

Female reproductive system

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Structure of female reproductive system

I. Primary sex organ (ovary)

- 1) Production of ova (**Oogenesis**).
- 2) Production of steroid hormones (**Estrogen & Progesterone**).

II. Secondary sex organs

(Fallopian tubes & Uterus & Cervix & Vagina & External genital organs).

- Ovaries in young female at menarche contain 400.000 follicles.
 - During reproductive period, only 500 follicles will complete their maturation to release ova and the others become atretic.
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Sex (Menstrual) cycle in female

Definition:

- It is a monthly rhythmic changes in the **rate of secretion** of female sex hormones with corresponding changes in 1ry & 2ry sex organs.

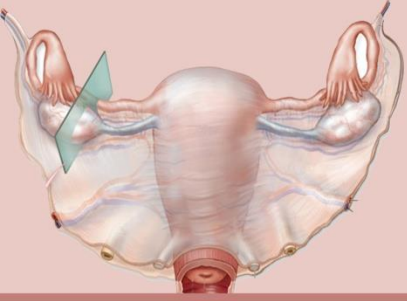
Due to: cyclic changes in hypothalamic **Gn-RH** & pituitary gonadotropins.

Aim: is periodic preparation for fertilization & pregnancy.

Length: 28 days for each cycle.

The sex (menstrual) cycle consists of:

1. Ovarian cycle
2. Uterine cycle
3. Vaginal cycle
4. Cyclic changes in cervix
5. Cyclic changes in breast

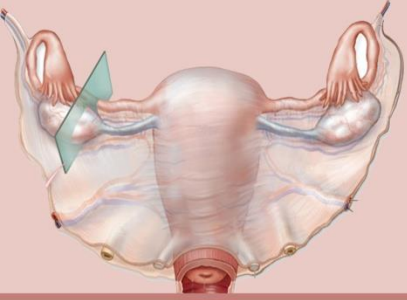


Ovarian cycle

- Ovarian cycle is composed of 3 phases

1) Follicular phase	14 days	<ul style="list-style-type: none">- Under control of FSH.- Secretion of large amount of estrogen.
2) Ovulation phase	Mid-cyclic	<ul style="list-style-type: none">- Caused by LH & FSH surge.
3) Luteal phase	14 days	<ul style="list-style-type: none">- Under control of LH.- Secretion of large amount of progesterone.





I. Follicular phase:

✦ At the start of each cycle:

- (6 – 12) **primordial follicles** enlarge to form **primary (pre-antral) follicles**.
- Under the effect of **FSH** which is released from anterior pituitary gland due to low level of estrogen.

✦ Composition of primary (pre-antral) follicle:

- **Primary oocyte** is increased in size.
- **Follicular cells** proliferate to form **granulosa cells** around the oocyte.
- **Ovarian stromal cells** proliferate to form **theca cells** around the follicle.

✦ Two cells mechanism for steroid production:

- 1) **Theca cells** synthesize **androgen** under the effect of **LH**.
- 2) **Granulosa cells** convert **androgen to estrogen** under the effect of **FSH**.

✦ Antral follicle:

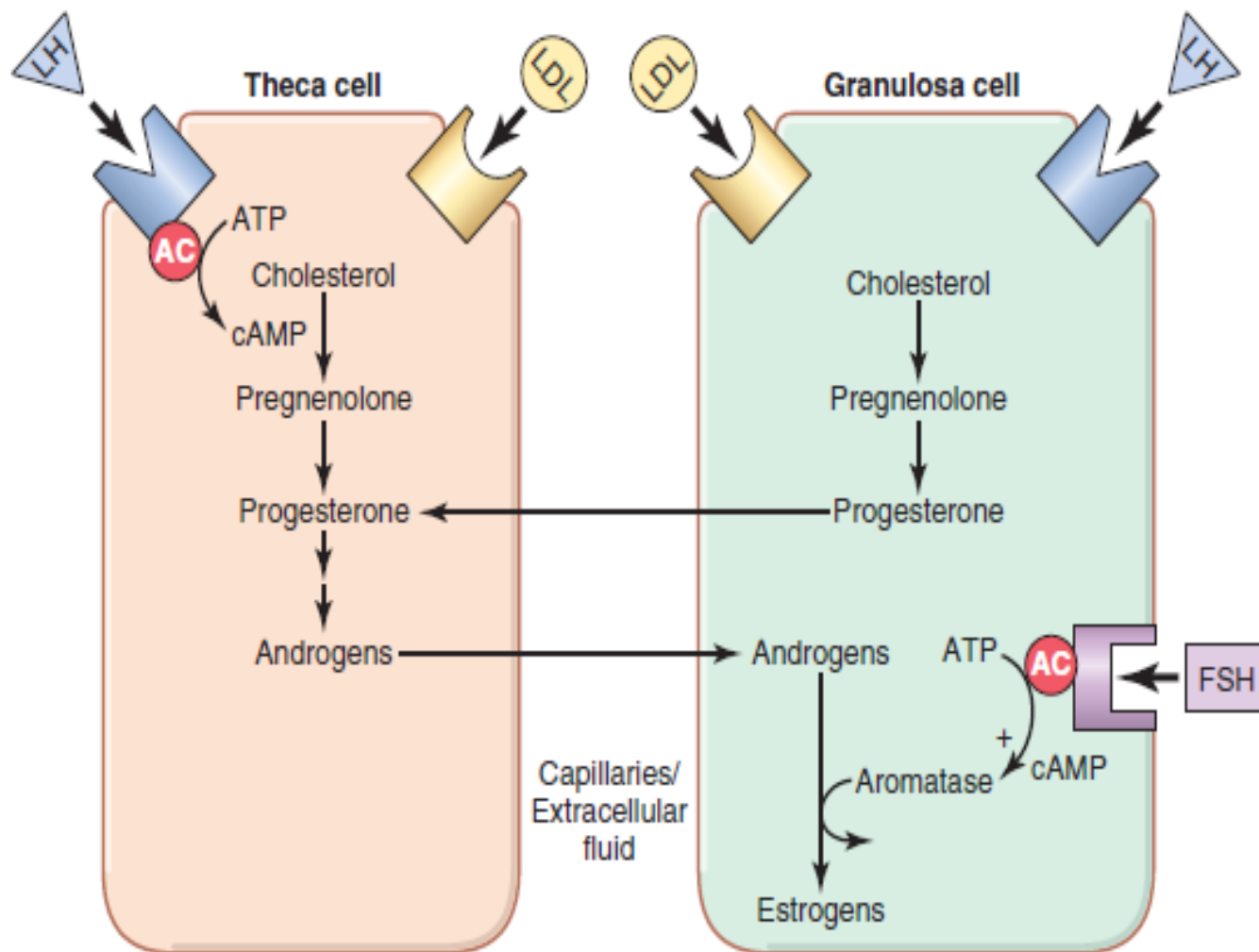
- After one week (at the 7th day of the cycle):

a) Largest follicle (first in phase) in one ovary enlarges & highly developed & secrete more estrogen.

It is called *antral follicle or dominant follicle*.

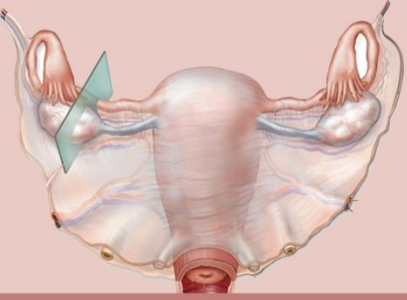
It contains a large cavity filled with fluid called the antrum.

b) Other follicles (competing follicles) regress & degenerate.



Interaction of follicular theca and granulosa cells for production of estrogens. The theca cells, under the control of luteinizing hormone (LH), produce androgens that diffuse into the granulosa cells.

In mature follicles, follicle-stimulating hormone (FSH) acts on granulosa cells to stimulate aromatase activity, which converts the androgens to estrogens.



Mechanism of uni ovulation

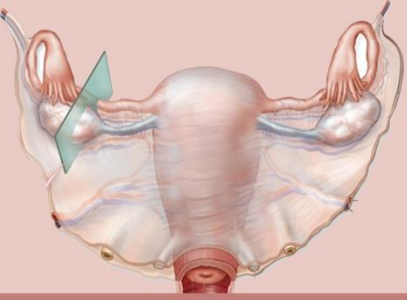
- The dominant follicle secretes large amount of estrogen.
- Estrogen from dominant follicle will cause the following:

1) Negative feedback on competing follicles:

- \uparrow Estrogen \Rightarrow \downarrow FSH secretion from anterior pituitary.
- \downarrow FSH \Rightarrow \downarrow growth of competing follicles \Rightarrow atretic follicles.

2) Positive feedback on dominant follicle:

- \uparrow Estrogen (in the follicle) \Rightarrow \uparrow number & sensitivity of FSH receptors on granulosa cells of dominant follicle \Rightarrow \uparrow response of granulosa cells to FSH in dominant follicle \Rightarrow \uparrow estrogen secretion from dominant follicle \Rightarrow more growth of the dominant follicle.
- Also, the dominant follicle secretes **inhibitory peptides** that cause degeneration of the competing follicles.

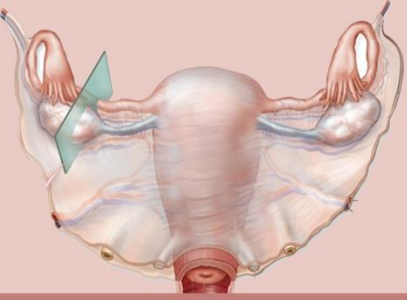


Just before ovulation:

The follicle becomes **mature graafian follicle** (reach 1 – 2 cm in diameter).

- The oocyte complete the **meiosis** reduction division to produce **secondary oocyte** and **first polar body**.
- The secondary oocyte is **arrested in the metaphase** until fertilization.

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- In **Antral follicle**, the spaces unite and give one large space,
 - **oocyte** is located in a mass of granulosa cells (**cumulus oophorus**) that project into antrum,
 - The first layer of granulosa cells that surround the oocyte and in close contact with **zona pellucida**, becomes elongated and is called **corona radiata**.
 - In presence of **FSH and increased estrogens**, outer layers of granulosa cells of large antral follicle synthesize **LH receptors**.
 - Just before ovulation, these cells begin to synthesize **progesterone** instead of converting androgens to estrogens.



II. Ovulation

- ✦ **Timing:** ovulation occurs at the **14th day** of the cycle. (mid-cyclic).
- ✦ **Cause of ovulation:** gonadotropin surge. (LH & FSH surge).

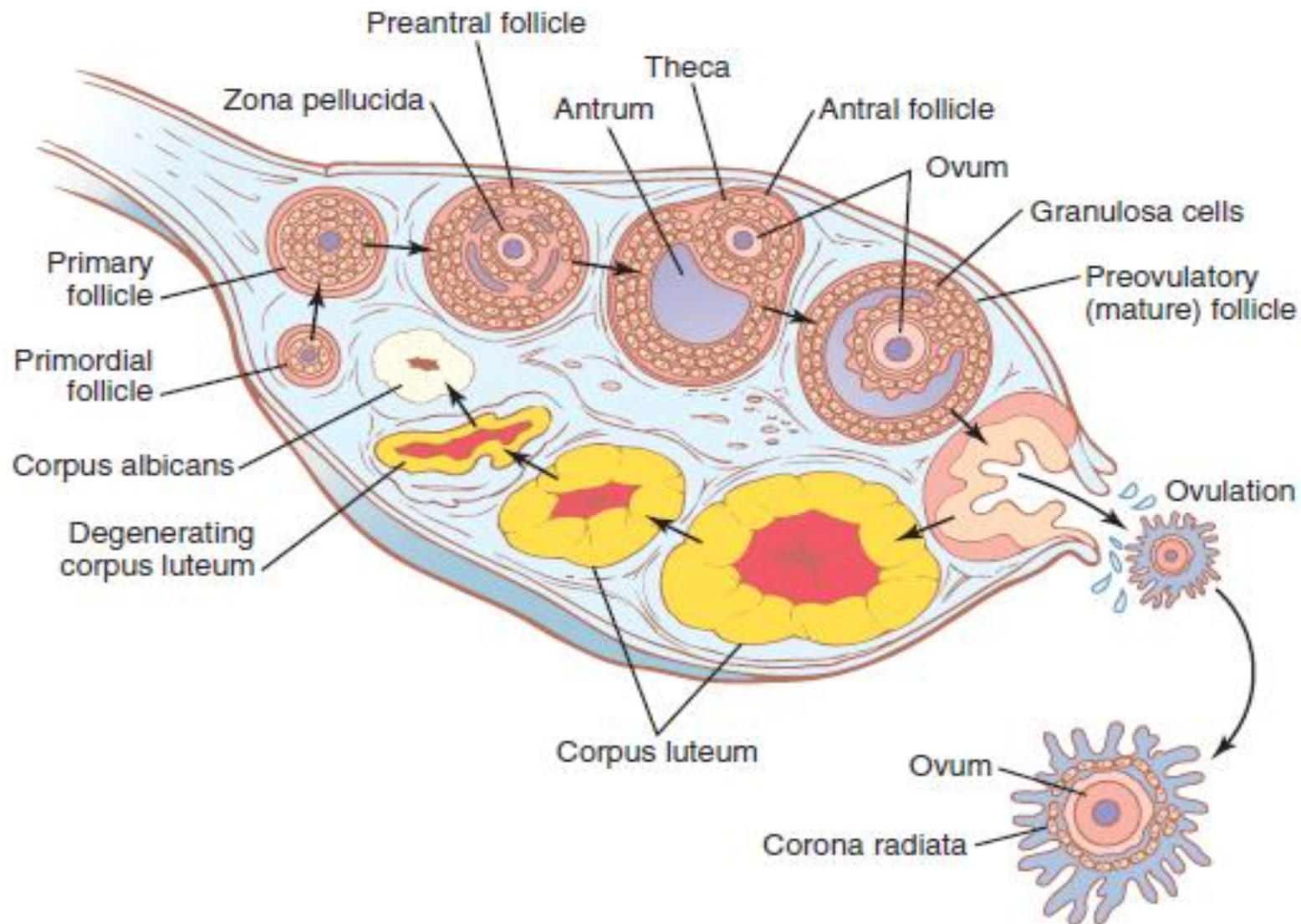
III. Luteal phase

✦ **Formation of corpus luteum:**

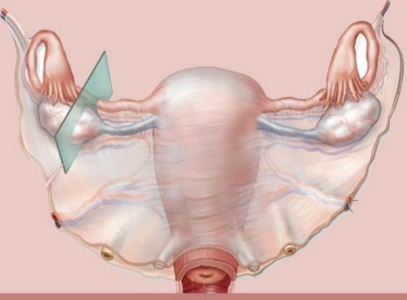
- After ovulation, the ruptured follicle becomes filled with blood forming corpus hemorrhagicum, then clotted blood is removed by phagocytosis.
- Then, it is converted to corpus luteum **under the effect of LH**.
- Both granulosa & theca cells are converted to **lutein cells**.
- Lutein cells are rich in lipids. So, corpus luteum is **yellow** in color.

✦ **Functions of corpus luteum:**

- It is a **temporary endocrinal** organ. Secretes progesterone & estrogen.
- So, after ovulation by **8 days**, there is **progesterone** peak with second peak of **estrogen**. (first estrogen peak is mid-cyclic).



Stages of follicular growth in the ovary, also showing formation of the corpus luteum



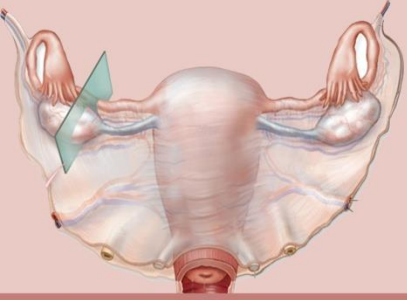
✦ **Fate of corpus luteum**

A. If no fertilization & no implantation:

- ↓ **LH** (due to high level of progesterone & estrogen) ⇒ **degeneration of corpus luteum** (luteolysis) ⇒ drop of progesterone & estrogen level **9 days** after ovulation.
- After **14 days** of ovulation, it becomes corpus albicans.
- Corpus albicans is removed by macrophages leaving fibrous scar.
- **Drop of progesterone & estrogen level lead to:**
 - a) Shedding of endometrium in uterus (menstruation).
 - b) Stimulation of FSH secretion to start another cycle.

B. If fertilization occurs:

- Corpus luteum is maintained by human chorionic gonadotropin (hCGn) for **6 months** and called corpus luteum of pregnancy ,Which secretes **progesterone** for stabilization of pregnancy.



Ovulation



Definition

- It is the process of **rupture** of **mature** graafian follicle and **expulsion of ovum** into the peritoneal cavity to be picked up by the fimbriated end of the fallopian tube.



Timing: Ovulation occurs at the 14th day of the cycle. (mid-cyclic).



Mechanism of ovulation

I. Before ovulation

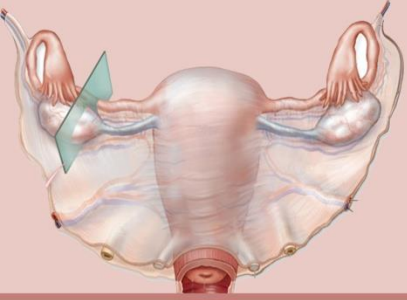
- Premature oocyte **maturation & luteinization** are prevented by:

1) Oocyte Maturation Inhibitor (OMI):

- It is formed by the granulosa cells.
- It prevents meiosis of the oocyte until the **pre-ovulatory LH surge** removes this inhibition.

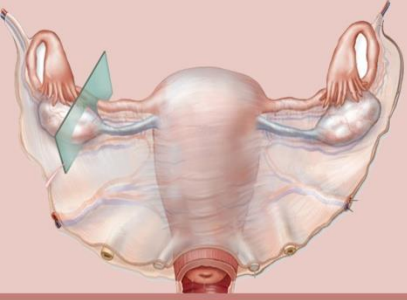
2) Luteinization Inhibitor (LI):

- It is formed by the granulosa cells.
- It inhibits luteinization until the **pre-ovulatory LH surge** removes this inhibition.



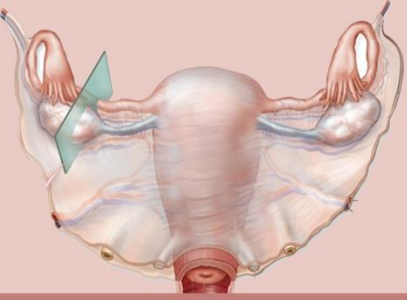
II. Gonadotropin surge

- **Definition:** it is mid-cyclic increase in gonadotropins level in blood.
- *Cause of gonadotropin surge*
 - When estrogen level in the blood reaches a **high critical level** and **maintained for a critical time**, it induce sudden increase in LH (**LH surge**).
- *Aim of gonadotropin surge*
 - 1) Final **maturation** of the oocyte.
By removal of the inhibitory effect of **Oocyte Maturation Inhibitor**
 - 2) Physical **release** of the oocyte from the mature graafian follicle.
By removal of the inhibitory effect of **Luteinization Inhibitor**



Functions of LH surge

1. **Complete the meiosis:** by removal of inhibitory effect of **OMI**
2. **Luteinization of granulosa cells:** by removal of inhibitory effect of **LI**
3. \uparrow **Progesterone synthesis** Progesterone leads to:
 - a) Hyperemia of follicle \Rightarrow **Plasma transudation** \Rightarrow swelling of the follicle.
 - b) \uparrow Distensibility of follicular wall to accommodate rapid increase in follicular fluid without marked change in the intra-follicular **Pressure**.
4. \uparrow **Proteolytic enzymes activity (collagenase)**
This leads to digestion of collagen in the follicular wall.



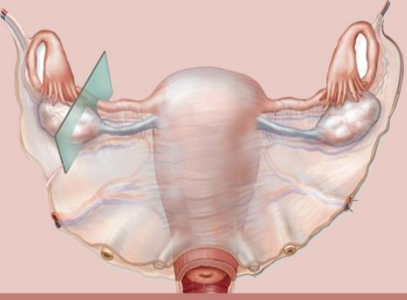
5. ↑ **Plasminogen activator**

This leads to conversion of plasminogen to plasmin (active proteolytic enzyme) \Rightarrow lysis of the follicular wall connective tissue.

6. ↑ **Prostaglandin synthesis (PGE & PGF)**

a) PG act to free lysosomal enzymes within the follicular fluid \Rightarrow digest the follicular wall.

b) PG contract the ovarian smooth muscles \Rightarrow help the expulsion of ovum into the peritoneal cavity.



Functions of FSH surge:

1. Increase number of **LH receptor** on the **granulosa cells** for luteinization and normal corpus luteum formation.
2. Stimulation of **granulosa cells** to produce **plasminogen activator**.

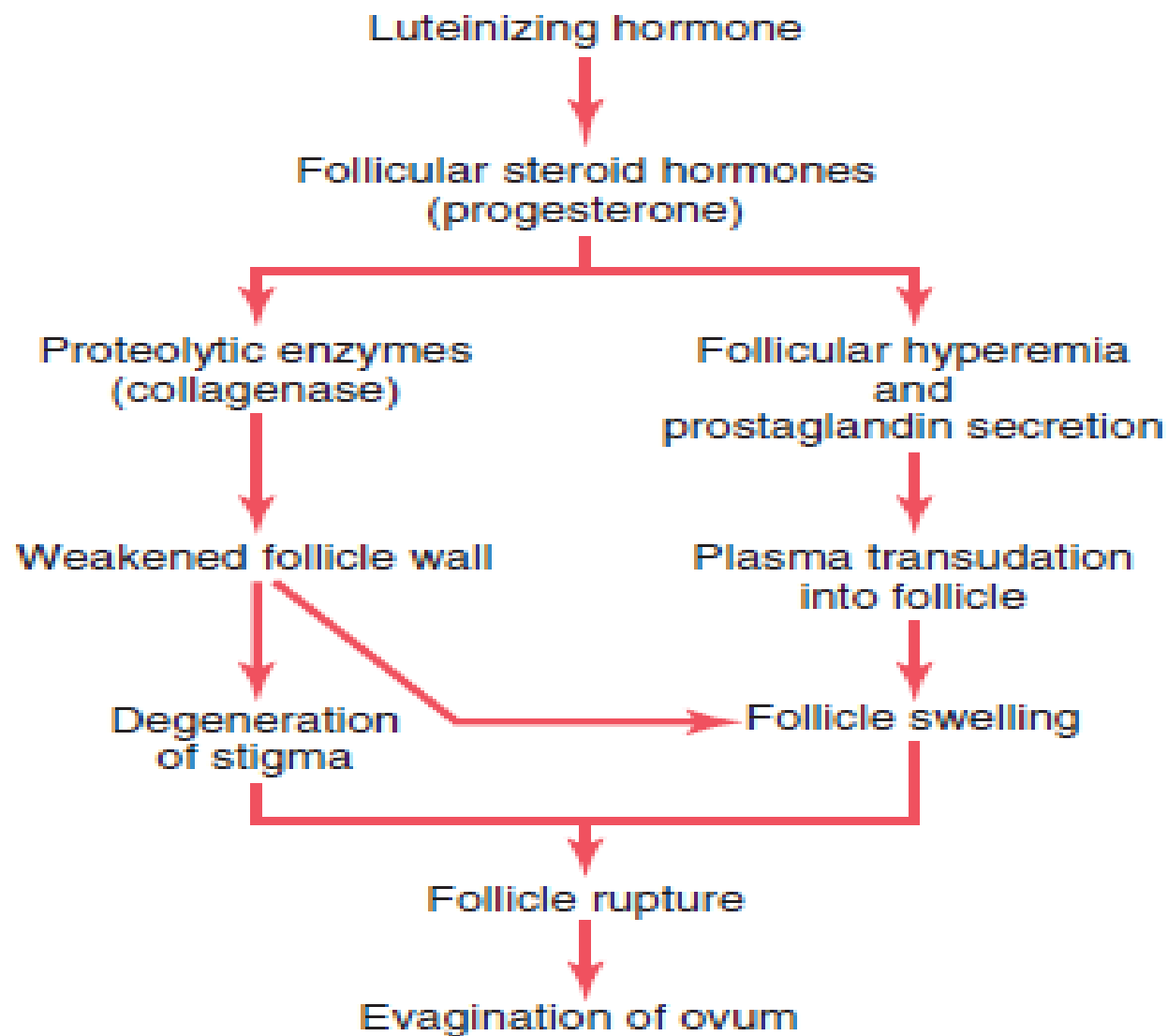
Indications (signs) of ovulation

- Ovulation occurs at the 14th day of the cycle. (mid-cyclic).
i.e. 14 days from the start of menstruation (if the cycle is regular).

Methods used to determine time of ovulation:

- Ovulation and **corpus luteum** formation is indicated by the presence of signs of **progesterone** release.

1. **LH surge**: ↑ **plasma LH** 9 – 11 hours before ovulation.
2. **Urine**: presence of **pregnandiol** (metabolic end product of progesterone).
3. **Temperature**: ↑ **body temperature** by **0.5 °C** at the time of ovulation, that persists until menstruation occurs. (must be morning temperature).
4. **Ovary**: lower abdominal pain at the time of ovulation.
5. **Ultrasound imaging**: to see the **mature graafian** follicle.

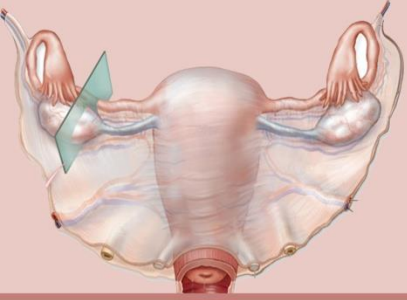


The postulated mechanism of ovulation



Failure of ovulation (non-ovulatory cycles)

- Non-ovulatory cycles are present normally in the first 1 - 2 years after the onset of puberty and before the menopause.
- Bleeding is due to withdrawal of estrogen due to atrophy of graafian follicle.
- Some women are infertile due to non-ovulatory cycles.
- non-ovulatory cycles occur also in women treated with contraceptive pills.



Uterine cycle

➤ **Definition:** - Cyclic changes of the endometrium under the effect of ovarian hormones.

➤ **Aim:** - Preparation of endometrium to receive zygote (implantation). - If no implantation, the prepared endometrium is destroyed as menstruation.

(So, menstruation is the crying of uterus for lack of a baby).

➤ **Phases:**

1. Proliferative phase
2. Secretory phase
3. Menstrual phase (Destructive phase)

1. Proliferative phase

Correspond to follicular phase in ovary.

From 5th to 14th day of the cycle.

Under the effect of **estrogen**
Secreted from the developing follicle.

Changes:

- **Endometrium:** rapid increase in thickness from 1 \Rightarrow 4 mm.
- **Uterine glands:** increase in length rapidly but with **no** secretions.
- **Epithelial cells:** contain little glycogen.
- **Vascularity:** blood vessels become more spiral but **not** tightly coiled.

2. Secretory phase

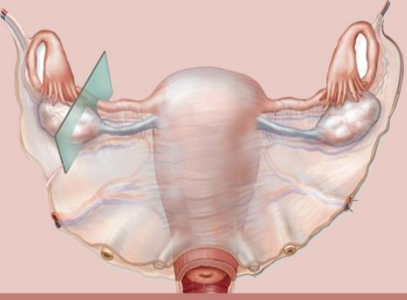
Correspond to luteal phase in ovary.

From 15th day to the beginning of next cycle.

Under the effect of **progesterone & estrogen**
Secreted from corpus luteum.

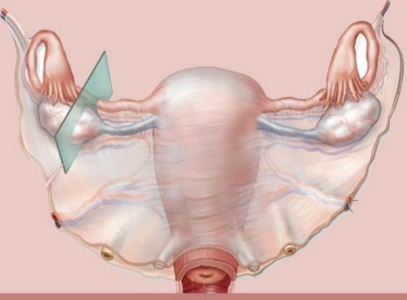
Changes:

- **Endometrium:** more increase in thickness from 4 \Rightarrow 8 mm.
- **Uterine glands:** become coiled with thick mucoid **secretion** rich in glycogen.
- **Epithelial cells:** rich in glycogen.
- **Vascularity:** blood vessels become tightly coiled.
- Connective tissue in lamina propria undergo decidual reaction.
- At the end of this phase, the endometrium can be divided into 3 regions:
 - a) **Compact:** neck of the glands.
 - b) **Spongy:** dilated part of the glands.
 - c) **Basal:** blind ends of the glands.
- **Functional layer =(compact & spongy)** are supplied by spiral arteries
- During menstruation the functional layer is lost while the basal remains.



3. Menstrual phase (Destructive phase)

- **Timing:** from the **first to the 5th** day of the cycle.
- **Cause:** due to degeneration of corpus luteum \Rightarrow removal of the hormonal support of the endometrium.
- **Mechanism:**
 - VC of spiral arteries \Rightarrow ischemia & necrosis of functional layer.
 - Then, VD of spiral arteries \Rightarrow rupture & hemorrhage.Finally, the endometrium is shed in patches soaked with blood.
 - The bleeding ends when the spiral arteries constrict again.
 - **The menstrual bleeding** is not clotted due to fibrinolytic system.



3- Vaginal cycle

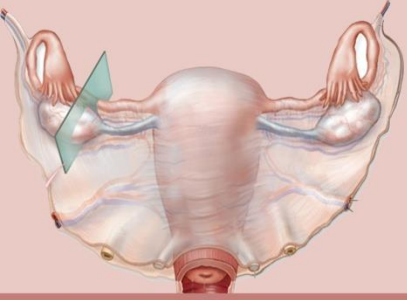
- **In the follicular stage** : under the effect of **estrogens** the vaginal epithelium becomes **cornified** (identified in the vaginal smear) and there is **acidic secretion** .
- **In the luteal stage** : under the effect of **progesterone** the vaginal **epithelium** proliferates .

4- Cyclic changes in cervix

- **In the follicular stage** : under the effect of **estrogen** there is thin , watery , alkaline mucous that **help transport and survival of sperm** and gives **positive fern pattern** arborization
- **In the luteal stage** : under the effect of **progesterone** there is thick , cellular secretion that gives **negative fern pattern** arborization .

5- Cyclic changes in breast

Ten days before menstruation, there is swelling, tenderness and pain the breast, probably due to **distension of ducts** , **hyperemia** and **edema of the interstitial tissue** of the breast , all these changes regress during menstruation .



Ovarian hormones

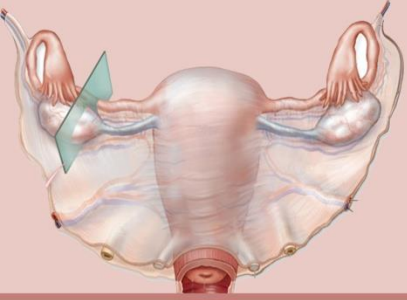
1. ESTROGENS

Steroid hormones .

- **Three types** of estrogens are secreted from the ovaries **Estradiol** (most potent) , **Estrone** , and **Estriol** .

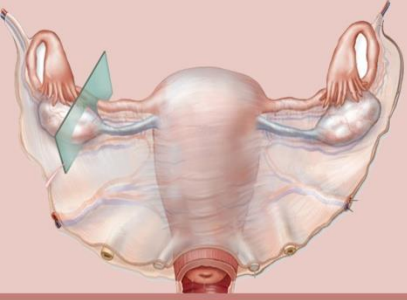
Secreted from :

- 1- Ovary from **growing follicles** and **corpus luteum** .
 - 2- Non ovarian sources : **placenta** and **suprarenal cortex** .
- **Transported** in blood in free form and bound with globulins .
 - **Metabolism** : mainly in liver
 - **Estrogen secretion is continuous** , however , it **shows cyclic variation in the rate of secretion** i.e. estrogen has 2 peaks :
 - (1) At time of ovulation .
 - (2) Mid-luteal phase which is less than pre-ovulatory peak .



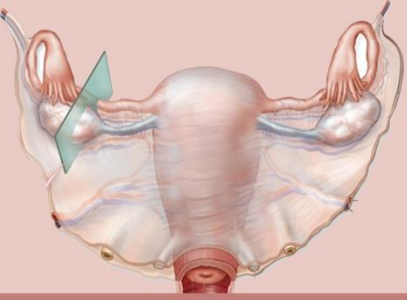
Actions :

- 1- **In the embryonic life** : Development of **uterus** and **vagina** .
- 2- **Pre-pubertal effect** : ↓ **Gonadotropin releasing factors**, due to high sensitivity of hypothalamic feedback mechanism.
- 3- **After puberty**:
 - a- **On the ovary** : growth and maturation of **oocyte** and **corpus luteum** .
 - b- **Effect on Secondary sex organs** :
 - Estrogen stimulate the growth of **secondary sex organs**
 - (uterus, tubes, vagina, external organs) .
 - They stimulate the proliferation of endometrium and vascularity (it responsible for **proliferative phase** of uterine cycle) .
 - They **increase** the motility of the fallopian tubes and **excitability of uterine muscles** and their sensitivity to oxytocin
 - They stimulate the **synthesis of progesterone** receptors in the uterine tissues



c- Effect on Female Sex characters :

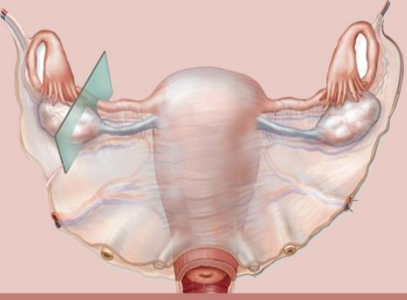
- They stimulate the development of the breast (duct system , increase the blood supply and pigmentation of areolae & nipples) .
- They are responsible for the female type of Fat and hair distribution .
- They keep the female voice high pitched .
- They are responsible for the broad female pelvis.



d- Metabolic effects :

- They stimulate union of the epiphysis and maturation of ossification centers .
- Estrogens are mild anabolic agents .
- They cause retention of Ca^{++} and ph-3 and formation of bone matrix .
- They include mild Na^+ and water retention responsible for the premenstrual tension .
- They decrease circulating cholesterol levels, they could be one of the factors responsible for **lower incidence of atherosclerosis** in females .
- Alters hepatic production of clotting factors so, promote thrombosis .
- Secretion of angiotensinogen .

e- Behavioral effect : increase lipido in human



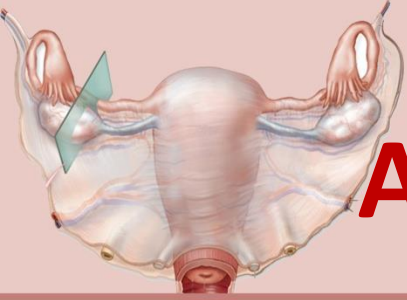
2- PROGESTERONE

- Steroid hormone.
- Secreted from :

Ovary : corpus luteum .

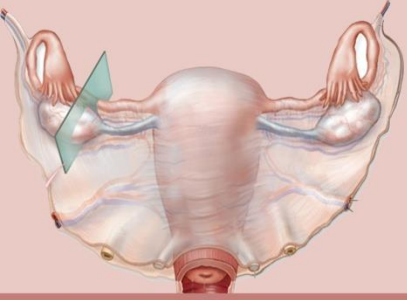
Non ovarian sources : placenta and suprarenal cortex.

- Transported in blood 2 % free & 98% bound to albumin and globulins.
- Metabolism mainly in liver and excreted in urine in the form of **pregnandiole**.



Actions Of Progesterone

1. It is responsible for the **secretory phase** in the endometrium .
2. It changes the **stroma cells** of the endometrium into **decidual cells** .
3. It is responsible for the **formation of placenta** and imbedding of the fertilized ovum .
4. It maintains pregnancy by **inhibiting uterine contraction** . It is antagonistic to **the effect of estrogens** , so that **the excitability of myometrium cells decreases** as does **their sensitivity to oxytocin** .
5. Inhibition of ovulation via inhibition of anterior pituitary gonadotropins secretion .
6. It stimulates the **growth of the secretory alveoli of mammary glands** & increase blood supply to the breast with more hyperemia.



7. **progesterone** has a **natriuretic effect** when present in high concentrations .
8. Increase **basal body temperature** by about **0.5 oC** due to its effect on hypothalamus and its permissive action on thyroid hormone .
9. **Behavioral effect** :
 - Increase appetite .
 - participates in onset and maintenance of maternal behavior.
10. Stimulate respiration due to increased **sensitivity of respiratory center to CO₂**.



THank you