Lectures 36,37&38

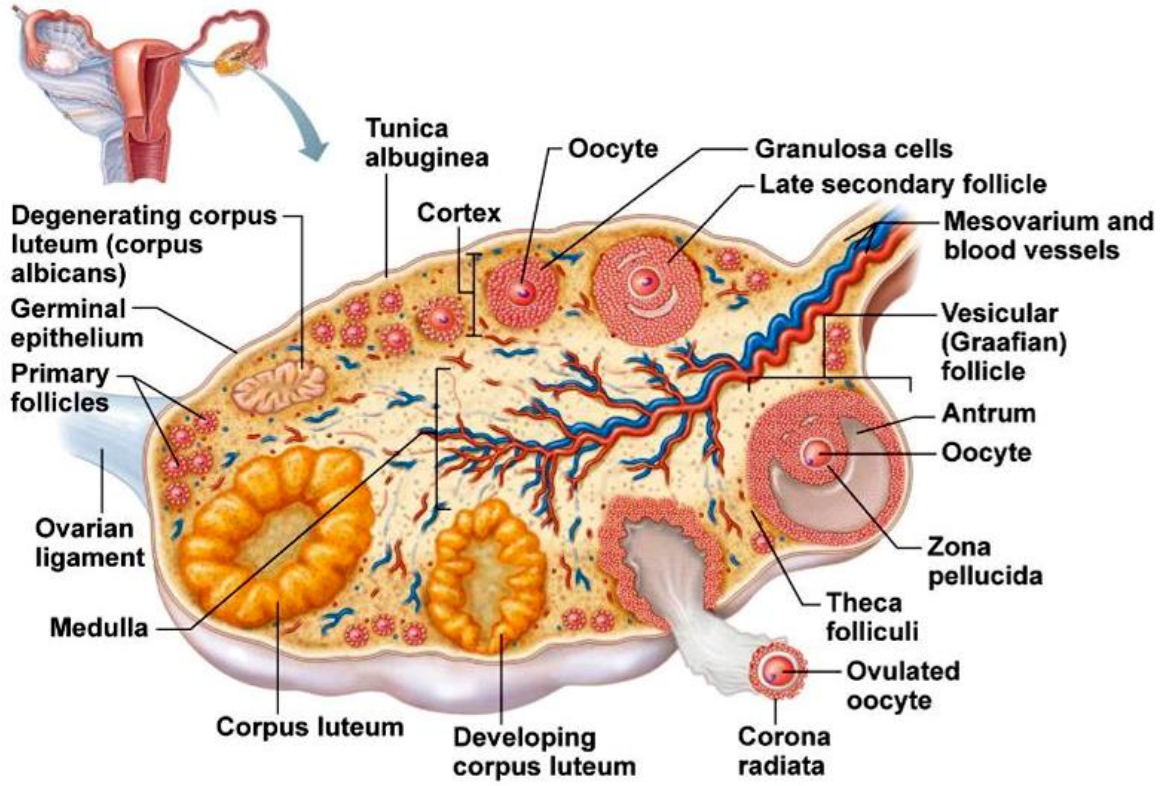
OOGENESIS, OVARIAN CYCLE AND OVULATION

Learning objectives
- Describe the components of the oogenesis.
- Describe maturation of oocytes at puberty.
- Describe the hormonal control of the oogenesis.
-Know ovarian cycle and ovulation (corpus luteum and corpus albicans).
- Know the oocyte transport.

OOGENESIS

DEFINITION: It is the process of transformation of the oogonia into mature ovum.

SITE AND TIME: The steps of oogenesis occur in the cortex of the ovary and accompanied by development of ovarian follicles. It starts as early as the embryonic life.



Diagrammatic view of an ovary sectioned to reveal the follicles in its interior.

STAGES: **-Prenatal maturation. -postnatal maturation**

PRENATAL MATURATION:

1. The embryonic (primordial) germ cells are derived from the endoderm of the wall of the yolk sac. During their migration to be attached to the developing ovary (urogenital ridge), they differentiate into **oogonia.**

2. At the 3rd month of embryonic development, the ovary contains nests of oogonia that proliferate (by mitosis)to produce **primary oocytes**, of which about 1-2 millions are present at birth. No primary oocytes form after birth (in contrast to the continuous production of primary spermatocytes in the male after puberty).

N.B.

♦*Ovarian stromal cells surround the developing primary oocyte to form a single layer of flattened follicular cells. The primary oocyte and its flattened follicular cells constitute* ***the primordial follicle***

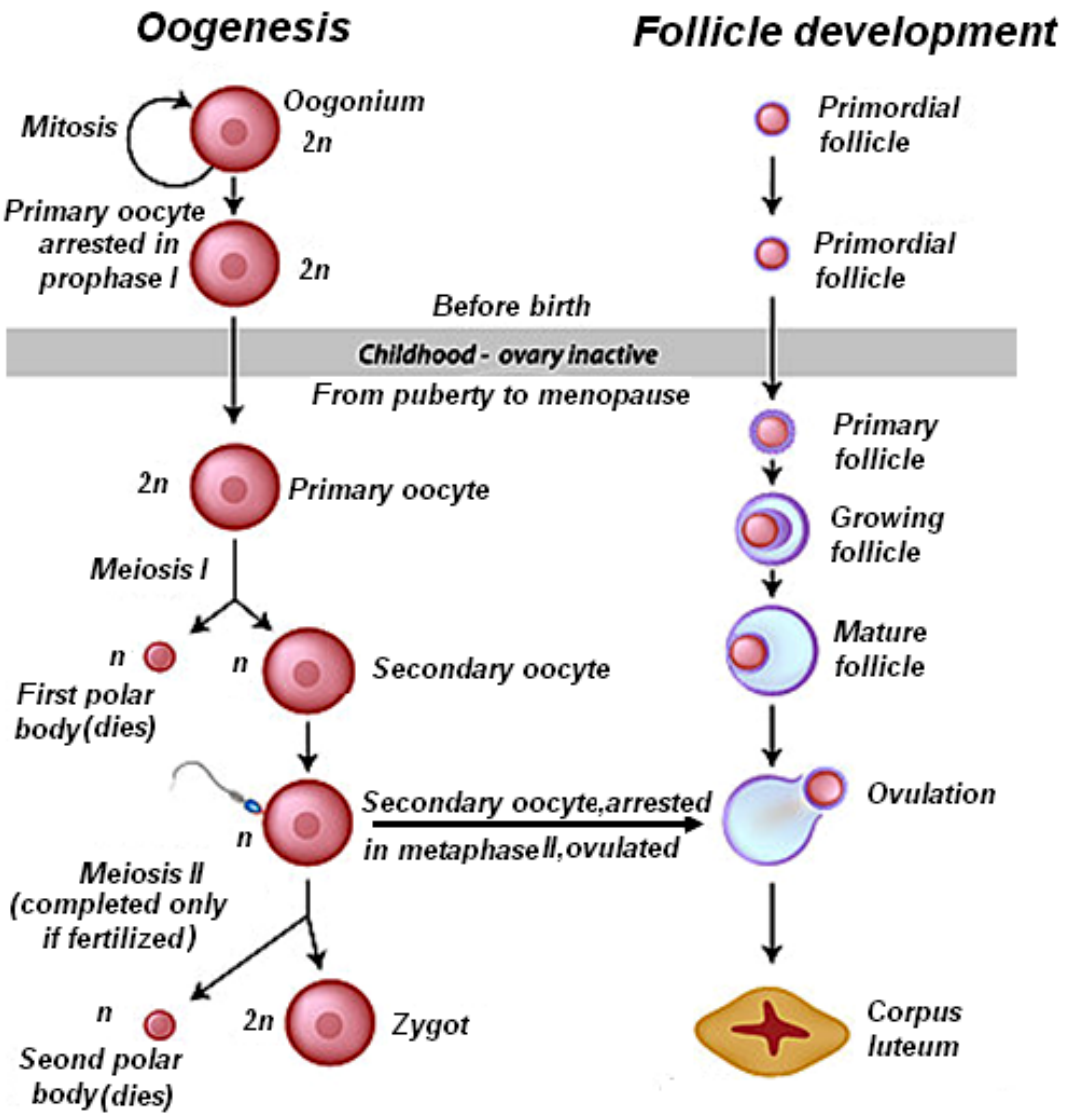
♦*The follicular cell layer becomes cuboidal as the primary oocyte enlarges at puberty and* ***a primary follicle*** *(early) is formed.*

♦*A primary follicle with more than one layer of cuboidal follicular cells is called* ***a growing follicle***

3. Primary oocytes begin the first meiotic division before birth but this division is not complete until after puberty.

4. By the time of birth, the female has only the primordial follicles with primary oocytes late in prophase stage of the first meiotic cell division.

5. From birth to puberty, the majority of the primordial follicles degenerate and so by the time of puberty there are about 30000-40000 primordial follicles. ***Only about 200-400 of these ever reach full maturity after puberty*** and are expelled at ovulation during the female's reproductive life. The remaining follicles undergo a degenerative process called ***atresia.***



Diagrammatic view of oogenesis associated with follicular development.

POSTNATAL MATURATION:

1. The primary oocytes stay dormant in the ovaries until puberty.

2. The primary oocyte increases in size and a membrane, **the zona pellucida**, forms around it as the follicle matures.

3. Just before or at the time of ovulation, the primary oocyte completes the first meiotic divisiongiving rise to two daughter cells; ***a) secondary oocyte*** and ***b) first polor body.*** Each cell contains the haploid (half) number of chromosomes = 23.

N.B. unlike its male counterpart, the division of cytoplasm is unequal. The secondary oocyte gets almost all the cytoplasm while the first polar body receives little cytoplasm and is a small, nonfunctional cell that later divides and degenerates.

4. At ovulation, the nucleus of the secondary oocyte begins the second meiotic division progressing only to metaphase, then division arrests.

If fertilization occurs, the second meiotic division is completed, and the **mature oocyte** retains most of the cytoplasm, whereas **the second polar body** is small and degenerates. Each cell contains 23 chromosomes.

5. The secondary oocyte released at ovulation is surrounded by the **zona pellucida** and a follicular cell layer, **the corona radiata**. It is a large cell.

6.Fertilization which is the fusion of one sperm with one secondary oocyte restores the diploid number of chromosomes = 46.

N.B.: The ovum remains viable for a maximum period of 24 hours. If fertilization does not take place it undergoes autolysis without completing the second meiotic division.

THE OVARIAN CYCLE

►DEFINTION:

Ovarian cycle (28 days) is the cyclic changes which take place in the ovary of fertile female every month, under the effect of hormones of the pituitary gland (F.S.H. and L.H.).

Notes:

-At puberty, a pool of growing follicles is established and continuously maintained from the supply of primordial follicles.

-With each ovarian cycle a number of follicles (15-20) begin to grow but usually only one reaches full maturity, the others degenerate and become atretic.

-In next cycle, another group of follicles begin to grow and again only one reaches maturity. Consequently the majority of follicles degenerates without reaching full maturity and become atretic follicles (corpus atreticum).

- Follicle stimulating hormone (F.S.H.) of the anterior pituitary initiates maturation of the primordial follicle to become the mature Graafian follicle.

- During maturation, the oestrogen hormone is secreted by the theca interna cells of the Graafian follicle.

The cycle is described in 3 phases:

1- Follicular phase.

2- Ovulation.

3- Luteal phase.

1- FOLLICULAR PHASE

Follicular development passes through stages:

A) Stage of primordial follicles.

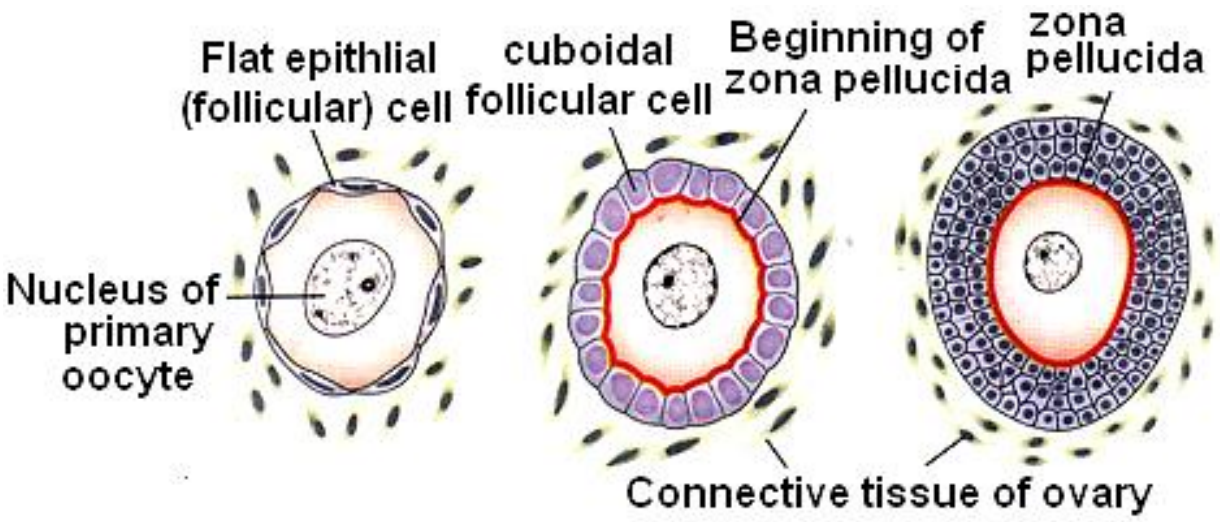
B) Stage of growing follicles.

C) Stage of mature graafian follicle.

A) Stage of primordial follicles.

About from 15-20 ***primordial ovarian follicles*** begin to grow under the effect of FSH.

Each consists of a primary oocyte covered by a single layer of flattened follicular cells.



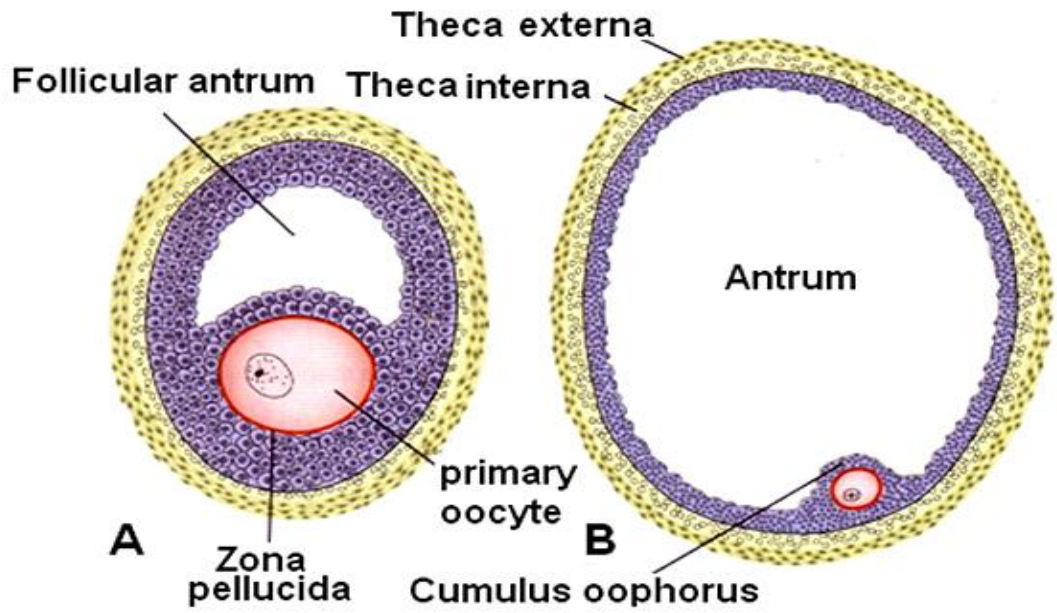
A. Primordial follicle consisting of a primary oocyte surrounded by a layer of flattened epithelial cells. B. Early primary or preantral stage follicle recruited from the pool of primordial follicles. As the follicle grows, follicular cells become cuboidal and begin to secrete the zona pellucida, which is visible in irregular patches on the surface of the oocyte. C. Mature primary (preantral) follicle with follicular cells forming a stratified layer of granulosa cells around the oocyte and the presence of a well-defined zona pellucida.

B) Stage of growing follicles:

♦The surrounding follicular cells change from flat to cuboidal layer ***(early primary follicles)***;and then proliferate to produce a stratified epithelium of **granulosa cells** around the oocyte**.**

♦ The granulosa cells and the oocyte secrete a layer of hyaline material (glycoprotein capsule);called the **zona pellucida**; on the surface of the oocyte separating it from the surrounding granulosa.

♦ Finally, the stroma around the basement membrane of the follicle develops to form a capsule like 'theca' (**theca folliculi**). It is now called ***mature primary follicles*****.**



A. Vesicular (antral) stage follicle. The oocyte, surrounded by the zona pellucida, is off-center; the antrum has developed by fluid accumulation between intercellular spaces. Note the arrangement of cells of the theca interna and the theca externa.
B. Mature vescular (graafian) follicle. The antrum has enlarged considerably, is filled with follicular fluid, and is surrounded by a stratified layer of granulosa cells.
- The oocyte is embedded in a mound of granulosa cells, the cumulus oophorus.

♦As follicles continue to grow; cells of the theca folliculi organize into an inner layer of secretory cells, the **theca interna,** and an outer fibrous capsule, the **theca externa.**

♦As development continues, fluid-filled spaces appear between granulosa cells. Coalescence of these spaces forms **the follicular cavity or antrum.** The antrum is crescent shaped. The fluid in the antrum is called **liquor folliculi** and the follicle is termed a ***secondary (vesicular, antral) follicle.***

C) Stage of mature graafian follicle

♦With time, the follicular and theca cells are still increasing in number causing an increase in the overall volume of the follicle.

♦,The antrum enlarges and the growth of the antrum pushes the ovum to one side of the follicle. Granulosa cells surrounding the oocyte remain intact and form the **cumulus oophorus.** A layer of granulosa cells rearrange themselves around the zona pellucidaand become columnar to form the **corona radiata.** The granulosacells surrounding the cavity are called **membrane granulose.**

♦The mature follicle is about 25 mm or more in diameter where it occupies most of the entire thickness of the ovary.

♦It is surrounded by the theca interna, which is composed of cells having characteristics of steroid secretion, rich in blood vessels, and the theca externa, which gradually mergeswith the ovarian stroma.

♦This follicle is termed as ***tertiary or mature graafian follicle.***

♦ The granulosa cells and cells of theca interna produce estrogen hormone under the control of F.S.H. produced by the pituitary gland.

2-OVULATION

●DEFINITION:

Ovulation is a process in which rupture of the mature graafian follicle occurs with liberation of the ovum into the peritoneal cavity.

●TIME:

Ovulation takes place approximately 14 days before the beginning of the next menstrual cycle i.e. in the middle of the menstrual cycle, around the 14^{th}day of a 28 day cycle.

●PROCESS:

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

♦ Coincident with final development of the vesicular follicle, there is an abrupt increase in lutenizing Hormone (**LH**) that causes the primary oocyte to complete meiosis **I** and the follicle to enter the preovulatory mature (Graafian) vesicular stage.

N.B. *In meiosis* ***I****, two cells are produced: the* ***larger secondary oocyte*** *that contains all of the cytoplasmic material and a smaller, inactive* ***first polar body.*** *Meiosis* ***II*** *follows at once but will be arrested in the metaphase and will so remain* ***until fertilization****.*

♦At the same time, the follicle approaches the surface of the ovary that begins to bulge locally, and at the apex, an avascular spot, the **stigma,** appears.

♦The ovum together with the cells of the corona radiate are detached from the wall of the follicle and float in the follicular fluid.

♦Capillary circulation in the area **of stigma** is stopped and tissue weakening proceeds to rupture of this weak area.

♦On rupturing of the follicle through the wall the ovary, the followings are expelled into the peritoneal cavity:

a- Secondary oocyte (in the metaphase stage of the second meiotic division) surrounded by the zona pellucida

b-The cells of the corona radiata.

c- Viscid liquor folliculi.

♦By the sweeping action of the tubal fimbriae, the oocyte is carried into the uterine tube where it may be fertilized.

The following factors contribute to the rupture of the follicle

1. A sudden growth spurt of the follicle.

2. Rise of the pressure of the fluid inside the follicular antrum

3. Decrease vascularity by the pressure exerted by the growing follicle on the overlying cortex of the ovary.

♦After ovulation, the granulosa cells and theca interna cells form a temporary endocrine gland called **corpus luteum.**

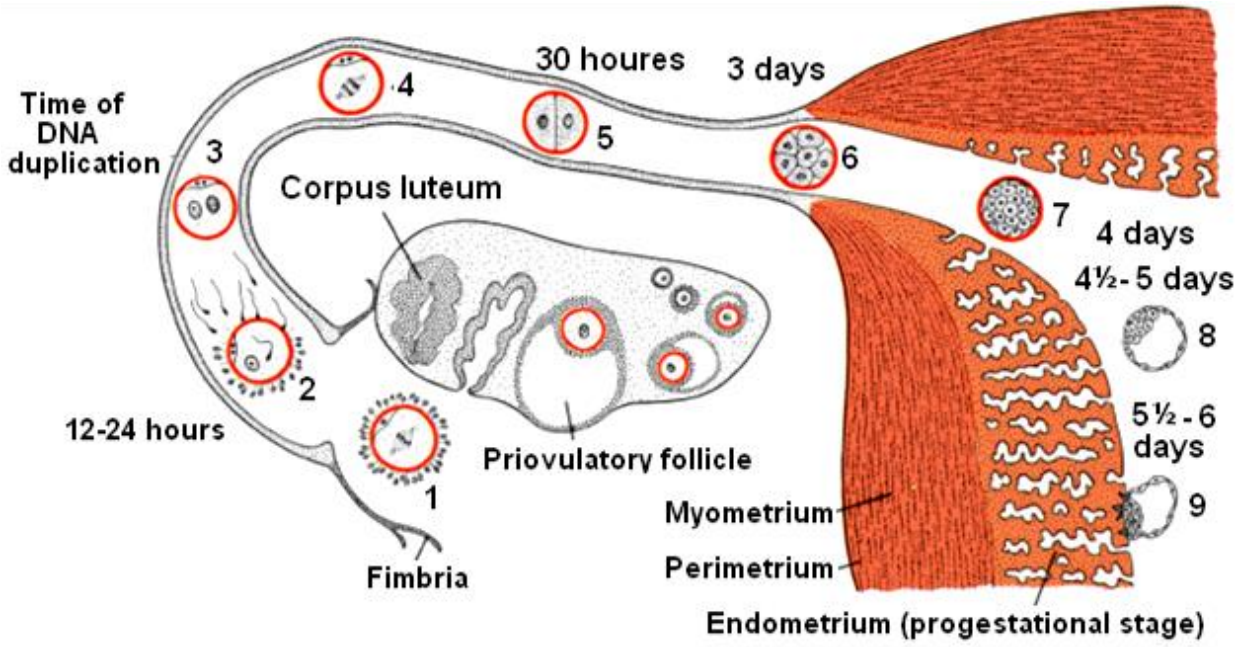
OOCYTE TRANSPORT AND VIABILITY

♣The oocyte surrounded by the zona pellucida and the cells of the corona radiata are carried into the tube by sweeping movements of the fimbriae over the surface of the ovary and by motion of cilia on the epithelial lining of the tube.

♣Once in the uterine tube, surrounding cells of corona radiate lose contact with the oocyte.

♣ The oocyte is propelled by cilia of the tubal mucosa and by the peristaltic muscular contraction of the uterine tube.

♣The ovum remains viable for a maximum period of 24 hours. If fertilization does not take place it undergoes autolysis without completing the second meiotic division. If fertilization takes place, the fertilized oocyte reaches the uterine lumen in approximately 3 to 4 days after ovulation.



- Events during the first week of human development.

1, Oocyte immediately after ovulation.

2, Fertilization, approximately 12 to 24 hours after ovulation.

3,Stage of the male and female pronuclei.

4, Spindle of the first mitotic division.

5, Two cell stage (approximately 30 hours of age).

6, Morula containing 12 to 16 blastomeres (approximately 3 days of age).

7, Advanced morula stage reaching the uterine lumen(approximately 4 days of age).

8, Early blastocyst stage (approximately 4.5 days of age).The zona pellucida has disappeared.

9, Early phase of implantation (blastocyst approximately6 days of age).

- The ovary shows stages of transformation between a primary follicle and a preovulatory follicle as well as a corpus luteum.

-The uterine endometrium is shown in the progestational stage.

3- LUTEAL PHASE (LUTINIZATION)
(FORMATION OF CORPUS LUTEUM)

♦The pituitary gland secretes the lutenizing hormone (L.H.) that stimulates formation of the corpus luteum after rupture of mature graffian follicle. This occurs by change of the membrane granulosa cells and cells of theca interna into **lutein** cells.

♦Following ovulation and release of the follicular fluid, the wall of the follicle (granulosa and theca cells) collapses and becomes folded and vascularized by blood vessels growing in from the periphery.

♦Granulosa cells begin to increase greatly in size, become polyhedral and develop lipids and yellowish pigments and they are now called ***granulosa lutein cells***.

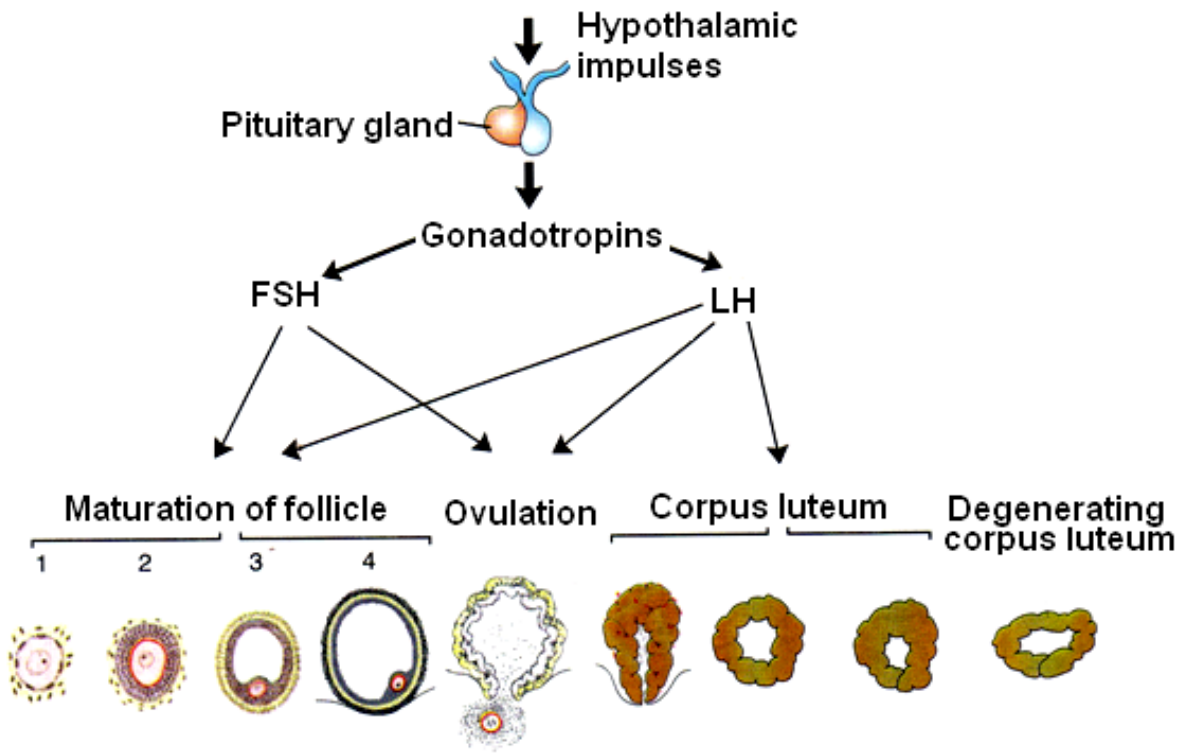


Fig 15: The role of the hypothalamus and pituitary gland in regulating the ovarian cycle. Under the influence of GnRH from the hypothalamus, the pituitary releases the gonadotropins, FSH, and LH. Follicles are stimulated to grow by FSH and to mature by FSH and LH. Ovulation occurs when concentrations of LH surge to high levels. LH also promotes development of the corpus luteum. 7, primordial follicle;2,growing follicle;3,vesicular follicle; 4, mature vesicular(graafian) follicle.

♦The cells of the theca interna are transformed into ***theca lutein cells.*** They are similar in structure to granulosa cells but are smaller. These cells also contribute to the formation of the corpus luteum.

♦Progesterone, together with some estrogenic hormones, secreted by the **corpus luteum** causes the uterine mucosa to enter the **progestational** or **secretory stage** in preparation for implantation of the blastocyst.

TYPES AND FATE OF CORPORA LUTEA

1. The Corpus Luteum of Menstruation

♦If the oocyte is not fertilized, the corpus luteum reaches maximum development approximately 9 days after ovulation (It will persist functioning during the second half of the menstrual cycle secreting progesterone).

♦10-14 days after ovulation, it shrinks and degenerates because of degeneration of lutein cells and form a mass of fibrotic scar tissue***, the corpus albicans.***

♦Simultaneously, progesterone production decreases, precipitating menstrual bleeding.

2. The Corpus Luteum of Pregnancy

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

♦The corpus luteum continues to increase in size up to about the end of the third month and it forms the **corpus luteum of pregnancy (corpus luteum graviditatis).**

♦It actively secretes progesterone till at least the end of the fourth month. Then it gradually declines very slowly and its function is taken over by the placenta, as secretion of progesterone by the trophoblastic component of the placenta becomes adequate for maintenance of pregnancy.

♦Removal of the corpus luteum of pregnancy before the fourth month usually leads to abortion.

♦However the corpus luteum continues to secrete progesterone till the end of pregnancy. After labour, it starts to involute to be changed into corpus albicans.

3. Corpus Albicans

After degeneration of the corpora lutea either of menstruation or of pregnancy, they are transformed into a scar of dense connective tissue. It appears as white bodies in the stroma of the ovary.

HORMONAL CONTROL OF REPRODUCTIVE CYCLE

♣At puberty, the female begins to undergo regular monthly cycles. These **sexual cycles** are controlled by the hypothalamus.

Gonadotrophin-releasing hormone (GnRH) produced by the hypothalamus acts on cells of the anterior pituitary gland, which in turn secrete **gonadotrophins (FSH and LH).**

♣These hormones, **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)**stimulate and control cyclic changes in the ovary.

♣**FSH** stimulates the growth of the ovarian follicles up to ovulation. It also stimulates the secretion of estrogen by the theca interna and granulose cells. Prior to ovulation, an abrupt increase of **luteinizing hormone (LH)** from the anterior pituitary is necessary for ovulation and formation of corpus luteum.

♣Levels of estrogen and progesterone produced by the growing follicles and by the corpus luteum are related to cyclic phases that occur in the endometrium.

♣Estrogen controls the proliferative phase while progesterone controls the secretory phase.

♣ By the feedback mechanism these hormones affect the **gonadotrophin-releasing hormone (GnRH)** produced by the hypothalamus. Estrogens inhibit the release of FSH and progesterone inhibits the release of LH.

♦The administration of progesterone will inhibit the process of ovulation.

♦The **contraceptive pills** are combination of estrogen and progesterone which together inhibit ovulation but permit menstruation.

- Both hormones act at the level of FSH and LH, preventing their release from the pituitary. The pills are taken for 21 days and then stopped to allow menstruation, after which the cycle is repeated.

- While administration of pituitary FSH followed by the chorionic gonadotrophic hormone may stimulate the ovaries to ovulate.