

Ovulation and Menstrual cycle

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- **OVULATION CYCLE**

- Cyclical changes in ovaries during 28 day reproductive cycle, terminating in the release of single mature ovum (ovulation) under the influence of anterior pituitary gonadotrophic hormones [follicle stimulating hormone (FSH) and luteinizing hormones (LH)]

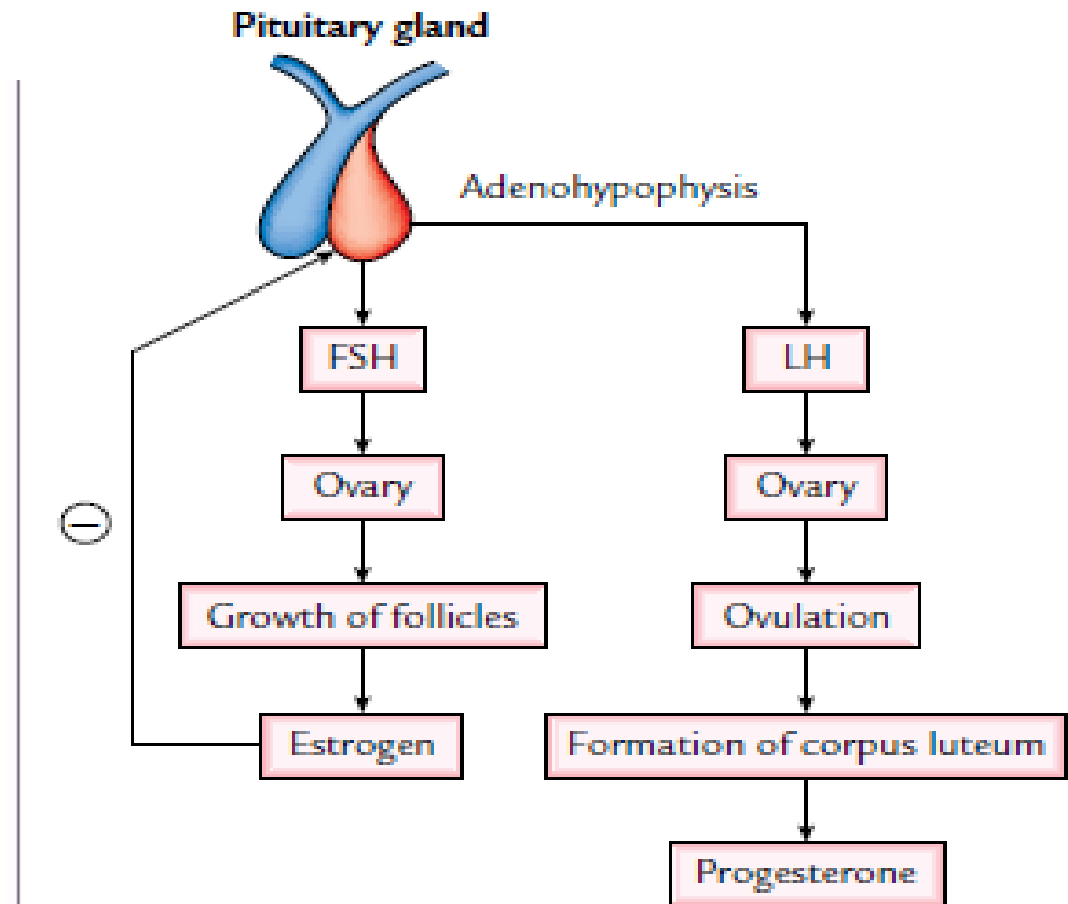
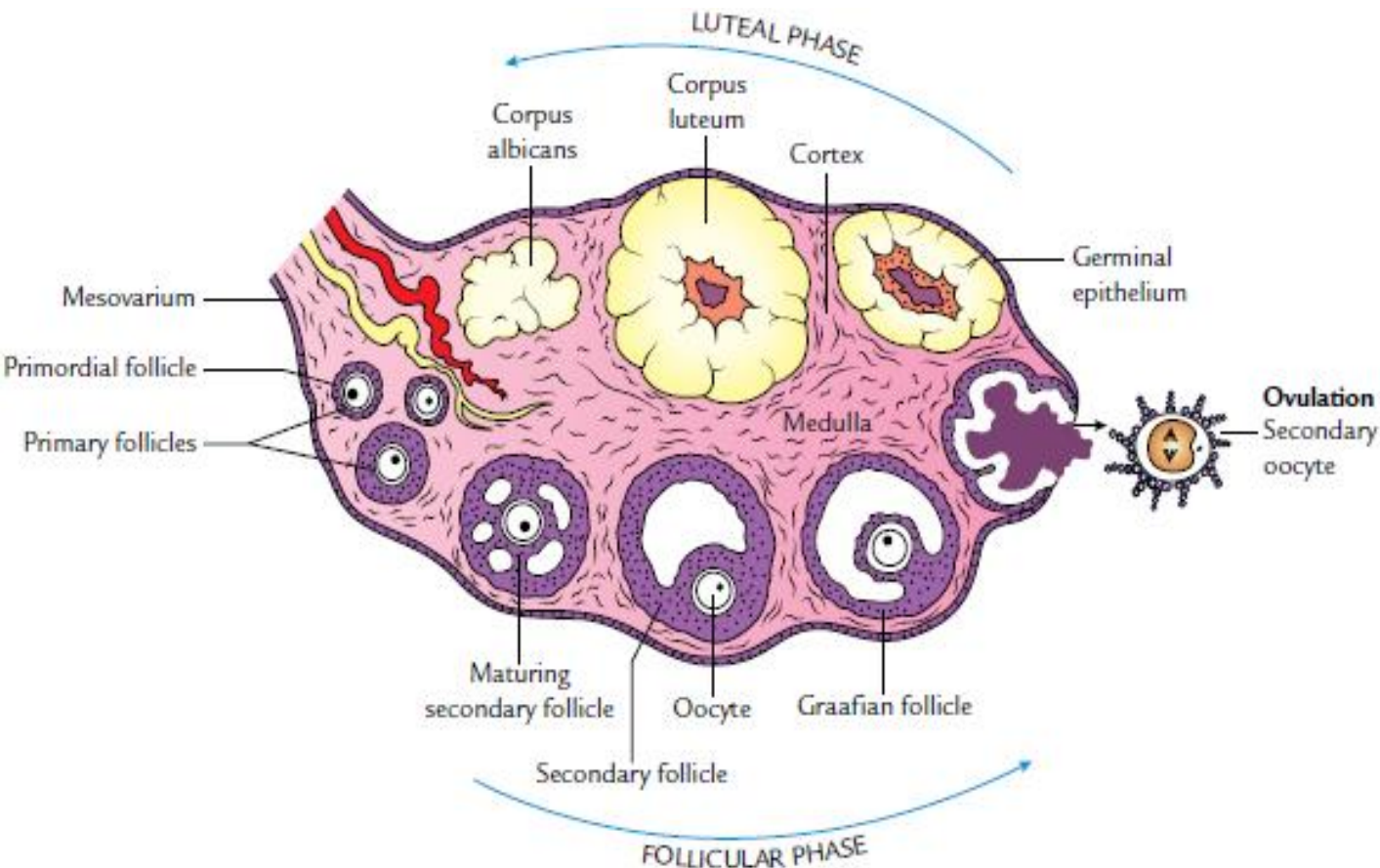


Fig. 2.5 Ovarian cycle.

Hormone –stimulated process by which the oocyte is released from the ovary.

Follicular Development

An *ovarian follicle* is a rounded structure that contains a developing ovum surrounded by follicular cells.

Development of an ovarian follicle is characterized by:

- Growth & differentiation of primary oocyte
- Proliferation of follicular cells
- Formation of zona pellucida
- Development of theca folliculi

- **Follicular Phase/ Development**

- FSH and LH secretion from the anterior pituitary gland is stimulated by **gonadotropin-releasing hormone (GnRH)** from the hypothalamus
- During each cycle, **FSH** promotes growth of several ***primordial follicles*** 5 to 15 start maturation by process known as ***folliculogenesis***
- only one follicle usually develops into a mature follicle
- ***folliculogenesis***
 - ❖ It is the process of maturation of ovarian follicles
 - ❖ various types of follicles that are formed during this process of maturation are ***primordial, primary, secondary, vesicular, tertiary*** and ***mature***

- **Primordial follicles –**

- formed during fetal life consist of a primary oocyte enveloped by a single layer of flattened follicular cells
- follicular cells **protect the ova** and form different types of follicle with progress in their development
- primary oocyte and granulosa cells are covered by a thin basement membrane

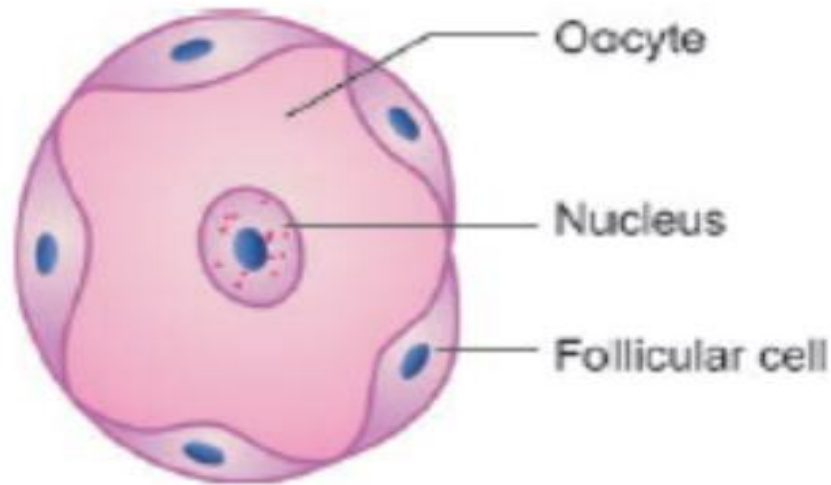
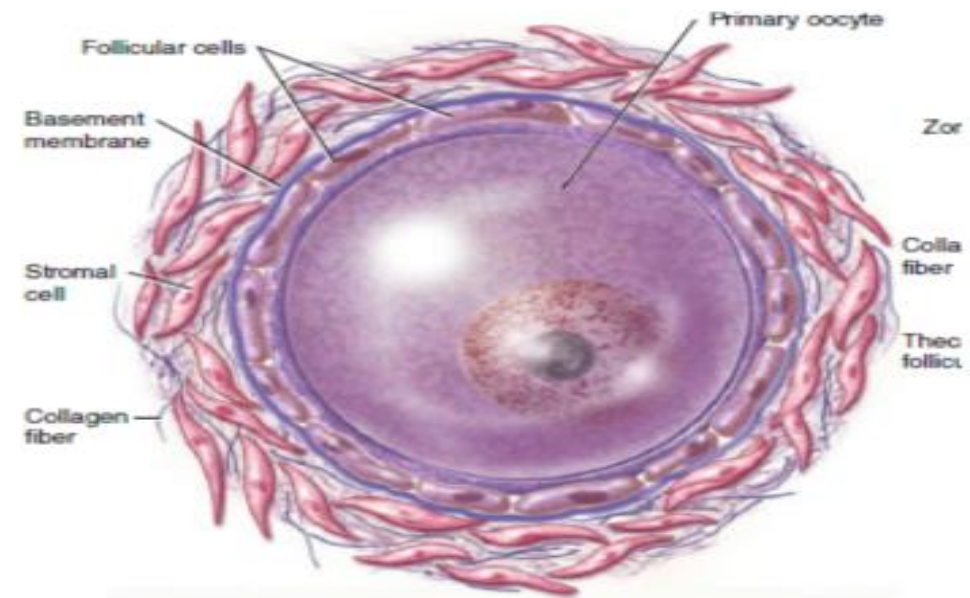


Fig. 3.14: Primordial follicle



(a) Primordial follicle

- ***Primary follicles***
- first indication that a primordial follicle is beginning to undergo further development is that the flattened follicular cells become columnar
- Primary follicle consists of primary oocyte surrounded by a layer of cuboidal or low columnar follicular cells
- growing follicle forms a homogenous layer of glycoprotein in between follicular cells & primary oocyte -***zona pellucida***

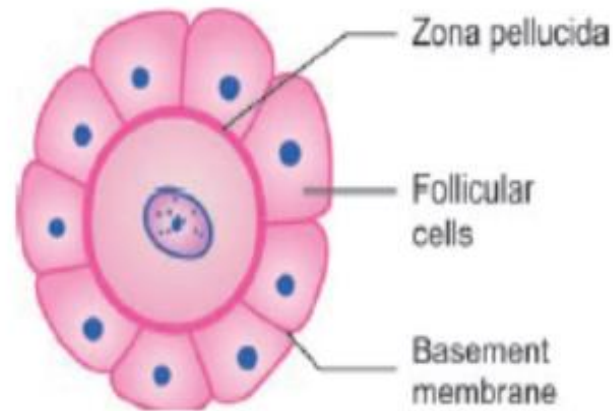
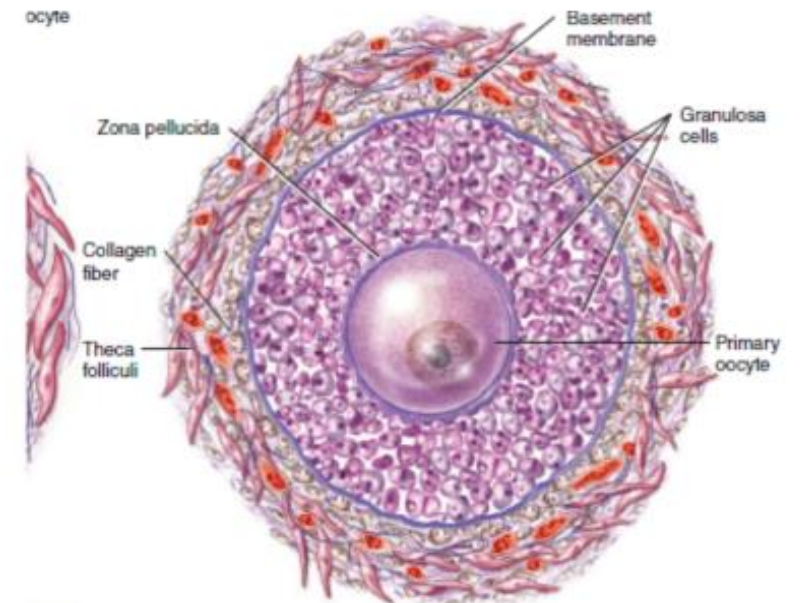


Fig. 3.15: Primary follicle



(b) Late primary follicle

- ***Secondary/ multilaminar follicle:***
- follicular cells undergo mitotic division
- form several layers of follicular cells surrounding the primary oocyte forming a multi-layered stratum granulosum
- primary oocyte increases in size
- follicular cells are now called as “**granulosa cells**”
- granulosa cells are in the form of a compact mass

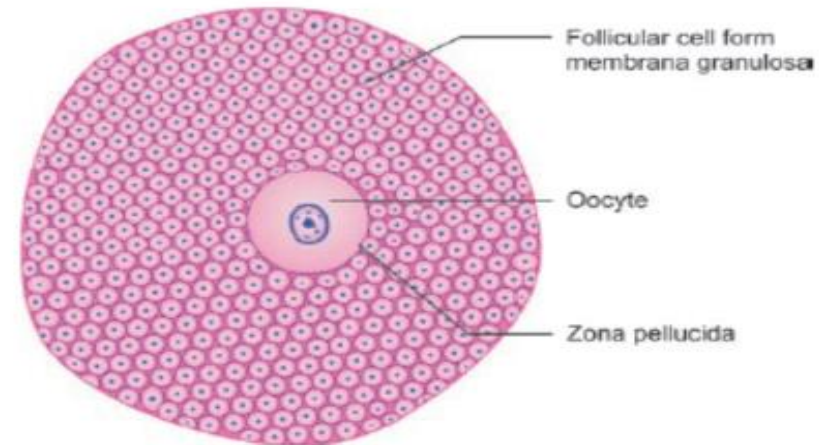


Fig. 3.16: Secondary follicle

- ***Preamtral follicle:***

- Fluid-filled spaces appear between granulosa cells- follicle is known as “**preamtral follicle**”
- fluid is secreted by granulosa cells

- ***Tertiary/Antral follicle:***

- fluid-filled spaces between granulosa cells coalesce
- form a bigger cavity known as “**follicular antrum**” pushes the primary oocyte with surrounding granulosa cells
- fluid in antrum is called **liquor folliculi**
- the proliferation of granulosa cells the size of the follicle increases

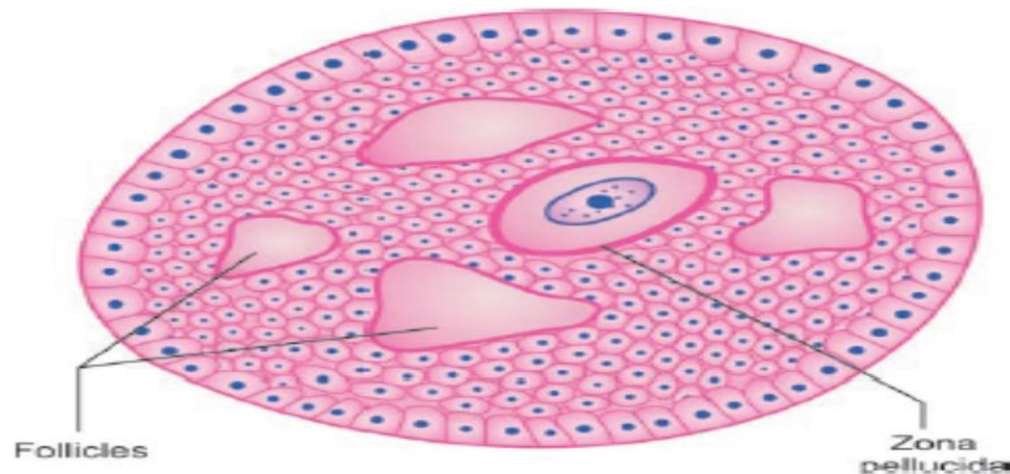
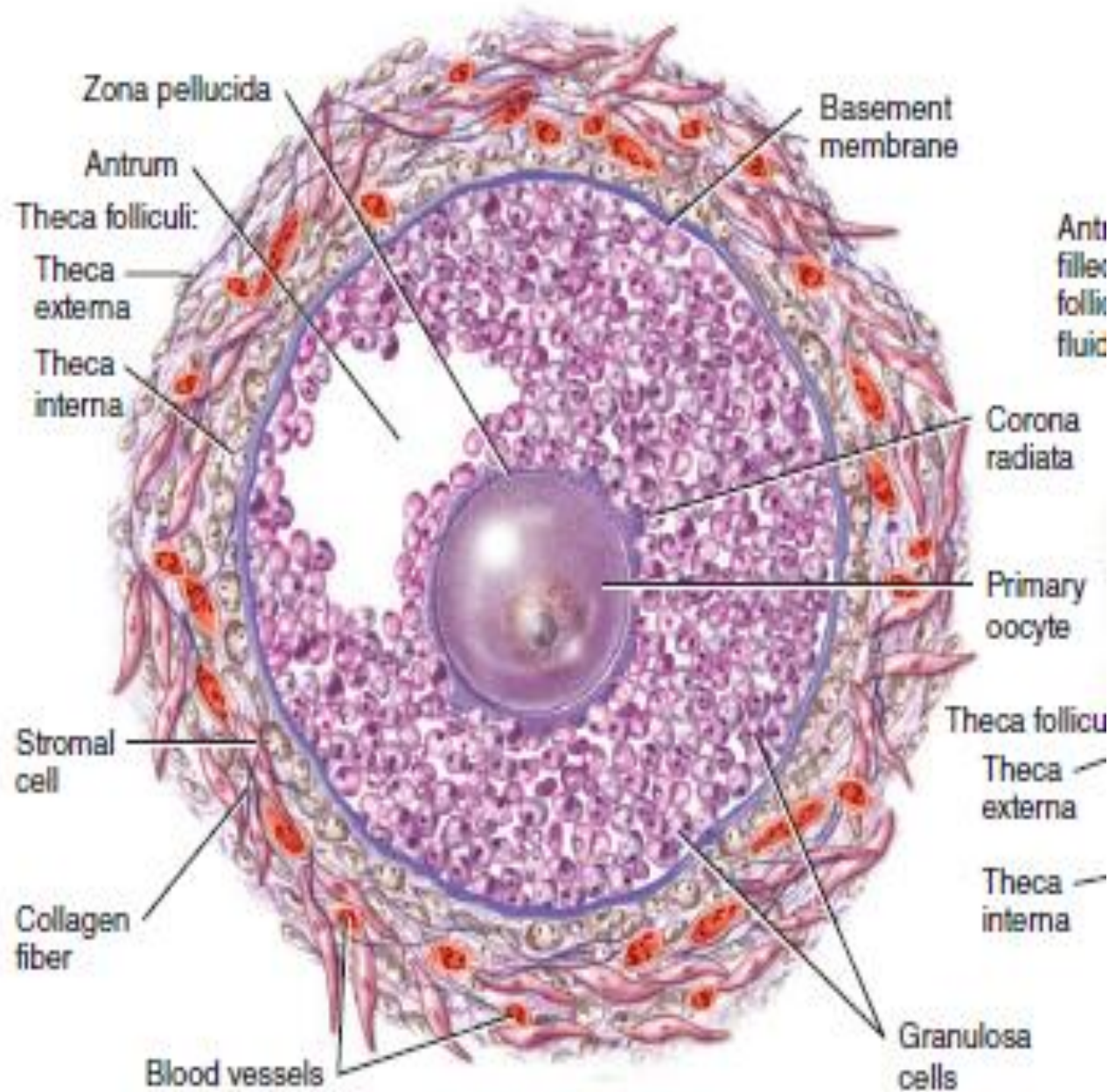


Fig. 3.17: Preamtral follicle



Fig. 3.18: Tertiary/Antral follicle



(c) Secondary follicle

- ***Mature/Graafian follicle***
- Around 7th day of sexual cycle one of the tertiary follicles increases in size in response to FSH and LH
- forms the largest mature follicle - **“Graafian follicle”**
- Remaining follicles degenerate and become atretic
- reaches the periphery of the cortex & starts projecting on to the surface of the ovary
- primary oocyte with a layer of covering cells move to one side of the follicle by the growing fluid filled antrum

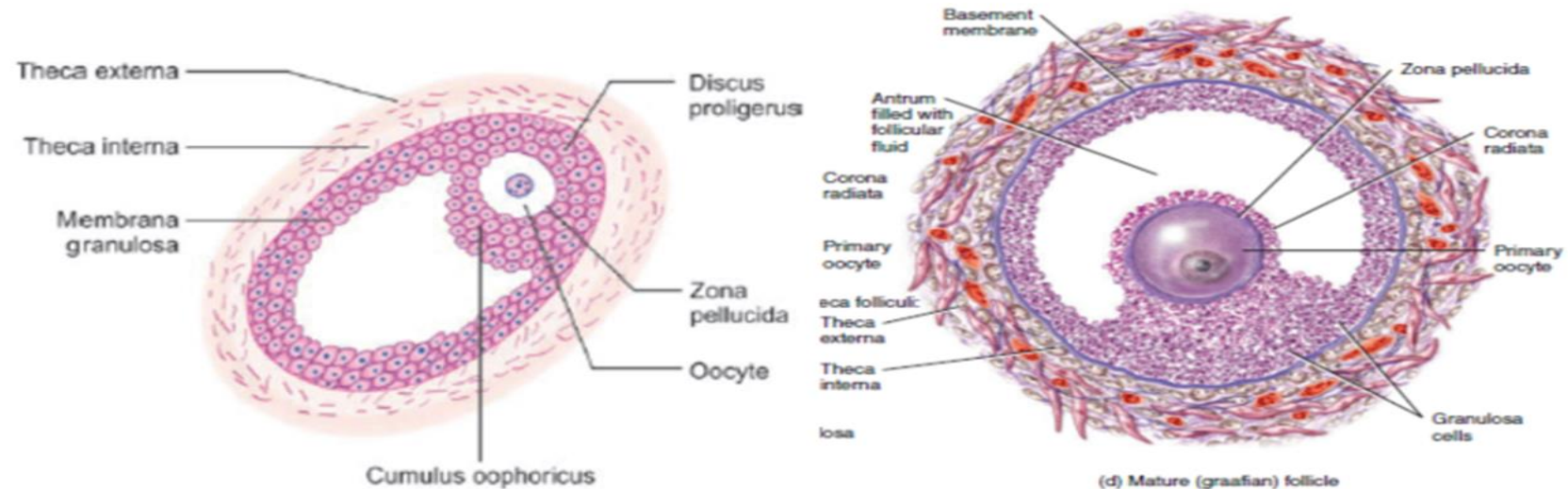


Fig. 3.19: Mature graafian follicle

- layer of cells immediately surrounding the oocyte & zona pellucida are called ***corona radiata cells***
- projection of granulosa cells covering the primary oocyte projecting into the follicular antrum is called ***cumulus oophorus***
- area of attachment of primary oocyte & corona radiata to the wall of follicle is called ***discus proligerus***

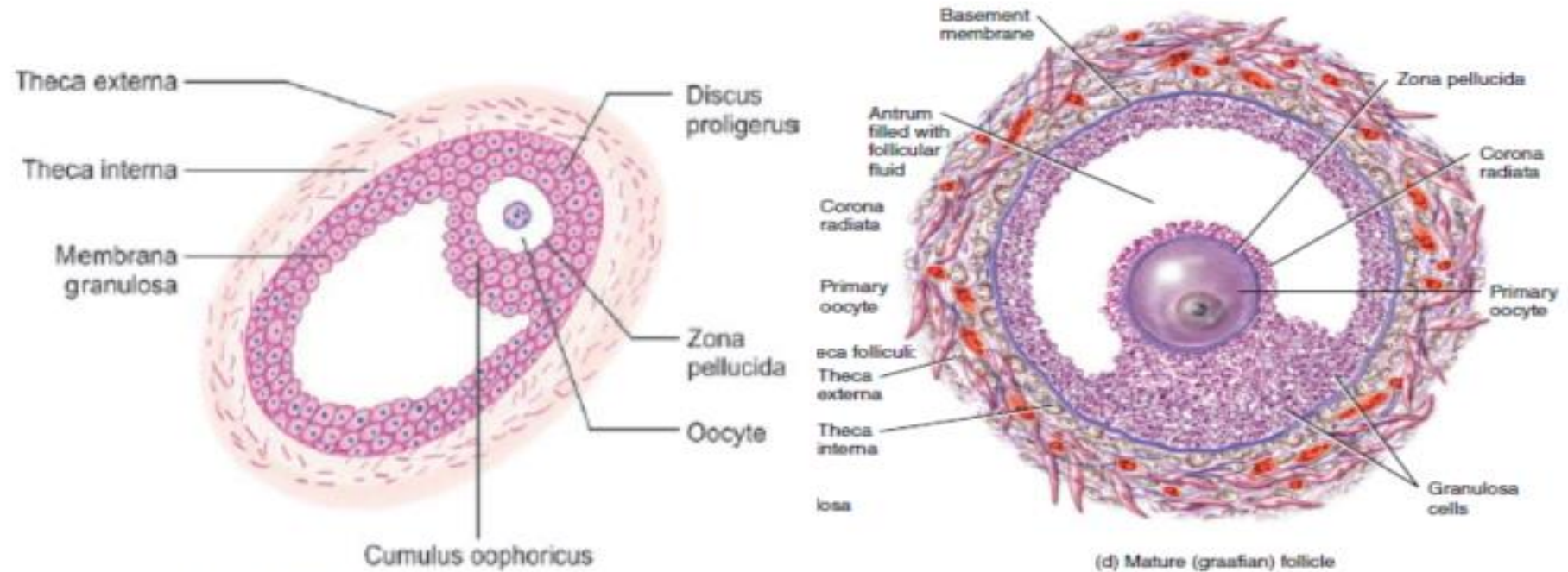
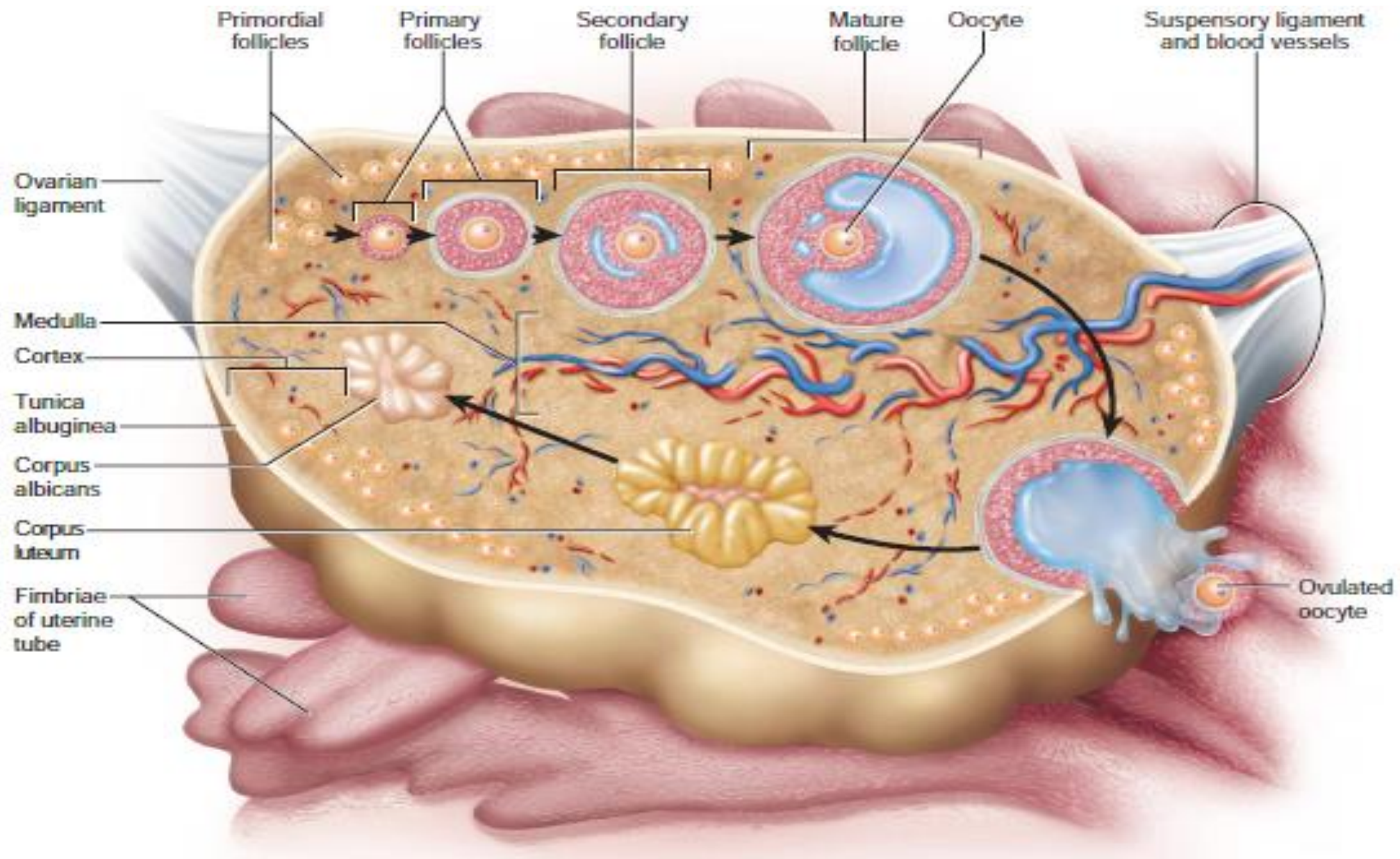


Fig. 3.19: Mature graafian follicle

(d) Mature (graafian) follicle



- stromal cells surrounding the membrana granulosa become condensed form a covering called ***theca interna***
- Theca interna increase in thickness & becomes more vascular
- secrete estrogen & called the cells of the thecal gland
- fibrous tissue becomes condensed to form another covering for the follicle called ***theca externa***

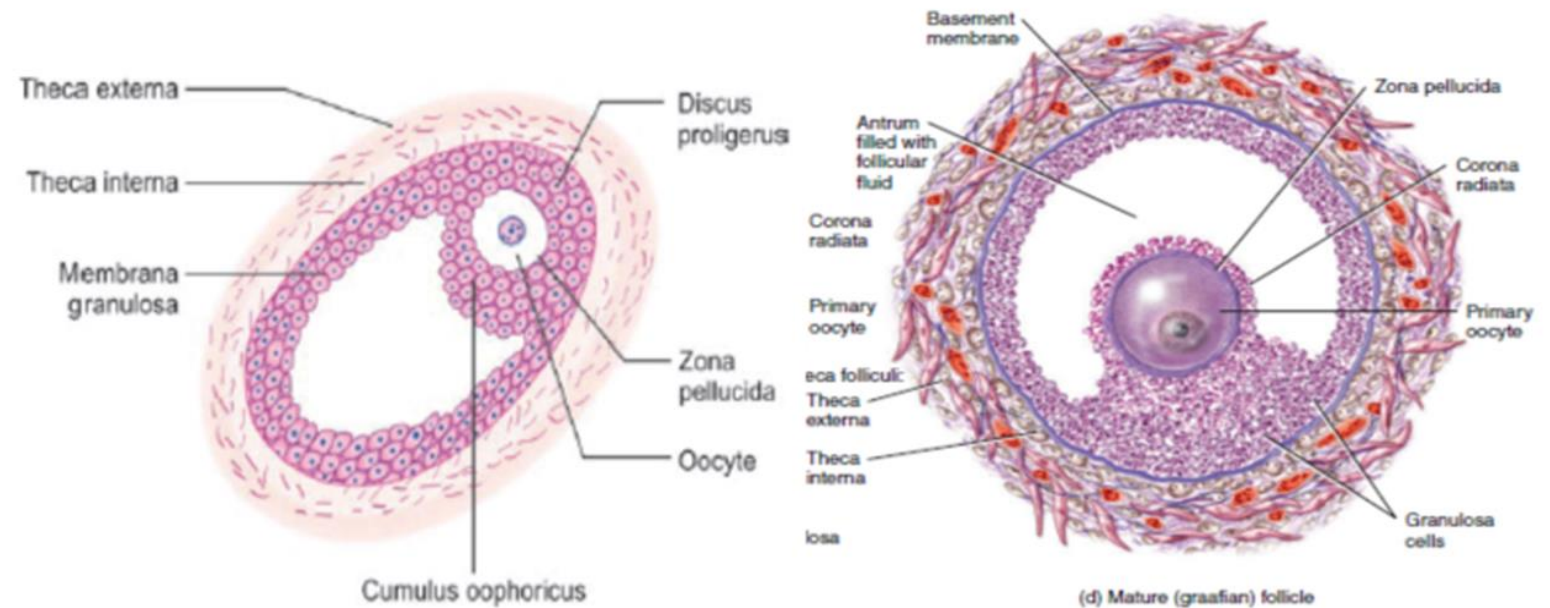
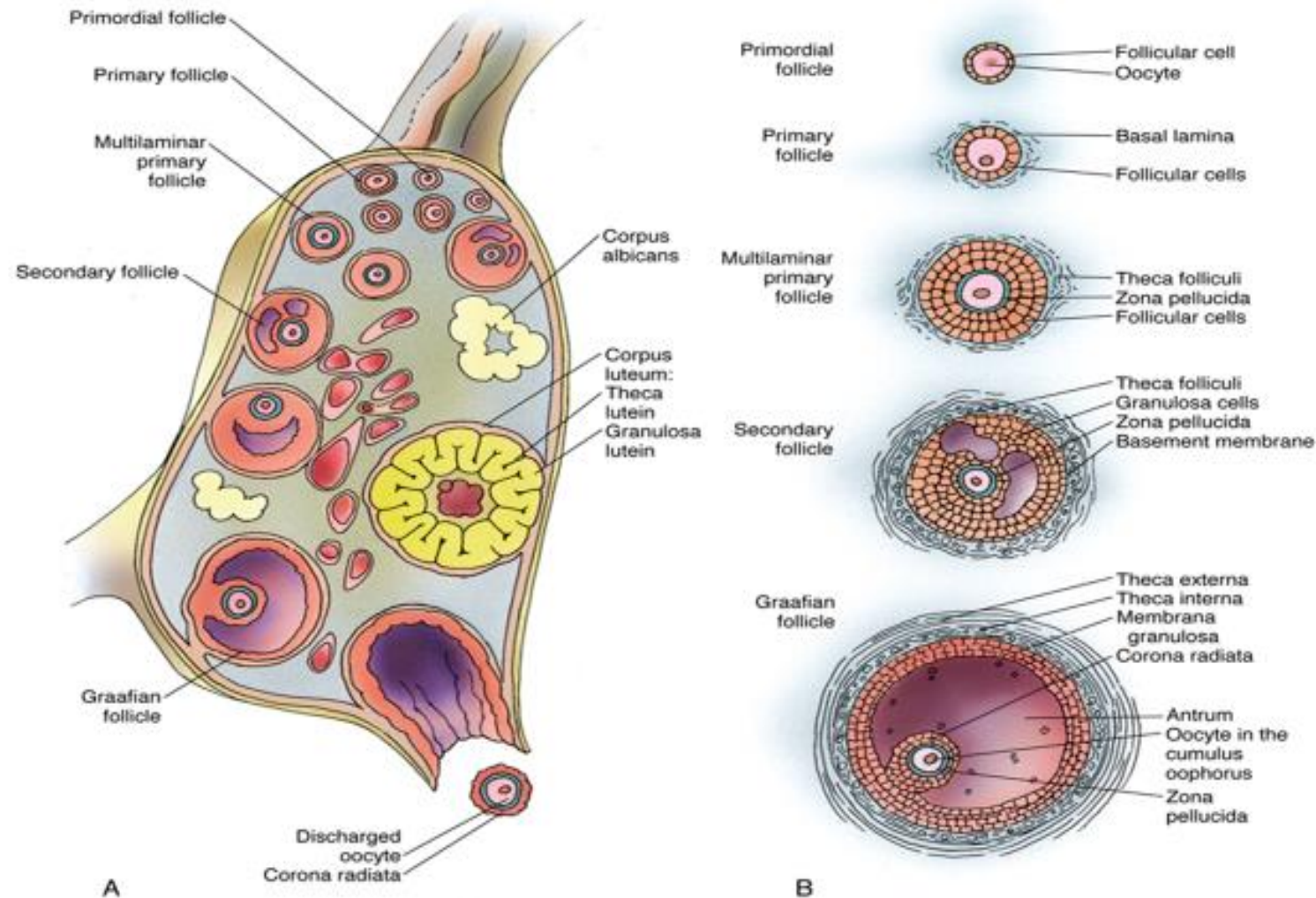


Fig. 3.19: Mature graafian follicle

- Just before ovulation the primary oocyte of mature Graafian follicle completes first meiotic division & forms secondary oocyte and first polar body



HOMORNES

- Early development of ovarian follicles require FSH
- FSH stimulates maturation of follicular (granulosa) cells surrounding oocyte
- Growing follicles produce oestrogens
- Final stages of maturation requires LH as well
- (a)LH elevates concentrations of maturation-promoting factor, causing primary oocytes to complete meiosis I and initiate meiosis II;
- (b) stimulates production of progesterone by follicular stromal cells
(luteinization)
- (c) causes follicular rupture and ovulation.

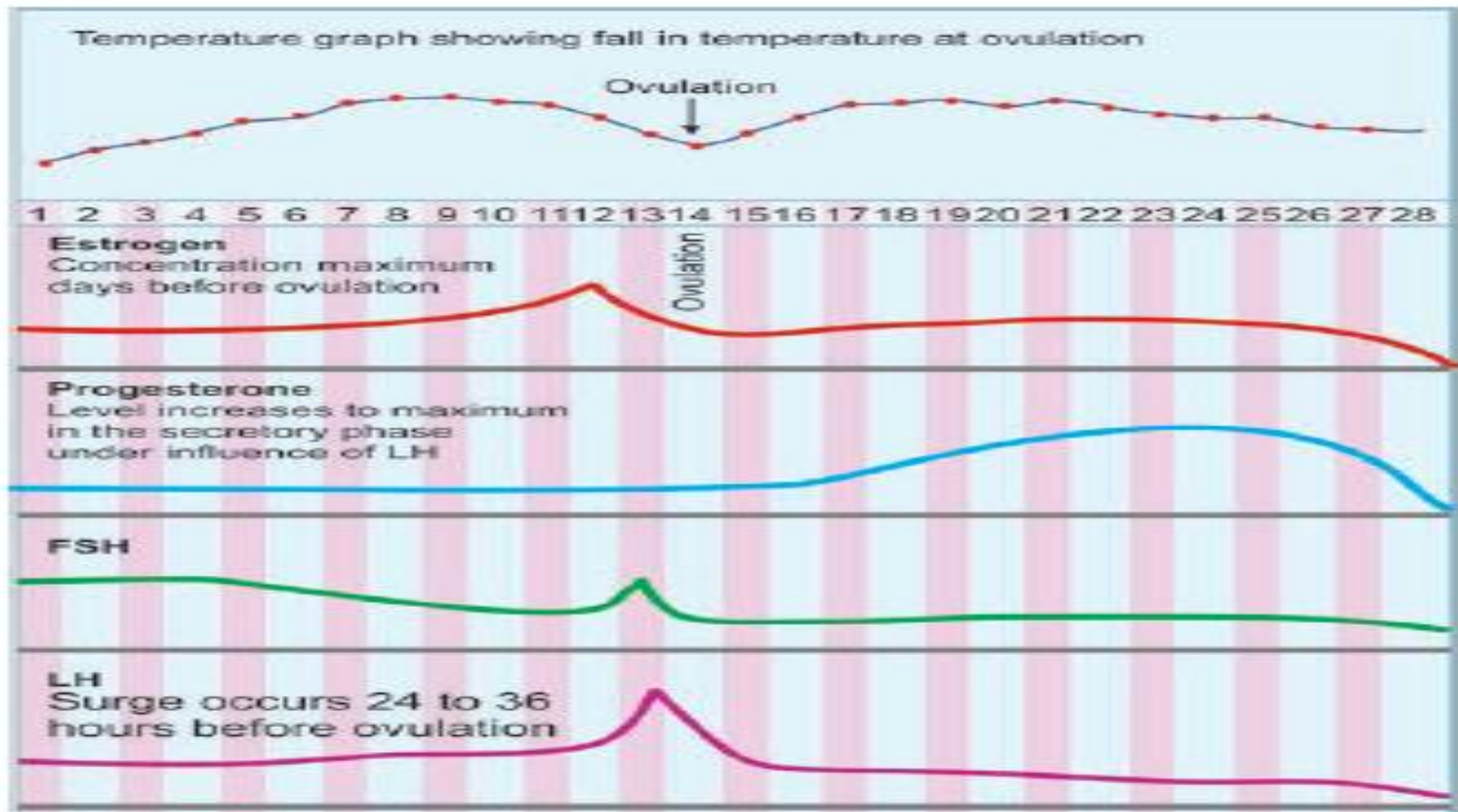


Fig. 3.22: Morning temperature and concentration of hormones FSH, LH, estrogen and progesterone during normal menstrual cycle. Ovulation occurs because of a LH surge just before ovulation

- **Ovulatory Phase**

- secondary oocyte - meiosis II begins but it is stopped in metaphase II
- ovarian follicle is at first very small compared to the thickness of the ovarian cortex
- Follicle enlarges reaches the surface of the ovary, forms a bulging in this situation
- An avascular area (***stigma***) appears over the most convex point of the follicle
- cells of the cumulus oophoricus become loosened by accumulation of fluid between them.

- the mature follicle ruptures & releases the secondary oocyte in metaphase of 2nd meiotic division.
- shedding of the ovum from the ovary is called **ovulation**
- ovum that is shed from the ovary is not fully mature
- secondary oocyte that is undergoing division to shed off the second polar body

- ***Structure of the Ovum at Ovulation***
- ovum that is shed from the ovary is not fully mature
- secondary oocyte that is undergoing division to shed off the second polar body
- it is surrounded by the zona pellucida
- surrounded by cells of the corona radiata
- No nucleus is seen, nuclear membrane has dissolved for the second meiotic division
- A spindle is present

- Between the cell membrane (or *vitelline membrane*) & the zona pellucida is the ***perivitelline space***
- first polar body lies in this space

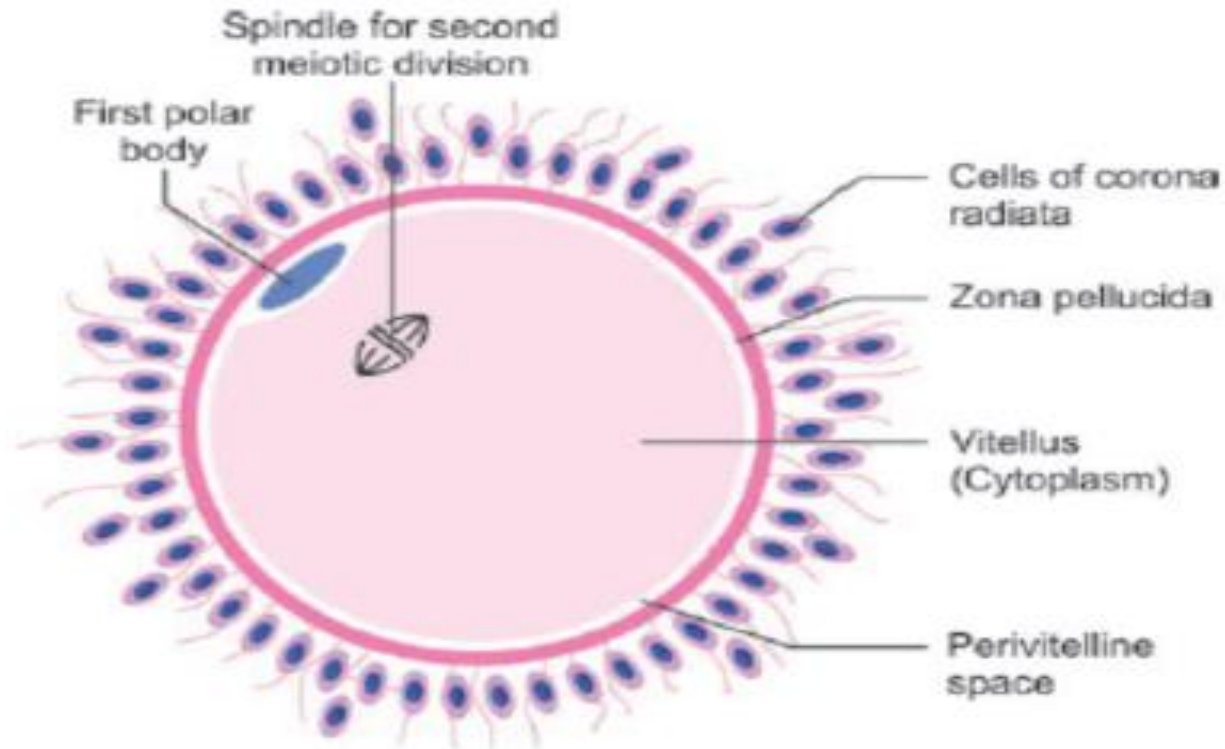
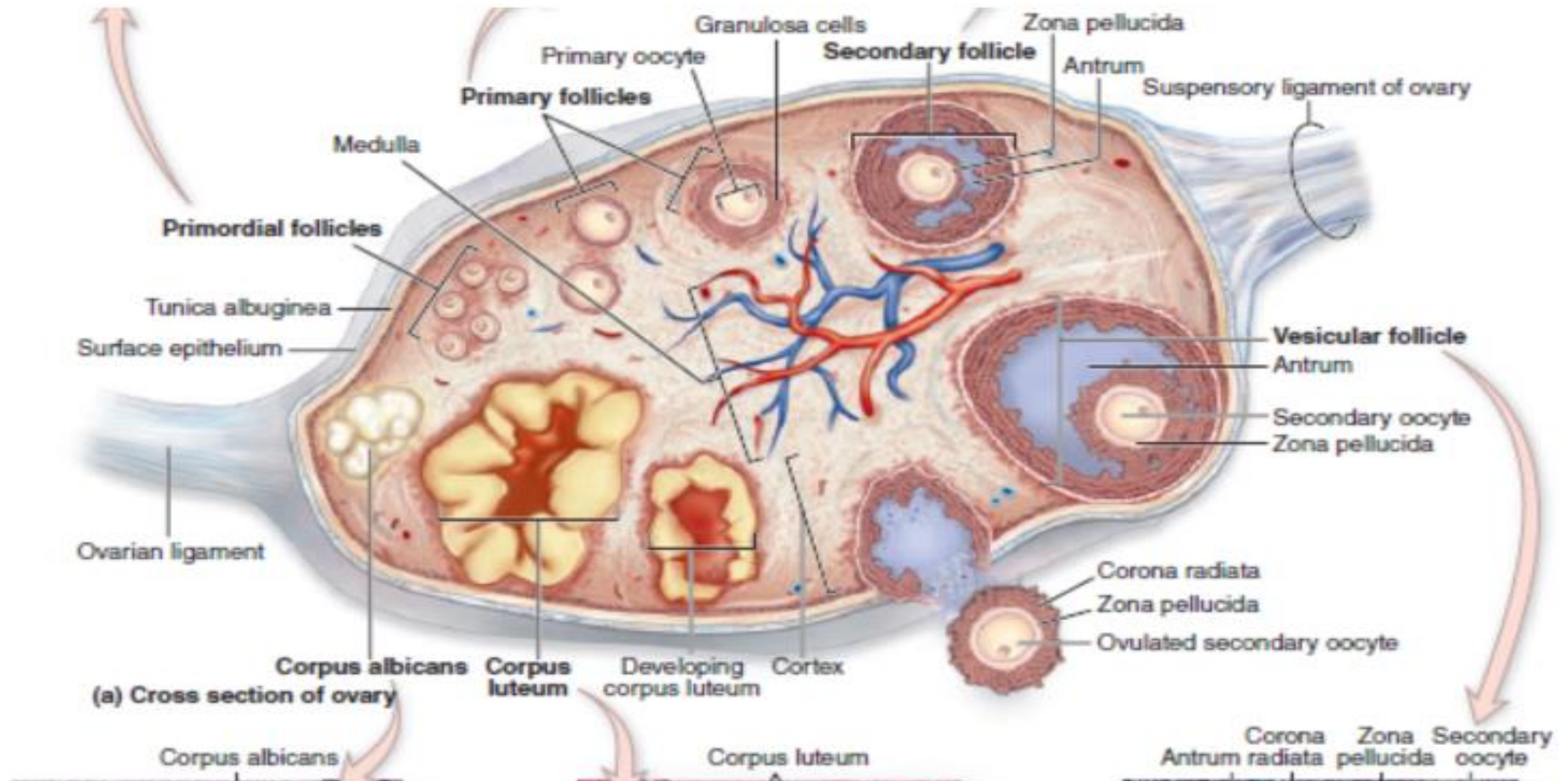
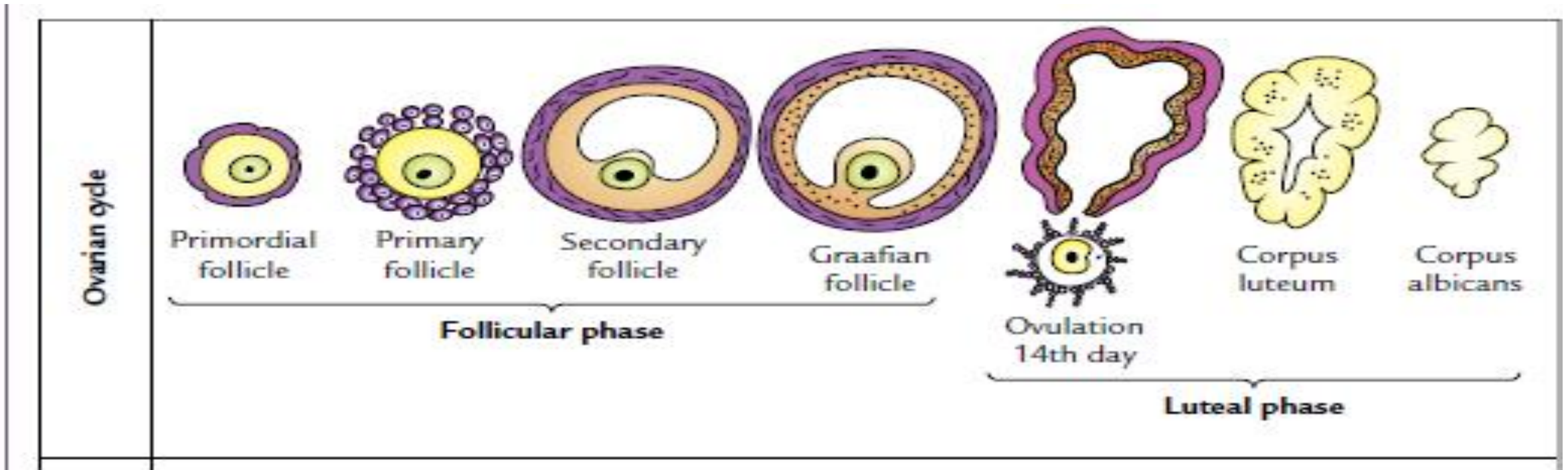


Fig. 3.21: Structure of ovum at the time of ovulation

- After ovulation, the remaining part of the follicle undergoes changes that convert it into an important structure called the ***corpus luteum***

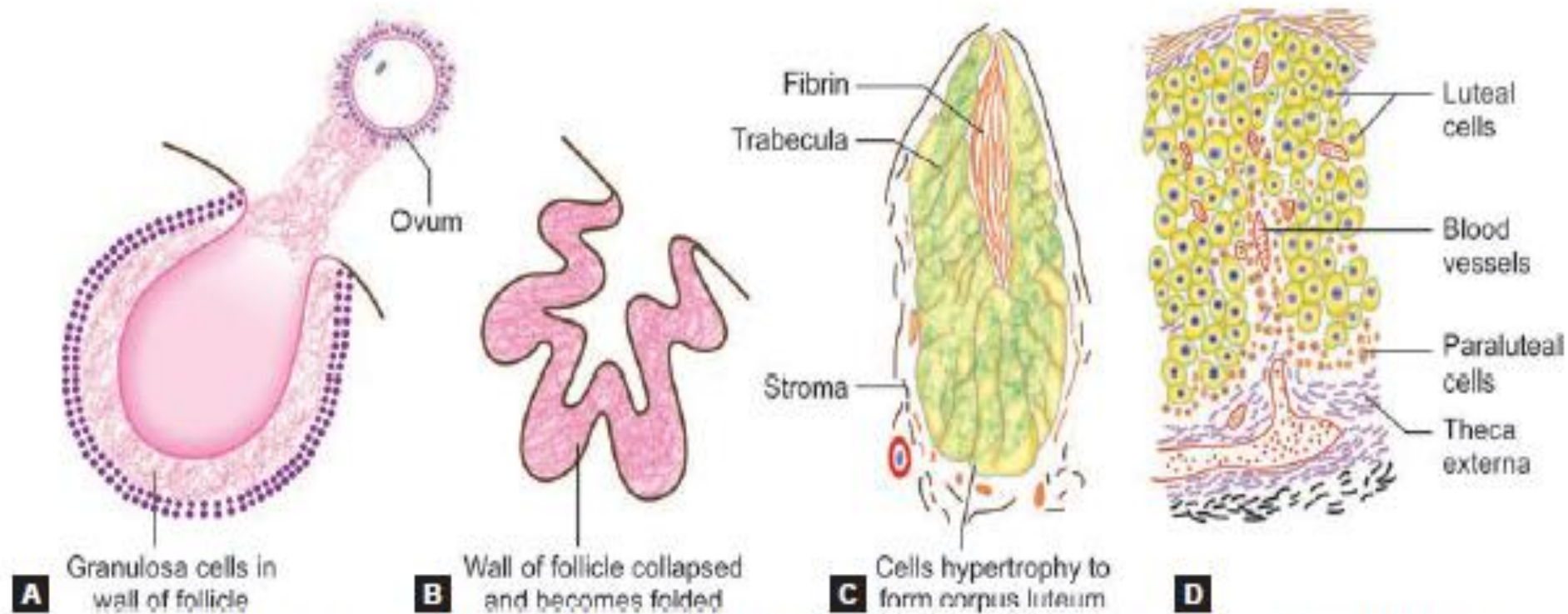


- ***Corpus Luteum***
- is an important structure
- secretes a hormone, ***progesterone***
- derived from the ovarian follicle, after the latter has ruptured to shed the ovum as follows:-
- (a) When the follicle ruptures its wall collapses and becomes folded
- Sudden reduction in pressure caused by rupture of the follicle results in bleeding into the follicle
- The follicle filled with blood is called the ***corpus haemorrhagicum***.



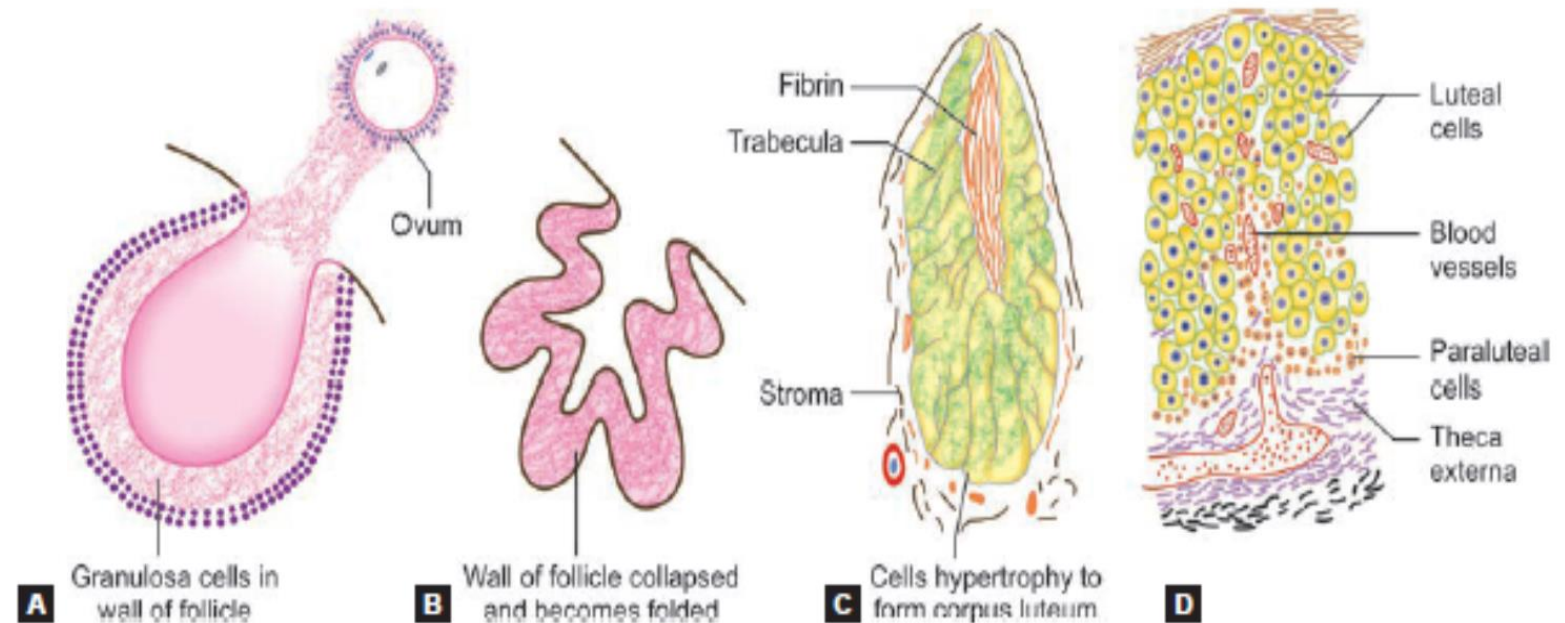
- **(b)** At this stage, the follicular cells are small and rounded
- They enlarge rapidly
- As they increase in size their walls press against those of neighbouring cells so that the cells acquire a polyhedral shape
- Their cytoplasm becomes filled with a yellow pigment called ***lutein***
- Now called ***luteal cells***
- The presence of this yellow pigment gives the structure a yellow colour hence **corpus luteum**
- Some cells of the theca interna also enlarge and contribute to the corpus luteum

- (c) the corpus luteum secretes progesterone
- This secretion has to be poured into blood like secretions of endocrine glands
- ovarian follicle itself has no blood vessels, but the surrounding theca interna has blood vessels
- When the corpus luteum is forming, blood vessels from the theca interna invade it and provide it with a rich blood supply



Figs 3.20A to D: Stages in the formation of corpus luteum and transformation of follicular cells to luteal cells

- subsequent fate of the corpus luteum depends on whether the ovum is fertilised or not
- (a) If the ovum is not fertilised, the corpus luteum persists for about 14 days
- During this period it secretes progesterone
- If fertilization does not occur, the granulosa cells produce **inhibin**, a protein that acts on adenohypophysis and inhibits the secretion of gonadotrophins, which leads to the regression of corpus luteum
- It remains relatively small & is called the **corpus luteum of menstruation**
- At the end of its functional life, it degenerates and becomes converted into a mass of fibrous tissue called the **corpus albicans**



Figs 3.20A to D: Stages in the formation of corpus luteum and transformation of follicular cells to luteal cells

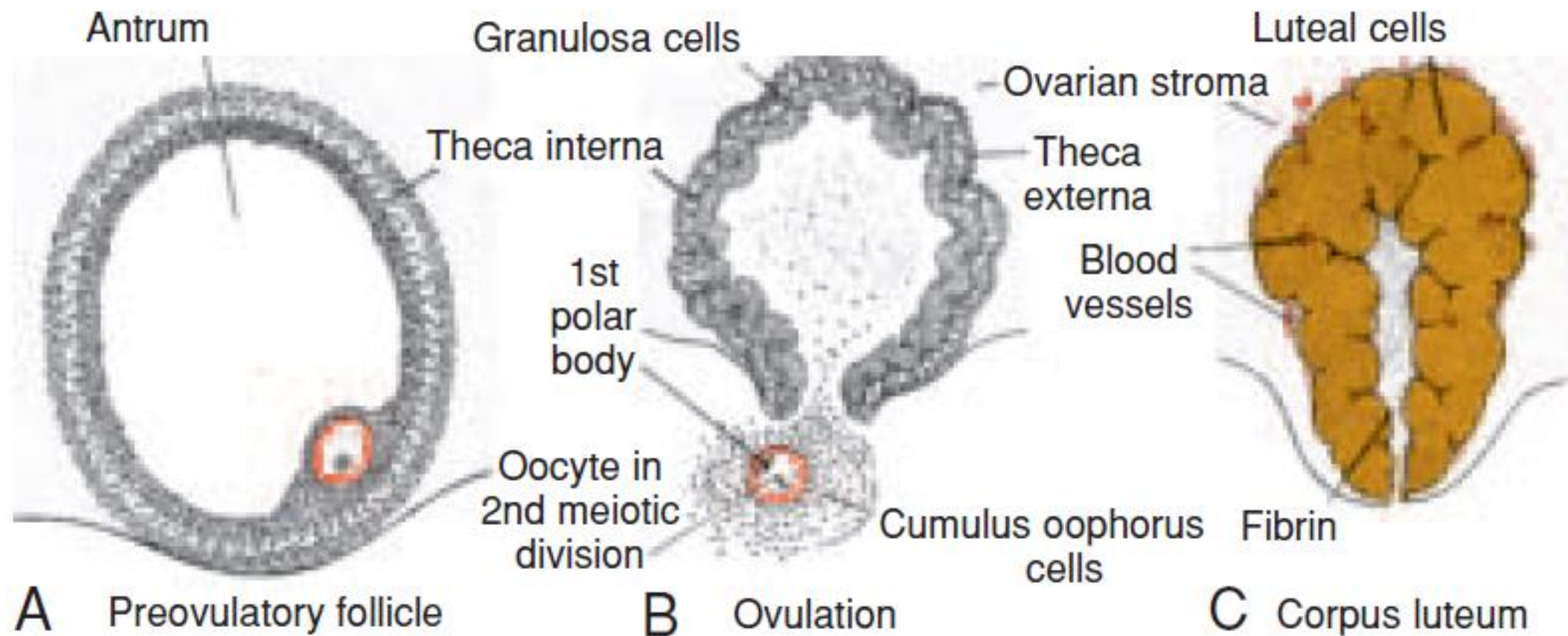


Figure 2.2 **A.** Preovulatory follicle bulging at the ovarian surface. **B.** Ovulation. The oocyte, in metaphase of meiosis II, is discharged from the ovary together with a large number of cumulus oophorus cells. Follicular cells remaining inside the collapsed follicle differentiate into luteal cells. **C.** Corpus luteum. Note the large size of the corpus luteum, caused by hypertrophy and accumulation of lipid in granulosa and theca interna cells. The remaining cavity of the follicle is filled with fibrin.

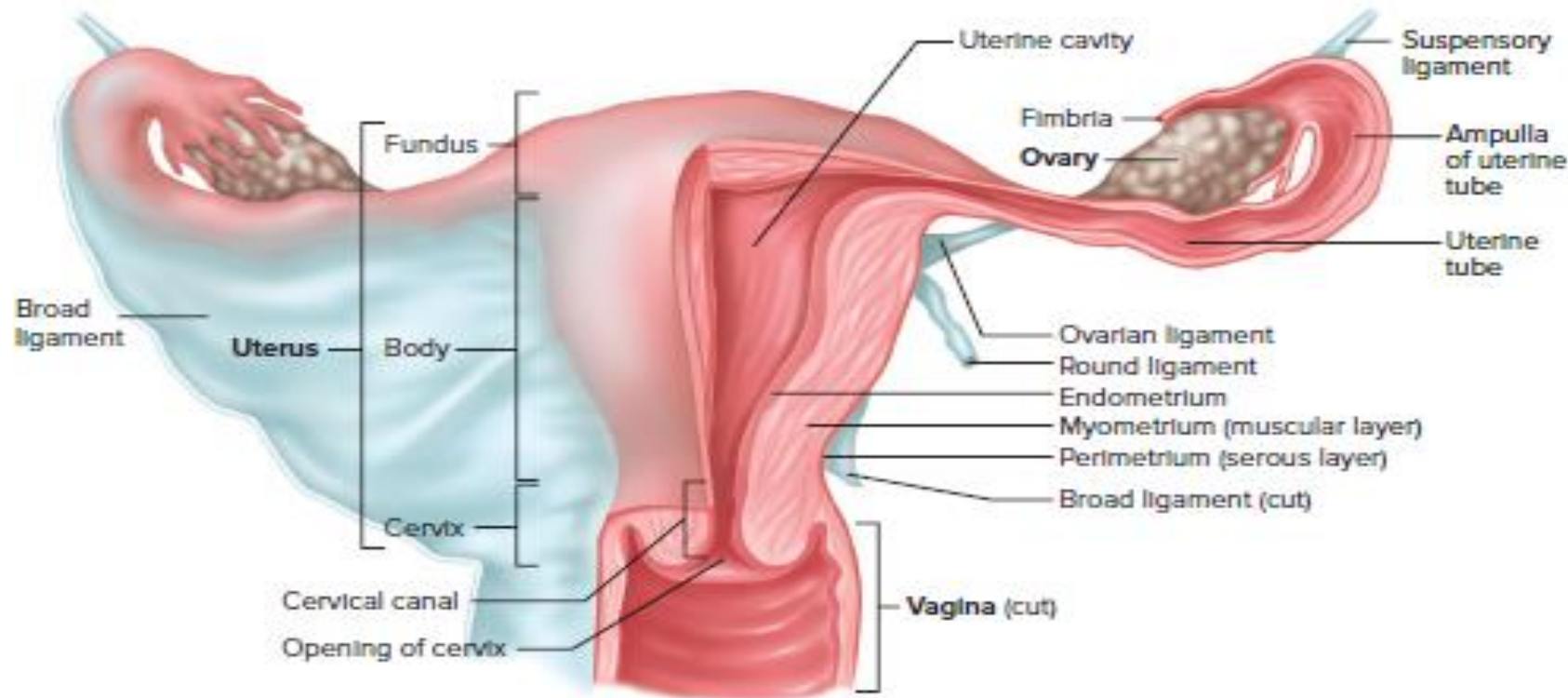
- Corpus luteum of pregnancy
 - That's if pregnancy occurs
 - Secret progesterone to maintain pregnancy for first few months
 - After 4 months the corpus disappears as the placenta start producing progesterone
- Series of events from formation of ovarian follicles , ovulation and to degeneration of the corpus luteum constitute **ovarian cycle**

- Corpus haemorrhagicum
 - Bleeding into the follicle
- Corpus Luteum (yellowish body)
 - Secret progesterone
 - Depends on whether the pregnancy occur or not
- Corpus luteum of menstruation
 - That's if egg is not fertilized
 - Persist for about 14 days
- Corpus albicans (white body)
 - Degenerated fibrous corpus luteum

• MENSTRUAL CYCLE

• Anatomy of Uterus

- uterus consists of 3 layers of tissue: perimetrium, myometrium & endometrium
- outer layer—**perimetrium** or serosa—is part of the peritoneum; it is composed of simple squamous epithelium and a thin layer of areolar connective tissue
- middle layer of the uterus, the **myometrium**
- consists of 3 layers of smooth muscle fibers that are thickest in the fundus & thinnest in the cervix



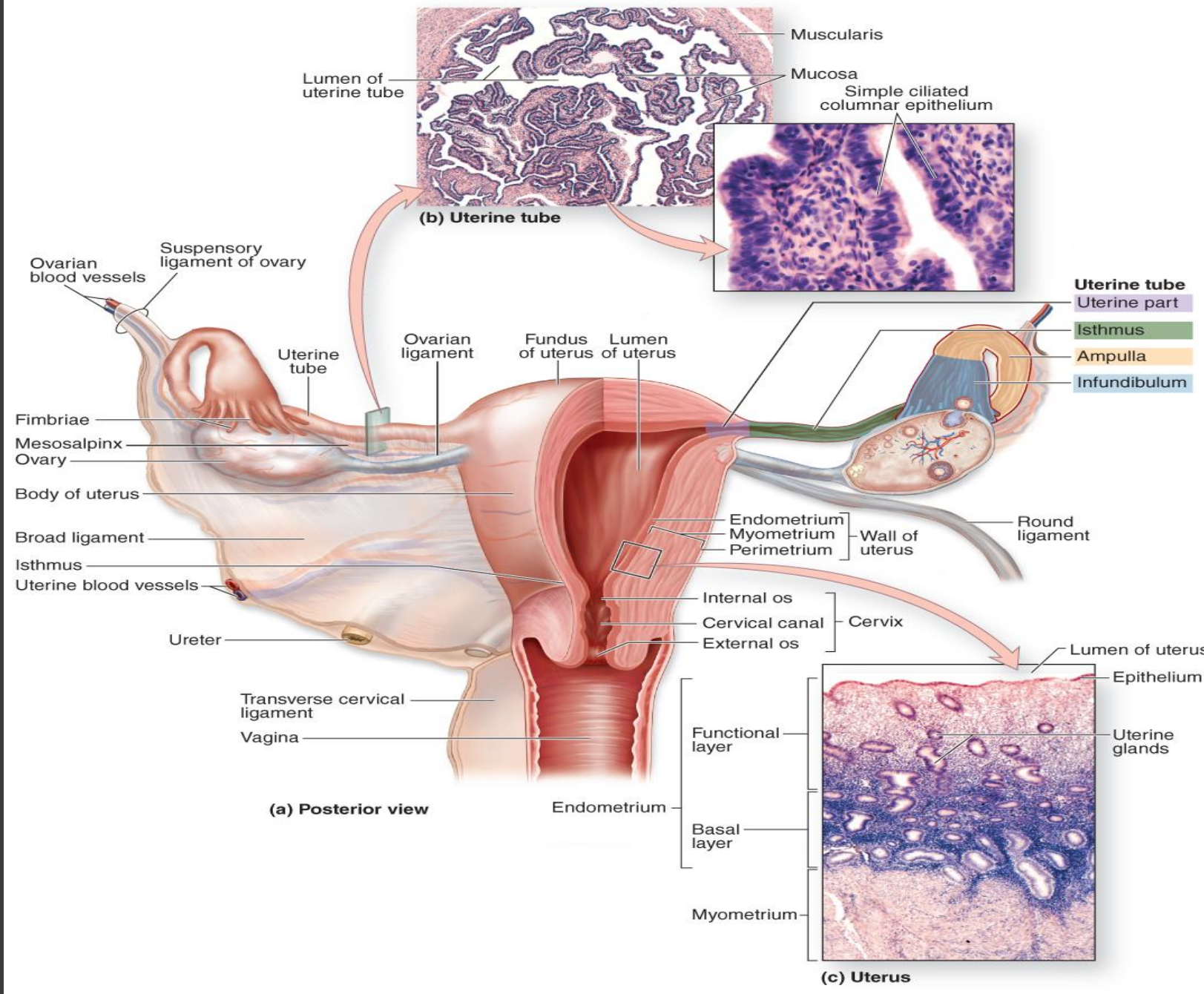


FIGURE 22-14

- inner layer of the uterus, the **endometrium** is highly vascularized and has three components:
- (1) An innermost layer composed of simple columnar epithelium (ciliated and secretory cells) lines the lumen
- (2) An underlying endometrial stroma is a very thick region of lamina propria (areolar connective tissue)
- (3) Endometrial (uterine) glands develop as invaginations of the luminal epithelium and extend almost to the myometrium

- endometrium is divided into two layers.
- The **stratum functionalis** (=functional layer) lines the uterine cavity(compact and spongy layers together form **stratum functionalis** (functional layer))
- sloughs off during menstruation as a result of declining levels of progesterone from the ovaries
- The deeper layer, the **stratum basalis** (=basal layer), is permanent and gives rise to a new stratum functionalis after each menstruation

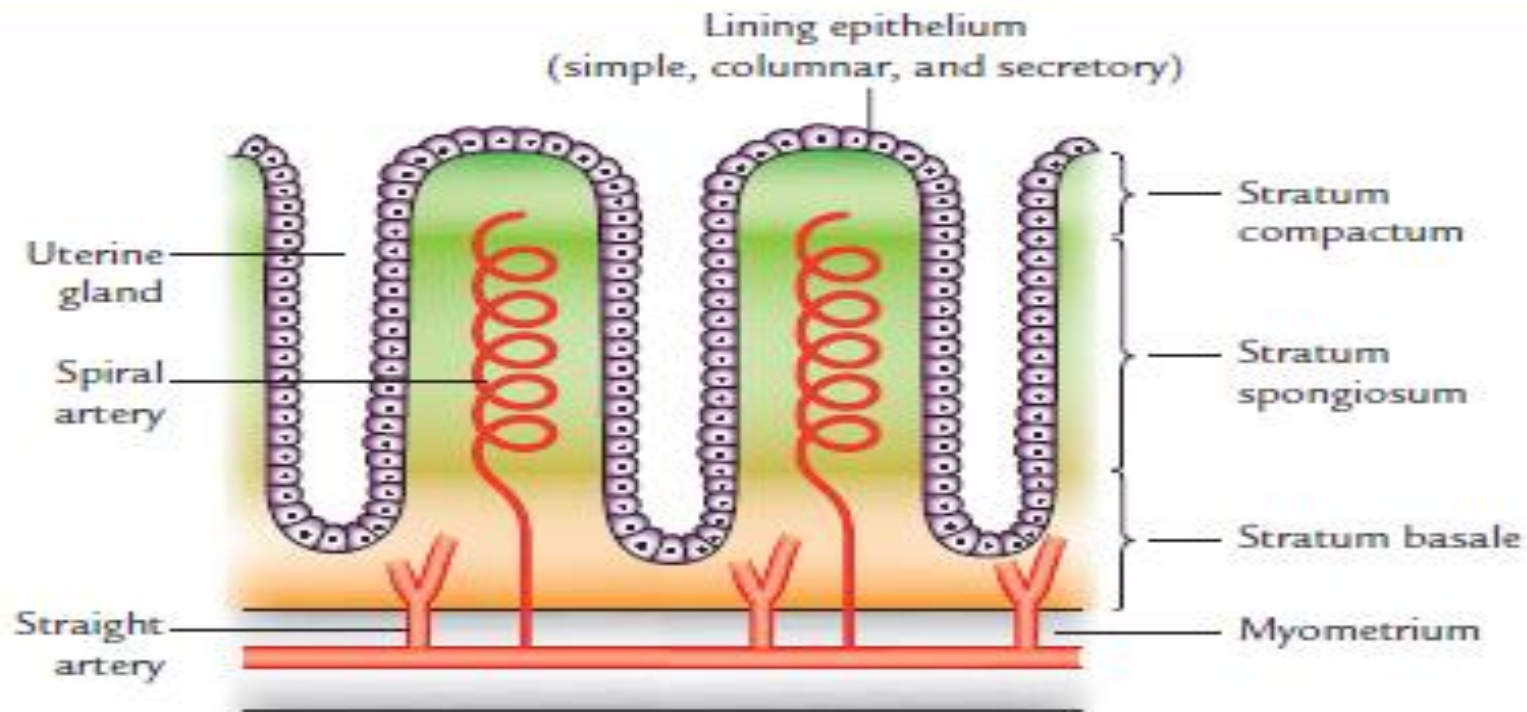
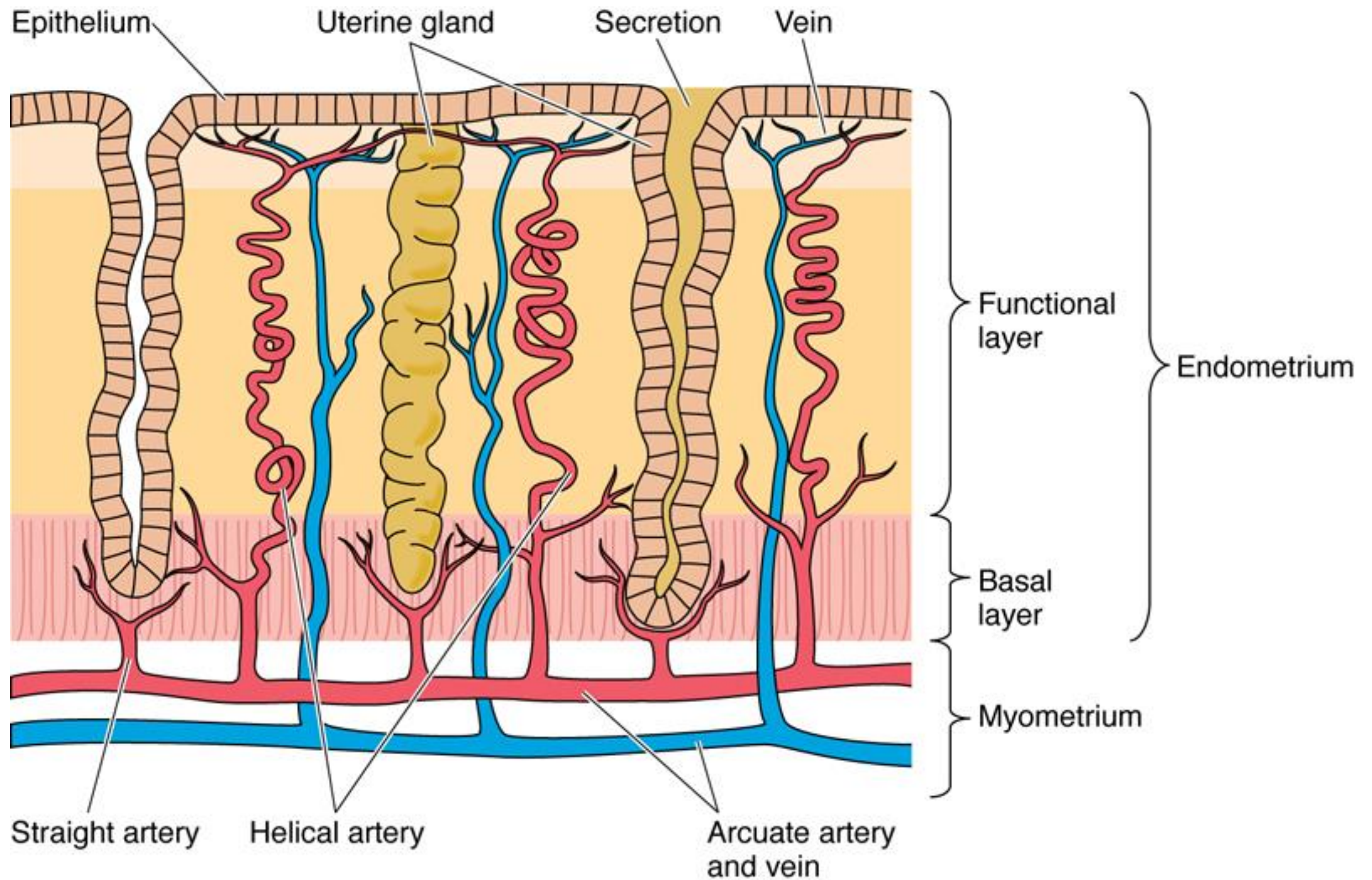
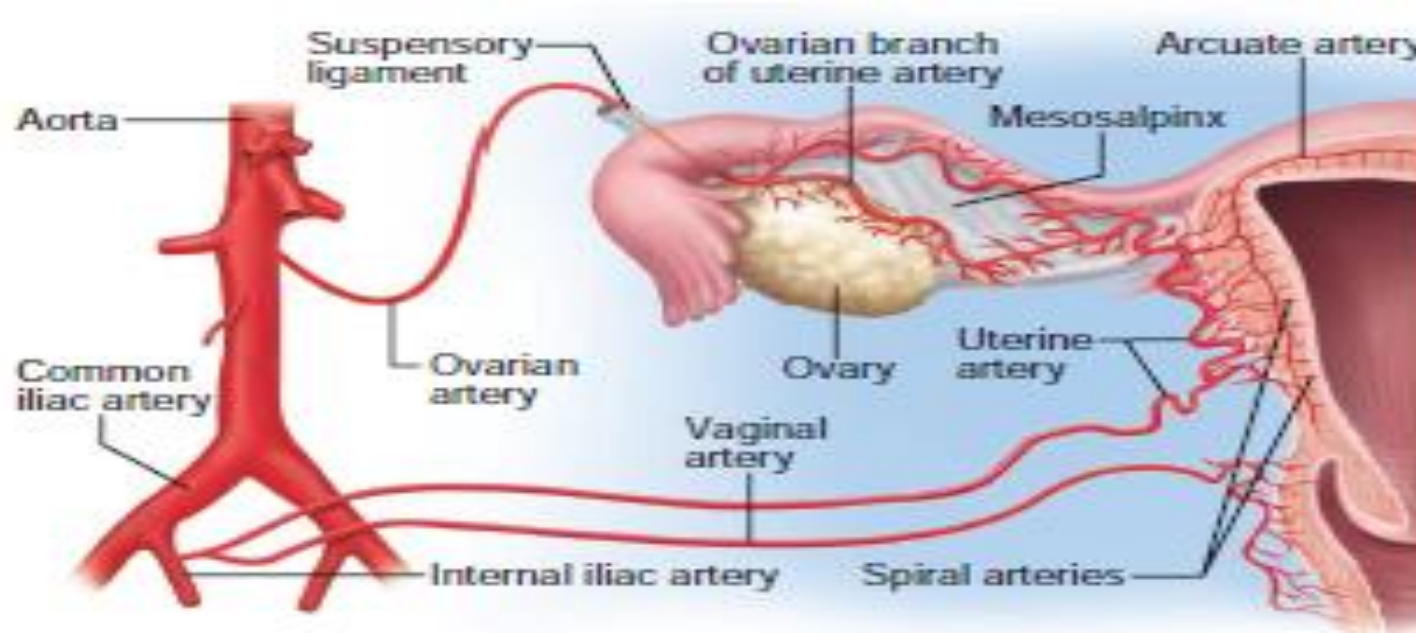


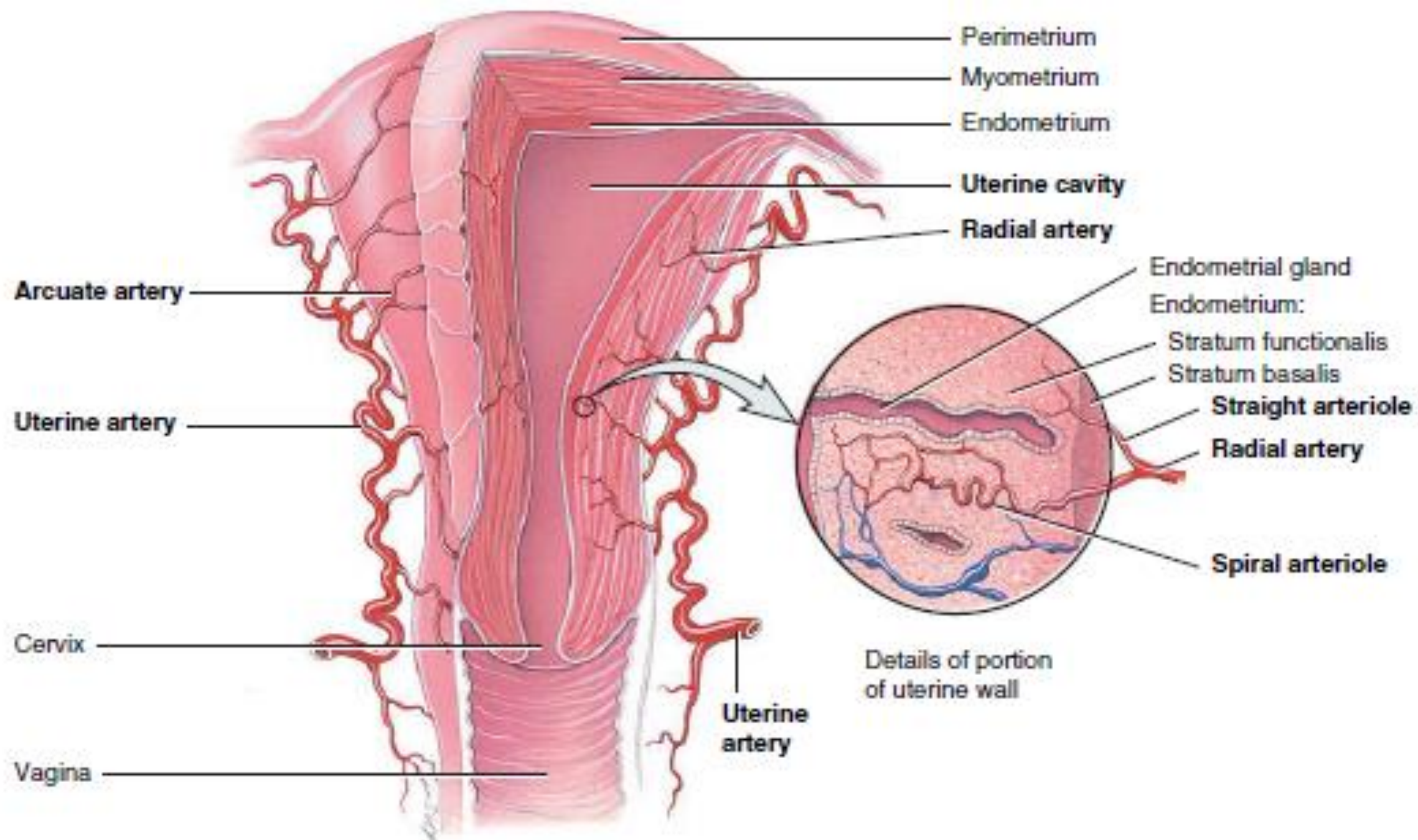
Fig. 2.7 Layers of endometrium.



- **Blood supply to the uterus**

- Branches of the internal iliac artery called **uterine arteries** supply blood to the uterus
- Uterine arteries give off branches called **arcuate arteries** that are arranged in a circular fashion in the myometrium
- These arteries branch into **radial arteries** that penetrate deeply into the myometrium
- Before the branches enter the endometrium, they divide into two kinds of arterioles: **Straight arterioles** supply the stratum basalis with the materials needed to regenerate the stratum functionalis
- **spiral arterioles** supply the stratum functionalis and change markedly during the menstrual cycle





Anterior view with left side of uterus partially sectioned

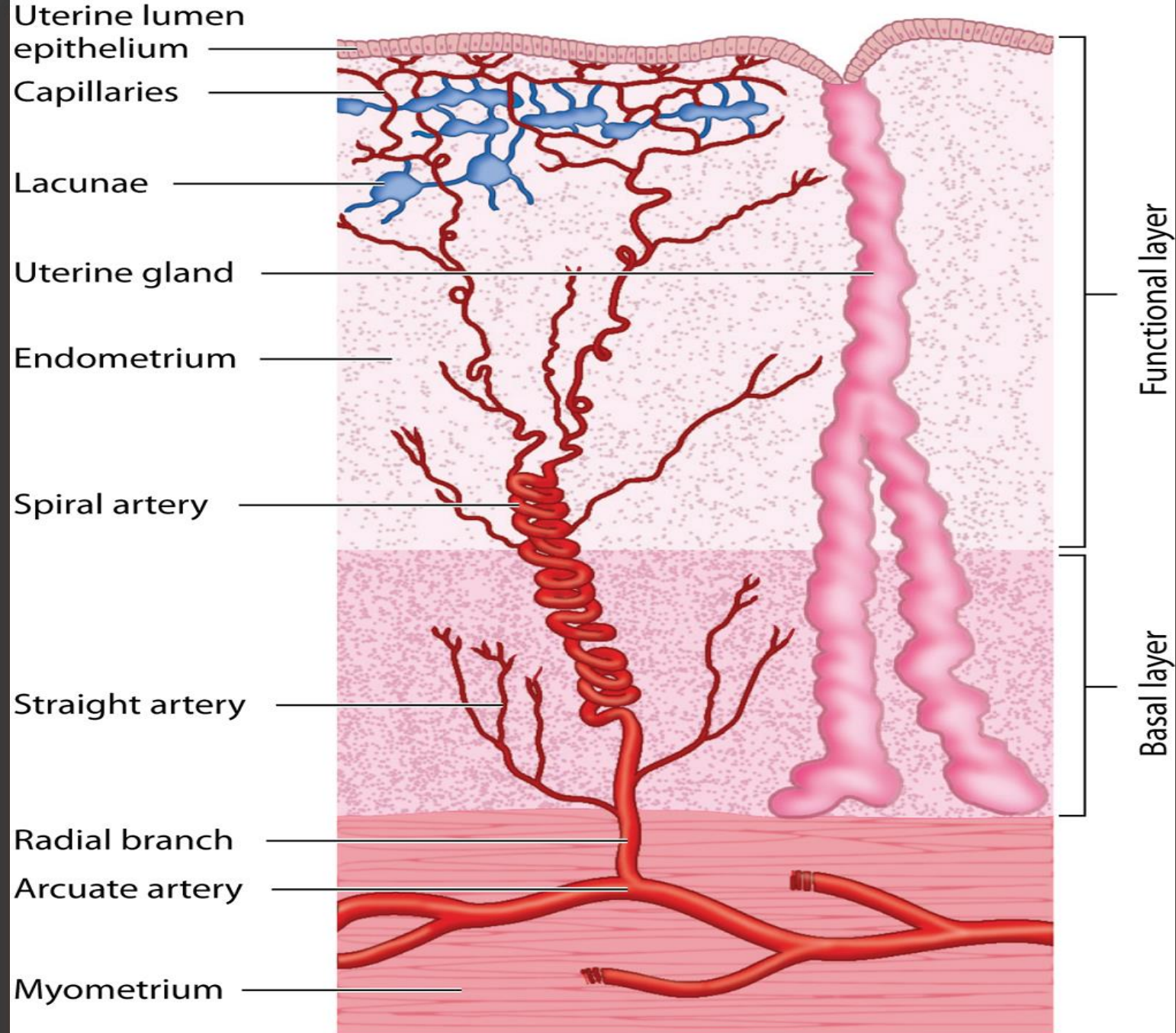
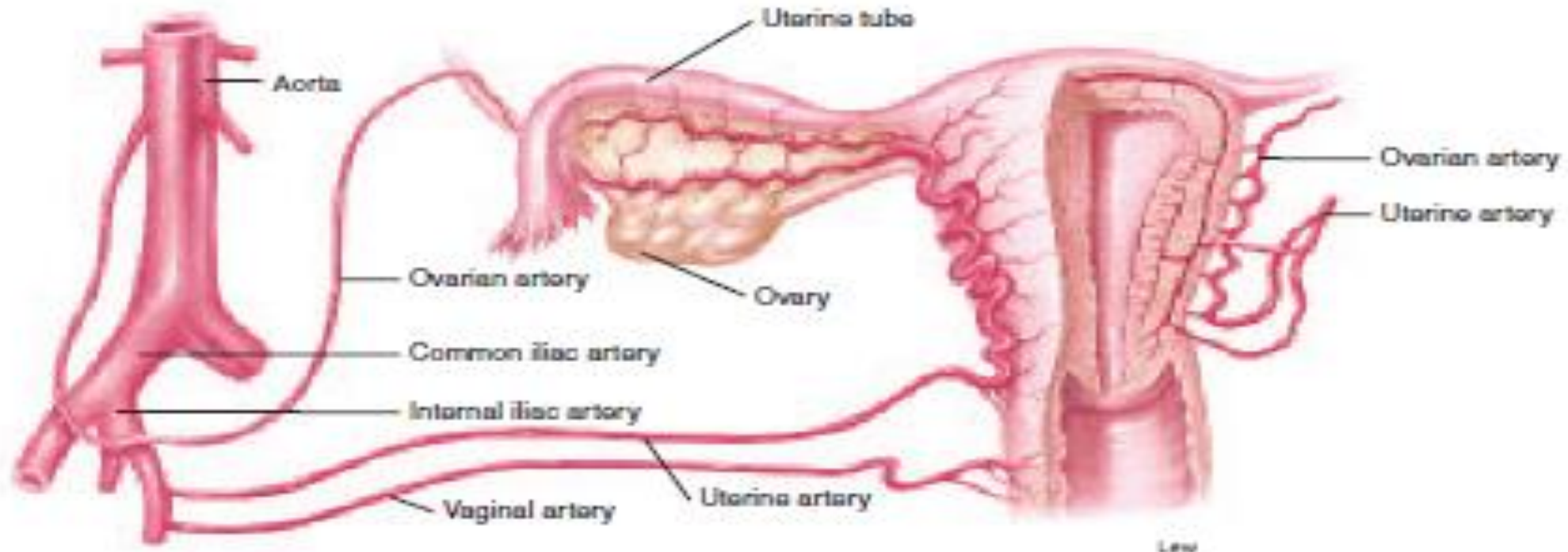


FIGURE 22-18

- The extensive blood supply of the uterus is essential to support **regrowth of a new stratum functionalis after menstruation, implantation of a fertilized ovum, and development of the placenta**
- the changes taking place in the uterine endometrium during the menstrual cycle occur under the influence of:
- (a) **oestrogens** produced by the thecal gland (theca interna) and by the interstitial gland cells, and possibly by granulosa cells.
- (b) **progesterone** produced by the corpus luteum



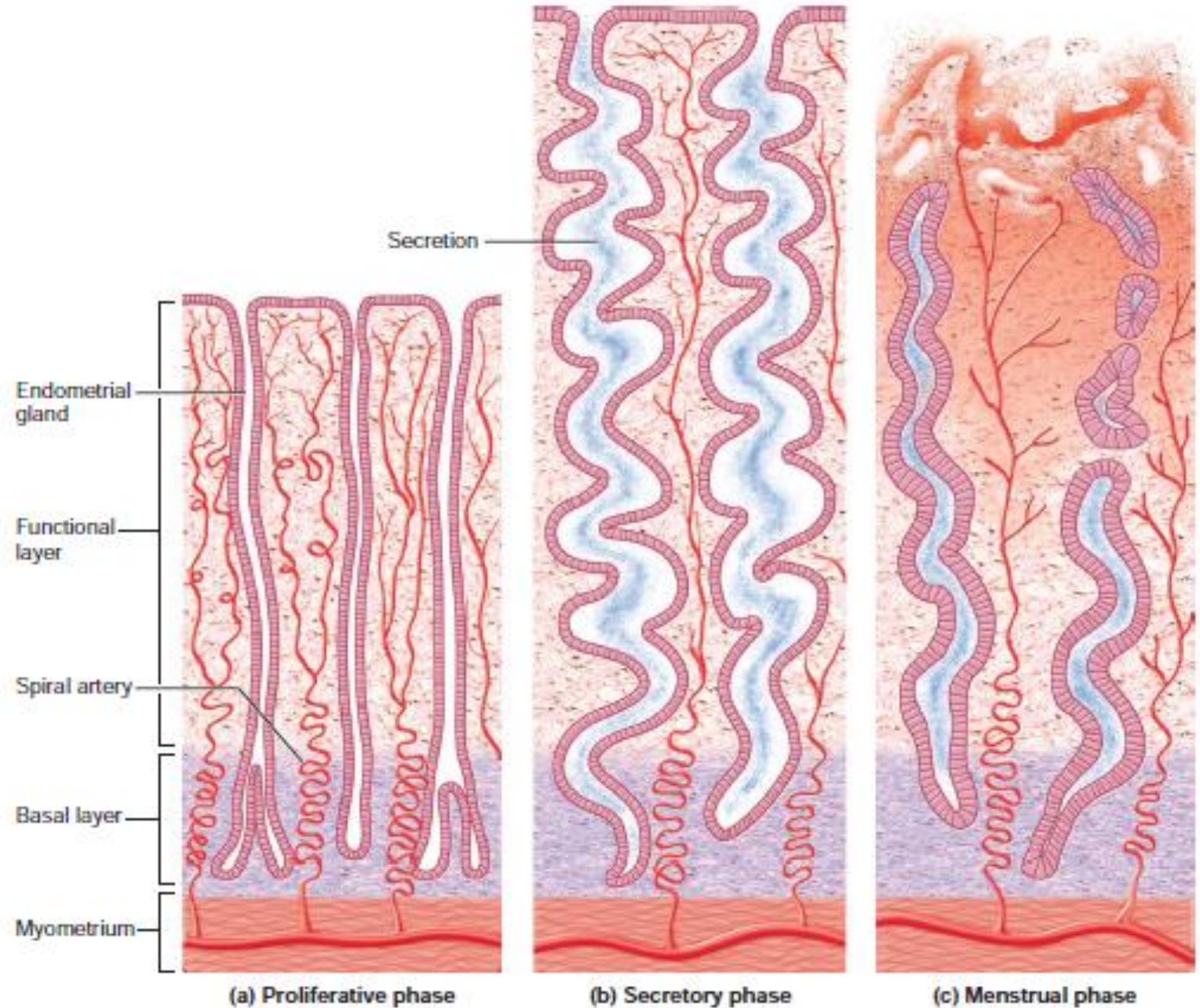
- **MENSTRUAL CYCLE**

- cyclical changes that occur in the endometrium every month also called *uterine cycle*
- visible feature is a monthly flow of blood (menstruation)
- The duration of blood flow is 3–7 days
- length of the cycle is usually of 28 days and can vary from 21–40 days
- 1st day of bleeding in the present cycle marks the beginning of the menstrual cycle.
- Ending of the cycle is the 1st day of bleeding of the next cycle

- The **hormones** produced by the **ovarian follicles** and **corpus luteum** (**oestrogen** and **progesterone**) produce cyclic changes in the endometrium
- These monthly changes in the internal layer of the uterus constitute the **endometrial cycle**, commonly referred to as the **menstrual cycle** or period
- Controlled by gonadotropins
- From puberty up to about 45-50 years
- Menarche
- Menopause

- purpose of menstrual cycle is to **prepare the endometrium for reception of fertilized ovum(implantation)**
- The main changes in the endometrium are:
 - (a) increase in thickness
 - (b) growth of uterine glands
 - (c) changes in epithelial cells lining the glands
 - (d) increase in thickness and fluid content of the endometrial stroma

- Divided into three major phases:-
 - Menstrual phase
 - Proliferative phase
 - Secretory phase
 - Ischemic phase



Menstrual phase/ period

- Begins with ovulated oocyte not fertilized and no implantation occurs in the uterus
- Lasts for 3 -7days on average(From day 1 to day 7)
- Is due to ↓progesterone and estrogen due to regressing corpus luteum
 - Spasm of muscle contraction
- ↓ level of these hormones stimulates release of prostaglandins induce intermittent constrictions of spiral arteries and interruption of blood flow to the functional layer of endometrium
 - Basalis layer is intact
 - This causes no oxygenated blood to functional layer and produce ischemia causing necrosis of cells in the wall of blood vessels and degeneration of the functional layer

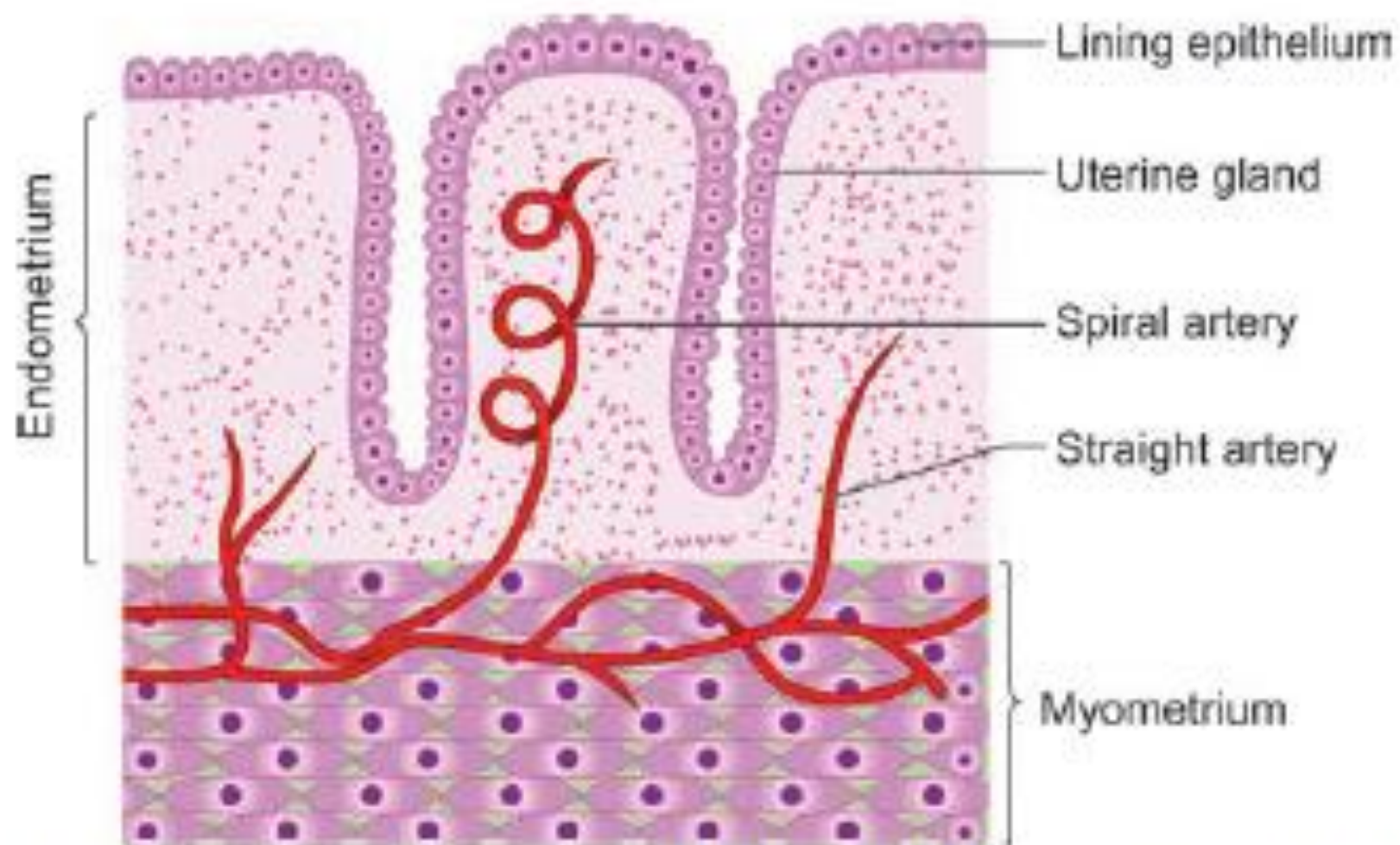
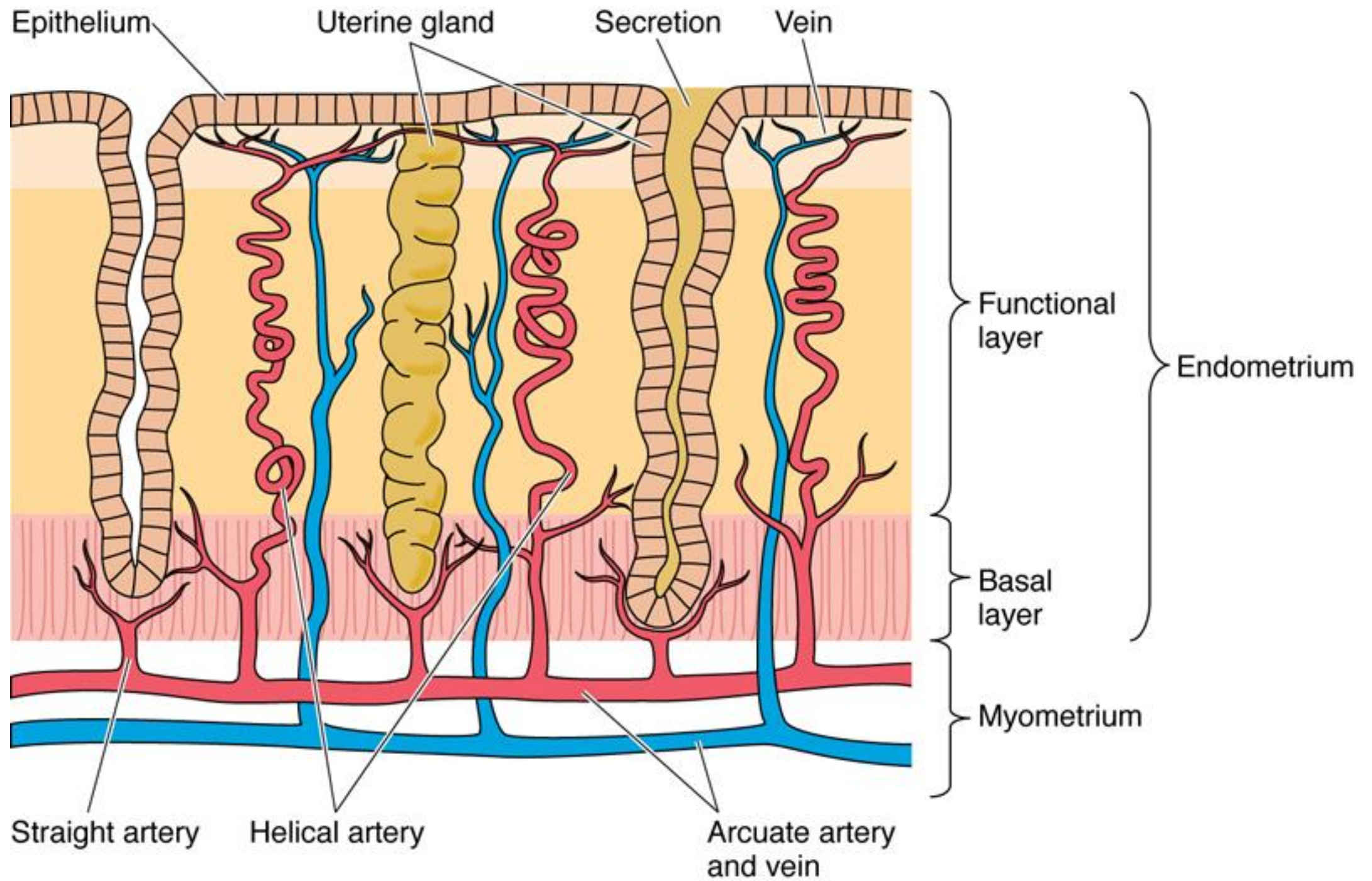


Fig. 3.6: Layers in the wall of uterus and components of uterine endometrium that undergo changes during menstrual cycle

- Spiral arteries dilate resulting in the rupture of their necrotic walls and hemorrhage into the stroma
- Functional layer detaches
- Blood, uterine fluid ,stromal cells secretory material and epithelial cells from functional layer mix to form the **menstrual flow**
- Amount of blood and endometrium lost varies among women and in same women at different times
- Blood combined with small pieces of endometrial tissue is discharged through the vagina



Proliferative Phase

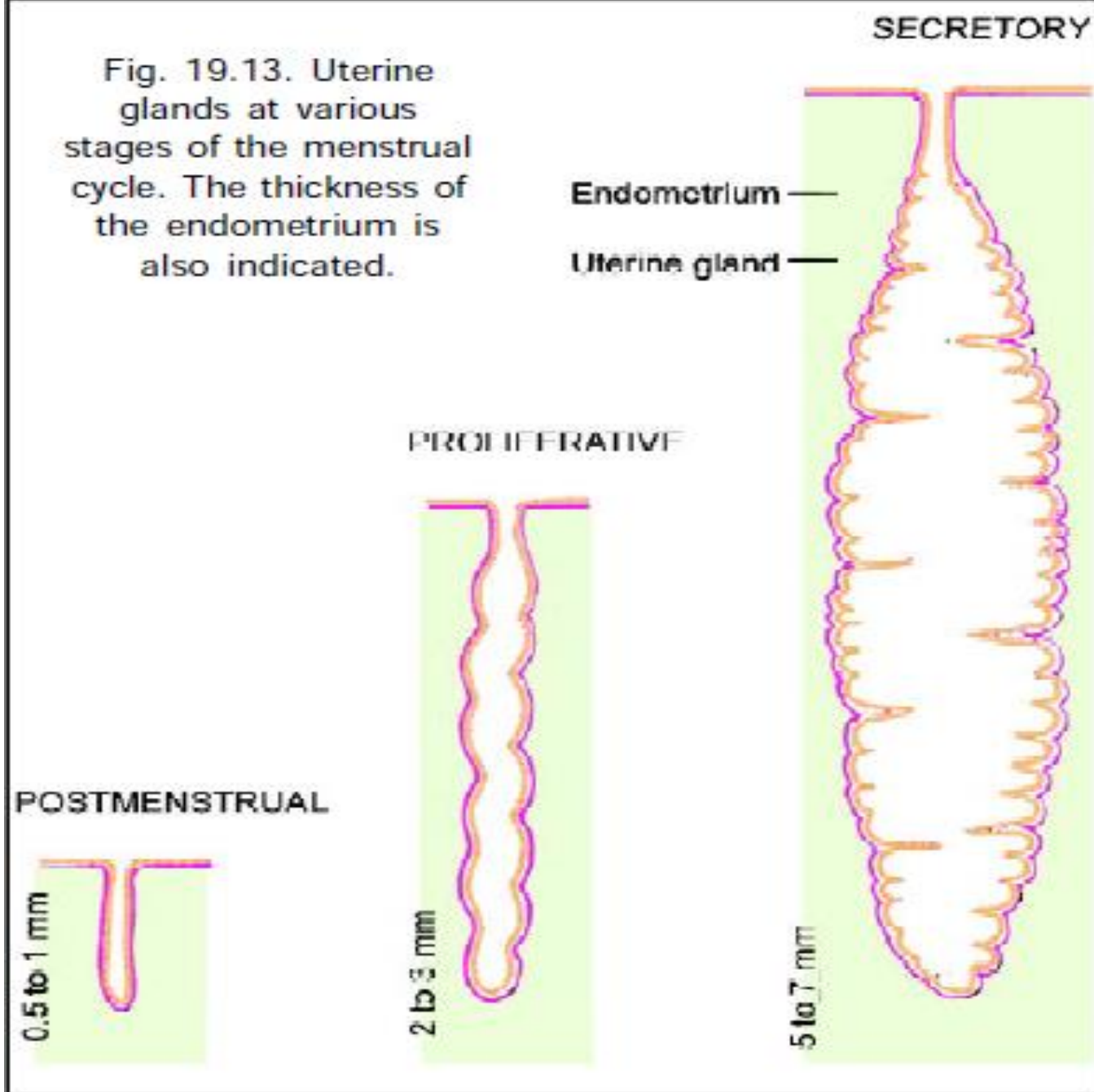
- Also known as Follicular / estrogenic phase
- Variable length, day 6 – 14
- Coincide with growing ovarian follicles
- Estrogen secreted from theca cells acts on endometrium
- Characterized by or result in regeneration of functional layer

- increase in the thickness of the endometrium and in its water content during this phase of repair and proliferation
- the superficial part of the stroma remains compact, but the part surrounding the bodies of the uterine glands becomes spongy
- The deepest part of the stroma also remains compact
- Spiral arteries lengthen and the glands increase in number
- About 3 - 3 mm thick layer is established

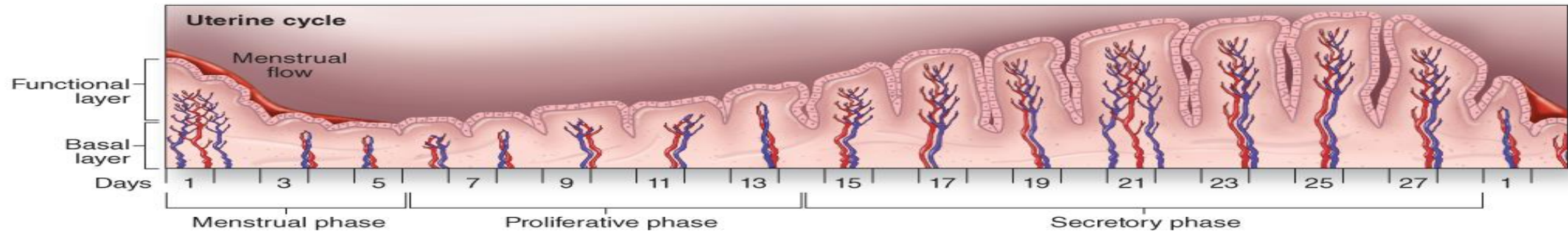
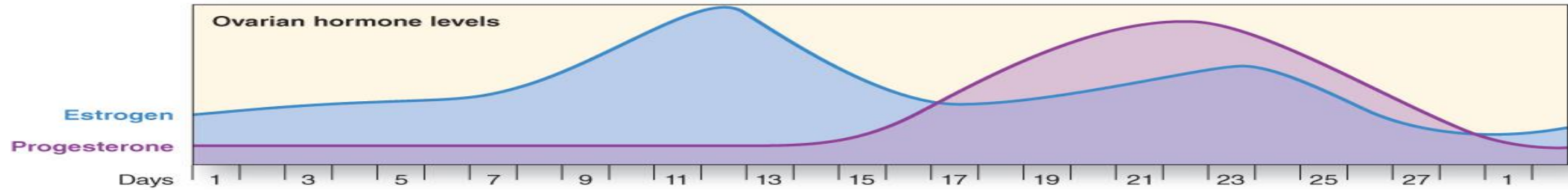
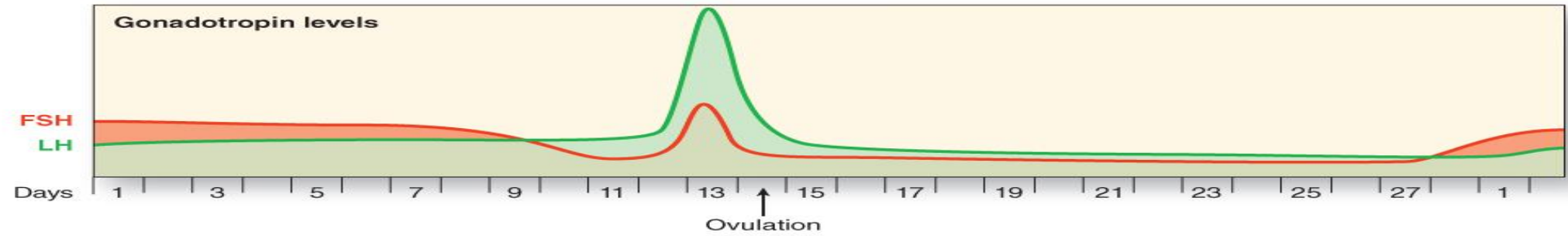
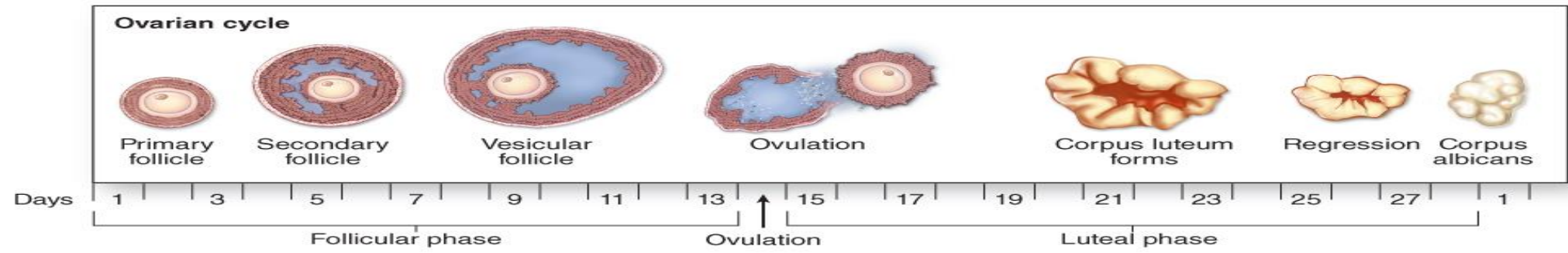
Secretory phase

- Also known as luteal phase
- Last for about 13 days starts on day 15
- The glands increase in number and length, and the spiral arteries elongate
- The glands become wide, tortuous, and saccular, and the endometrium thickens
- High progesterone and oestrogen levels and increased fluid in the connective tissue
- Wide and tortuous glands
- Ready for implantation

Fig. 19.13. Uterine glands at various stages of the menstrual cycle. The thickness of the endometrium is also indicated.



- Ischemic phase
- occurs when the oocyte is not fertilized
- Spiral arteries constrict, giving the endometrium a pale appearance
- constriction results from the decreasing secretion of hormones, primarily progesterone, by the degenerating corpora lutea
- Also causes stoppage of glandular secretion, a loss of interstitial fluid, and a marked shrinking of the endometrium



- **CLINICAL APPLICATION**

- **ENDOMETRIOSIS**

- In this condition fragments of endometrial tissue are present in the uterine tubes, on the ovary, and in the peritoneum of the pelvic cavity.
- Normal are suppose to be found only in the uterus.
- explanation for this out-of-place endometrium is that a reflux of menstrual fluid spreads endometrial cells from the uterus through the uterine tubes
- the uterine tubes open into the peritoneum, endometrial cells may also spread to the peritoneum

- In endometriosis, the pain associated with menstruation is extreme because the endometrial
- fragments respond to the circulating ovarian hormones by building up endometrial tissue and bleeding
- Blood accumulates in the pelvic cavity, forms cysts, and exerts pressure
- causes one-third of all cases of infertility in women, when ectopic endometrial tissue covers the ovaries or blocks the uterine tubes

- Treatment involves drugs that halt the secretion of estrogens and suppress menstruation,
- Use of lasers to vaporize patches of ectopic endometrium, and hysterectomy

- An **ovarian cyst** is a fluid-filled sac in or on an ovary
- the etiology is unclear, although increased androgen production by the ovaries or adrenals is likely involved
- Such cysts are relatively common, usually noncancerous, and frequently disappear on their own
- Cancerous cysts are more likely to occur in women over 40
- Ovarian cysts may cause pain, pressure, a dull ache, or fullness in the abdomen; pain during sexual intercourse;
- delayed, painful, or irregular menstrual periods; abrupt onset of
- sharp pain in the lower abdomen; and/or vaginal bleeding
- Most ovarian cysts require no treatment, but larger ones (more than 5 cm or 2 in.) may be removed surgically

- ***Abnormal menstrual cycles***
- **Amenorrhea**
- is the absence of menstruation.
- The most common causes of amenorrhea are pregnancy and menopause
- In female athletes, amenorrhea results from reduced secretion of gonadotropin-releasing hormone, which decreases the release of LH and FSH
- As a result, ovarian follicles fail to develop, ovulation does not occur, synthesis of estrogens and progesterone wanes, and monthly menstrual bleeding ceases
- may be of two types: primary and secondary.
- (a) *Primary amenorrhea*: It is the condition when menstrual bleeding does not occur after 16 years of age.
- (b) *Secondary amenorrhea*: It is stoppage of menstrual cycles with normally occurring menstrual cycles before

- **Dysmenorrhea:** Painful menses
- ***Hypomenorrhea:*** It is scanty blood flow during the menstrual cycle
- ***Menorrhagia:*** It is profuse blood flow during the menstrual cycle
- ***Metrorrhagia:*** It is the occurrence of bleeding between the menstrual cycles
- ***Oligomenorrhea:*** It is reduced frequency of menstrual cycles

- ***Use of hormones in birth control (contraceptive) pills:***
- sex hormone estrogen with or without progesterone is used in the preparation of contraceptive pills
- These hormones in contraceptive pills act on the hypothalamus and pituitary gland resulting in inhibition of secretion of GnRH, and FSH and LH the secretion of which is essential for ovulation to occur
- **The suppression of ovulation is the basis for the contraceptive pills**