

Histology of female genital system

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Female genital system

The female genital system is composed of:

1. Primary sex organs: Two ovaries which have an endocrine function (secretion of estrogen and progesterone), and an exocrine function (secretion of the female gametes: oocytes).

2. Secondary sex organs:

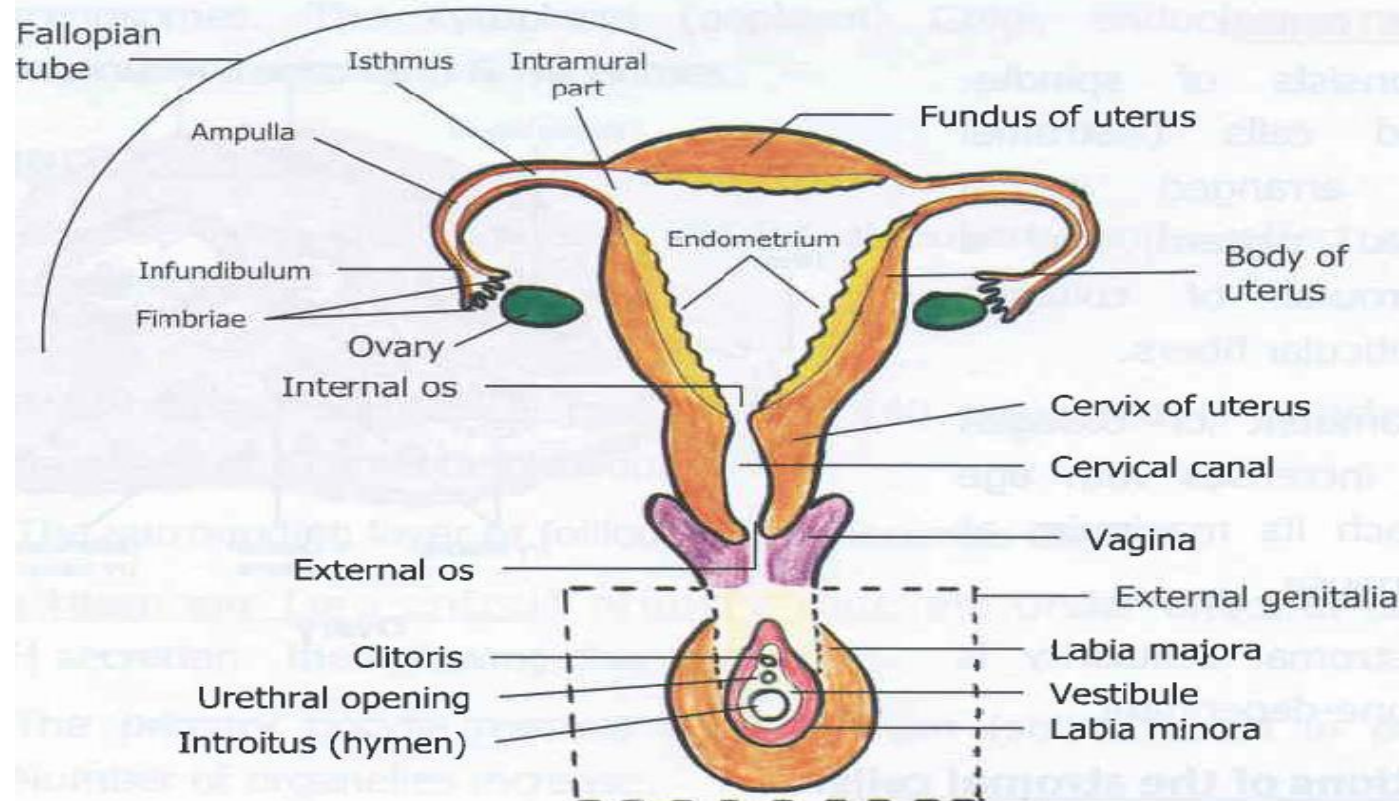
Two fallopian tubes.

Uterus.

Vagina.

External genitalia.

Two mammary glands.



THE OVARY

It is a paired ovoid organ lying in the right and left pelvic cavity. The adult ovary consists of:

1. Germinal Epithelium:

- It is a single layer of cuboidal epithelium which commonly transforms to flat cells with increasing of age.
- The term germinal is a misnomer as its epithelial cells are not the source of female gametes.

2. Tunica Albuginea: It is a layer of dense white fibrous C.T. located between the germinal epithelium and the underlying cortex.

3. Outer Cortex:

- It is present under tunica albuginea, in the peripheral portion of the ovary.
- It is formed of richly cellular supporting stroma (cortical stroma), and different types of ovarian follicles containing the oocytes.

4. Inner Medulla: It is located in the central portion of the ovary. It is formed of loose highly vascular C.T., lymphatics & nerves.

Ovarian Hilum:

It is the route whereby blood vessels, lymphatics and nerves enter and leave the ovary.

Cortical Stroma:

It consists of spindle- shaped cells (=stromal cells) arranged in whorled pattern, on a background of collagen and reticular fibers.

The amount of collagen fibers increases with age to reach its maximum at menopause.

The stromal cellularity is hormone-dependant .

Functions of the stromal cells:

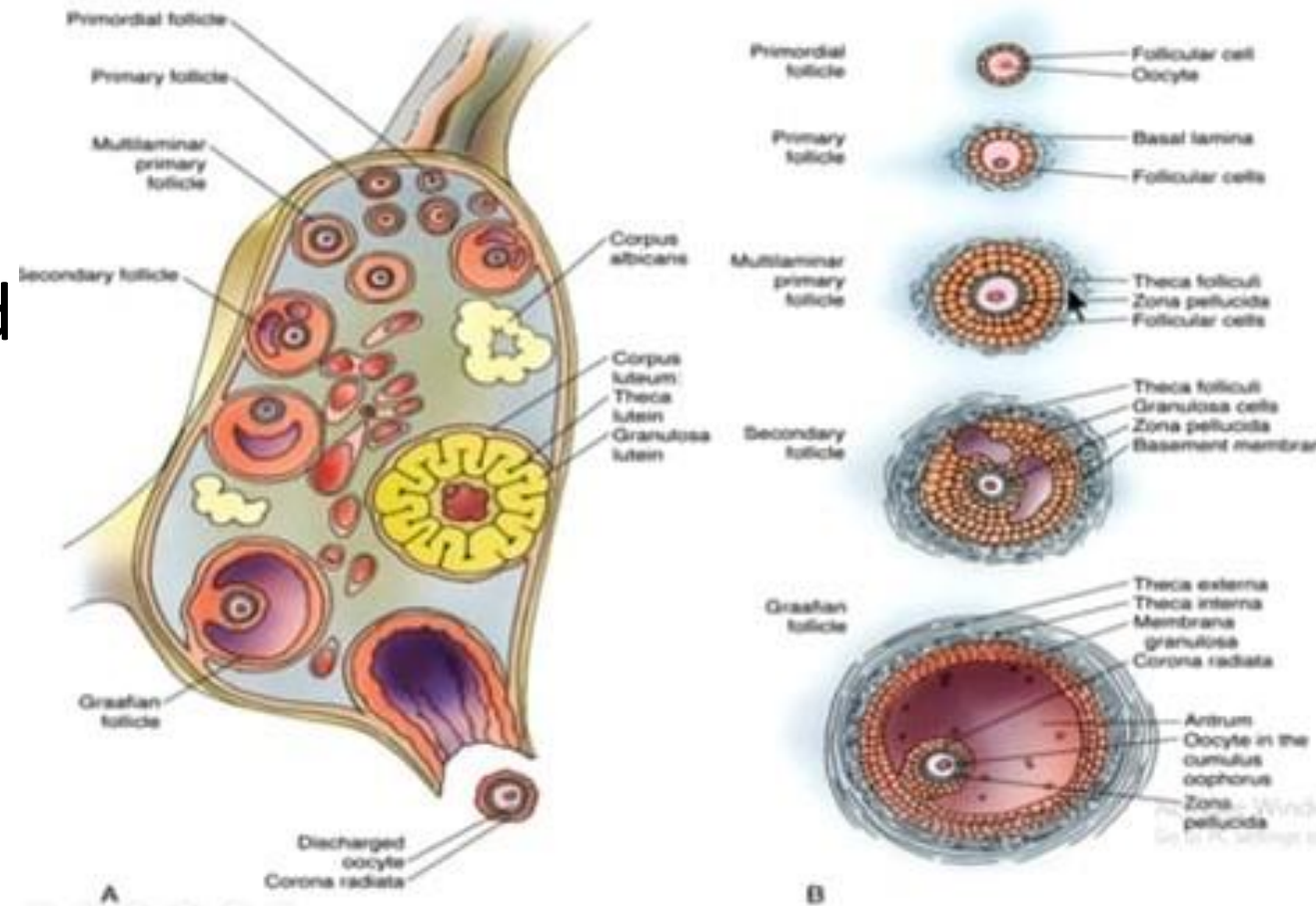
- a. Providing support for the developing ova.
- b. Giving rise to the theca folliculi cells.
- c. Secrete steroid hormones (estrogen-androgen).

Ovarian Follicles

They are distributed in the stroma of the ovarian cortex. They provide the microenvironment for the developing oocyte. They are variable in size, each containing a single oocyte.

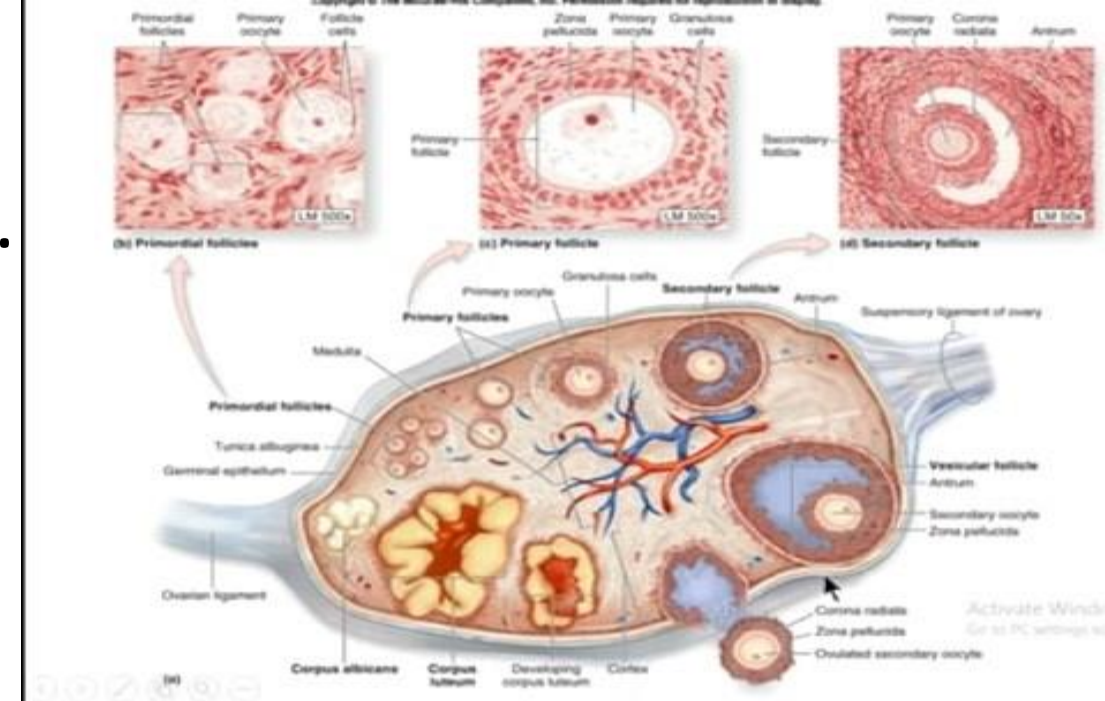
Types:

1. Primordial follicles
2. Primary follicles: Unilaminar and multilaminar (pre-antral).
3. Secondary (Antral) follicles
4. Mature Graafian follicles
5. Atretic follicles.



1. Primordial Follicles:

- Located directly under tunica albuginea.
- They are formed between 6-9th month of fetal life. At birth the cortex is packed by large number of them.



- Each consists of a primary oocyte surrounded by a single layer of flat follicular cells. The primary oocyte is about 25 μm in diameter with a large eccentric vesicular nucleus and clear 1-2 nucleoli. Nucleus contains diploid number of chromosomes. The cytoplasm (ooplasm) Golgi, endoplasmic reticulum, numerous mitochondria & lysosomes.

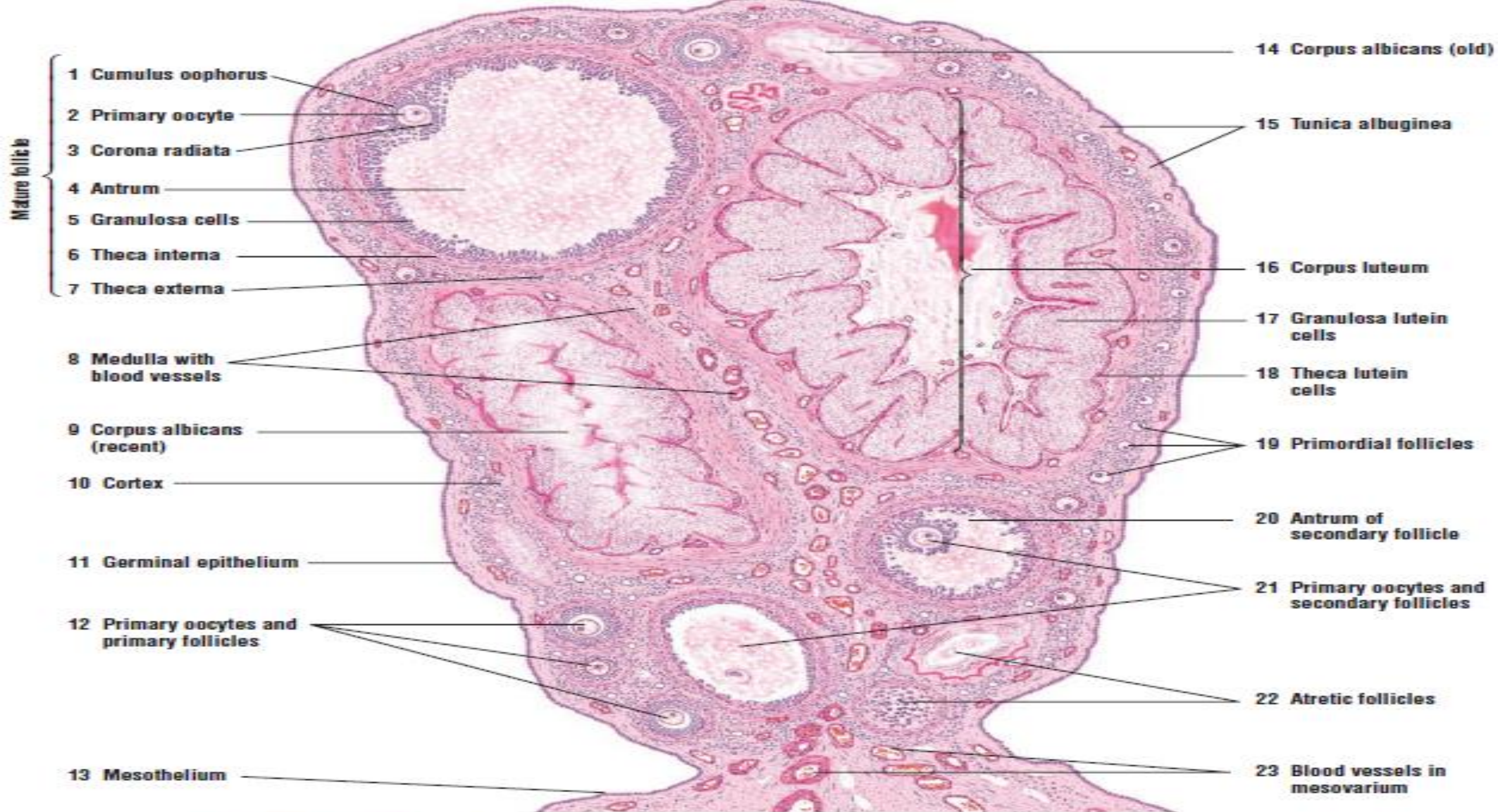


FIGURE 19.1 ■ Ovary (panoramic view). Stain: hematoxylin and eosin. Low magnification.

2. Primary Follicles:

They develop from the primordial follicles at puberty under effect of FSH of anterior pituitary.

a. Unilaminar primary follicles:

The primary oocyte enlarges in size (40 μm), and is arrested in the prophase of 1 meiotic division.

The surrounding layer of follicular cells becomes cuboidal.

b. Multilaminar (pre-antral) primary follicles: Under effect of continuous FSH secretion the following changes occur:

The primary oocyte reaches about 50 μm (still arrested in prophase).
number of organelles increase.

The surrounding follicular cells proliferate (by mitotic division) to form several layers of polyhedral granulosa cells.

A thick homogeneous deeply staining acidophilic layer rich in glycosaminoglycans and glycoprotein, called the zona pellucida, is formed between the primary oocyte and the granulosa cells. Both the oocyte and granulosa cells are believed to be responsible for synthesis of this layer.

Ovarian stromal cells become arranged in concentric layers around the enlarging follicle forming a capsule-like structure called theca folliculi. As the follicle enlarges, it moves to the deeper areas of the cortex.

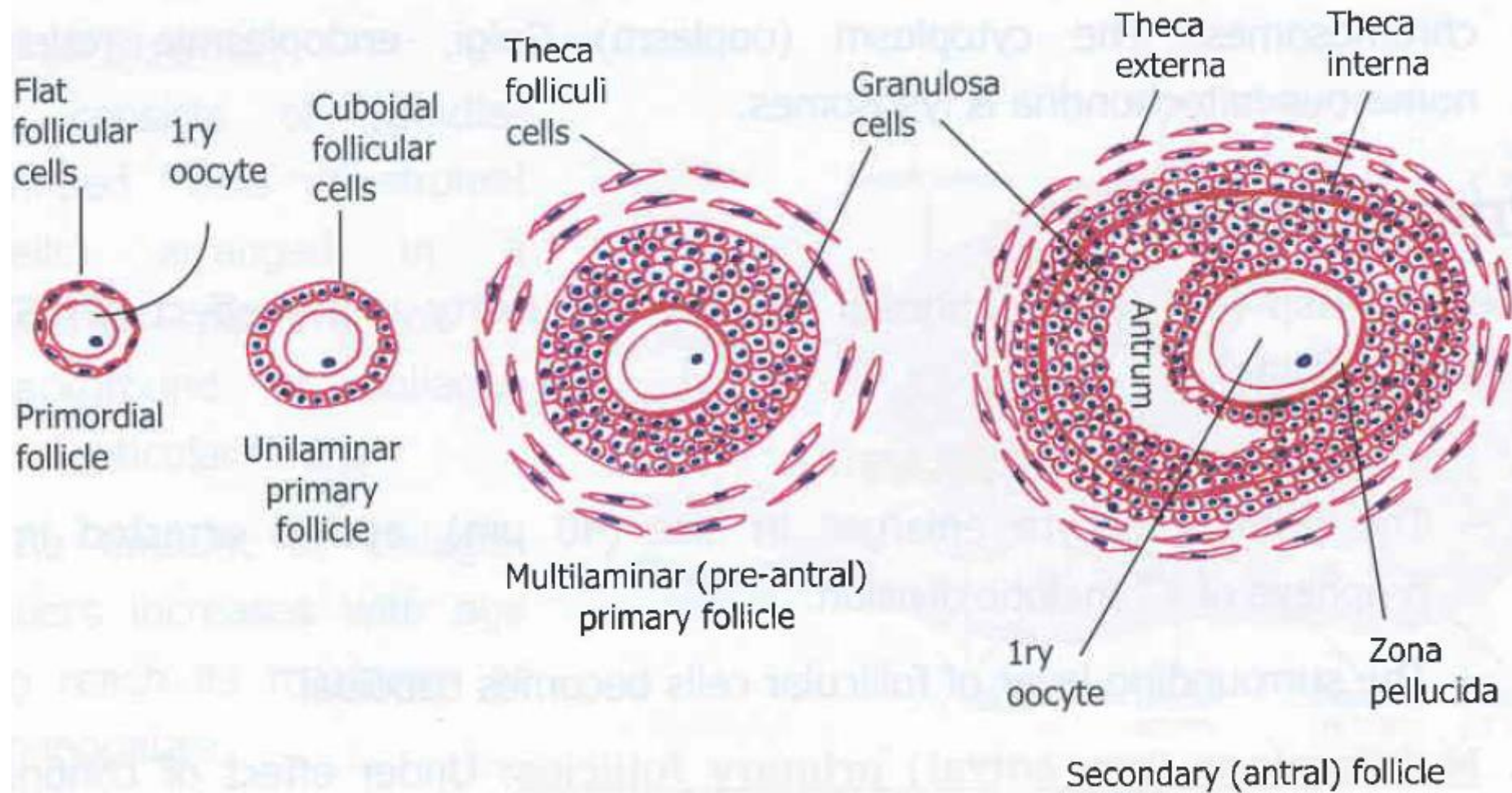
3. Secondary (Antral) Follicles:

A liquid (liquor folliculi) is secreted by granulosa cells and begins to accumulate between them. This fluid contains glycosaminoglycans and several proteins (steroid-binding proteins).

The small spaces between the granulosa cells that contain the liquor folliculi coalesce together to form a large cavity called the antrum.

The primary oocyte enlarges in size (120 μm) and is pushed to one side.

The theca folliculi differentiates into an inner theca interna layer and an outer theca externa layer.



Primary & secondary ovarian follicles.

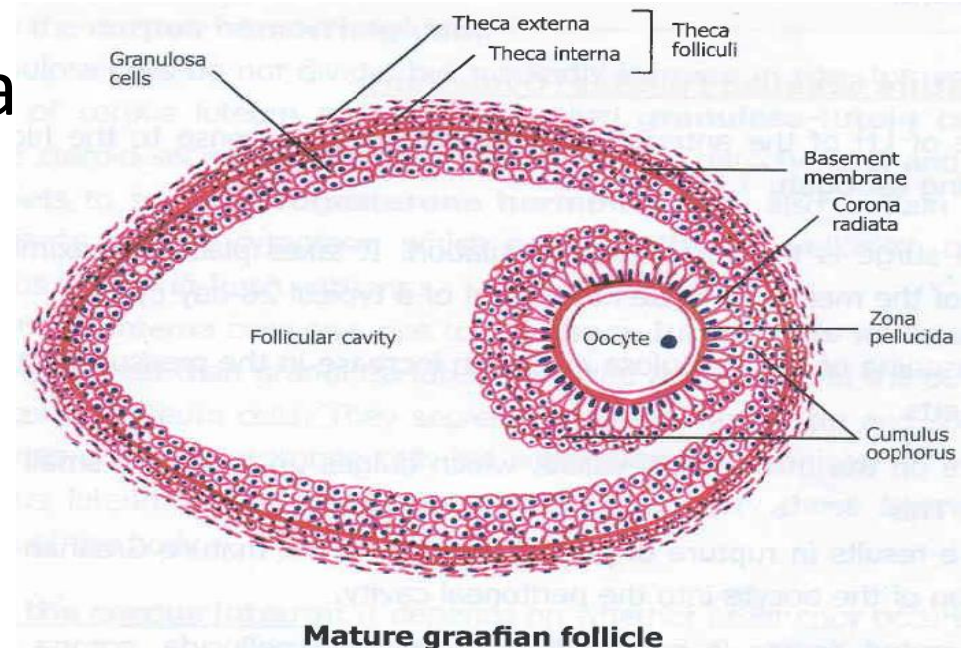
4. Mature Graafian (Tertiary) Follicles:

- It is a large structure that reaches 2-2.5 cm in diameter. It occupies the whole thickness of the ovarian cortex and bulges from the ovarian surface.
- It consists of:
 - a. Primary oocyte: 150 μm in diameter. It changes into the secondary oocyte with haploid number of chromosomes just before ovulation.
 - b. Zona pellucida: a glycoprotein layer which directly surrounds the oocyte.
 - c. Corona radiata: a layer of the granulosa cells acquiring a columnar shape and surrounding the oocyte. Thin cytoplasmic processes from the corona radiata cells penetrate the zona pellucida to make contact with microvilli projecting from the oocyte via gap junctions.

d. Cumulus oophorus: a group of granulosa cells surrounding the corona radiata and protruding towards the antrum separating the oocyte from the follicular fluid.

e. Granulosa Cells: formed of 3-4 layers of polyhedral cells lining the follicular cavity and secrete the follicular fluid. It is believed that these cells also secrete an enzyme (aromatase) that converts androgen hormone coming from theca interna cells into estrogen.

f. Basement membrane: separating granulosa cells from theca folliculi cells.



g. Theca interna:

Large polyhedral cells concerned with the secretion of estrogen hormone directly, or by secretion of androgen which is converted into estrogen by aromatase enzyme of granulosa cells.

By EM they show the features of steroid-secreting cells: abundant SER, many mitochondria and lipid droplets.

The cells enclose a prominent capillary network which carries estrogen to be distributed to all parts of the body.

h. Theca externa

Small compact layer of fibroblast-like cells.

They have no secretory function, There is no clear boundary between the theca interna and theca externa or between the theca externa and the surrounding stroma.

5. Atretic Follicles:

Up to 20 primary follicles are activated every month, only one follicle reaches maturation & ovulates liberating one oocyte each menstrual cycle. The remainder undergoes atresia (degeneration).

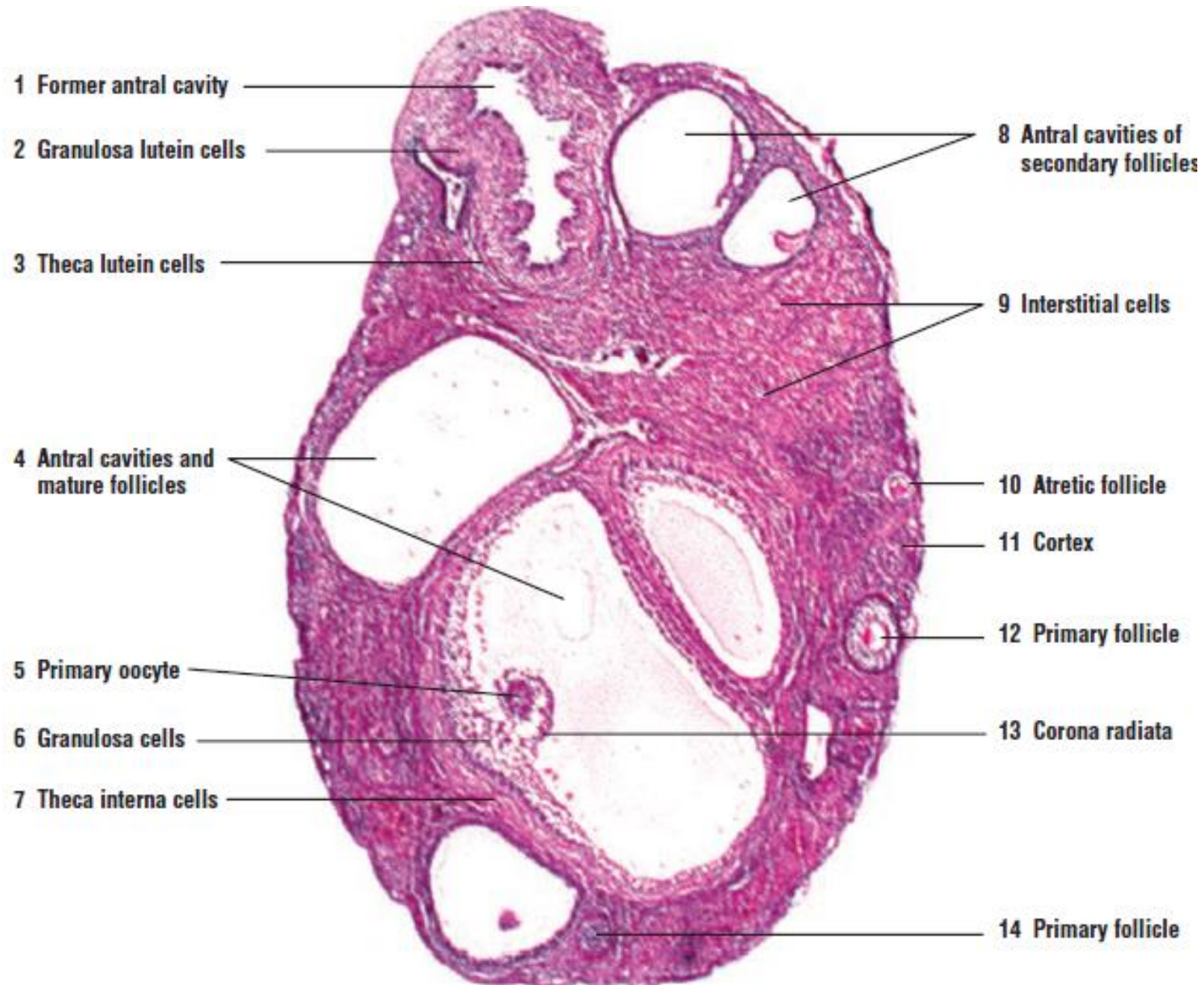
The atresia (degeneration) occurs at any stage of the developing follicles (primordial, primary, secondary or tertiary)

It is characterized by death of the oocyte and, degeneration of surrounding cells. Macrophages invade the follicle to phagocytose the debris.

When small follicles (primordial and primary) degenerate, complete resorption occurs leaving no scar. However, secondary and tertiary follicles leave a scar of collagen which lasts for a long time.



FIGURE 19.1 ■ Ovary (panoramic view). Stain: hematoxylin and eosin. Low magnification.



Fate of Mature Graafian Follicles (Ovulation):

A surge of LH of the anterior pituitary occurs in response to the high levels of circulating estrogen.

This LH surge is the stimulus for ovulation. It takes place approximately in the middle of the menstrual cycle i.e. day 14 of a typical 28-day cycle.

- The loosening of the granulosa cells with increase in the pressure of the follicular fluid exerts pressure on the thin cortical tissue, which bulges up to form a small cone called stigma. This pressure results in rupture of part of the wall of the mature Graafian follicle with liberation of the oocyte into the peritoneal cavity.

The liberated oocyte is surrounded by the zona pellucida, corona radiata and some of the cumulus oophorus cells is picked up by the fallopian tube. The oocyte remains viable for a maximum of 24 hours, after which it undergoes autolysis.

The follicular fluid with some blood from the highly vascular theca interna is expelled into the peritoneal cavity.

The follicular antrum is filled with a blood clot. The remaining granulosa and theca interna cells form the corpus luteum.

The Corpus Luteum:

- After ovulation and under the effect of LH, the granulosa and theca interna cells undergo luteinization to form a temporary endocrine organ called corpus luteum which is embedded in the ovarian cortex. It produces high levels of progesterone and moderate levels of estrogen.

Formation and structure of corpus luteum:

As the result of the release of the follicular fluid, the follicle collapse, so the wall of the corpus luteum is folded.

Some of the blood flows into the follicular cavity where it forms a blood clot which is gradually removed. In animals this central blood clot is present to form the corpus hemorrhagicum.

Granulosa cells do not divide, but markedly increase in size, forming the main bulk of corpus luteum and are now called granulosa-lutein cells. These large steroid-secreting cells become rich in sER, mitochondria and many lipid droplets to secrete progesterone hormone. They also contain lipochrome pigments in their cytoplasm which produces the yellowish color of the corpus luteum in fresh sections.

The theca interna cells give rise to the theca-lutein cells which are smaller, deeply stained than granulosa-lutein cells and are located in the outer folds of the corpus luteum cells. They secrete estrogen hormone and show the EM features of steroid secreting cells but with fewer lipid droplets.

Corpus luteum has a rich vascular network to carry these hormones to all parts of the body.

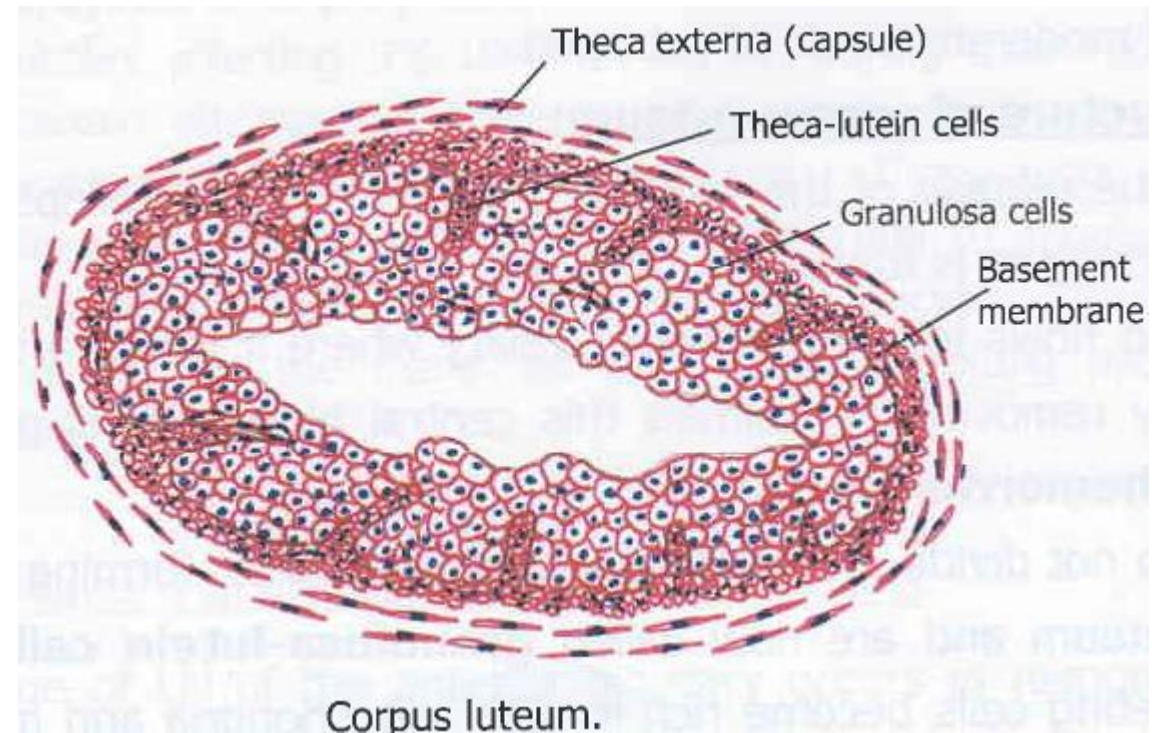
Fate of the corpus luteum: It depends on whether pregnancy occurs or not:

a. **If no pregnancy occurs:** No further hormonal stimulation takes place with the drop in LH level, the corpus luteum is called corpus luteum of menstruation and it degenerates within 10-12 days. Its cellular components are phagocytosed by macrophages and the fibroblasts invade the area producing a dense white C.T. body called corpus albicans (white body).

b. If pregnancy occurs: The trophoblast cells of the implanted embryo secrete a hormone called human chorionic gonadotropin (HCG) whose action is similar to LH, This HCG stimulates further growth of the corpus luteum to secrete progesterone and estrogen to maintain the integrity of the uterine mucosa and glands important for nutrition of the embryo, until the placenta becomes fully functioning. This is called corpus luteum of pregnancy and it lasts about 4-5 months, after that it degenerates and is replaced by the corpus albicans.

N.B.: Types of corpora in the ovary

- 1) Corpus hemorrhagicum.
- 2) Corpus luteum of menstruation.
- 3) Corpus luteum of pregnancy.
- 4) Corpus albicans.



Ovogenesis

It is the process responsible for female gamete production. Primordial germ cells (oogonia) develop in the endoderm of the yolk sac and then migrate to the developing ovary in the embryo. Ovogenesis includes three phases:

1. **Proliferation:** In the ovary of the developing embryo, the oogonia divide by mitosis to give rise to a large number of oogonia during the 1st trimester of pregnancy (about 7 millions in both ovaries).

2. Growth: During the 2nd trimester of pregnancy, mitotic division stops. The oogonia grow, increase in size and are called now the primary oocyte. These primary oocytes enter the prophase of the 1st meiotic division where they are arrested and do not progress to the other stages of meiosis. By the 7th month of pregnancy, most oogonia have become primary oocytes. However, many oocytes are lost and undergo atresia such that at puberty both ovaries contain about 300,000 primary oocytes only.

3. Maturation: At puberty and just before ovulation, the primary oocyte ($2N$) continues the 1st meiotic division to give the 2ry oocyte(N) and a 1st polar body.

After ovulation, the 2ry oocyte enters the 2nd meiotic division (which will be completed only after fertilization) to give the mature ovum and a 2nd polar body.

Fallopian Tubes (Oviducts)

They are two muscular tubes of great mobility; each is about 10-12 cm in length.

They are responsible for conveying the ova from the ovaries to the uterus. They are also the site of fertilization.

Anatomically, each is formed of four segments which are different histologically in amount of the muscles, degree of folding of their epithelium and percentage of ciliated cells:

1. Intramural segment: a short part which passes through the wall of the uterus to open into it.
2. Isthmus: narrow, short, thick-walled segment.
3. Ampulla: thin-walled segment where fertilization takes place.
4. Infundibulum: has finger-like extensions called the fimbriae and opens into the peritoneal cavity.

Histologically, the wall of the oviduct is formed of three layers:

1. Mucosa:

It has many folds.

It is composed of simple columnar, partially ciliated epithelium lying on a C.T. lamina propria.

a) Ciliated cells: Their cilia beat towards the uterus to push the ovum. At time of ovulation they become taller and more ciliated.

b) Non-ciliated (secretory) cells: They produce watery fluid which has a nutritive function for the oocyte and helps in capacitation of the spermatozoa.

2. Musculosa:

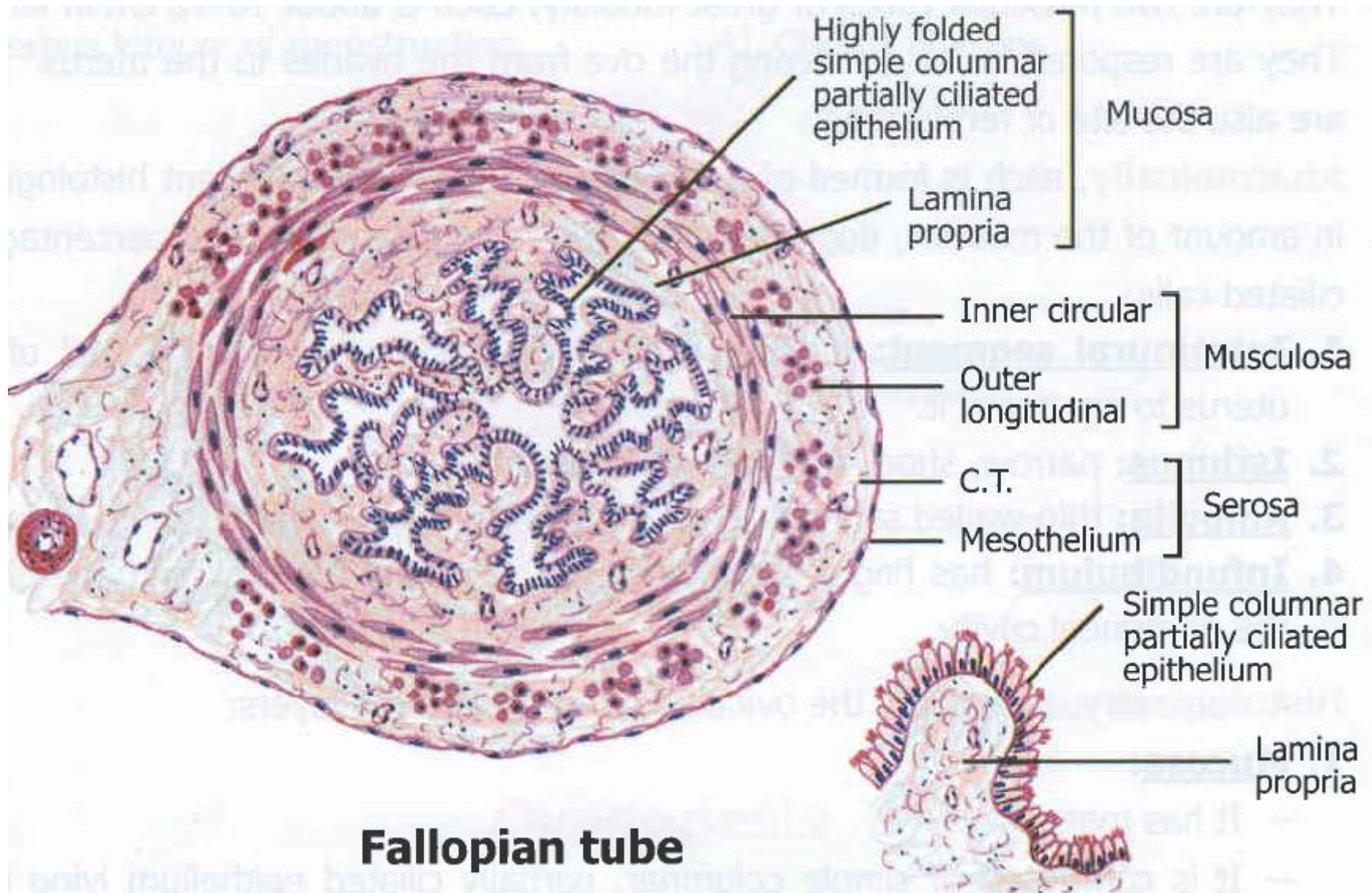
Formed of inner circular and outer longitudinal smooth muscle layer.

Their peristalsis plays a greater role than the cilia in pushing the ovum (fertilized or not) towards the uterus.

3. Serosa: Loose C.T. covered with simple squamous mesothelium.

Modifications in the different anatomical parts of the oviduct:

- * The mucosal folds are most numerous in the ampulla.
- * The ciliated cells are most numerous in the infundibulum.
- * The secretory cells are most numerous in the intramural segment.
- * The musculosa is thickest in the isthmus and intramural parts.



The Uterus

A pear-shaped organ which receives the fallopian tubes in its upper part and its lower part opens into the vagina.

It is divided into three parts: Fundus, body, and cervix. The fundus and body are histologically similar, while the cervix is different.

Fundus & Body of Uterus

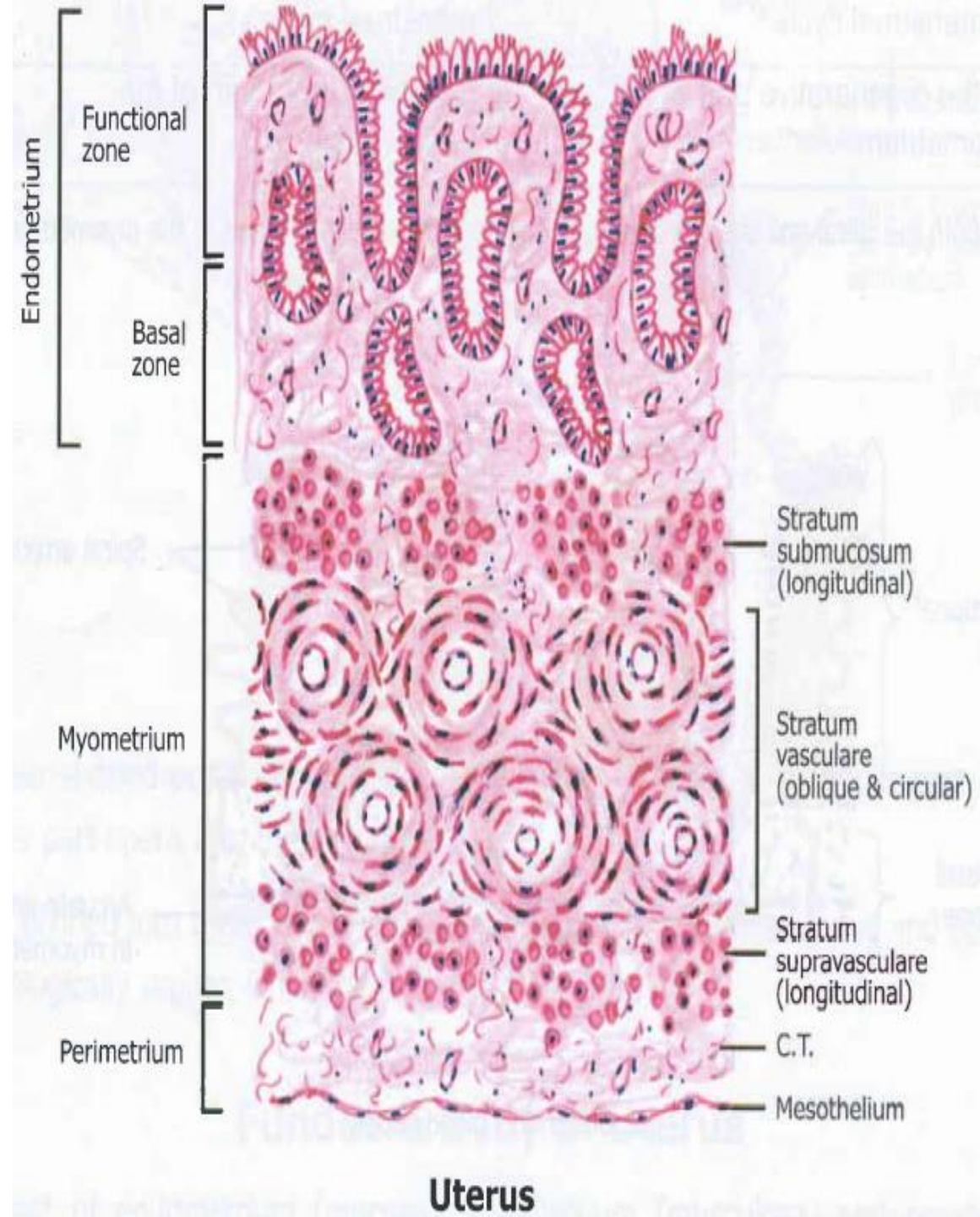
Consist of endometrium (mucosa), myometrium (musculosa) and perimetrium (serosa)

1. Endometrium:

Lined by simple columnar partially ciliated epithelium (secretory and ciliated cells), resting on a C.T. lamina propria.

It also contains endometrial (simple tubular) glands lined by the same surface epithelium but with very few ciliated cells.

Functionally, the endometrium is divided into two zones:



Functional zone	Basal zone
It is superficial part of the endometrium	It is deep part of endometrium adjacent to the myometrium
Contains the surface epithelium + the upper part of lamina propria + the superficial part of the endometrium.	Contain the deep part of lamina propria + the basal part of the endometrium.
Supplied by spiral arteries	Supplied by straight arteries
Undergoes marked changes during the menstrual cycle	Remained unchanged during the menstrual cycle
It is the reparative part of the endometrium	It is reserve part of the endometrium

2. Myometrium:

- It is the thickest layer of the uterus.
- It is hormone-sensitive and undergoes both hyperplasia (increase in cell number) and hypertrophy (increase in cell size) during pregnancy. It returns to its normal size (involution) within few weeks after delivery.
- With cessation of hormonal stimuli after menopause smooth muscle fibers undergo atrophy, while the fibrocollagenous tissue between the muscles become very obvious.
- It is composed of three poorly-defined layers of smooth muscles:
 - a) Stratum submucosum: longitudinal layer of muscles.
 - b) Stratum vasculare: of circular and oblique muscles arranged in 8- shaped figures enclosing large blood vessels.
 - c) Stratum supravasculare: longitudinal layer of muscles.

3. Perimetrium: Loose C.T. covered by simple squamous mesothelium.

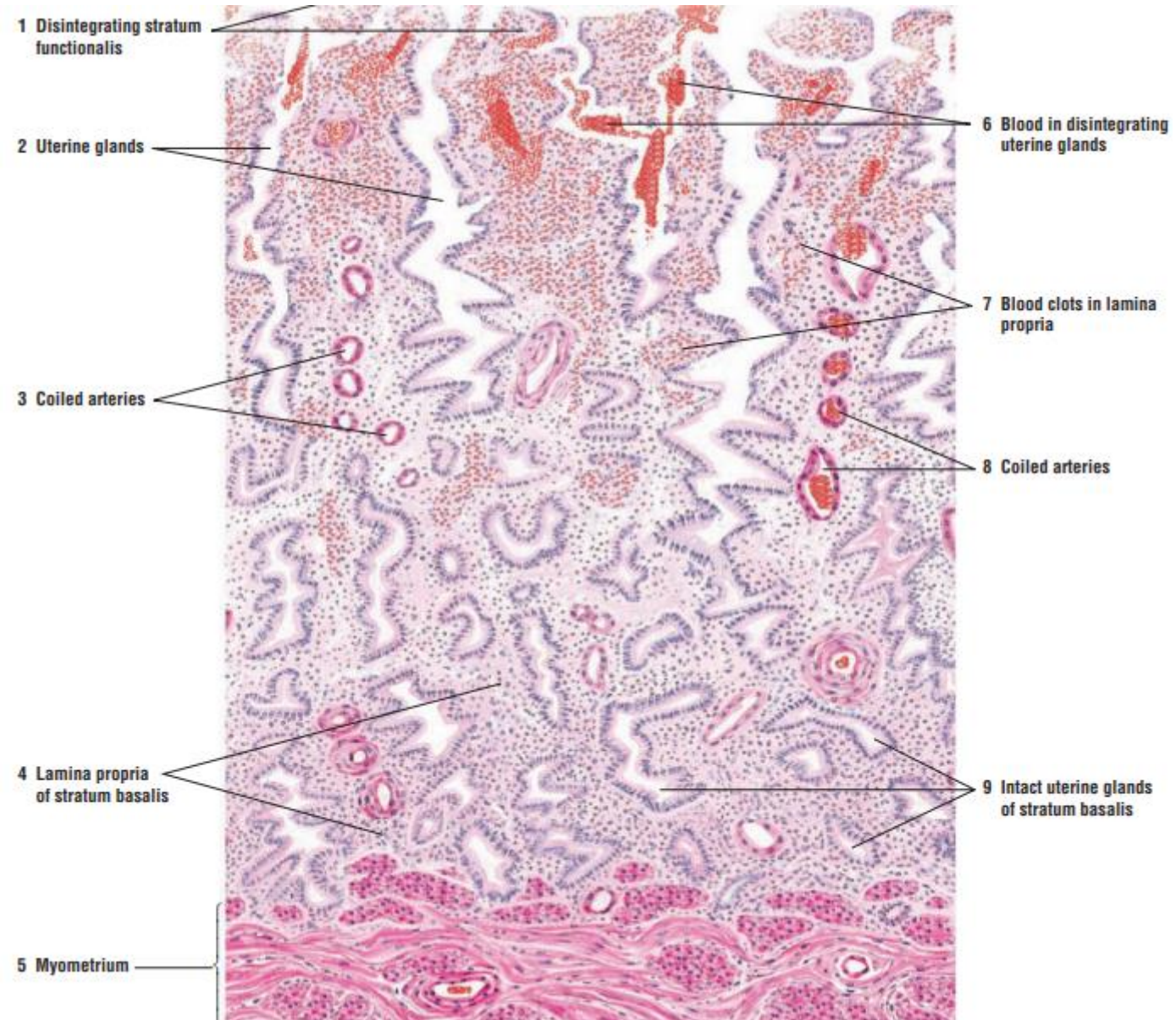
The Menstrual Cycle:

- The menstrual cycle starts at the age between 12-15 years and continues till age of about 45-50 years.
- At puberty the ovarian hormones (estrogen and progesterone), under the control of FSH and LH from the anterior pituitary, causes the endometrium to undergo cyclic structural changes during the menstrual cycle.
- The duration of the menstrual cycle is variable and averages about 28 days.
- The menstrual cycle includes three phases. Its beginning is taken as the day when the menstrual bleeding starts.

1. Menstrual (destructive) phase: (from 1st to 5th day)

When fertilization does not occur, the corpus luteum stops functioning 10-12 days after ovulation. As a result, levels of estrogen and progesterone in blood drops rapidly causing constriction of the spiral arteries supplying the functional zone, producing ischemia, As a result death of the walls of the spiral arteries and part of the functional zone occurs. The blood vessels rupture and bleeding begins with shedding of the dead functional zone leaving the basal zone (about 0.5 mm thick).

The basal zone acts as a cellular reserve from which the functional zone regenerates in the following phase.



2. Proliferative (follicular estrogenic) phase: (from 5th to 14th day)

The growing ovarian follicles begin to secrete estrogen under control of pituitary FSH. Estrogen stimulates the mitotic activity of the cells in the basal zone of the endometrium resulting in endometrial proliferation and regeneration.

The endometrium resumes its covering simple columnar partially ciliated epithelium.

The regenerated glands are straight with narrow lumens and their cells show no secretory function.

At the end of this phase, the endometrium is about 2-3 mm thick.

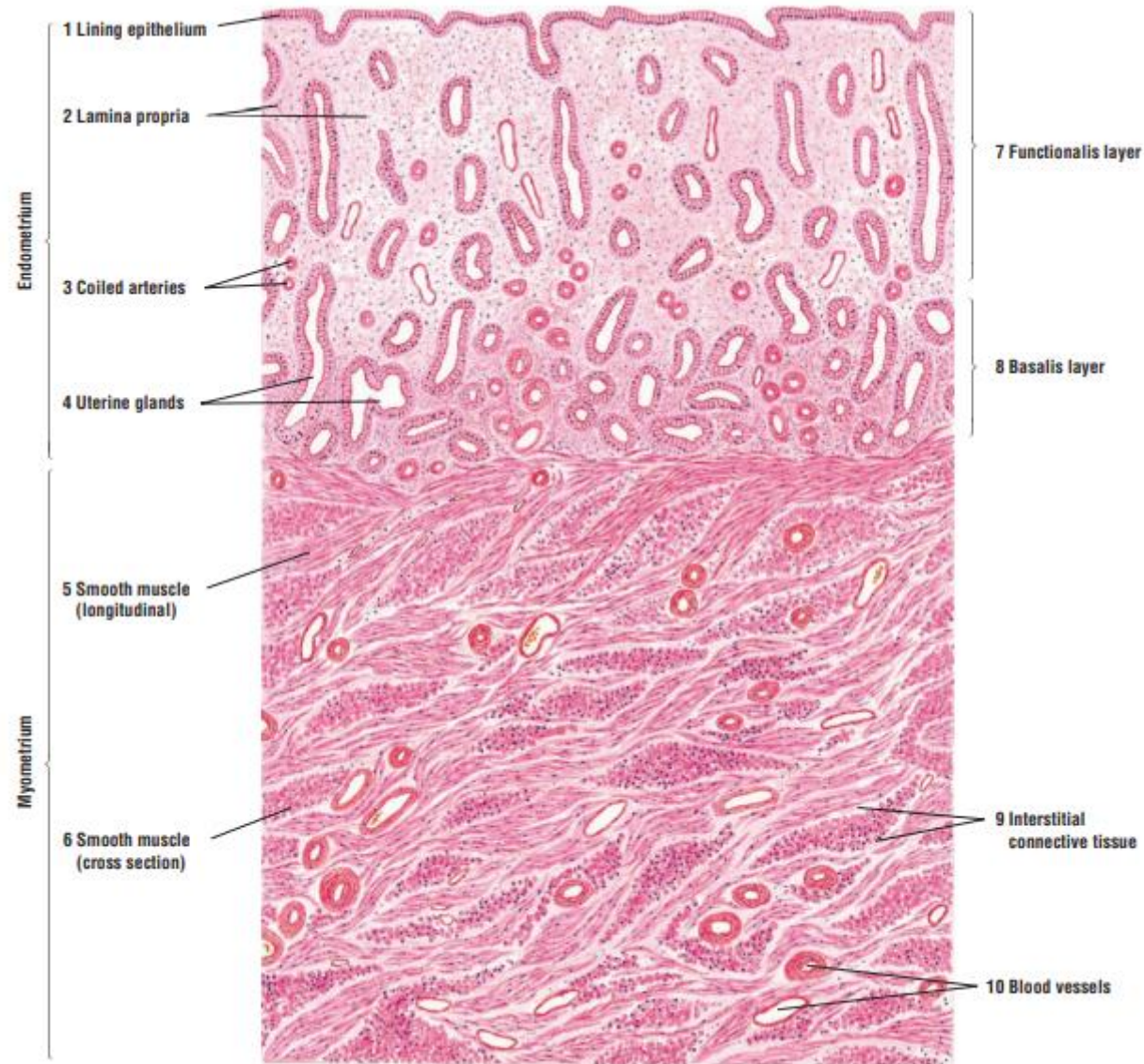


FIGURE 19.12 ■ Uterine wall: proliferative (follicular) phase. Stain: hematoxylin and eosin.

3. Secretory (Luteal-progestational) phase: (from 14th day till onset of next bleeding)

- It starts after ovulation under the effect of progesterone secreted by the corpus luteum, controlled by pituitary LH

It includes the following changes:

- a) Endometrial glands: become long, highly tortuous. In early secretory phase, the cells of the endometrial glands accumulate glycogen in their basal parts. In late secretory phase, the glycogen is accumulated in the apical parts of the cells and the lumens of the glands are distended with secretion.
- b) Endometrial thickness: increases reaching its maximum (5 mm).
- c) Spiral arteries. elongate and become highly coiled and congested,
- d) Stroma (surrounding CT of lamina propria) become edematous and the stromal cells enlarge and show features of protein synthesizing cells and are called decidual cells. These changes are referred to as decidual reaction.

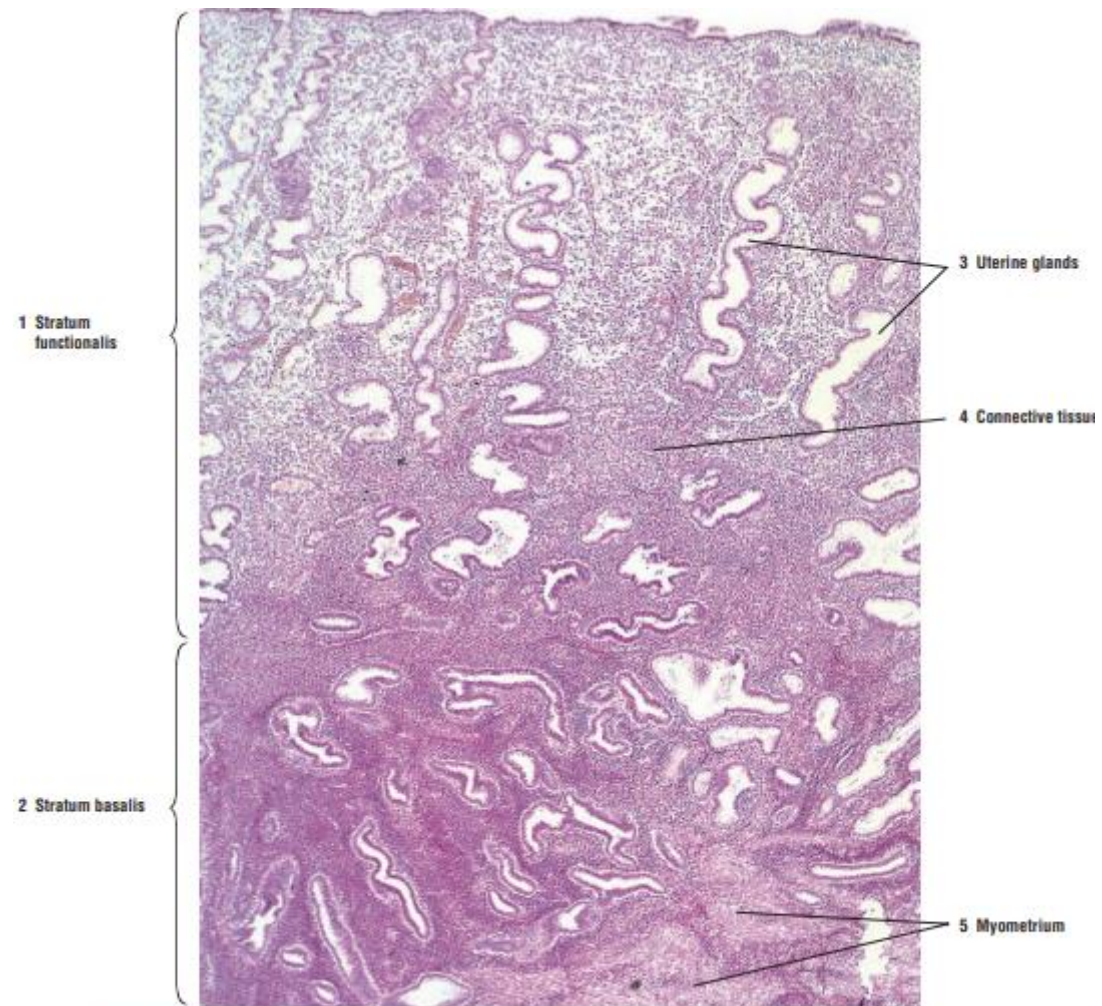
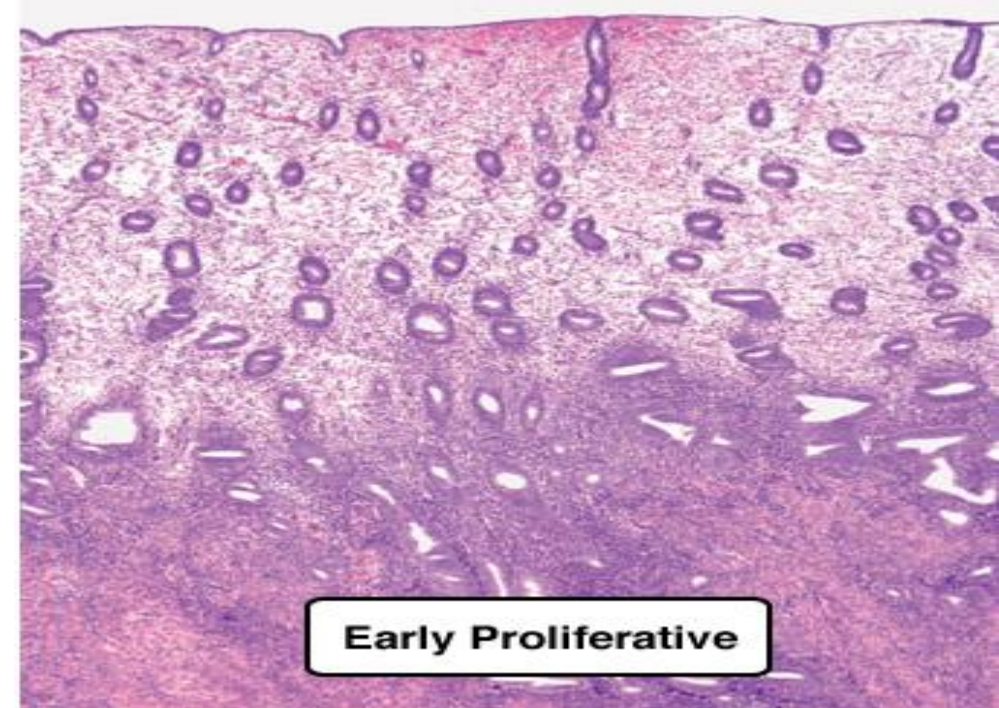


FIGURE 19.14 ■ Uterine wall (endometrium): secretory (luteal) phase. Stain: hematoxylin and eosin. $\times 10$.



Cervix of the Uterus

- It is the lower cylindrical part of the uterus (3 am long) that protrudes into the vagina.
- The junction between the cervix and the uterine body is called the internal os. The cervical lumen is narrow (1 cm in diameter), and opens into the vaginal cavity at the external os.
- Histologically, it is formed of mucosa lying on a surrounding stroma:

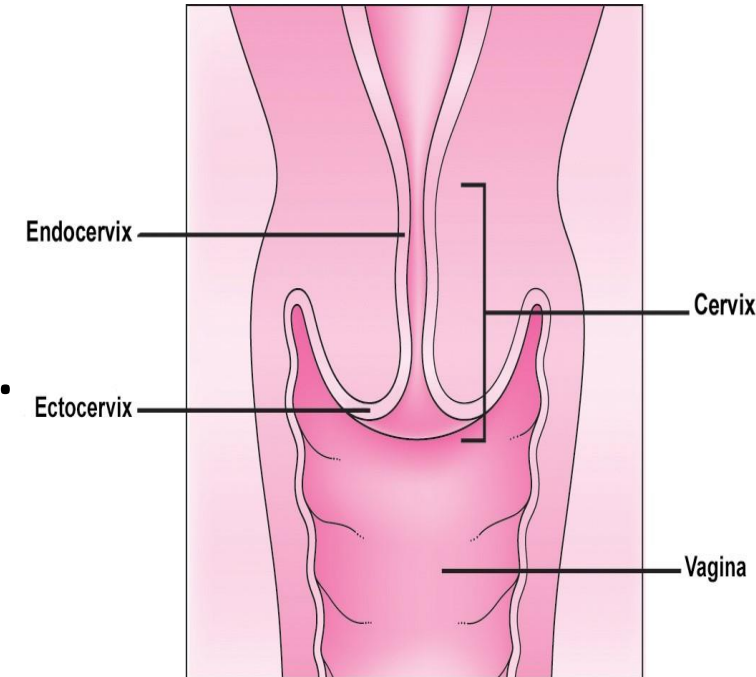
1. Mucosa of the cervix:

a) The endocervix:

It is the lining of the cervical canal.

It is lined by mucus-secreting simple columnar cells.

It contains mucous-secreting glands which are branched tubuloalveolar glands and lined by simple columnar cells.



b) The ectocervix:

It is the external aspect of the cervix that bulges into the lumen of the vagina

It is covered by non-keratinized stratified squamous epithelium.

N.B. The cervical mucosa does not undergo remarkable changes and does not shed during the menstrual cycle.

2. Stroma of the cervix.

- It is formed of dense C.T. with few smooth muscle fibers. This makes the cervix firm and rubbery.

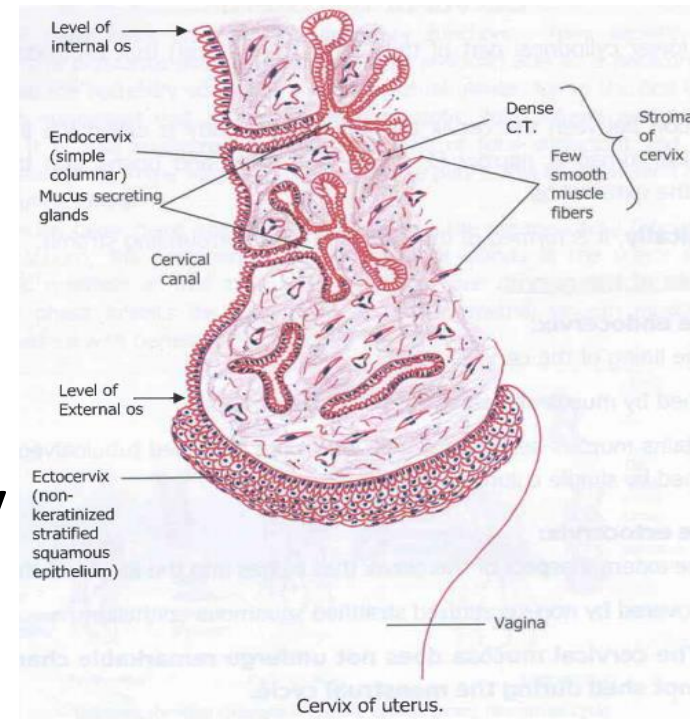
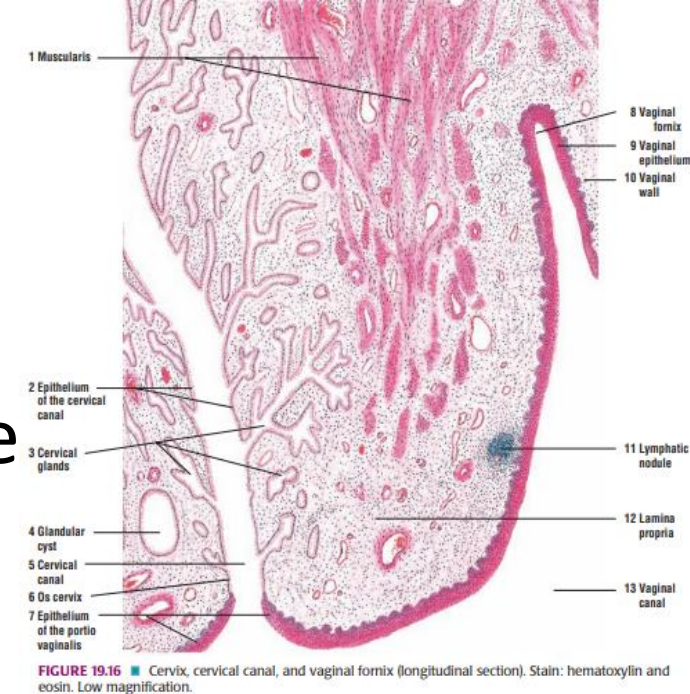
During labour, under control of relaxin hormone from the placenta, cervical softening and dilatation occurs as a result of separation and the haphazard arrangement of the collagen fibers of the cervical stroma instead of their parallel arrangement (a process known as collagenolysis).

Cervical mucus:

- It plays a significant role in fertilization of the oocyte.

. During the proliferative phase of the menstrual cycle and at time of ovulation, the cervical mucus is thin, watery and abundant to facilitate the movement of the spermatozoa to penetrate the uterus.

After ovulation (in the secretory phase), or if pregnancy occurs, the cervical mucus becomes more viscous and scanty thus preventing passage of spermatozoa as well as microorganisms into the body of the uterus.



The Vagina

It is a fibromuscular tube (7-9 cm long), which is capable of marked distension. It consists of three layers: mucosa, muscularis and adventitia.

1.Mucosa: formed of epithelium and lamina propria.

a. Epithelium:

Non-keratinized stratified squamous epithelium.

- Under the effect of estrogen, the vaginal epithelium synthesizes and accumulates great amounts of glycogen.
- When the vaginal cells desquamates, this glycogen is deposited into the vaginal lumen, where bacteria (lactobacilli) breakdown this glycogen to form lactic acid

The formed lactic acid results in an acidic pH in the vaginal lumen which provides protection against harmful bacteria and fungi (candida albicans),

b. Lamina propria: It is formed of loose C.T. very rich in elastic fibers.

2. Musculosa: It is formed of inner circular and outer longitudinal smooth muscle fibers.

3. Adventitia: It is formed of dense C.T. rich in elastic fibers.

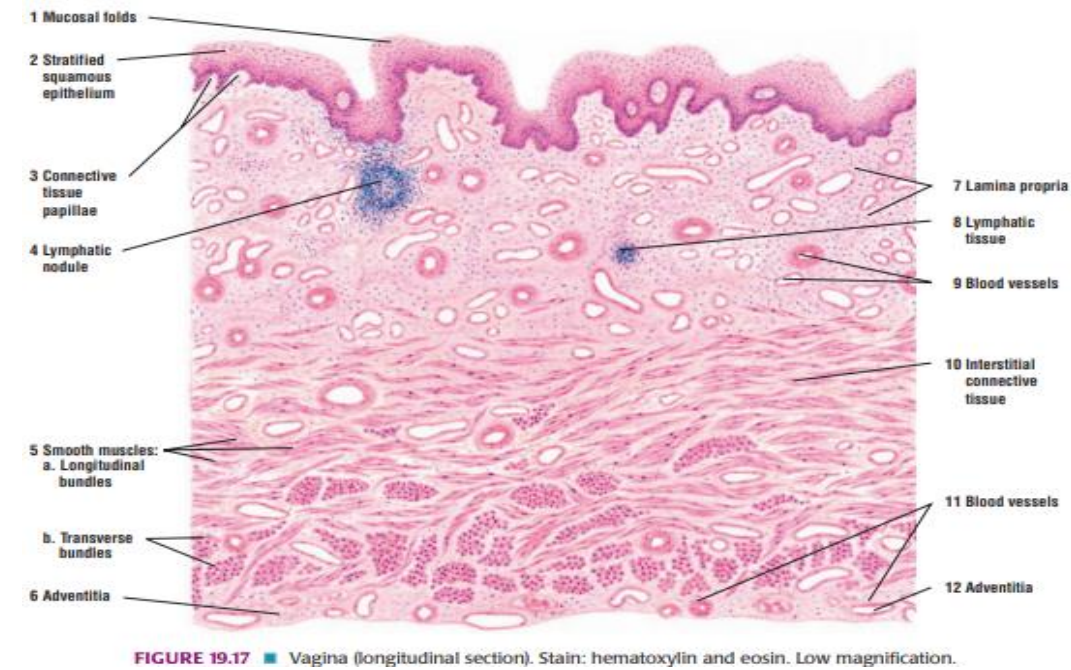
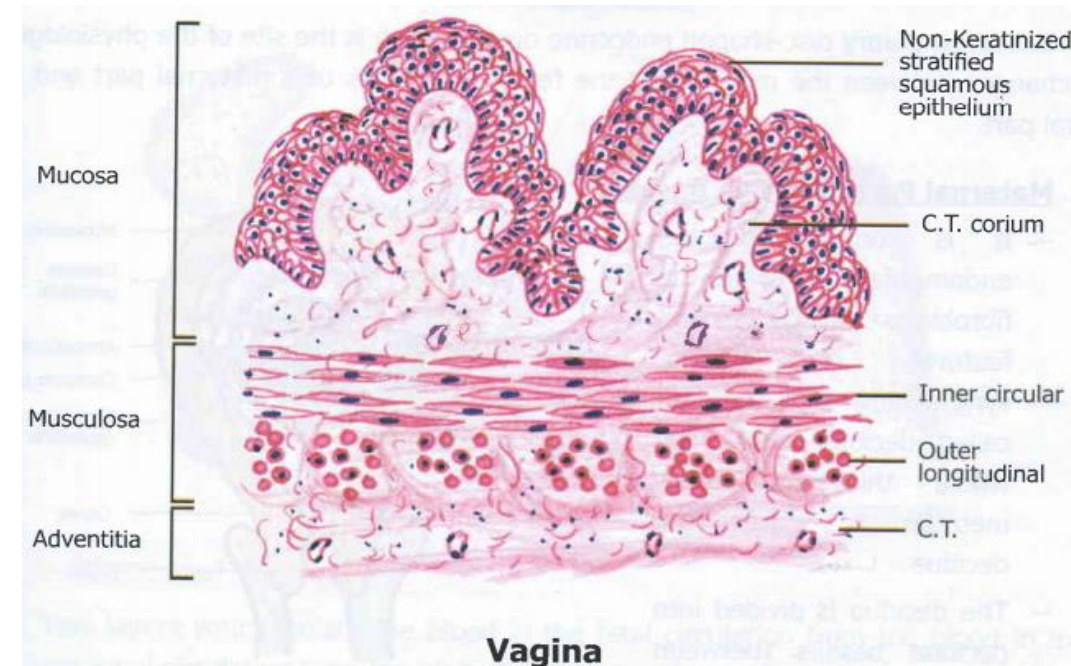


FIGURE 19.17 ■ Vagina (longitudinal section). Stain: hematoxylin and eosin. Low magnification.



The External Genitalia

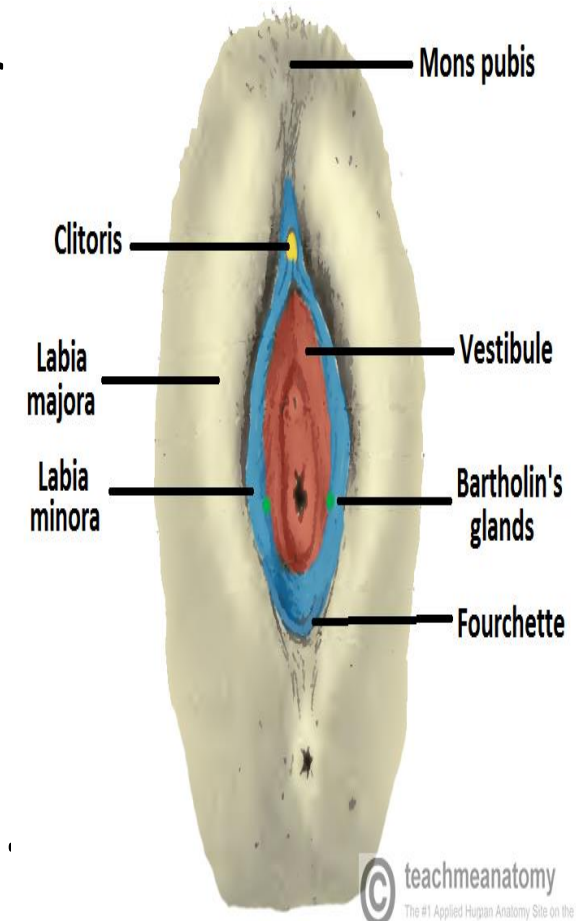
Labia Majora:

They are two folds of skin containing large quantity of adipose tissue and a thin layer of smooth muscles. Their inner surface has no hair follicles, while their external surface is covered by hairy skin with sebaceous and sweat glands.

Labia Minora:

They are two folds of skin (with no hair follicles) with a core of spongy C.T. rich in elastic fibers. Sebaceous and sweat glands are present on its inner and outer surfaces.

The space between the two labia minora is called the vestibulum.



Clitoris: It is formed of two corpora cavernosa (erectile vascular C.T.), which are covered by thin skin with no hair follicles, sebaceous or sweat glands.

Hymen: It is a perforated membrane of C.T. at the lower end of the vagina, and is covered by stratified squamous epithelium on both sides. It is regarded as a junction between external and internal genitalia.

Bartholin's gland: They are situated on either sides of the vestibulum of the labia minora. They are mucus-secreting glands.

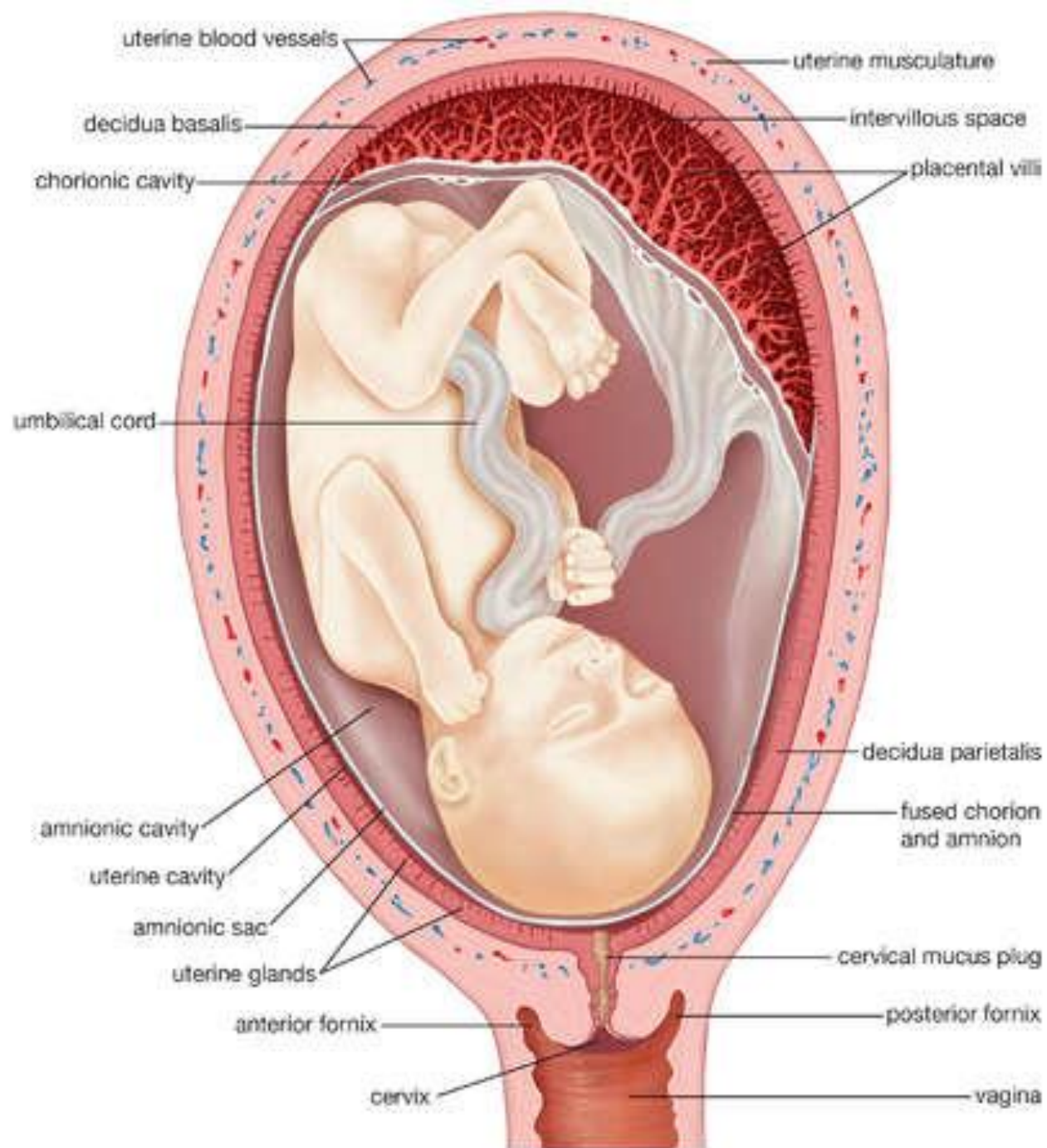
N.B.: External genitalia, especially the clitoris, are abundantly supplied by sensory nerve endings including Meissner's and Pacinian corpuscles for sexual arousal.

The Placenta

It is a temporary disc-shaped endocrine organ, which is the site of the physiologic exchanges between the mother and the fetus. It consists of a maternal part and a fetal part.

A. Maternal Part (Decidua Basalis):

- It is formed by the endometrial C.T. where the fibroblasts enlarge, exhibit features of protein synthesizing cells and are basalis called decidual cells. The whole thickened endometrium is called the decidua.
- The decidua is divided into decidua basalis (between embryo and myometrium), decidua capsularis (between embryo and lumen of uterus) and decidua parietalis (endometrium lining the rest of uterine cavity).
- The decidua basalis is the most important part that enters in the formation of the placenta.



B. Fetal Part (Chorionic Villi):

- They arise as finger-like projections from the outer wall of the blastocyst (stage at which the embryo arrives at the uterus). They branch and anastomose to become embedded in the decidua basalis. They are separated by intervillous spaces which contain the maternal blood.
- Each chorionic villus consists of:
 1. Central core of C.T. containing fetal blood vessels. The C.T. contains large motile macrophages (Hofbauer cells).
 2. Trophoblast, which is an epithelial covering consisting of two layers:

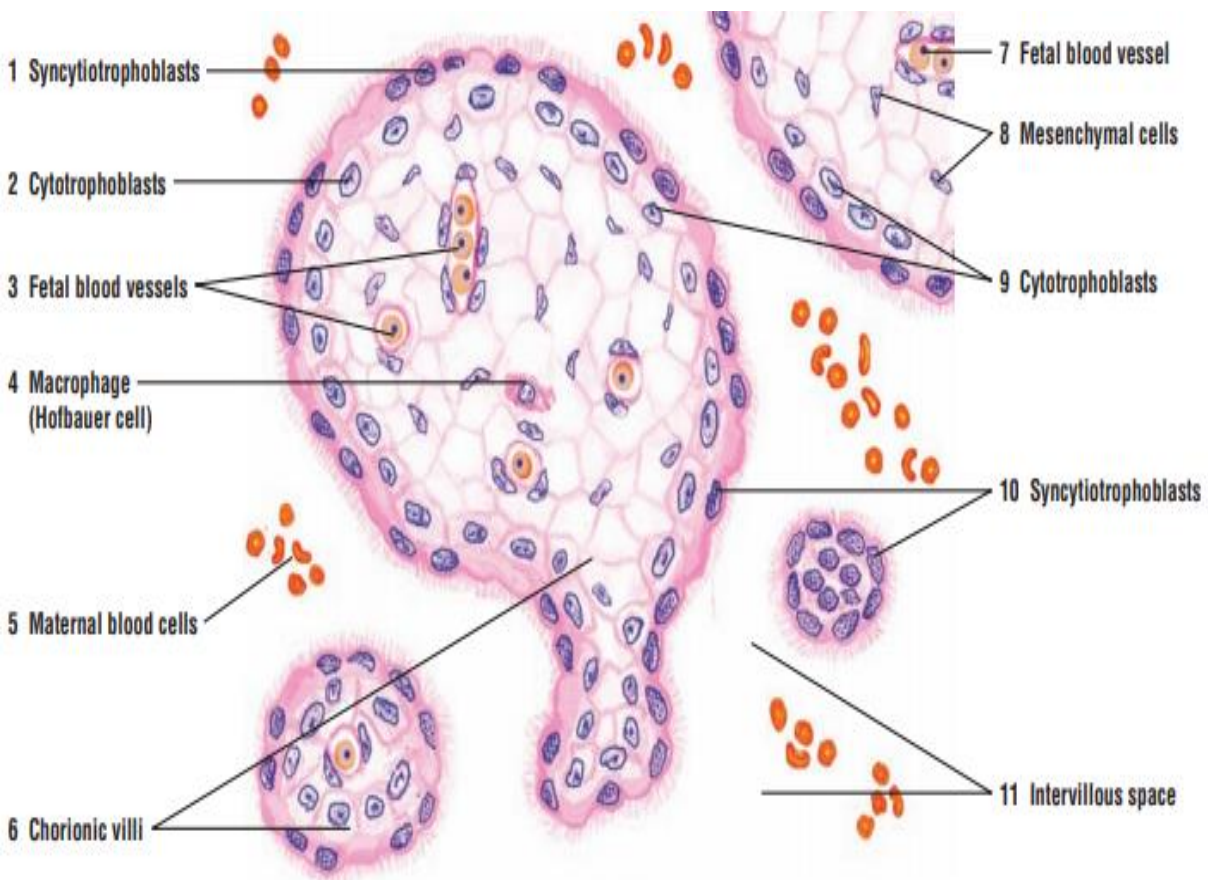


FIGURE 19.22 ■ Chorionic villi: placenta during early pregnancy. Stain: hematoxylin and eosin. High magnification.

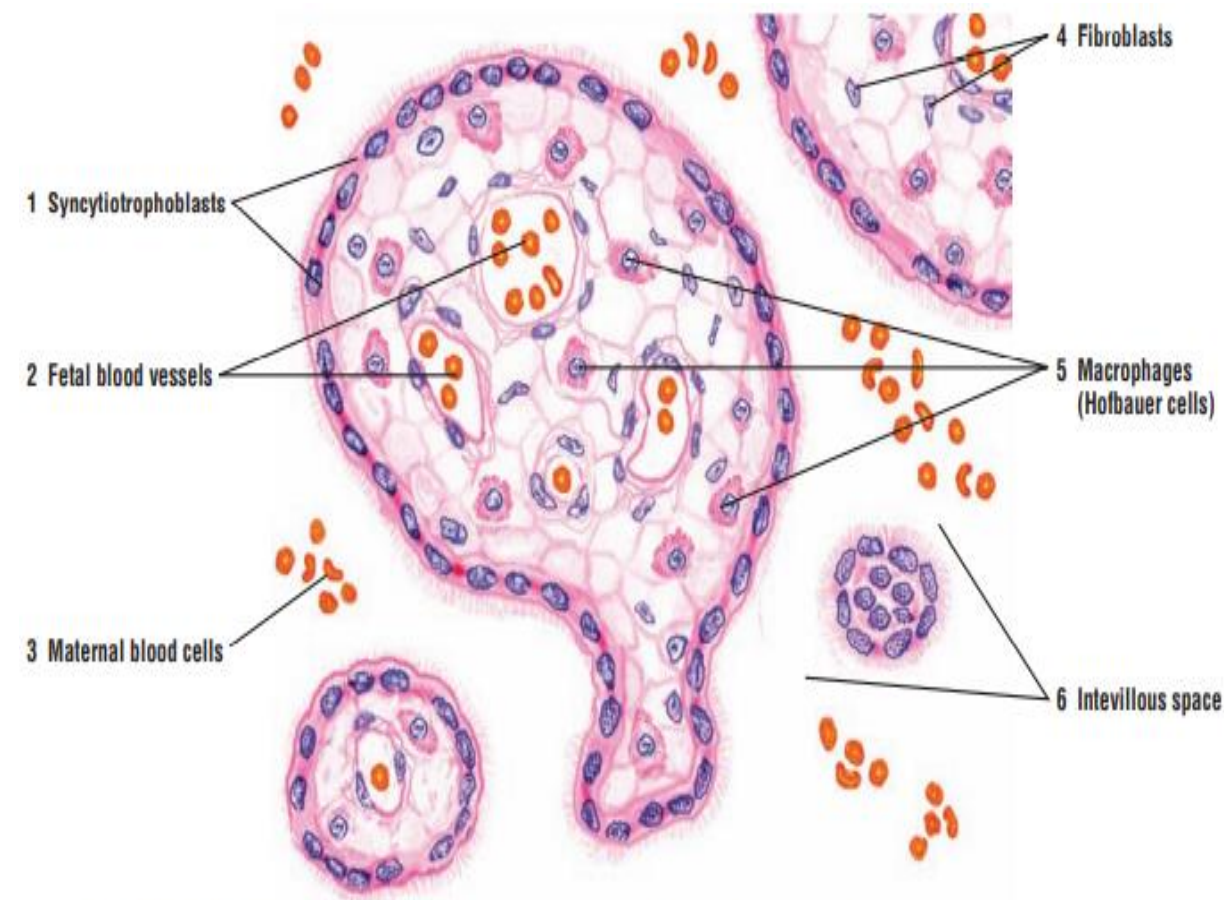


FIGURE 19.23 ■ Chorionic villi: placenta at term. Stain: hematoxylin and eosin. High magnification.

a. Inner cytotrophoblast: a continuous single layer of cuboidal cells with pale-staining cytoplasm. The cytotrophoblast disappears by the end of the 4th month of pregnancy.

b. Outer syncytiotrophoblast: a thin layer of deeply stained cells with no clear cell boundaries, thus appearing as a thin multinucleated syncytial layer. The syncytiotrophoblast has numerous surface microvilli to invade the decidua basalis.

The Placental Barrier:

- This layers which isolate the blood in the fetal circulation from the blood in the maternal circulation form the placental barrier.
- It is composed of:
 - The trophoblast (syncytiotrophoblast and cytotrophoblast in the 1st 4months of pregnancy, and syncytiotrophoblast only in the last five months).
 - Basement membrane of the trophoblast.
 - C.T. core containing Hofbauer cells.
 - Basement membrane of fetal capillary.
 - Endothelium of fetal capillary.

Functions of the Placenta:

1. It allows the passage of nutrients, oxygen, antibodies and hormones from mother to the fetus.
2. It removes waste products and carbon dioxide.
3. Endocrine function: the syncytiotrophoblast secretes the following:
 - a. Human chorionic gonadotropin: responsible for maintaining the corpus luteum of pregnancy after cessation of LH stimulus from the pituitary gland.
 - b. Human chorionic somatomammotropin: which has lactogenic and growth stimulating activity.
 - c. Estrogen and progesterone.

d. Chorionic thyrotropin (similar to TSH) and chorionic corticotropin (similar to ACTH).

e. Relaxin: responsible for the softening and dilatation of the cervix during labour.

4. Placental barrier function:

It prevents the passage of harmful microorganisms (bacteria) to the developing embryo.

It allows the passage of maternal immunoglobulins to the fetal circulation which passively immunizes the fetus against some bacteria.

