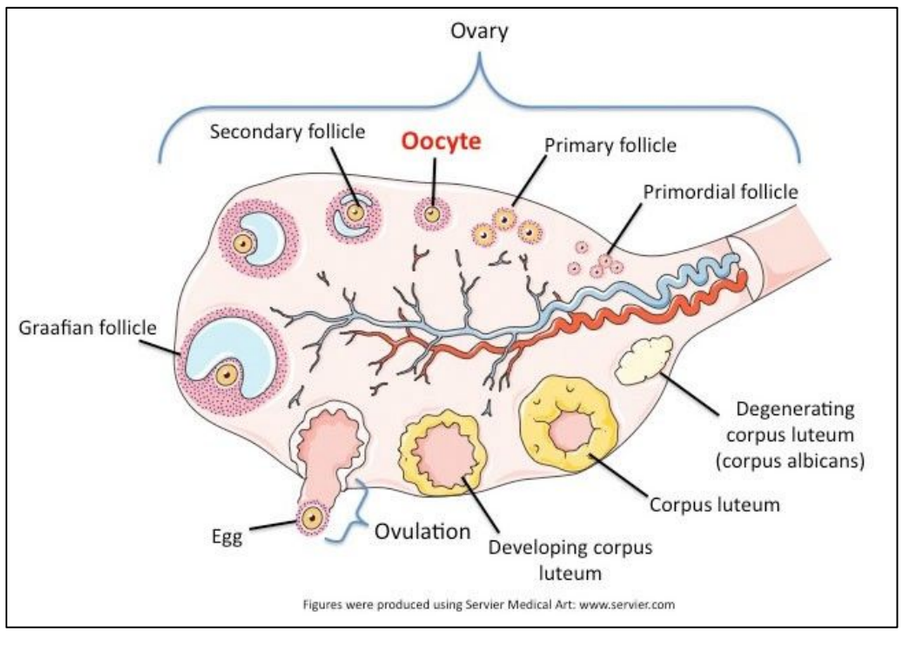
Further Reading

Female Menstrual Cycle

(the cycle will be discussed in the next lecture, in a somewhat less detailed manner)

- The primary female reproductive organ are the ovaries, an almond-shaped organ in the lower abdomen.
- The ovaries produce eggs or the ovum, the functional unit of the ovaries are the follicles. Females are born with immature follicles called "primordial follicles", a follicle of this type consists of a primary oocyte (an immature ovum), surrounded by a relatively flat layer of epithelium, these epithelial cells are known as "granulosa cells".
- Follicles remain immature in the primordial stage throughout childhood, but then suddenly are triggered into maturity during puberty due to the sudden rise in GnRH (GnRH secretion remains low throughout childhood but increases in late childhood to trigger puberty) with subsequent rise in FSH and LH.
- Puberty immediately triggers the the menstrual cycle, which lasts for 28 days monthly, and are divided into two subcycles, an ovarian cycle (which we will discuss), and a uterine cycle (discussed in lecture three, involves menstrual blood). However these cycles occur simultaneously, don't worry, all will be clear by the next lecture.
- Ovulation occurs at day 14 of this cycle. (all days mentioned subsequently are approximations)
- Usually only 6-12 follicles participate in menstrual cycles, with only one follicle releasing its ovum to be fertilized.
- The ovaries contain around 300-500 thousand follicles, 6-12 of which are usually responsive to participate in the menstrual cycle each month, with only one follicle releasing its ovum and the remaining follicles simply degenerate.



Preovulatory (Follicular) Stage: Day 1-11 (High FSH, LH and an initially low Estrogens and Progesterone)

- The cycle start when estrogen and progesterone levels are low, this creates a sudden surge in **FSH** and **LH** secretion which act as trophic factors on the primordial follicles. (They act through cAMP 2nd messenger system, which as we remember can result in increased protein synthesis and trophic effects)
- **FSH** (and to lesser extent LH) binds to the flat granulosa cells surrounding of the primordial follicles and causes them to assume a cuboidal shape and proliferate into multiple layers, the primary oocyte itself enlarges, and some cells from the surrounding connective tissue are recruited to surround the follicles, such cells are called theca cells, these changes cause the primordial follicle (which was lined by a single layer of granulosa cells) to become a primary follicle which harbors a primary oocyte in meiosis I.

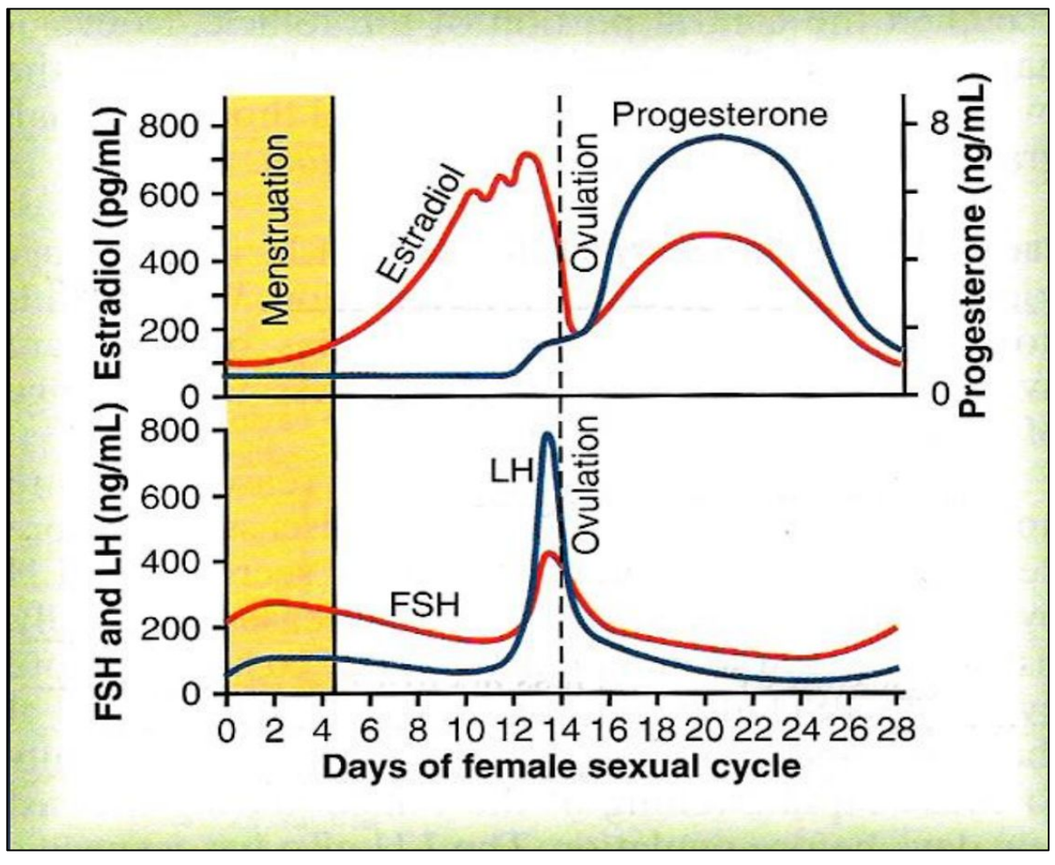
- Granulosa cells are stimulated to secrete estrogen, and theca cells differentiate into theca interna and theca externa. Theca interna turn into secretory cells that secrete androgens (converted by granulosa cells into estrogen by aromatase enzyme), and theca externa form a capsule around the ovary.
- FSH causes granulosa cells to secrete increasing amount of estrogens, which is secreted both into blood and also towards the ovum, not only that, non-selective secretion of fluid and electrolytes also occurs. This causes a pool of fluid and hormones to form inside the follicles, such pool is called an “antrum” , the formation of the antrum causes the primary follicle to become a secondary follicle (as seen in the figure above)
- The secondary follicle then upregulate its LH receptors due to the high amount of estrogen and FSH through complex intracellular pathways, LH causes the cells to proliferate, causes increased proliferation theca cells and the ovum also enlarges almost fourfolds and starts meiosis II and is called a secondary oocyte, and the secondary follicle is now called a tertiary or graafian or vesicular follicle.
- All of these events usually occurs first in a single, dominant follicles before the remaining 5-11 follicles, this follicle then due to its intensive secretion of estrogen causes inhibition of FSH and LH secretion, thus it inhibits the growth of other follicles except itself (its upregulation of FSH and LH receptors causes it to be more sensitized and protected and it will continue to grow)

Preovulatory (Follicular) Stage: Day 7-12 (Low FSH, LH and High Estrogen)

- One dominant follicle continue to grow, while the others lose their trophic support from FSH and LH and become atrophied and fibrosed (atretic follicles)

Preovulatory (Follicular) Stage: Day 12-13 (High FSH, Very High LH, and High Estrogen and Progesterone) and **Ovulatory Stage:** Day 14 (High FSH, Very High LH, and High Estrogen and Progesterone)

- For an unknown reason, one day before ovulation the high level of progesterone and estrogens cause a surge in LH secretion and a slightly lesser increase in FSH secretion. LH causes an increase in progesterone synthesis.
- LH causes the follicles to swell and rupture by promoting swelling (it activates fibroblasts surrounding the follicles, which make more blood vessels around the follicles and it also increases prostaglandin synthesis, which causes increased vascular permeability of those new vessels, therefore swelling of the insides of the follicles occurs) releasing the secondary oocyte into the abdominal cavity to be picked up by the fallopian tubes where fertilization occurs.



Postovulatory (Luteal) Stage: Day 14-25 (Low FSH, Low LH, High Estrogen and Very High Progesterone)

- The ruptured tertiary follicle will contain blood from ruptured blood vessels which will soon clot, and under the effect of LH, the cells will be luteinized (be made yellow) and the tertiary follicle will now be corpus luteum (refer to the figure of the previous page), which is devoid of an ovum.
- LH causes granulosa and theca interna cells to secrete much higher amounts of progesterone than estrogen, progesterone prepares the endometrium of the uterus for implantation, therefore the timing of its release is very strategic.
- The high secretion of progesterone and estrogen will ultimately decrease the levels of FSH and LH, therefore the corpus luteum cells will lose their trophic support and become atrophied, they will be replaced by white fibrous tissue called corpus albicans.

Postovulatory (Luteal) Stage: Day 26-28 (Increasing FSH, Increasing LH, Low Estrogen and Low Progesterone)

- As the corpus luteum become atrophied, the secretion of estrogen and progesterone gradually decreases, FSH and LH increase in their secretion due to loss of negative feedback.
- Now we are back to the hormonal state of day one, a new cycle can thus be initiated.