Physiology of Ovarian Cycle

GUYTON & HALL, Chapter 81

DR.MOHAMMED ALOTAIBI

ASSISTANT PROFESSOR OF PHYSIOLOGY

COLLEGE OF MEDICINE

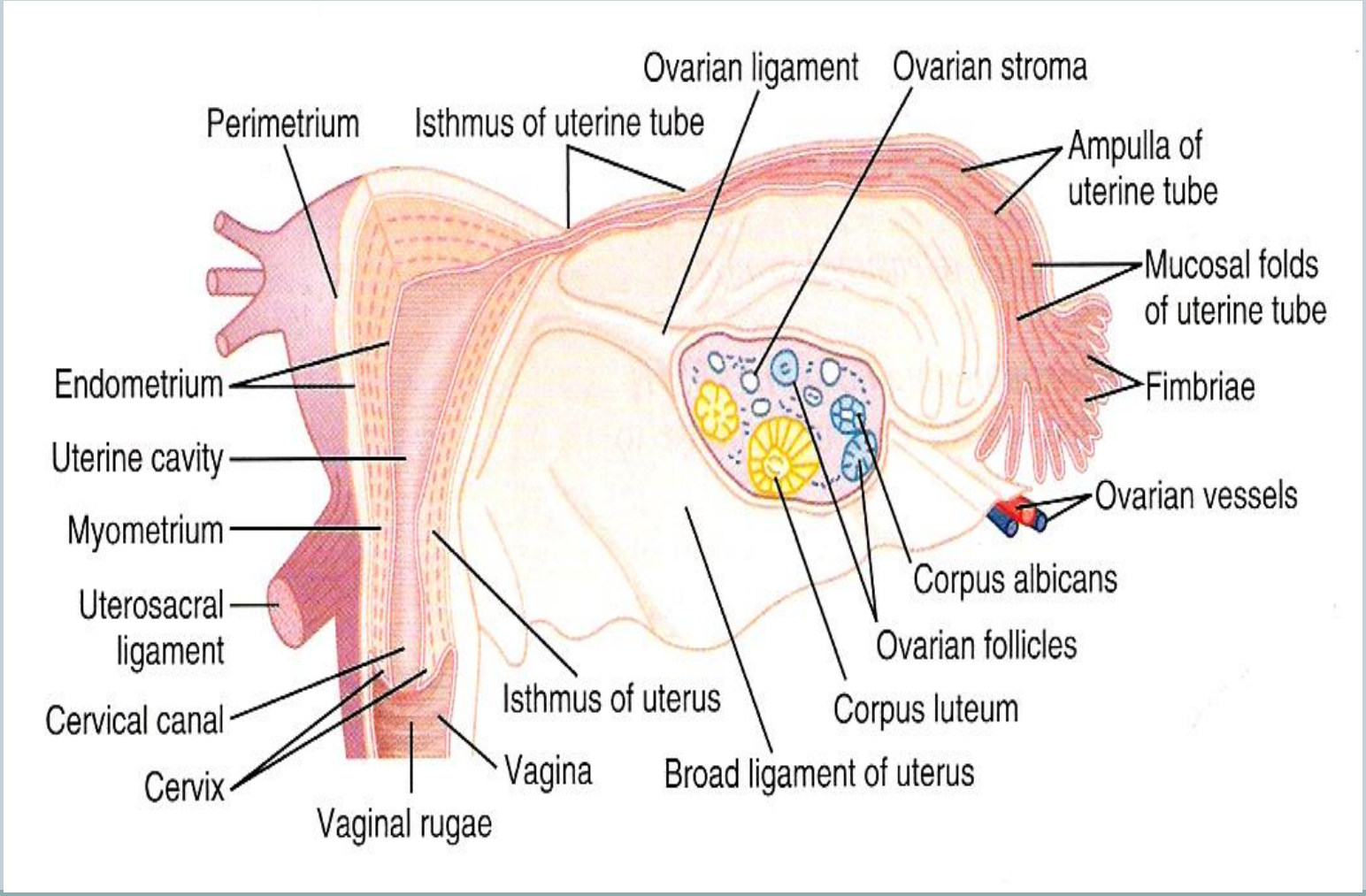
KING SAUD UNIVERSITY

Objectives

By the end of this lecture, you should be able to:

1. Recognize the hypothalamic- *pituitary-ovarian-axis*
2. Describe the physiological phases of ovarian cycles
3. Describe the changes that occur in the ovaries leading to ovulation
4. Describe the development and the fate of corpus luteum

Physiologic Anatomy of the Female Sexual Organs



Female Reproductive Physiology

Normal repr. Years of female → Monthly rhythmical changes in the rates of secretion of female hormones & corresponding physical changes in the ovaries & other sexual organs (menstrual/sexual cycle)

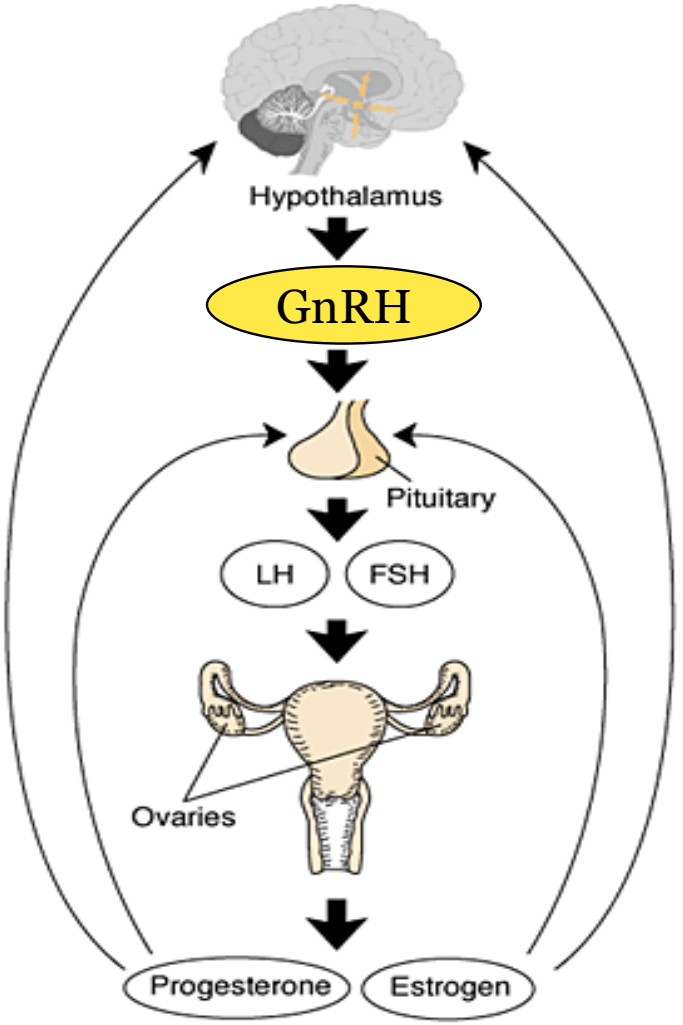
Duration of the cycle averages **28 days** (20-45 days).

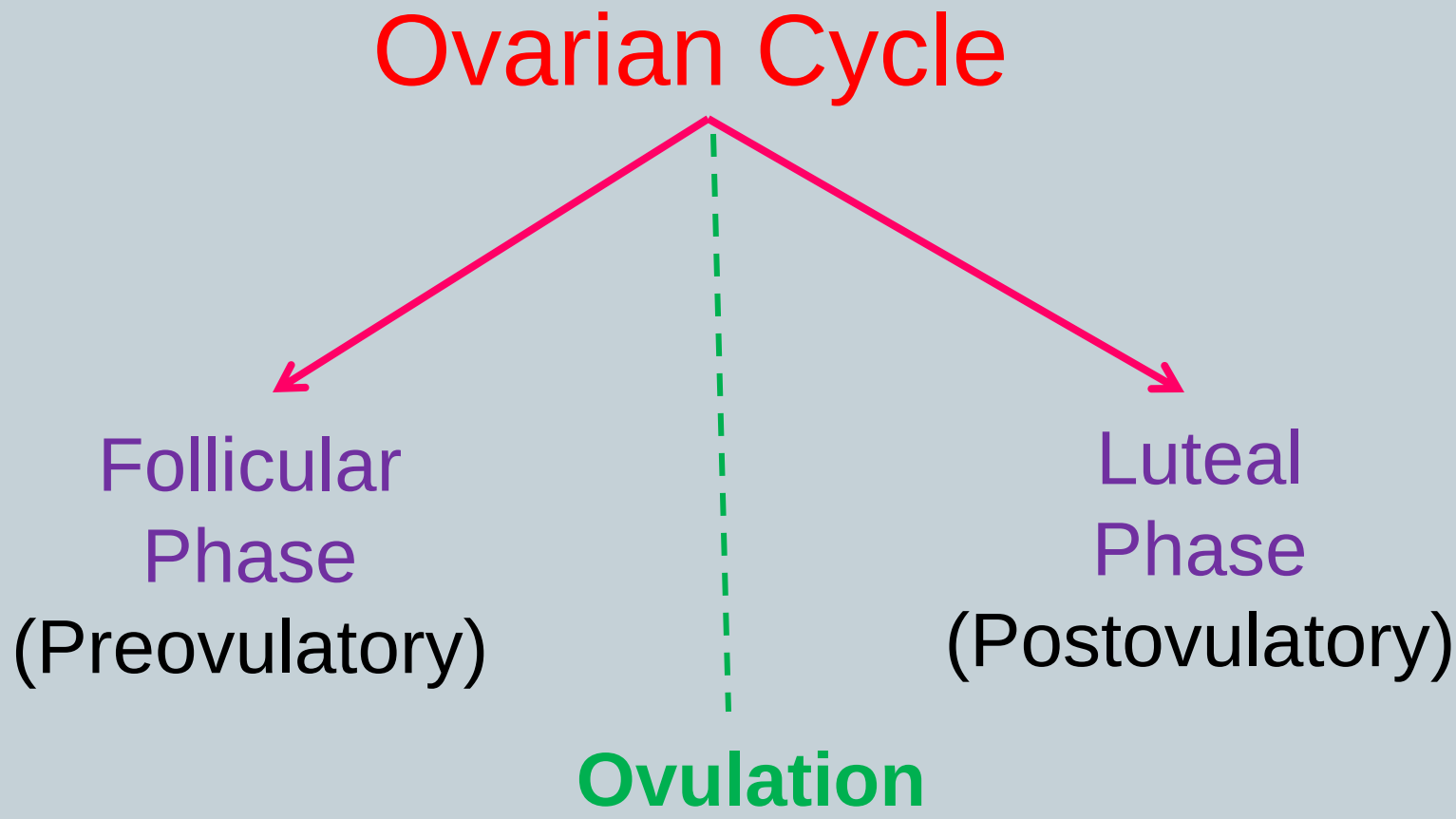
There are 2 results of the female sexual cycle:

1. *Single* ovum is released from the ovaries each month
2. Uterine endometrium is prepared for implantation of the fertilized ovum.

Gonadotropic hormones and their effects on the ovaries

- The **ovarian changes** during the sexual cycle depend completely on FSH & LH secreted by AP.
- **Both FSH and LH** stimulate their ovarian target cells by combining with highly specific receptors leading to an increase in the cells rates of secretion, growth & proliferation.

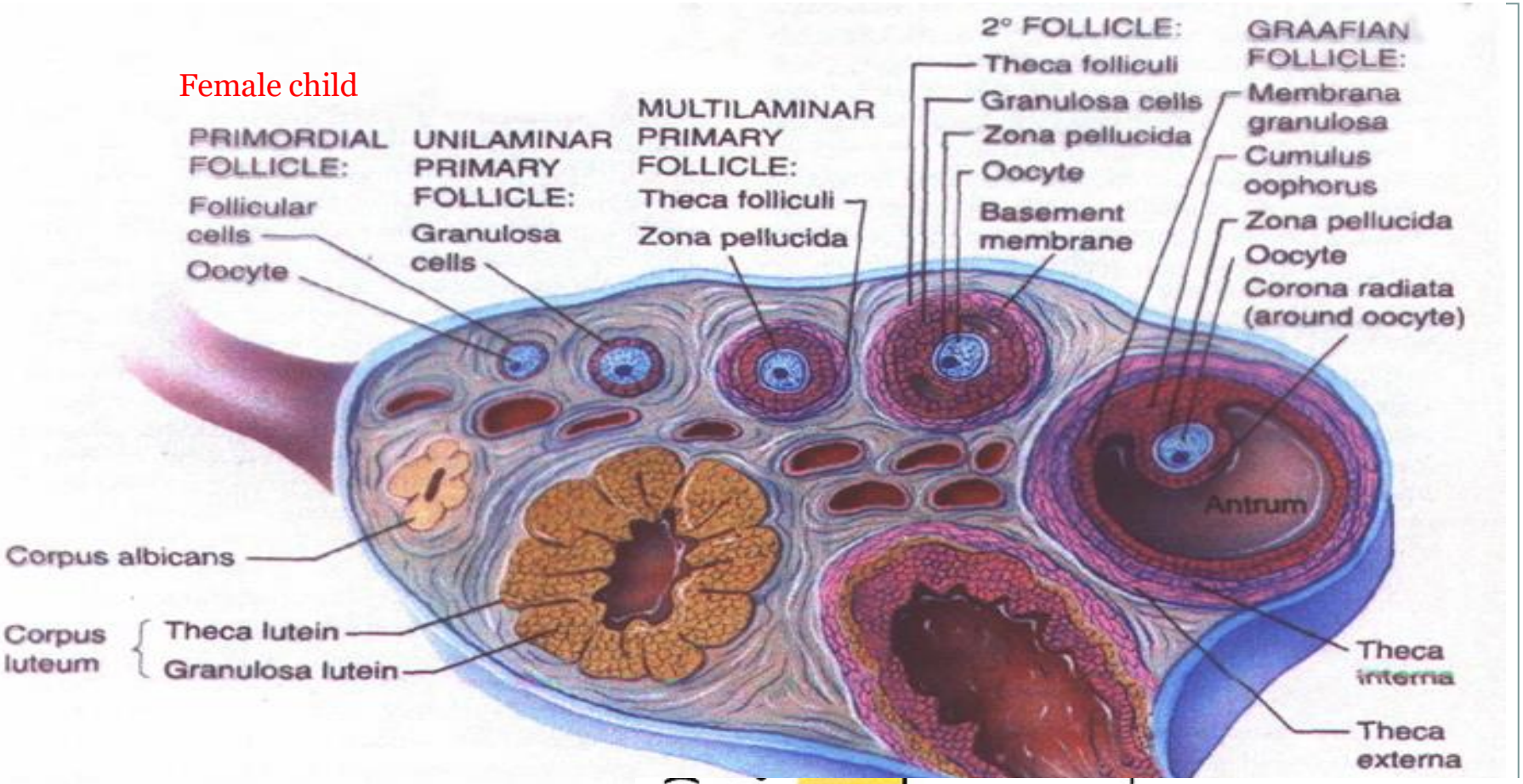


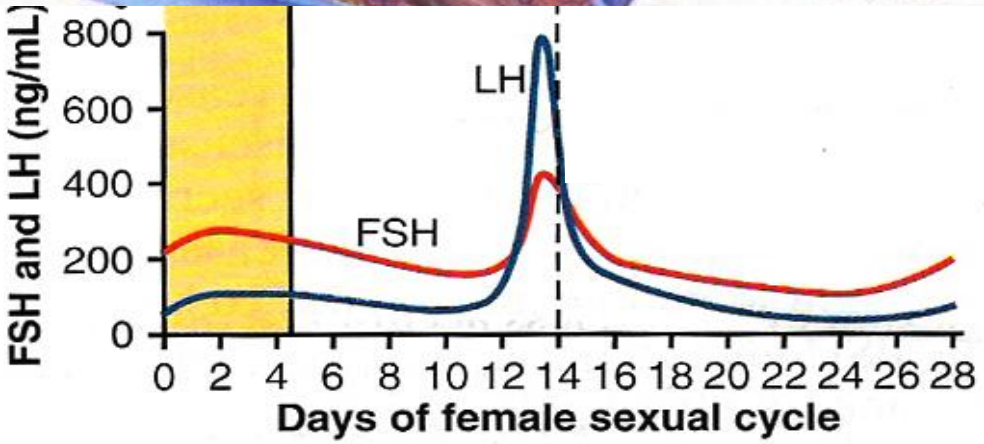

Ovarian Cycle
Follicular Phase (Preovulatory)
Ovulation
Luteal Phase (Postovulatory)

“Follicular” phase of the ovarian cycle:

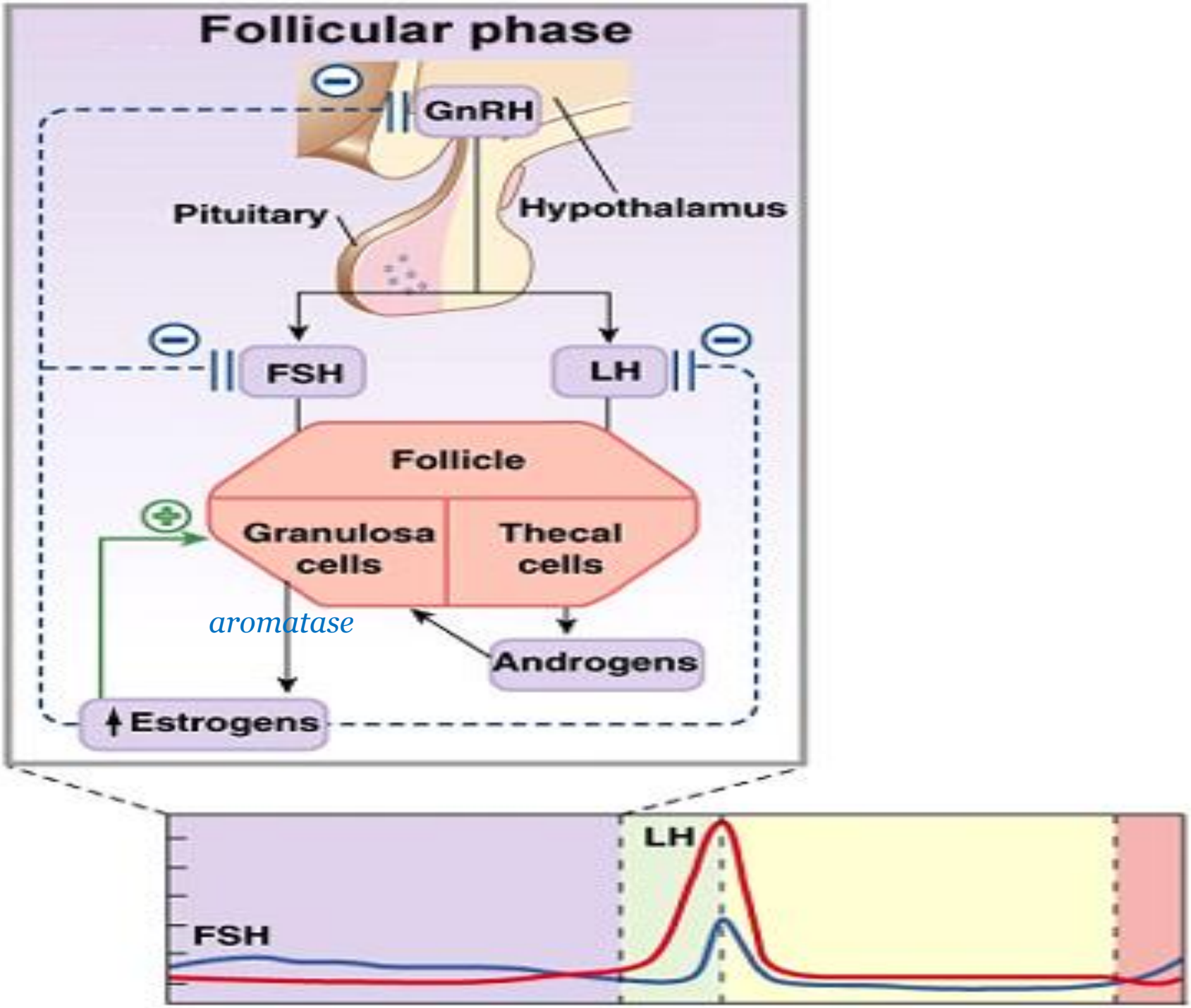
(Ovarian follicle growth)

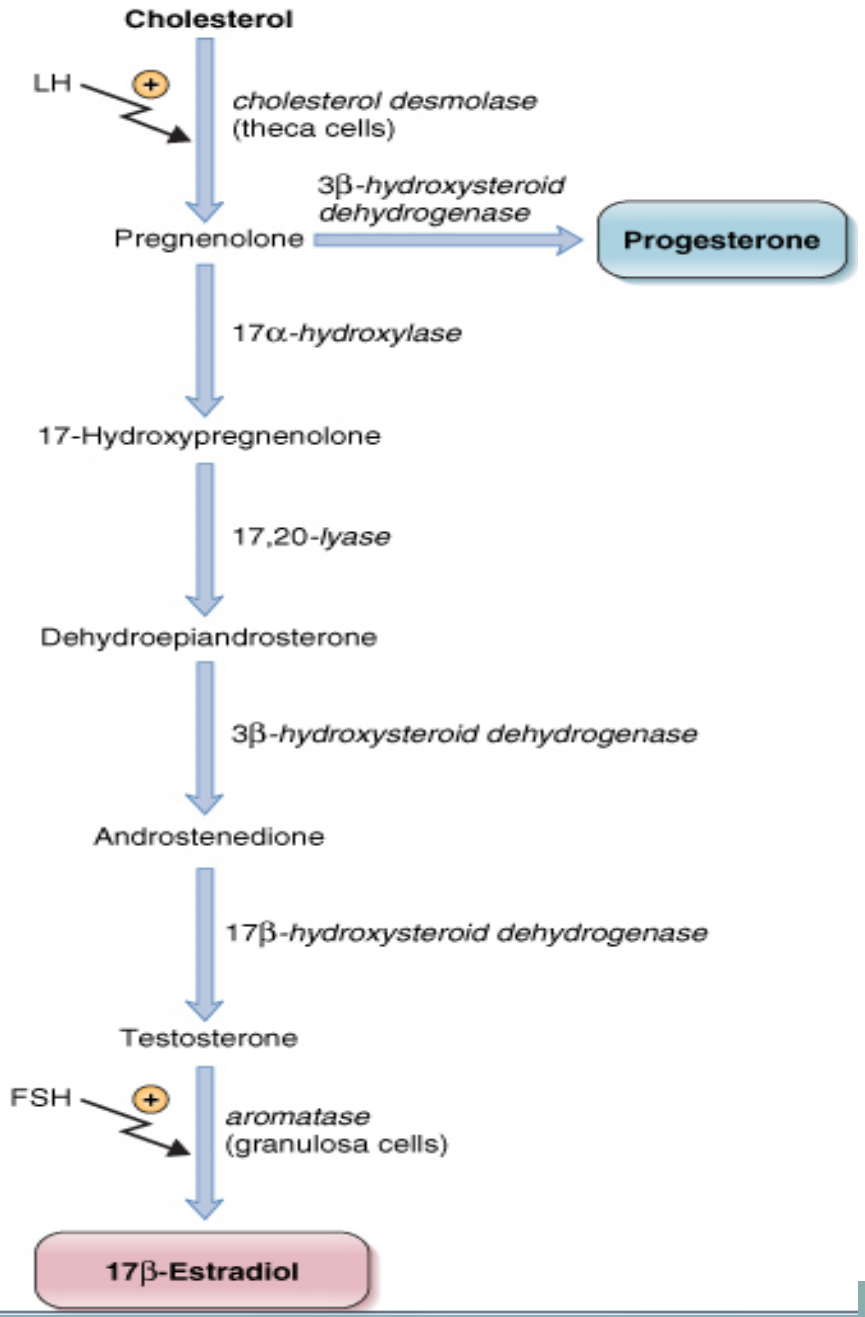
Female child





During ***the first few days*** of the monthly female sexual cycle there is an increase secretion of **FSH, LH**


Follicular phase
GnRH
Pituitary
Hypothalamus
FSH
LH
Follicle
Granulosa cells
Thecal cells
aromatase
Androgens
Estrogens
LH
FSH

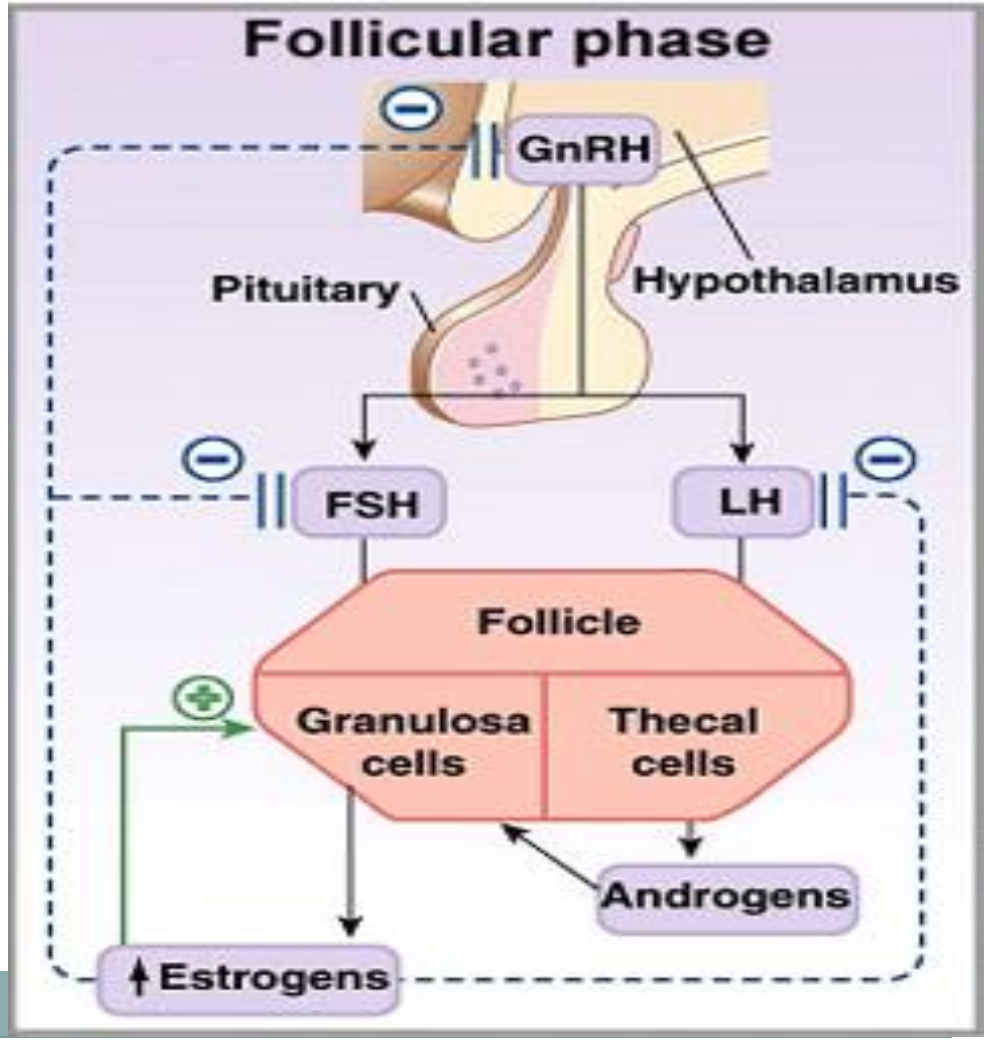

Cholesterol
LH
+
cholesterol desmolase
(theca cells)
3β-hydroxysteroid
dehydrogenase
Pregnenolone
Progesterone
17α-hydroxylase
17-Hydroxypregnenolone
17,20-lyase
Dehydroepiandrosterone
3β-hydroxysteroid dehydrogenase
Androstenedione
17β-hydroxysteroid dehydrogenase
Testosterone
FSH
+
aromatase
(granulosa cells)
17β-Estradiol

The early growth of the primary follicle up to the antral stage is under FSH stimulation only. Then there is **accelerated growth** of the follicle to larger follicle called vesicular follicle (Graffian) caused by:

1. Estrogen ↑ FSH receptors **(positive feedback effect).**

2. Estrogen & FSH combine to promote **LH** receptors on the original granulosa cells in addition to FSH stimulation.

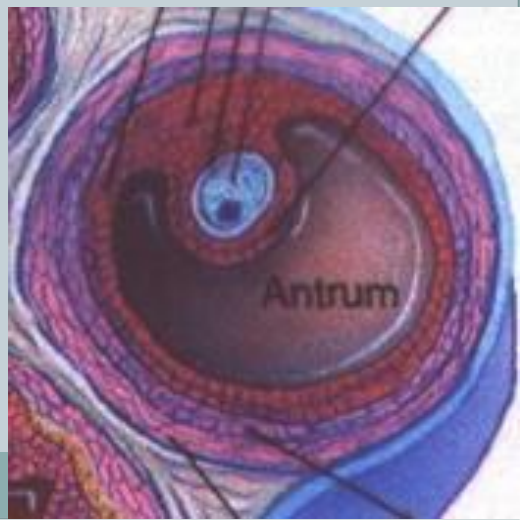
Proliferation of the follicular theca cells & increase their secretion.



Ovarian follicle growth

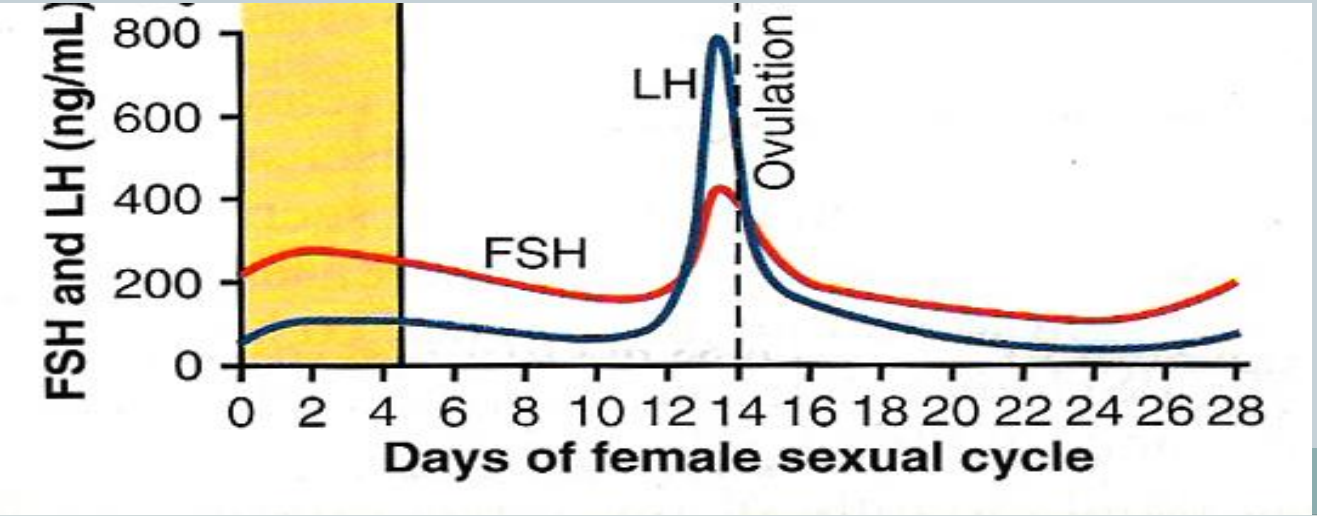
- The **antral follicles** begin to grow. The ovum enlarges & remains embedded at one pole of the granulosa cells of the follicle

- After a week or more of growth—but before ovulation occurs—one of the follicles begins to outgrow all the others, and the remaining 5 to 11 developing follicles involute (a process called *atresia*)



Ovulation

- Ovulation in a woman who has a normal **28-day** female sexual cycle occurs **14 days** after the onset of menstruation.
- Without LH hormone, ovulation will not occur
- 2 days before ovulation → rate of LH secretion ↑ to 6-16 fold & peaks about 16 hrs before ovulation.

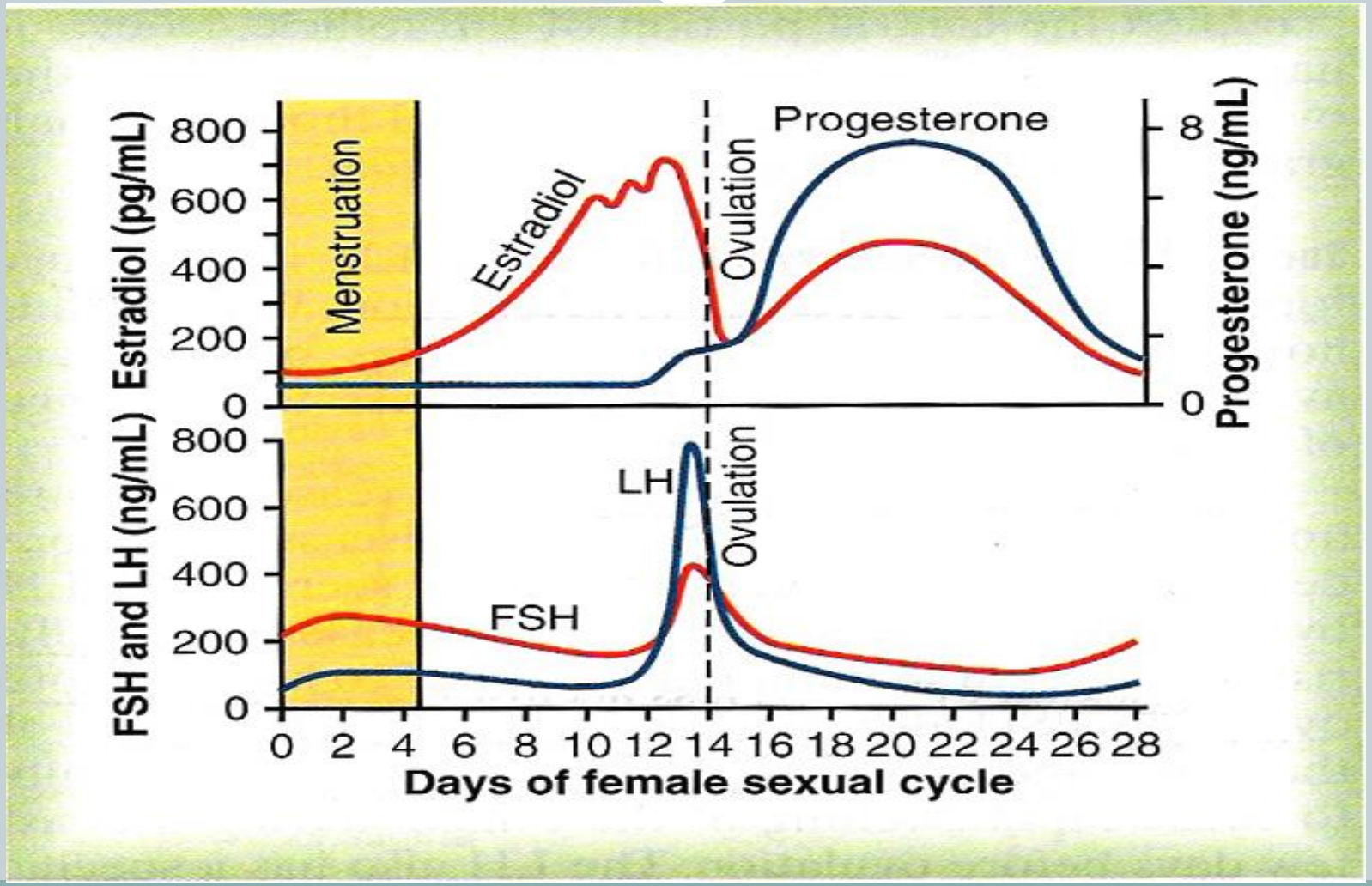


Ovulation

LH surge is necessary for final follicular growth and ovulation:

- FSH also ↑ 2 to 3 fold & acts synergistically with LH to cause swelling of the follicle before ovulation.

- LH has specific effect on the granulosa cells & theca cells converting them to *progesterone-secreting cells* ⟶ rate of estrogen secretion ↓ about 1 day **before ovulation** while progesterone secretion begin to ↑


Estradiol (pg/mL)
800
600
400
200
0
Menstruation
Estradiol
Ovulation
Progesterone
8
0
Progesterone (ng/mL)
FSH and LH (ng/mL)
800
600
400
200
0
LH
Ovulation
FSH
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days of female sexual cycle

Initiation of ovulation

Large quantity of LH causes rapid secretion of progesterone from the follicle. Within a few hours 2 events occur which are necessary for ovulation:

1) the **theca externa** begins to secrete proteolytic enzymes & causes weakening of the wall resulting in swelling of the follicle & degeneration of the stigma

2) rapid growth of **new blood vessels** into the follicle wall & prostaglandins are secreted into the follicular tissue.

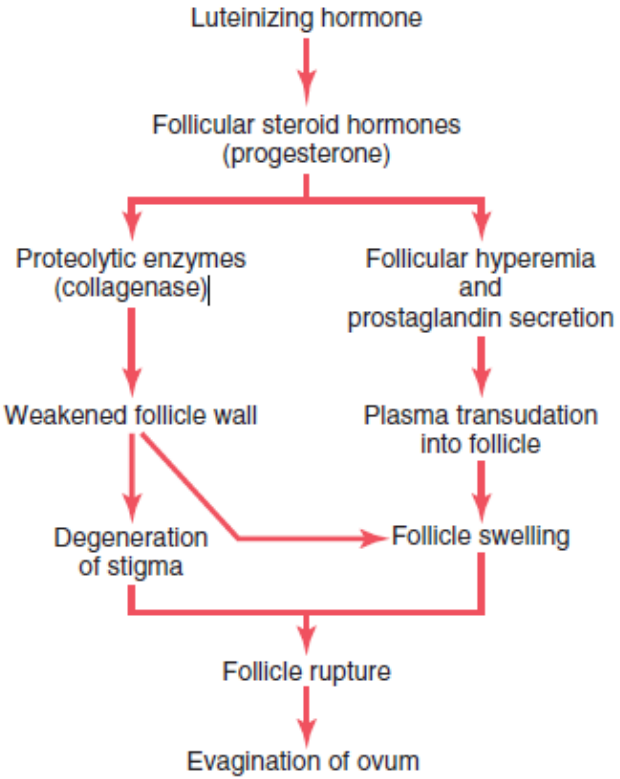
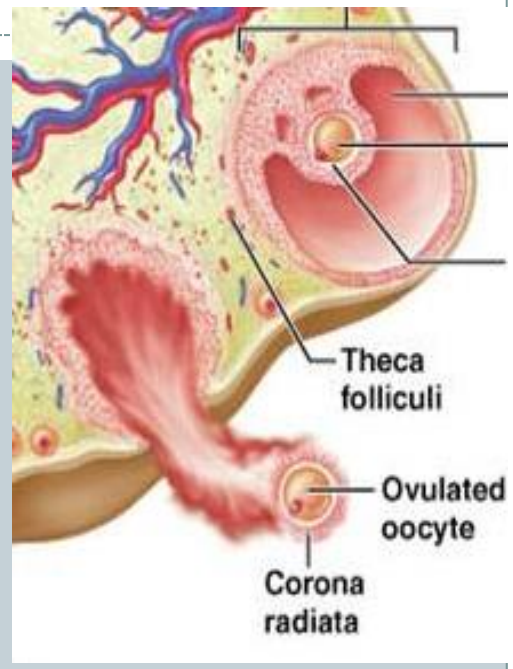
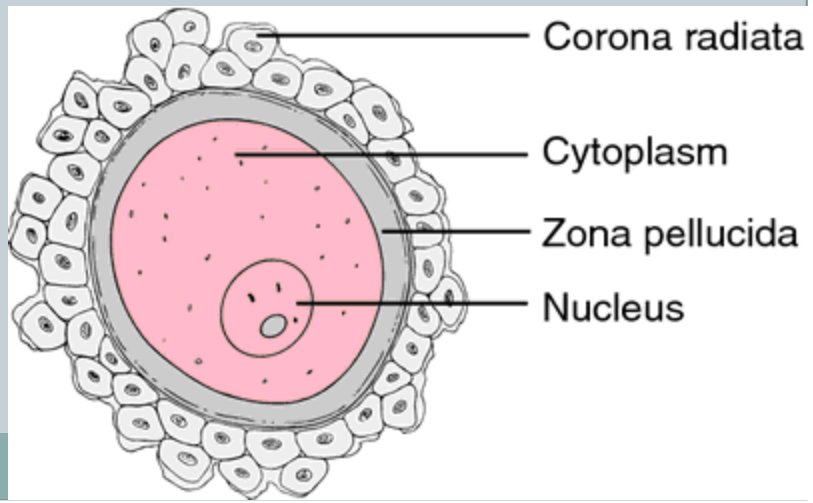


Figure 82-6. The postulated mechanism of ovulation.

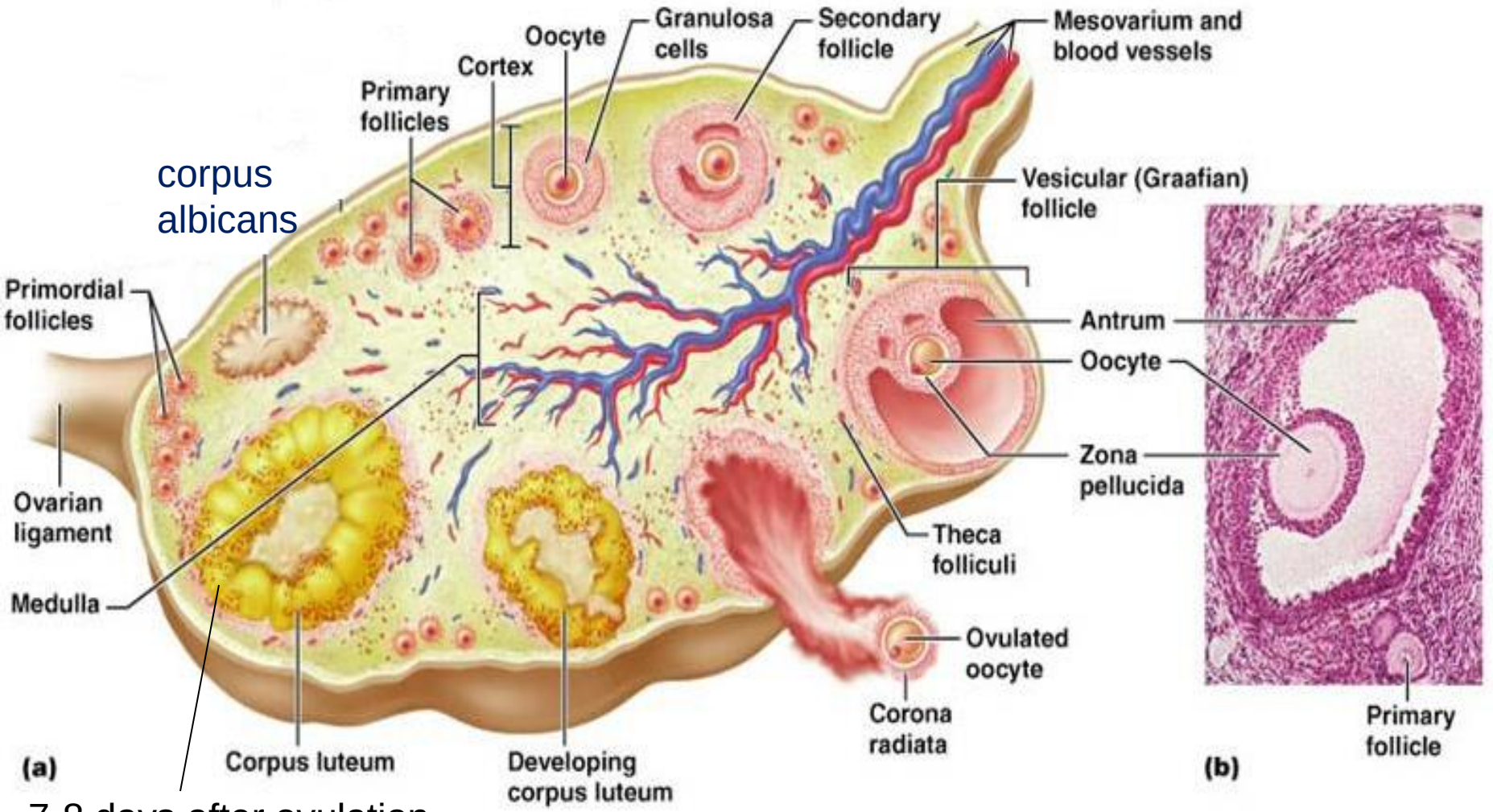
Ovulation

During ovulation, stigma protrudes & fluids ooze from the follicle & the stigma ruptures allowing more viscous fluid outward carrying with it the ovum surrounded by mass of granulosa cells called corona radiata





Corpus Luteum



7-8 days after ovulation
~ 1.5 cm in diameter

The granulosa cells with the theca cells are called **corpus luteum.**

Corpus Luteum

"Luteal" phase of the ovarian cycle

- After expulsion of the ovum from the follicle, the remaining granulosa & theca interna cells change to **lutein cells** & become filled with *lipid inclusions* giving them yellowish appearance.

- The granulosa cells in corpus luteum form large amount of **progesterone** & estrogen. The theca cells form mainly androgens which are converted by granulosa cells into female hormones and small amount can appear in plasma.

Corpus Luteum

Function of LH:

1-Change of granulosa and theca interna cells into **lutein cells**.

2- Causes ovulation.

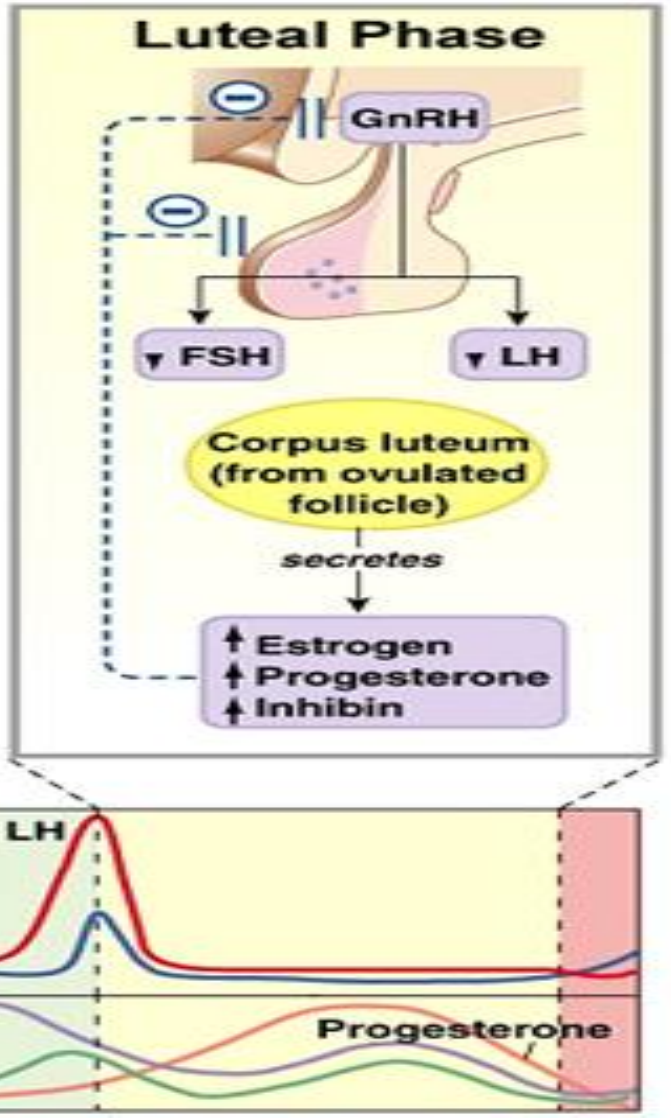
3- Maintains secretion of progesterone & estrogen from the corpus luteum.

Involution of the corpus luteum and onset of the next ovarian cycle

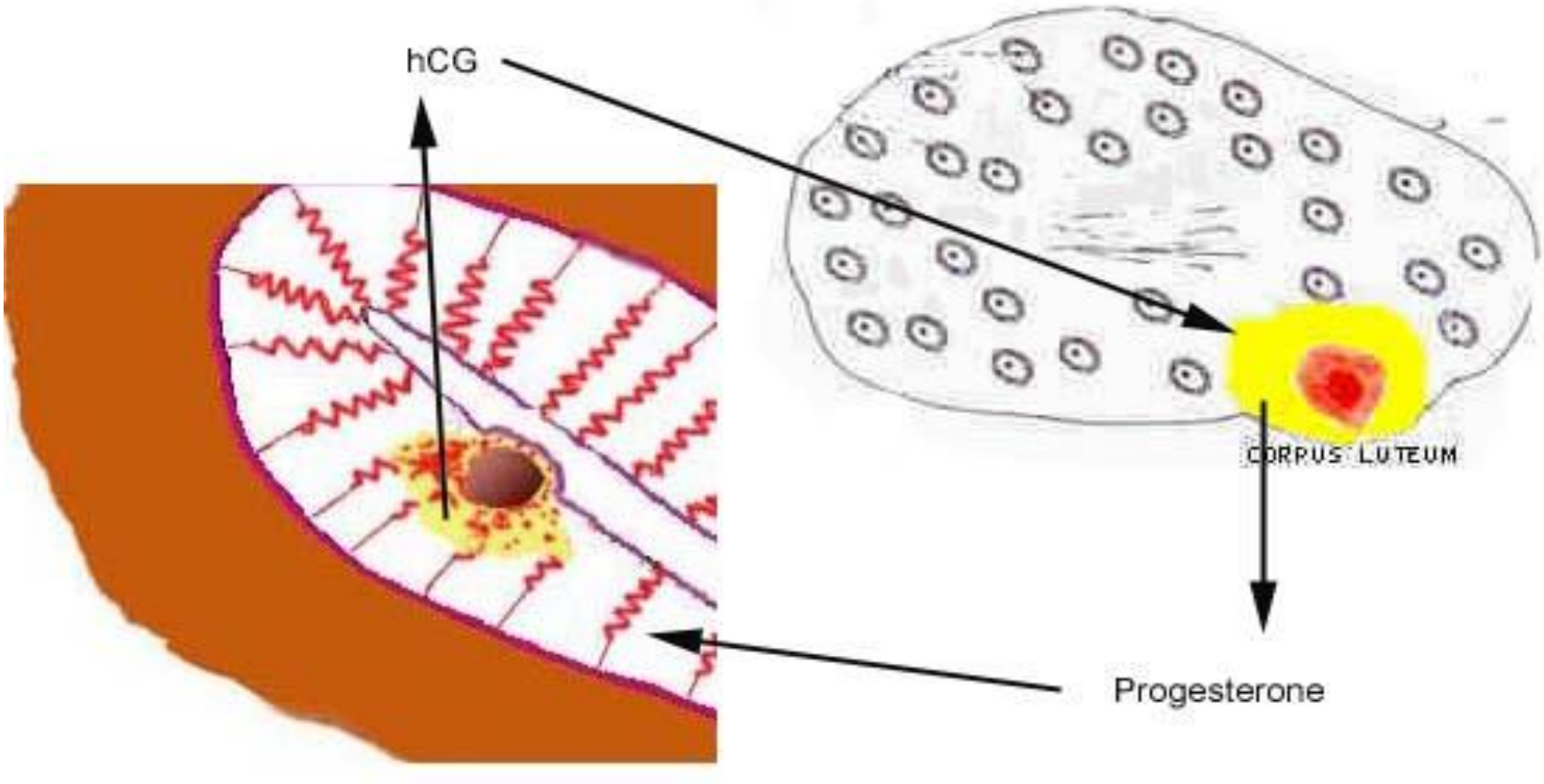
1- Estrogen & progesterone have strong negative feedback on AP and ↓ FSH & LH

2- The **lutein cells** secrete small amounts of inhibin

3- Around **26th days** of normal sexual cycle & after involution of corpus luteum, sudden cessation of estrogen, progesterone & inhibin removes the negative feedback inhibition of the AP & allowing ↑ secretion of FSH & LH again.

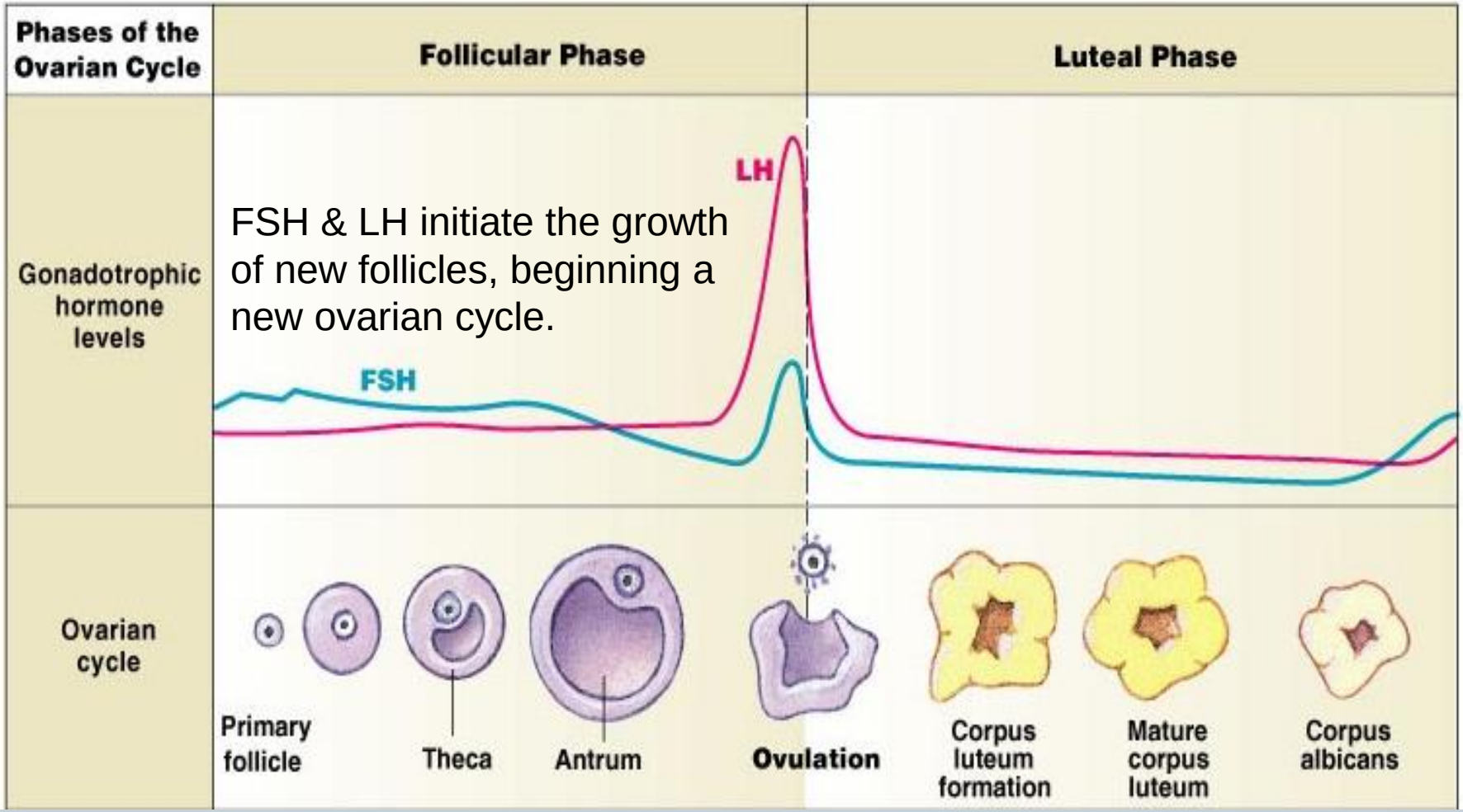


Corpus Luteum



- **<u>If pregnancy occurs</u>, the hCG from the Trophoblast acts on the corpus luteum to prolong its life for 2 to 4 months of pregnancy**

Corpus Luteum



Physiology of Uterine (Endometrial) Cycle

GUYTON & HALL, Chapter 81

DR.MOHAMMED ALOTAIBI

ASSISTANT PROFESSOR OF PHYSIOLOGY

COLLEGE OF MEDICINE

KING SAUD UNIVERSITY

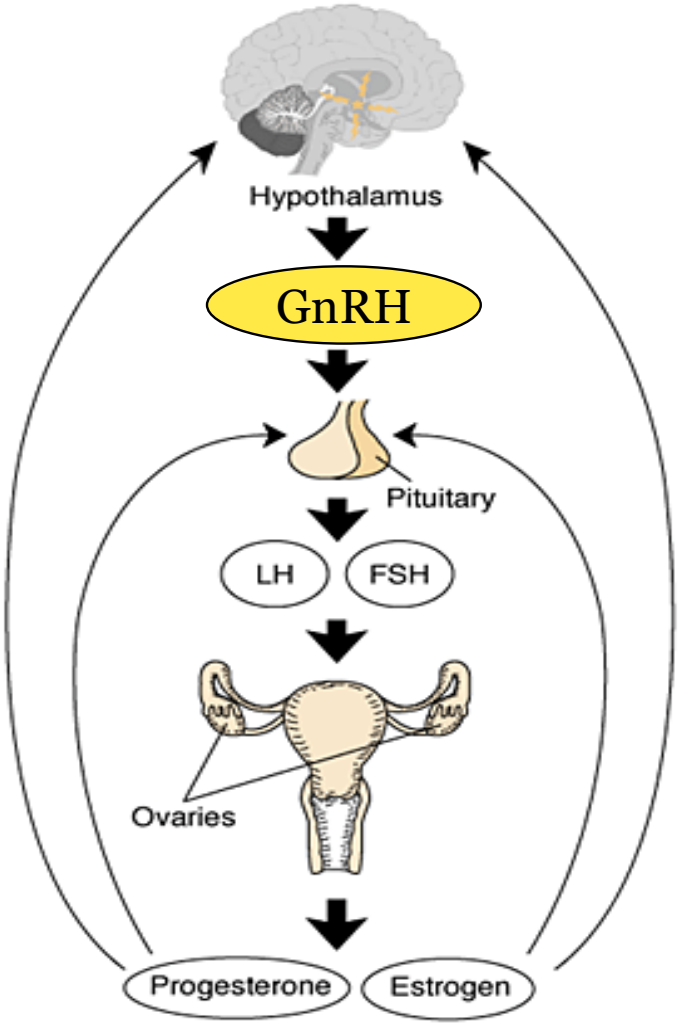
Objectives

By the end of this lecture, you should be able to:

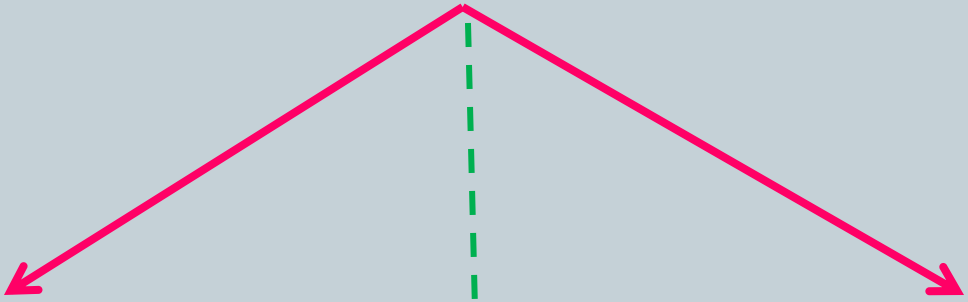
1. Describe the normal phases of menstrual cycle
2. Discuss the ***structural changes*** that occur in the endometrium during the menstrual cycle and explain how these changes are hormonally controlled
3. List the hormones of female reproduction and describe their physiological functions
4. Describe the physiology of menopause and the disorders of menstruation

Monthly endometrial cycle and menstruation

- It is associated with the monthly cyclical production of estrogens & progesterone by the ovaries in the lining of the uterus



Uterine (endometrial) Cycle



Proliferative phase **(estrogen Phase)** (Preovulatory)

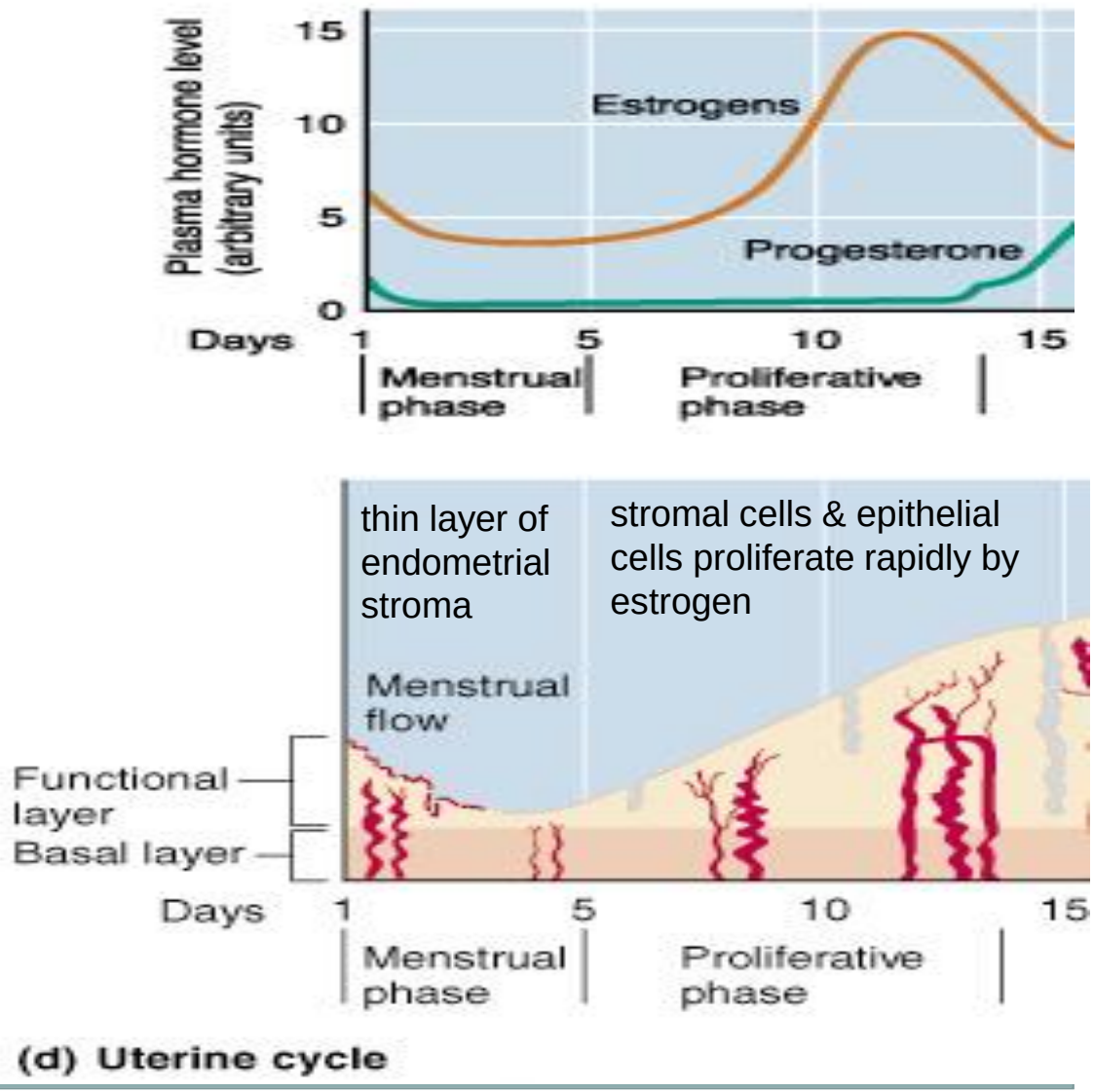
Ovulation

Secretory phase **(progestational phase)** (Postovulatory)

Proliferative phase (estrogen phase)

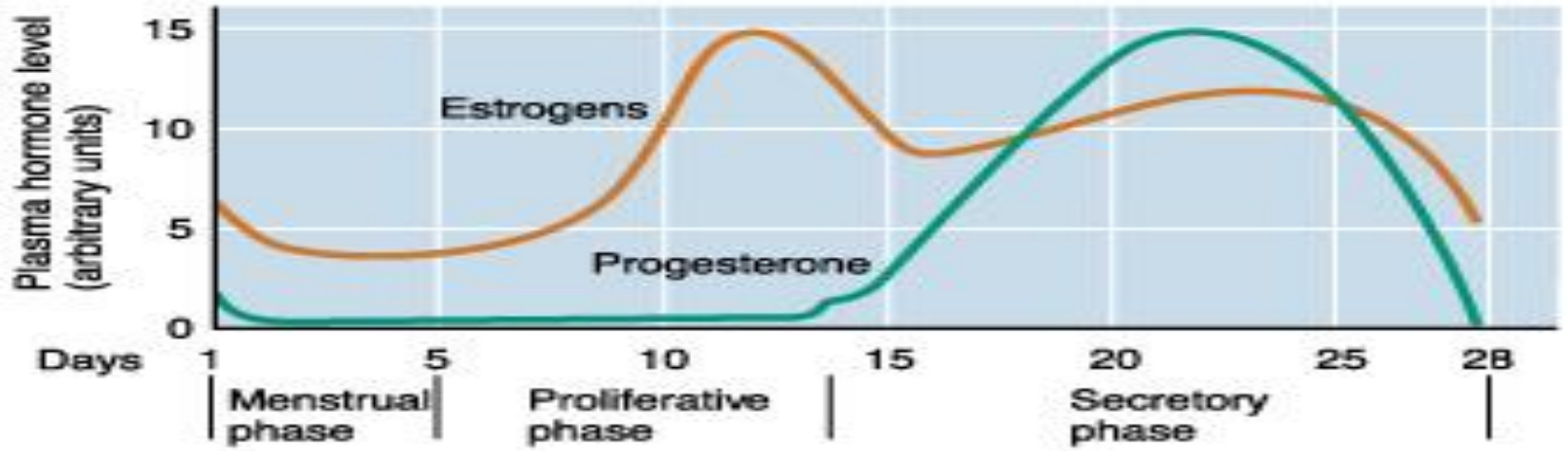
The endometrial surface re-epitheliazed within 4-7 days after the beginning of menstruation. The endometrium thickness increases, due to increase numbers of stromal cells &progressive growth of the glands & new blood vessels.

At the time of ovulation, the endometrium is **3-5 mm thick**. The endometrial glands, cervical region secrete a thin, stringy mucus which helps to guide sperm in the proper direction from the vagina into the uterus.



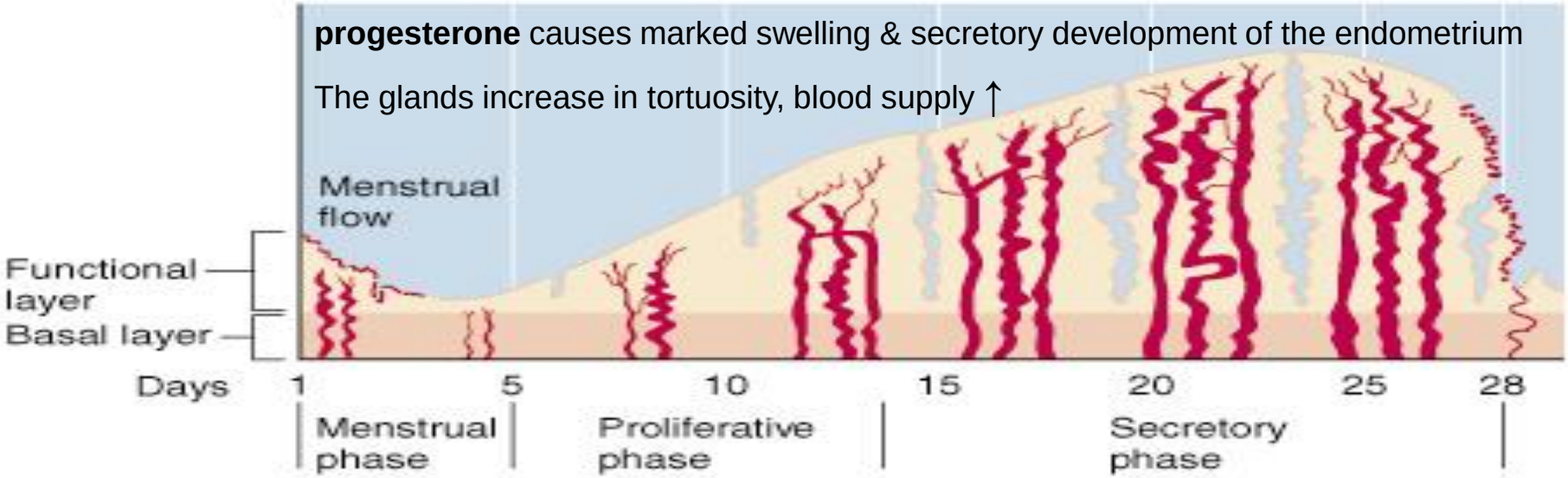
(d) Uterine cycle

Secretory phase (progestational phase)



progesterone causes marked swelling & secretory development of the endometrium

The glands increase in tortuosity, blood supply ↑



Stromal cells cytoplasm increase lipid &glycogen deposits, 1 week after ovulation, endometrium thickness is 5-6 mm . Uterine secretions called **"uterine milk"** provide nutrition for the dividing ovum.

Menstruation

- -If the ovum is not fertilized, about 2 days before the end of the monthly cycle, the corpus luteum in the ovary suddenly involutes and the ovarian hormones (estrogens and progesterone) decrease to low levels of secretion,

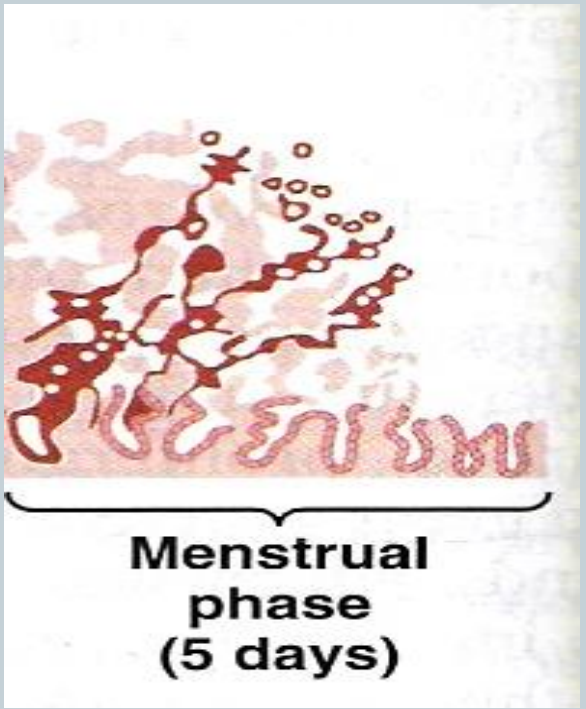
- Necrosis is initiated in the endometrial blood vessels, due to:

1) vasospasm

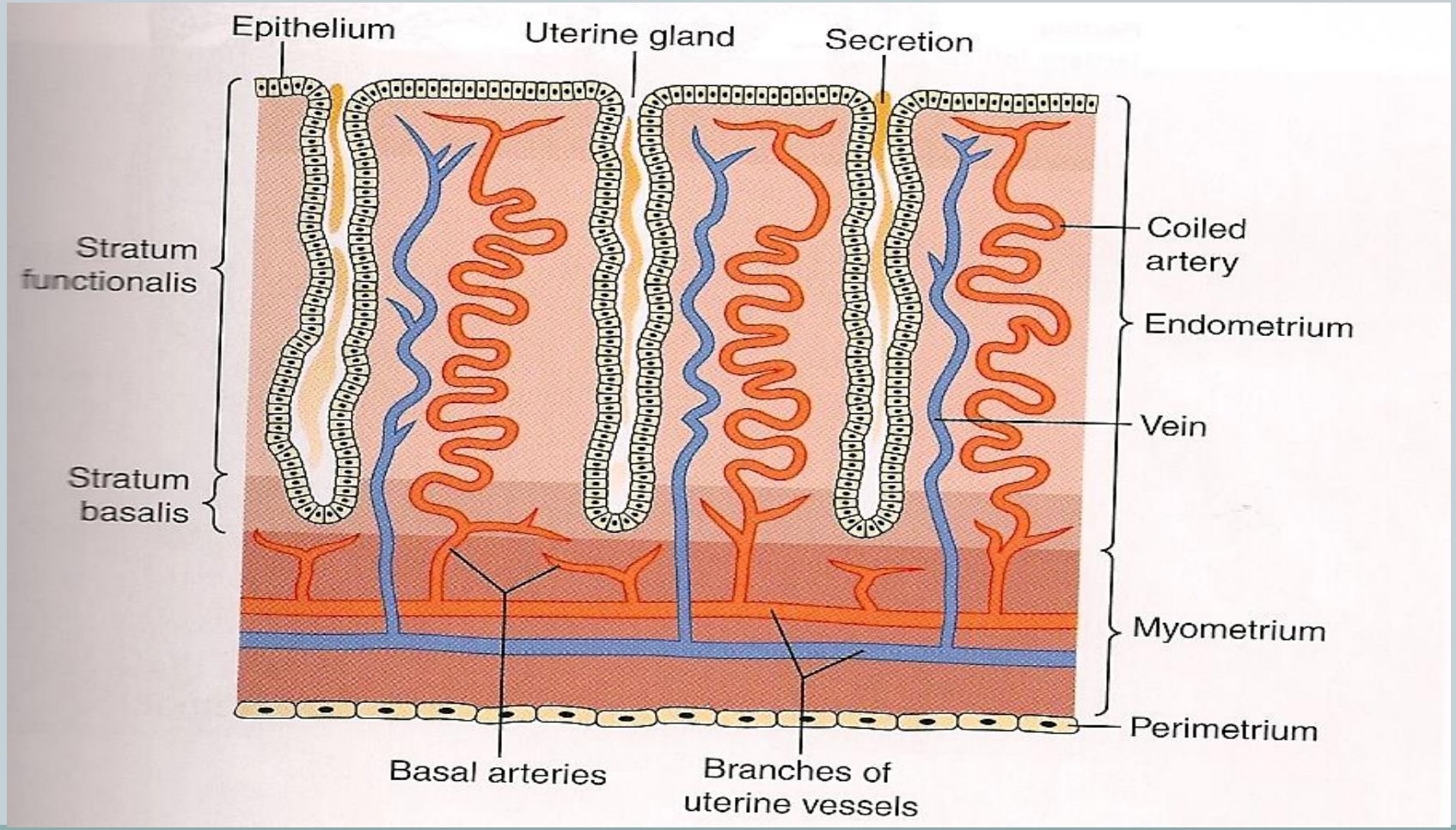
2) decrease nutrients to the endometrium

3) loss of the hormonal stimulation

- The mass of desquamated tissue & blood plus the contractile effects of prostaglandins all initiate contractions which expel the uterine contents.



Uterine (endometrial) Cycle



Menstruation

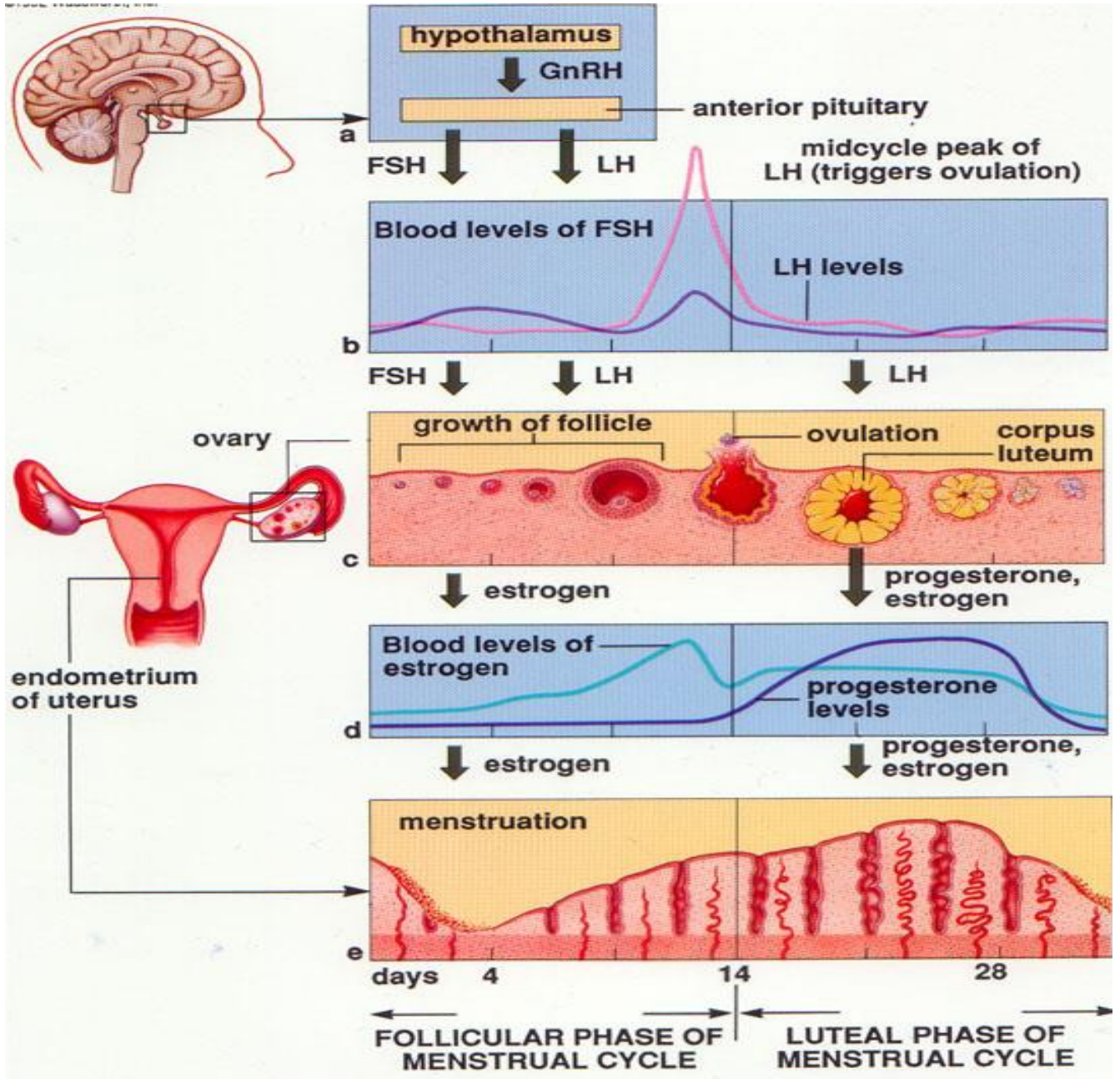
- **In normal menstruation**, about 40 ml of blood + 35 ml of serous fluid are lost. The menstrual blood is normally non-clotting due to the presence of fibrinolysin.

-Within 4 to 7 days after menstruation, the loss of blood ceases & the endometrium become re-epithelialized.

Leukorrhea during menstruation:

During menstruation, leukocytes are released with the necrotic material & blood so the uterus is highly resistant to infection during menstruation as protective mechanism.

Summary



Changing hormone levels during the menstrual cycle.

Functions of Estrogens

- Estrogens increase the size of ovaries, fallopian tubes, uterus, and external genitalia.
- Estrogens cause marked proliferation of the endometrial stroma and greatly increased development of the endometrial glands.
- Estrogens cause (1) development of the stromal tissues of the breasts, (2) growth of an extensive ductile system, and (3) deposition of fat in the breasts.
- Estrogens stimulate bone growth and slightly increase protein deposition.
- Estrogens increase body metabolism and fat deposition.
- Estrogens cause sodium and water retention by the kidney tubules.

Functions of progesterone

- Progesterone promotes the secretory changes in the uterine endometrium.
- Progesterone promotes increased secretion by the mucosal lining of the fallopian tubes.
- Progesterone promotes development of the lobules and alveoli of the breasts, causing the alveolar cells to proliferate, enlarge, and become secretory.
- Progesterone decreases the frequency and intensity of uterine contractions.

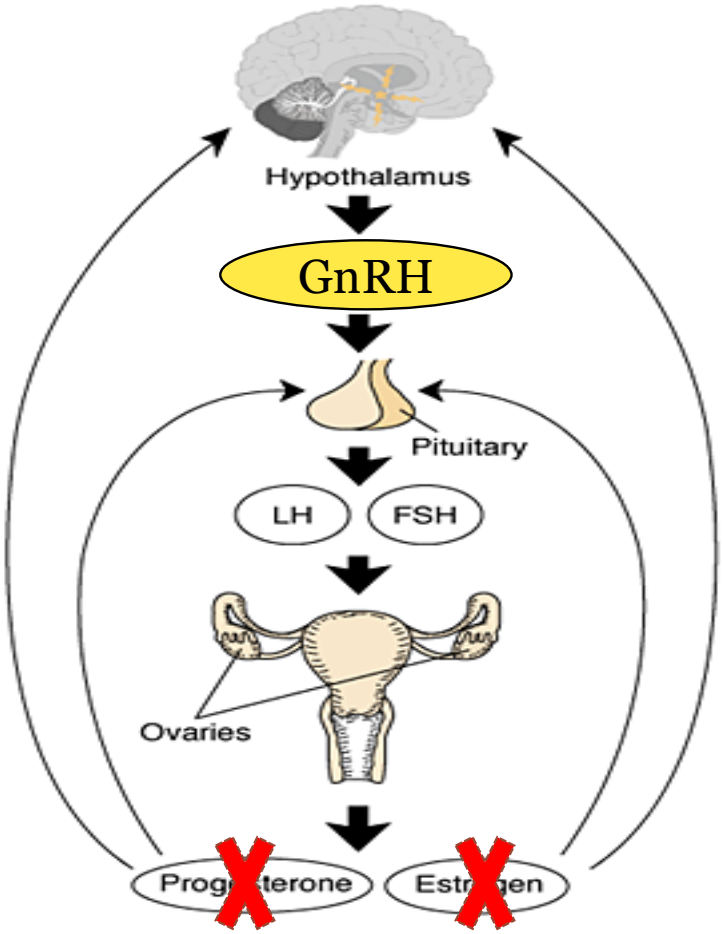
Menopause and the Disorders of Menstruation

Menopause

At the age of 40 to 50 years, the sexual cycle becomes irregular, ovulation fails to occur & the cycle ceases

The loss of estrogens causes marked physiological changes in the function of the body including:

"hot flushes" characterized by extreme flushing of the skin, psychic sensations and dyspnea, Irritability, fatigue, anxiety, occasionally various psychotic states, decreased strength and calcification of bones throughout the body.



Disorders of Menstruation

Amenorrhea: Is absence of menstrual period either

- Primary amenorrhea in which menstrual bleeding has never occurred.
- Secondary amenorrhea cessation of cycles in a woman with previously normal periods, caused by:
  - Pregnancy (is the most common cause)
  - Emotional stimuli and changes in the environment.
  - Hypothalamic diseases (↓ GnRH pulses)
  - Pituitary disorders
  - Primary ovarian disorders and various systemic disease.

Menorrhagia: Refer to abnormally heavy or prolonged bleeding.

Hypomenorrhea: Refer to scanty flow.

Dysmenorrhea: Painful menstruation (cramps due to accumulation of prostaglandins in the uterus and treatment with inhibitors of prostaglandin synthesis).

The End

Thank You