



# Urogenital System

Sheet 2

Subject | Physiology

Done by | Raghad Ahmad

Correction | Rawan Almujaibel

Doctor | Ebaa Alzayadneh



## female reproductive system

The main function of the female reproductive system is:

1. to prepare the body to conceive a baby
2. to take care of the baby while it is developing (during pregnancy).

### The physiologic anatomy of the female reproductive system:

The **gonads (the ovaries)** are the primary organ of the female reproductive system where at least one ovum will be produced every month. The ovum will be expelled into the abdomen and taken by the **fallopian tube** and transported along it. If it was fertilized, the zygote will be implanted in the **uterus**. Then it will grow as a fetus until it is ready to be delivered through the **cervix** and the **exterior vaginal organ**.

After puberty, in the normal years of the reproductive function, there will be monthly rhythmic changes of secretion of female hormones and they correspond to the physical changes occurring in the ovaries and the other reproductive organs. These rhythmic changes are recognized by the monthly menstrual cycle (monthly female sexual cycle).

There is another cycle which is the ovarian cycle which refers to the changes that take place according to different stages of the development of the ovum in the ovary. The duration of the cycle is 28 days on average and the range is (20-45) days.

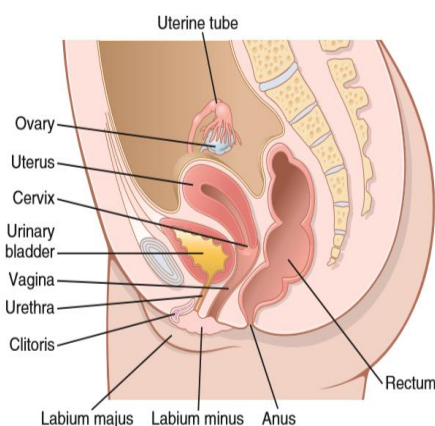


Figure 82-1. The female reproductive organs.

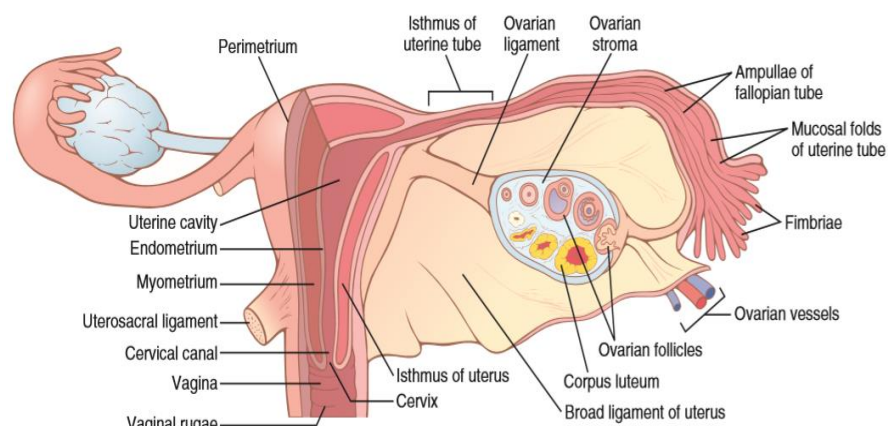


Figure 82-2. Internal structures of the uterus, ovary, and a uterine tube.

## The results of the female sexual cycle:

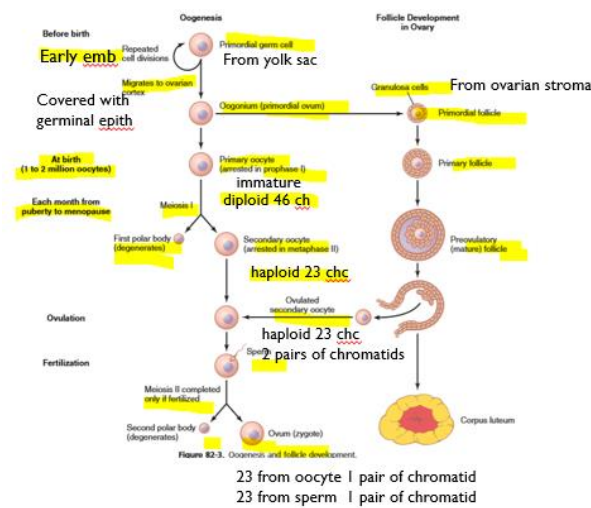
1. A single ovum is released from the ovaries each month.
2. Uterine endometrium is prepared for implantation of the fertilized ovum.

**Oogenesis** is a series of steps that involve the development and differentiation of immature egg (oocyte) into a mature egg (ovum). It is one of the female reproductive system main functions to produce an ovum every month to be fertilized by the sperm.

1. In the early embryonic life, primordial cells that originate from the yolk sac will migrate to the outer surface of the ovary and start proliferating very repetitively.
2. Then they reach the cortex substance of the ovaries. At this stage, we call them oogonia or primordial ovum. They will collect or attract a layer of ovary stromal cells which are called **granulosa cells**, they look like epithelioid cells. This structure (the oogonia and the granulosa layer) is called **primordial follicle**.
3. The oocyte is called **primary oocyte** and it will be arrested at the prophase of meiosis 1 (they have 46 chromosomes /diploid). This takes place at the fifth month of gestation.
4. At birth, the baby will have about 1 -2 million oocytes (fixed number, they will not increase or proliferate).
5. After puberty, each month, a primary oocyte will complete meiosis 1 to produce **one secondary oocyte** (haploid, 23 chromosomes) and a smaller cell called the first polar body which will degenerate eventually. The secondary oocyte will be arrested at the metaphase of meiosis 2 until fertilization takes place.

On the other side of the photo, we see the primordial follicle which becomes a primary follicle, then the stages of ovulation that we will talk about later. The primary follicle will mature in several events including building and secreting fluid inside the follicle. We will have different layers of cells called theca cells. **[It will be explained later]**. Then the ovulation will take place when the ovum is expelled into the abdomen to be taken by the fimbria of the fallopian tube. The expelled egg is a secondary oocyte that is arrested in the metaphase of meiosis 2. Only after being fertilized by the sperm, it will finish up meiosis 2.

producing an ovum( which is forming a zygote with the sperm) and a second polar body which will degenerate.



## The regulation of the ovarian function:

There are 3 hormonal systems that are regulating the ovarian function, similar to what we have seen in the male reproductive system. The first hormone is the hypothalamic releasing hormone (**Gonadotropin releasing hormone**). Once it is stimulated and released, it will activate the anterior pituitary sex hormone secretion which are called Gonadotropins: **follicle stimulating hormone (FSH) and the leutenizing hormone (LH)**. The third hormones are the ovarian hormones (**Estrogens and**

**progesterone**) which are stimulated by FSH and LH. They are parallel to Testosterone in the male reproductive system.

Without secretion of GRH, there will be no FSH or LH, that what happens during childhood, so the ovaries are inactive.

After puberty, GRH is secreted, FSH and LH will be secreted from the anterior pituitary, then the ovaries start functioning.

The ovarian changes during the sexual cycle depend completely on FSH & LH rhythmic secretion by the anterior pituitary gland.

Both FSH and LH stimulate their ovarian target cells by combining with highly specific receptors leading to a modulation (increase) in the cells rates of secretion, growth & proliferation.

The ovulatory cycle is divided into 2 phases: **the follicular phase (preovulatory)** and **the luteal phase (postovulatory)**. It is divided by the **ovulation** event.

**The follicular phase:** 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 (at the age of 11-13 years), AP secretes FSH and LH (after being stimulated by GRH) resulting in ovum to increase in size & growth of additional layers of granulosa cells of some follicles known as primary follicles. Then the interstitium of the ovary will build another group of cells that are called theca cells outside the granulosa cells. It is divided into 2 layers: theca interna and theca externa.

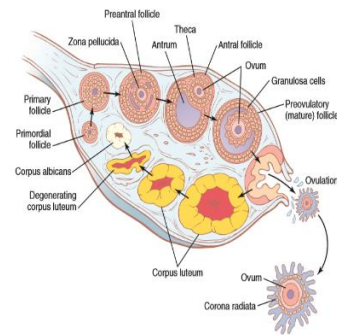
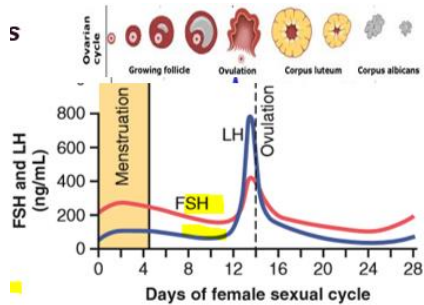
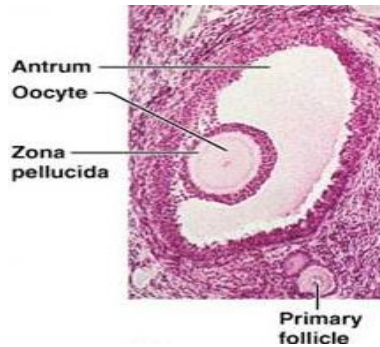


Figure 82-5. Stages of follicular growth in the ovary, also showing formation of the corpus luteum.



The cyclic changes in the rates of secretion of the anterior pituitary hormones FSH and LH will affect the growth and development of the ovarian follicles. For example, during the first few days (the first 2 weeks) of the monthly female sexual cycle there is an increase in the 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.

GRH stimulates the release of FSH and LH with slightly more FSH. FSH has a positive effect on granulosa cells to secrete Estrogens as they have the aromatase enzyme needed for this. LH will stimulate theca cells to produce androgens which can be further converted to estrogens in the granulosa cells after they diffuse to them.

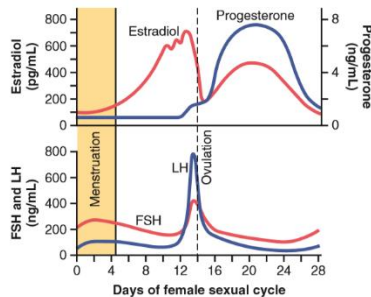
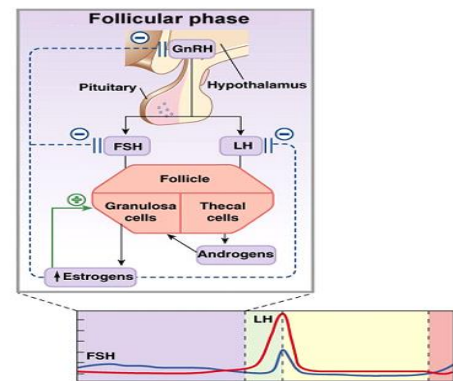
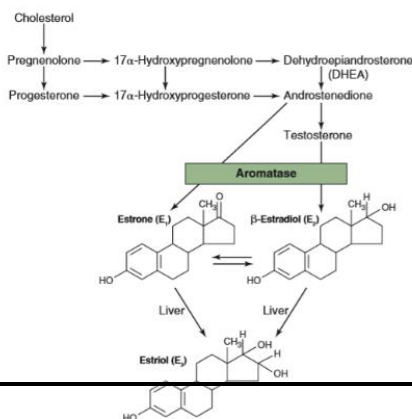


Figure 82-4. Approximate plasma concentrations of the gonadotropins and ovarian hormones during the normal female sexual cycle. FSH, follicle-stimulating hormone; LH, luteinizing hormone.

At menstruation (day zero), the levels of estrogens and progesterone are very low (almost zero). At this stage, we see increasing levels of FSH and LH (with slightly more FSH). This is mainly due to the absence of the negative feedback of estrogens and progesterone on the AP. With the increasing levels of FSH and LH, granulosa cells will start secreting more estrogens leading to a peak of estrogens at the first 2 weeks. This is accompanied with a reduction in the levels of FSH and LH (negative feedback inhibition). Just before the ovulation, there will be a surge in the LH (mainly) and FSH, that is accompanied with increase in the progesterone secretion and decrease in the estrogens secretion. This is contradictory with the negative feedback effect principle. It is a characteristic for the ovarian cycle. (The effect of estrogens on the AP is different according to the stage of the cycle).



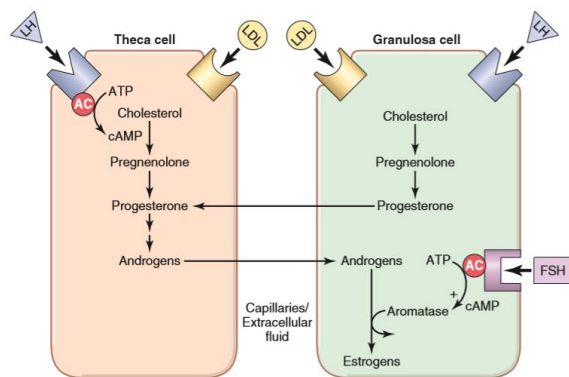
Estrogen hormones in a nonpregnant woman are mainly synthesized by the ovaries (granulosa cells specifically) by aromatase which can give the different forms of Estrogen. They differ from each other in the



potency or in the availability. Beta estradiol is the primary and major estrogen in nonpregnant females. Estrone is found in less amount and its potency is 12 times less than that of beta estradiol. Estriol is the least potent one with a potency that is 80 times less than that of beta estradiol. All these forms are produced from cholesterol and androgens (Testosterone, Progesterone, Dehydroepiandrosterone, Androstenedione). In pregnant females, estrogens can be produced by the placenta.

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 forming the **antral follicle**. The antrum is surrounded by granulosa cells that secrete the fluid. The early growth of the primary follicle up to the antral stage is under FSH stimulation only. The antral follicles begin to grow and increase in size. The ovum enlarges & remains embedded at one pole of the granulosa cells of the follicle forming the preovulatory mature follicle (the antrum is large and the ovum is at one pole). It is called also the **vesicular follicle (Graffian)**. This is caused by:

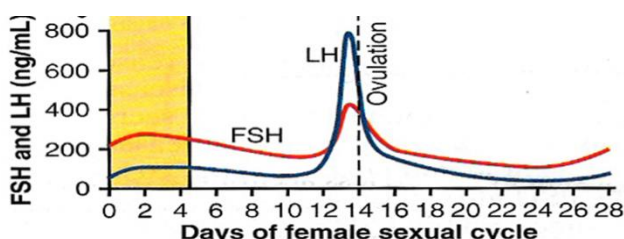
1. Estrogen secreted into the follicle causes the granulosa cells to increase FSH receptors which causes positive feedback effect to increase estrogens secretion.
2. Both estrogen & FSH combine (synergistic effect) to promote LH receptors on the original granulosa cells in addition to FSH stimulation, 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 of androgens.



This figure shows the interaction between theca and granulosa cells and the effects of LH and FSH. Granulosa cells have FSH receptors and LH receptors which induce the cell by producing cAMP mainly, to increase the synthesis of estrogen. In theca cells, LH will bind to its membrane receptor to induce the 2<sup>nd</sup> messenger cAMP to produce androgens which diffuse from theca to granulosa cells to be converted to estrogens by aromatase.

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 rest of the oogonia will undergo **atresia** (involute).

## Ovulation



It happens after the maturation of the follicle by expelling the ovum from the graafian follicle. LH is necessary for final follicular growth and ovulation. Absence of LH will lead to failure of ovulation even if the growth of the

follicle was going very well. 2 days before ovulation, the rate of LH secretion will increase significantly to 6-16 fold & peaks about 16 hrs before ovulation. FSH also increases 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 will decrease about 1 day before ovulation while progesterone secretion begins to increase. LH surge will cause an increase in the Progesterone and a decrease in the estrogen.

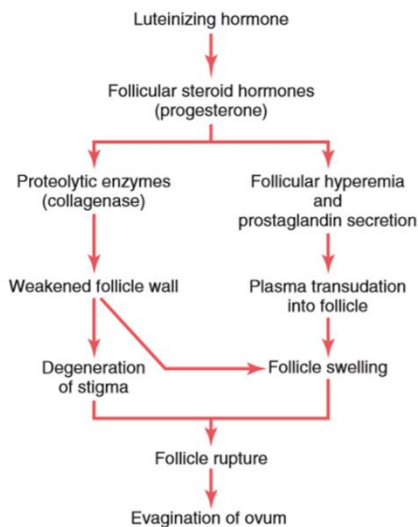
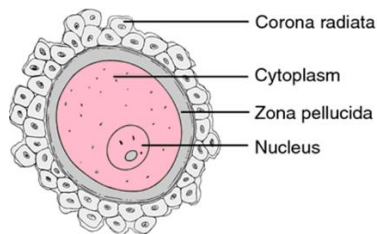


Figure 82-6. The postulated mechanism of ovulation.



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 enzyme and weakens the wall resulting in swelling of the follicle & degeneration of the stigma (a small protrusion in the follicular wall).

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

The prostaglandins will give signals to the follicle to undergo swelling which stimulates the rupture of the follicle, so the ovum is expelled.

Ovulation occurs 14 days after the onset of menstruation in 28 days cycle. During ovulation, stigma protrudes & fluids go outside from the follicle (from the antrum) & the stigma ruptures allowing more viscous fluid to go outward carrying with it the ovum surrounded by mass of granulosa cells called corona radiata. Inside, there is a layer of zona pellucida surrounding the ovum.

After the ovum is expelled, the remaining granulosa cells with the theca cells are called corpus luteum. After 7-8 days of ovulation, it will be 1.5 cm in diameter.

One of the methods to identify the day of ovulation is to measure the body temperature during the ovarian cycle; because the secretion of progesterone after ovulation is accompanied with increase of body temperature about .5 F. It can be used by women for conceiving purposes.

## “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 a 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.

Both LH and FSH have a positive effect on the corpus luteum to secrete progesterone and estrogens as well as an inhibitory factor called inhibin. These 3 hormones have a negative feedback to the hypothalamus and AP. The inhibition of secreting GRH, FSH and LH by estrogens, progesterone and inhibin is a very important characteristic of the luteal phase. So after ovulation, the levels of FSH & LH decrease while the levels of estrogen & progesterone increase.

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 (human chorionic gonadotropin hormone) from the placenta acts on the corpus luteum similar to the action of LH to prolong its life for 2 to 4 months of pregnancy & promote the secretion of progesterone and estrogens.

If there was no fertilization and no pregnancy, the corpus luteum will involute and the next ovarian cycle will begin:

- 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. This causes reduction in FSH & LH & loss of these hormones leading to 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 increased secretion of FSH & LH again. This is characteristic for the beginning of a new ovarian cycle.

**Good Luck**

الله يوفقكم جميعاً :