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# LECTURE 2
# PHYSIOLOGY OF OVARIAN CYCLE

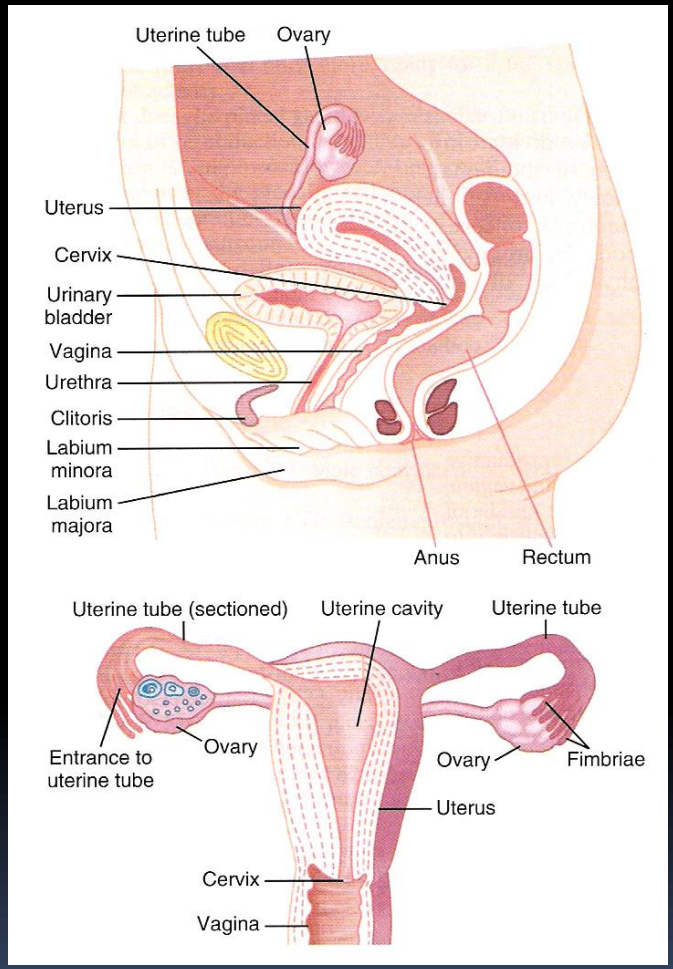
# Objectives

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. Describe the pituitary ovarian axis and in correlation with the changes that occur in the ovaries leading up to and following ovulation during an ovarian cycle

Keywords: 17β-estradiol, progesterone, graafian follicle, ovulation, corpus luteum

# Anatomy of the female sexual organs



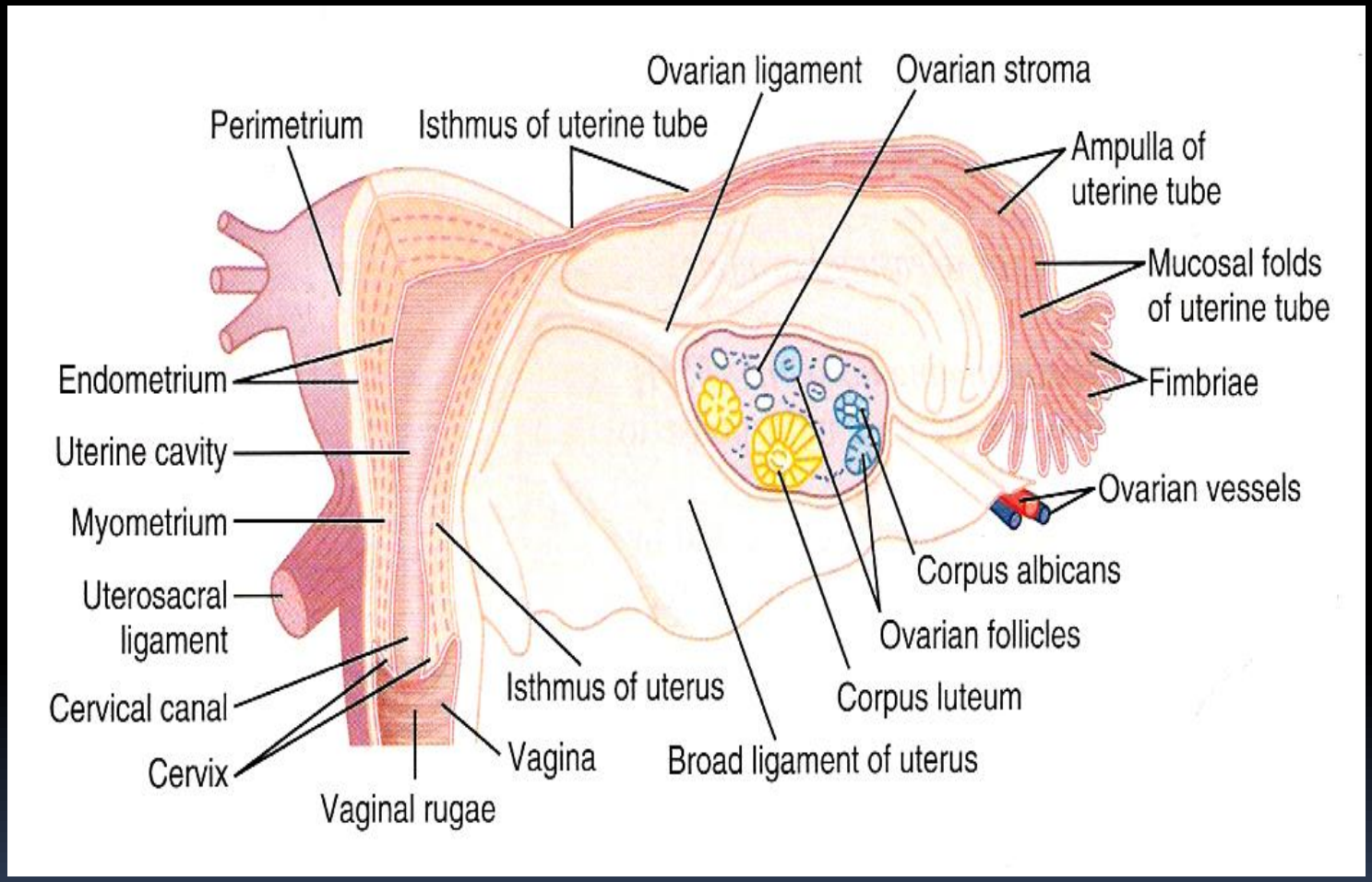
**Monthly ovarian cycle:**

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).

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 for the fertilized ovum.


Ovarian ligament
Ovarian stroma
Perimetrium
Isthmus of uterine tube
Ampulla of uterine tube
Mucosal folds of uterine tube
Endometrium
Fimbriae
Uterine cavity
Ovarian vessels
Myometrium
Corpus albicans
Uterosacral ligament
Ovarian follicles
Isthmus of uterus
Corpus luteum
Cervical canal
Vagina
Broad ligament of uterus
Cervix
Vaginal rugae

**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.

## Ovarian follicle growth:-

## “Follicular” phase of the ovarian cycle:

- In female child  each ovum is surrounded by single granulosa cell sheath 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.
- After puberty, AP secrete FSH and LH which stimulate the ovaries with some follicles to grow. This begins with enlargement of the ovum to increase in size & growth of additional layers of granulosa cells of some follicles & known as primary follicles.

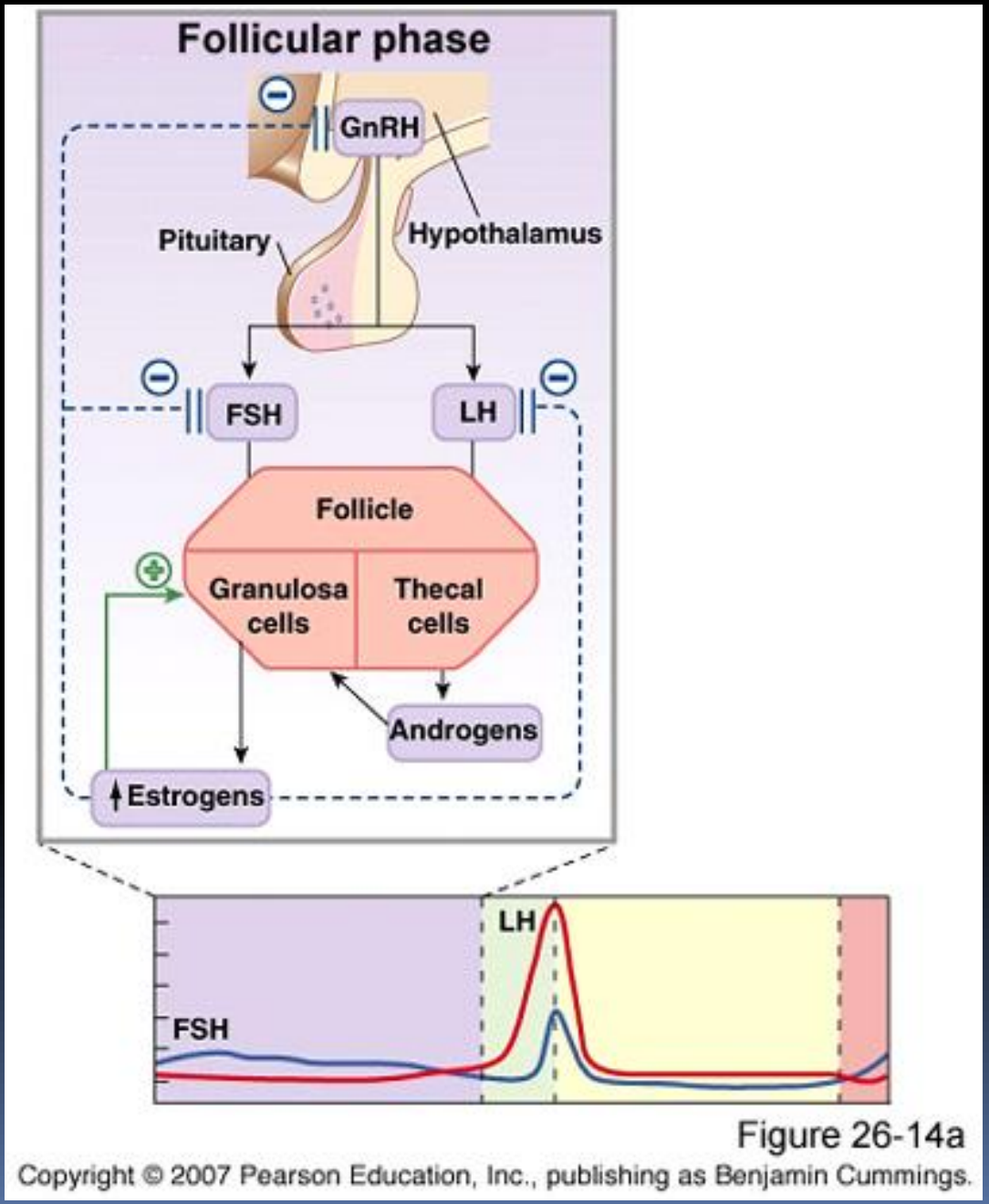
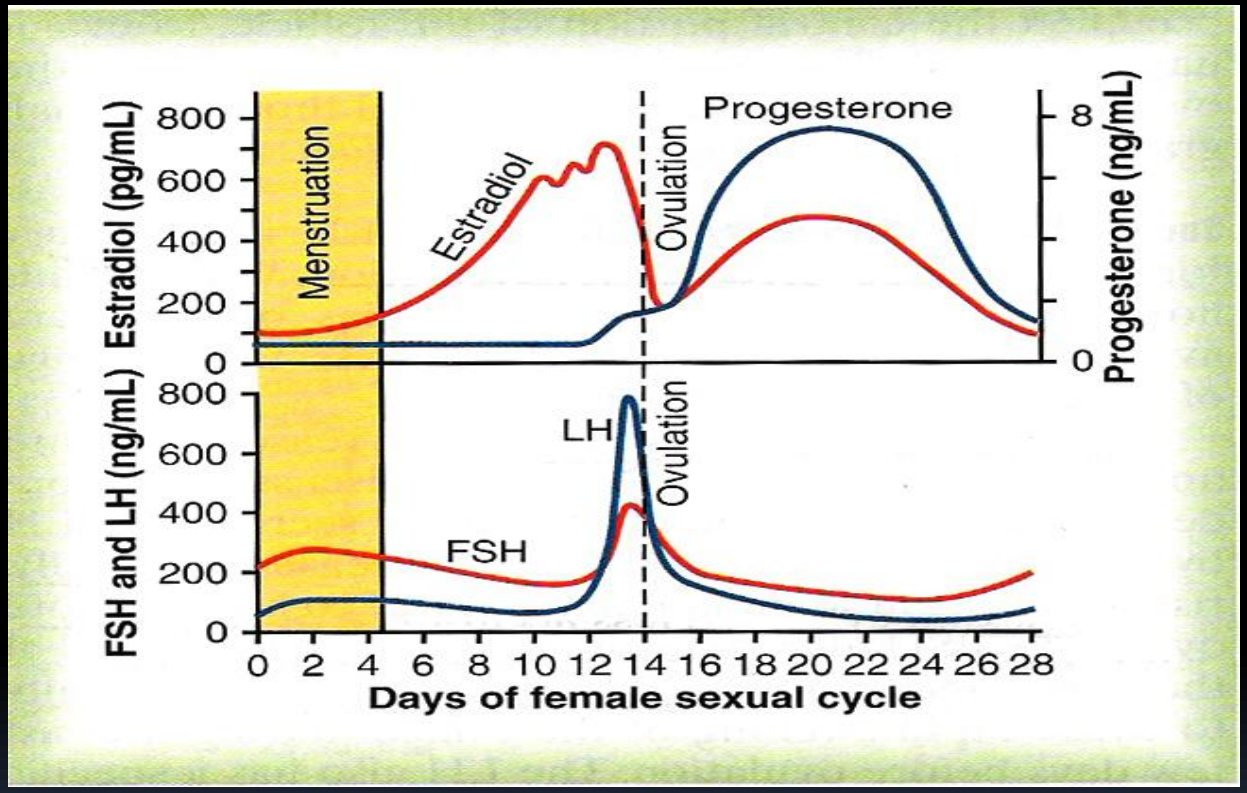



Figure 26-14a


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

During the first few days of the monthly female sexual cycle there is 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. There is proliferation of the granulosa cells to many layers. The ovary interstitium collect in several layers outside the granulosa cells to form a second mass of cells called **theca.**

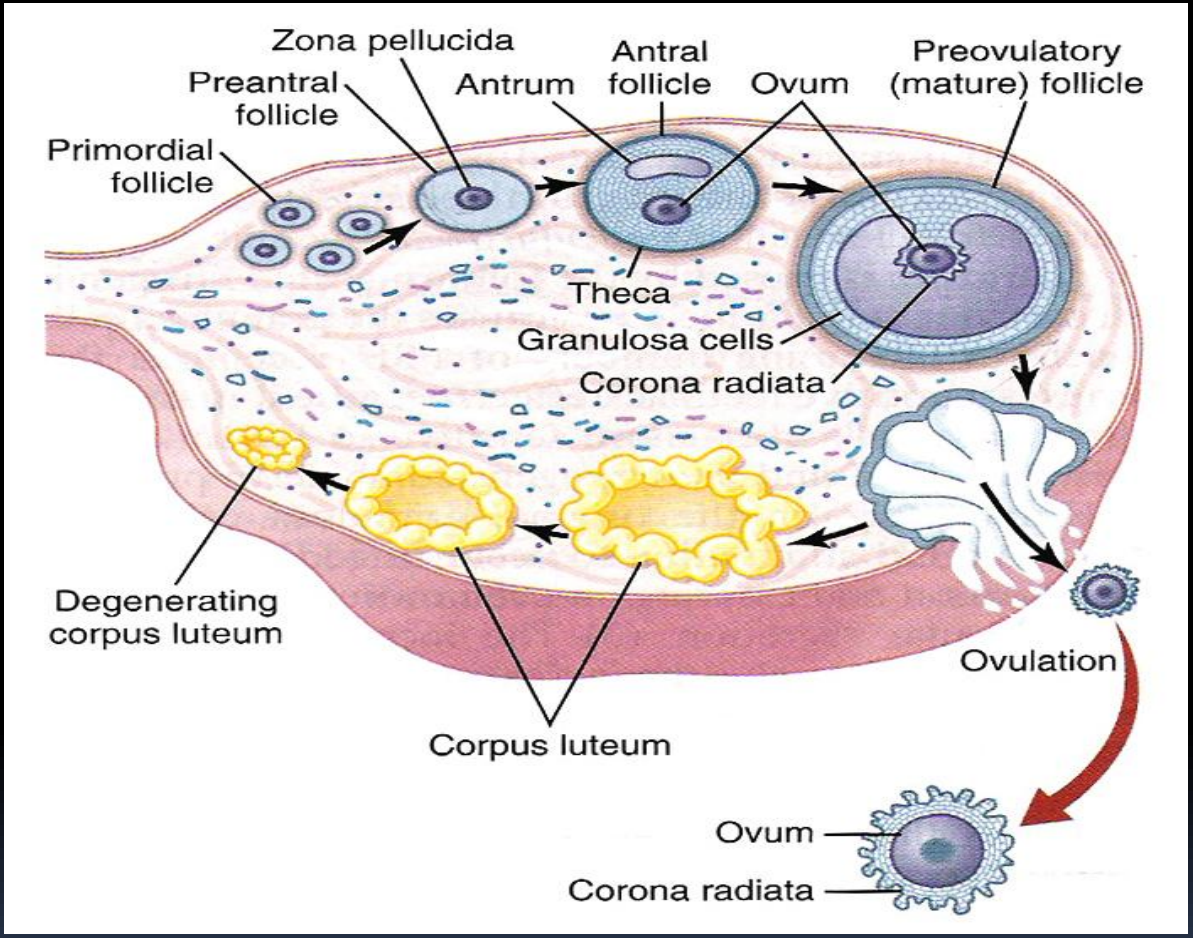
## This theca is divided into 2 layers:

1. theca interna, the cells have epitheloid characteristics and similar to the granulosa cells and secrete sex hormones (estrogen and progesterone)
2. theca externa, the outer layer, develops into a highly vascular connective tissue capsule of the developing follicle.

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 early growth of the follicle up to the antral is under FSH stimulation. Then there is accelerated growth of the follicle to larger follicle called vesicular follicle 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 granulosa cells, allowing more increase 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.


Zona pellucida
Preantral follicle
Primordial follicle
Antrum
Antral follicle
Ovum
Preovulatory (mature) follicle
Theca
Granulosa cells
Corona radiata
Degenerating corpus luteum
Corpus luteum
Ovulation
Ovum
Corona radiata

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

- 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 positive feedback effect & mature follicle reach about 1 to 1.5 cm.

# Ovulation:

It occurs 14 days after the onset of menstruation in 28 days cycle. Before ovulation, small area in the center of the follicle called stigma protrude & 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.

## LH surge is necessary for ovulation:

2 days before ovulation, the rate of LH secretion from the AP increase markedly to 6-16 fold & peak about 16 hrs before ovulation.

- FSH also increases to 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 so the rate of estrogen secretion begins to fall about 1 day before ovulation while progesterone secretion begin to increase.

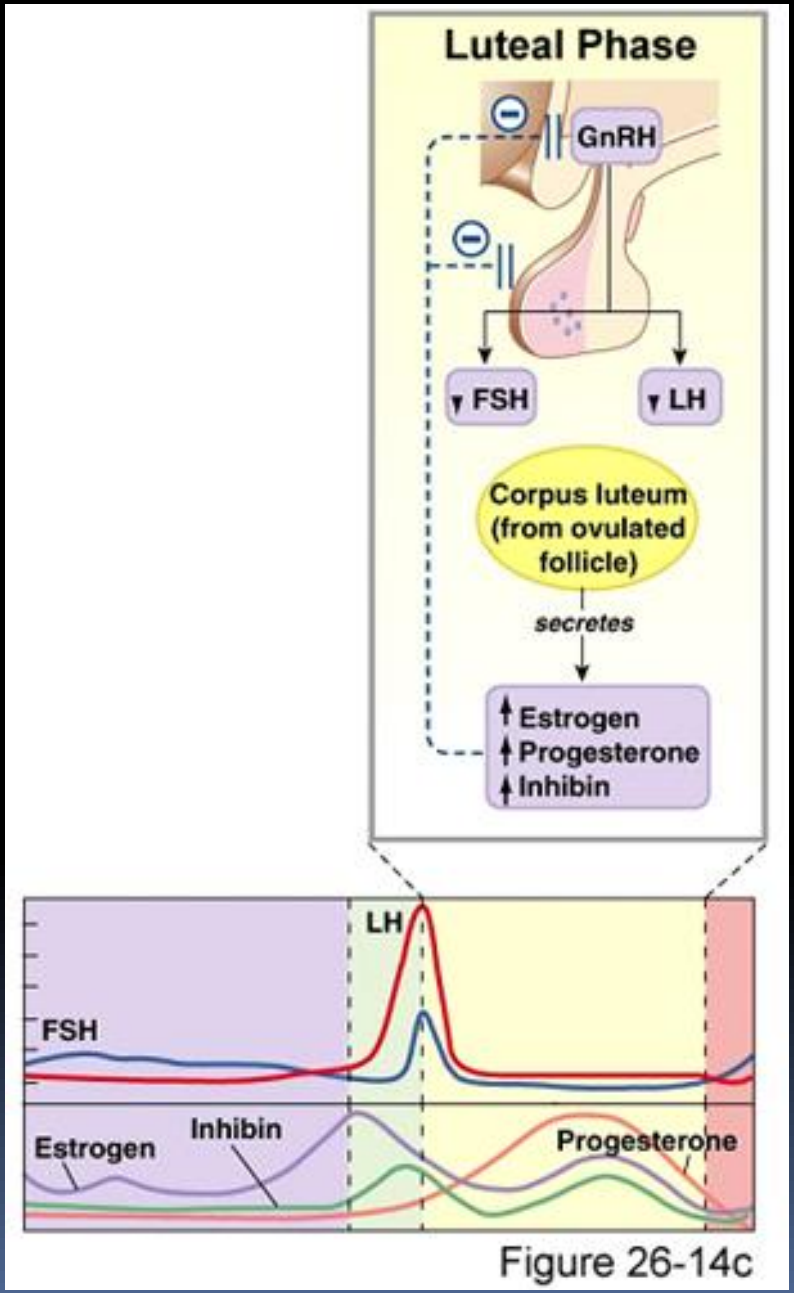
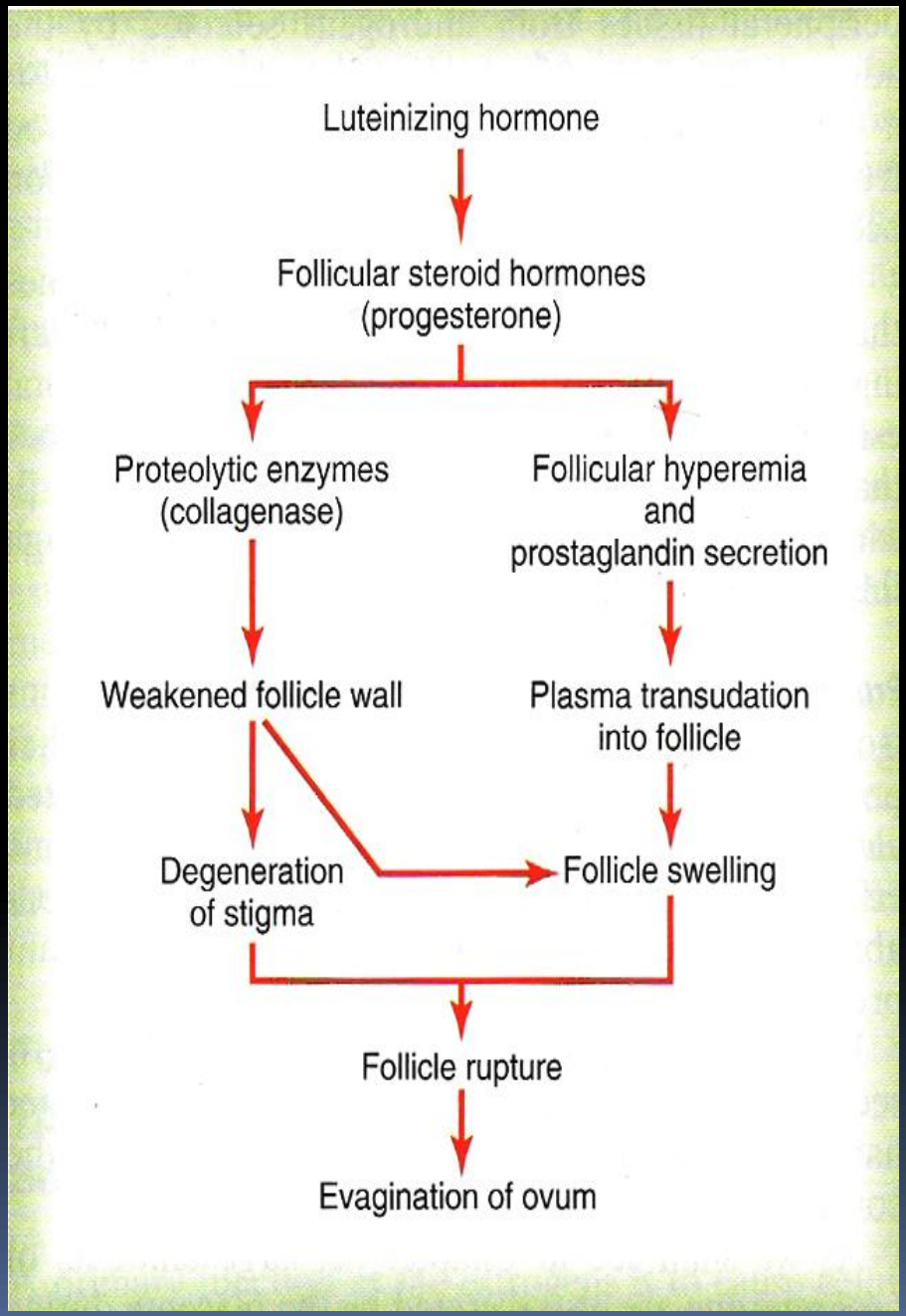


Figure 26-14c


Luteinizing hormone
Follicular steroid hormones (progesterone)
Proteolytic enzymes (collagenase)
Follicular hyperemia and prostaglandin secretion
Weakened follicle wall
Plasma transudation into follicle
Degeneration of stigma
Follicle swelling
Follicle rupture
Evagination of ovum

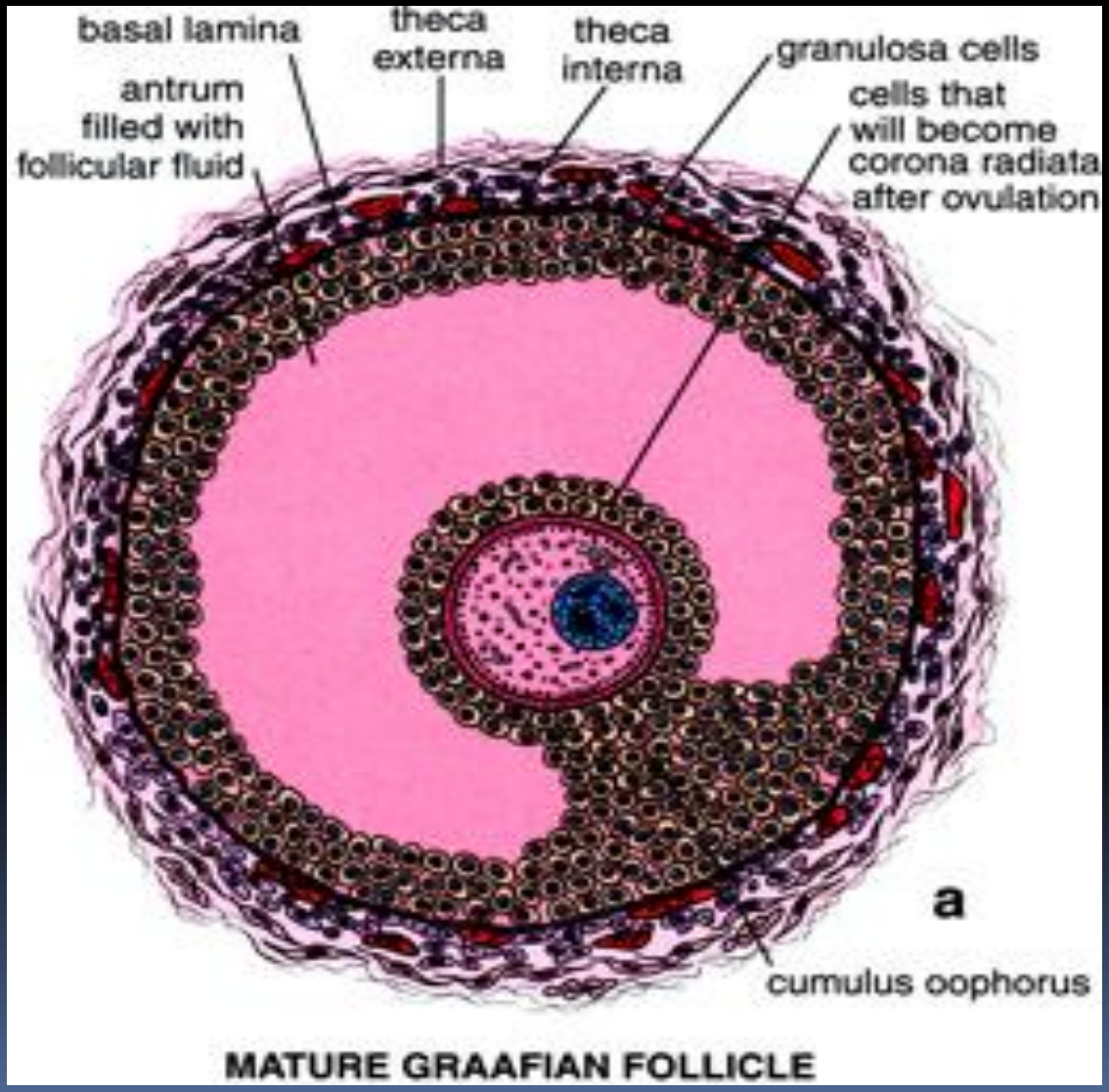
## Initiation of ovulation:

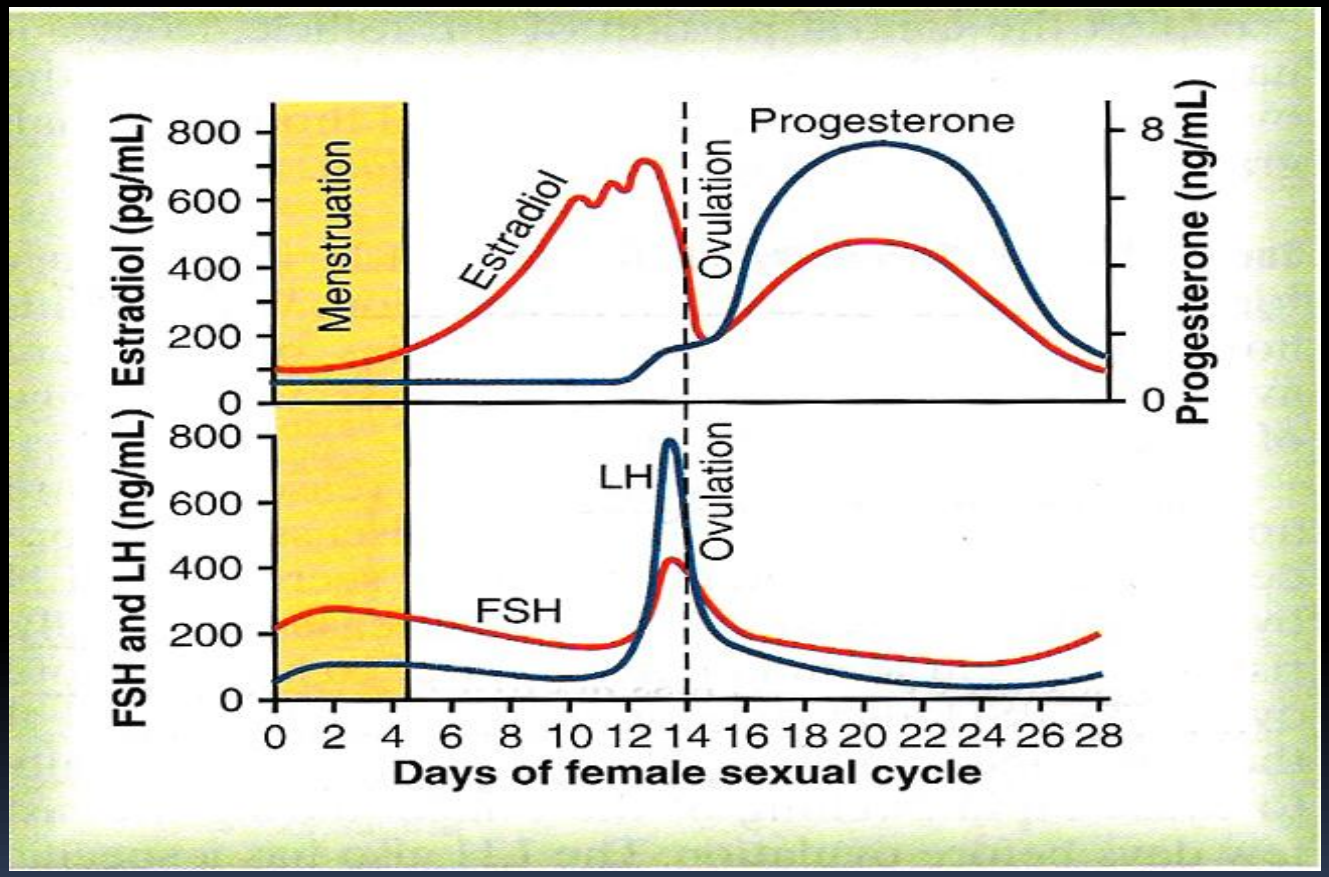
Large quantity of LH secreted by the AP causes rapid secretion of progesterone from the follicle few hours & 2 events occur which are necessary for ovulation:

1) the theca externa begins to secrete proteolytic enzymes & causes weakening of the wall result 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.

-The two effects causes swelling of the follicle & plasma transudation into the follicle & degeneration of the stigma with discharge of the ovum.

# Mature Graffian Follicle

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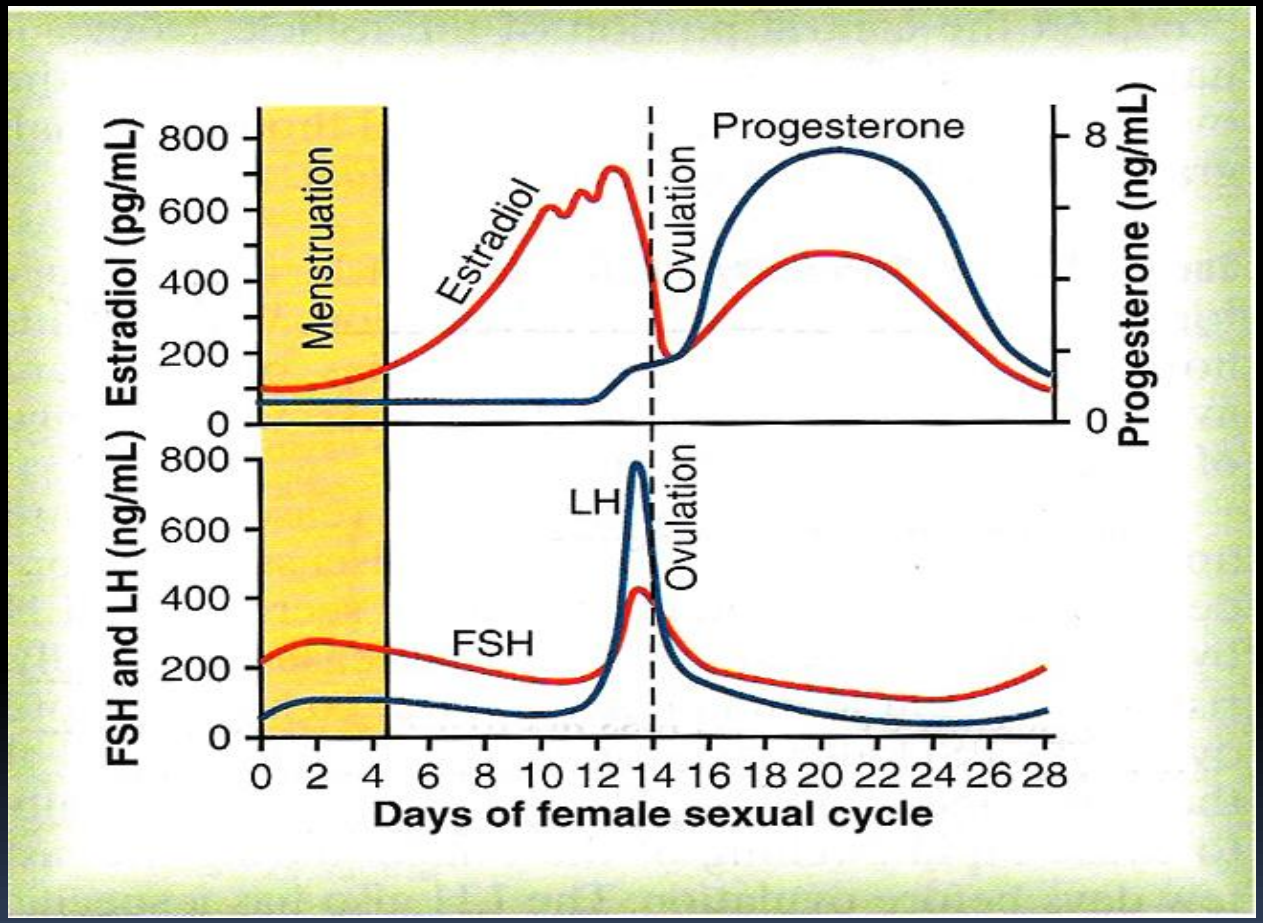
FSH
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days of female sexual cycle

## Luteal phase of the ovarian cycle:

- After expulsion of the ovum from the follicle, the remaining granulosa & theca internal cells change to lutein cells & become filled with lipid inclusions giving them yellowish appearance. The granulosa cells with the theca cells called corpus luteum.

- The granulosa cells in corpus luteum develop extensive intracellular endoplasmic reticula & form large amount of progesterone & estrogen. The theca cells form mainly androgens which are converted by granulosa cells into female hormones.

- The corpus luteum grow to about 1.5 cm in diameter, at about 7 to 8 days after ovulation .Then begins to involute & losses its secretory function & its yellowish characteristic about 12 days after ovulation & becomes corpus albicans & replaced by connective tissue & absorbed.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LH
Ovulation
FSH
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days of female sexual cycle

# Luteinizing function of LH:

1- The change of granulosa and theca interna cells into lutein cells.

2- Extrusion of the ovum from the follicle Uncharacterized local hormone in the follicular fluid called luteinization – inhibiting factor hold the luteinization process until after ovulation.

3- Secretion of progesterone & estrogen from the corpus luteum.

- If pregnancy occur, the chorionic gonadotropin from the placenta act on the corpus luteum to prolong its life for 2 to 4 months of pregnancy.

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

1- Estrogen & progesterone secreted by the corpus luteum in 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 levels of both FSH & LH & loss of these hormones causes the corpus luteum to degenerate completely, called involution of the corpus luteum.

3- Around 26th days of normal sexual cycle & after involution of corpus luteum, sudden cessation of secretion of estrogen, progesterone & inhibin removes the feedback inhibition of the AP & allowing increase secretion of FSH & LH again. FSH & LH initiate the growth of new follicles, beginning a new ovarian cycle.

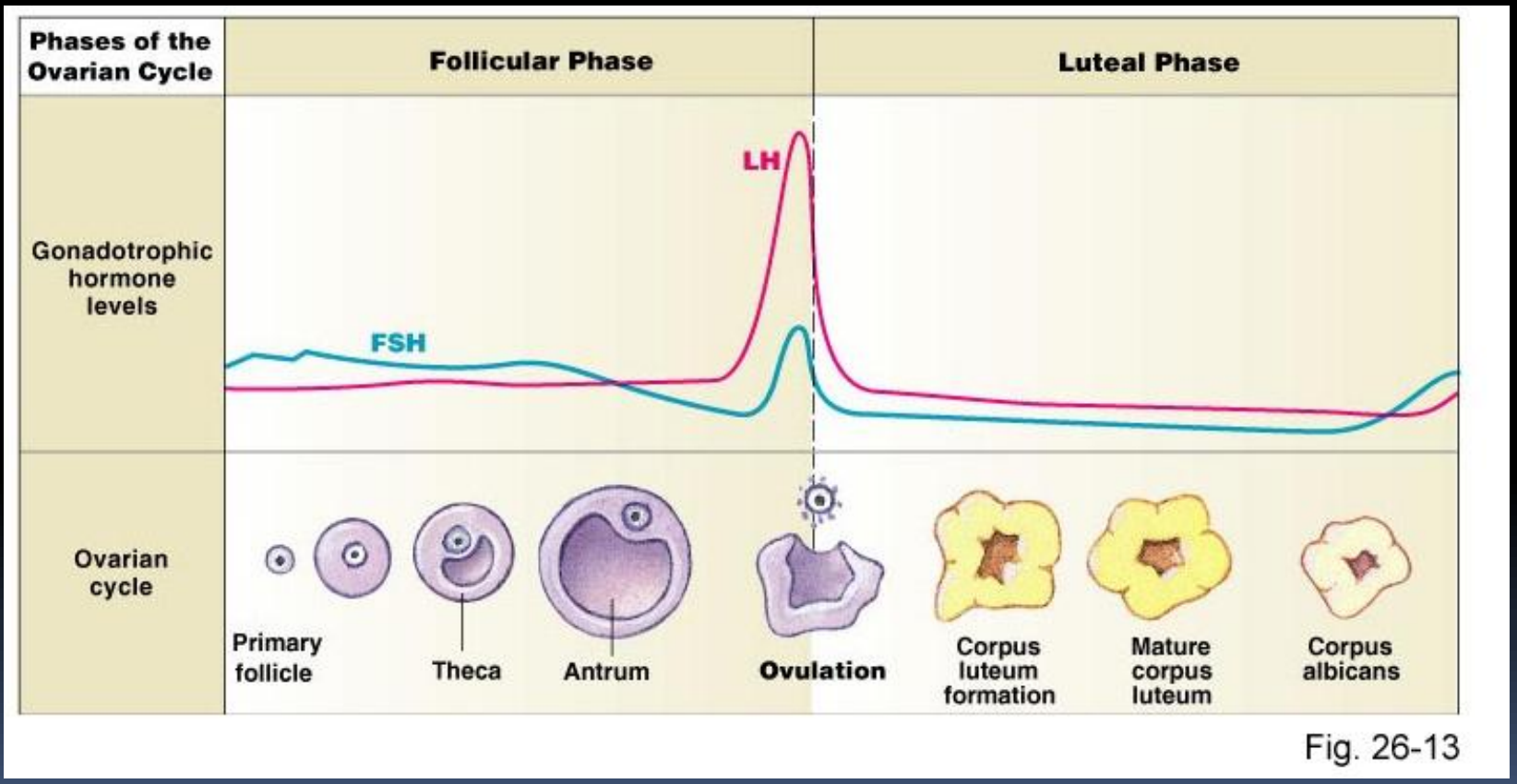

Phases of the Ovarian Cycle
Follicular Phase
Luteal Phase
Gonadotrophic hormone levels
LH
FSH
Ovarian cycle
Primary follicle
Theca
Antrum
Ovulation
Corpus luteum formation
Mature corpus luteum
Corpus albicans

Fig. 26-13

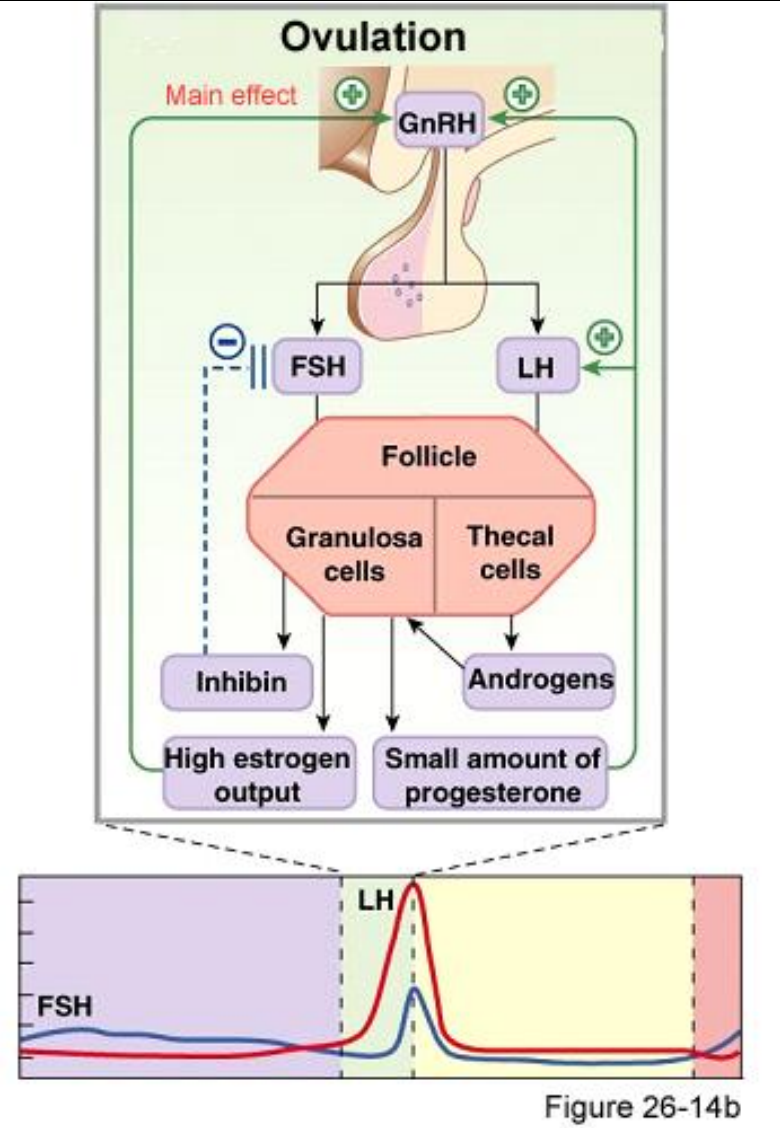
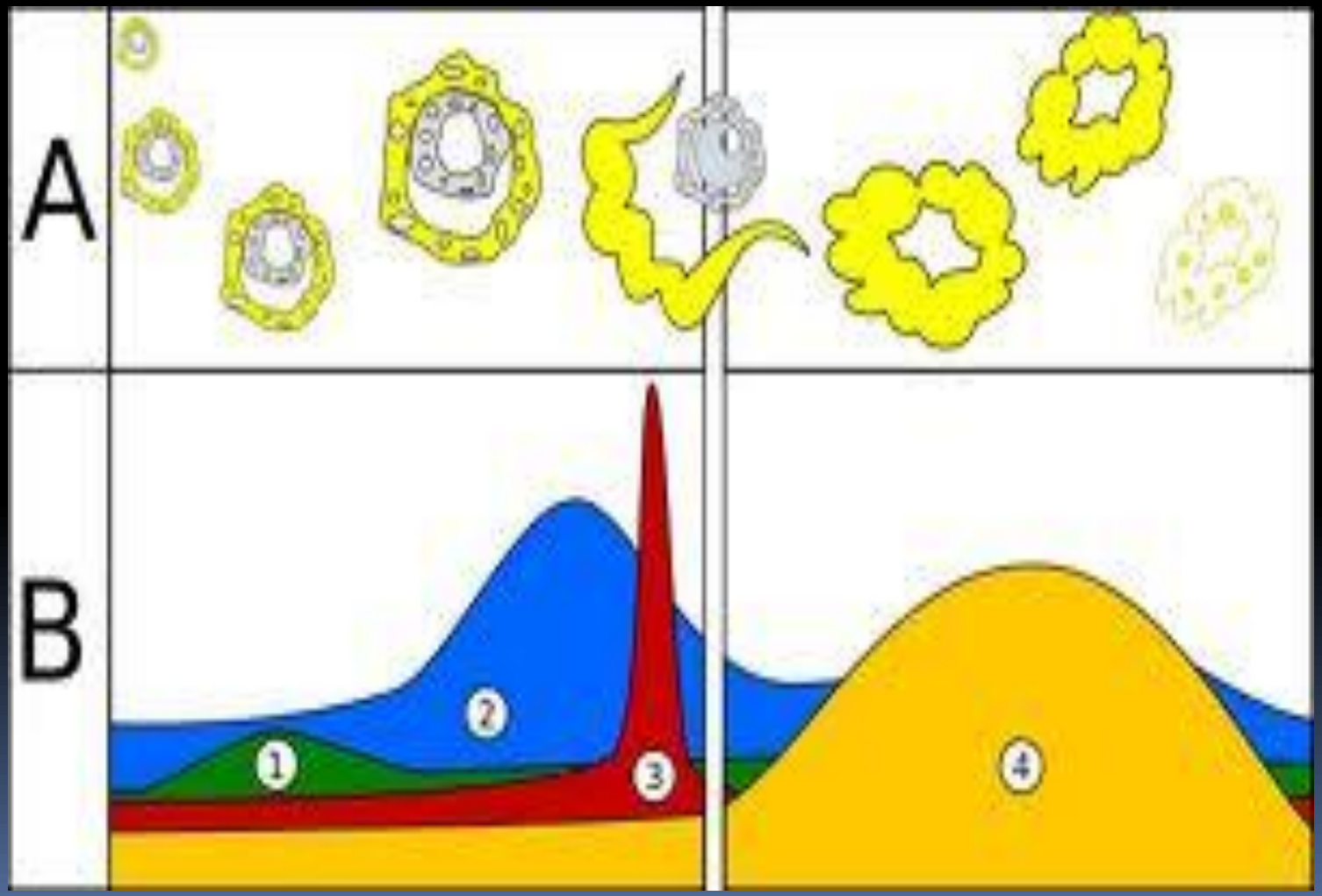
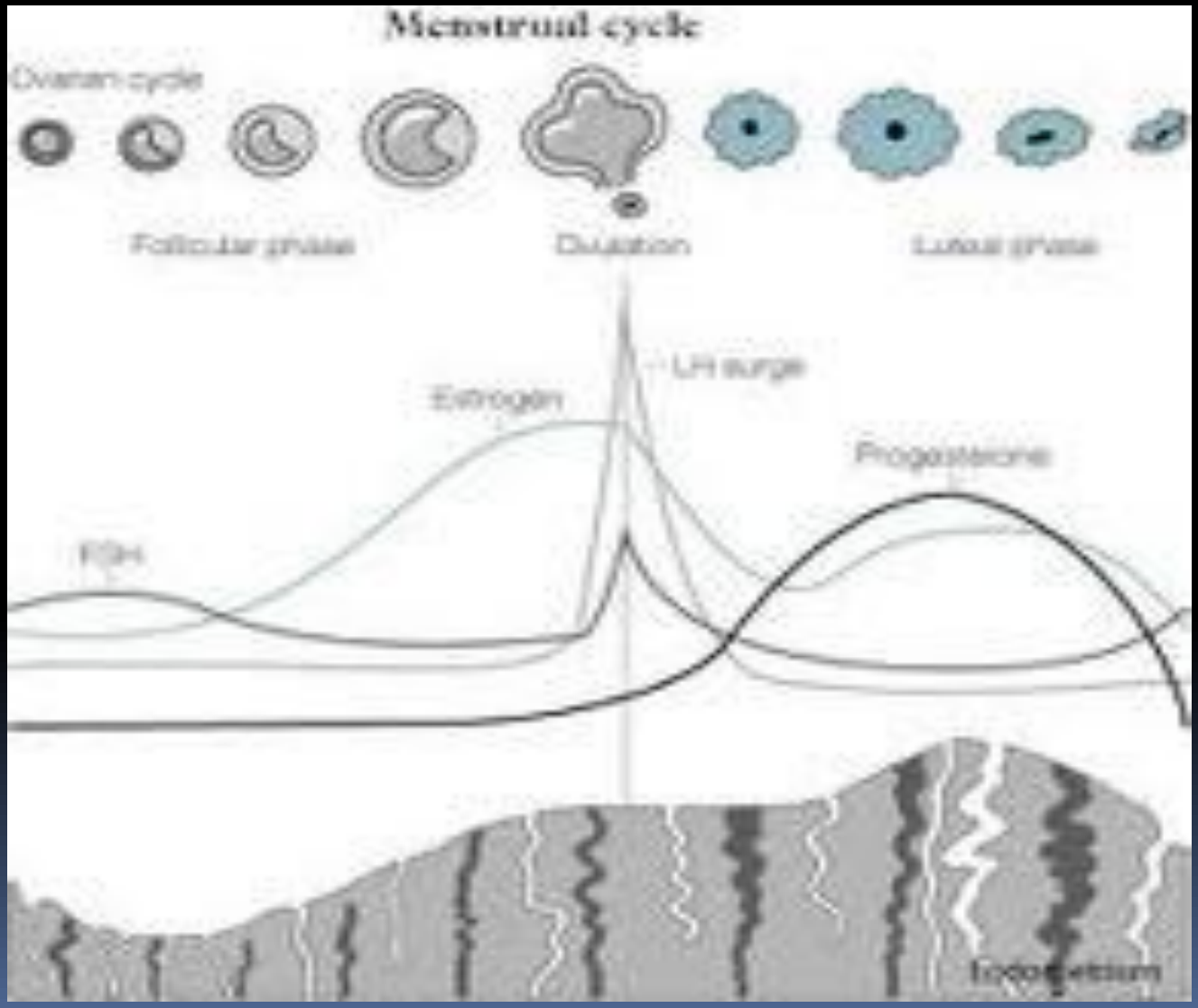


Figure 26-14b


A
B
1
2
3
4


Menstrual cycle
Ovarian cycle
Follicular phase
Ovulation
Luteal phase
LH surge
Estrogen
Progesterone
FSH