G.U.S. Physiology

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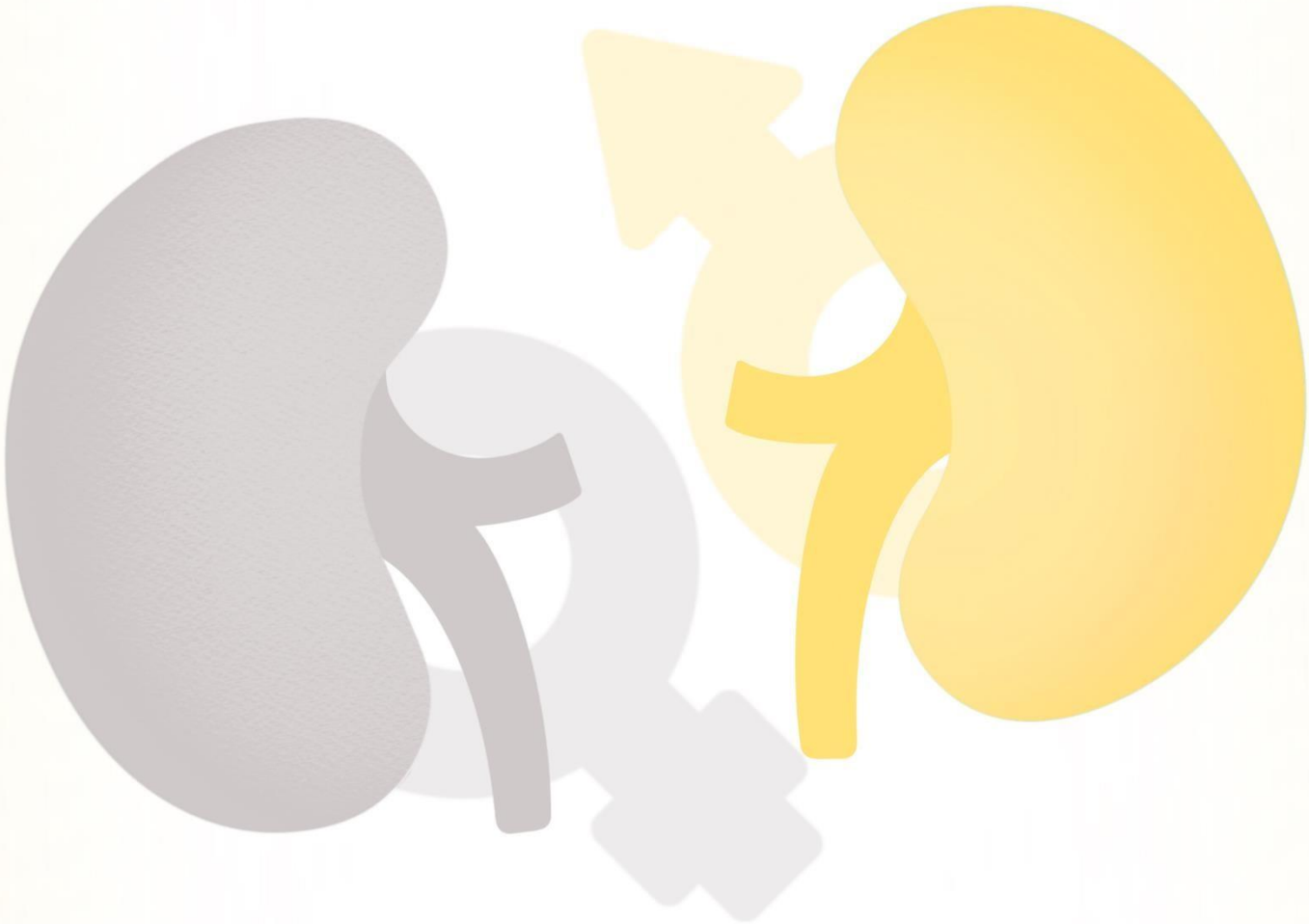

Sheet: female reproductive system

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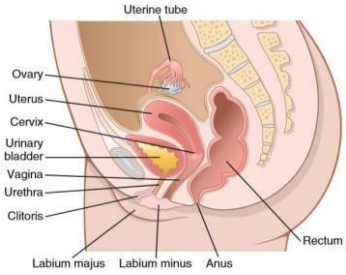
female reproductive system



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 (pregnancy).

The physiologic anatomy:

gonads (ovaries) are the primary organ, where <u>at least one</u> 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 **uterus cervix** and **exterior vaginal organ**.

monthly menstrual cycle (monthly female sexual cycle):

After puberty a monthly rhythmic changes in rate of secretion of female hormones &corresponding physical changes in ovaries and other sexual organs.

duration of the cycle is 28 days on average and range is (20-45) days.

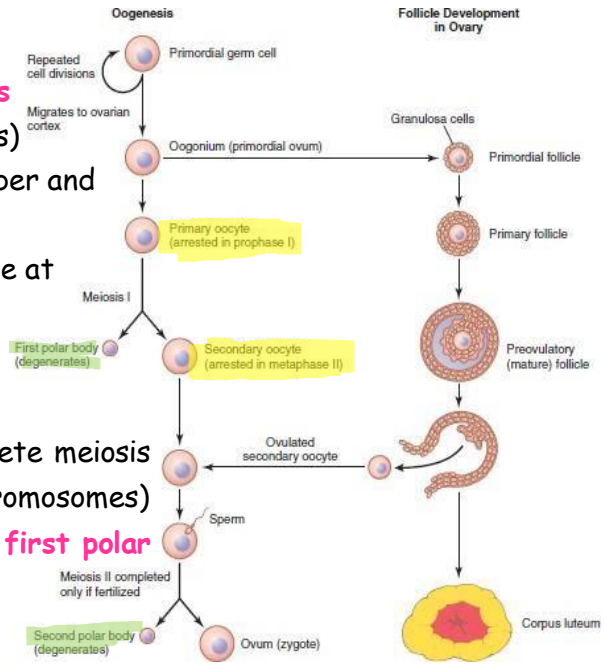
ovarian cycle: changes that take place according to different stages of ovum in the ovary.

<u>results of female sexual cycle:</u> 1-single ovum is released from ovaries every month.

2-uterine endometrium is prepared for implantation of fertilized ovum

Oogenesis: a series of steps that involve the development and differentiation of immature egg (oocyte) into a mature egg (ovum).

1. **In early embryonic life,** primordial cells that originate from yolk sac will migrate to ovaries outer surface and start proliferating repetitively.



2.when it reaches ovaries cortex, we call them **oogonia or primordial ovum,** that will collect around it **granulosa cells** (a layer of ovary stromal cells that look like epithelioid cells) forming **primordial follicle** as these layers increase in number and thickness it's called **primary(immature) oocyte**, arrested in prophase of meiosis 1 (46 chromosomes /diploid). takes place at 5th month of gestation.

3. **At birth,** baby will have about 1 -2 million oocytes (fixed number, don't increase or proliferate).

4 **After puberty,** each month **a primary oocyte** will complete meiosis 1 to produce **one secondary oocyte** (haploid,23 chromosomes) arrested at metaphase of meiosis 2 until fertilization, and **first polar body**(a smaller cell which will degenerate eventually.

when **the primary follicle** start secreting fluids inside and become surrounded by different layers of cell (mainly theca cells) we call it **pre ovulatory follicle (mature).**

Ovulation will take place when **ovum (secondary oocyte)** is expelled out of the follicle into abdomen to be taken up by the fimbria of the fallopian tube (ovum is arrested in metaphase2 until fertilization)

5. **after being fertilized**, **(secondary oocyte)** will finish up meiosis 2 producing an **ovum (zygote)** 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.

1- hypothalamic releasing hormone **(Gonadotropin releasing hormone)** which activates,

2- anterior pituitary sex hormone secretion (Gonadotropins): **follicle stimulating hormone (FSH) and the luteinizing hormone (LH),** that stimulate,

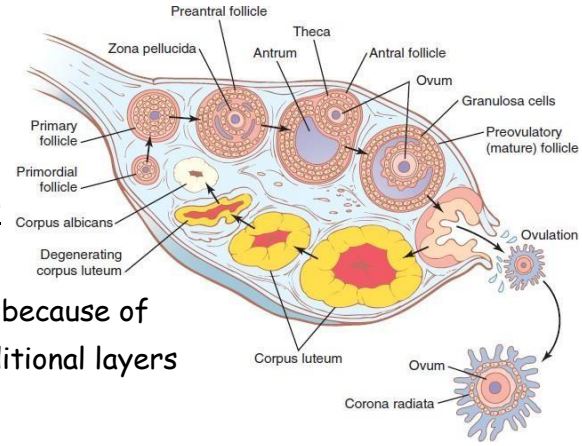
3- ovarian hormones (**Estrogens and progesterone**). parallel to Testosterone in Male

during childhood, without secretion of GnRH, no FSH or LH, so the ovaries are inactive.
After puberty, GnRH is secreted, FSH and LH will be secreted, then the ovaries start functioning.

**The ovarian changes during sexual cycle depend completely on FSH & LH rhythmical secretion. 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 phases:

The follicular phase(preovulatory):



1- In a female child each ovum is surrounded by primordial follicle (single granulosa cell sheath) which provides nourishment for ovum & secrete oocyte maturation-inhibiting factor which keeps the ovum in its primordial state.

2- After puberty (11-13 years), FSH and LH secretion starts because of GnHR -> resulting in: an increase in ovum size & growth of additional layers of granulosa cells forming primary follicles.

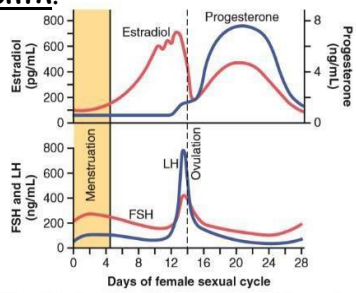
3- Then ovary interstitium collects in several layers outside the granulosa cells to form a second mass of cells called theca (theca interna and theca externa.)

The cyclic changes in the rates of secretion of A pituitary hormones FSH and LH will affect the growth and development of the ovarian follicles. For example, during the first few days (first 2 weeks) of the monthly female sexual cycle there is an increase in the secretion of FSH and LH. which causes the acceleration of growth of **many primary follicles each month**.

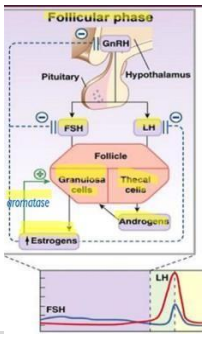
** FSH increase is slightly more & earlier.

FSH has a + effect on granulosa cells to secrete Estrogen as they have the aromatase enzyme needed for this.

LH will stimulate theca cells to produce androgens which can be converted to estrogen in granulosa cells after they diffuse to them



At menstruation (day 0), levels of estrogen and progesterone are very low (almost 0) with increasing levels of FSH and LH. This is mainly due to absence of estrogen and progesterone negative feedback on A pituitary. With the increasing levels of FSH and LH more estrogens is secreted leading to a peak in estrogen during first 2 weeks, accompanied with a reduction in the levels of FSH and LH (negative feedback inhibition). Just before the ovulation, a surge in LH (mainly) and FSH, that is accompanied with increase in progesterone secretion and decrease in estrogen secretion.



(contradictory to negative feedback effect principle, a characteristic for ovarian cycle, the effect of estrogens on the AP is different according to the stage of the cycle).

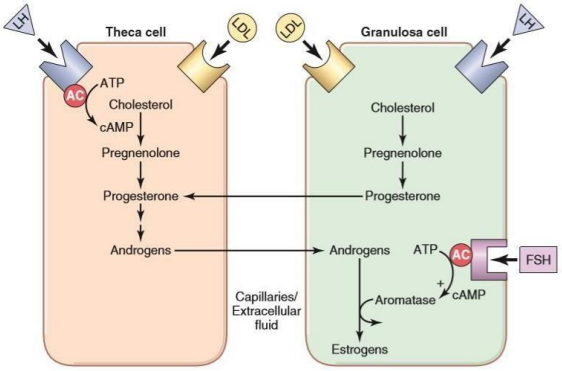
**Estrogen in a nonpregnant woman are mainly synthesized by ovaries (granulosa cells specifically) by aromatase which can give different forms of Estrogen. That differ in potency or availability.
All these forms are produced from cholesterol and androgens (Testosterone, Progesterone, Dehydroepiandrosterone, Androstenedione).
**In pregnant females, estrogen can be produced by placenta.

Beta estradiol: is the primary and major estrogen in nonpregnant females.
Estrone: is found in less amount and its potency < by X 12 times.
Estriol: least potent < X 80 than beta estradiol.

4- Few days after follicles proliferation & growth granulosa cells secrete follicular fluids that contain high concentration of estrogen, which accumulates to form **antrum** forming **antral follicle** (antrum surrounded by granulosa cells that secrete the fluid). 5- The ovum enlarges & remains embedded at one pole of granulosa cells of the follicle forming **preovulatory mature follicle** = **vesicular follicle (Graffian).** (antrum is large and the ovum is at one pole). *Caused by:*

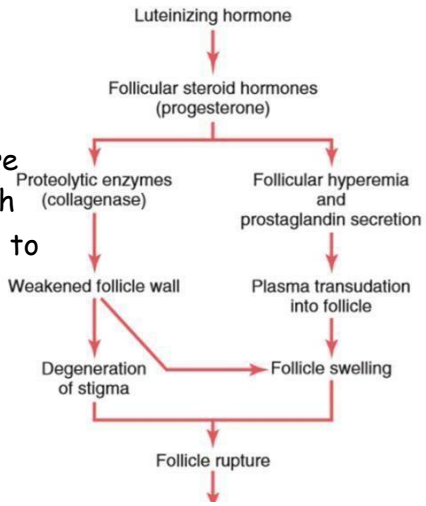
1. Estrogen secreted into follicle causes granulosa cells to increase FSH receptors which causes positive feedback effect to increase estrogens secretion.
2. Both estrogen & FSH combine (synergistic effect) to promote LH receptors on granulosa cells in addition to FSH stimulation, allowing more rapid increase in follicular secretion.
3. The increasing estrogen from follicle plus increasing LH from A pituitary causes proliferation of follicular theca cells & increase their secretion of androgens.

**The early growth of primary follicle up to antral stage is under FSH stimulation only.



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 2nd messenger cAMP to produce androgens which diffuse from theca to granulosa cells to be converted to estrogens by aromatase. During all reproductive years of adult life (13- 46 years), 400- 500 of primordial follicles develop enough to expel their ova—**one** each month. The rest of oogonia will undergo **atresia** (involute).

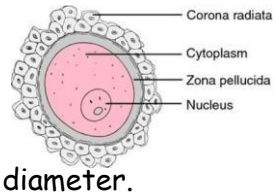
Ovulation



expelling the ovum from graafian follicle. LH is necessary for final follicular growth and ovulation. 2 days before ovulation, the rate of LH secretion will increase significantly 6-16 folds & peaks about 16 h before ovulation, it's absence leads to failure of ovulation even if follicle growth is going very well. FSH increases 2-3 folds & acts synergistically with LH to cause swelling of follicle before ovulation.

**LH has specific effect on granulosa & 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. 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) theca externa begins to secrete proteolytic enzyme and weakens the wall resulting in swelling of the follicle & degeneration of stigma (a small protrusion in the follicular wall).
2) rapid growth of new blood vessels into follicle wall & prostaglandins secreted into follicular tissue gives signals to follicle to undergo swelling stimulating the rupture of the follicle (ovum is expelled).



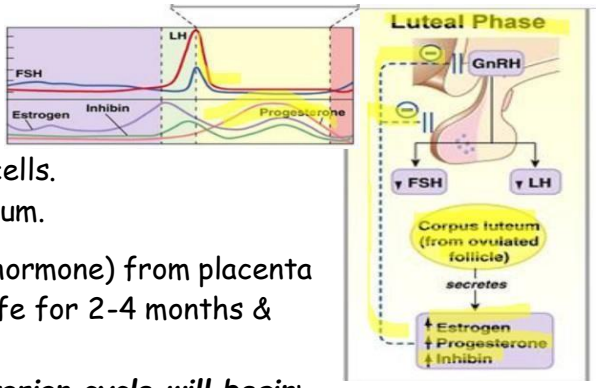
Ovulation occurs 14 days after onset of menstruation in 28 days cycle. During ovulation, stigma protrudes & fluids leaves the follicle, the stigma ruptures allowing more viscous fluid to go outward carrying the ovum surrounded by mass of granulosa cells **corona radiata** and a layer of **zona pellucida.**
The remaining granulosa & theca = **corpus luteum**. 7-8 days after ovulation 1.5 cm in diameter.

**A method to identify day of ovulation: measure body temperature during ovarian cycle because progesterone secretion after ovulation is accompanied with increase of body temperature about .5 F.

"Luteal" phase of the ovarian cycle

- After ovum expulsion, the remaining granulosa & theca interna cells change to **lutein cells** & become filled with lipid inclusions giving them yellowish appearance.
- Granulosa cells in corpus luteum form large amount of progesterone & estrogen.
- Theca cells form mainly androgens which are converted by granulosa cells into female hormones.

Both LH and FSH have a positive effect on corpus luteum to secrete progesterone and estrogens and **inhibin** (inhibitory factor). These 3 hormones have a negative feedback to hypothalamus and AP.
** inhibition of secreting GnRH, FSH and LH while levels of estrogen & progesterone increase is a characteristic of this phase.



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 corpus luteum.

- If pregnancy occurs, **hCG** (human corionic gonadotropin hormone) from placenta acts on corpus luteum similar to LH action to prolong its life for 2-4 months & promote secretion of progesterone and estrogens.
- no pregnancy, corpus luteum will involute and the ***next ovarian cycle will begin***:
1- Estrogen & progesterone from corpus luteum have strong negative feedback effect on AP to inhibit FSH & LH secretion at the end of the cycle.

2- The lutein cells secrete small amounts of inhibin which inhibit secretion of FSH by A pituitary, reduction in FSH & LH which lead 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 on AP & allowing increased secretion of FSH & LH again. A characteristic for the beginning of a new ovarian cycle.

Good luck.