of ovary above follicle loses its blood supply (stigma), degenerates and causes opening between the peritoneal cavity and the antrum. The oocyte with surrounding granulosa cells and liquor is released.

The remnants of the Graafian follicle are converted into corpus hemorrhagicum and then in corpus luteum.

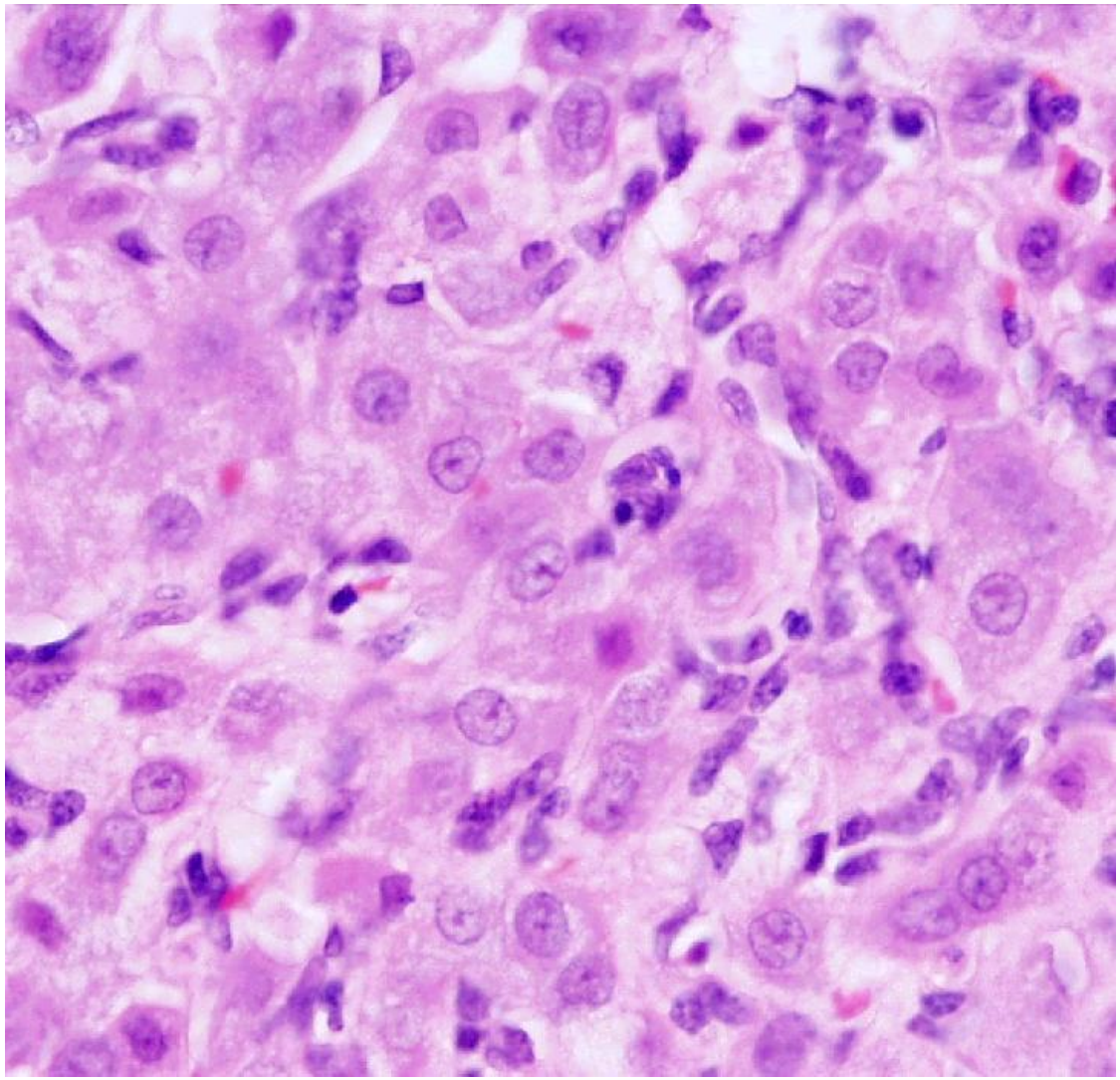
Corpus luteum of menstruation



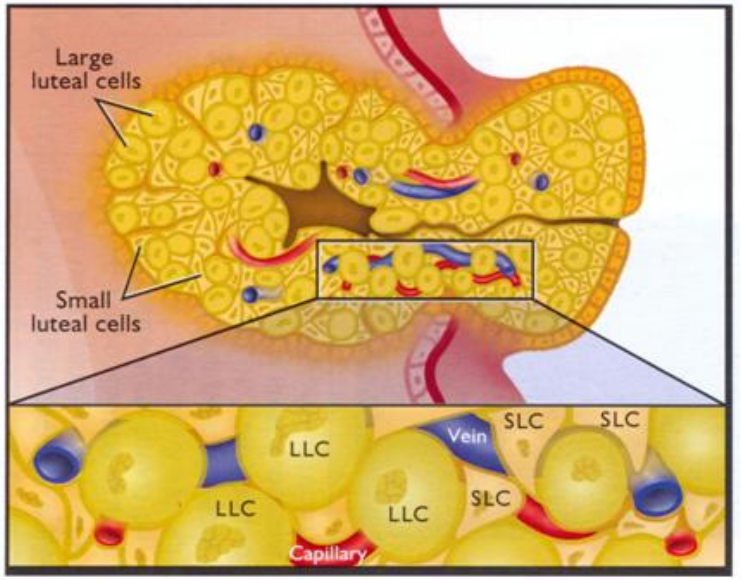
The remnants of follicle collapse and become folded, ruptured blood vessels leak blood into follicular cavity, forming a central clot – **corpus hemorrhagicum**. The phagocytes remove the clot and under influence of LH c.h. is transformed into corpus luteum, which functions as a temporary endocrine gland.

It is composed of 2 types of cells: **granulosa-lutein cells** (modified granulosa cells) and **theca lutein cells** (modified theca interna cells).

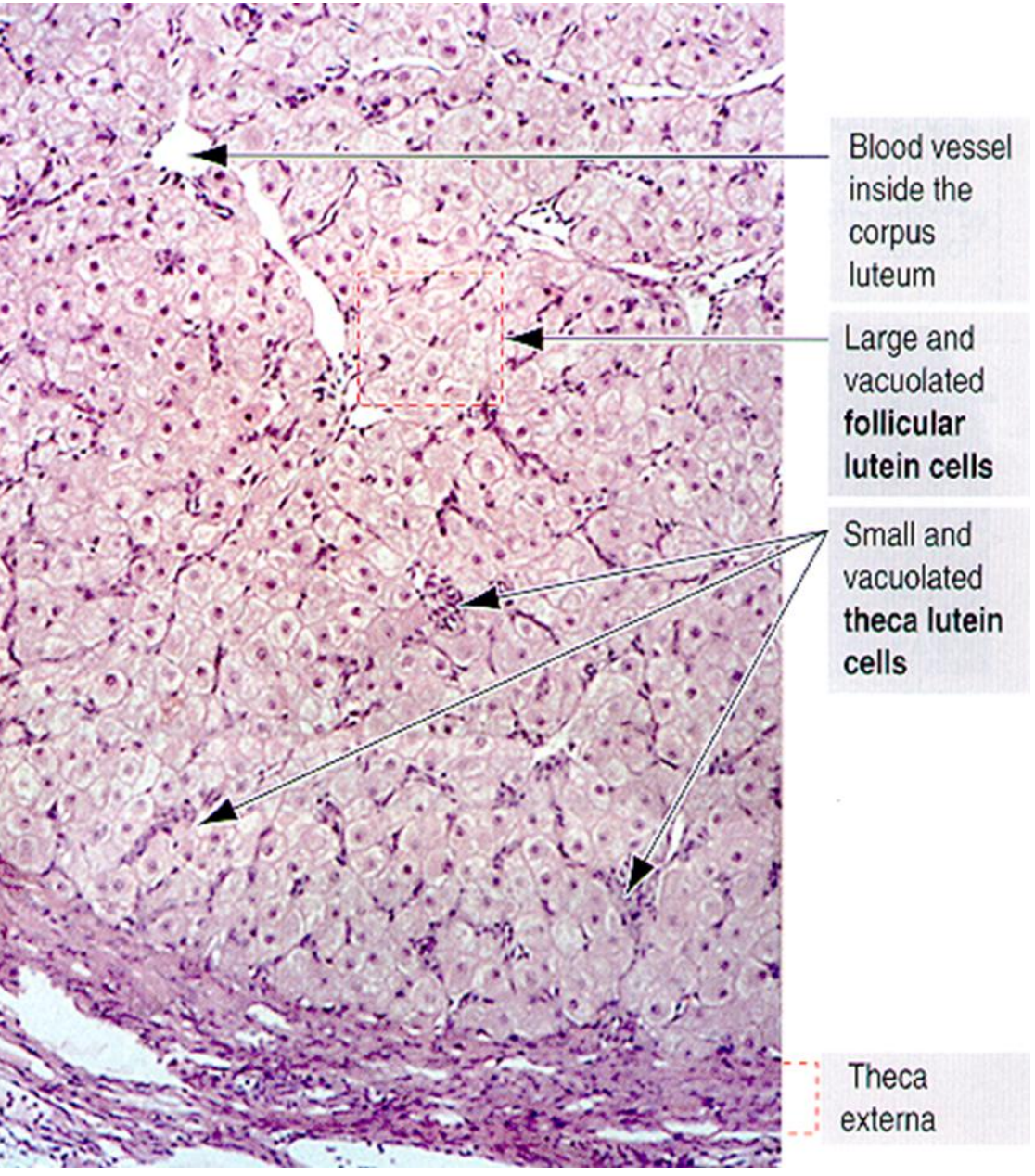
Granulosa - lutein cells



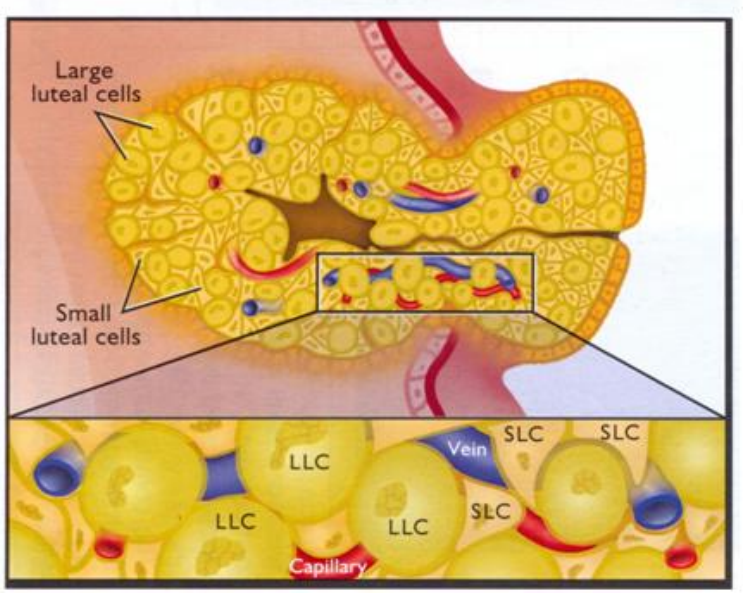
Granulosa cells (account 80% of the cell population) increase in size and transform into **granulosa-lutein cells**.
These cells produce **progesterone** and convert androgens produced by theca-lutein cells into **estrogens**.



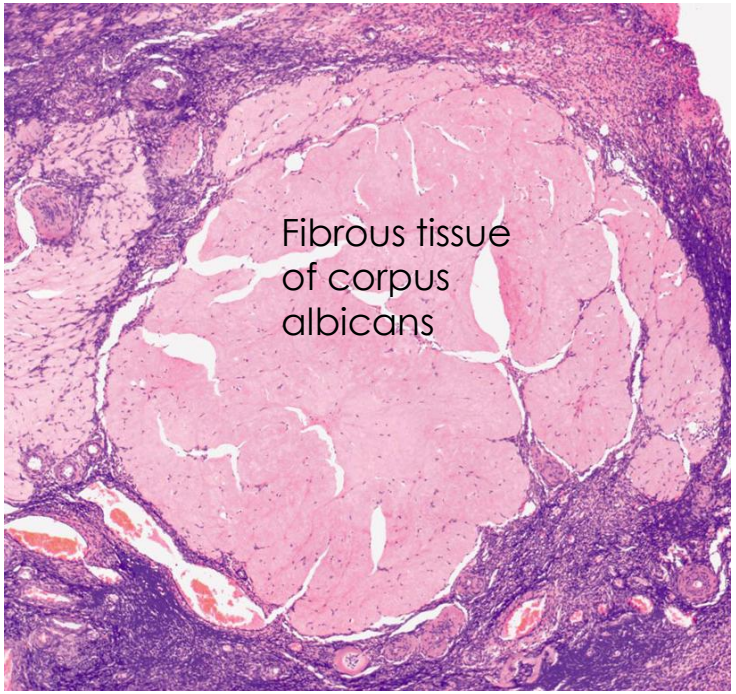
Theca and granulosa lutein cells CORPUS LUTEUM (slide no. 94)



Theca-lutein cells (derived from the **theca interna**) account 20% of the cell population. They produce **progesterone**, some estrogens and androgens.



Degeneration of corpus luteum

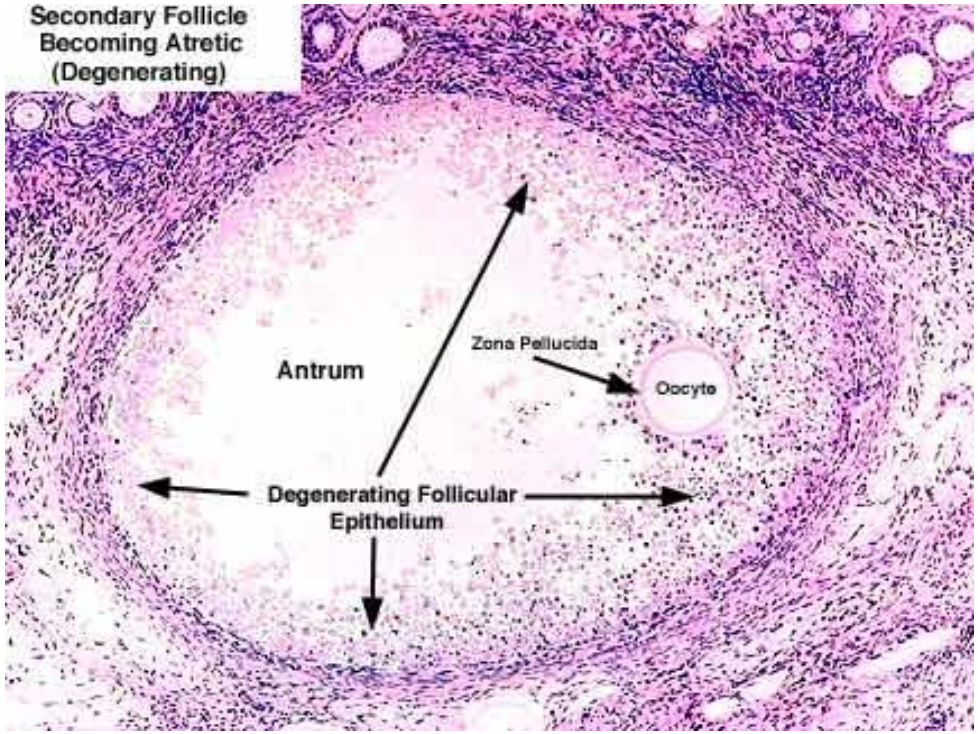


Progesterone and **estrogens** inhibit the secretion of **LH** and **FSH**. The absence of FSH prevents the development of new follicles. If pregnancy does not occur, the absence of LH leads to degeneration of the corpus luteum – **corpus luteum of menstruation**..

The fibrous connective tissue is called – **corpus albicans** and later is undergoes autolysis and are phagocytosed by macrophages.
The remnants – scar on the surface of ovary.

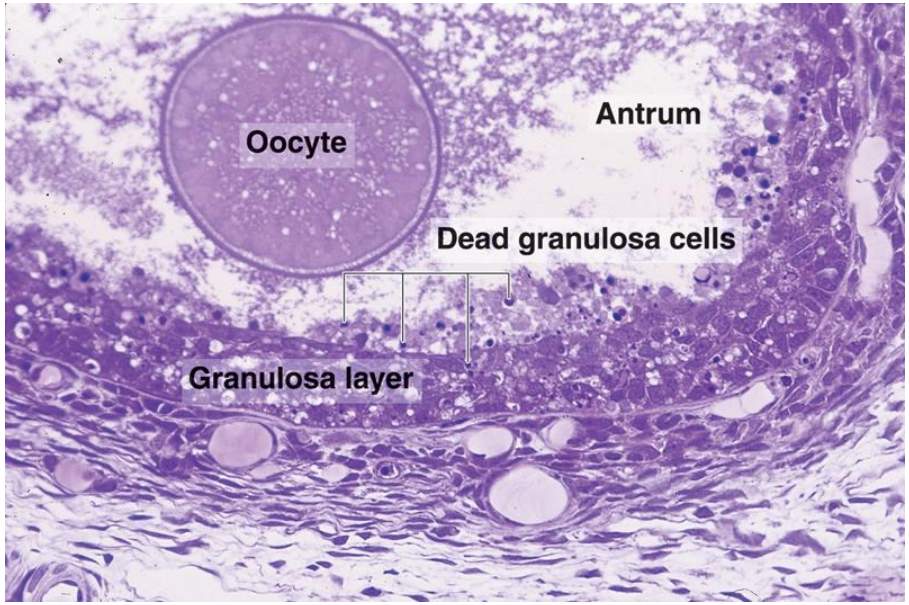
If preganacy occurs human chorionic gonadotropin (placenta) maintains the corpus luteum for 3 months– **corpus luteum of pregnancy**.
Later the corpus luteum (both types) is invaded by fibroblasts, becomes fibrotic.

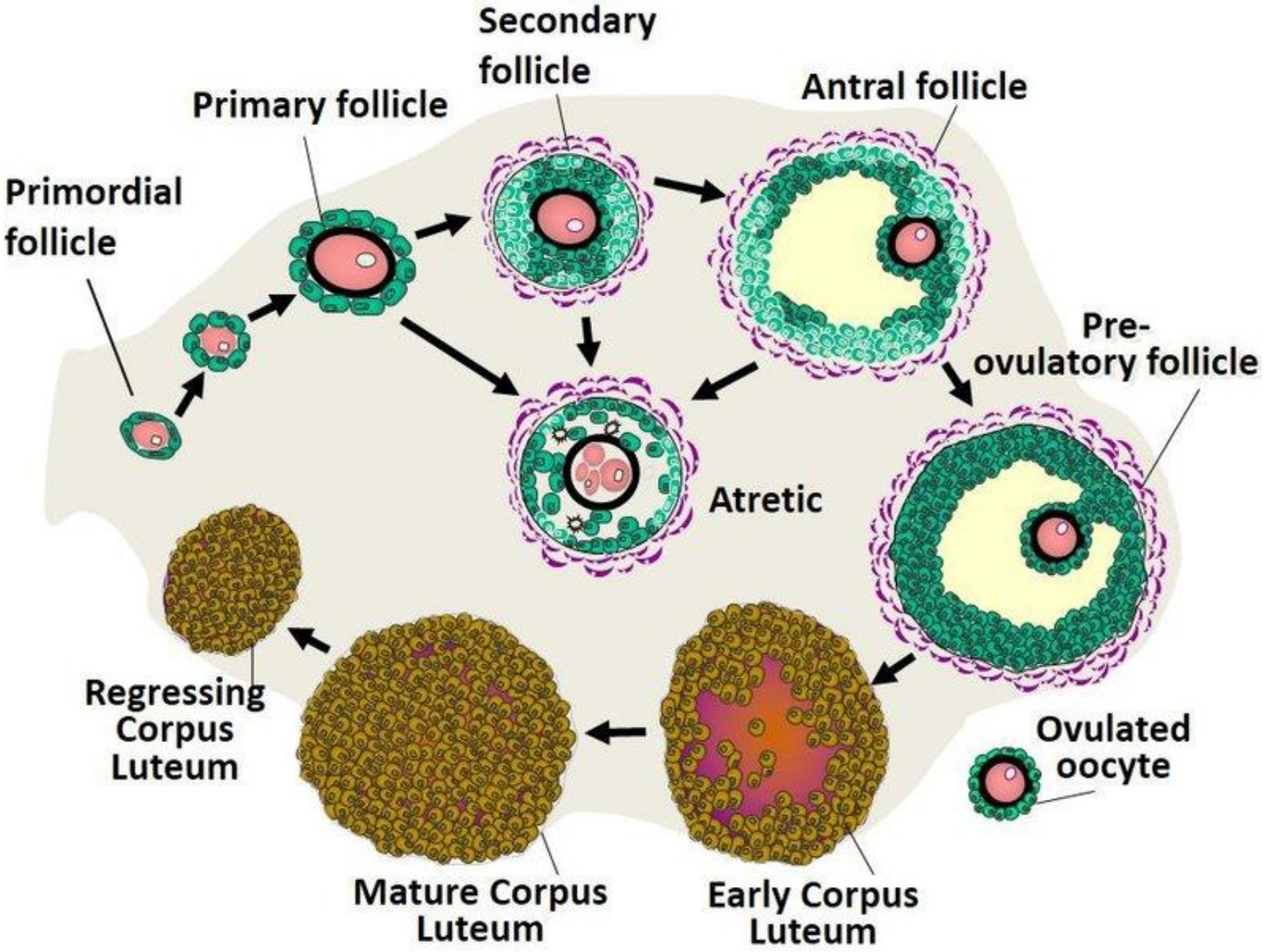
Atretic follicles



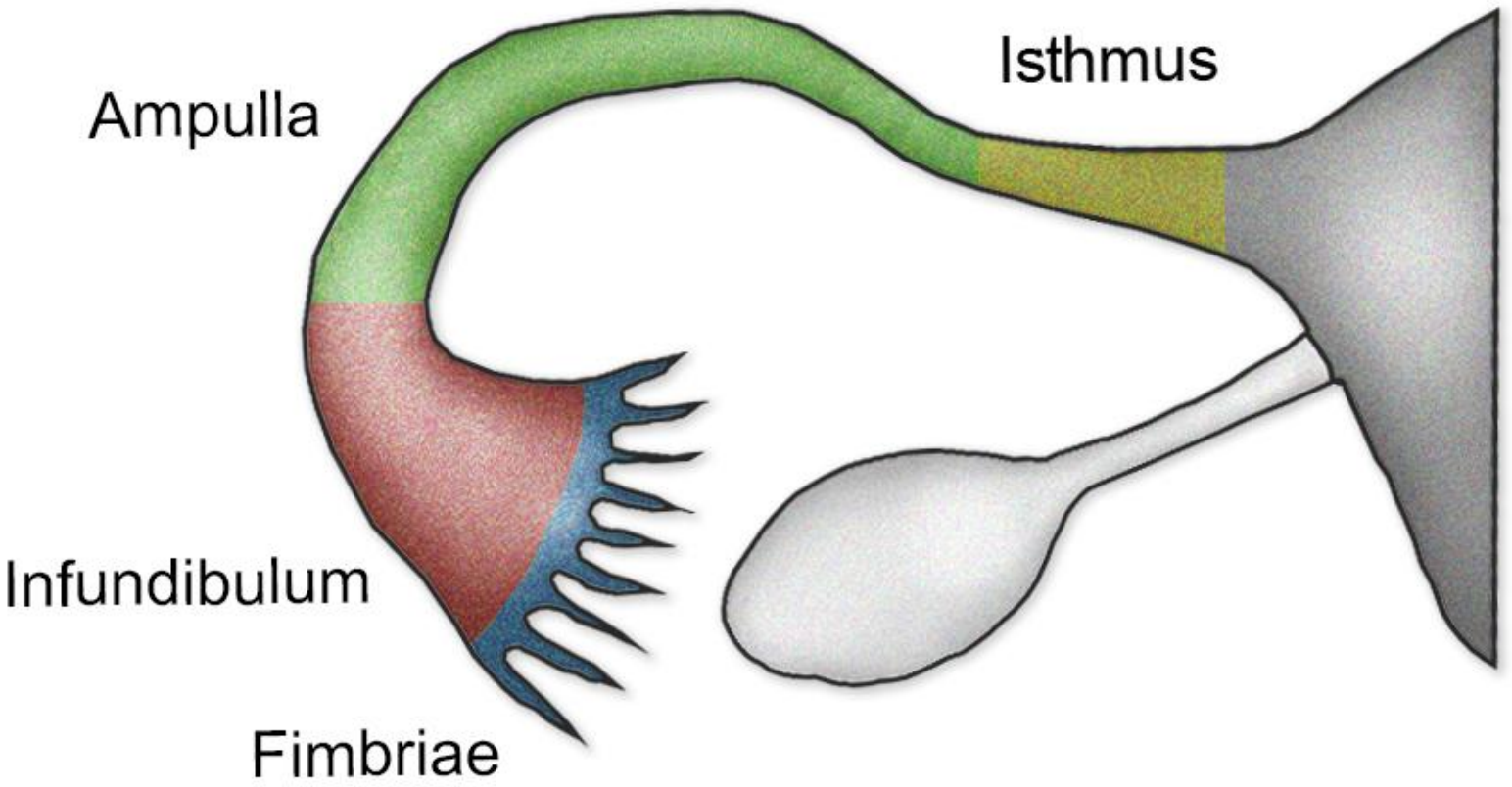
The ovaries contain a lot of follicles. Most of them degenerate, but multiple develop during each menstrual cycle. Only one of them ovulates, the remaining undergo atresia and are phagocytosed by macrophages.

Atresia of a follicle characterized by:
(1) the death of granulosa cells, many of which are seen loose in the antrum; (2) loss of the cells of the corona radiata;
(3) the oocyte floating free within the antrum.



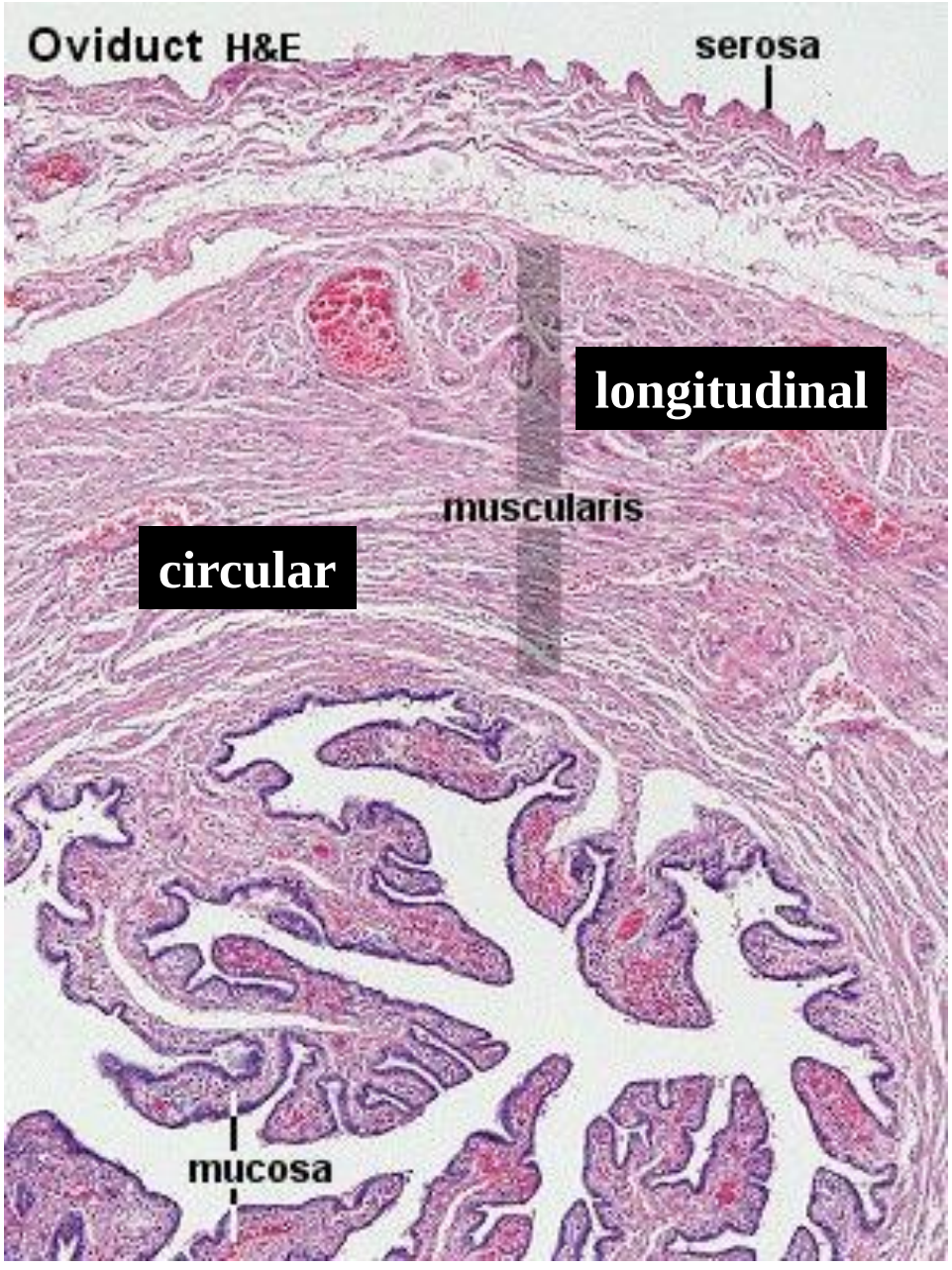

Secondary follicle
Primary follicle
Antral follicle
Primordial follicle
Pre-ovulatory follicle
Atretic
Regressing Corpus Luteum
Ovulated oocyte
Mature Corpus Luteum
Early Corpus Luteum

Oviduct (fallopian tube)



- infundibulum with fimbriae, which help to capture oocyte
- ampulla – the place of fertilization
- isthmus – the narrowed portion
- intramural region – passing through the uterine wall.

Oviduct – microscopic structure



Simple columnar epithelium

Mucosa with many folds most pronounced in the ampulla (l**amina propria of mucosa**) – loose connective tissue

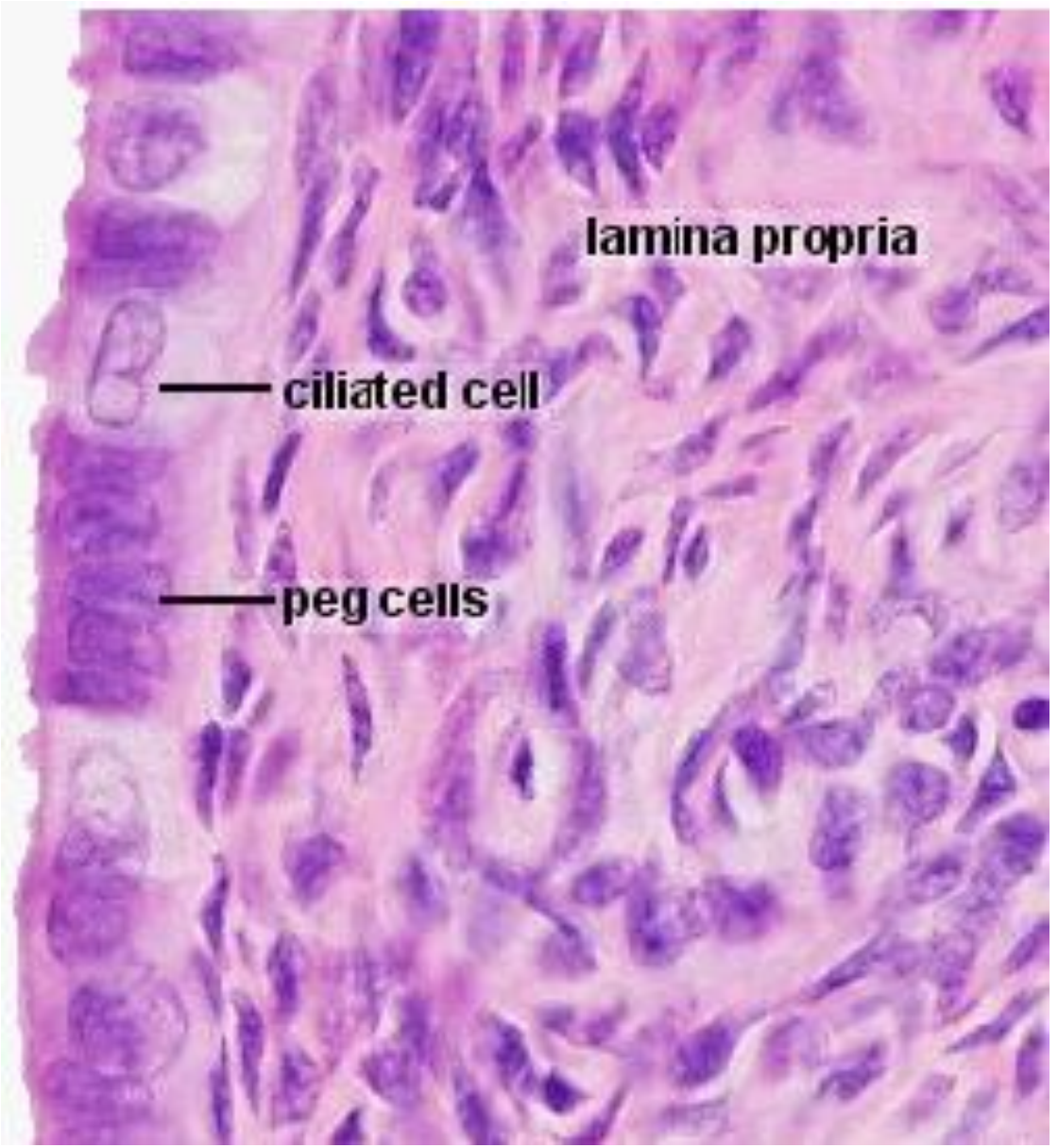
Muscularis - 2 poorly defined layers of smooth muscle cells.

Serosa – loose connective tissue with many blood vessels covered with simple squamous epithelium.

Oviduct – microscopic structure

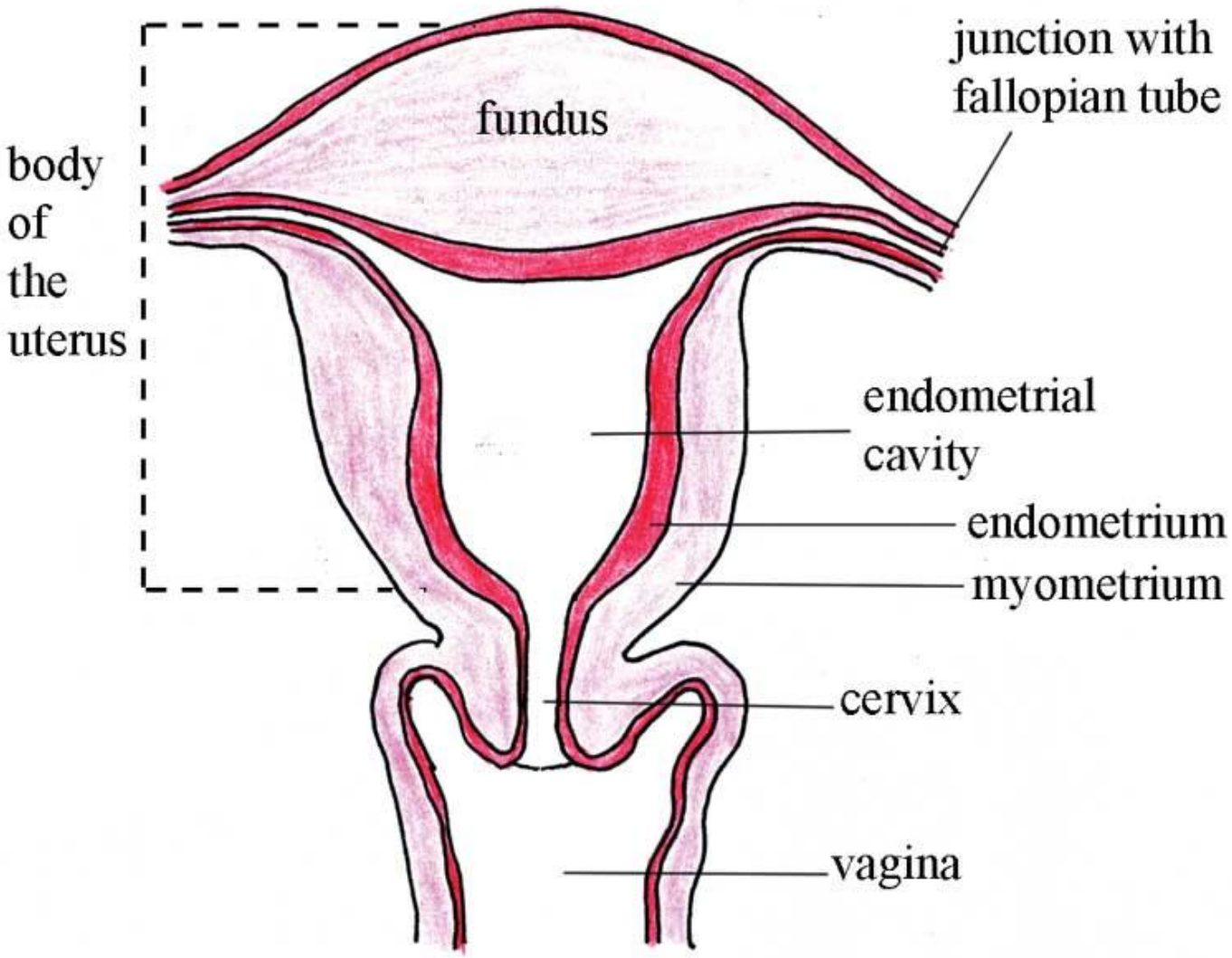
Ciliated cells
The cilia beat in unison toward the uterus. As the result a fertilized ovum (and spermatozoa, fluid) is propelled toward the uterus.

Peg cells – without cilia, secretory function, nutrition and protection of spermatozoa, oocyte and embryo during initial phase of development.



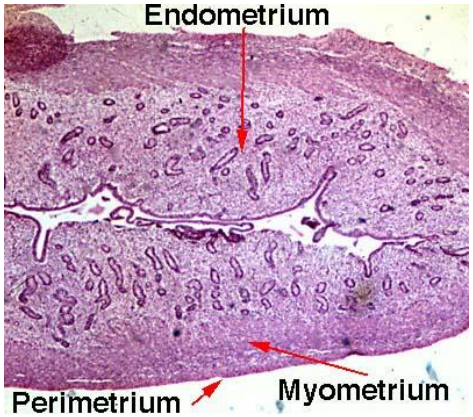
Two regions of an oviduct

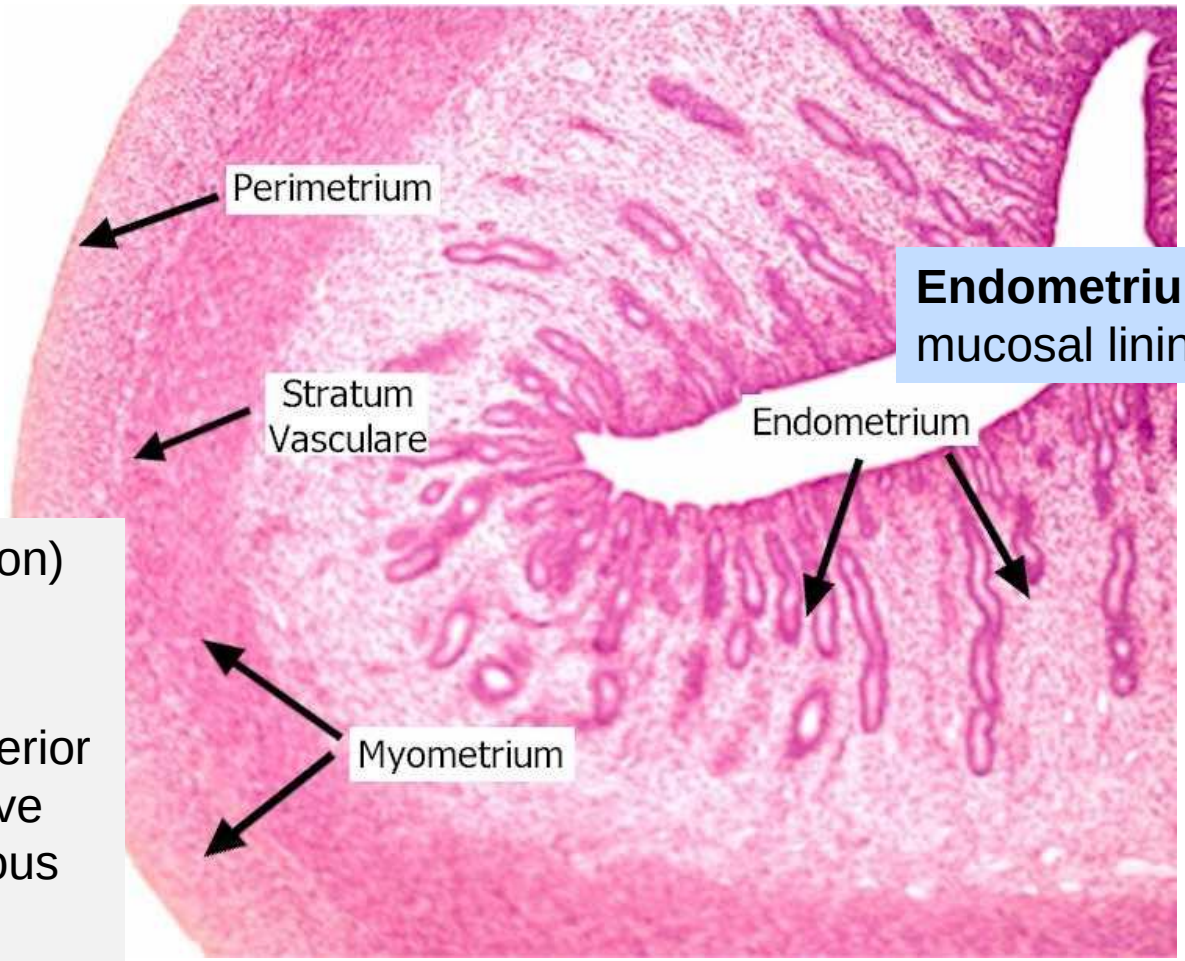
UTERUS – GENERAL DESCRIPTION



THE WALL OF UTERUS

The uterine wall of the body and the fundus is composed of:





Endometrium – mucosal lining

Adventitia -(anterior portion) connective tissue

or

Serosa -(fundus and posterior portion) –areolar connective tissue with simple squamous epithelium -mesothelium**.**

Myometrium – smooth muscle cells layers

Endometrium - simple columnar epithelium and a lamina propria.

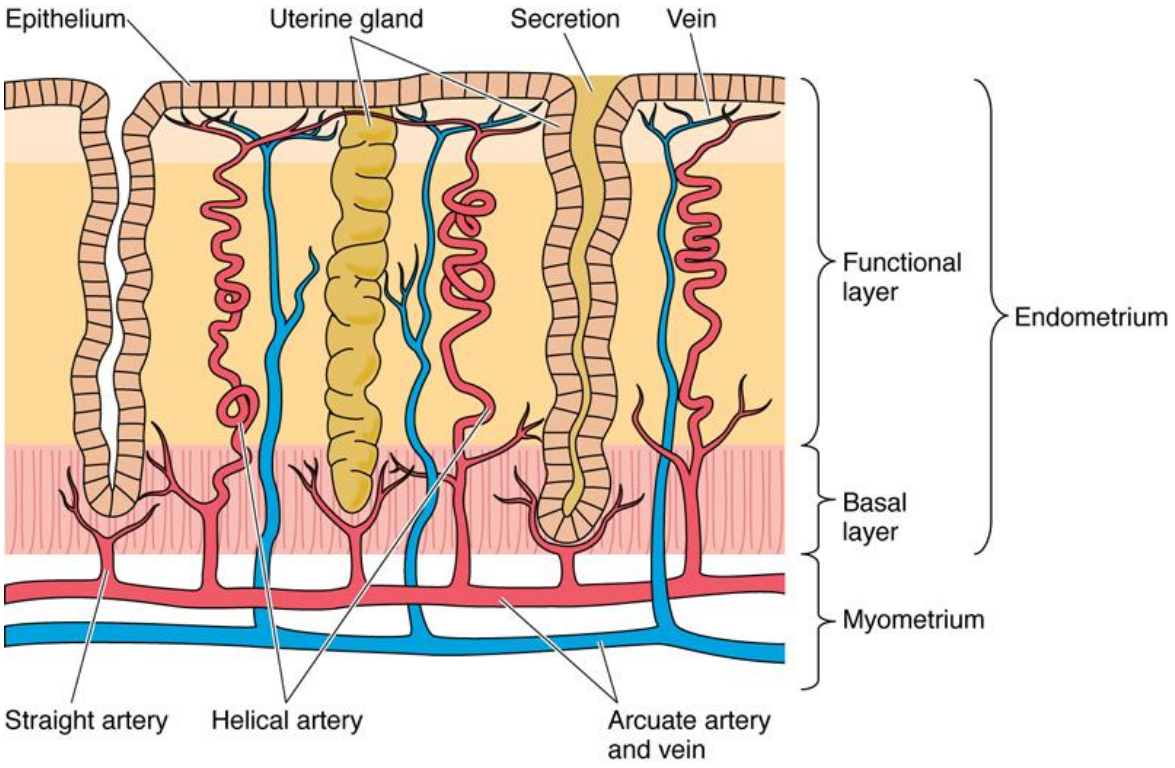
Epithelium - **nonciliated secretory columnar cells** and **ciliated cells**

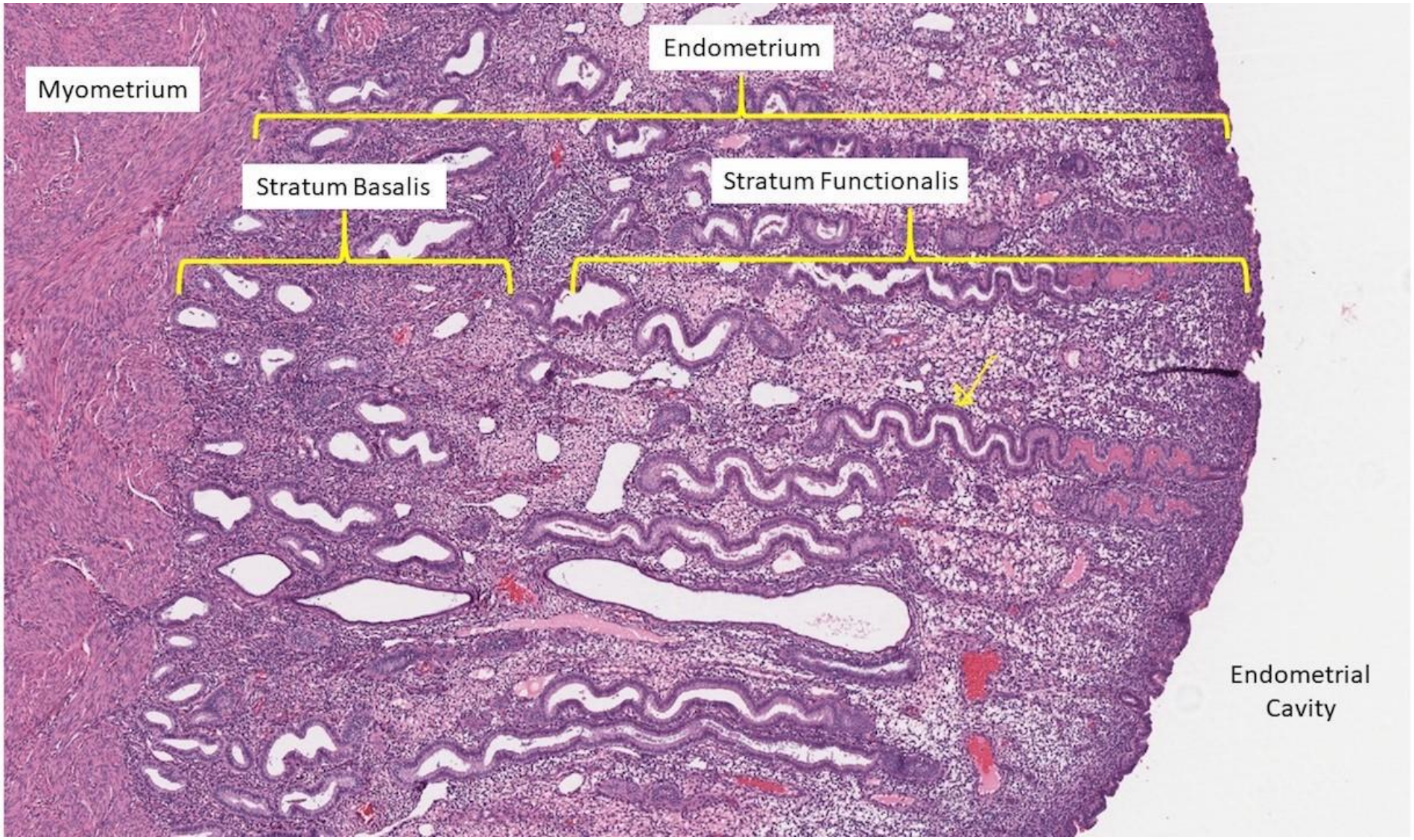
Lamina propria - simple branched **tubular glands.**

Two layers of endometrium:

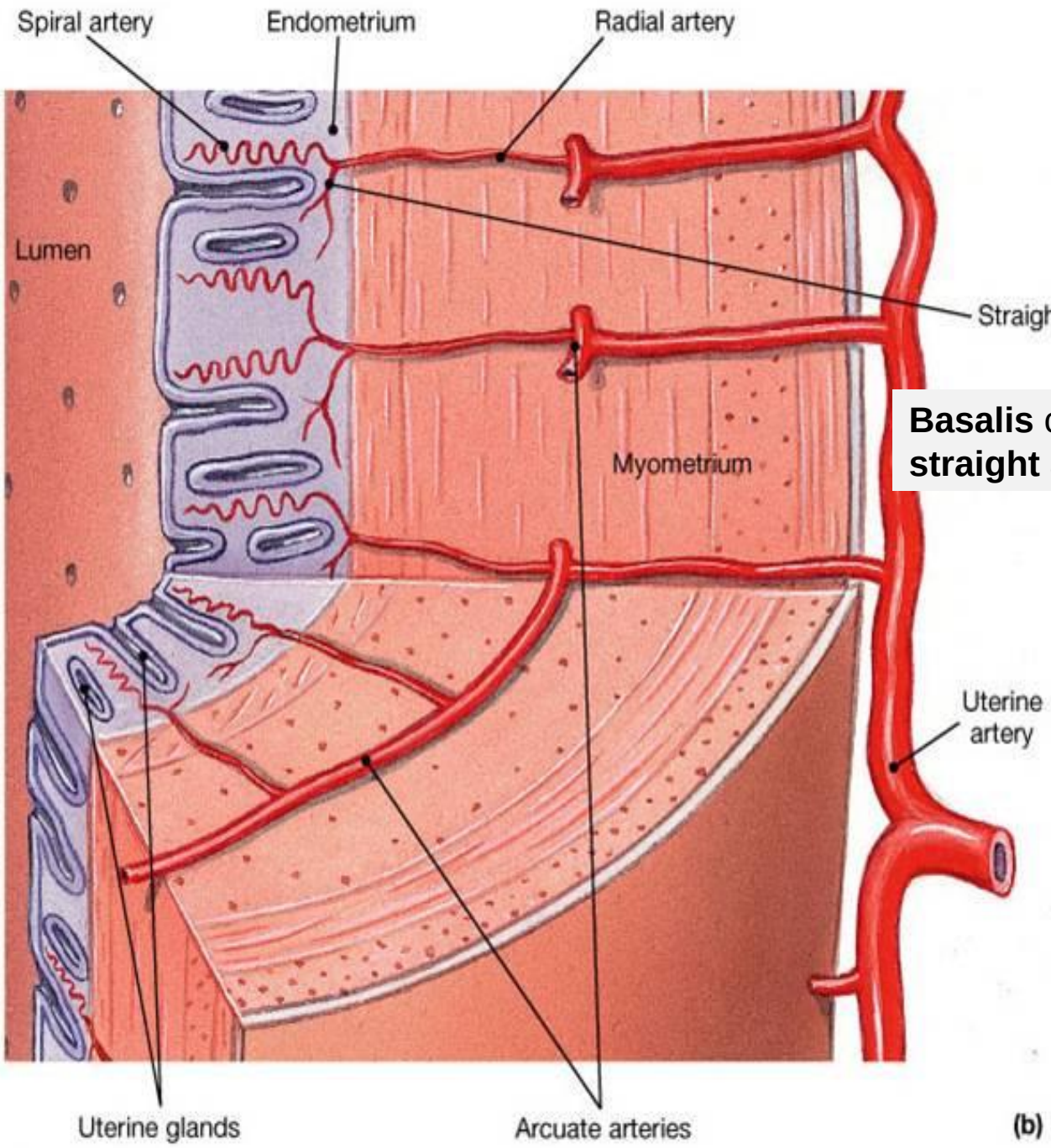
Functionalis, a thick, superficial layer that is sloughed at menstruation

Basalis, a deep, narrow layer whose glands and connective tissue cells proliferate and thereby regenerate the functionalis during each menstrual cycle.

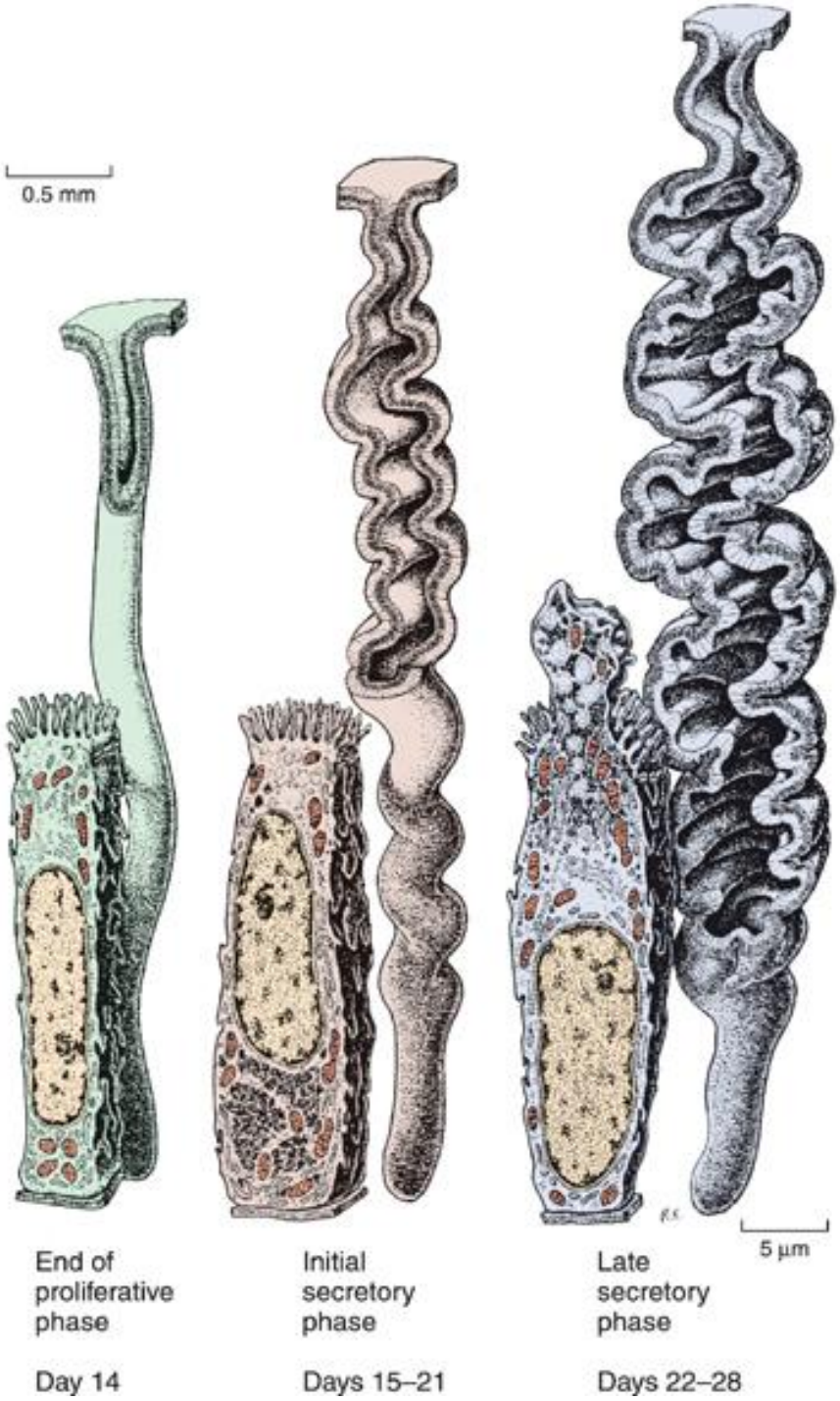



Myometrium
Endometrium
Stratum Basalis
Stratum Functionalis
Endometrial Cavity

Functionalis is vascularized by numerous **coiled helical (spiral)** arteries



Basalis contains **straight arteries**

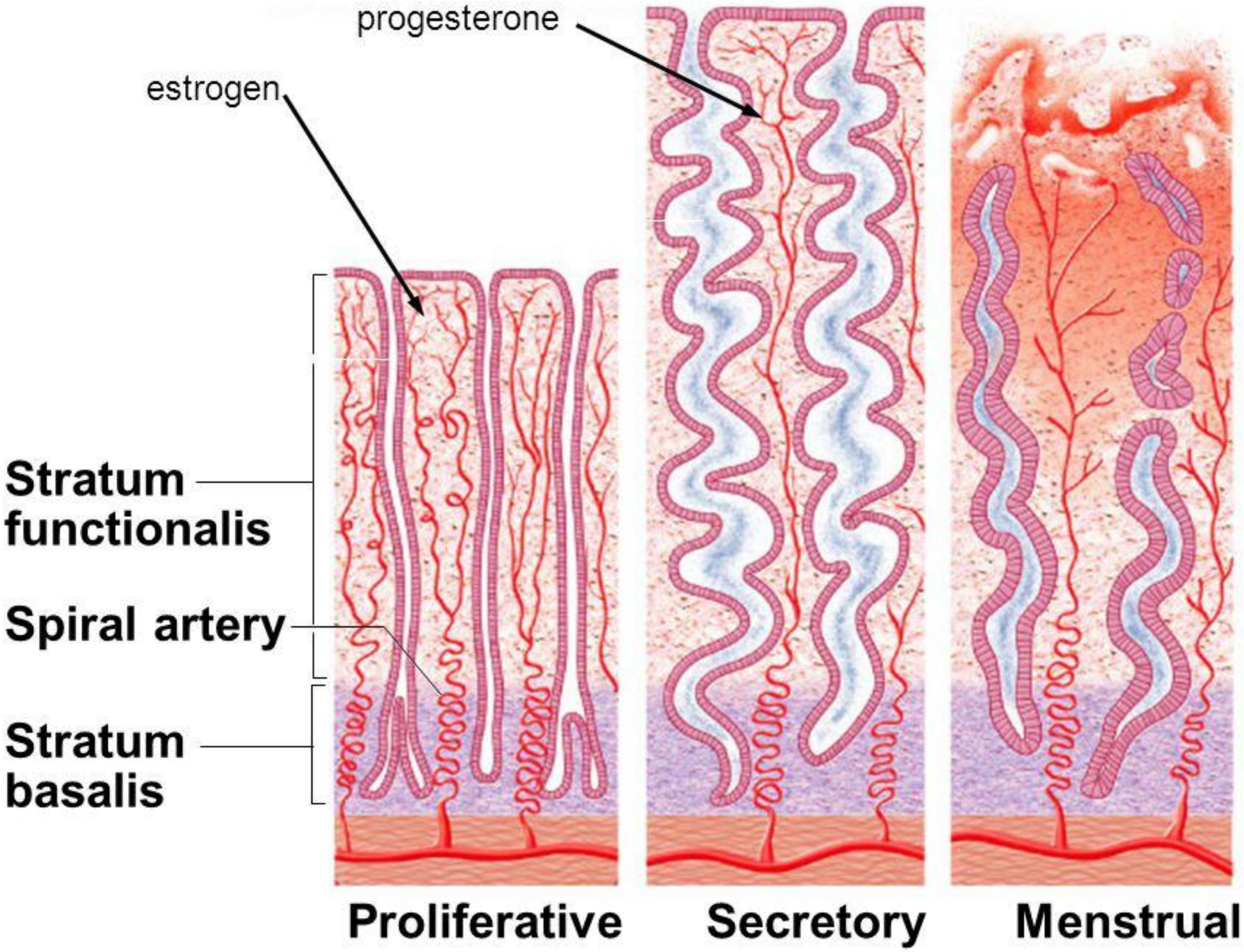


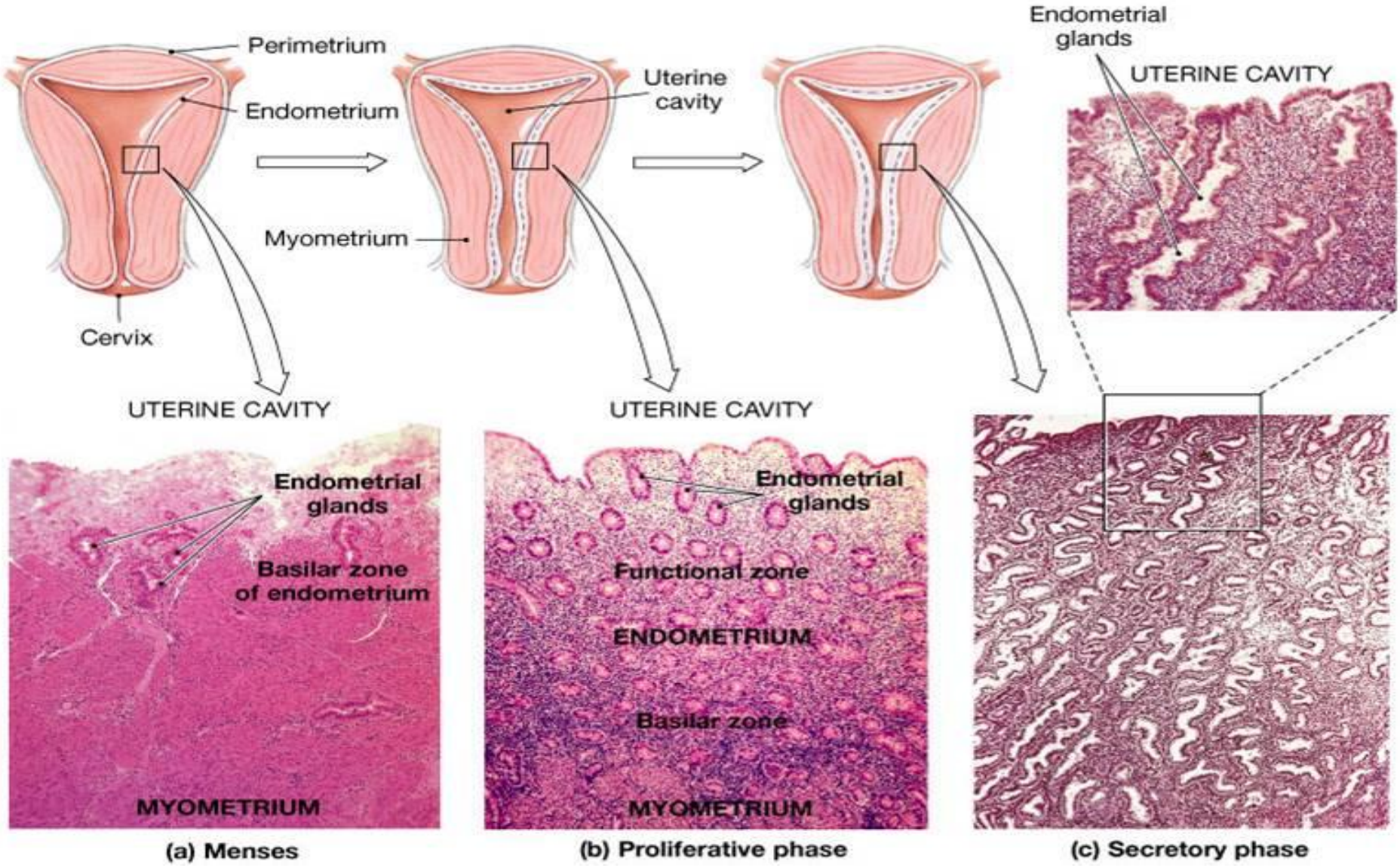
CHANGES IN THE UTERINE GLANDS AND IN THE GLAND CELLS DURING THE MENSTRUAL CYCLE.

In the proliferative stage the glands are straight tubules, and their cells show no secretory activity.

In the initial secretory phase the glands begin to coil, and their cells accumulate glycogen in the basal region.

In the late secretory phase the glands are highly coiled, and their cells present secretory activity at their apical portion.


progesterone
estrogen
Stratum functionalis
Spiral artery
Stratum basalis
Proliferative
Secretory
Menstrual

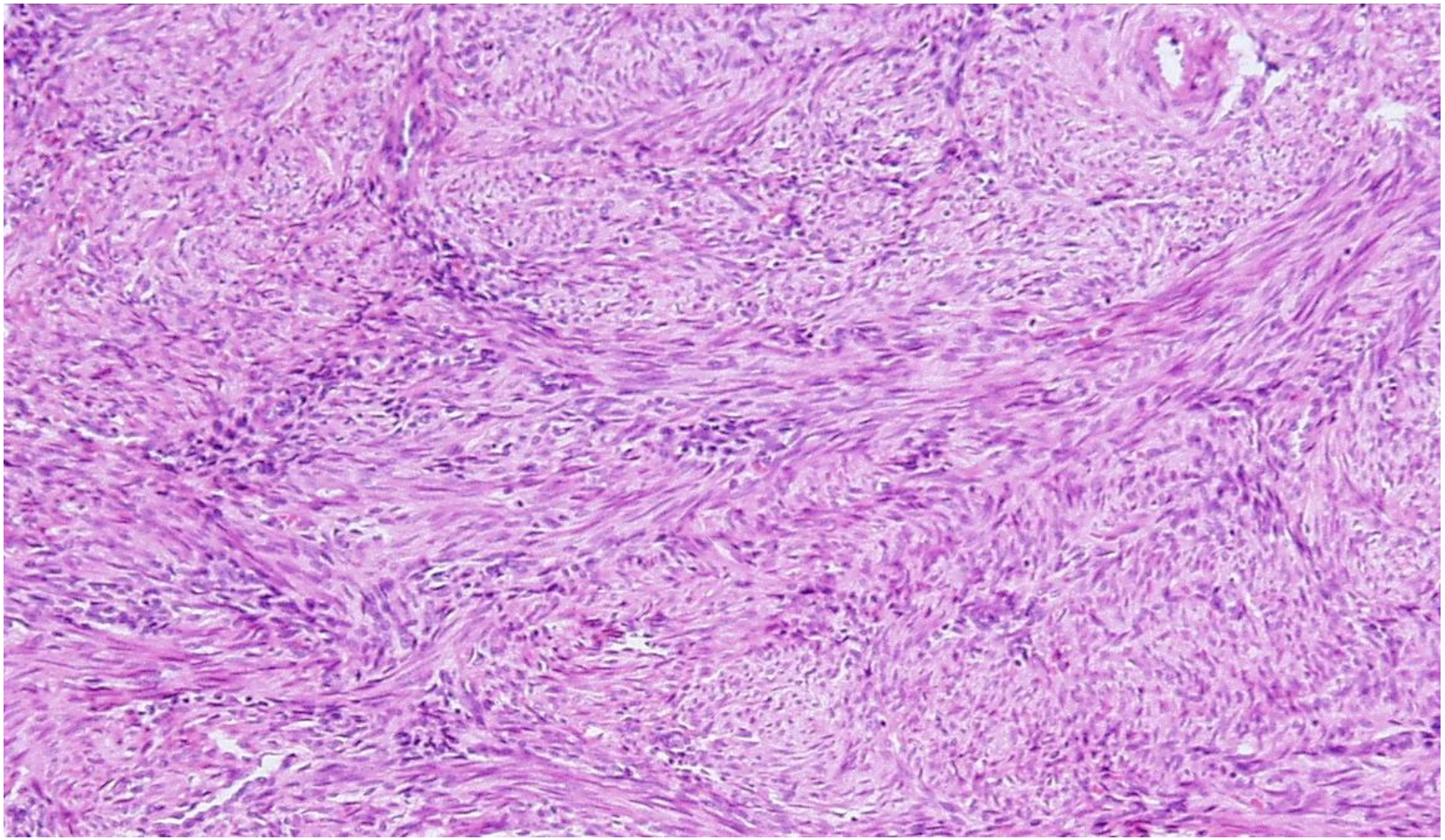


(a) Menses

(b) Proliferative phase

(c) Secretory phase

MYOMETRIUM



Three layers of smooth muscle cells: inner longitudinal, middle circular and outer longitudinal

Cicular layer houses arcuate arteries (stratum vasculare).

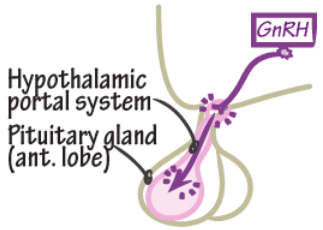
OVARIAN & UTERINE CYCLES

- ✓ Hypothalamic-pituitary-ovarian axis regulates oocyte development and release.
- ✓ Ovarian follicle produces hormones that prepare endometrium for implantation of fertilized oocyte.

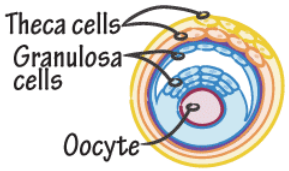
Dysmenorrhea
Painful cramping with menstruation; treatable with OTC drugs and hormonal contraceptives.

TWO PATHWAYS:
- ✓ If fertilization and implantation occur, corpus luteum and, therefore, endometrium are maintained.
- ✓ If implantation does NOT occur, corpus luteum involutes, hormone levels fall, menses begins.

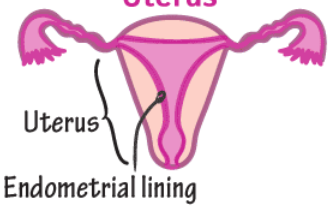
Hypothalamus & Pituitary Gland

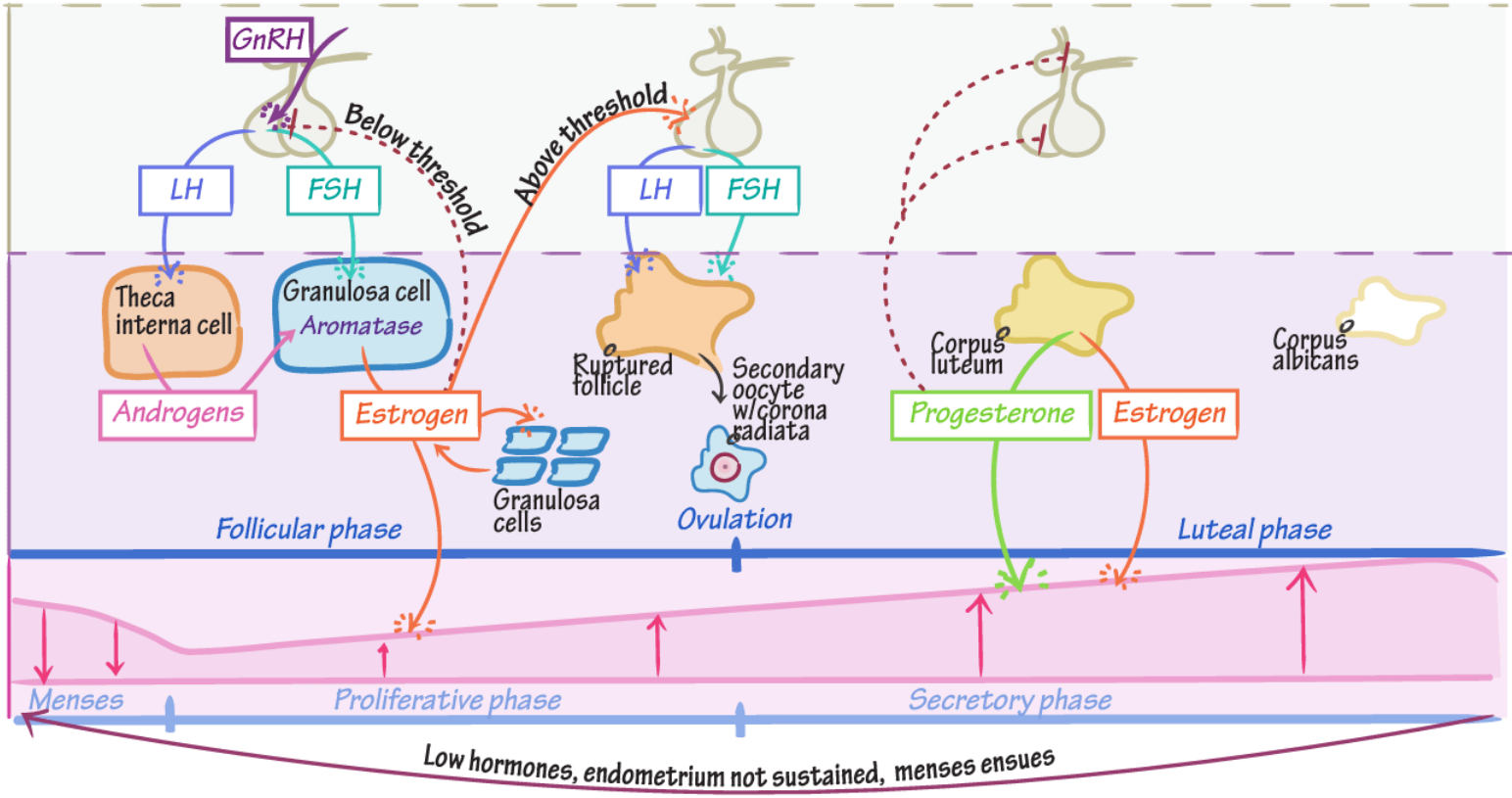


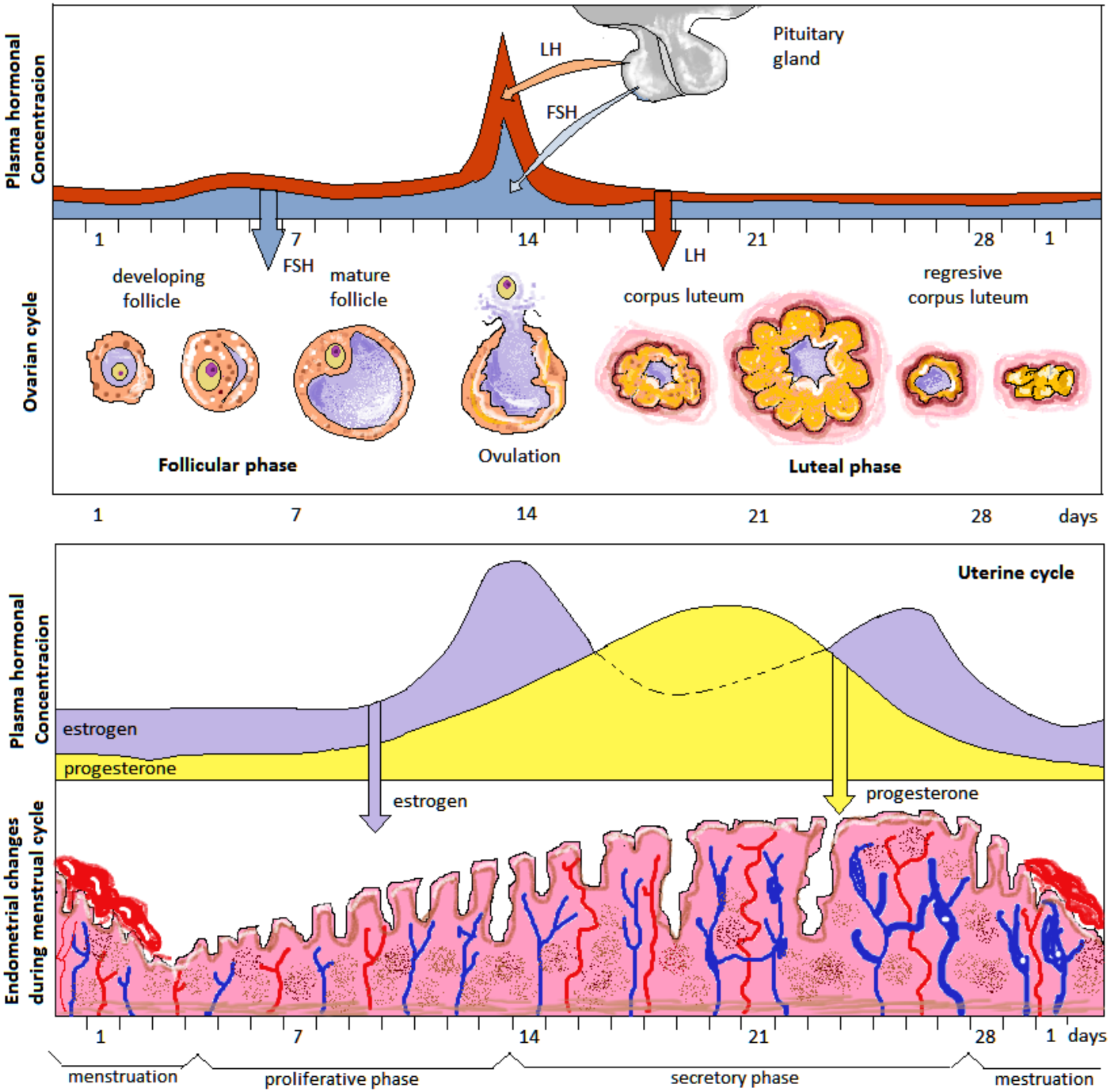
Ovarian Follicle



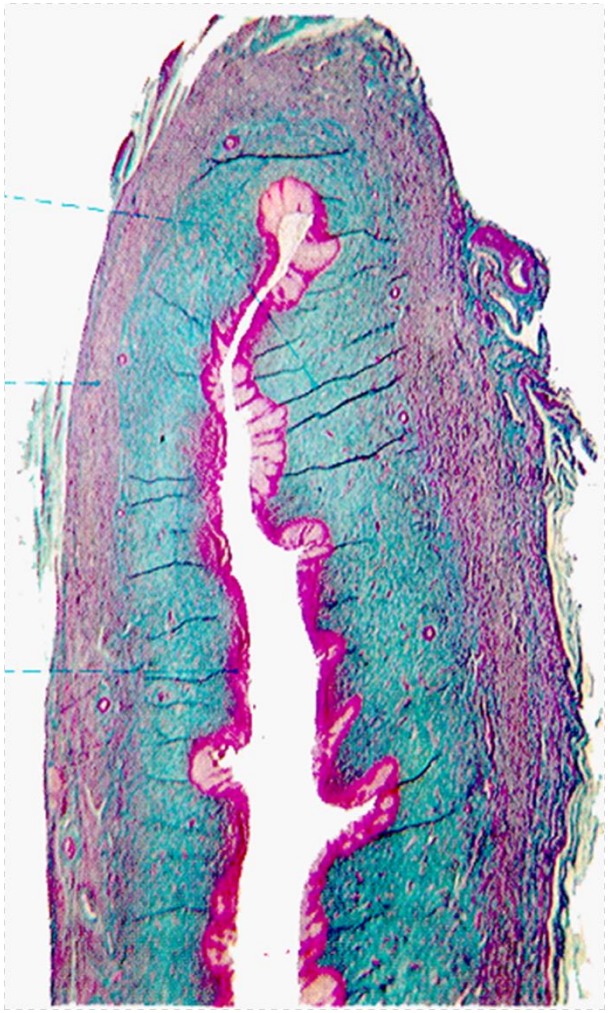
Uterus

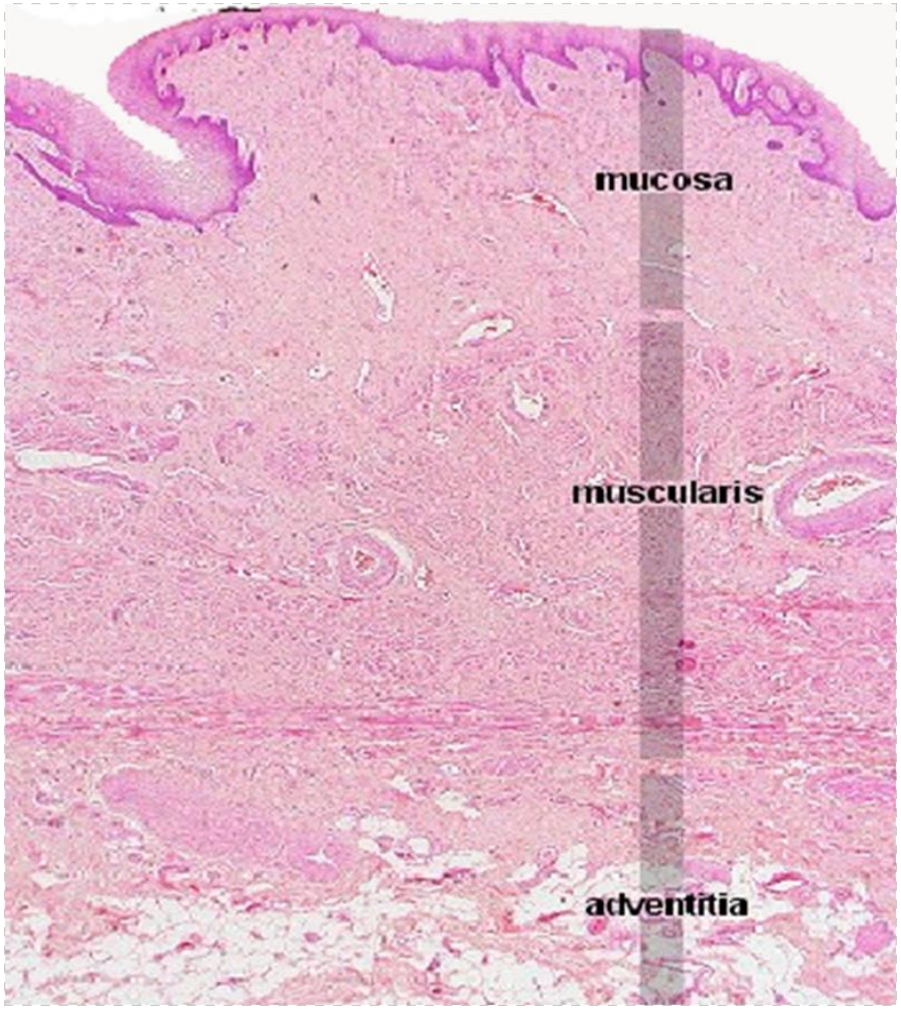





Plasma hormonal Concentracion
LH
FSH
Pituitary gland
1
7
14
21
28
1
FSH
LH
Ovarian cycle
developing follicle
mature follicle
corpus luteum
regresive corpus luteum
Follicular phase
Ovulation
Luteal phase
1
7
14
21
28
days
Plasma hormonal Concentracion
Uterine cycle
estrogen
progesterone
estrogen
progesterone
Endometrial changes during menstrual cycle
1
7
14
21
28
1
days
menstruation
proliferative phase
secretory phase
mestruation

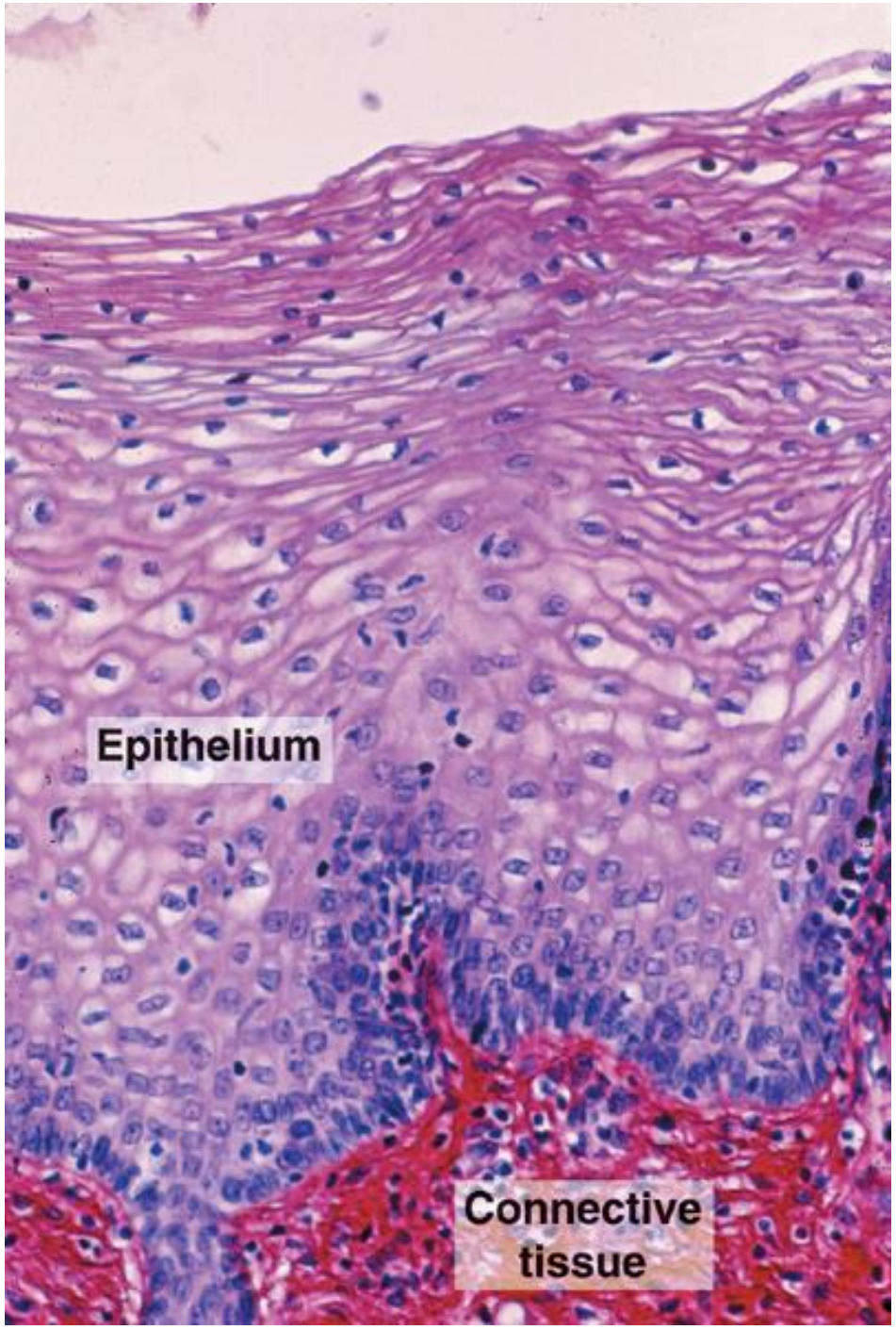
Vagina – general morphology





1. Mucosa - epithelium and lamina propria (loose fibroelastic connective tissue)
2. Muscularis – smooth muscle cells and sphincter composed of skeletal muscle cells
3. Adventitia – dense fibroelastic connective tissue

VAGINA



Stratified squamous nonkeratinized epithelium of vagina undergoes cyclic changes during menstrual cycle.

In secretory phase, under influence of estrogens epithelial cells accumulate glycogen. The cytoplasm of these cells is clear because of accumulated glycogen, which is metabolized by *Lactobacillus acidophilus* to lactic acid. Low pH (3.5-4.9) of vaginal contents prevents bacterial contamination.

During secretory phase superficial layer of epithelium is desquamated.

THANK YOU!