THE FEMALE REPRODUCTIVE SYSTEM

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The Ovaries

The ovaries have *two functions - "production" and ovulation of oocytes and the production and secretion of hormones.* The ovary is attached to the broad ligament by a short fold of peritoneum, called the *mesovarium* (or ligament of the ovary), through which vessels and nerves pass to the ovary and enter it at the hilus of the ovary.

The surface of the ovary is covered by a single layer of cuboidal epithelium, also called *germinal epithelium.* It is continuous with the peritoneal mesothelium. Fibrous connective tissue forms a thin capsule, the *tunica albuginea*, immediately beneath the epithelium.

the ovary is divided into an outer *cortex* and an inner *medulla*. The cortex consists of a very cellular connective tissue stroma in which the ovarian follicles are embedded. The medulla is composed of loose connective tissue, which contains blood vessels and nerves.
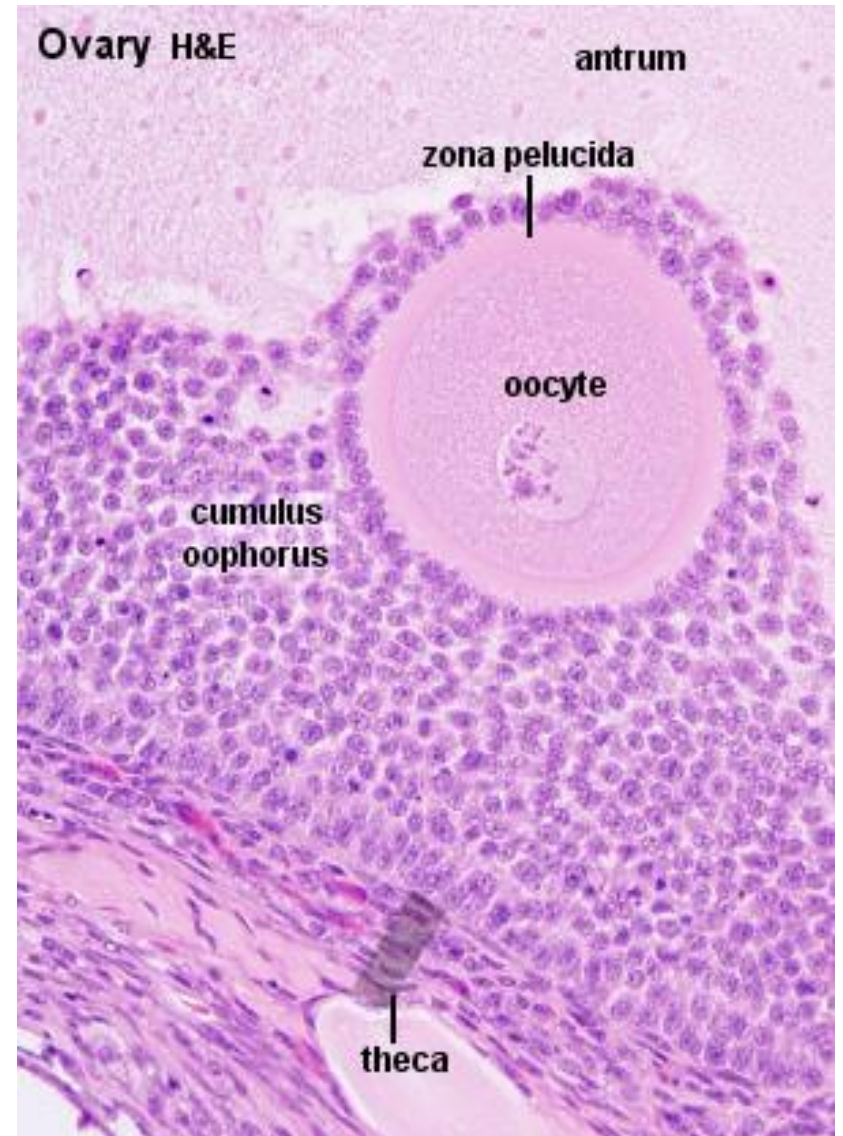
Ovarian Follicles

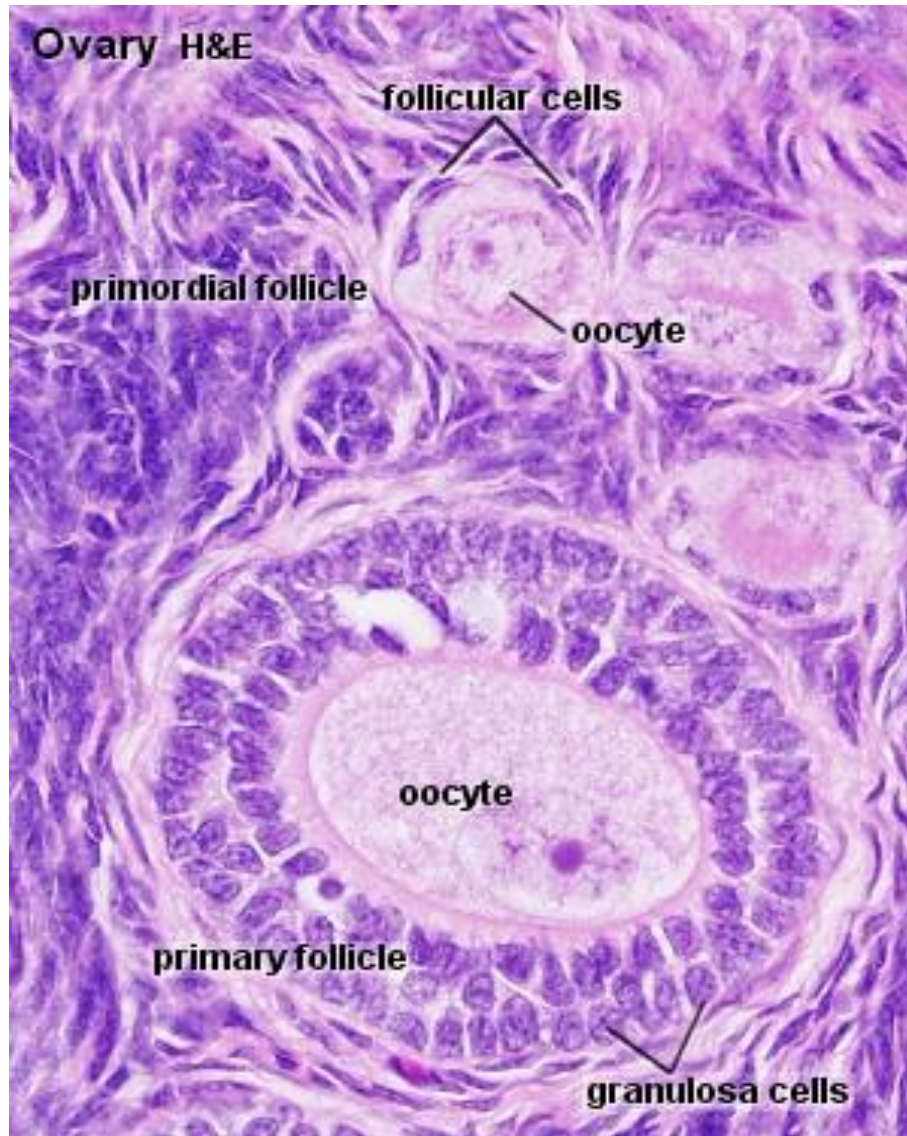Ovarian follicles consist of one oocyte and surrounding follicular cells. Follicular development can be divided into a number of stages.

Primordial follicles

are located in the cortex just beneath tunica albuginea. One layer of flattened follicular cells surround the oocyte (about 30 μm in diameter). The nucleus of the oocyte is positioned eccentric in the cell. It appears very light and contains a prominent nucleolus. Most organelles of the oocyte aggregate in the centre of the cell, where they form the vitelline body (probably not visible in any of the available preparations).

The primary follicle

is the first morphological stage that marks the onset of follicular maturation (Which hormone stimulates follicular maturation and where is this hormone produced?). The previously flattened cell surrounding the oocyte now form a cuboidal or columnar epithelium surrounding the oocyte. Their cytoplasm may have a granular appearance, and they are for this reason also called granulosa cells. The continued proliferation of these cells will result in the formation of a stratified epithelium (with a distinct basement membrane) surrounding the oocyte. The **zona pellucida** (glycoproteins between interdigitating processes of oocyte and granulosa cells) becomes visible. Parenchymal cells of the ovary surrounding the growing follicle become organised in concentric sheaths, the theca folliculi.

Ovary H&E

follicular cells

primordial follicle

oocyte

oocyte

primary follicle

granulosa cells

Ovary H&E

antrum

zona pelucida

oocyte

cumulus oophorus

theca

FEMALE REPRODUCTION

- Unlike males, who are able to produce sperm cells throughout their reproductive lives, females produce a finite number of egg cells.

- During early fetal development germ cells migrate into the ovaries and differentiate into oogonia

100 μm
Cat Ovary
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Secondary follicle

Small fluid-filled spaces become visible between the granulosa cells as the follicle reaches a diameter of about 400 µm. These spaces enlarge and fuse to form the follicular antrum, which is the defining feature of the secondary follicle. The oocyte is now located eccentric in the follicle in the cumulus oophorus, where it is surrounded by granulosa cells. The theca folliculi differentiates with the continued growth of the follicle into a theca interna and a theca externa. Vascularization of the theca interna improves, and the spindle-shaped or polyhedral cells in this layer start to produce oestrogens. The theca externa retains the characteristics of a highly cellular connective tissue with smooth muscle cells. The oocyte of the secondary follicle reaches a diameter of about 125 µm. The follicle itself reaches a diameter of about 10-15 mm.

The mature or tertiary or preovulatory or Graafian follicle

increases further in size (in particular in the last 12h before ovulation). The Graafian follicle forms a small "bump" on the surface of the ovary, the stigma (or macula pellucida). The stigma is characterised by a thinning of the capsule and a progressive restriction of the blood flow to it. Prior to ovulation the cumulus oophorus separates from the follicular wall. The oocyte is now floating freely in the follicular antrum. It is still surrounded by granulosa cells which form the corona radiata. The follicle finally ruptures at the stigma and the oocyte is released from the ovary.

OVARIES

- Each follicle consists of an immature egg called an oocyte
- Cells around the oocyte are called:
    - Follicle cells (one cell layer thick)
        - Stimulated to mature by FSH from the pituitary gland
    - Granulosa cells (when more than one layer is present)
    - Thecal cells: Cells in the ovarian stroma
- Thecal & granulosa cells work together to produce estrogen
- A protective layer of glycoprotein forms around the egg called the zona pellucida

FOLLICLE DEVELOPMENT

1. **Primordial follicle**: one layer of squamous-like follicle cells surrounds the oocyte
2. **Primary follicle:** two or more layers of cuboidal granulosa cells enclose the oocyte
3. **Secondary follicle:** has a fluid-filled space between granulosa cells that coalesces to form a central antrum
4. **Graafian follicle**: secondary follicle at its most mature stage that bulges from the surface of the ovary
5. **Corpus luteum** : ruptured follicle after ovulation

Atresia

Atresia is the name for the degenerative process by which oocytes (and follicles) perish without having been expelled by ovulation. Only about 400 oocytes ovulate - about 99.9 % of the oocytes that where present at the time of puberty undergo atresia. Atresia may effect oocytes at all stages of their "life" - both prenatally and postnatally. By the sixth month of gestation about 7 million oocytes and oogonia are present in the ovaries. By the time of birth this number is reduced to about 2 million. Of these only about 400.000 survive until puberty.

Atresia is also the mode of destruction of follicles whose maturation is initiated during the cyclus (10-15) but which do not ovulate. Atresia is operating before puberty to remove follicles which begin to mature during this period (none of which are ovulated). Given that atresia affects follicles at various stages of their development it is obvious that the process may take on quite a variety of histological appearances.
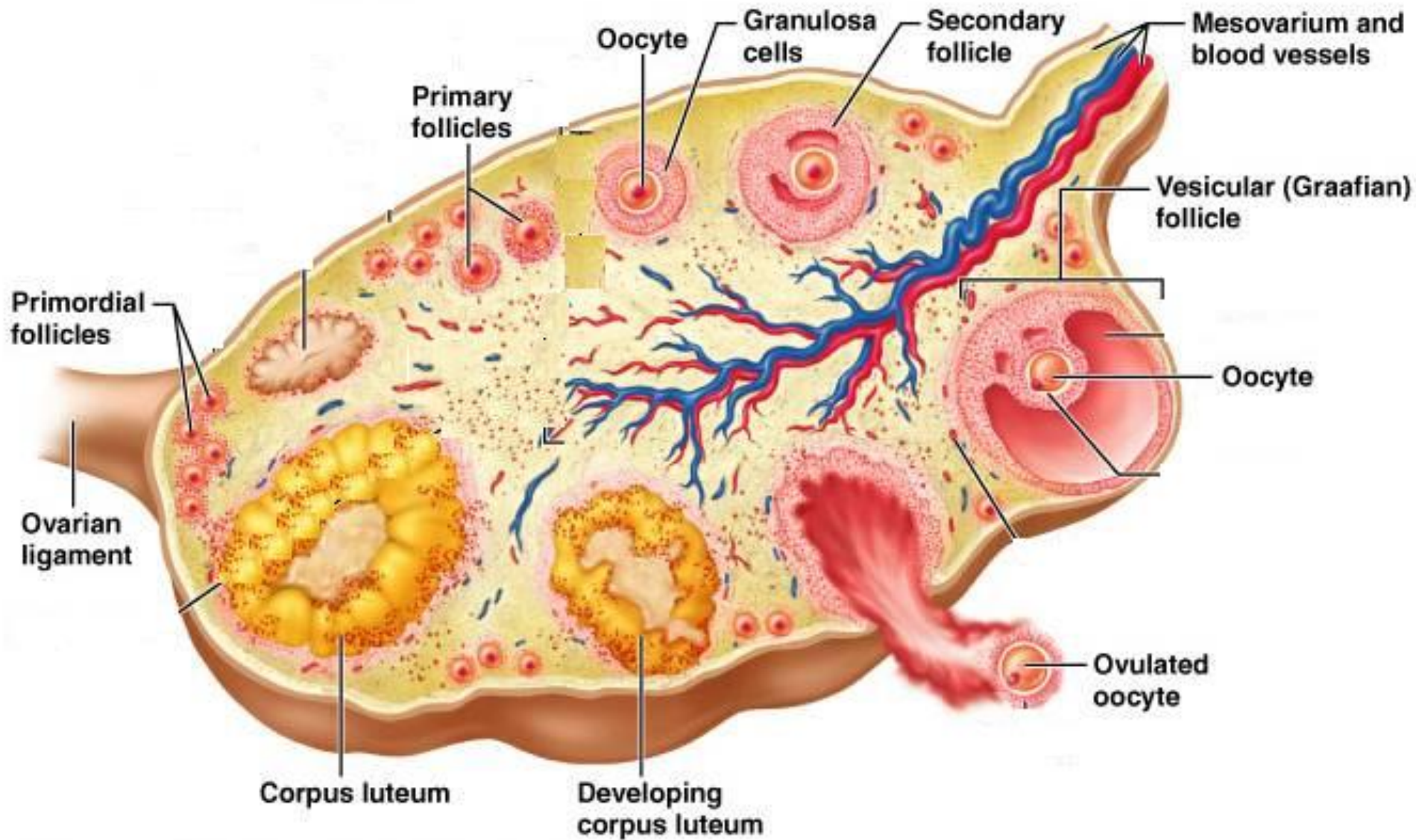
The Corpus luteum

The corpus luteum is formed by both granulosa cells and thecal cells after ovulation has occurred. The wall of the follicle collapses into a folded structure, which is characteristic for the corpus luteum. Vascularization increases and a connective tissue network is formed. Theca interna cells and granulosa cells triple in size and start accumulating lutein (Which hormone stimulates this process? Where is this hormone produced?) within a few hours after ovulation. They are now called granulosa lutein cells and theca lutein cells and produce **progesterone and oestrogens.**

Hormone secretion in the corpus luteum ceases within 14 days after ovulation if the oocyte is not fertilised. In this case, the corpus luteum degenerates into a corpus albicans - whitish scar tissue within the ovaries.
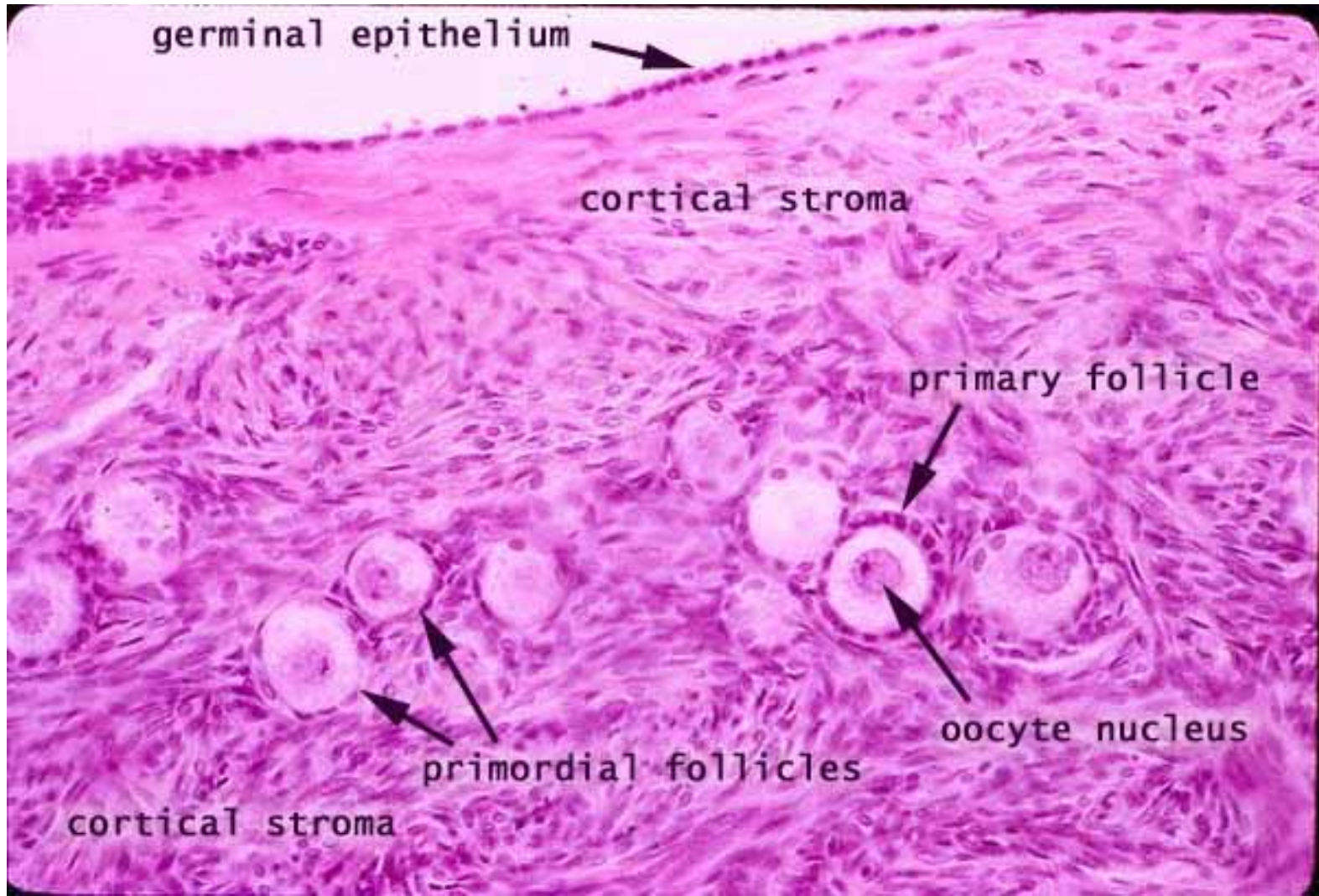
Hormone secretion continues for 2-3 month after ovulation if fertilisation occurs.
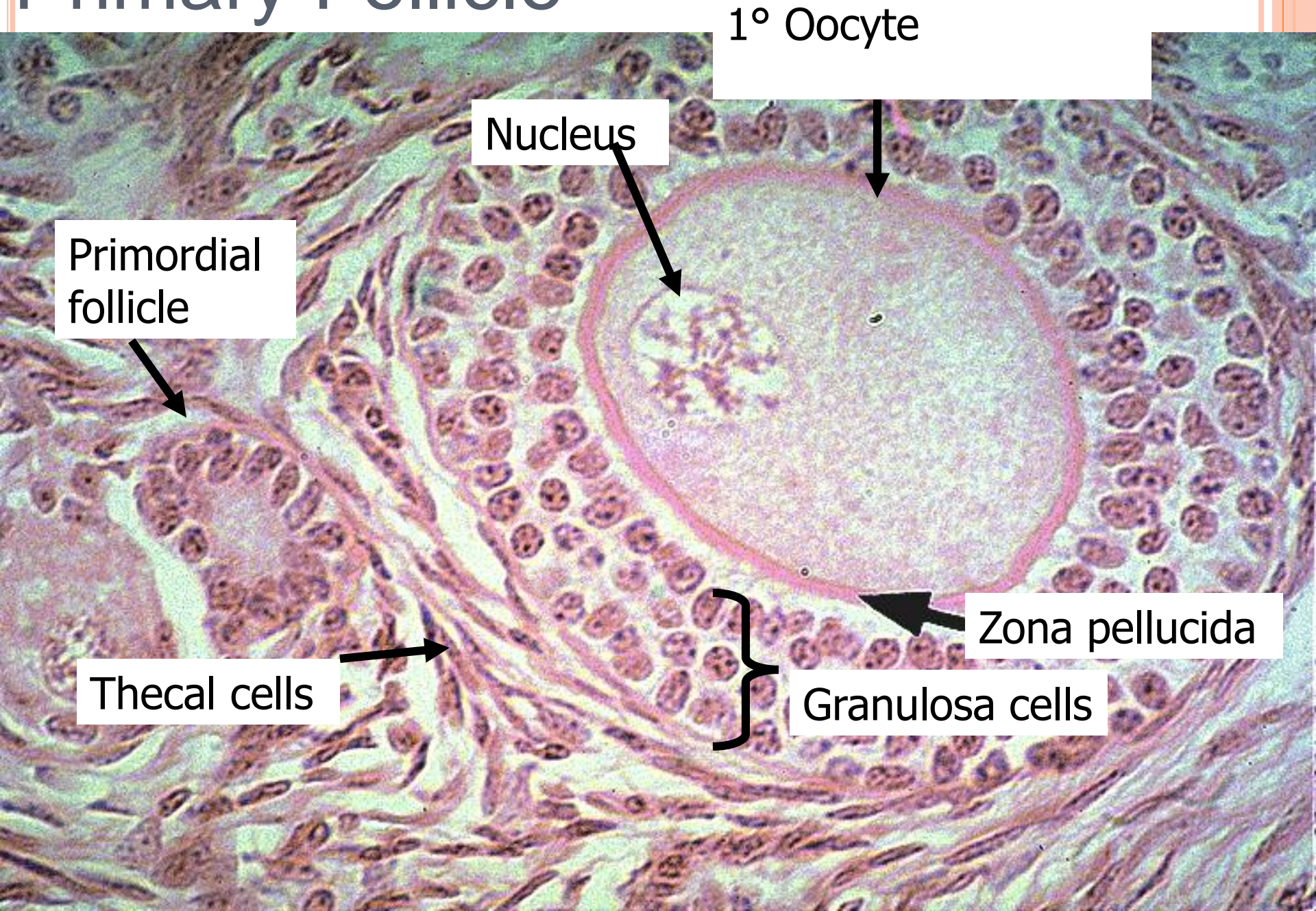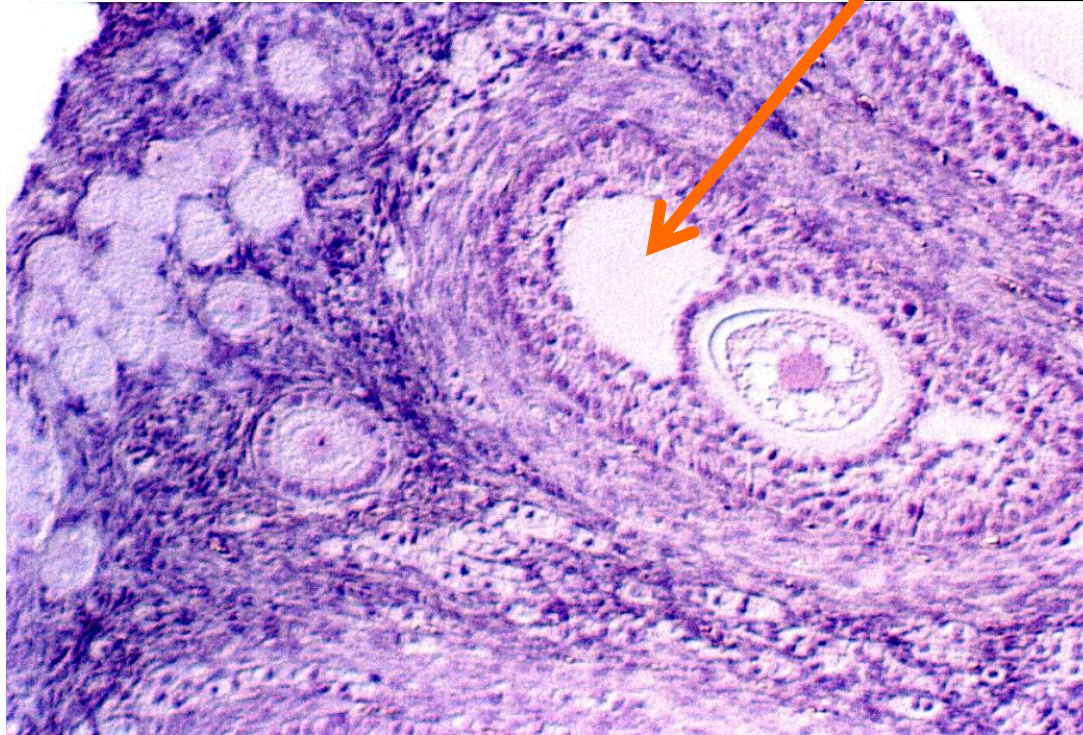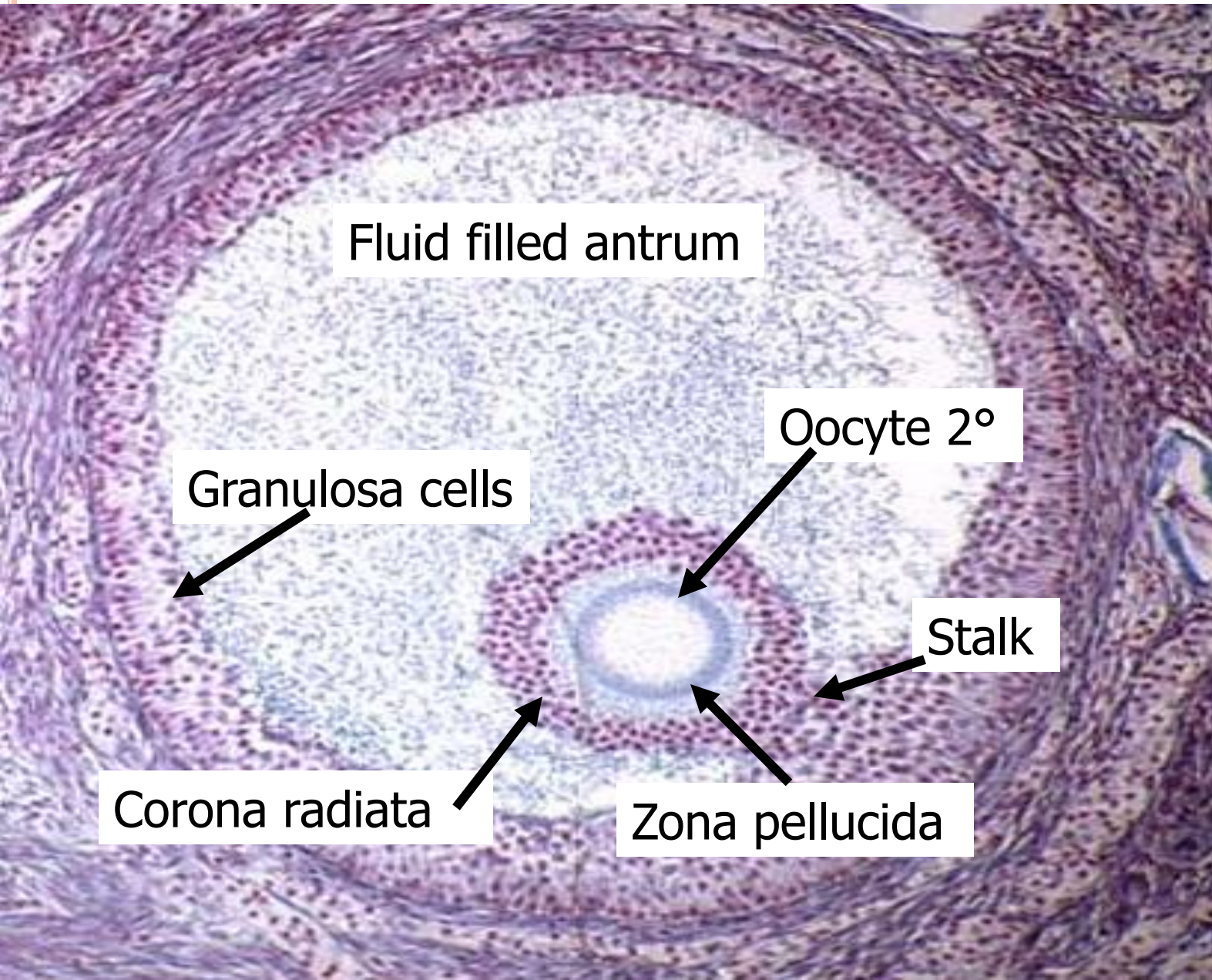
OVARY HISTOLOGY

OVARY HISTOLOGY

Primary Follicle

1° Oocyte

Nucleus

Primordial follicle

Thecal cells

Zona pellucida

Granulosa cells

Secondary Follicle

Fluid-filled antrum

GRAAFIAN FOLLICLE

Fluid filled antrum

Oocyte 2°

Granulosa cells

Stalk

Corona radiata

Zona pellucida

Corpus luteum

- After ovulation, the remains of the follicle are transformed into a structure called the **corpus luteum**.

- If a pregnancy occurs, it produces **progesterone** to maintain the wall of the uterus during the early period of development.

corpus luteum

cortex

CORPUS ALBICANS

- If fertilization does not occur, the corpus luteum will begin to break down about 2 weeks after ovulation.

- Degeneration occurs when fibroblasts enter the corpus luteum and a clump of scar tissue forms called the **corpus albicans**.

Slide 17 Ovary

Corpus albicans
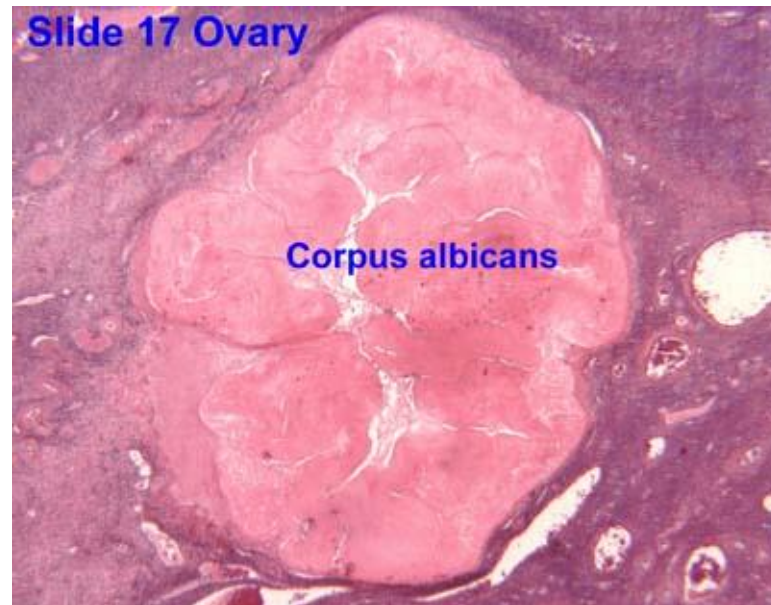
The Oviduct (Fallopian tube)

The oviduct functions as a conduit for the oocyte, from the ovaries to the uterus. Histologically, the oviduct consists of a mucosa and a muscularis. The peritoneal surface of the oviduct is lined by a serosa and subjacent connective tissue.

The mucosa

is formed by a ciliated and secretory epithelium resting on a very cellular lamina propria. The number of ciliated cells and secretory cells varies along the oviduct. Secretory activity varies during the menstrual cycle, and resting secretory cells are also referred to as peg-cells. Some of the secreted substances are thought to nourish the oocyte and the very early embryo.

The muscularis

consists of an inner circular muscle layer and an outer longitudinal layer. An inner longitudinal layer is present in the isthmus and the intramural part of the oviduct. Peristaltic muscle action seems to be more important for the transport of sperm and oocyte than the action of the cilia.

four subdivisions of the oviduct.

1-The infundibulum : is the funnel-shaped (up to 10 mm in diameter) end of the oviduct. Finger-like extensions of its margins, the fimbriae, are closely applied to the ovary. Ciliated cells are frequent. Their cilia beat in the direction of
2-the ampulla of the oviduct. Mucosal folds, or plicae, and secondary folds which arise from the plicae divide the lumen of the ampulla into a very complex shape. Fertilization usually takes place in the ampulla.
3-The isthmus : is the narrowest portion (2-3 mm in diameter) of the parts of the oviduct located in the peritoneal cavity. Mucosal folds are less complex and the muscularis is thick. An inner, longitudinal layer of muscle is present in the isthmus and the
4- **intramural part of the oviduct:** which penetrates the wall of the uterus. The term "intramural" should be familiar to you ..... The mucosa is smooth, and the inner diameter of the duct is very small.
Obstruction of the oviduct as a consequence of salpingitis is one possible cause of infertility, and alterations of luminal structure by inflammatory processes are a risk factor for tubal pregnancies.

Oviduct H&E

serosa

muscularis

mucosa

Oviduct H&E

lamina propria

ciliated cell

peg cells
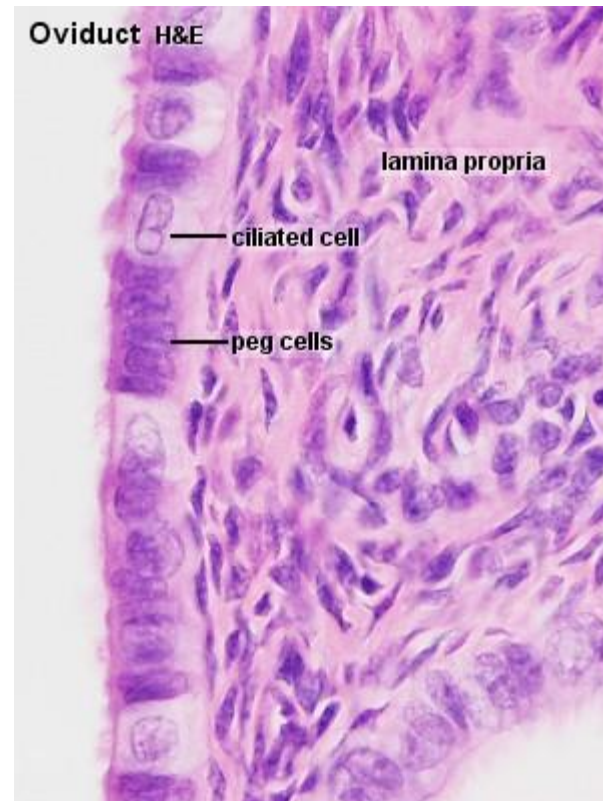
The Uterus

The uterus is divided into body (upper two-thirds) and cervix. The walls of the uterus are composed of a mucosal layer, the endometrium, and a fibromuscular layer, the myometrium. The peritoneal surface of the uterus is covered by a serosa.

Myometrium

The muscle fibres of the uterus form layers with preferred orientations of fibres (actually 4), but this is very difficult to see in most preparations. The muscular tissue hypertrophies during pregnancy, and GAP-junctions between cells become more frequent.

Endometrium

The endometrium consists of a simple columnar epithelium (ciliated cells and secretory cells) and an underlying thick connective tissue stroma. The mucosa is invaginated to form many simple tubular uterine glands. The glands extend through the entire thickness of the stroma. The stromal cells of the endometrium are embedded in a network of reticular fibres. The endometrium is subject to cyclic changes that result in menstruation. Only the mucosa of the body of the uterus takes part in the menstrual cycle.
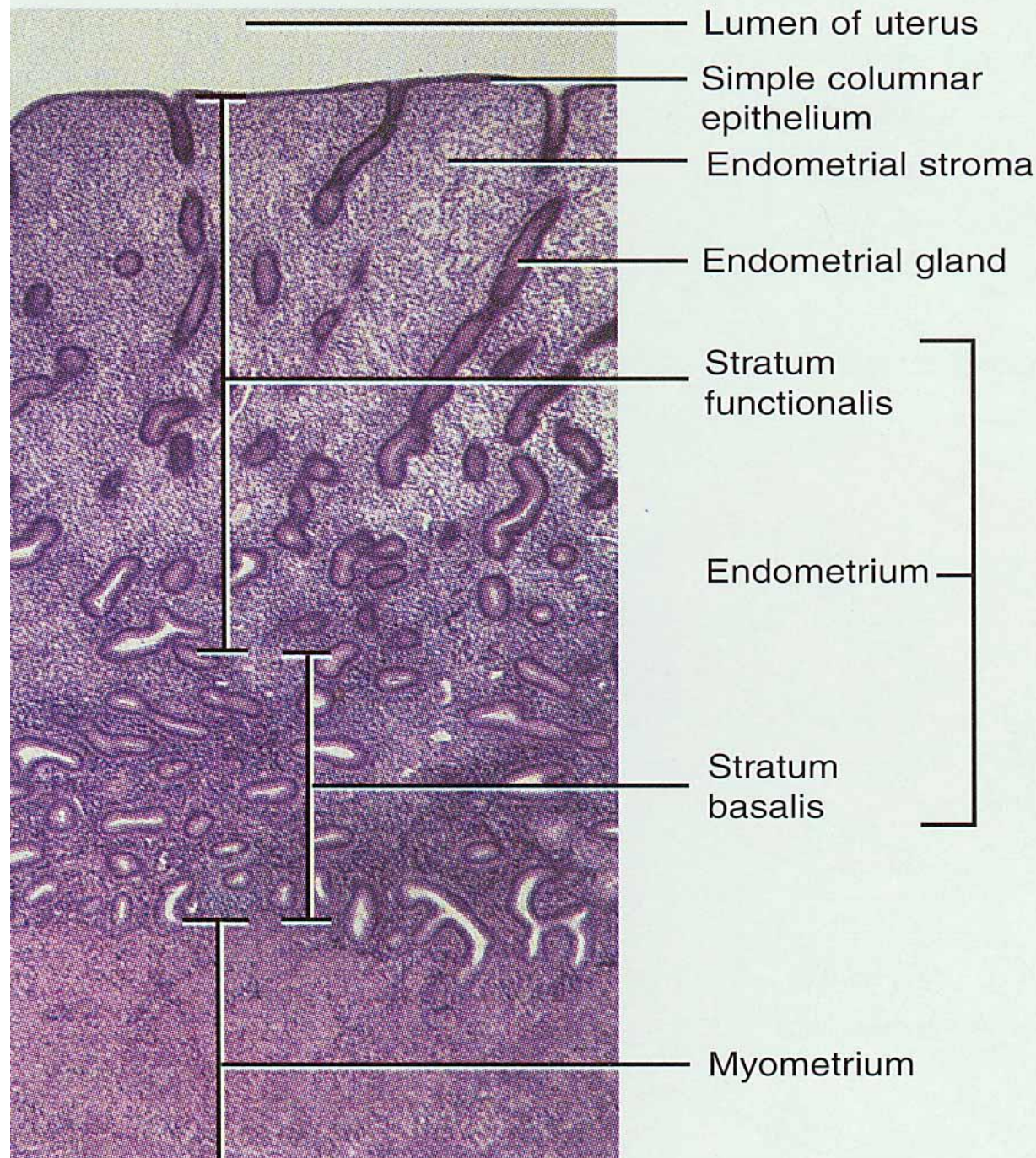
The endometrium can be divided into two zones based on their involvement in the changes during the menstrual cycle: the **basalis and the functionalis.**
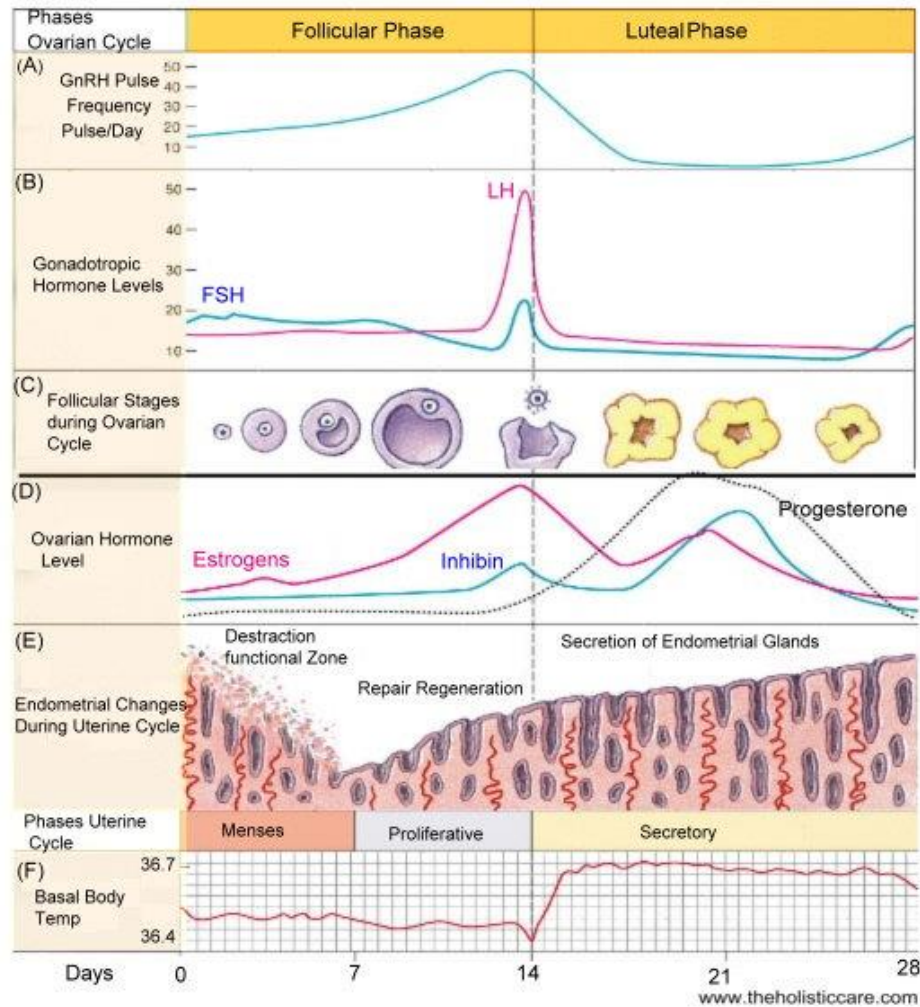
The **basalis** is not sloughed off during menstruation but functions as a regenerative zone for the functionalis after its rejection.

The functionalis is the luminal part of the endometrium. It is sloughed off during every menstruation and it is the site of cyclic changes in the endometrium. These cyclic changes are divided into a number of phases: proliferative (or follicular), secretory (or luteal), and menstrual

UTERINE HISTOLOGY

Lumen of uterus

Simple columnar epithelium

Endometrial stroma

Endometrial gland

Stratum functionalis

Endometrium

Stratum basalis

Myometrium

Ovarian and Uterine Cycles

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Cervix

- Narrow lower neck of the uterus which projects into the vagina inferiorly
- Cervical canal – cavity of the cervix that communicates with:
  - The vagina via the external os
  - The uterine body via the internal os
- Cervical glands secrete mucus that covers the external os and blocks sperm entry except during midcycle

Fallopian tube

Uterus

Ovary

Cervix

Internal os

Endocervical canal

External os

Fornix

Vagina

A.D.A.M.
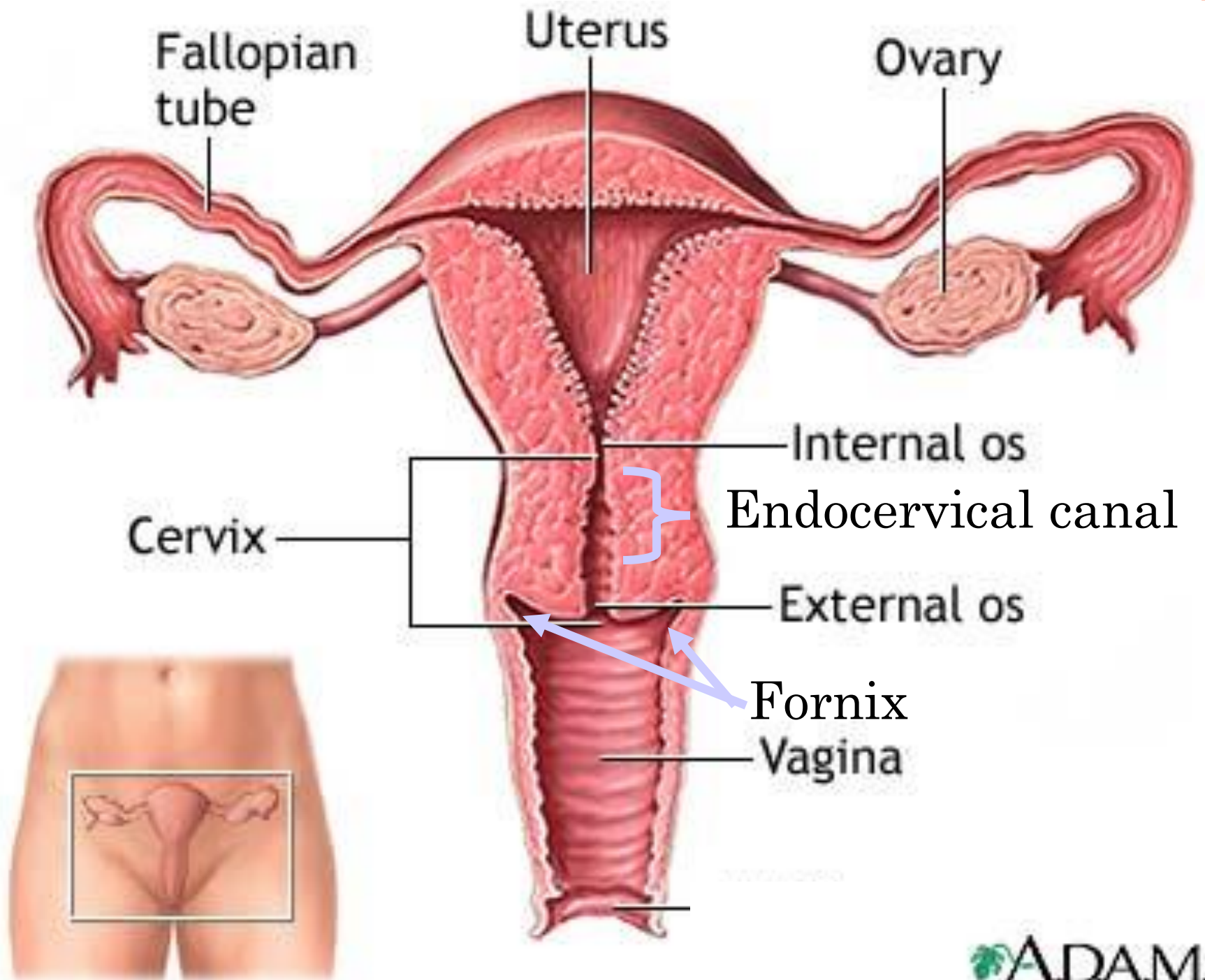
Vagina

The vagina is a fibromuscular tube with a wall consisting of three layers: the mucosa, muscularis and adventitia of the vagina

Mucosa

The stratified squamous epithelium (deep stratum basalis, intermediate stratum spinosum, superficial layers of flat eosinophilic cells which do contain keratin but which do not normally form a true horny layer) rests on a very cellular lamina propria (many leukocytes). Towards the muscularis some vascular cavernous spaces may be seen (typical erectile tissue).

Muscularis

Inner circular and outer longitudinal layers of smooth muscle are present. Inferiorly, the striated, voluntary bulbospongiosus muscle forms a sphincter around the vagina.

Adventitia

The part of the adventitia bordering the muscularis is fairly dense and contains many elastic fibres. Loose connective tissue with a prominent venous plexus forms the outer part of the adventitia.