PHYSIOLOGY OF OVARIAN CYCLE

GUYTON & HALL, CHAPTER 82

EBAA M ALZAYADNEH, PHD

ASSISTANT PROFESSOR, PHYSIOLOGY AND BIOCHEMISTRY DEPARTMENT/SCHOOL OF MEDICINE

THE UNIVERSITY OF JORDAN

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

PHYSIOLOGIC ANATOMY OF THE FEMALE SEXUAL ORGANS

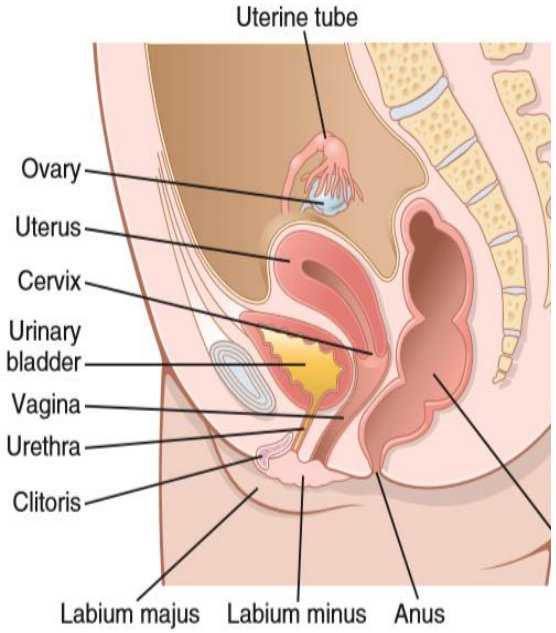


Figure 82-1. The female reproductive organs

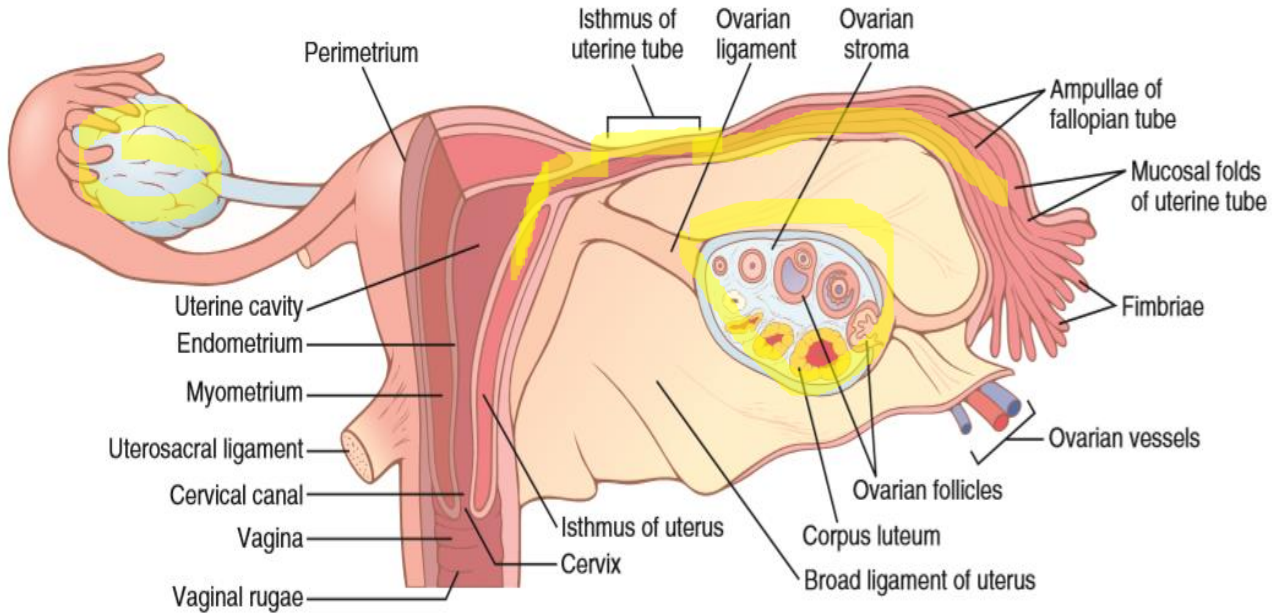


Figure 82-2. Internal structures of the uterus, ovary, and a uterine tube.

Monthly Menstrual Cycle

Normal reproductive years of female ⟶ Monthly rhythmical changes in the rates of secretion of female hormones & corresponding physical changes in the ovaries & other sexual organs.

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

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.

OOGENESIS

- A developing egg (oocyte) differentiates into a mature egg (ovum) through a series of steps called oogenesis .

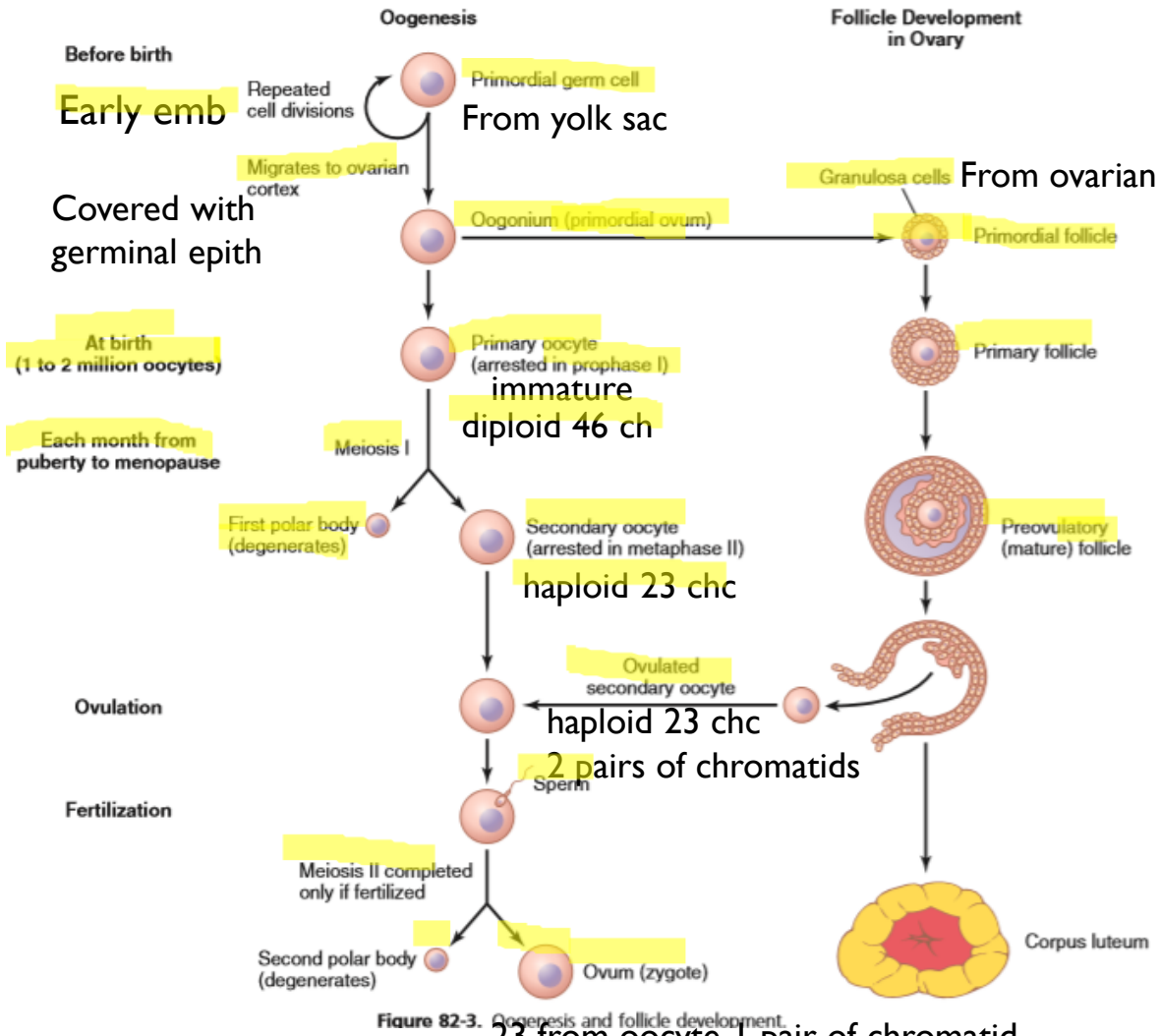


Figure 82-3. Oogenesis and follicle development.

23 from oocyte 1 pair of chromatid
23 from sperm 1 pair of chromatid

Regulation of Ovarian Function

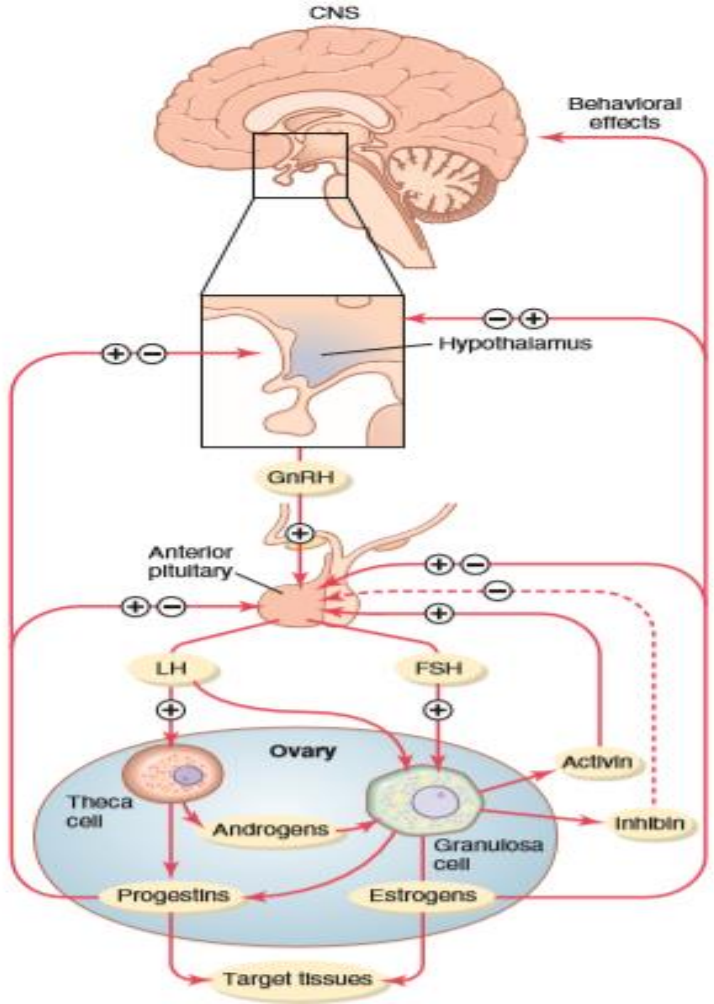
1. Gonadotropin-releasing hormone (GnRH)

2. The anterior pituitary sex hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH), stimulated by the GnRH.

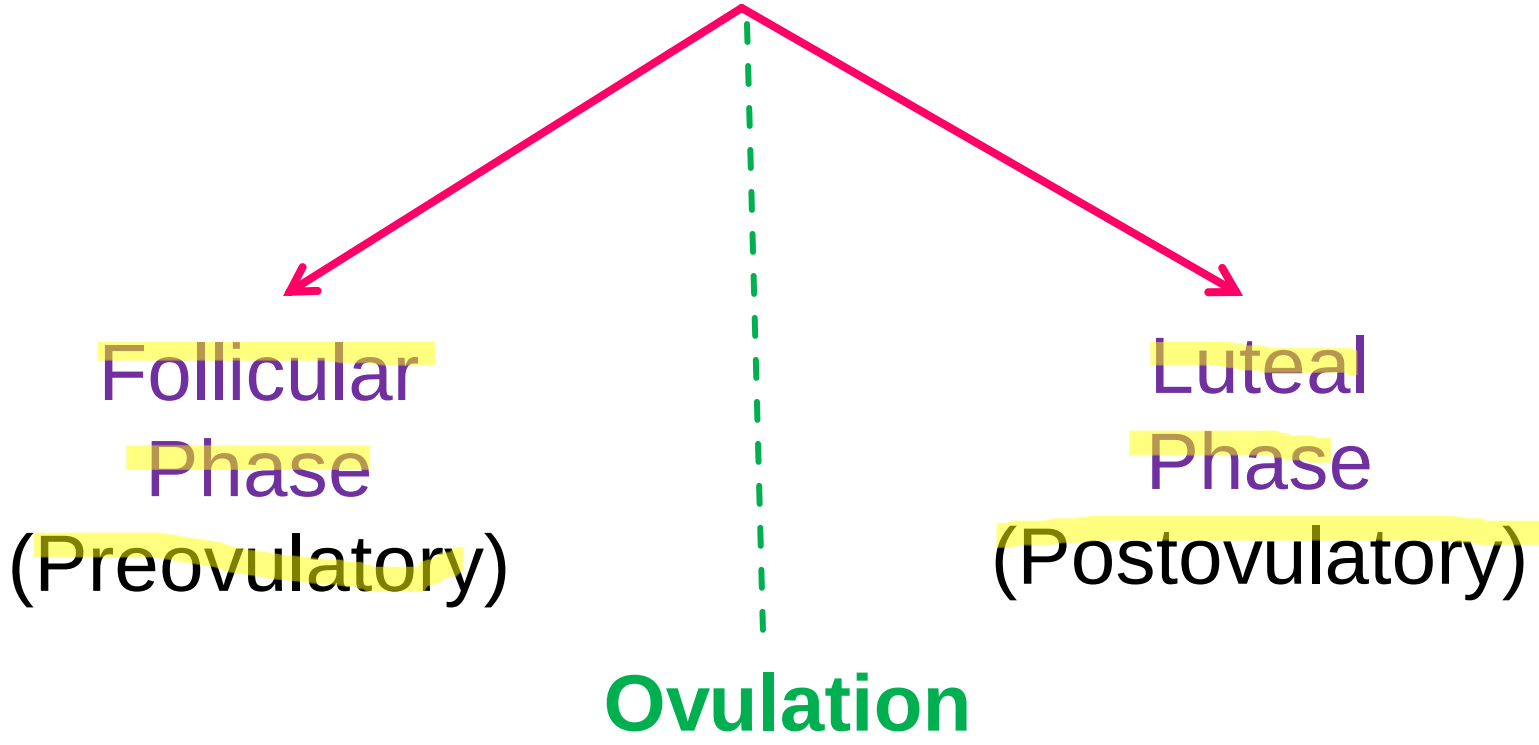
3. The ovarian hormones, estrogen and progesterone, which are secreted by the ovaries in response to FSH and LH

❖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

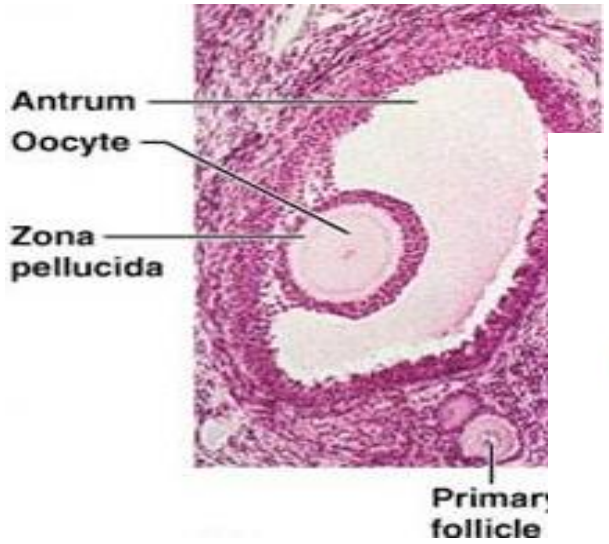


Ovarian follicle growth

- **“Follicular” phase of the ovarian cycle:**

- In female child each ovum is surrounded by single granulosa cell sheath called *primordial follicle* which provides nourishment for the ovum & secrete oocyte *maturation-inhibiting factor* which keeps the ovum in its primordial state

- After puberty, AP secretes FSH and LH resulting in ovum to increase in size & growth of additional layers of granulosa cells of some follicles known as primary follicles



- There is proliferation of the
- granulosa cells to many layers.
- The ovary interstitium Collects in several layers outside the granulosa cells to form a second mass of cells called **theca**

The theca is divided into 2 layers:

1. ***theca interna***
2. ***theca externa***,

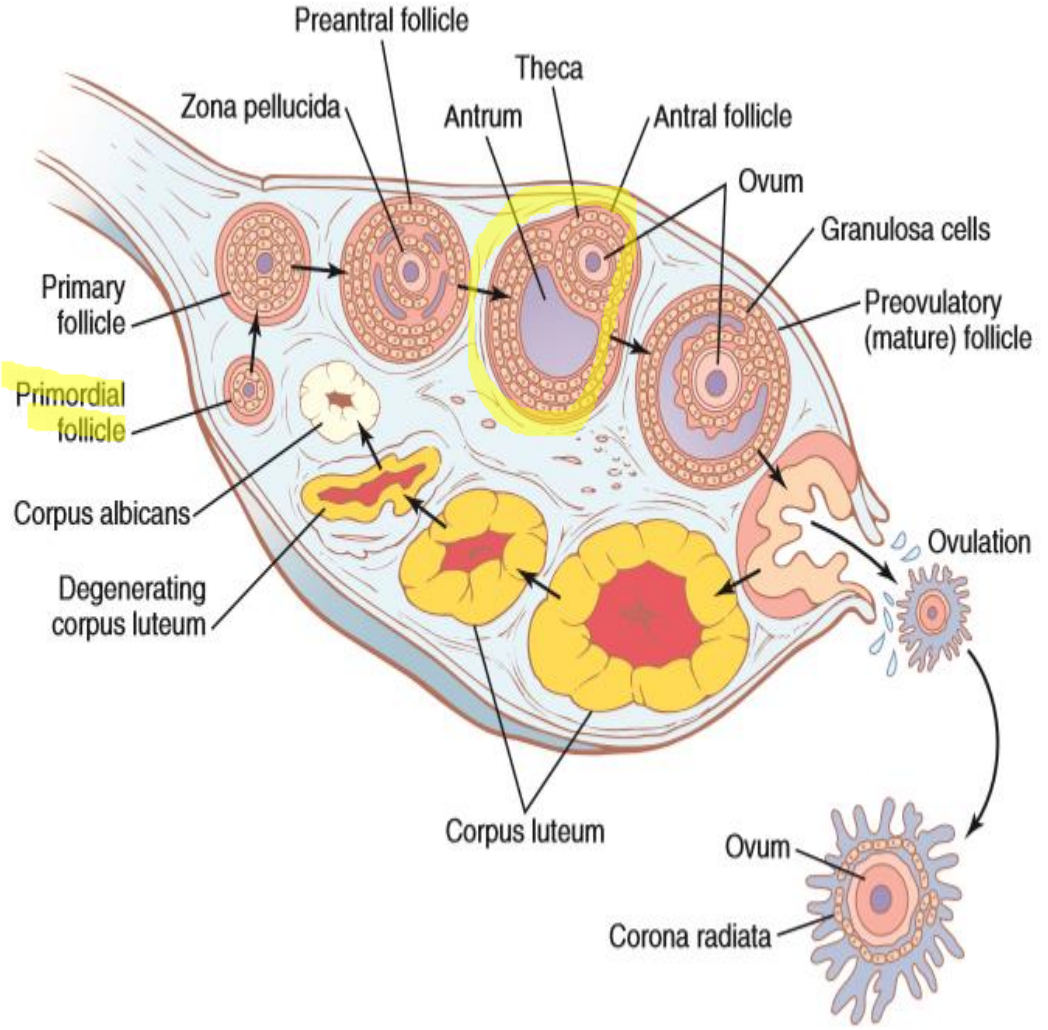


Figure 82-5. Stages of follicular growth in the ovary, also showing formation of the corpus luteum.

Ovarian follicle growth

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

- **FSH** increase is slightly more & earlier than LH which causes the acceleration of growth of many primary follicles each month.
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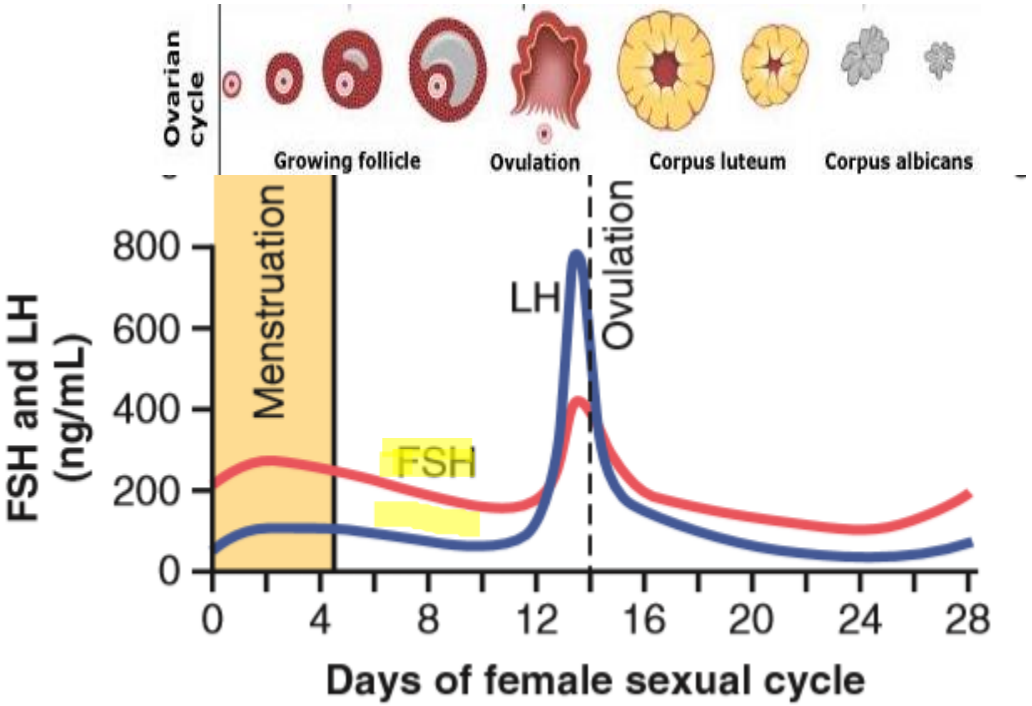
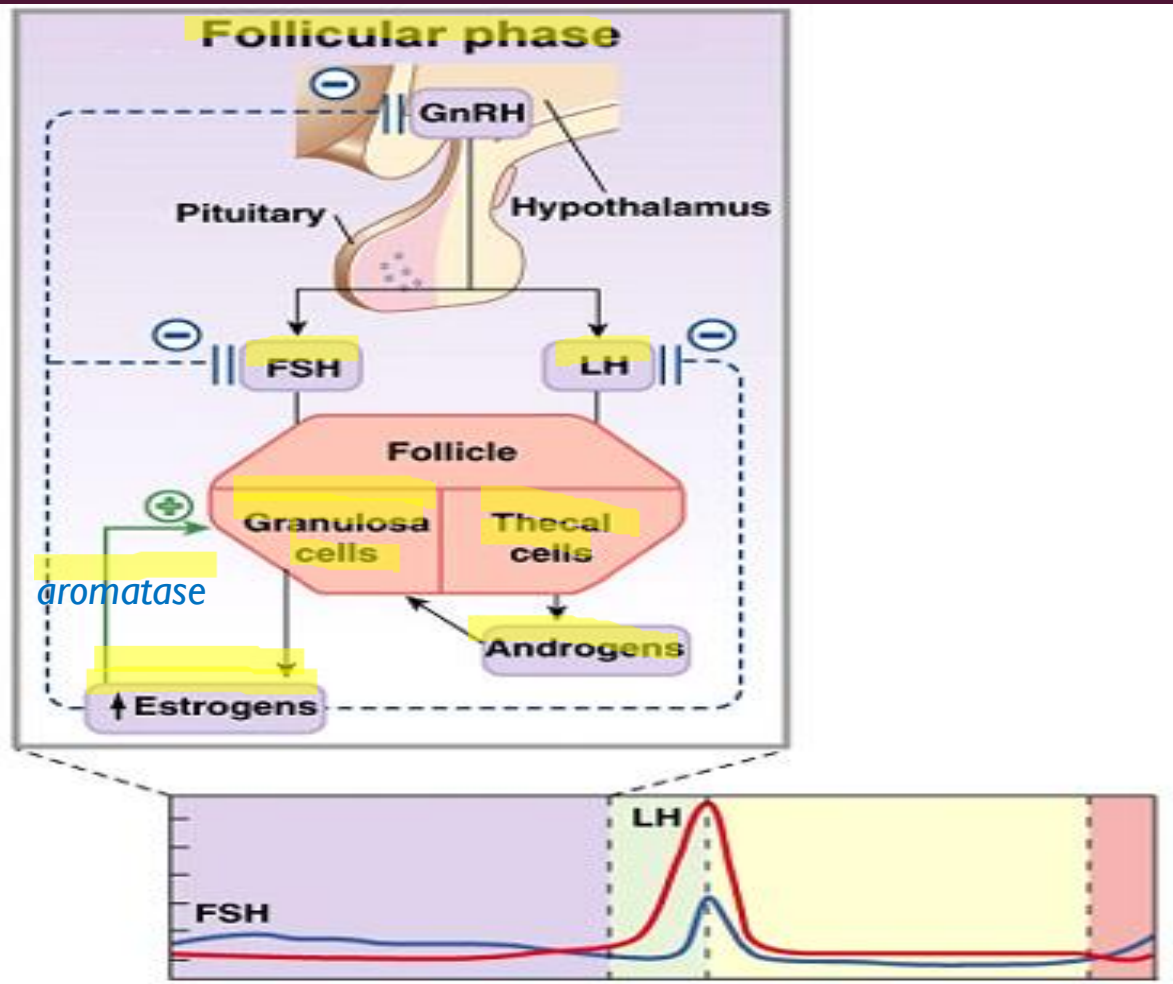



Follicular phase
GnRH
Pituitary
Hypothalamus
FSH
LH
Follicle
Granulosa cells
Thecal cells
aromatase
Androgens
Estrogens
LH
FSH

EFFECT OF ESTROGEN AND PROGESTRONE ON GONADOTROPINS

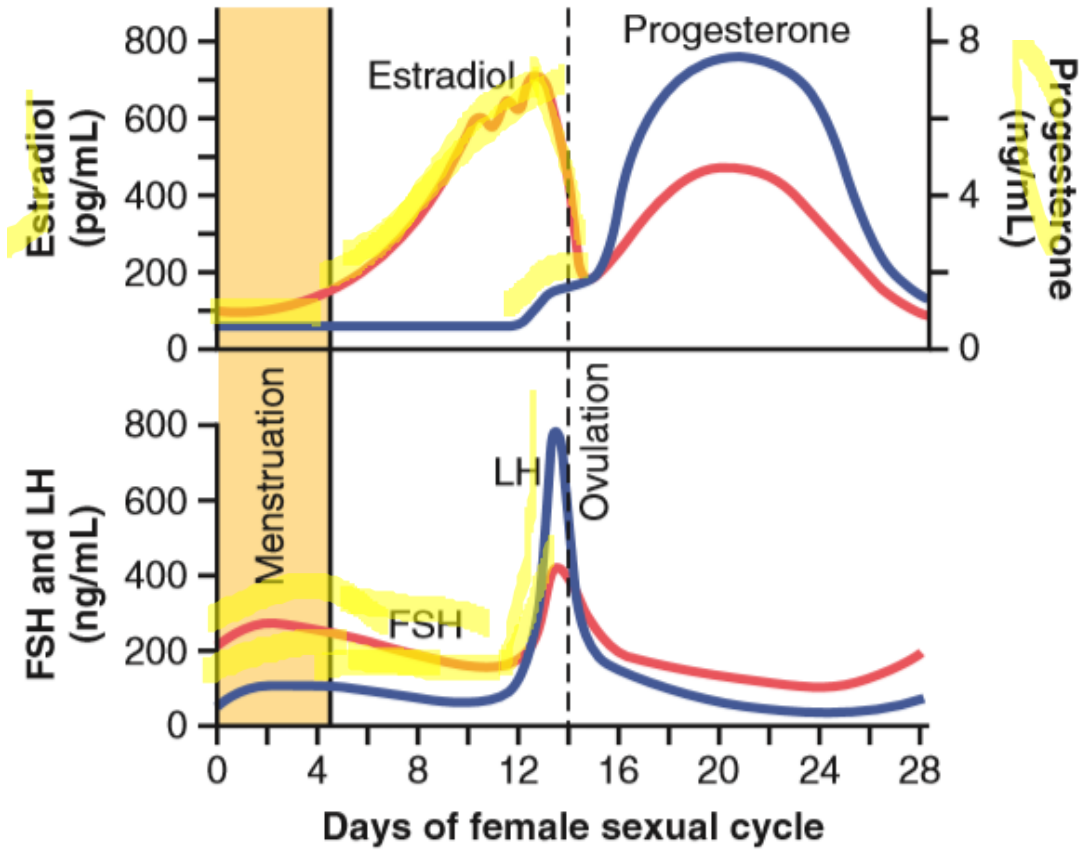
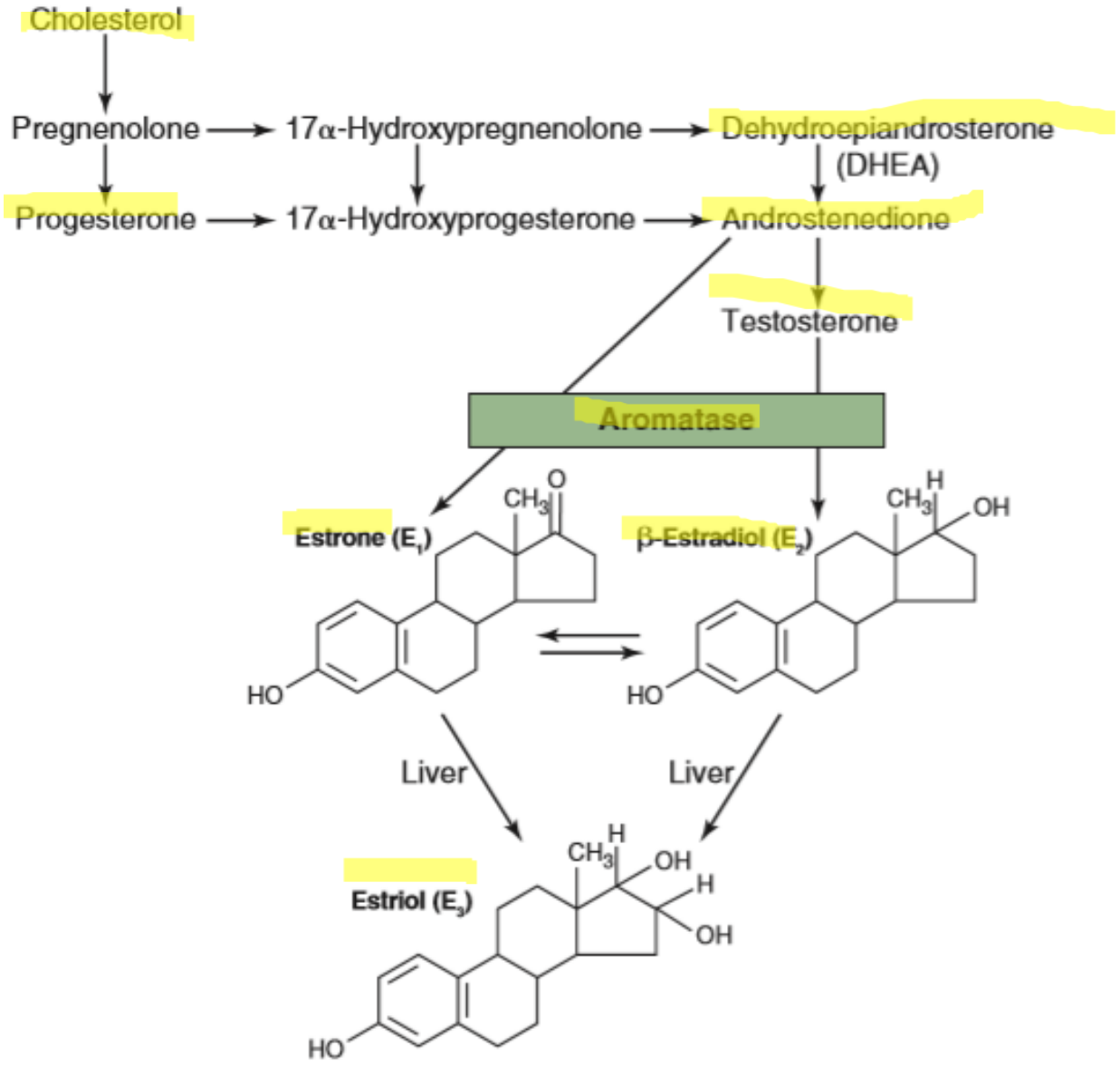


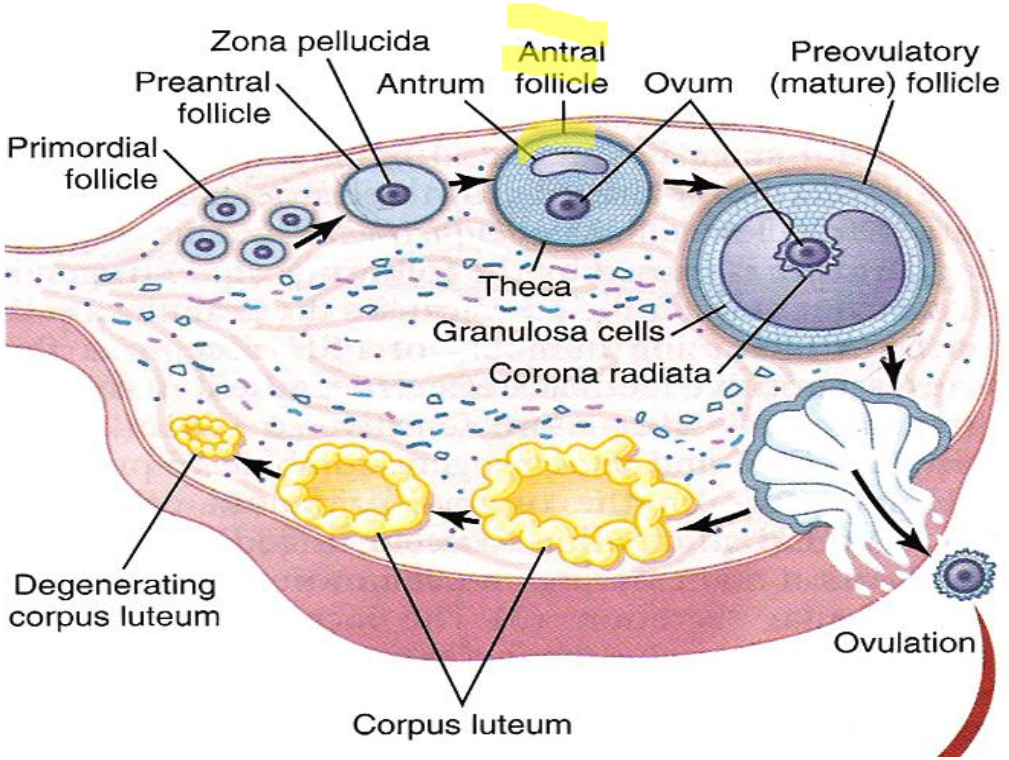
Figure 82-4. Approximate plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle. FSH, follicle-stimulating hormone; LH, luteinizing hormone.



2-7. Synthesis of the principal female hormones. The chemical structures of the precursor hormones, including progesterone, are
Figure 78-2.

Ovarian follicle growth

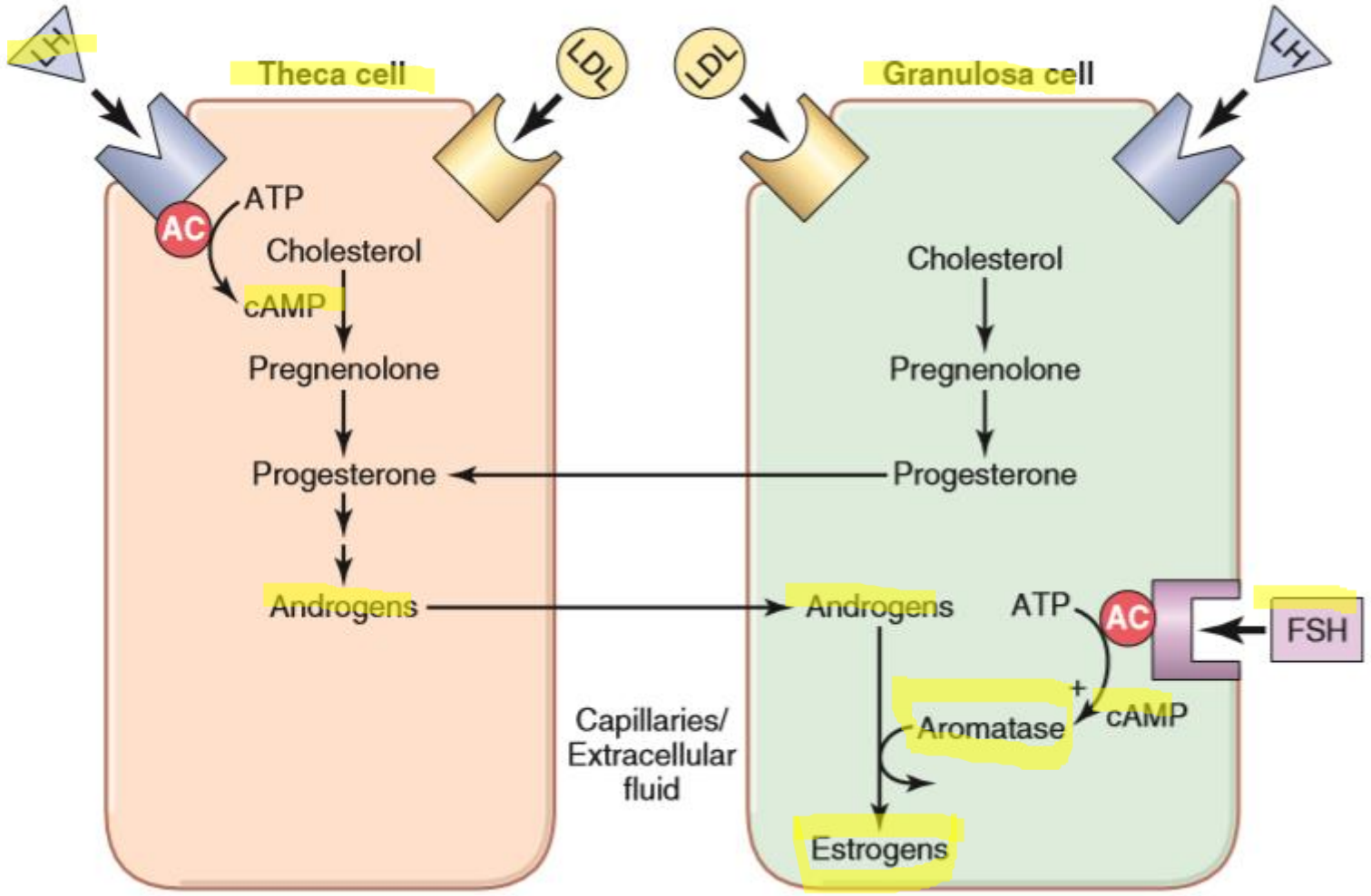
Few days after proliferation & growth of the follicles, the granulosa cells secrete follicular fluids that contain high concentration of **estrogen**. This fluid accumulates to form **antrum** within the mass of the granulosa cells



Ovarian follicle growth

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 secreted into the follicle caused the granulosa cells to increase FSH receptors which causes **positive feedback effect**
2. both estrogen & FSH combine to promote LH receptors on the original granulosa cells in addition to FSH stimulation, allowing more rapid increase in follicular secretion
3. the increasing estrogen from the follicle plus increasing LH from the AP causes proliferation of the follicular theca cells & increase their secretion

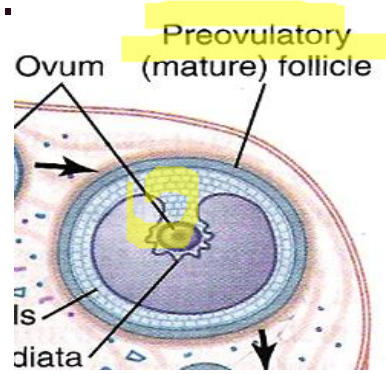

LH
LDL
Theca cell
LDL
Granulosa cell
LH
ATP
AC
Cholesterol
cAMP
Pregnenolone
Progesterone
Androgens
Cholesterol
Pregnenolone
Progesterone
Androgens
ATP
AC
FSH
+
cAMP
Aromatase
Capillaries/
Extracellular
fluid
Estrogens

Ovarian follicle growth

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

- 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.

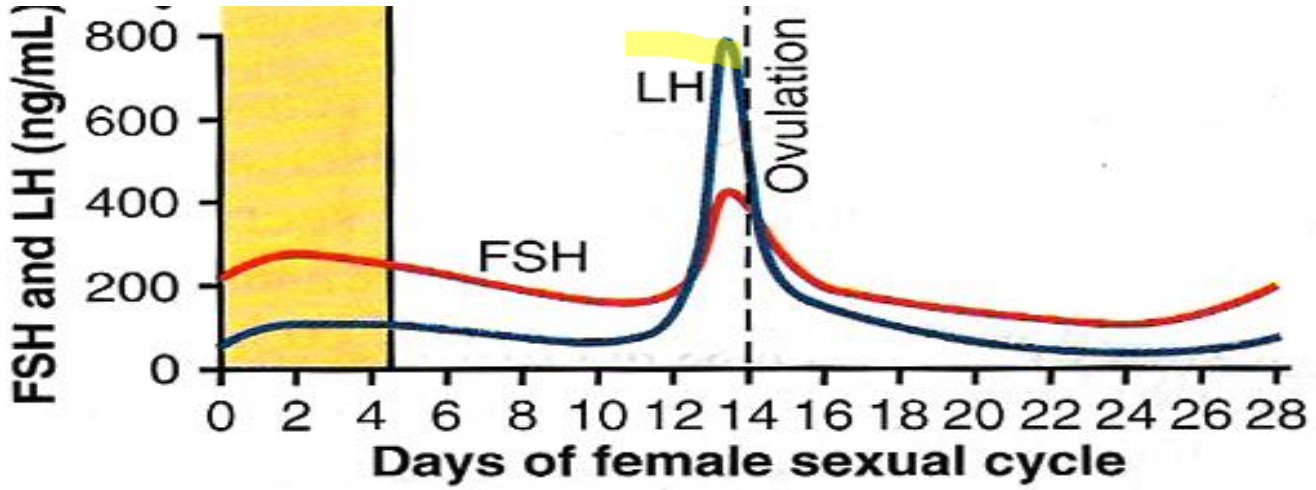
- The remaining follicles (5 to 11) undergo ***atresia*** or involute



Ovulation

LH is necessary for final follicular growth and ovulation:

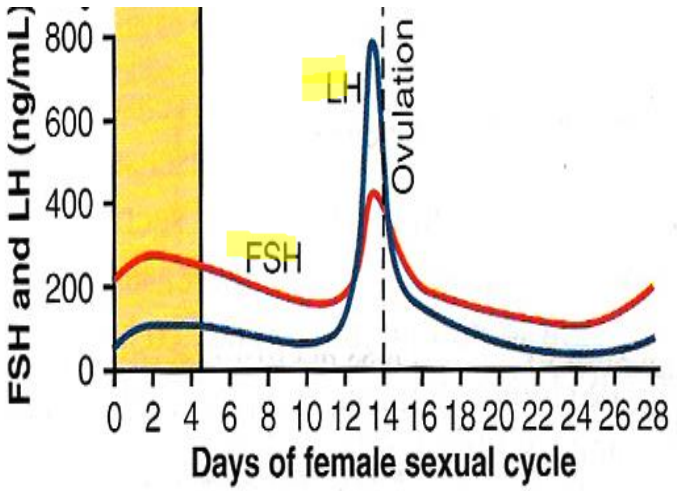
2 days before ovulation → rate of LH secretion ↑ to 6-16 fold & peaks about 16 hrs before ovulation.



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 ↓ abou 1 day **before ovulation** while progesterone secretion begin to ↑



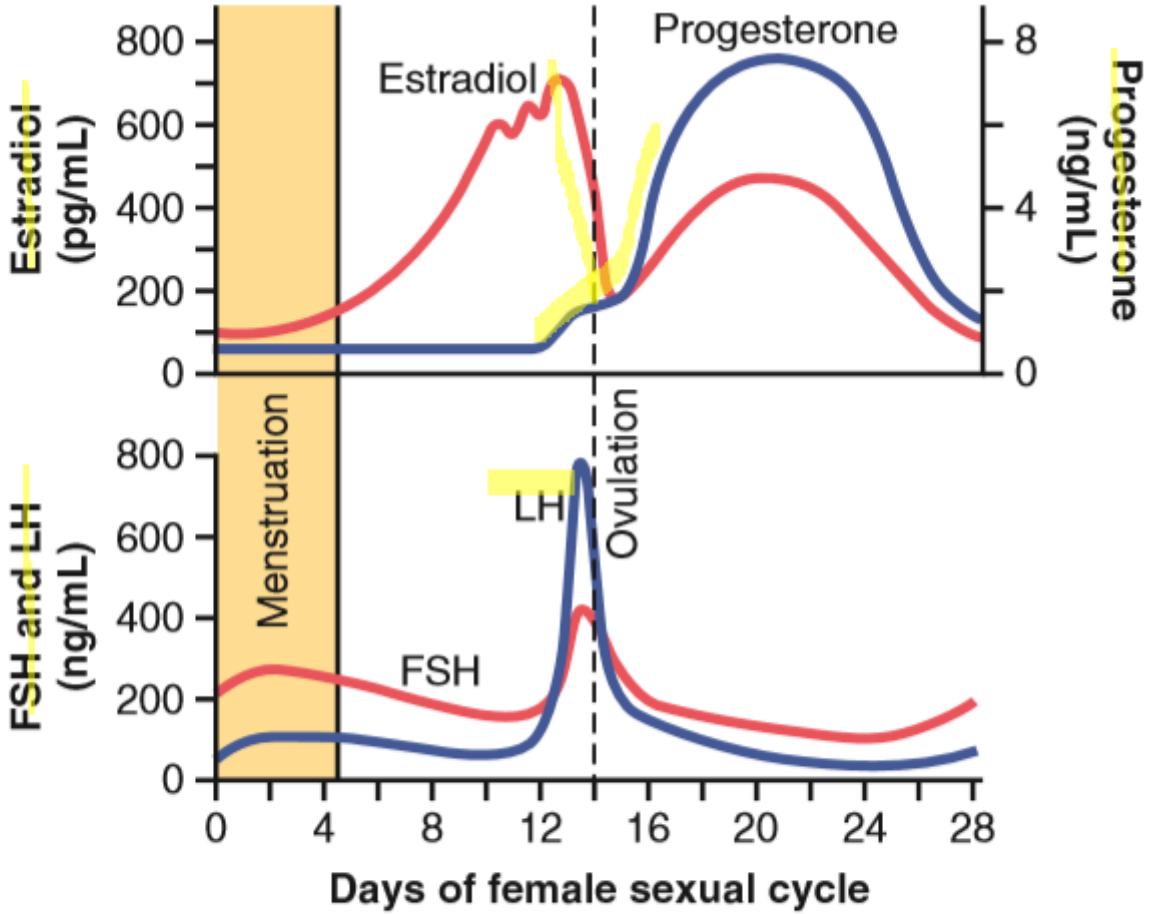
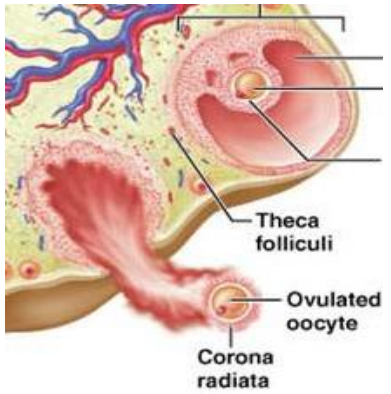
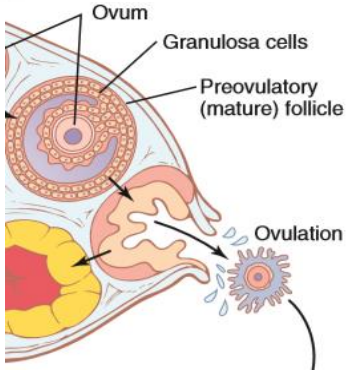


Figure 82-4. Approximate plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle. FSH, follicle-stimulating hormone; LH, luteinizing hormone.

Initiation of ovulation

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





1) the **theca externa** begins to secrete proteolytic enzyme and weakens 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.

OVULATION

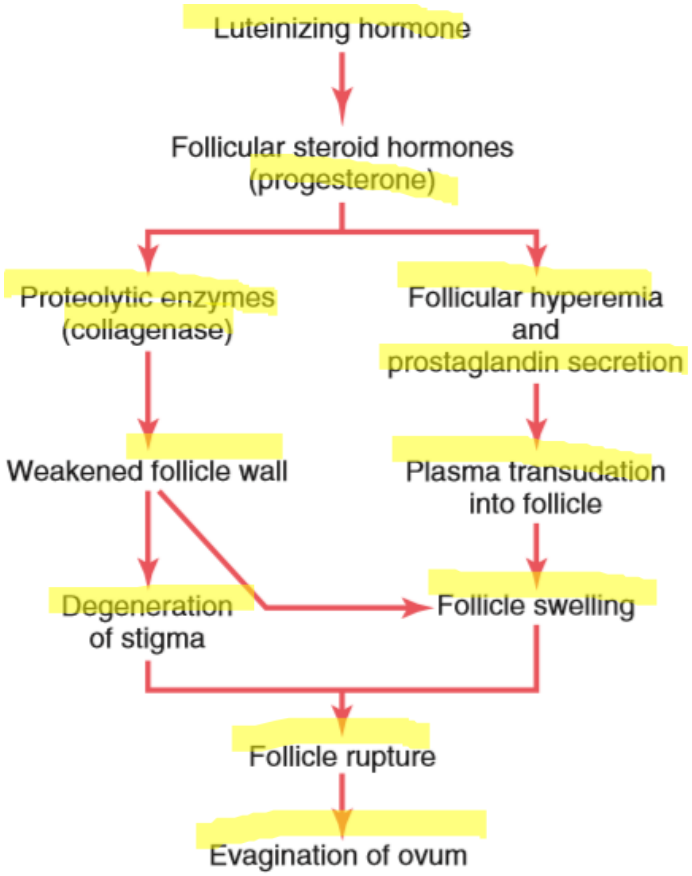
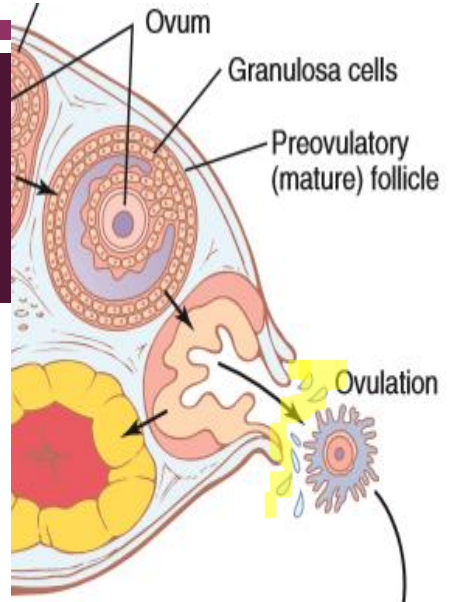


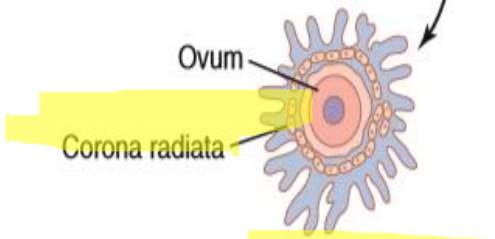
Figure 82-6. The postulated mechanism of ovulation.

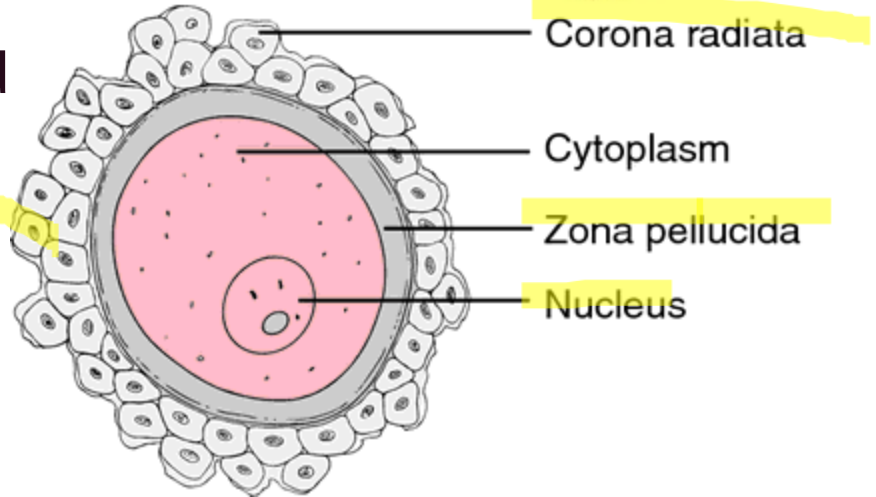
Ovulation

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

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

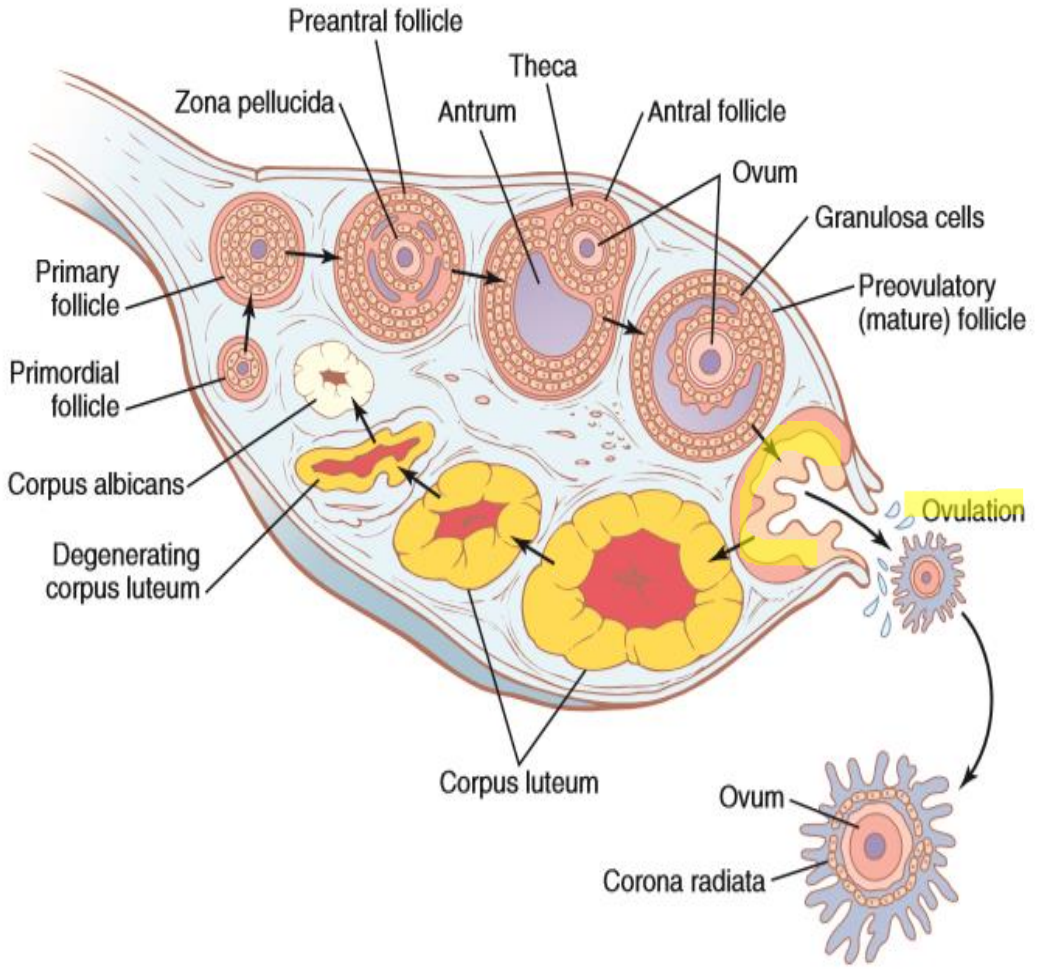
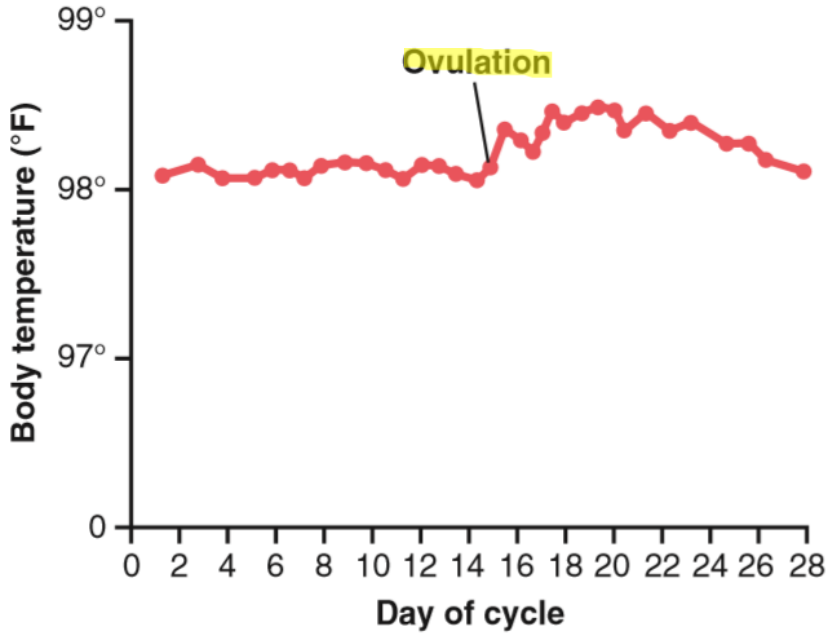


Figure 82-5. Stages of follicular growth in the ovary, also showing formation of the corpus luteum.

7-8 days after ovulation ~ 1.5 cm in diameter

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

Ovulation



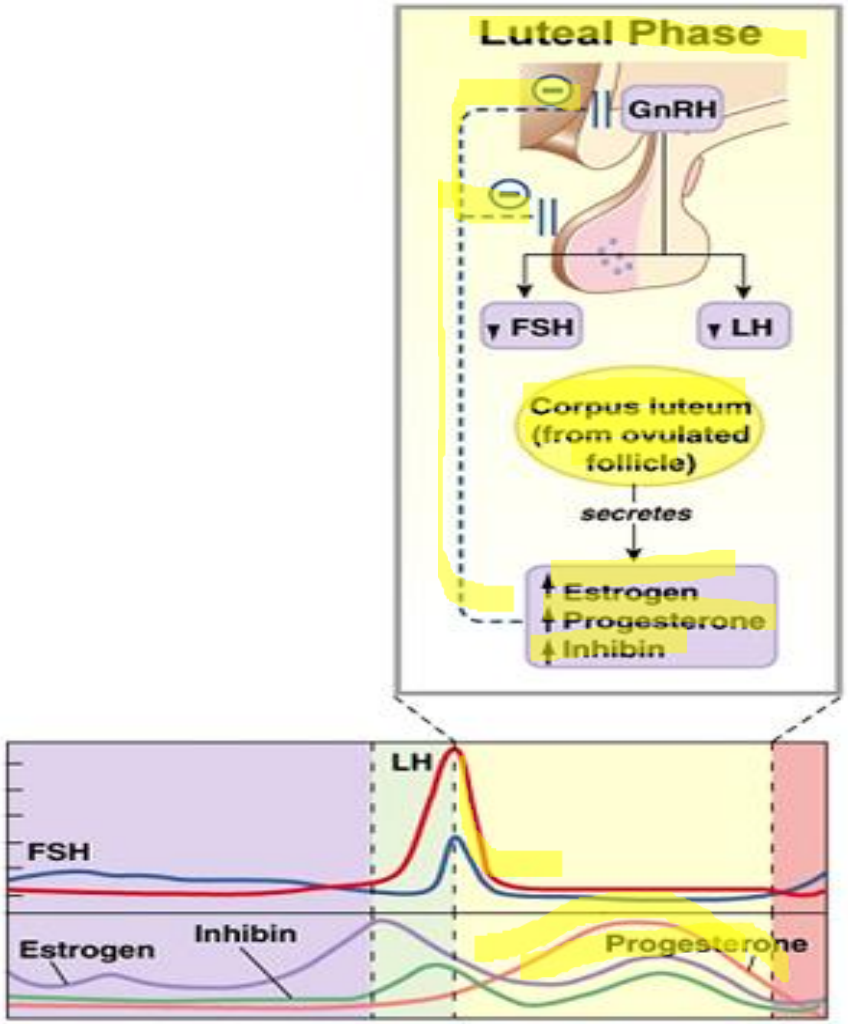
Secretion of progesterone during the latter half of the cycle raises the body temperature about 0.5°F, with the temperature rise coming abruptly at the time of ovulation.

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.


Luteal Phase
GnRH
FSH
LH
Corpus luteum (from ovulated follicle)
secretes
Estrogen
Progesterone
Inhibin
LH
FSH
Estrogen
Inhibin
Progesterone

Corpus Luteum

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 from the placenta acts on the corpus luteum to prolong its life for 2 to 4 months of pregnancy

Corpus Luteum

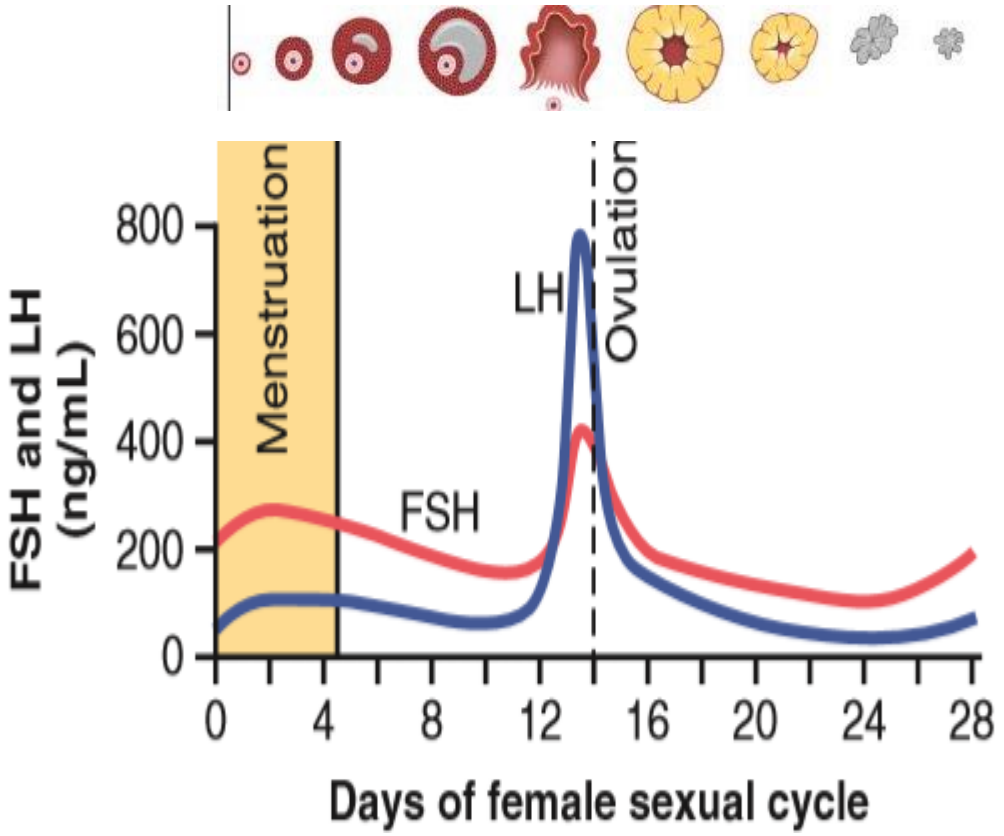
Involution of the corpus luteum and onset of the next ovarian cycle:

1- Estrogen & 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. ↓ FSH & LH & loss of these hormones >> complete degeneration of corpus luteum (involution)

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



7-8 days after ovulation ~ 1.5 cm in diameter

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