Physiology

● Sheet ○ Slide ○ Handout

Number

12

Subject

Female reproductive system

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Date:

Price:

Notes:
1- This sheet was written according to the record of section 1.
2- This sheet has some added information from different sources (Guyton, Dr. Faraj...) in order to make it easier and more understandable.
3- The arrangement of topics is a little different from the record.
4- The first part of this sheet will continue to talk about male reproductive system, then we will start talking about the female reproductive system.

Semen:

The semen is composed of 10% sperms and the rest are secretions. 60% of these secretions are from the seminal vesicle, 20% are from the prostate, and the other 10% come from the mucus glands especially the bulbourethral glands. The secretions from these accessory glands promote sperm survival and fertility.

The semen contains fructose which is essential for the nourishment of the sperms; it also contains enzymes, amino acids, acids, electrolytes, etc. Some of these enzymes in the semen were not intended to have their action on the sperm; rather they were intended to work on the ovum, such as *proteolytic enzymes* and hyaluronidase *enzyme.*

Hyaluronidase enzyme function is to lyse the tissue around the ovum ([Guyton: Hyaluronidase depolymerizes the hyaluronic acid polymers in the intercellular cement that holds the ovarian granulosa cells together] - you will understand this sentence at the end of the sheet). This enzyme is not a product of the accessory glands; rather its source is from the sperm. It's used widely in the dental field especially against inflammation and infection of the gums, and is also used in cosmetics.

In addition, the semen contains clotting enzymes from the prostate (these enzymes are different from the clotting enzymes in the blood). When the semen is ejaculated in the female reproductive system it immediately clots, and after few minutes this clot dissolves (liquefies) under the effect of fibrinolysin enzyme which is a product of the prostate also. The purpose of this clotting is to prevent the loss of the ejaculated semen ([Guyton: it holds the semen in the deeper regions of the vagina where the uterine cervix lies.]) and it gives some time for the capacitation process to occur).

Note: according to the anatomy lectures, Dr. Faraj said that the secretions of the prostate glands contain proteolytic enzymes which lyse the fibrin clot caused by the seminal vesicle fluids.

Reproductive dysfunction:

If we want to know the causes of reproductive dysfunction for a patient we should do physical examination for him, ask for his medical history, perform semen analysis, hormone stimulation test, and genetic analysis.

Semen analysis: this test is performed 3-5 days after sexual abstinence.

- The first value in this test is the volume of semen ejaculated which is usually 3-4 ml, but it can range from 1-7 ml (follow the table below).
- The second value is sperm count. Usually 100 million sperm/ml, ranging from 20 million to 120 million in 1 ml of semen. Below 20 million the male is considered infertile.

Oligospermia: low sperm count (below 20 million).

Azospermia: no sperms at all.

Table 8.2 Seminal fluid — mean values for a fertile semen

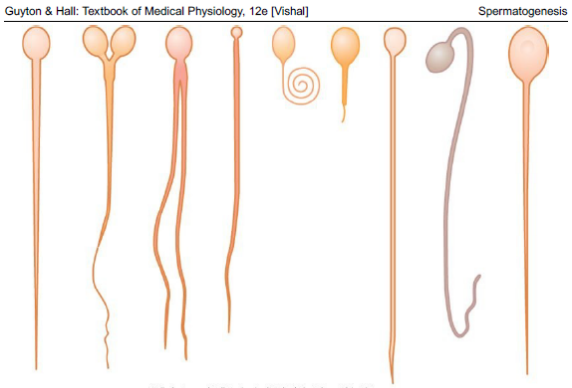
Volume	3.5 ml (Range 1-7 ml)
Sperm count	100 million/ml (minimum 20 million/ml)
Motility	Normal in more than 60 per cent of total
Morphology	Normal in more than 60 per cent of total
Secondary liquefaction	Complete within fifteen minutes
Fructose content	2.2 g/l

Inflammatory cells and blood elements should be absent; spermatozoal precursor cells should not exceed 10 per cent of sperm count

* Oligospermia: Low sperm count (below 20 millions/ml.
* Azospermia: No sperms at all.

- The third value is motility. Not all the sperms are motile; normally 70% of sperms in the semen are motile (ranging from 65% to 75%).
- The fourth value is morphology. Normal morphology should be found in more than 70% of the sperms (ranging from 65% to 75%).

This picture shows abnormal morphology of the sperms. The right one is normal and the others are abnormal (two heads, two tails...)



Hall: Guyton and Hall Textbook of Medical Physiology, 12th Edition

Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.

- The fifth value is secondary liquefaction. As said earlier, after ejaculation the semen clots, and after few minutes it liquefies. Normal liquefaction time is 15-30 minutes. If it takes more than 1 hour, the male may be infertile. That's because the sperms after 1 hour in the "clot state" will become immotile.
- The sixth value is fructose content. Normally it's 2.2g/L.

Note: no inflammatory cells or any blood elements should be found in semen.

The sperm should reach the fertilization site (upper third of oviduct) within 30 minutes up to 60 minutes after ejaculation. The percentage of sperms reaching the fertilization site is 0.001%. That's why the male ejects a large number of sperms per semen, so that a sufficient amount can reach the fertilization site, and one of them can be able to penetrate and fertilize the ovum.

Side effects of testosterone injection:

Testosterone injections can decrease the level of LH in the body (-ve feedback), consequently it decreases the level of testosterone produced from natural sources. Also, it can lead to homosexuality (similar to steroids).

These are the only information that were mentioned by Dr. Khresha assuming we talked about all these topics in histology lectures.

Now, we will start talking about female reproductive system.

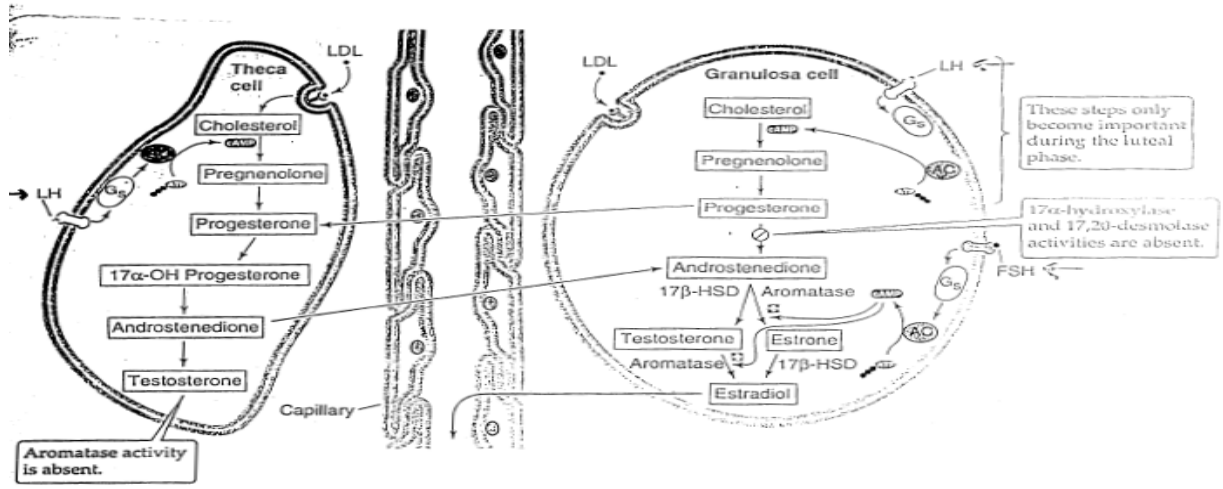
Overview:

The ultimate goal in the female reproductive system is to have normal levels of sex hormones during the different life events (adolescence, pregnancy...) because these hormones regulate most of the physiological actions in the reproductive tract.

Two types of cells regulate the endocrine function of the female sex hormones. These two cells are *theca interna* cells and *granulosa* cells.
Note: the ovum in the female is surrounded by a follicle. it starts as primordial follicle and differentiates to → unilaminar primary follicle → multilaminar primary follicle → secondary follicle → graafian mature follicle. We will reach all these stages before ovulation. In the primary multilaminar follicle will start having 2 types of cells: theca interna + granulosa.

Theca interna cells have receptors for LH hormone, which induce it to make andrognes (testosterone/androstenedlone - a precursor of testosterone). Here estradiol can't be produced from testosterone because the enzyme responsible for this process -*aromatase enzyme*- is missing from theca interna cells.

Granulosa cells, which have the aromatase enzyme, **"absorb" the androgens produced by theca interna cells**. The following actions will take place in granulosa cells under the effect of **FSH**:

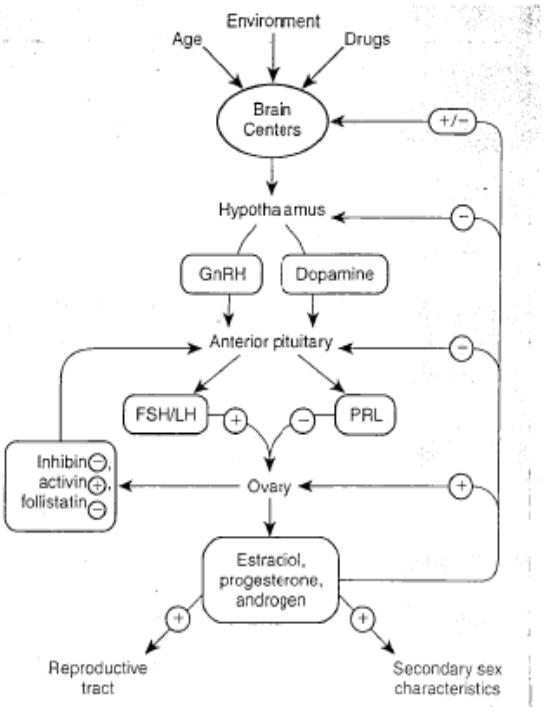


1- Converting testosterone to estradiol by aromatase enzyme.
2- Converting androstenedione by 17β-HSD enzyme to testosterone then to estradiol by aromatase enzyme.
3- Converting androstenedione to estrone by aromatase enzyme then to estradiol by 17β-HSD enzyme.
LH hormone also has an effect on granulosa cells, especially in the luteal phase (will be explained later) of the menstrual cycle. Under the effect of LH progesterone is produced from cholesterol. Progesterone can't produce androstenedione in the granulosa cells because the enzyme required for this -*Desmolase enzyme*- is absent. Instead, progesterone passes to theca interna cells and there, under the effect of LH also, it can be converted to androstenedione.
So, these two cells function as one unit; they can't work alone.

Regulation of the reproductive tract in the female:

The regulation here is kind of similar to what we have in the male.
Age, environment, drugs, endogenous hormonal state, stress levels, and diseases affect the brain centers➔Brain centers affect the hypothalamus which in turn releases GnRH and dopamine➔ GnRH and dopamine affect the anterior pituitary which secretes prolactin and gonadotropins (FSH/LH)➔

a. Prolactin has an:1) inhibitory effect on producing hormones from ovaries, and by that it can inhibit the pregnancy. Actually in 50% of the females who are subjected to prolactin can't be pregnant. 2) Prolactin induces milk formation in nursing mothers; so 50% of nursing mothers can't be pregnant.
b. FSH/LH have a stimulatory effect on ovaries to produce androgens, estradiol, and progesterone. Both LH and FSH regulate follicular steroidogenesis and androgen and estradiol secretion, and LH regulates the secretion of progesterone from the corpus luteum (will be explained later).



Androgens, estradiol, and progesterone have negative feedback effect on the anterior pituitary (They inhibit the release of FSH and LH).
Ovaries also produce Inhibin, Activins, and Follistatin.
Inhibin and follistatin have a negative feedback on FSH release from the anterior pituitary. Activin increases the secretion of FSH.
Note: Inhibins and activins can be produced from granulosa cells, pituitary, brain, adrenal glands, kidney, bone marrow, corpus luteum and placenta. Their activity is confined to the reproductive system.

Ovaries, hormones, and reproductive system cycles:

Ovaries are the primary sex organs in the female. They produce hormones (estrogens and progesterone) and ova.

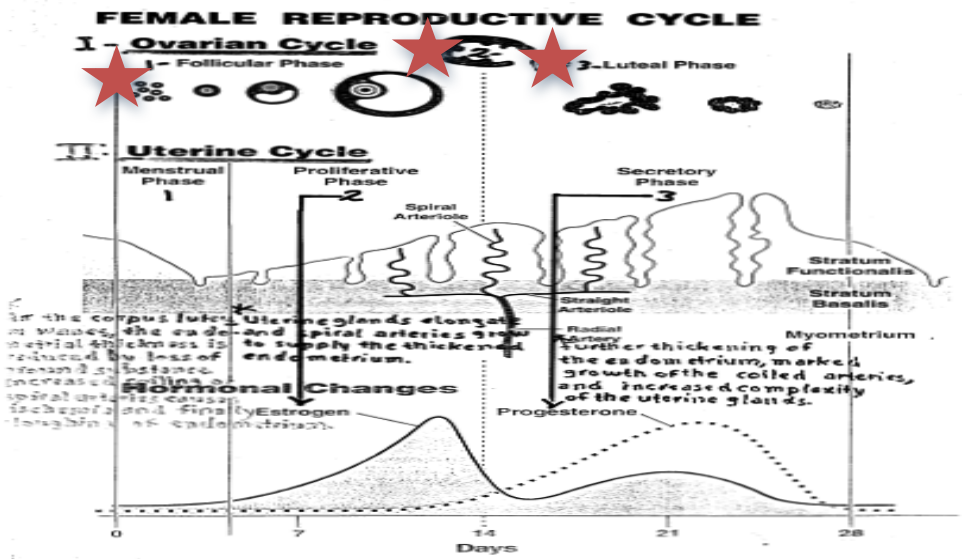
Estrogens are responsible for the female phenotype (female characteristics). It's responsible for the development of secondary sex characteristics and sex organs at puberty (ovaries, fallopian tubes, uterus, and vagina).
Progesterone is considered as pregnancy hormone.

The ovum produced is surrounded by a *follicle*. Follicle and ova formation starts early in the fetal life, at the 30th week of gestation 7 million ova are present in the two ovaries. 2 million of them will be present at birth and the others will degenerate. Only 300,000 - 400,000 will be available at puberty.
During all the reproductive years (13-50 years old) about 450 ova are ovulated, one each month substituting between the two ovaries (if the first ovary ovulates in this month, the second ovary will ovulate in the next month and so on - but this rule could be broken).
Throughout the reproductive life, 90% to 95% of all follicles are found as primordial follicles (the first stage of follicle development. They are a non growing-inactive follicles).
Throughout the fetal life and childhood, some primordial follicles develop to primary follicles, but they degenerate eventually (they don't reach mature state).

There are two *cycles* that occur in the female reproductive system at puberty: ovarian cycle and uterine cycle. These two are part of the menstrual cycle.

> Wiki note: The menstrual cycle is the regular natural change that occurs in the female reproductive system (specifically the uterus and ovaries) that makes pregnancy possible.

When these two cycles begin, they don't stop until reaching menopause (except pregnancy and diseases). They occur regularly every 28 days. The ovarian cycle dominates the uterine cycle , that means if the ovarian cycle didn't occur, then the uterine cycle won't occur either.
The first day of the menstrual cycle is counted when the woman has menses (when she bleeds). In the day 14 (in the middle of the cycle) ovulation occurs.



The ***ovarian cycle*** is composed of three phases: follicular phase, ovulation phase, and luteal phase:-

- When the female infant is born, she has follicles called primordial follicles which will undergo further development at the time of puberty in order to be ovulated. At the *follicular phase* **(day 0-14 of the menstrual cycle)** the follicles develop, they are activated and get ready to be ovulated.

-*follicular phase*: 2-3 days before the end of the previous cycle, genetically induced, FSH levels get slightly high, and about 10 follicles start the process of maturation under the effect of FSH, they develop from primordial follicles to become primary follicles. These primary follicles can produce estrogen. One of them will get very large, have a lot of blood supply, and will be very sensitive to FSH, it's called dominant follicle [Note: the dominant follicle because of its big size will release high levels of estrogen which works on the granulosa cells and make more receptors for FSH on it, thus being more sensitive to FSH]. The high amount of estrogen released, as a negative feedback, will reduce FSH secretion from the anterior pituitary. The small amount of FSH will be sufficient for the dominant follicle to continue developing since it's more sensitive, but it's not sufficient for the others (they will degenerate). There is another reason for the degeneration of the other follicles, which states that they don't produce sufficient amounts of the estrogens, instead, they concentrate the androgens inside them in the form of dihydrotestosterone which can't be used to synthesize estrogens.

The primary surviving follicle will develop to secondary follicle, and eventually to mature graafian follicle.

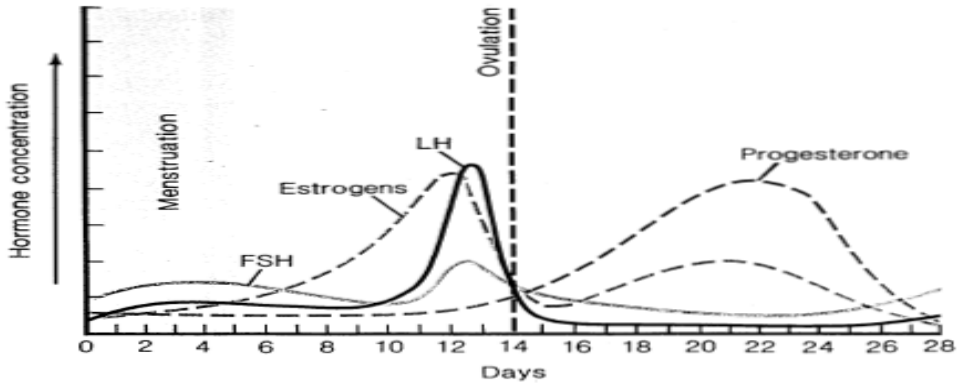
Shortly before the ovulation, the graafian follicle will start to rupture and to be filled with fluid, which eventually leads to the explosion of the ovum from the follicle. So that at the time of ovulation, we will have the ovum and the ruptured follicular cells (follicle remnants).

- At the *ovulation phase*, a mature graafian follicle will be ovulated. This happens in the middle of the menstrual cycle at **day 14**.

-At the *luteal phase* **(day 14-28)** the *corpus loteum* will be formed. After ovulation, the follicle remnants under the effect of LH will form the corpus loteum. Corpus luteum in turn will produce progesterone (mainly) and estrogens. If there was pregnancy, corpus luteum will produce progesterone and estrogens until the 3rd month of pregnancy, after that the placenta will do the job. If there was no pregnancy, the corpus luteum will degenerate forming corpus albicans.
So, in the first half of the menstrual cycle we have only estrogen from the follicle itself; in the second half we have progesterone mainly and estrogens from the corpus luteum.

[Note: this part was not mentioned by the doctor. In the ***uterine cycle*** we have 3 phases: menstrual phase, proliferative phase, and secretory phase.
The *menstrual phase* extends from day 0-4. It's characterized by bleeding from the vagina which indicates the collapse of the previously built endometrium.
The *proliferative phase* extends from day 4-14. In this phase the endometrium is being built, it increases in thickness and spiral arteries develop under the effect of estradiol.
The *secretory phase* extends from day 14-28. It includes glandular development in the endometrium under the effect of progesterone (it matches the luteal phase).]

Hormones:



In the beginning of the menstrual cycle, all of the hormones found in low levels except for FSH (Remember: FSH starts to rise 2-3 days before the previous cycle. it induces the development of primordial follicles to primary follicles) .
After day 10, the estrogen level increases dramatically with its peak at day 13 (remember the dominant follicle).
This very high level of estrogen will lead to a very high LH secretion and less FSH secretion (will be explained in a moment) leading to what is called *LH Surge* which triggers the ovulation process [Note: LH causes rapid swelling of the follicle during the last few days before ovulation, leading eventually to its ovulation] .
So we can say ***estrogen induced LH surge*** **leads to ovulation**.
After ovulation, the follicle remnants will form corpus luteum which will produce progesterone mainly and estrogen as said earlier, so we will very have high levels of progesterone in the second half of the cycle.
In the second half of the cycle, when the level of estrogen and progesterone are high, we will have low levels of FSH and LH (negative feedback mechanisms).

How estrogens stimulate LH release?
The normal level of estrogens is 72 pg/mL. Below 200 pg/mL estrogen has negative effect on LH and FSH release, above 200 pg/mL (and that's the level we reach before LH surge) estrogen has positive effect on LH and FSH release. The effect on LH release is more potent than the effect on FSH.

Thank You!