The ovarian cycle

The ovary

- An ovary contains many follicles, and each one contains an immature egg, called an oocyte.
- A female is born with as many as two million follicles, but the number is reduced to 300.000-400.000 by the time of puberty.

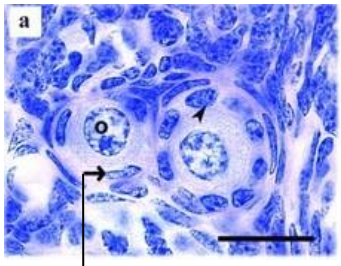
- During the lifetime of a female, only 400 follicles mature.

- As the follicle matures during the **ovarian cycle**, it changes from a primary to a secondary to a vesicular (graafian) follicle, **Figure (1)**.

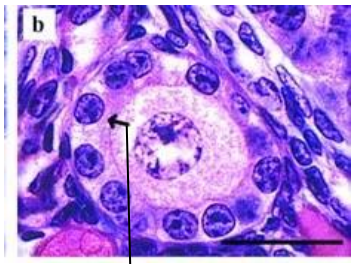
- ***Primary follicle***: epithelial cells of a primary follicle surround a primary oocyte.
A primary oocyte undergoes **meiosis I**, and the resulting cells are haploid with **23 chromosomes** one of these cells is called a polar body. Primary follicle produces estrogen.

- ***Secondary follicle***: pools of follicular fluid bathe the secondary oocyte in a secondary follicle.
A secondary oocyte undergoes **meiosis II**, but only if it is fertilized by a sperm. Secondary follicle produces estrogen and some progesterone, **Figure (2)**.
If the secondary oocyte remains unfertilized, it never completes meiosis and will die after being released from the ovary.

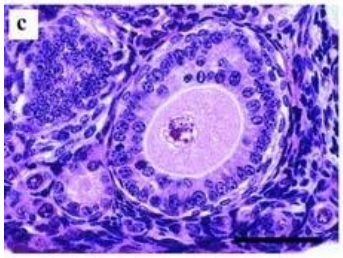
- ***Vesicular (graafian) follicle***: the fluid-filled cavity increases to the point that the follicle wall balloons out on the surface of the ovary. Eventually, the vesicular follicle ruptures, and the secondary oocyte (often called egg) is released. The follicle then becomes the corpus luteum, which produces progesterone and some estrogen.



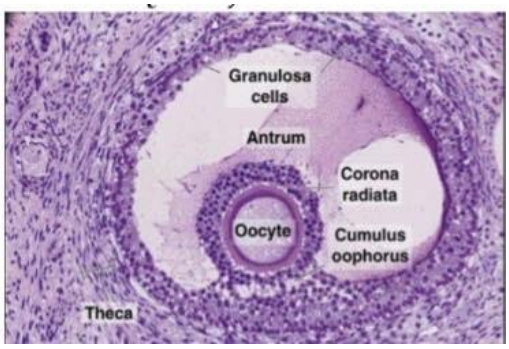
(a)- Primordial follicles were defined as an oocyte (o) surrounded by a layer of squamous (flattened) granulosa cells (arrow).



(b)- Primary follicles possessed an oocyte surrounded by a single layer of cuboidal granulosa cells (arrow).



(c)- Secondary follicles were surrounded by more than one layer of cuboidal granulosa cells, with no visible antrum.



(d)- Graafian follicles were the largest of the follicular types, possessed a clearly antral space and a cumulus granulosa cell layer

Figure- 1 Maturation of a follicle

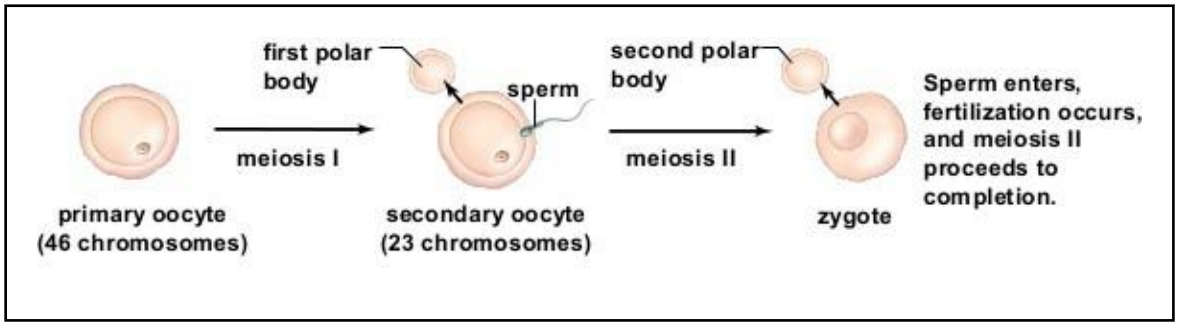


Figure -2: Oocyte development

At puberty, the female begins to undergo regular monthly cycles. These sexual cycles are controlled by the hypothalamus. Gonadotropin-releasing hormone (GnRH), produced by the hypothalamus, acts on cells of the anterior lobe (adenohypophysis) of the pituitary gland, which in turn secrete gonadotropins, which include :

- Follicle-stimulating hormone (FSH)

- Luteinizing hormone (LH)

These hormones stimulate and control cyclic changes in the ovary, fig. (3).

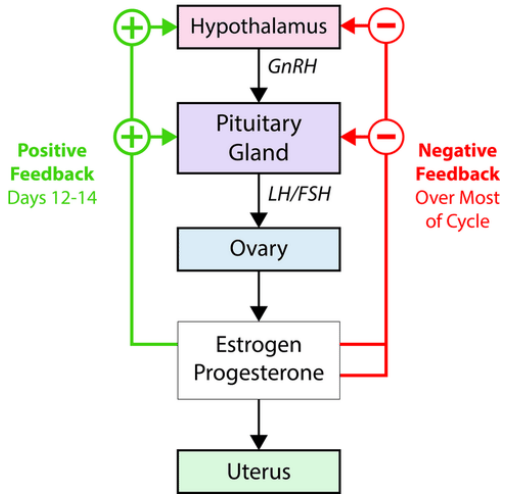


Figure- 3: Hormonal control of ovarian cycle

Phases of the ovarian cycle

- Follicular phase

- FSH promotes the development of follicles that primarily secrete estrogen.

- Due to a positive feedback effect, an estrogen spike causes a sudden secretion of a large amount of GnRH from the hypothalamus. This leads to a surge of LH production by the anterior pituitary and to ovulation at about the 14^{th} day of a 28-day cycle.

- Luteal phase

- During the luteal phase of the ovarian cycle, LH promotes the development of the corpus luteum, which secretes primarily progesterone.
- When pregnancy does not occur, the corpus luteum regresses, and a new cycle begins with menstruation.

Beginning of ovarian cycle

- 15-20 primary follicles are stimulated to grow under the influence of FSH.

- Under normal conditions, only one of these follicles reaches full maturity, and only one oocyte is discharged at ovulation; the others degenerate and become atretic.

- FSH stimulates maturation of follicular (granulosa) cells surrounding the oocyte.

- Proliferation of follicular cells is mediated by growth differentiation factor 9 (GDF-9), a member of the transforming growth factor-β (TGF-β) family.

- Theca interna and granulosa cells produce estrogens

[Theca interna cells produce androstenedione and testosterone, and granulosa cells convert these hormones to estrone and 17 β- estradiol].

Effects of estrogen production

- The uterine endometrium enters the follicular or proliferative phase.

- Thinning of the cervical mucus occurs to allow passage of sperm.

- Stimulate the anterior lobe of the pituitary gland to secrete LH.

At mid ovarian cycle

There is an LH surge that:

- Elevates concentrations of maturation promoting factor, causing oocyte to complete meiosis I and initiate meiosis II.

- Stimulates production of progesterone by follicular stromal cells (luteinization) **(Luteinization: is the process of transformation of follicular granulosa cells into lutein cells).**

- Causes follicular rupture and ovulation.

After ovulation and during the luteal phase of the ovarian cycle

- LH promotes the development of the corpus luteum

- Progesterone in particular causes the endometrial lining to become secretory

When progesterone production declines to a low level; menses occur.

[Menses due to the breakdown of the endometrium], fig. (4).

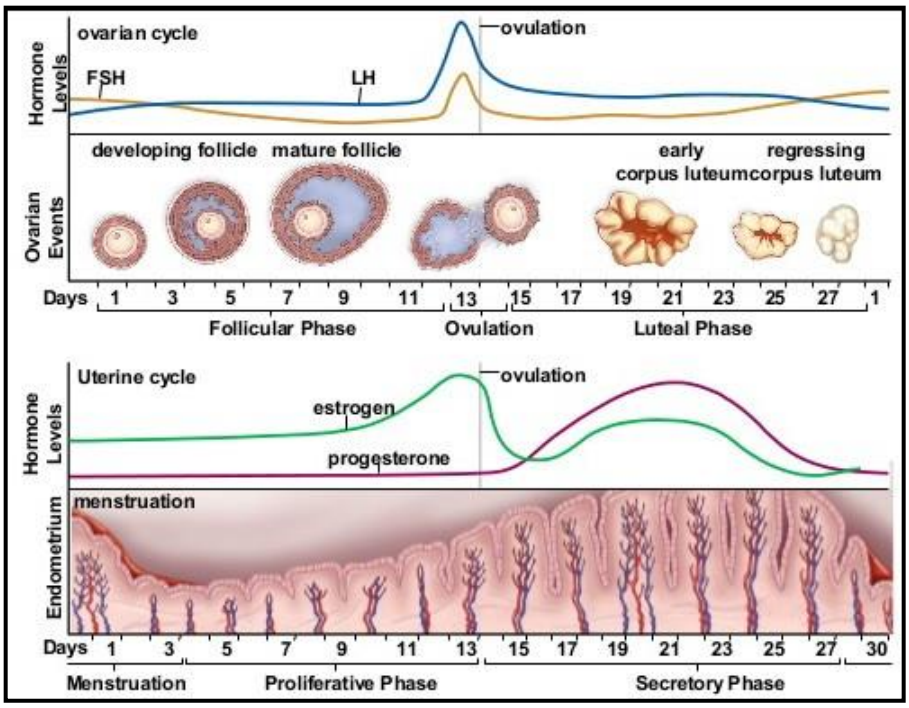


Figure-4: Female hormone levels in the ovarian and uterine phases

Embryology: Study of development of the embryo**.**

- Embryo: implantation to 8 weeks

- Fetus: after 8 weeks

- Gestation: carrying of an embryo/fetus inside a female

Embryonic development

In animal, embryonic development includes five essential stages:

1) Gametogenesis: gamete production

2) Fertilization: gamete ⟶ zygote

3) Cleavage: zygote ⟶ blastula

4) Gastrulation: blastula ⟶ gastrula

5) Organogenesis: organ formation

i.e. Neurulation: gastrula ⟶ Neurula

First week of human embryonic development: Ovulation to implantation

Ovulation

- In the days immediately preceding ovulation, under the influence of FSH and LH, the follicle grows rapidly to a diameter of **25 mm** to become a mature vesicular (graafian) follicle.

- With final development of the vesicular follicle, estrogens, produced by follicular and thecal cells, stimulate increased production of LH that causes the follicle to enter the mature vesicular (graafian) stage.

- Primary oocyte complete meiosis I and enter meiosis II, but the oocyte is arrested in metaphase approximately 3 hours before ovulation.

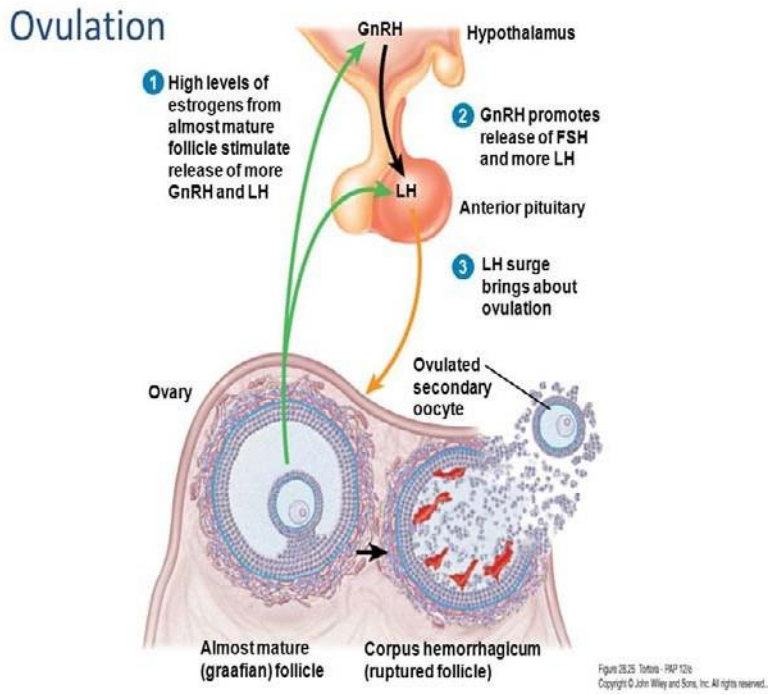
- In the meantime, the surface of the ovary begins to bulge locally, and stigma appears

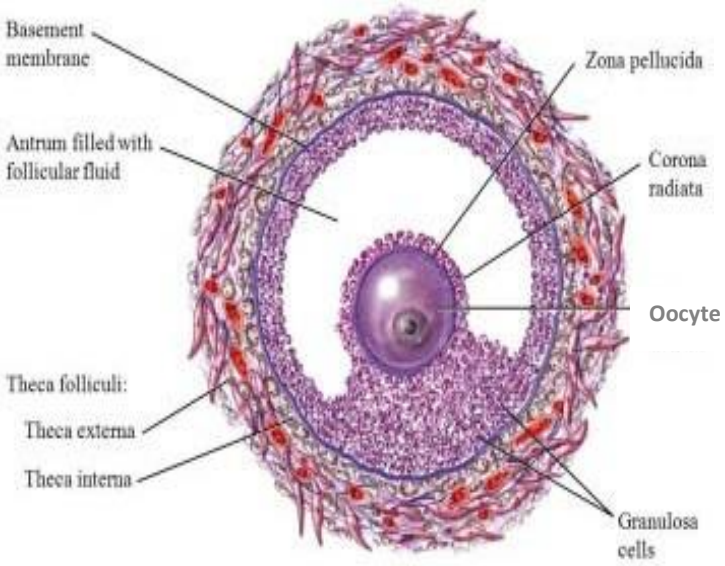
- High concentration of LH increases collagenase activity, resulting in digestion of collagen fibers surrounding the follicle.

- Prostaglandin levels also increase in response to the LH surge and cause local muscular contractions in the ovarian wall.

- Those contractions extrude the oocyte together with its surrounding granulosa cells from the region of the cumulus oophorus and floats out of the ovary.

- Then some of the cumulus oophorus cells rearrange themselves around the zona pellucid to form the corona radiate.





Mature (graafian) follicle

Corpus luteum

After ovulation, granulosa cells remaining in the wall of the ruptured follicle, together with cells from the theca interna, are vascularized by surrounding vessels. Under the influence of LH, these cells change into lutein cells, which form the corpus luteum and secrete **estrogen** and **progesterone.** Progesterone, together with some estrogen, causes the uterine mucosa to enter the **progestational or secretory stage** in preparation for implantation.

If the oocyte is fertilized, degeneration of the corpus luteum is prevented by **human chorionic gonadotropin** (is a hormone secreted by the syncytiotrophoblast of the developing embryo).

- Yellowish luteal cells continue to secret progesterone until the end of the fourth month.

- Thereafter, luteal cells regress slowly.

- Secretion of progesterone by the trophoblastic component of the placenta becomes adequate for maintenance of pregnancy.

- Removal of the corpus luteum before the fourth month leads to abortion.

Corpus albicans

If fertilization does not occur:

- The corpus luteum reachs maximum development approximately **9 days** after ovulation.

- Then, the corpus luteum shrinks because of degeneration of lutein cells **(luteolysis**) and forms the corpus albicans.

- Progesterone production decreases therefore menstruation occurs.

Oocyte transport

- Before ovulation, fimbriae of the uterine tube (fallopian tube) sweep over the surface of the ovary and the tube begins to contract rhythmically.

- The oocyte surrounded by some granulosa cell is passed into the tube by these sweeping movements of the fimbriae and by movement of cilia on the epithelial lining.

- In the tube, granulosa cells remove from the zona pellucid and lose contact with the oocyte.

- In the uterine tube, oocyte pushes by muscular contractions and by cilia in the tubal mucosa with endocrine regulation.

- The fertilized oocyte reaches the uterine lumen in approximately 3-4 days, fig. (5).

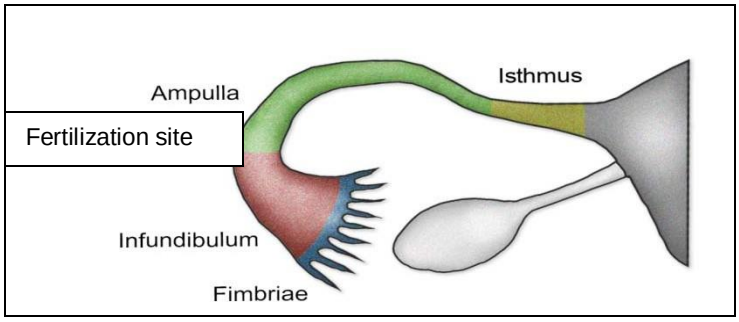


Figure-5: The fallopian tube