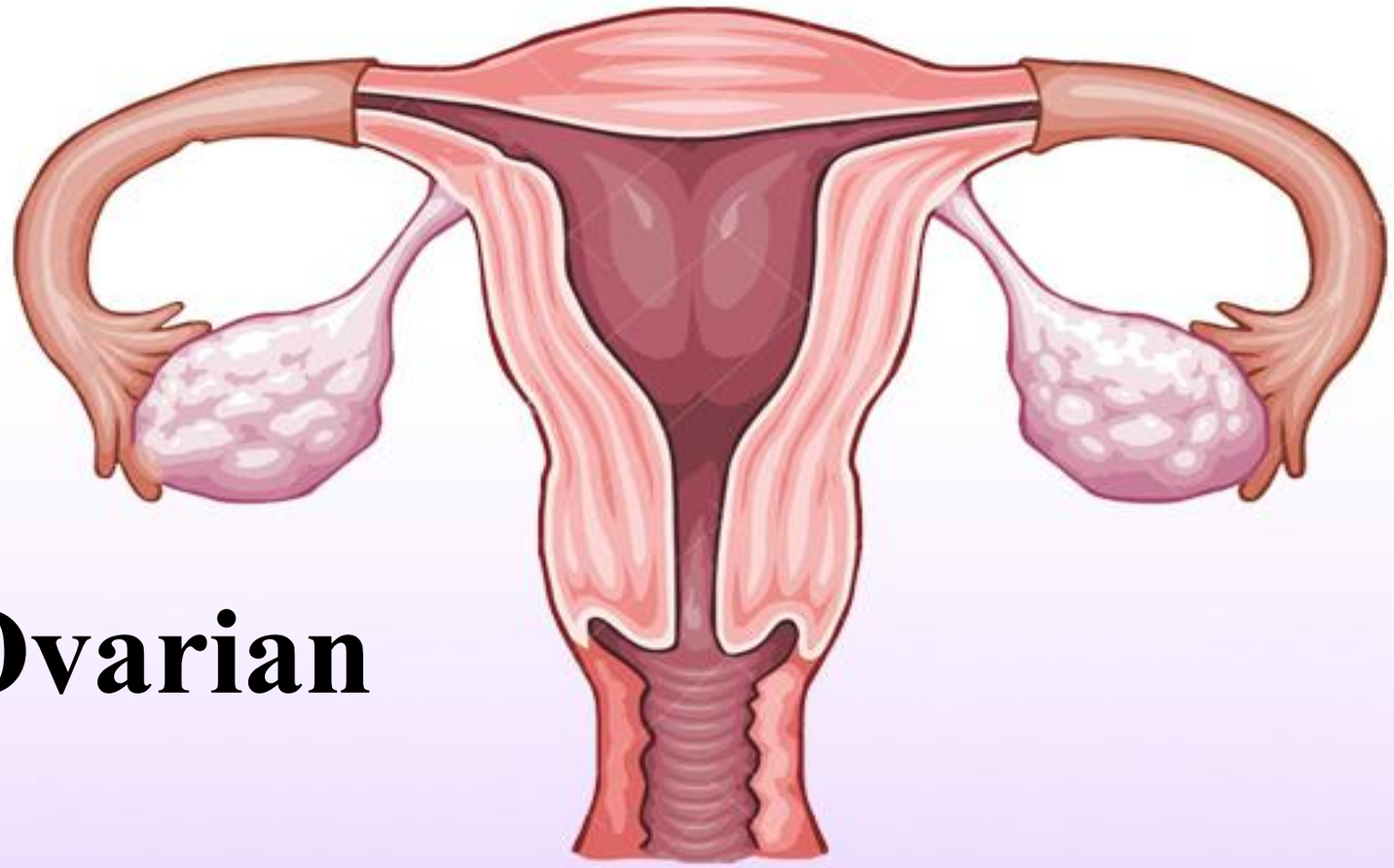
Physiology team



L4-Physiology of Ovarian Cycle

Sources:

✓ **Male slides**

Objectives

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

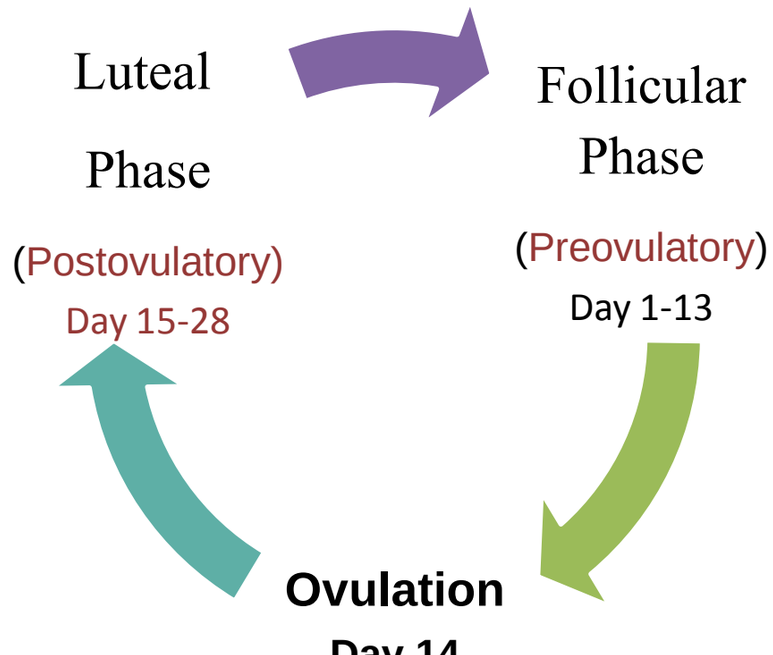
1-List the hormones of female reproduction and describe their physiological functions

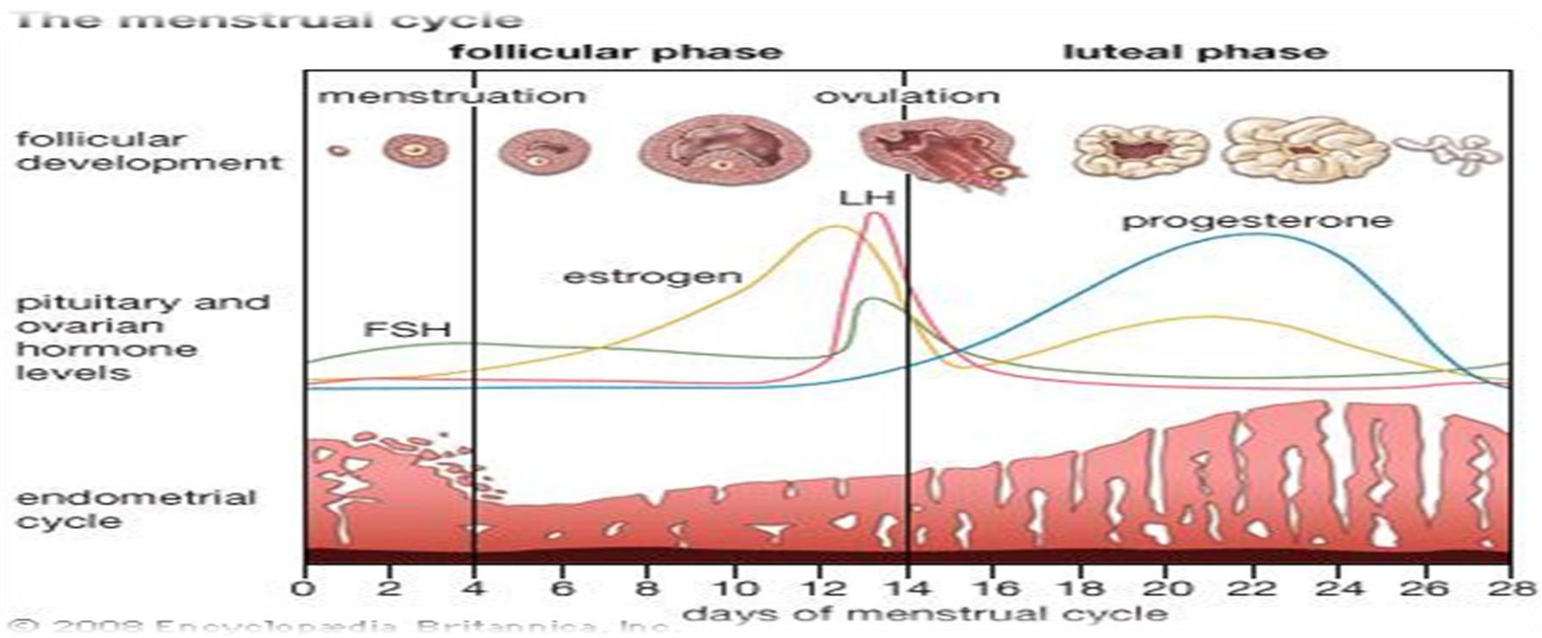
2- Describe the changes that occur in the **ovaries** during the menstrual cycle

3-Describe the hormonal control of the development of ovarian follicles, mature oocytes and corpus luteum

4- Recognize the pituitary-ovarian-axis and the changes that occur in the ovaries leading to ovulation

Ovarian Cycle





Ovarian cycle

Monthly ovarian cycle:

monthly rhythmical changes in the rates of secretion of female hormones & corresponding physical changes in the ovaries & other sexual organs.

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

Results of the female sexual cycle:

1. Single ovum is released from the ovaries each month

2. Uterine endometrium is prepared for implantation for the fertilized ovum.

Gonadotropic hormones and their effects on the ovaries:

-The ovarian changes during the sexual cycle depend on FSH & LH secreted by AP. In the absence of these hormones, the ovaries remain inactive throughout childhood.

-At puberty, the AP starts to secrete FSH & LH which lead to the beginning of monthly sexual cycles.

-First menstrual cycle is called menarche.

- Both FSH and LH, stimulate their ovarian target cells by combining with highly specific receptors lead to increase the cells rates of secretion, growth & proliferation of the cells.

1-Follicular Phase (Ovarian follicle growth)

1. Childhood

Primordial follicles

- The ovarian changes that occur during the sexual cycle depend completely on **the gonadotropic hormones FSH and LH, secreted by the anterior pituitary gland.**

- **In the absence of these hormones (during childhood),** the ovaries remain inactive, when almost no pituitary gonadotropic hormones are secreted.

❖ **Female child:** each ovum (called primary oocyte at this time) is surrounded by a **single layer of granulosa cells**, both they called **primordial follicle.**

❖ During childhood, the granulosa cells provide nourishment for the ovum & secrete **oocyte maturation inhibiting factor** which keeps the ovum in its primordial state.

2. Puberty

Primary follicles

- At age 9 to 12 years, the pituitary **begins to secrete progressively more FSH and LH** "FSH increase is slightly more & earlier than LH" , which leads to onset of normal monthly sexual cycles beginning between the ages of 11 and 15 years. **This period of change is called puberty.**

After puberty: Enlargement of the ovum to increase in size & growth of **additional layers** of granulosa cells of some follicles & known as **primary follicles.**

Continue Primary follicles

The **ovary interstitium** collect in several layers outside the granulosa cells to form a second mass of cells called theca.

This theca is divided into 2 layers:

1. theca interna, the cells have epitheloid characteristics and similar to the granulosa cells and secrete **Androgens which converted to estrogen by <u>aromatase</u> enzyme in granulosa cells "during follicular phase" and Progesterone "during luteal phase"**

2. theca externa, the outer layer, develops into a **highly vascular connective tissue capsule** of the developing follicle.

Antral Secondary Follicles

Few days after proliferation & growth of the follicles, the granulosa cells secrete follicular fluids contain **high concentration of estrogen.** This fluid accumulate to form antrum within the mass of the granulosa cells.

The previous stages under control of FSH only

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

Then there is accelerated growth of the follicle to larger follicle called **vesicular follicle** caused by:-

1. **Estrogen secreted into the follicle cause:** increase FSH receptors in granulosa cells which causes positive feedback effect. (granluosa cells become more sensitive to FSH)

2. **Both estrogen& FSH combine to:** promote LH receptors on the granulosa cells, allowing more increase follicular secretion.

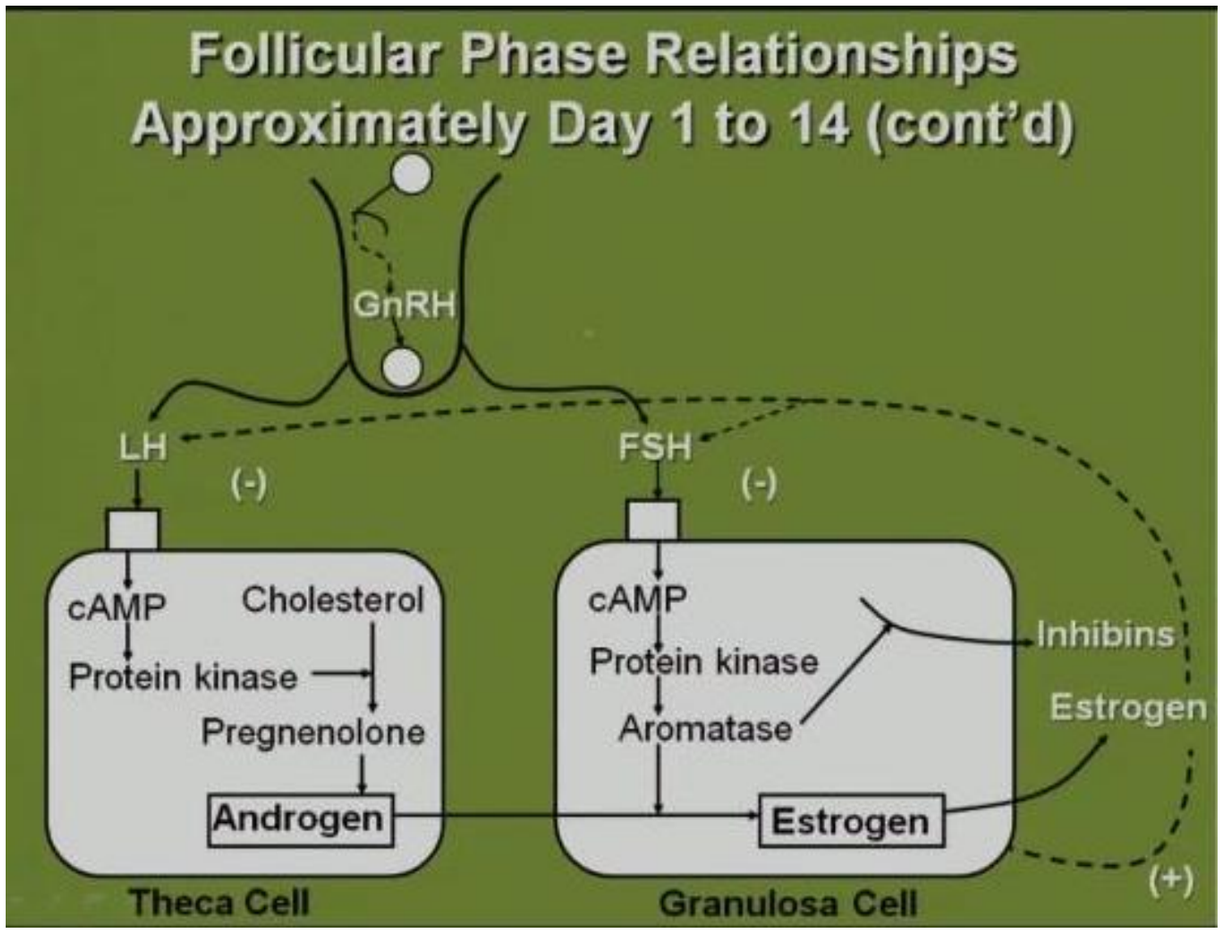
3. **Increasing estrogen from the follicle and LH from the AP causes:** proliferation of the follicular theca cells & increase their secretion.

Mature Follicles

Only one follicle continue to grow & the remaining follicles (5 to 11) undergo **atresia** or **involute** the cause is unknown or could be that large amount of estrogen from the growing follicle inhibit further FSH secretion from the AP, while the largest follicle continue to grow because of the intrinsic positive feedback effect & **mature follicle reach about 1 to 1.5 cm.**

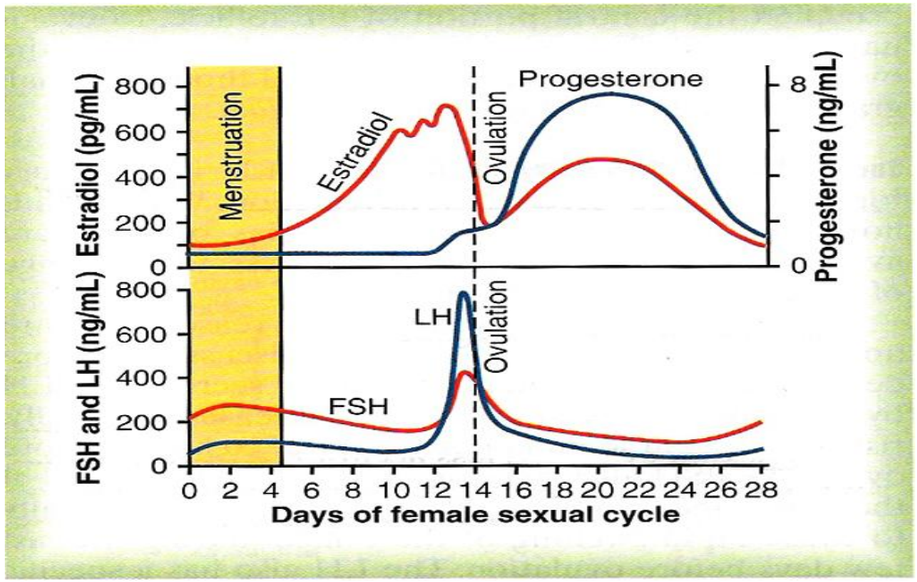
NOTE : During all the reproductive years of adult life, between about 13 and 46 years of age, **400 to 500** of the primordial follicles develop enough to expel their ova—**one** each month

"Understanding Figure"



Ovulation

Ovulation occurs 14 days after the onset of menstruation in 28 days cycle.



Before Ovulation:

LH is necessary for final follicular growth and ovulation

- **2** days before ovulation → rate of **LH** secretion ↑ to 6-16 fold & peaks about 16 hrs before ovulation.
- **LH** has specific effect on the granulosa cells & theca cells converting them to *progesterone-secreting cells*
- About 1 day **before ovulation** while progesterone secretion begin to increase rate of estrogen secretion decrease
- **FSH** also ↑ 2 to 3 fold & acts synergistically with LH to cause swelling of the follicle before ovulation)

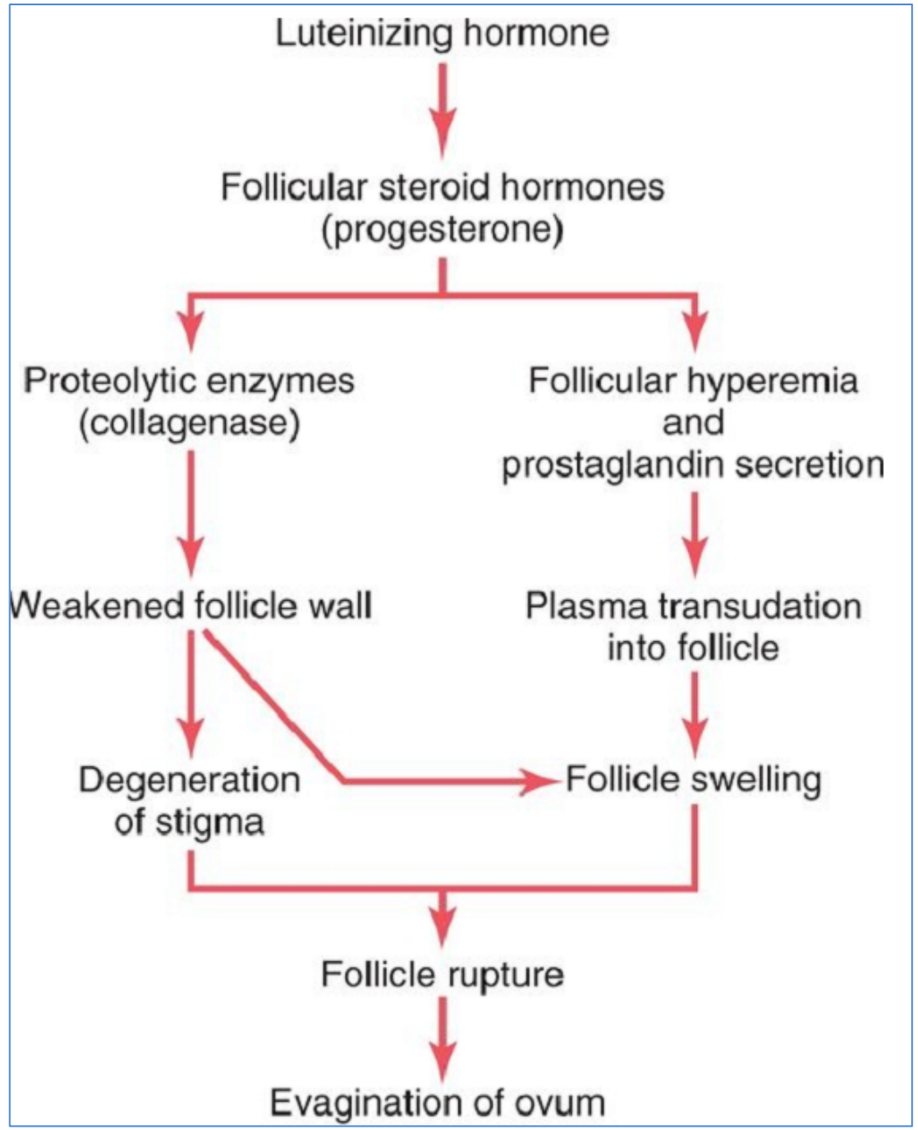
Ovulation

Important

Initiation of ovulation:

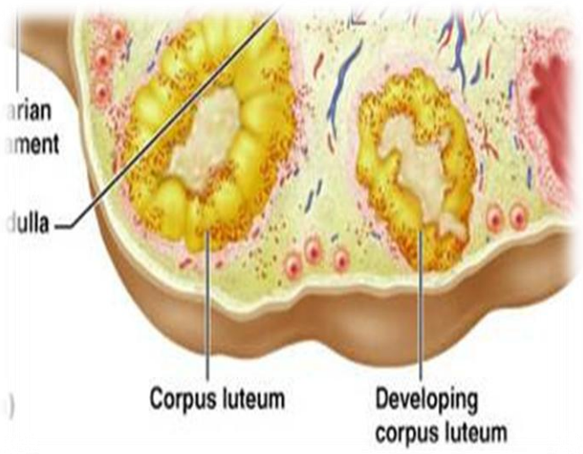
Large quantity of LH causes rapid secretion of progesterone from the follicle to Initiate the ovulation

ovulation: (1) The *theca externa* (the capsule of the follicle) begins to release proteolytic enzymes from lysosomes, and these cause dissolution of the follicular capsular wall and consequent weakening of the wall, resulting in further swelling of the entire follicle and degeneration of the stigma. (2) Simultaneously there is rapid growth of new blood vessels into the follicle wall, and at the same time, prostaglandins (local hormones that cause vasodilation) are secreted into the follicular tissues. These two effects cause plasma transudation into the follicle, which contributes to follicle swelling. Finally, the combination of follicle swelling and simultaneous degeneration of the stigma causes follicle rupture, with discharge of the ovum.



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**

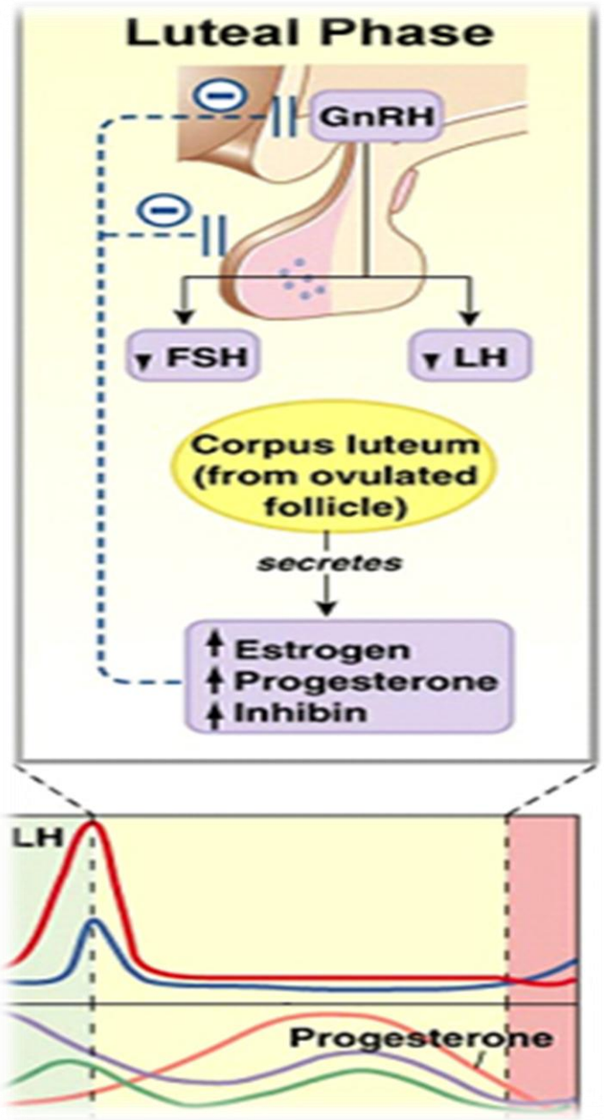
2-Luteal phase



Corpus Luteum:

•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**.

•This process called **luteinizing** because it under effect of **LH** and total mass called **corpus luteum**



• **The granulosa cells** in corpus luteum form large amount of **progesterone "mainly"** & **estrogen.**

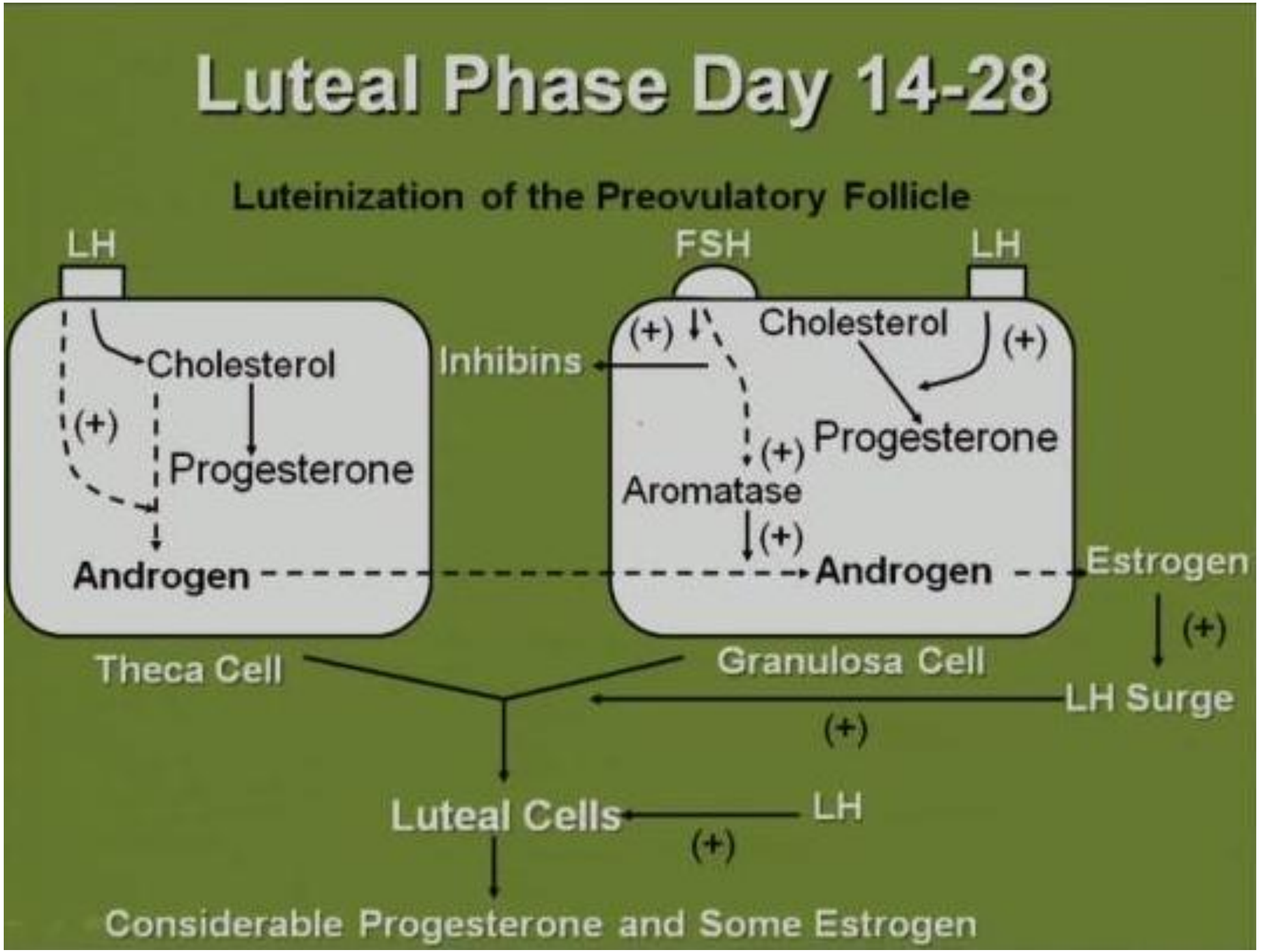
• **The theca cells** form mainly **androgens** which are converted by granulosa cells into female hormones

•**Luteinizing function of LH:**

1- Extrusion of the ovum from the follicle.	2- Change of granulosa and theca interna cells into **lutein cells**	3- Secretion of progesterone & estrogen from the corpus luteum

If pregnancy occurs

, the hCG "mimic LH hormone" from the placenta acts on the corpus luteum to prolong its life for 2 to 4 months of pregnancy


Luteal Phase Day 14-28
Luteinization of the Preovulatory Follicle
LH
FSH
LH
Cholesterol
(+)
Progesterone
Androgen
Inhibins
(+)
Cholesterol
(+)
(+)
Progesterone
Aromatase
(+)
Androgen
Estrogen
(+)
Theca Cell
Granulosa Cell
LH Surge
(+)
Luteal Cells
LH
(+)
Considerable Progesterone and Some Estrogen

Corpus Luteum

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

1- **Estrogen and progesterone** from corpus luteum (luteal phase) have strong **negative feedback effect on AP to inhibit the secretion of FSH & LH.**

2- The **lutein cells** secrete small amounts of **inhibin** which **inhibit secretion of FSH** by AP.

Low concentration of FSH & LH lead to complete degeneration of corpus luteum (involution)

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

Summery

A. Synthesis of estrogen and progesterone (Figure 7-18)

- **Theca cells** produce testosterone (stimulated at the first step by LH). Androstenedione diffuses to the nearby **granulosa cells,** which contain 17β-hydroxysteroid dehydrogenase, which converts androstenedione to testosterone, and aromatase, which converts testosterone to 17β-estradiol (stimulated by FSH).

B. Regulation of the ovary

1. **Hypothalamic control—GnRH**
   - As in the male, pulsatile GnRH stimulates the anterior pituitary to secrete FSH and LH.
2. **Anterior lobe of the pituitary—FSH and LH**
   - FSH and LH stimulate the following in the ovaries:
     a. Steroidogenesis in the ovarian follicle and corpus luteum
     b. Follicular development beyond the antral stage
     c. Ovulation
     d. Luteinization
3. **Negative and positive feedback control—estrogen and progesterone** (Table 7-13)

C. Actions of estrogen

1. Has both negative and positive feedback effects on FSH and LH secretion.
2. Causes maturation and maintenance of the fallopian tubes, uterus, cervix, and vagina.
3. Causes the development of female secondary sex characteristics at puberty.
4. Causes the development of the breasts.
5. Up-regulates estrogen, LH, and progesterone receptors.

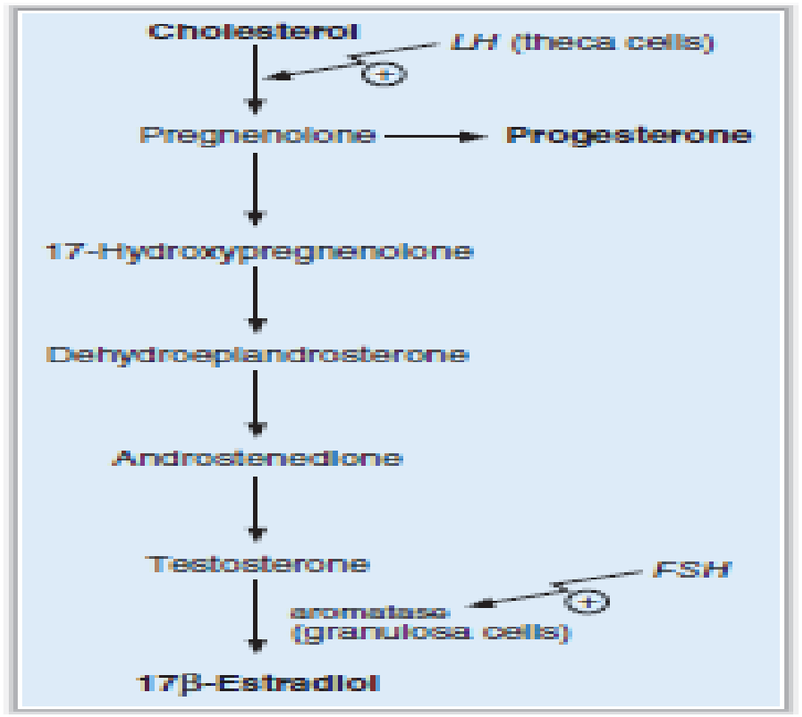


FIGURE 7-18 Synthesis of estrogen and progesterone. FSH — follicle-stimulating hormone; LH — luteinizing hormone.

Summery

table 7-13 Negative and Positive Feedback Control of the Menstrual Cycle

Phase of Menstrual Cycle	Hormone	Type of Feedback and Site
Follicular	Estrogen	Negative; anterior pituitary
Midcycle	Estrogen	Positive; anterior pituitary
Luteal	Estrogen	Negative; anterior pituitary
	Progesterone	Negative; anterior pituitary

6. Causes proliferation and development of ovarian granulosa cells.
7. Maintains pregnancy.
8. Lowers the uterine threshold to contractile stimuli during pregnancy.
9. Stimulates prolactin secretion (but then blocks its action on the breast).

D. Actions of progesterone

1. Has negative feedback effects on FSH and LH secretion during luteal phase.
2. Maintains secretory activity of the uterus during the luteal phase.
3. Maintains pregnancy.
4. Raises the uterine threshold to contractile stimuli during pregnancy.
5. Participates in development of the breasts.

MCQs

1-which cell produces estrogen that mainly enters the follicular fluid ?

a) Theca cell
b) Leyding cell
c) luteal cell
d) granulose cell

2-which hermone causes ovulation?

a) LH hormone
b) FSH hormone
c) Estrogen
d) progesterone

3-Which hormone is acting on corpus luteum to prolong its life during pregnancy?

A) Chorionic gonadotropin.
B) Human placental lactogen.
C) Progesterone.
D) Androgen.

4- The level of estrogen secretion 1 day before ovulation?

A) The same as progesterone.
B) Increase.
C) Decrease.
D) Constant.

5-The theca cells in corpus luteum secrete?

A) Adrenaline.
B) Androgen.
C) Estrogen.
D) Progesterone.

1-d 2-a 3-a 4-c 5-b

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