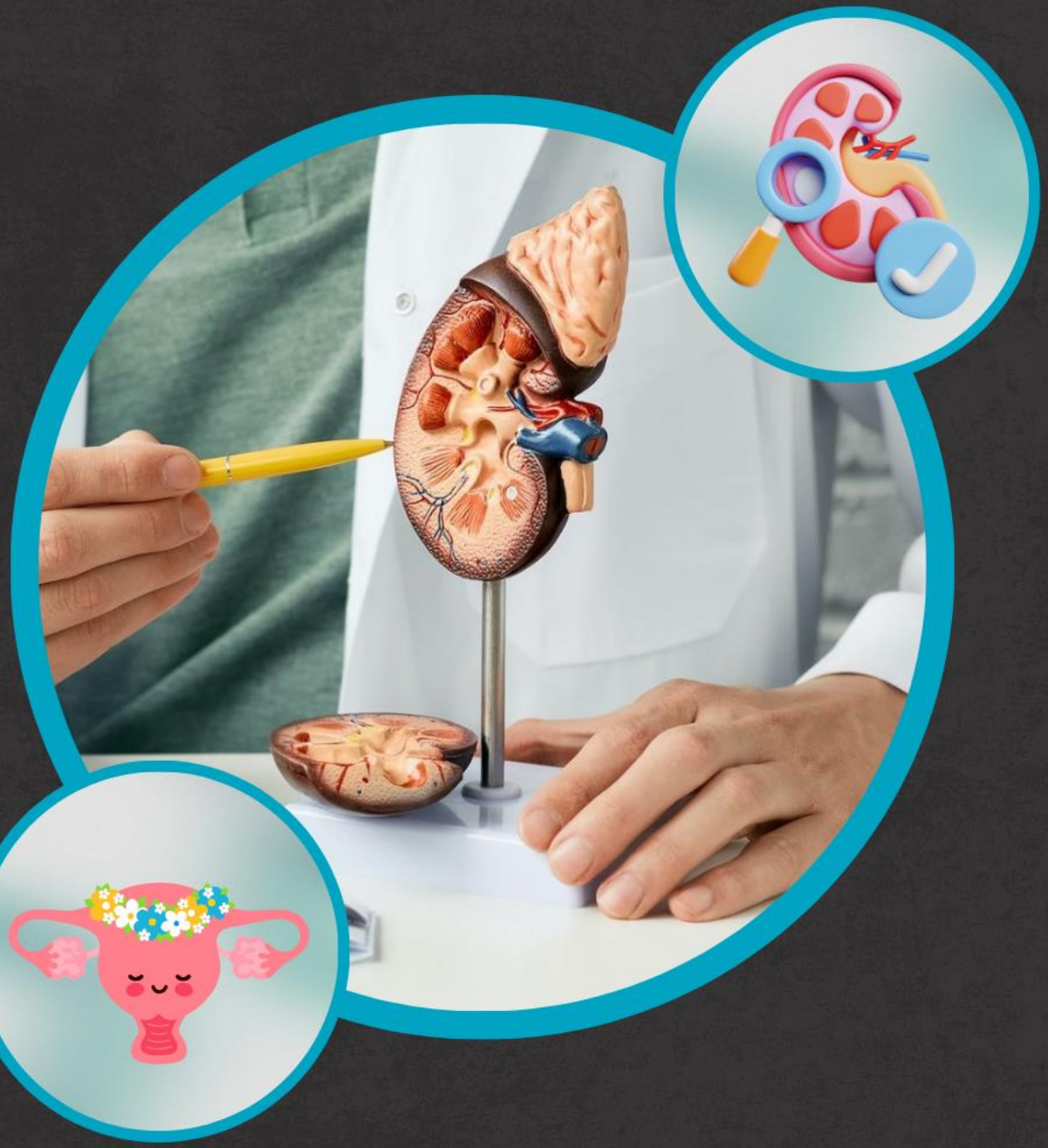


PHYSIO

MODIFIED NO. 14

الكُتّاب: زيد المنسي و محمد مجيد

المدققين: عدي الشنيطي

الدكتور/ة: الاء بواعنة

NOTES

Notes under the slides from doctor will be in this box

Color code

- Slides
- Doctor
- Additional info
- Important

Chick the additional Sourses in the last slide

Reproductive Physiology

Female Physiology Before Pregnancy and Female Hormones
Female reproductive functions

Chapter 82

In previous lecture, we talked about ovarian cycle, follicular phase (preovulatory phase) and ovulation.

We said that follicular phase is under the control of FSH hormone (released from anterior pituitary) > stimulate more than one follicle at the same time (8 – 12) follicle, but only one of them will reach the ovulatory stage.

This successful follicle will inhibit the Anterior pituitary from releasing high amounts of FSH > degradation of other follicles.

This follicle will stimulate high levels of Estrogen > High LH hormone before ovulation (15-24 hours) > rupture of the follicle > release (ovulation) of the 2ndary oocyst into fallopian tube.

These are the first 2 phases, now, we will talk about 3rd phase.

The Luteal Phase

After ovulation. The follicle will remain in the ovaries > swelling > fat accumulation > yellow appearance = Corpus Luteam.

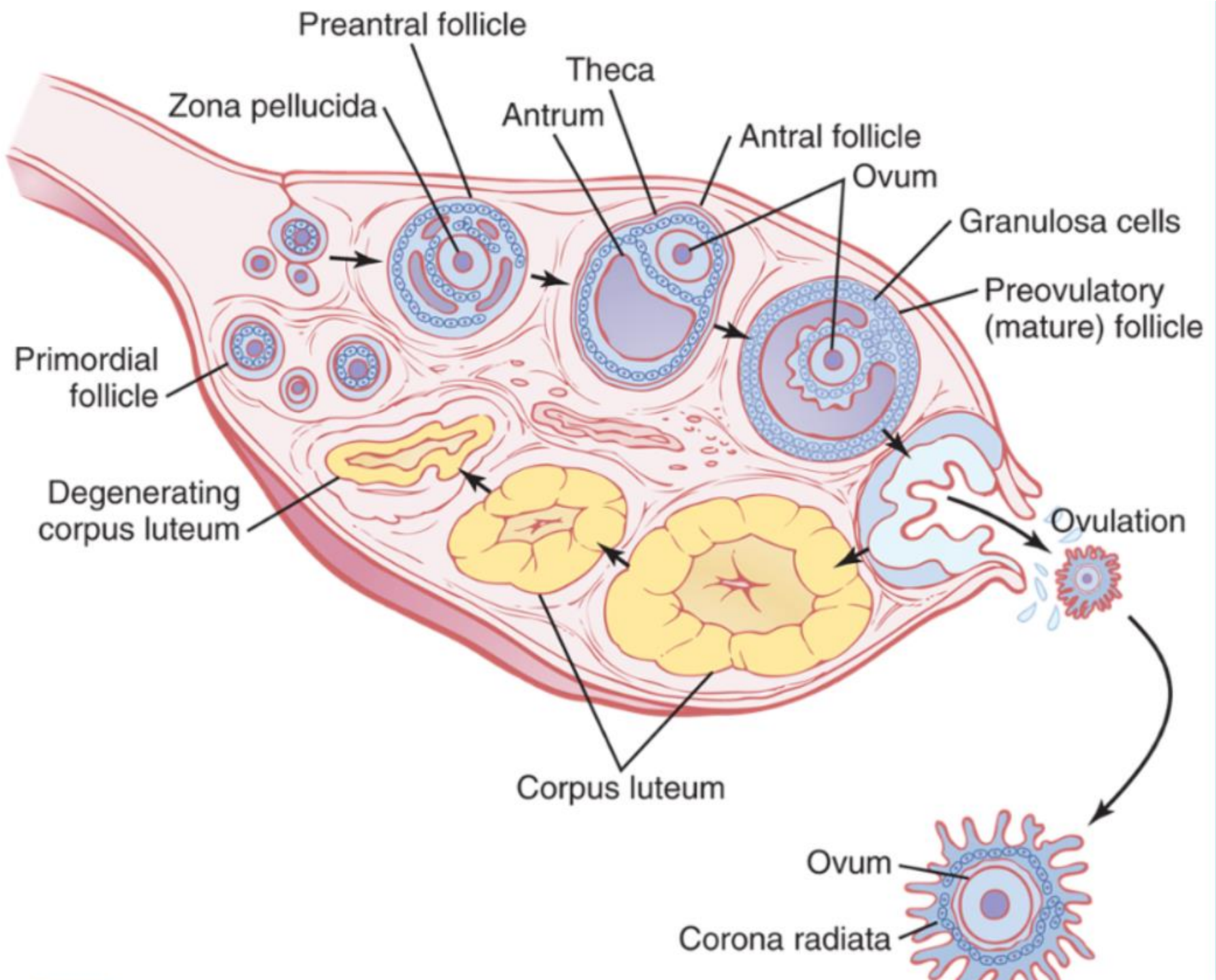
Corpus luteam plays a crucial role in the second cycle of follicular phase (preovulatory) = Progesterone production.

Corpus luteam will stay for 2 weeks, waiting for secondary oocyst (if it will be fertilized or not).

If fertilization occurs > Implantation of the fertilized egg in the uterus > keeping pregnancy inside the uterus.

Progesterone produced by Corpus luteam will help in maintaining the pregnancy inside the uterus.
LH from Ant.pituitary will keep Corpus luteam functional.

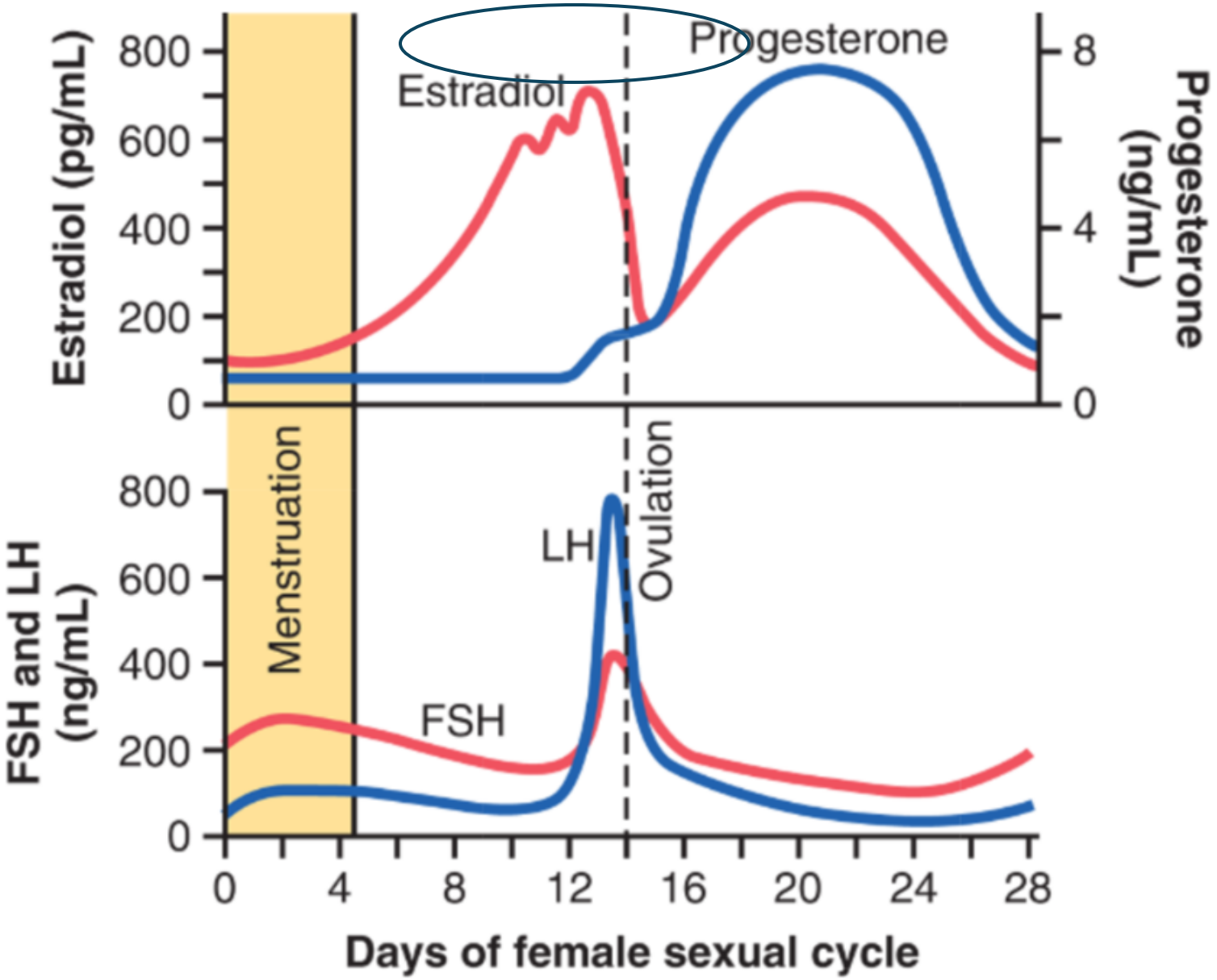
If no fertilization takes place > Corpus luteam will loose its charachteristics (loose fat, become white) > scarr inside ovary = Corpus albicans.


Preantral follicle
Theca
Zona pellucida
Antrum
Antral follicle
Ovum
Granulosa cells
Preovulatory
(mature) follicle
Primordial
follicle
Degenerating
corpus luteum
Ovulation
Corpus luteum
Ovum
Corona radiata

Note:
Estradiol = Estrogen

ماشيين مع بعض
Estradiol //// FSH

This cycle is not always 28 days, it might be longer or shorter, but post ovulatory phase is always 14 days (always fixed).
So, to know the day of ovulation = Cycle length – 14



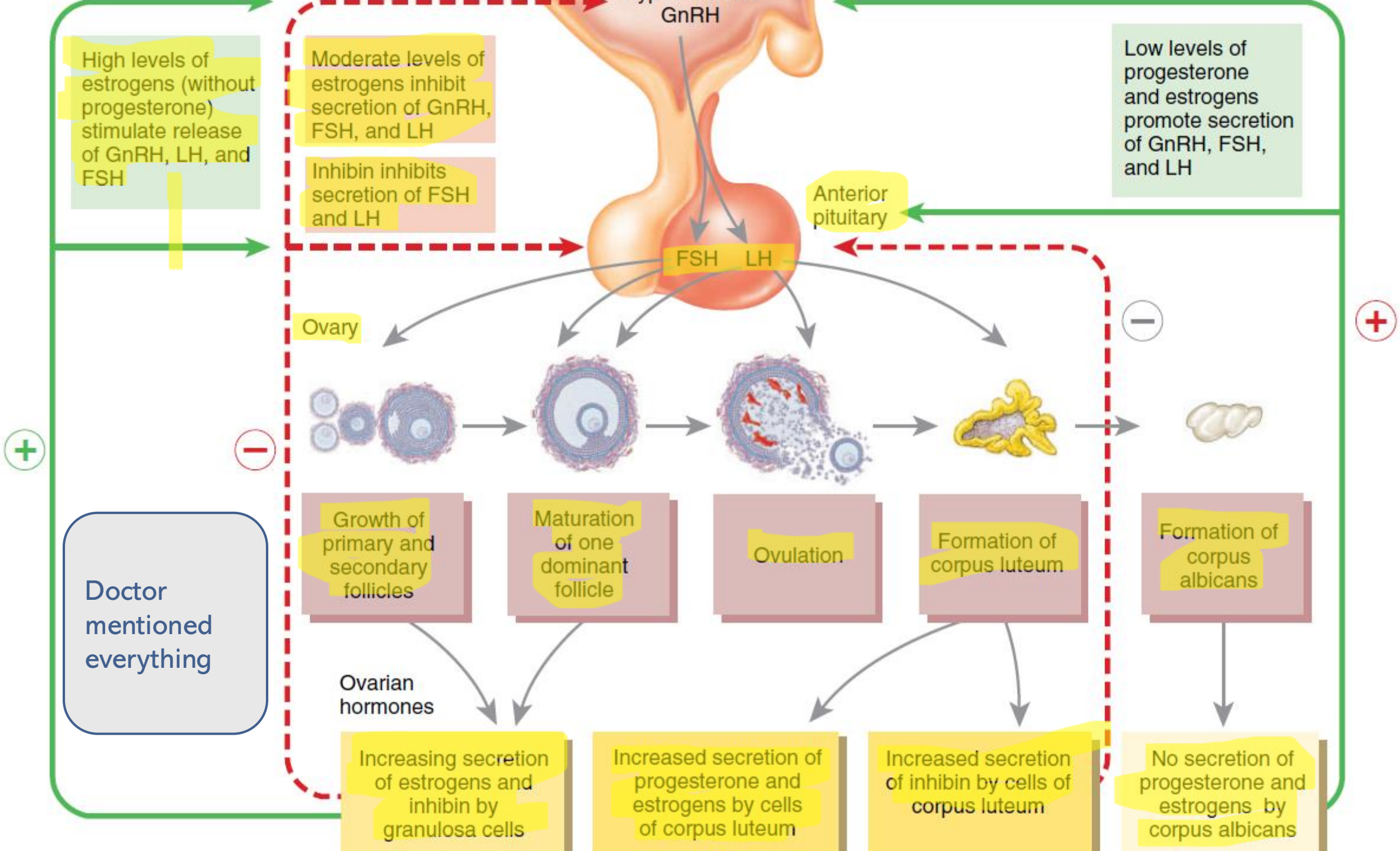
The first part of ovarian cycle, only FSH hormone is responsible for follicle maturation.

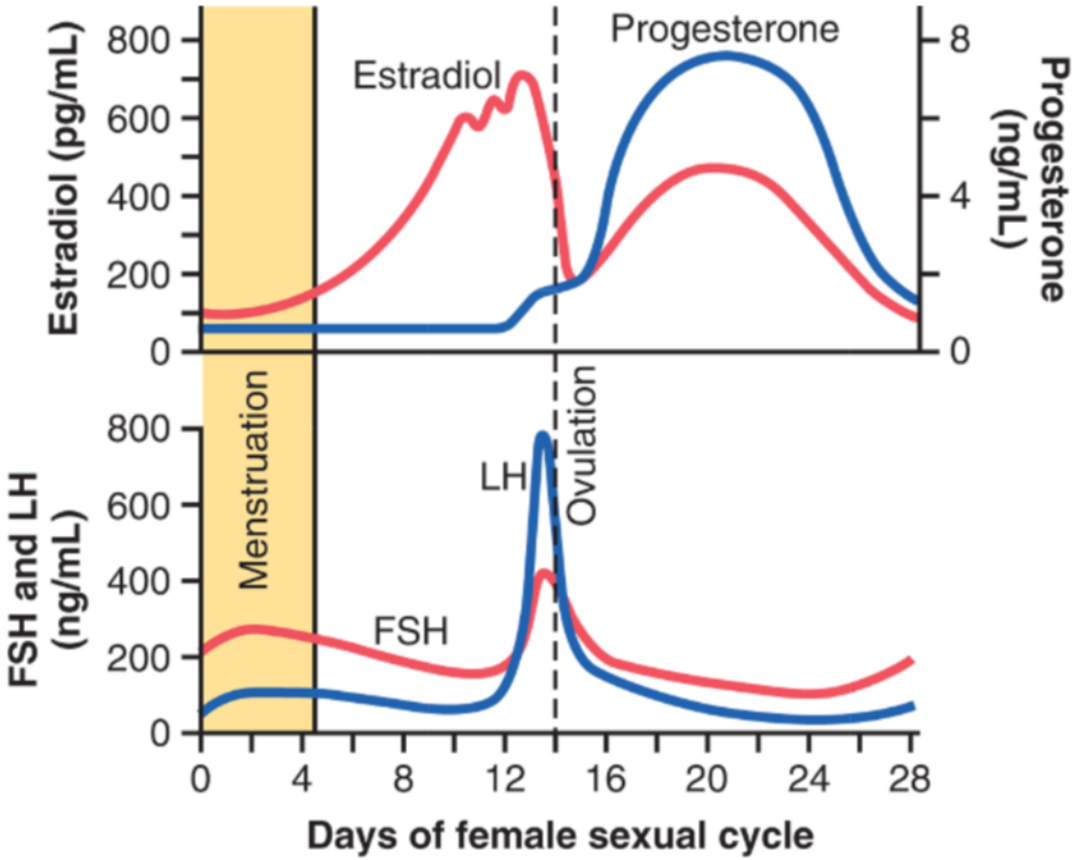
Only LH surge is responsible for ovulation process.

After the second part of the cycle, FSH and LH hormone will be reduced.

Corpus Luteum

- During the first few hours after expulsion of the ovum from the follicle, the **remaining granulosa and theca interna** cells change rapidly into **lutein cells.**
- They **enlarge** in diameter two or more times and become filled with **lipid inclusions** that give them a **yellowish appearance**.
- 12 days after ovulation → the corpus luteum begins to **involute** and eventually **loses its secretory function** and its **yellowish, lipid characteristic** about, becoming the corpus albicans; during the ensuing few weeks, the corpus albicans is **replaced by connective tissue** and over months is **absorbed.**


GnRH
High levels of estrogens (without progesterone) stimulate release of GnRH, LH, and FSH
Moderate levels of estrogens inhibit secretion of GnRH, FSH, and LH
Inhibin inhibits secretion of FSH and LH
Low levels of progesterone and estrogens promote secretion of GnRH, FSH, and LH
Anterior pituitary
FSH
LH
Ovary
Growth of primary and secondary follicles
Maturation of one dominant follicle
Ovulation
Formation of corpus luteum
Formation of corpus albicans
Ovarian hormones
Increasing secretion of estrogens and inhibin by granulosa cells
Increased secretion of progesterone and estrogens by cells of corpus luteum
Increased secretion of inhibin by cells of corpus luteum
No secretion of progesterone and estrogens by corpus albicans
Doctor mentioned everything

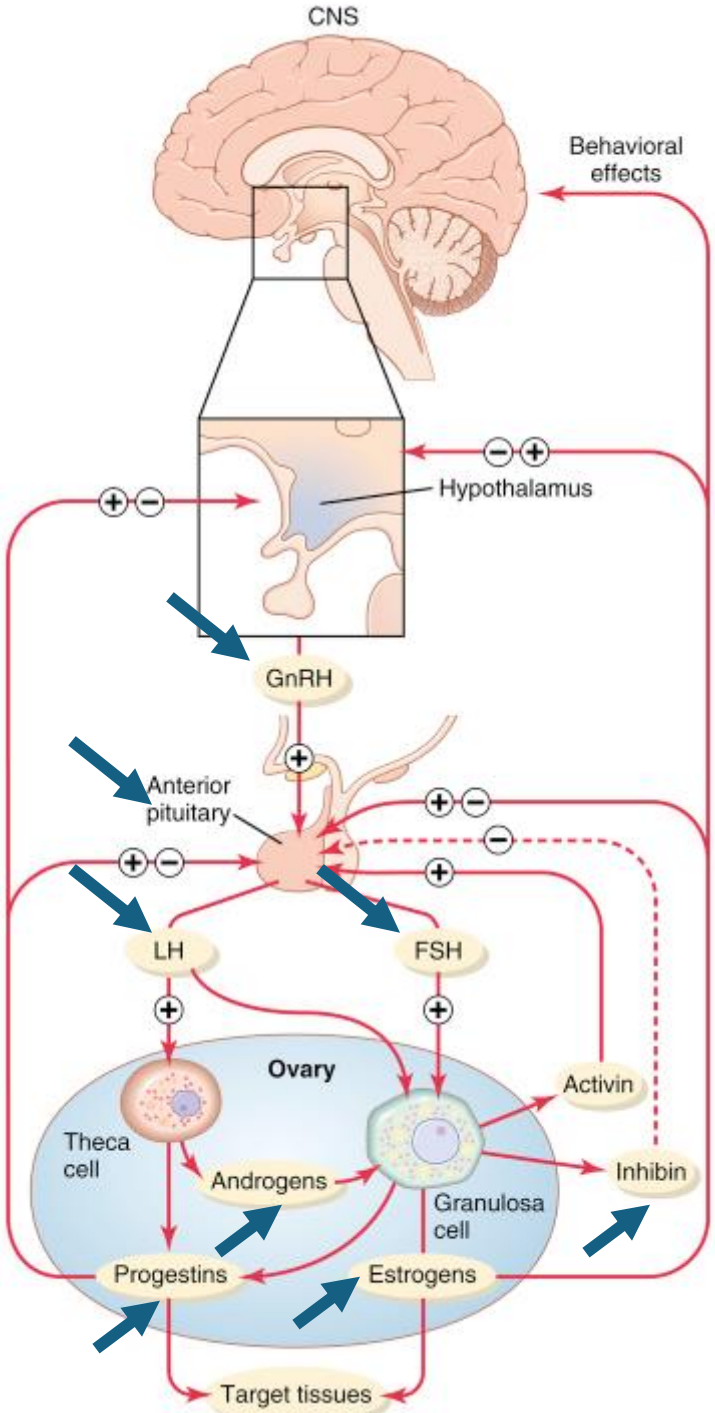


Summary

- High Estrogen, Low Progesterone = Positive feedback. (At the beginning)
- Low Estrogen, Low Progesterone = Positive feedback.
- High Estrogen, High Progesterone = Negative feedback. (Luteal phase).
- Moderate Estrogen, Moderate Progesterone = Negative feedback.

Gonadotropic Hormones and Their Effects on the Ovaries

- The ovarian changes that occur during the sexual cycle depend completely on the gonadotropic hormones FSH and LH.
- In the absence of these hormones, the ovaries remain inactive, which is the case throughout childhood, when almost no pituitary gonadotropic hormones are secreted.
- At age 9 to 12 years, the pituitary begins to secrete progressively more FSH and LH, which leads to onset of normal monthly sexual cycles beginning between the ages of 11 and 15 years.
- This period of change is called *puberty*, and the time of the first menstrual cycle is called *menarche*.


CNS
Behavioral effects
Hypothalamus
GnRH
Anterior pituitary
LH
FSH
Ovary
Theca cell
Androgens
Progestins
Granulosa cell
Estrogens
Activin
Inhibin
Target tissues

Summary (Female hormones)

- The amount of GnRH released from the hypothalamus increases and decreases much less drastically during the monthly sexual cycle. It is secreted in short pulses averaging once every 90 minutes.
- During the first few days of each monthly female sexual cycle, the concentrations of FSH and LH increase slightly to moderately, with the increase in FSH slightly greater than that of LH and preceding it by a few days.
- FSH, cause accelerated growth of 6 to 12 primary follicles each month.
- During growth of the follicles, estrogen is mainly secreted.

Summary (Female hormones)

- 2 days before ovulation there is a surge of LH, initiation of secretion of progesterone, and diminished estrogen secretion.
- Estrogen in particular and progesterone to a lesser extent, secreted by the corpus luteum during the luteal phase, have strong negative feedback effects on FSH and LH.
- In addition, the lutein cells secrete inhibin. This hormone inhibits FSH secretion.
- Low blood concentrations of FSH and LH result in corpus luteum involution.

Monthly Endometrial Cycle and Menstruation

I highly recommend you to watch ninja nerd's video about menstrual cycle, click here

First what is the endometrium? It is the inner lining of the uterus.

So, when we talking about female sexual cycle, we already went over the ovarian cycle, and now we will talk about the endometrial cycle.
At the same time as the follicular phase, ovulatory phase , and luteal phase occur, the endometrium also undergoes several changes in parallel.
We have three phases in endometrial cycle: 1.menstruation. 2.proliferative. 3.secretory.

Female sexual cycle: Menstrual cycle

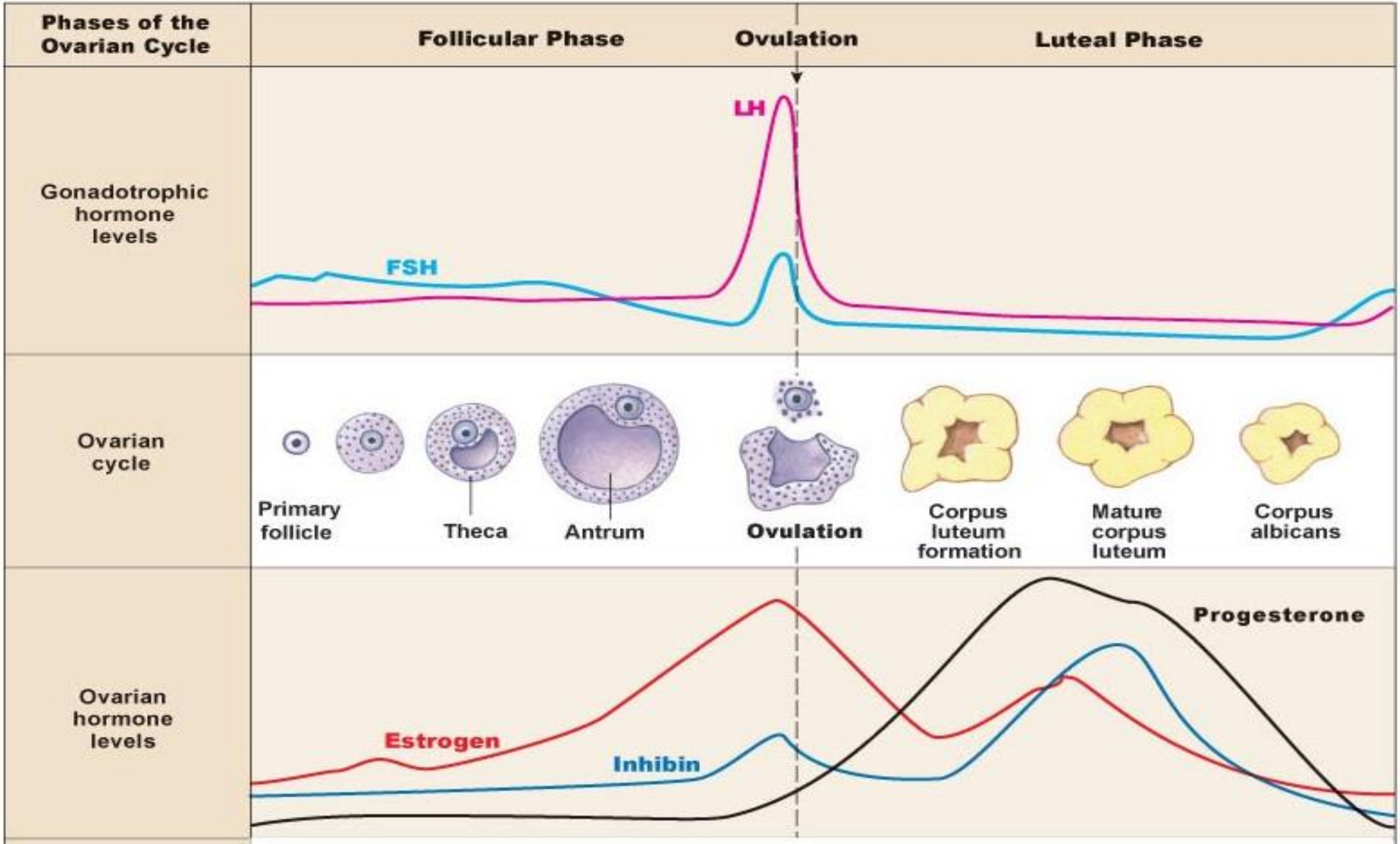
The normal reproductive years of the female are characterized by monthly (28d) rhythmical changes in the rates of secretion of the female hormones and corresponding physical changes in the ovaries and other sexual organs.

Ovarian Cycle

Follicular phase
Ovulatory phase
Luteal phase

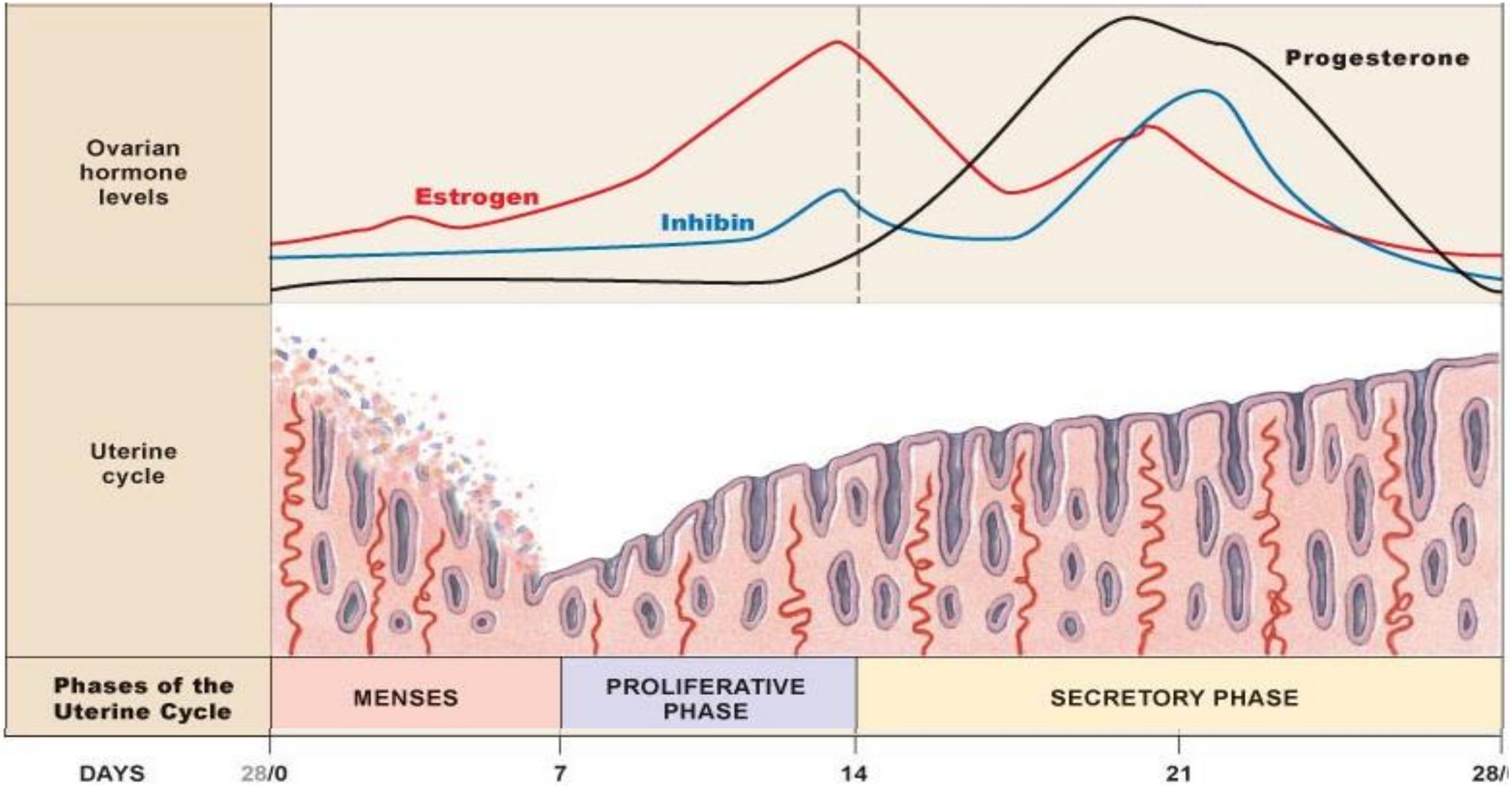
Endometrial Cycle

Menstruation
Proliferative phase
Secretory phases


Phases of the Ovarian Cycle
Follicular Phase
Ovulation
Luteal Phase
Gonadotrophic hormone levels
LH
FSH
Ovarian cycle
Primary follicle
Theca
Antrum
Ovulation
Corpus luteum formation
Mature corpus luteum
Corpus albicans
Ovarian hormone levels
Progesterone
Estrogen
Inhibin

Now let's talk about the next slide:
The ovaries will be secreting estrogen in the first phase of the cycle, then at the ovulation the estrogen will start going down, and the progesterone will start going up, and in the luteal phase the estrogen and progesterone will be released.
(الاستروجين والبروجستيرون على الرسمة تتبع)

So how that can be translated in the uterus?
the estrogen and progesterone levels at the beginning of the cycle will be very low. Now let's see during the menses or menstruation (the first phase of endometrium which is 28 days) the endometrium is undergoing sloughing and bleeding, so the first day in the female sexual cycle or menstrual cycle is the first day of bleeding.
Now go to the next box.


Ovarian hormone levels
Estrogen
Inhibin
Progesterone
Uterine cycle
Phases of the Uterine Cycle
MENSES
PROLIFERATIVE PHASE
SECRETORY PHASE
DAYS
28/0
7
14
21
28/


Ovarian cycle
Follicular phase
Luteal phase
Endometrial cycle
Menses
Proliferative phase
Secretory phase
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28–0
Days

After we said that the first day of menstrual cycle is the first day of bleeding, now this bleeding from the previous cycle, the endometrium was ready to accept the fertilized egg but there was no fertilization, so whatever the endometrium did to prepare itself is going away, so when the bleeding occurs The endometrium → فبصرله يكون مليان اوعية دموية حthickening so anything exceeding the normal thickness will be lost, so this is what we call the menstruation or the bleeding.

Menstruation

- If the ovum is not fertilized, about 2 days before the end of the monthly cycle, the corpus luteum in the ovary suddenly involutes, ovarian hormones (estrogens and progesterone) decrease to low levels of secretion.
- 24 hours preceding the onset of menstruation, vasospasm (increase release of prostaglandins), decrease in nutrients to the endometrium, and the loss of hormonal stimulation initiate necrosis in the endometrium.

Menstruation

- Hormonal stimulation initiate necrosis in the endometrium.
- Hemorrhagic areas → superficial layers of the endometrium have desquamated →uterine contractions to expel the uterine contents (prostaglandins).
- Menstrual flow from the uterus consists of 50–150 mL of blood, tissue fluid, mucus, and epithelial cells shed from the endometrium.
- Tremendous numbers of leukocytes are released along with the necrotic material and blood (resistant to infection).

Check the next slide and doctor's notes.

.There will be a lot of WBC because this sloughing and injuries to the endometrial wall (which is causing the pain due to prostaglandins secretion) this may increase the infection probability so there will be a leukorrhea which is the leukocytes will go out with a bleeding,
So all of this will reduce probability of getting an infection during the menstrual cycle.

Also there during the bleeding there should be no clotting normally, but if the bleeding was very heavy some clot are acceptable.
why should be no clotting? Because in the bleeding there is a fibrinolysin which is an anticoagulant that will prevent the clots from happening.

Doctor's notes

Menstruation is caused by the reduction of estrogens and progesterone, **especially progesterone, at the end of the monthly ovarian cycle.
**During normal menstruation, approximately 40 milliliters of blood and an additional 35 milliliters of serous fluid are lost. The menstrual fluid is normally nonclotting because a fibrinolysin is released along with the necrotic endometrial material.
**If heavy bleeding occurs from the uterine surface (first 2d), the quantity of fibrinolysin may be insufficient to prevent clotting, resulting in the passage of blood clots.

the period of the menstruation and the bleeding it's different, it could take 1,3,5 or 7 days it depends on what?
The female genetics, the environment (hot or cold), her diet, her family, her blood (blood flow and pressure), and if she has any diseases.

Proliferative Phase (Estrogen Phase) because the estrogen is the responsible for this phase

- Under the influence of estrogens, the stromal cells and the epithelial cells proliferate rapidly.
- The endometrial surface is re-epithelialized within 4 to 7 days after the beginning of menstruation.
- During the next week and a half, under the control of estrogen the endometrium increases greatly in thickness, owing to **increasing numbers of stromal cells** and to progressive growth of the **endometrial glands** and **new blood vessels** into the endometrium.
- At the time of ovulation, the endometrium is 3 to 5 mm thick.

Check doctor's notes in the next slide

Doctor's notes

**At the beginning of each monthly cycle, most of the endometrium has been desquamated by menstruation.
**After menstruation, only a thin layer of endometrial stroma remains and the only epithelial cells that are left are those located in the remaining deeper portions of the glands and crypts of the endometrium.

After the menstruation is happened and gone then the endometrium will back to it's original thickness which is 1 or 2 mm.

Secretory Phase (Progestational Phase) because the progesterone is the responsible here

- The estrogens cause slight additional cellular proliferation in the endometrium during this phase of the cycle.
- **Progesterone** causes marked swelling and secretory development of the endometrium.
- The glands increase in tortuosity; an excess of secretory substances accumulates in the glandular epithelial cells.
- lipid and glycogen deposits increase greatly in the stromal cells.
- Further Increase blood supply to the endometrium

Secretory Phase (Progestational Phase)

- From the time of fertilization until the time implantation, the uterine secretions, called “uterine milk,” provide nutrition for the early dividing ovum.
- Then, once the ovum implants in the endometrium, the trophoblastic cells on the surface of the implanting ovum (in the blastocyst stage) begin to digest the endometrium and absorb the endometrial stored substances, thus making great quantities of nutrients available to the early implanting embryo.

Check doctor's notes in the next slide

Doctor's notes

**At the peak of the secretory phase, about 1 week after ovulation, the endometrium has a thickness of 5 to 6 millimeters.
****The whole purpose of all these endometrial changes is to produce a highly secretory endometrium that contains large amounts of stored nutrients to provide appropriate conditions for implantation of a *fertilized* ovum during the latter half of the monthly cycle.

After the ovulation the estrogen will go down and the progesterone will go up.
The progesterone is the hormone for that is responsible for increasing the thickness more and more in the endometrium and there will be more glands and the vascularity will be more tortious (معقدة وملتوية), and the endometrium will be filled with collagen but why?
When the fertilized egg comes to implant there, it needs nourishment, which is provided by collagen, this is called uterine milk. The corpus luteum stopped producing estrogen and progesterone after 14 days because fertilization did not occur. As a result, the corpus luteum turned into the corpus albicans, and the levels of estrogen and progesterone dropped. When these hormone levels fall, the endometrium begins to shed. The built-up lining starts to break down and bleed, and thus, we enter the next endometrial cycle.

Function of sex hormones

Ovarian sex hormones

- Estrogens and the progestins.
- The most important of the estrogens → estradiol.
- The most important progestin → progesterone.
- The estrogens → mainly **promote proliferation** and **growth** of specific cells in the body that are responsible for development of most **secondary sexual characteristics** of females that appears after puberty(الهرمون الانثوي المسؤول عن التغيرات في جسم الانثى)
- The progestins → function mainly to **prepare the uterus for pregnancy** and the **breasts for lactation**.

Functions of Estrogens

- Effect of Estrogens on the Uterus and External Female Sex Organs
- Transform the female sex organs from those of a child → an adult.
- The ovaries, fallopian tubes, uterus, and vagina all increase several times in size.
- Deposition of fat and enlargement of external genitalia (Females have fat in their bodies, particularly in the breasts and hips, and estrogen is responsible for the distribution of this fat).
- Change the vaginal epithelium from a cuboidal into a stratified type why? After puberty, the female becomes sexually active, and the cuboidal cells are highly sensitive to bleeding and infection, which is considerably more resistant to trauma and infection so it will decrease the infection and the trauma.
- Estrogens cause marked proliferation of the endometrial stroma and greatly increased development of the endometrial glands, which will later aid in providing nutrition to the implanted ovum.

Functions of Estrogens on the breast tissue

- Effect of Estrogens on the Breast
- Development of the stromal tissues of the breasts.
- Growth of an extensive ductile system..
- Deposition of fat in the breasts.

The effect of estrogen on the breast tissue:
The breast is composed mainly of 1.fat 2.ducts 3.alveoli to produce milk.
The estrogen is responsible for fat deposition and the development of the ductile system(بيبني القنوات الحليبية), but it does not form the cells, build the alveoli, or help in milk production.

Doctor's notes

estrogens initiate growth of the breasts and of the milk-producing apparatus. They are also responsible for the characteristic growth and external appearance of the mature female breast. However, they do not complete the job of converting the breasts into milk-producing organs.

Functions of Estrogens

- Effect of Estrogens on the Skeleton
- Estrogens inhibit osteoclastic (which causes destruction of the bone tissue) activity in the bones and therefore stimulate bone growth.(بحافظ على الكالسيوم بالعظام)
- They cause uniting of the epiphyses with the shafts of the long bones.
- After menopause → increased osteoclastic activity, decreased bone matrix, and decreased deposition of bone calcium and phosphate →osteoporosis → fracture

Doctor's notes

This effect of estrogen (uniting epiphyses)in the female is much stronger than the similar effect of testosterone in the male. As a result, growth of the female usually ceases several years earlier than growth of the male.

Functions of Estrogens

- Effect of Estrogens on metabolism
- Estrogens **Slightly** Increase Protein Deposition.
- Estrogens increase the whole-body metabolic rate **slightly.**
- Increased deposition of fat in the subcutaneous tissues, breasts, buttocks and thighs.

Doctor's notes

increase protein deposition à This effect mainly results from the growth-promoting effect of estrogen on the sexual organs, the bones, and a few other tissues of the body.

Functions of Progesterone

(which works mainly on breast tissue and uterus)

- Progesterone promotes **secretory changes** in the uterus, also increases uterine thickness and enhances the tortuosity and glandular tissue in the uterus during the menstrual cycle.
- Progesterone decreases the frequency and intensity of uterine contractions, thereby helping to prevent expulsion of the implanted ovum.
- Progesterone promotes development of the lobules and alveoli of the breasts, causing the alveolar cells to proliferate, enlarge, and become secretory in nature.

Progesterone is released by the corpus luteum to help stabilize the uterus and support implantation, thus maintaining the pregnancy so it will decrease the contractions of the uterus.

Important question:

If a pregnant woman experiences bleeding in early pregnancy and visits the doctor, she may be given a hormone, what is the hormone?

The hormone is progesterone. This hormone helps maintain the pregnancy by stabilizing the endometrium, preventing uterine contractions, and avoiding cervical dilation.

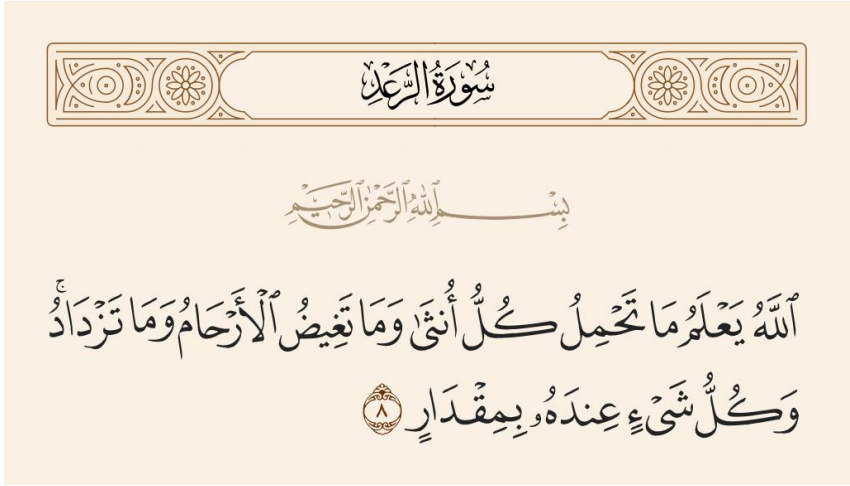
Doctor's notes

progesterone does not cause the alveoli to secrete milk; milk is secreted only after the prepared breast is further stimulated by 1. Oxytocin and 2.*prolactin* from the anterior pituitary gland.

Progesterone also causes the breasts to swell. Part of this swelling is due to the secretory development in the lobules and alveoli, but part also results from increased fluid in the tissue.

Additional sources (klick on the name to go to the lecture)

1. Doctor's lecture
2. Ninja nerd



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!