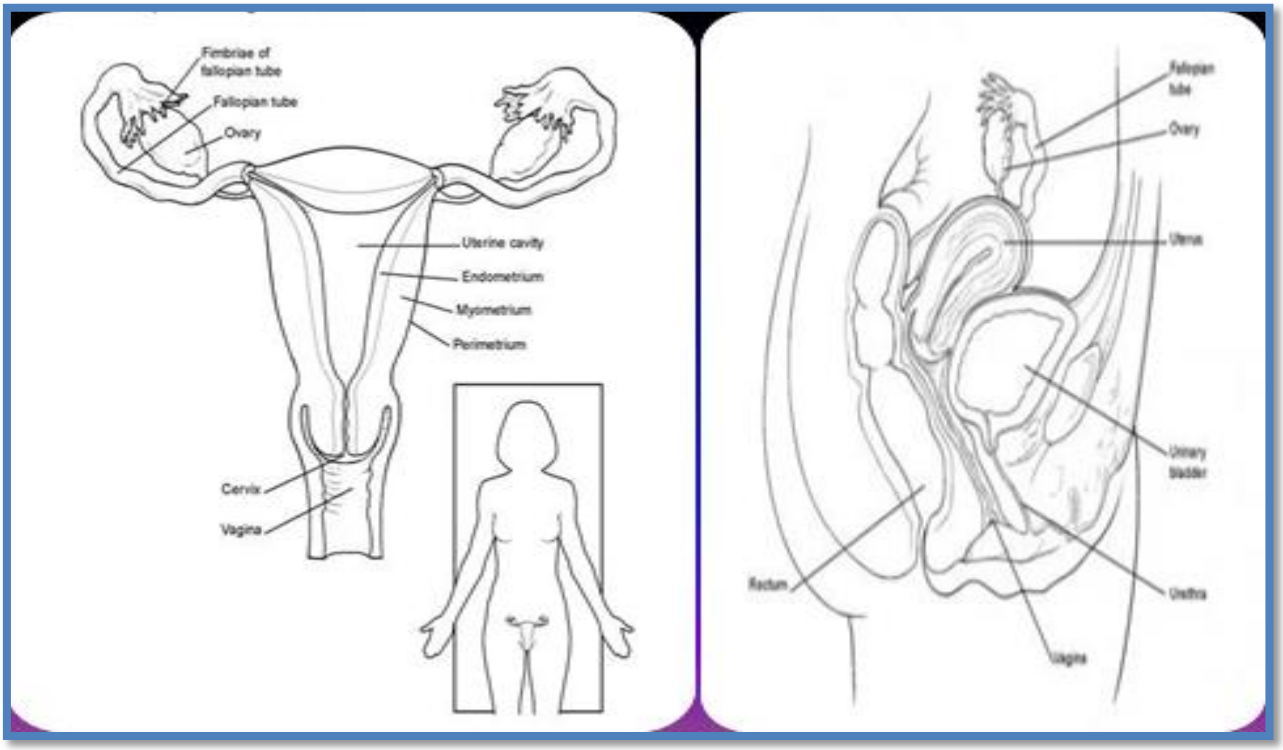
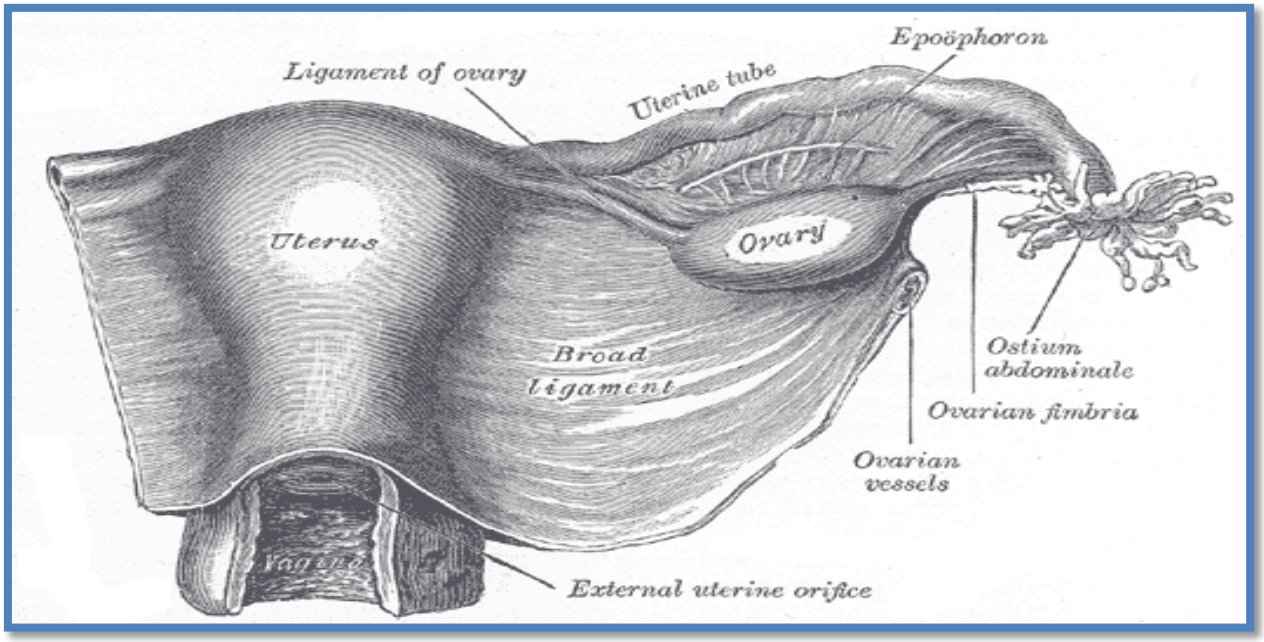
OVARIES

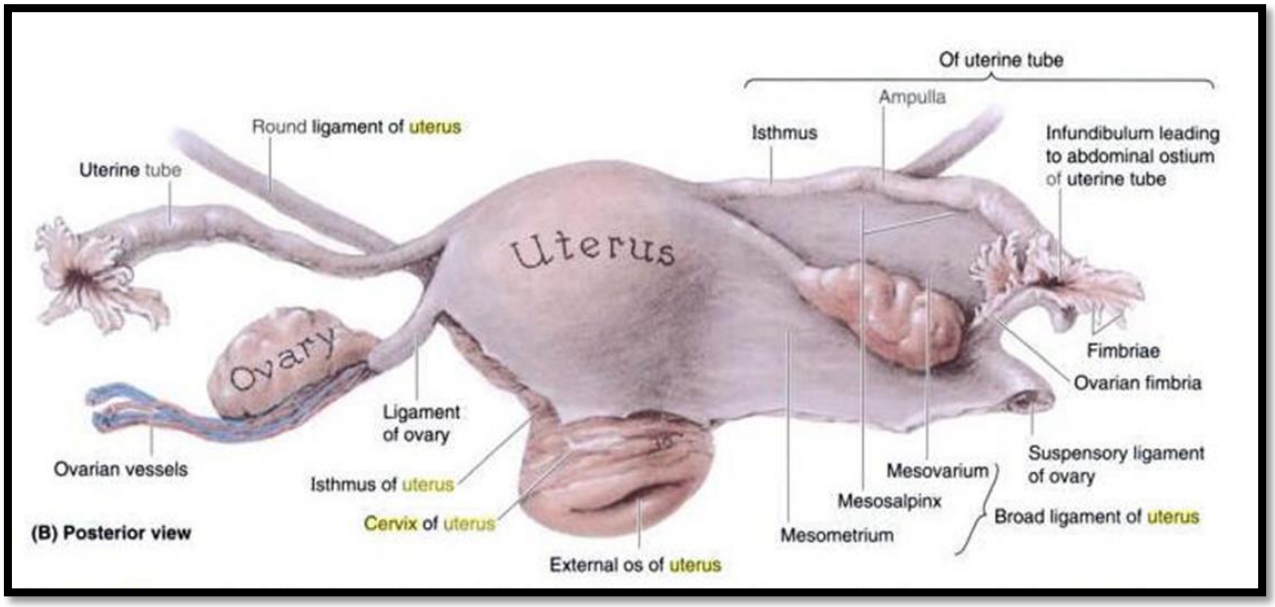
The **ovaries** are the female pelvic reproductive organs that house the **ova** and are also responsible for the production of sex hormones. They are paired organs located on either side of the **uterus** within the broad ligament below the **uterine** (**fallopian**) **tubes**. The **ovary** is within the **ovarian fossa**, a space that is bound by the **external iliac vessels**, **obliterated umbilical artery**, and the **ureter**. The **ovaries** are responsible for housing and releasing **ova**, or **eggs**, necessary for reproduction. At birth, a female has approximately **1** -**2** million **eggs**, but only **300** of these **eggs** will ever become mature and be released for the purpose of fertilization.

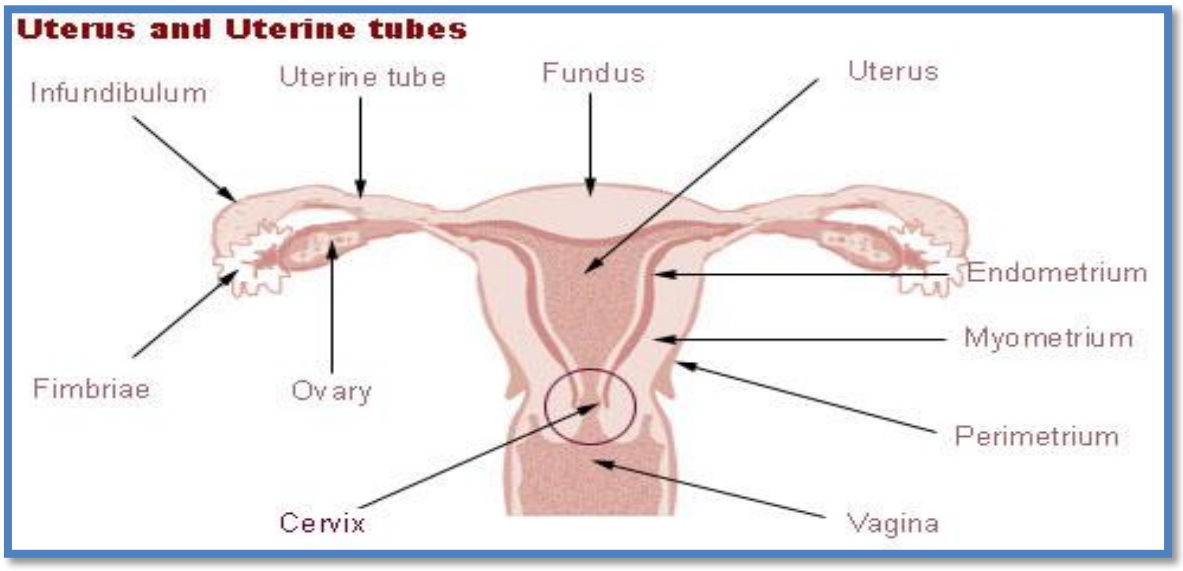


The **ovaries** are small, **oval-shaped**, and grayish in color, with an uneven surface. located alongside the **lateral wall** of the **uterus** in a region called the **ovarian fossa**. The **ovarian fossa** is the region that is bounded by the **external iliac artery** and in front of the **ureter** and the **internal iliac artery**. This area is about 4 cm x 3 cm x 2 cm in

size. The **ovaries** are surrounded by a **capsule**, and have an outer **cortex** and an inner **medulla.** The actual size of an **ovary** depends on a woman's age and hormonal status; the **ovaries**, covered by a modified **peritoneum**, are approximately **3-5** cm in length during childbearing years and become much smaller and then **atrophic** once menopause occurs. A cross-section of the **ovary** reveals many **cystic structures** that vary in size. These **structures** represent **ovarian follicles** at different stages of development and degeneration.







Usually, **ovulation** occurs in one of the two **ovaries** releasing an **egg** each menstrual cycle; however, if there was a case where one **ovary** was absent or dysfunctional then the other **ovary** would continue providing **eggs** to be released without any changes in cycle length or frequency. The side of the **ovary** closest to the **fallopian tube** is connected to it by **infundibulopelvic ligament**, and the other side points downwards attached to the **uterus** via the **ovarian ligament**.

OTHER STRUCTURES AND TISSUES OF THE OVARIES INCLUDE:

- HILUM OF OVARY
- CAPSULE OF OVARY

THE OVARY ALSO CONTAINS BLOOD VESSELS AND LYMPHATICS.

1. Hilum of ovary

- **Ligaments**

The **ovaries** lie within the pelvic cavity, on either side of the **uterus**, to which they are attached via a **fibrous cord** called the **ovarian ligament**. The ovaries are uncovered in the peritoneal cavity but are tethered to the body wall via the **suspensory ligament** of the **ovary**

which is a posterior extension of the **broad ligament** of the **uterus**. The part of the **broad ligament** of the **uterus** that covers the **ovary** is known as the **mesovarium**.

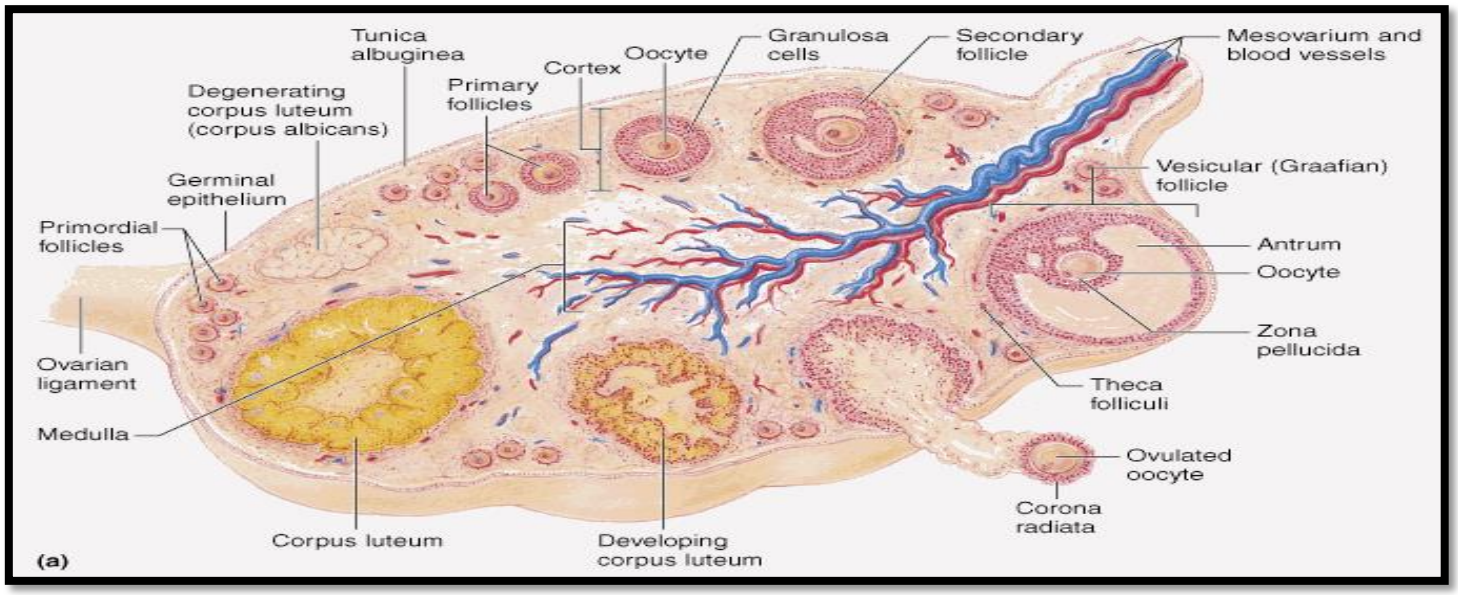
- **Microanatomy**

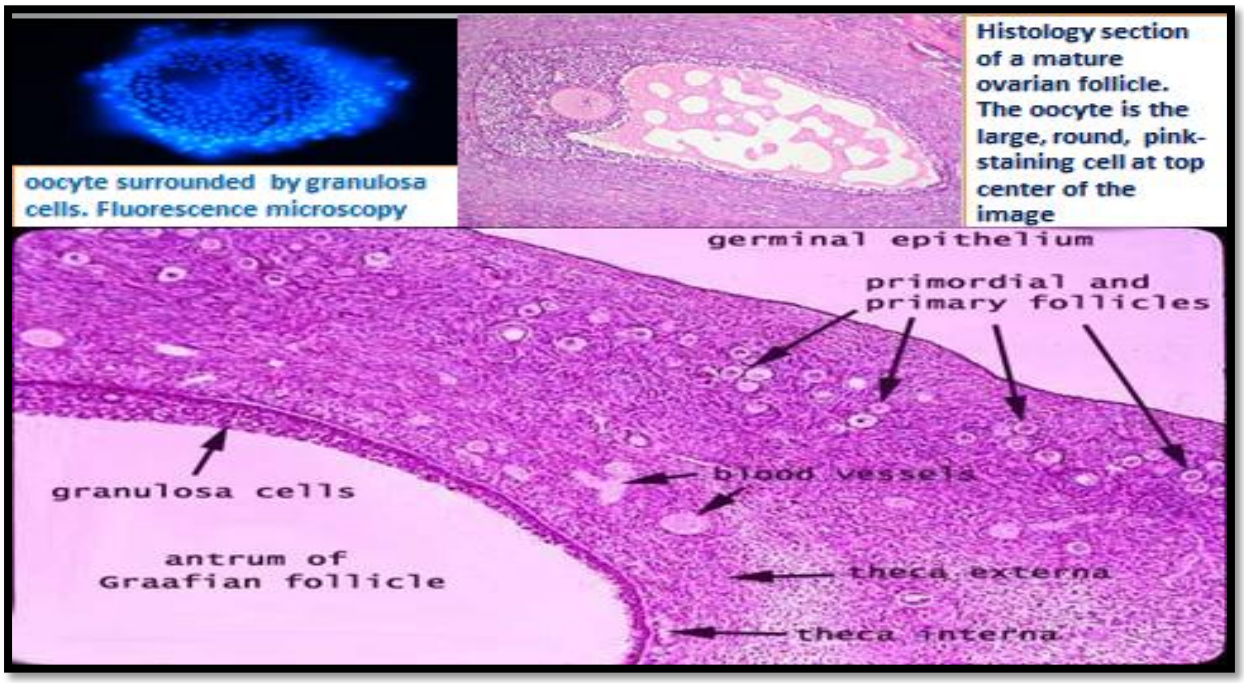
The surface of the **ovaries** is covered with membrane consisting of a lining of **simple cuboidal-to-columnar** shaped mesothelium.

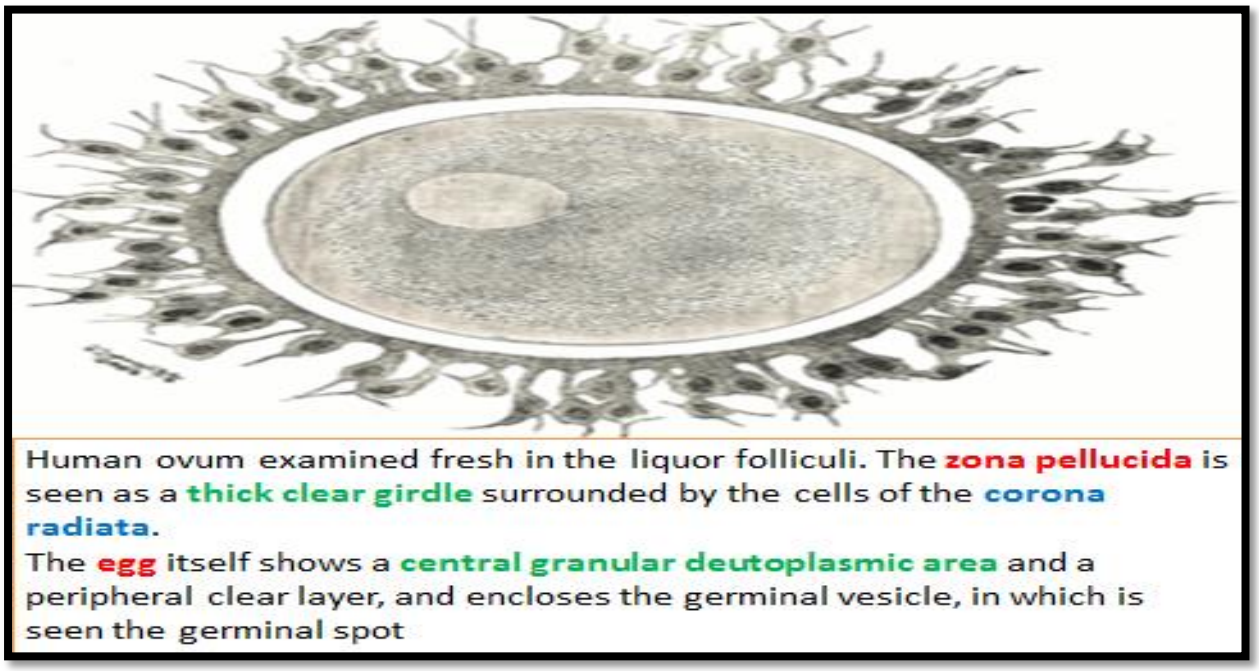
The outermost layer is called the **germinal epithelium**.

The outer layer is the **ovarian cortex**, consisting of **ovarian follicles** and **stroma** in between them. Included in the follicles are the **cumulus oophorus**, **membrana granulosa** (and the **granulosa cells** inside it), **corona radiata**, **zona pellucida**, and **primary oocyte.** **Theca** of follicle, **antrum** and **liquor folliculi** are also contained in the follicle. Also in the **cortex** is the **corpus luteum** derived from the follicles. **The innermost layer** is the **ovarian medulla**. It can be hard to distinguish between the **cortex** and **medulla**, but follicles are usually not found in the **medulla**.

Follicular cells flat epithelial cells that originate from surface epithelium covering the **ovary**, are surrounded by **Granulosa cells** - that have changed from flat to cuboidal and proliferated to produce a stratified epithelium.

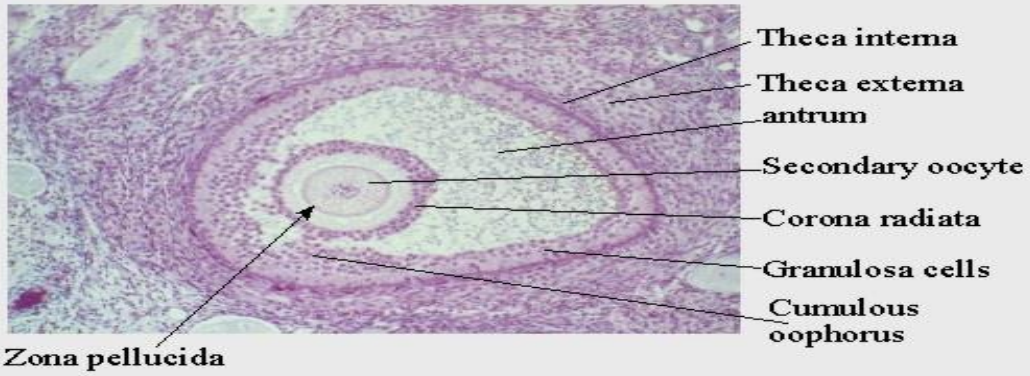






Human ovum examined fresh in the liquor folliculi. The **zona pellucida** is seen as a **thick clear girdle** surrounded by the cells of the **corona radiata**.
The **egg** itself shows a **central granular deutoplasmic area** and a peripheral clear layer, and encloses the germinal vesicle, in which is seen the germinal spot

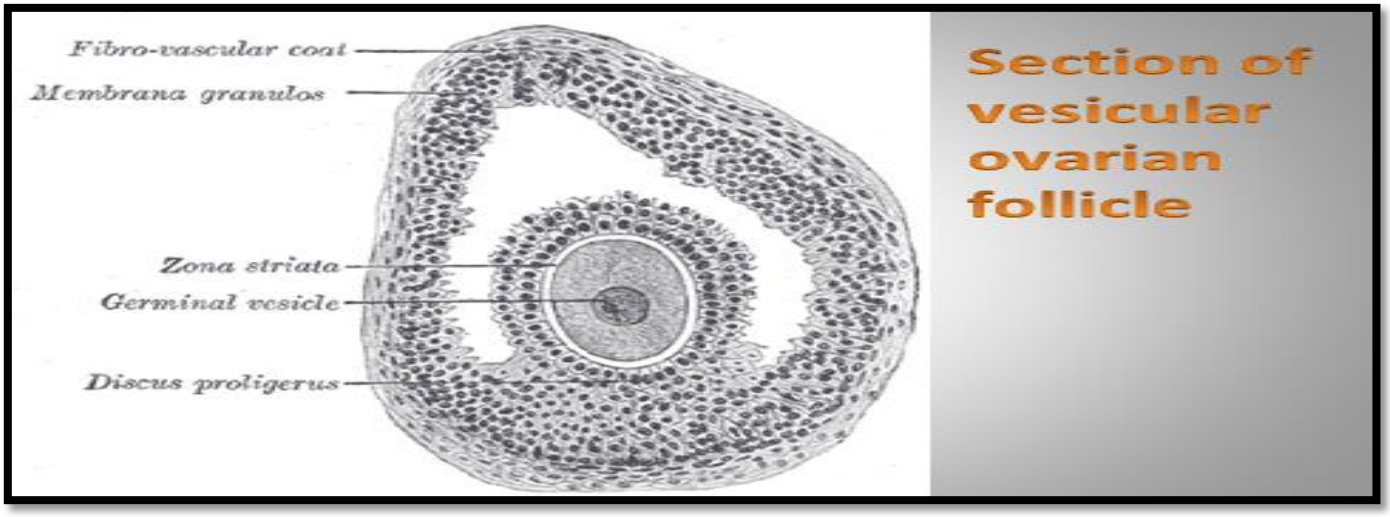
Mature (Vesicular) Follicle



At puberty, the **ovary** begins to secrete increasing levels of hormones. Secondary sex characteristics begin to develop in response to the hormones. The ability to produce **eggs** and reproduce develops. The **ovary** changes structure and function beginning at **puberty**.

Gamete production (Oogenesis)

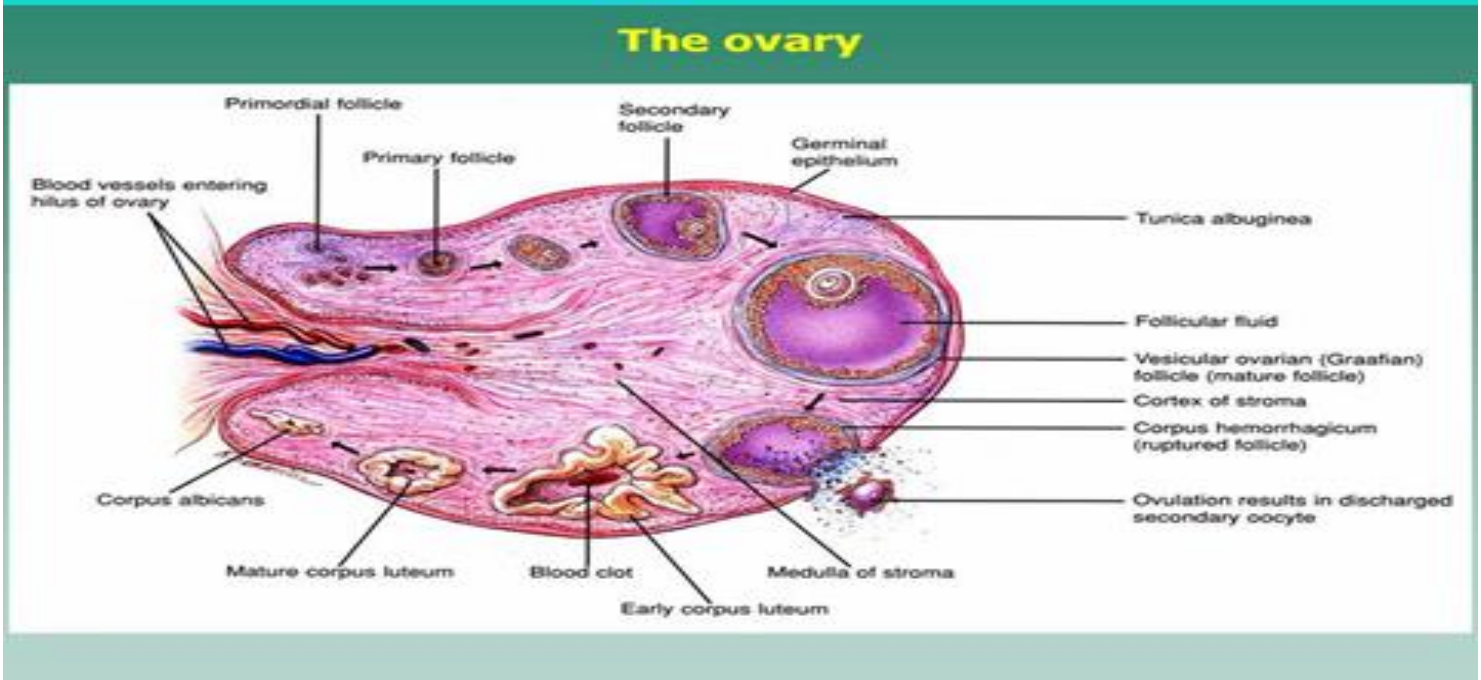
The **ovaries** are the site of production and periodical release of **egg** cells, the **female gametes**. In the **ovaries**, the developing **egg** cells (or **oocytes**) mature in the fluid-filled follicles. Typically, only one **oocyte** develops at a time, but others can also mature simultaneously. Follicles are composed of different types and number of cells according to the stage of their **maturation**, and their **size** is indicative of the stage of oocyte development, When the **oocyte** finishes its maturation in the **ovary**, a surge of luteinizing hormone secreted by the pituitary gland stimulates the release of the **oocyte** through the rupture of the follicle, a process called **ovulation**. The follicle remains functional and reorganizes into a **corpus luteum**, which secretes **progesterone** in order to prepare the **uterus** for an eventual implantation of the **embryo**



Hormone secretion

At maturity, **ovaries** secrete **estrogen**, **testosterone**,**inhibin**, and **progesterone**. In women, fifty percent of **testosterone** is produced by the **ovaries** and **adrenal glands** and released directly into the blood stream. **Estrogen** is responsible for the appearance of secondary sex characteristics for females at **puberty** and for the maturation and maintenance of the reproductive organs in their mature functional state.

Progesterone prepares the **uterus** for pregnancy, and the mammary glands for lactation. **Progesterone** functions with **estrogen** by promoting menstrual cycle changes in the endometrium



THE FEMALE CYCLE (MENSTRUAL CYCLE)

The **menstrual cycle** is the regular natural change that occurs in the female reproductive system (specifically the **uterus** and **ovaries**) that makes pregnancy possible. The cycle is required for the production of **ovocytes**, and for the preparation of the **uterus** for pregnancy. Up to **80**% of women report having some symptoms during the one to **two** weeks prior to menstruation. Common

symptoms include **acne**, **tender breasts**, **bloating**, **feeling tired**, **irritability** and **mood changes**. These symptoms interfere with normal life and therefore qualify as premenstrual syndrome in **20** to **30**% of women. In **3** to **8**%, they are severe.

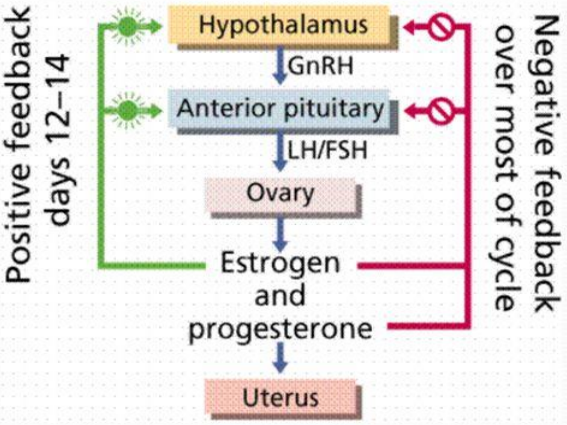
The first period usually begins between **twelve** and **fifteen** years of age, a point in time known as **menarche**. They may occasionally start as early as **eight**, and this onset may still be normal. The typical length of time between the first day of one period and the first day of the next is **21** to **45** days in young women and **21** to **35** days in adults (an average of **28** days). **Menstruation** stops occurring after **menopause** which usually occurs between **45** and **55** years of age. Bleeding usually lasts around **2** to **7** days.

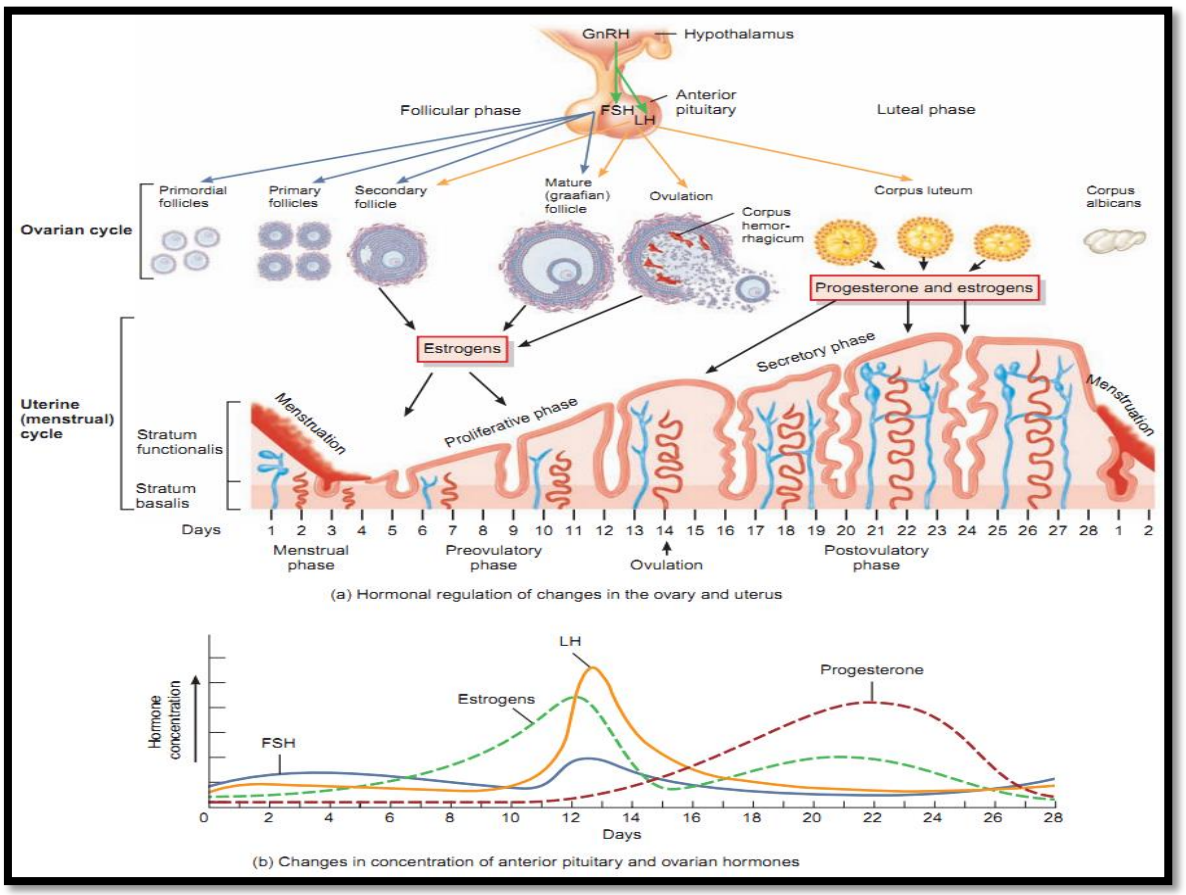
The **menstrual cycle** is governed by hormonal changes. These changes can be altered by using hormonal birth control to prevent pregnancy. Each cycle can be divided into **three phases** based on events in the **ovary** (**ovarian cycle**) or in the **uterus** (**uterine cycle**). The **ovarian cycle** consists of the **follicular phase**, **ovulation**, and **luteal phase** whereas the **uterine cycle** is divided into **menstruation**, **proliferative phase**, and **secretory phase**.

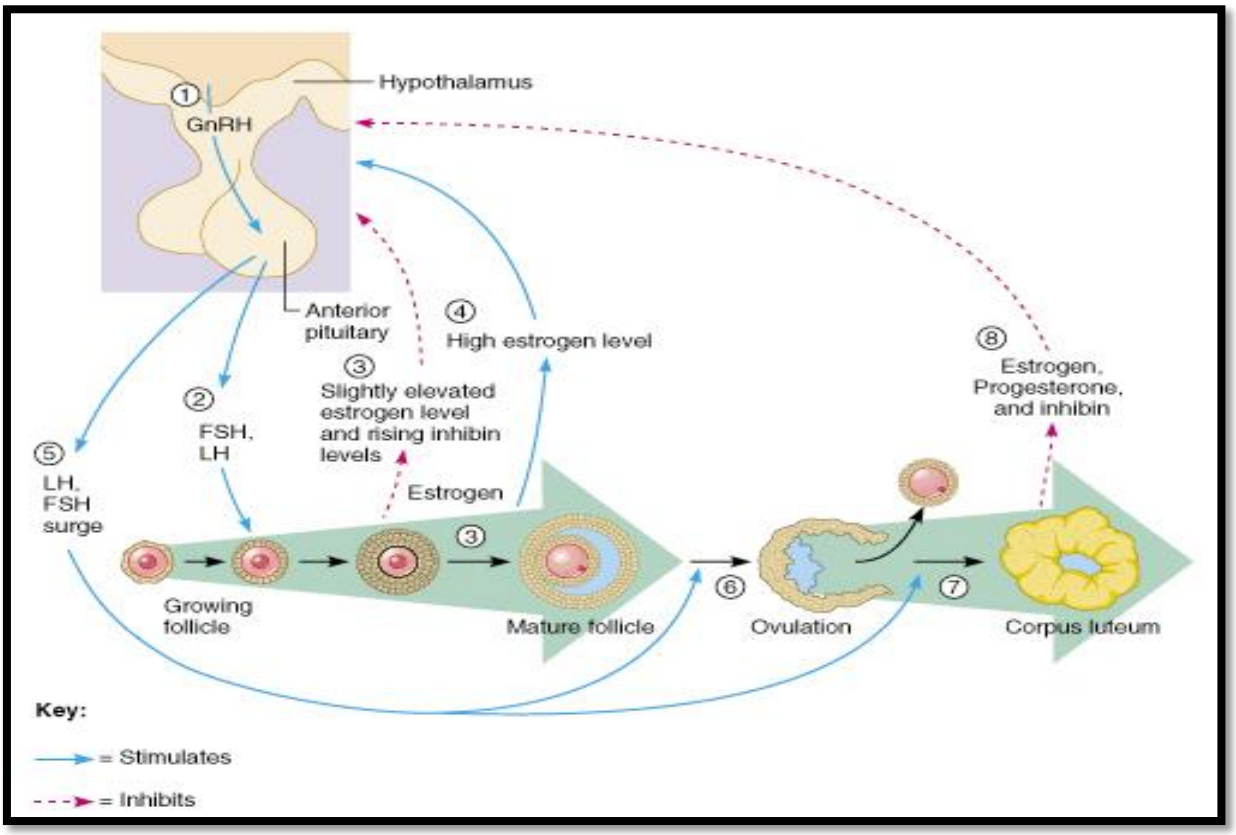
Stimulated by gradually increasing amounts of **estrogen** in the **follicular phase**, discharges of blood (menses) flow stop, and the lining of the **uterus** thickens. Follicles in the **ovary** begin developing under the influence of a complex interplay of hormones, and after **several** days one or occasionally **two** become dominant (non-dominant follicles shrink and die).

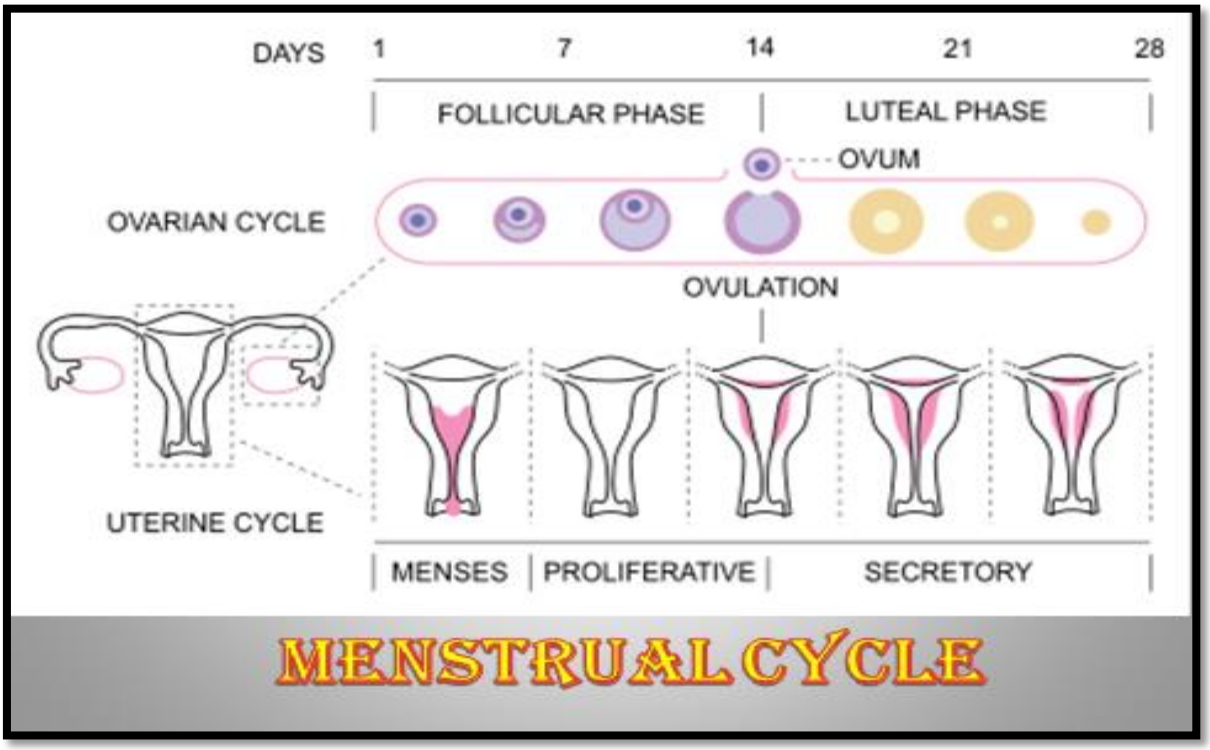
The Feedback Loop

- Hypothalamus releases gonadotropic releasing hormone (GnRH) to the pituitary
- Pituitary releases FSH to stimulate the follicles in the ovary to mature
- The follicle releases estrogen which causes the endometrial lining of the uterus to thicken
- This estrogen, at midcycle, also causes the pituitary to release LH and stop secreting FSH.






Hypothalamus
1
GnRH
Anterior pituitary
2
FSH, LH
3
Slightly elevated estrogen level and rising inhibin levels
4
High estrogen level
5
LH, FSH surge
Estrogen
3
Growing follicle
Mature follicle
6
Ovulation
7
Corpus luteum
8
Estrogen, Progesterone, and inhibin
Key:
= Stimulates
= Inhibits


DAYS
1
7
14
21
28
FOLLICULAR PHASE
LUTEAL PHASE
OVUM
OVARIAN CYCLE
OVULATION
UTERINE CYCLE
MENSES
PROLIFERATIVE
SECRETORY
MENSTRUAL CYCLE

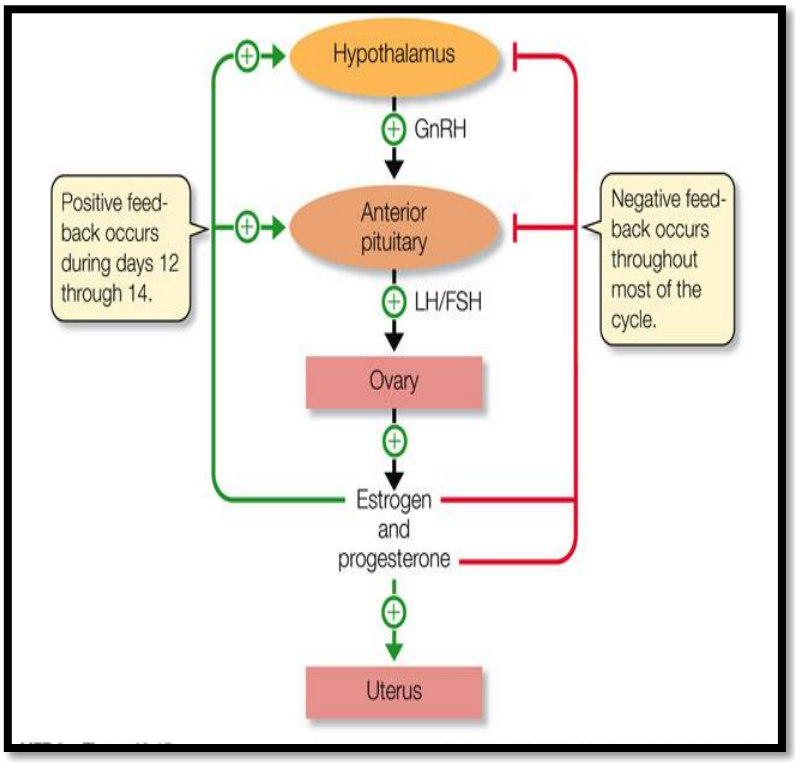
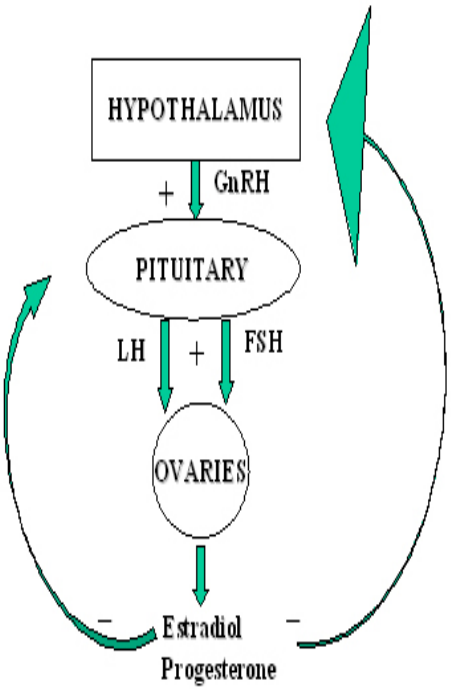
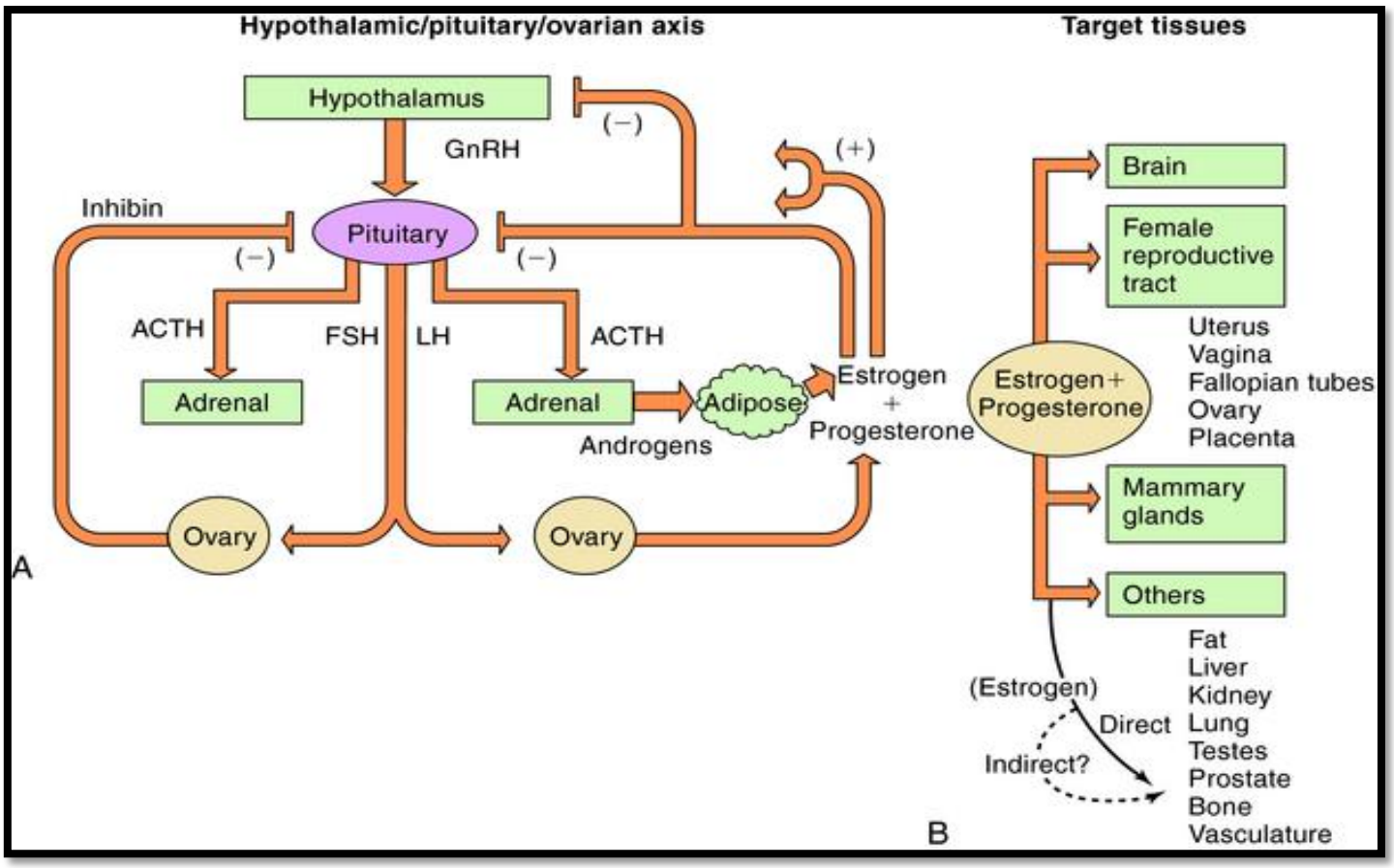

Hypothalamus
GnRH
Anterior pituitary
LH/FSH
Ovary
Estrogen and progesterone
Uterus
Positive feed-back occurs during days 12 through 14.
Negative feed-back occurs throughout most of the cycle.

Figure 1


HYPOTHALAMUS
+ GnRH
PITUITARY
LH + FSH
OVARIES
Estradiol
Progesterone


Hypothalamic/pituitary/ovarian axis
Target tissues
Hypothalamus
GnRH
(−)
(+)
Inhibin
Pituitary
(−)
(−)
ACTH
FSH
LH
ACTH
Adrenal
Adrenal
Adipose
Androgens
Estrogen + Progesterone
Ovary
Ovary
A
Brain
Female reproductive tract
Uterus
Vagina
Fallopian tubes
Ovary
Placenta
Estrogen + Progesterone
Mammary glands
Others
Fat
Liver
Kidney
Lung
Testes
Prostate
Bone
Vasculature
(Estrogen)
Direct
Indirect?
B

FERTILIZATION

usually occurs in the Fallopian tubes and marks the beginning of **embryogenesis**. The **zygote** will then divide over enough generations of cells to form a **blastocyst**, which implants itself in the wall of the **uterus**. This begins the period of **gestation** and the **embryo** will continue to develop until full-term. When the **fetus** has developed enough to survive outside the **uterus**, the **cervix** dilates and contractions of the **uterus** propel the **newborn** through the birth canal (the **vagina**).

HORMONAL CHANGES DURING PREGNANCY

Plasma levels of **human chorionic gonadotropin** increase immediately upon implantation of the **ovum**; the hormone is detectable in urine within **2** wk of implantation. It reaches a peak at ≈**8** wk of gestation and then declines to a stable plateau until birth. **Human chorionic gonadotropin** maintains **corpus luteum** function for **8**–**10** wk. **Human placental lactogen** (also called **human chorionic somatomammotropin**) has a structure that closely resembles **growth hormone**, and its rate of secretion appears to parallel placental growth and may be used as a measure of placental function. At its peak, the rate of secretion of **placental lactogen** is **1**–**2** g/d, far in excess of the production of any other hormones.

Placental lactogen stimulates **lipolysis**, antagonizes **insulin** actions and may be important in maintaining a flow of energy-yielding substrates to the **fetus**. **Placental lactogen** along with **prolactin** from the pituitary may promote mammary gland growth. After delivery, **placental lactogen** rapidly disappears from the circulation.

The **placenta** becomes the main source of steroid hormones at weeks **8–10** of gestation. Before then, **progesterone** and **estrogens** are synthesized in the maternal **corpus luteum**. These hormones play essential roles in maintaining the early uterine environment and development of the **placenta**. The **placenta** takes over **progesterone** production, which increases throughout pregnancy.

Progesterone, known as the hormone of pregnancy, stimulates **maternal respiration**; **relaxes smooth muscle**, notably in the **uterus** and **gastrointestinal tract**; and may act as an immunosuppressant in the **placenta**, where its concentration can be **50** times greater than in plasma. **Progesterone** may promote lobular development in the **breast** and is responsible for the inhibition of milk secretion during pregnancy.

The functions of high **estrogen** levels in pregnancy include stimulation of **uterine growth**, enhancement of uterine blood flow and possibly promotion of **breast** development. Because **estrogen** precursors originate in the **fetus**, **maternal estrogen** levels can be used as a measure of **fetal** viability.

The increased amount of **estrogens** during pregnancy also stimulates a population of cells (**somatotrophs**) in the maternal pituitary to become **mammotrophs**, or **prolactin-secreting cells**. The increased **prolactin** secretion probably helps promote mammary development. In addition, the increased number of pituitary **mammotrophs** at the end of pregnancy provides the large amounts of **prolactin** necessary to initiate and maintain lactation.

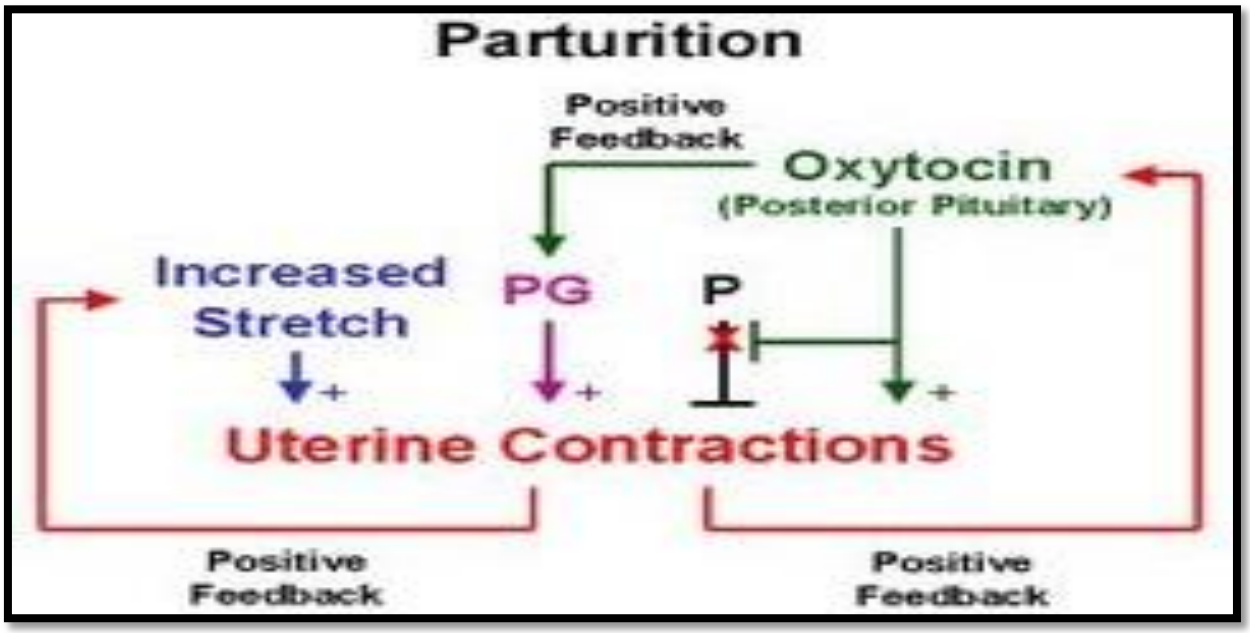
ENDOCRINE REGULATION OF LACTATION

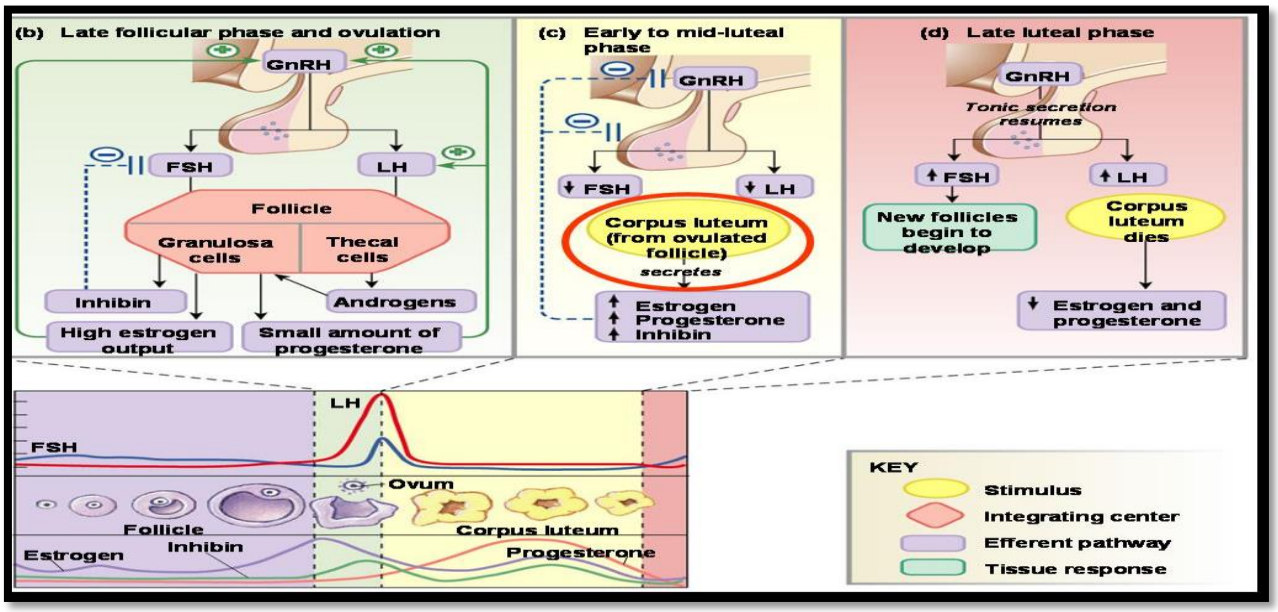
The establishment and maintenance of human lactation are under the influence of complex neuroendocrine control mechanisms (28).

After parturition, elevated levels of prolactin and withdrawal of estrogens and progesterone results in the onset of milk secretion (lactogenesis).

The **breasts** must have undergone appropriate growth and development beginning in puberty and completed during pregnancy for milk secretion to occur. The initiation of **lactogenesis** does not require infant sucking but lactation cannot be maintained unless the infant is put to the **breast** by **3** or **4** d postpartum. For the first **3**–**5** d postpartum the mammary secretion is termed "**colostrum**." This early milk is thick and straw-colored, rich in minerals and immune factors (i.e., lactoferrin and secretory immunoglobulin A) and low in lactose and total protein. The concentration of lactose increases and that of sodium and chloride decrease as milk secretion is enhanced. The characteristics of mature milk are evident by day **10** of lactation. With established lactation, **prolactin** is required for maintenance of milk production. **Prolactin** release into the circulation from **mammotrophs** in the anterior pituitary is in response to sucking. **Prolactin** secretion is mediated by a transient decline in the secretion of **dopamine** from the **hypothalamus**, which normally inhibits its secretion. Milk secretion continues as long as the infant continues to nurse more than **once** a day. The daily milk volume transferred to the infant increases through lactation. Most women can secrete considerably more milk than needed by a single infant. Milk secretion is continuous and the quantity produced is principally regulated by infant demand. **Oxytocin** release from the **posterior pituitary** results from neural impulses reaching the **hypothalamus** caused by sucking of the nursing infant. Circulating **oxytocin** causes contraction of **myoepithelial cells** that surround mammary alveoli

and ducts, forcing milk into ducts of the nipple so that it can be removed by the infant. This response is termed "**milk ejection**" or "**let-down**" and can be initiated by the mere sight of the infant or by hearing the infant cry. Milk secretion ceases in **1** or **2** d when infant sucking or milk removal is terminated.





PUBERTY AND MENARCHE

Puberty means the onset of adult sexual life, and *menarche* means the beginning of the cycle of menstruation. The period of puberty is caused by a gradual increase in gonadotropic hormone secretion by the pituitary, beginning in about the eighth year of life , and usually culminating in the onset of puberty and menstruation between ages 11 and 16 years in girls (average, 13 years).

In the female, as in the male, the infantile pituitary gland and ovaries are capable of full function if they are appropriately stimulated. However, as is also true in the male, and for reasons that are not understood, the hypothalamus does not secrete significant quantities of GnRH during childhood. Experiments have shown that the hypothalamus is capable of secreting this hormone, but the appropriate signal from some other area of the brain to cause the secretion is lacking. Therefore, it is now believed that the onset of puberty is initiated by some maturation process that occurs elsewhere in the brain, perhaps somewhere in the limbic system.