



Sheets

Physiology

Number

14

Doctor

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Correction

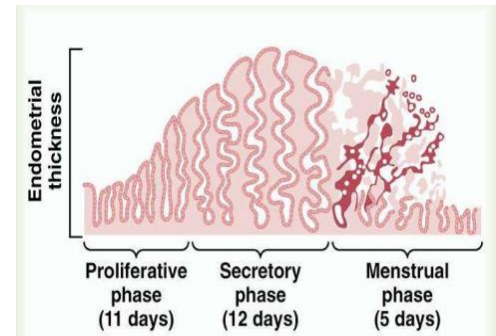
Dina Dahabreh

-Monthly Endometrial Cycle and Menstruation-

In the past, the only thing people knew about menstrual cycle is that there is vaginal bleeding that lasts for a few days, then they discovered that this bleeding is associated with **hormonal changes** in the female body. It is called **menstrual cycle** although menstruation is only the last step of the endometrial cycle.

The endometrial cycle is associated with the monthly cyclical production of estrogen and progesterone by the ovaries which causes changes in the lining of the uterus that happen through the following stages:

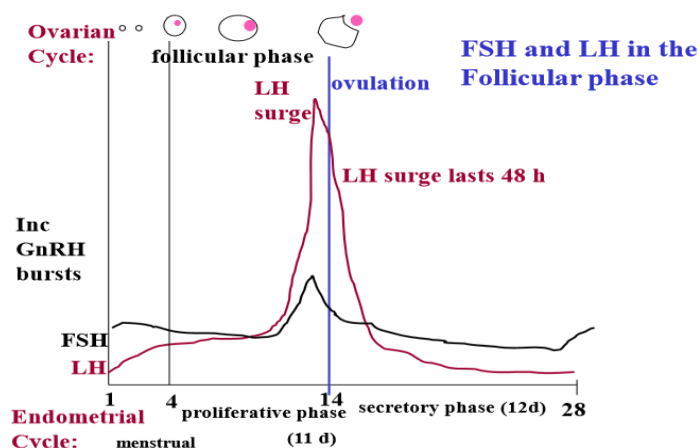
- (1) **Proliferation** of the uterine endometrium.
- (2) Development of **secretory** changes in the endometrium.
- (3) **Desquamation** of the endometrium, which is known as **menstruation**. (Last step)



The hormonal changes are: Progressive **rise in estrogen** followed by progressive **rise in progesterone** followed by a **decrease in progesterone secretion**. (No rise in estrogen = no menstrual bleeding/ no rise or withdrawal of progesterone = no menstrual bleeding).

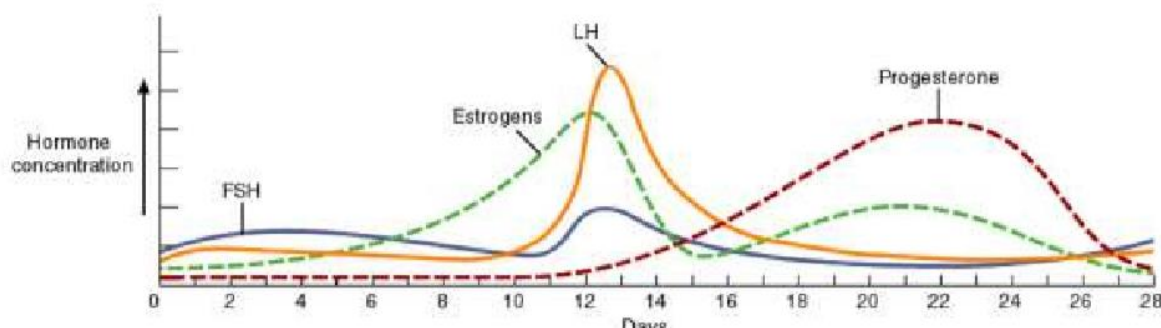
The rise in estrogen levels will cause what we call **structural priming** (formation of different layers in the endometrium) followed by the functional development in the vascular and secretory functions, the withdrawal of progesterone will give less and less support to the endometrial layers until its amount is not enough to maintain their function leading to tissue death.

This tissue death will be followed by **sloughing of that tissue and bleeding**.



Functions of Estrogen:

- 1- Induces mitosis of endometrial cells.
- 2- Induces mitosis of follicles.
- 3- Allows the growth and development of female sex organs (its function in females is like the function of testosterone in males), and after puberty we will have more estrogen because of this cyclicity meaning more development of the female genital system.
- 4- Responsible for secondary sex characteristics (fat distribution, enlarged breasts, skin texture, body contour, widened hips...)
*hair distribution is dependent on androgen (small amount in females, comes from the adrenal glands), responsible for pubic and axillary hair.
- 5- Along with other growth hormones, it helps with the development of bones and muscles.
- 6- Changes the secretory pattern of the cervix and vagina at the end of the proliferative phase to increase receptivity to spermatozoa.



Functions of Progesterone:

- 1- Endometrial metabolic function.
- 2- It rises in the luteal (postovulatory) phase to antagonize the function of estrogen, by the end of the proliferative phase we made the cervix more receptive to spermatozoa by thin secretions, progesterone will antagonize this effect by thick secretions that make the cervix less receptive and more hostile to spermatozoa.
- 3- Changes the thermal state of the body during the luteal phase (increases by about 1 C°).
- 4- Both progesterone and estrogen are important for breast development during puberty stage.

- ➔ Estrogen and progesterone are steroid hormones (can cross membranes without receptors and have an intra-cellular receptor that acts as a transcription factor), any steroid hormone is composed of rings and side chains. The core structure (rings) of progesterone is the exact same one as glucocorticosteroid and mineral corticosteroid, but they differ in side chains; (glucocorticosteroids have hydroxyl groups on C11, C17 and C21 while mineral corticosteroids have two hydroxyl groups and one aldehyde group). When there is high concentration of progesterone, it can bind to mineral corticosteroid receptors and act as a mineral corticosteroid causing more fluid retention in the second half of the cycle since progesterone concentration is high, fluid retention will cause breast congestion (the retention is systemic but can be observed in breasts).

Note that:

- Increased body temperature and breast congestion are signs of increased progesterone concentration.
- Testosterone secretion in males is in continuous patterns (pulsatile actually, but does not have as many variations in concentration as the estrogen and progesterone in the female body which have a cyclic pattern of secretion).

- ➔ Estrogen and progesterone both have **nuclear receptors** to make proteins through mRNA, still, they also have **membrane receptors** for the purpose of **faster action**.

*In general; lipid soluble hormones can have a small percentage of membrane receptors, and water soluble hormones can have a small percentage of nuclear receptors as well.

Differences between Spermatogenesis and Oogenesis

Spermatogenesis	Oogenesis
Spermatogonia proliferate only after puberty. A huge number is produced.	Mitotic proliferation of oogonia occurs prior to birth. A limited number is produced.
Meiotic divisions of primary spermatocyte produce 4 mature spermatozoa.	Meiotic divisions of oocyte produce only one mature ovum.
The products of meiosis (spermatids) undergo substantial differentiation in the maturing process.	Second meiotic division is completed only upon fertilization.
Equal division in all steps.	Unequal division in terms of cytoplasm.
The final product (spermatozoa) will exit the male body.	The final product (ovum) will be sent to the pelvis.

Spermatogenesis:

Migrated cells from yolk sac to genital ridge start to divide but will be arrested as **spermatogonia**, but during development they will be integrated in the seminiferous tubules which are connected to the epididymis then vas deferens until reaching the external genitalia.

After puberty, **almost all** spermatogonia are activated, the second meiotic division is completed in the testis but more maturation will happen in the epididymis.

Oogenesis:

Integration within certain cells called **primordial follicles**. The primordial follicles are not connected to the external genitalia, after reaching the maximum number of follicles, most of these primordial follicles will degenerate.

After puberty: only a few follicles are stimulated, we still have the destructive activity which will reduce the follicle count. There is no second **meiotic** division unless it gets fertilized.

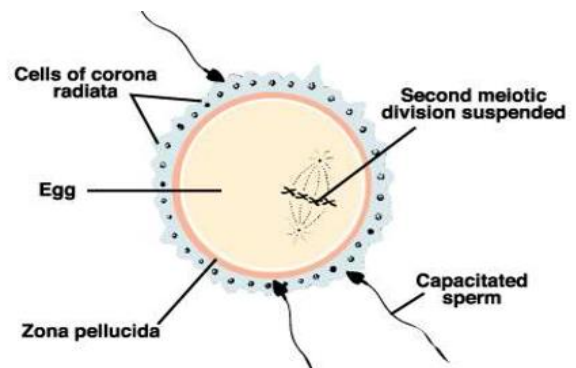
-Fertilization-

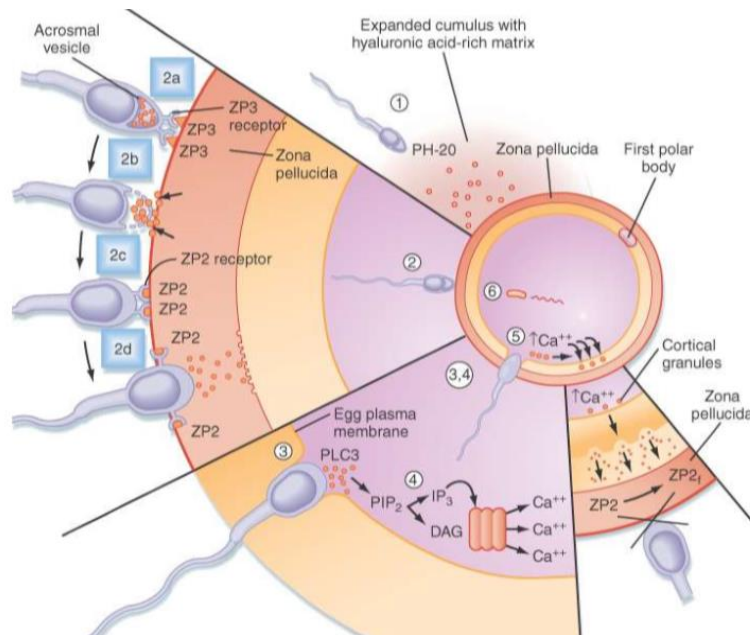
The goal of spermatogenesis and oogenesis is to maintain human race by fertilization (the oocyte will leave the ovary and the spermatozoa should reach the oocyte).

The cervix is hostile to semen except the time just before ovulation when it becomes non-hostile to spermatozoa, once semen is deposited most of it will go outside the vagina. **Seminal plasma will not cross the cervix**, what crosses the cervix is **spermatozoa**, and remember that most of the spermatozoa are abnormal in shape or structure, **very few will cross the cervix only when the environment allows it** (at the end of the follicular phase when estrogen is at its highest). So out of these millions of spermatozoa, very few will get across the uterus, once they cross they may continue their way towards the right or the left (randomly).

The spermatozoa **cannot** penetrate cells other than the oocyte because of certain mechanisms of inhibition.

While a spermatozoid is in semen, it cannot fertilize any oocyte, it has to be **capacitated** in order to fertilize the oocyte, which happens when the sperm leaves the semen that contains inhibitory enzymes





Ovulation happens either in right or in left ovary, the fimbria of the uterine tube will pick up the oocyte. The oocyte wall is composed of these layers: **corona radiata, zona pellucida and cortical granules**. Zona pellucida contains certain proteins (ZP2, ZP3) that act as **receptors** and bind to certain proteins on the head of a spermatozoid (that's why a spermatozoid cannot penetrate cells other than oocyte).

More than one sperm can bind to zona pellucida, **but once a single sperm gets past zona pellucida there will be changes that prevent other sperms from entering.**

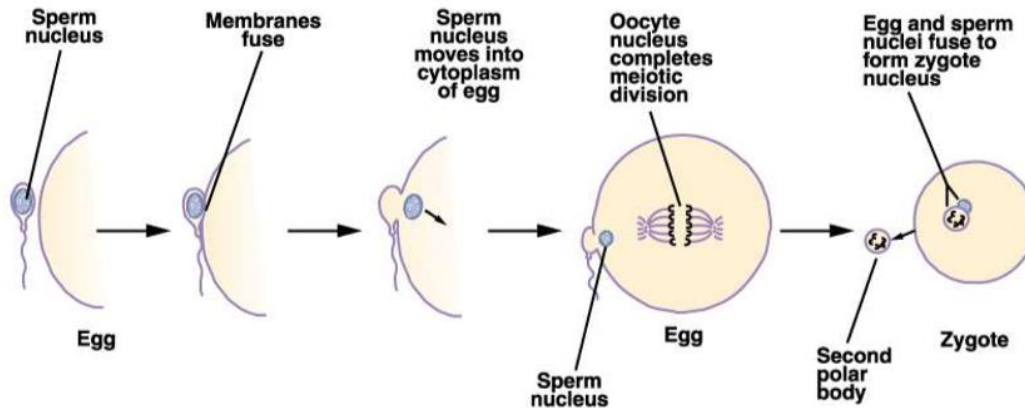
First of all, there will be a **reverse in polarity (electrical changes)**, which will prevent sperms outside from penetrating the oocyte.

Then there will be release of Ca^{+2} and subcapsular proteins which will increase the osmotic pressure creating a barrier of fluid to prevent other sperms from passing.

Once the membrane of the spermatozoid fuses with the membrane of the oocyte it will eject its content (nuclear material) into the cytoplasm, stimulating two important things:

- **The enzymatic machinery of the cell.**
- **The second meiotic division of the oocyte.**

The nuclear material of the oocyte and sperm fuse creating a **zygote**, the meiotic division also produces a **second polar body** (containing very little amount of cytoplasm) which will degenerate.



- Sixteen hours are needed from penetration until reaching the state of zygote.
- Oocyte can stay in the fallopian tube up to 16 hours.
- Spermatozoa can stay in the female reproductive system up to 96 hours.

The zygote will start mitotic divisions (doesn't have to be $1 \rightarrow 2 \rightarrow 4 \rightarrow 8 \rightarrow 16 \dots$, one cell may be dividing faster than another), the maternal cytoplasm contains nutrient material that can help the structure survive up to 2 days depending on cytoplasm alone (it can take nutrient material from the surroundings). Divisions continue until we reach the **blastocyst** stage in 4-5 days, before this stage all the cells are **totipotent** which means that any cell can make up an individual, so this structure can form more than one individual, but after (or even a little before) reaching the blastocyst stage we **cannot make more than one individual, which means that we started to have differentiation of cells**. A blastocyst is formed of:

- **Inner cell mass** that forms the **embryo**.
- **Outer cell mass** that forms the **placenta**.

Fertilization happens normally in **the ampulla of the fallopian tube** (still ectopic pregnancy can happen), it needs five days to reach the endometrium (blastocyst stage at this time). The nutrient material in the cytoplasm would have been consumed by this time and it will depend on the secretions of the uterine tube and the endometrium for nutritional support.

Five days after fertilization we will have a rise in progesterone level (secretory endometrium which is rich in fluids and lipoproteins) creating an appropriate media to contain the blastocyst, diffusion will not be enough to meet the needs of the embryo, that's why we will need to find another way to fulfil the needs of the developing blastocysts, which starts by **implanting** the cyst in the endometrial wall.

-Implantation-

About 6 days after fertilization, it needs:

- **a receptive secretory endometrium**
- **a functionally normal blastocyst**
- **an adequate cross-communication**

We said earlier that the cyst has inner cell mass and outer cell mass, the outer cell has two important functions:

- **build a vascular interaction with the endometrial wall** to gain nutrients and get rid of waste products.
- secretion of a glycoprotein **hormone called human chorionic gonadotropin (hCG)**.

Human chorionic gonadotropin hormone has 2 subunits:

- Alpha
- Beta: which has LH activity (mostly) and FSH activity.

Once hCG is secreted (about day 7, even in small amounts) it can be absorbed by endometrial wall to reach the maternal circulation going everywhere in the female body, including **corpus luteum**, preventing it from degenerating.

*Thanks everyone for the awesome three years, hope the rest
would be even better.*

Good Luck!