PHYSIO

MODIFIED NO. 13

الكُتّاب: نغم العمري و ميس قشّوع

المدققين: عمر عنانزة

الدكتور/ة: آلاء بواعنة

Reproductive Physiology

Color code

Slides

Doctor

Additional info

Important

NOTES

Notes under the slides from doctor will be in this box

How to Study!

- Slides (check the notes).
- Lecture.
- Reference book: Guyton and Hall Textbook of Medical Physiology (John E. Hall; Michael E. Hall). (14th edition)

Please note that there is huge similarity between doctor explanation and notes

Female Physiology Before Pregnancy and Female Hormones
Female reproductive functions

Chapter 82

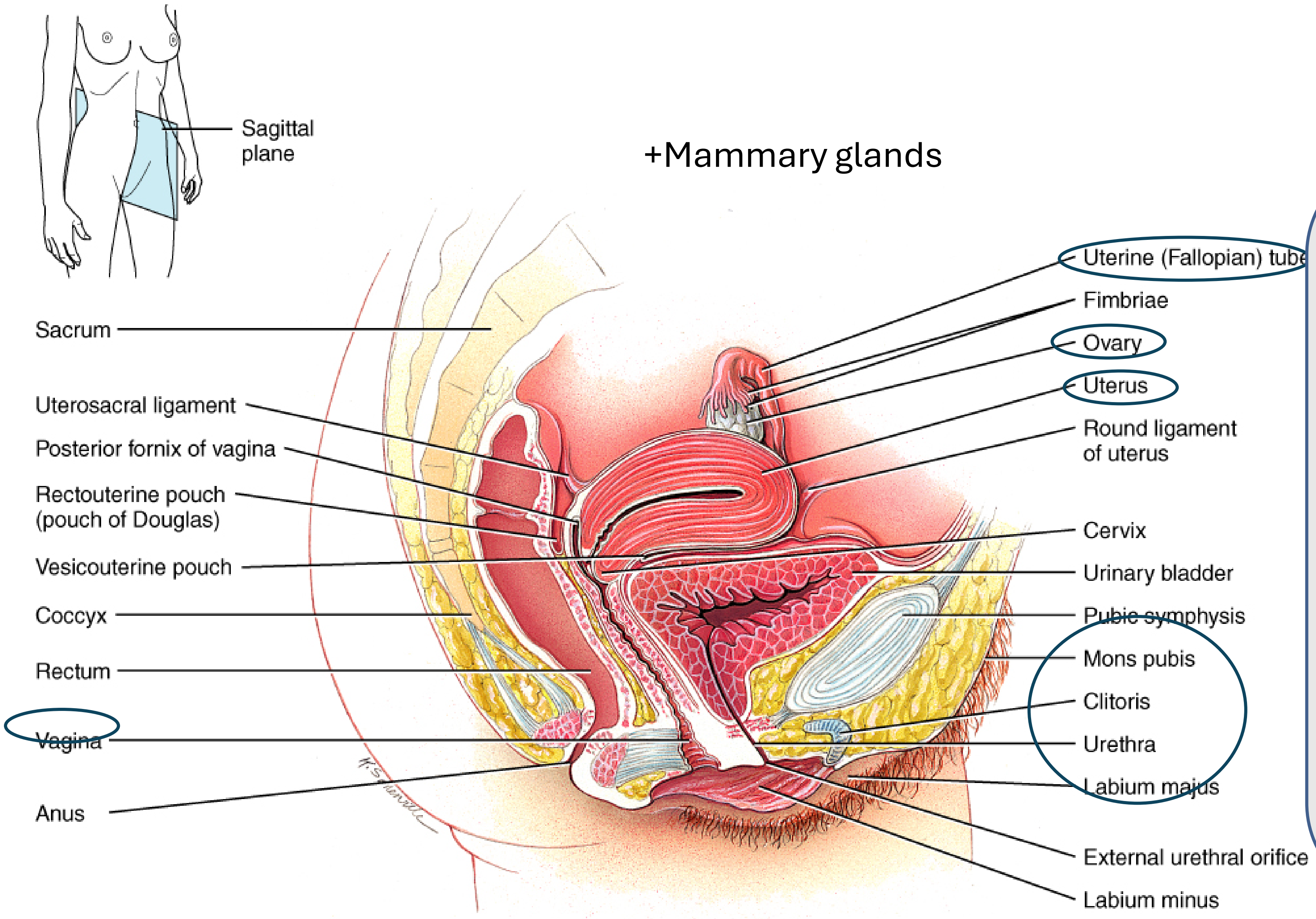
Female Reproductive Functions:

1) Preparation of the female body for conception and pregnancy

(2) The period of pregnancy itself.

Female reproductive organs

+Mammary glands

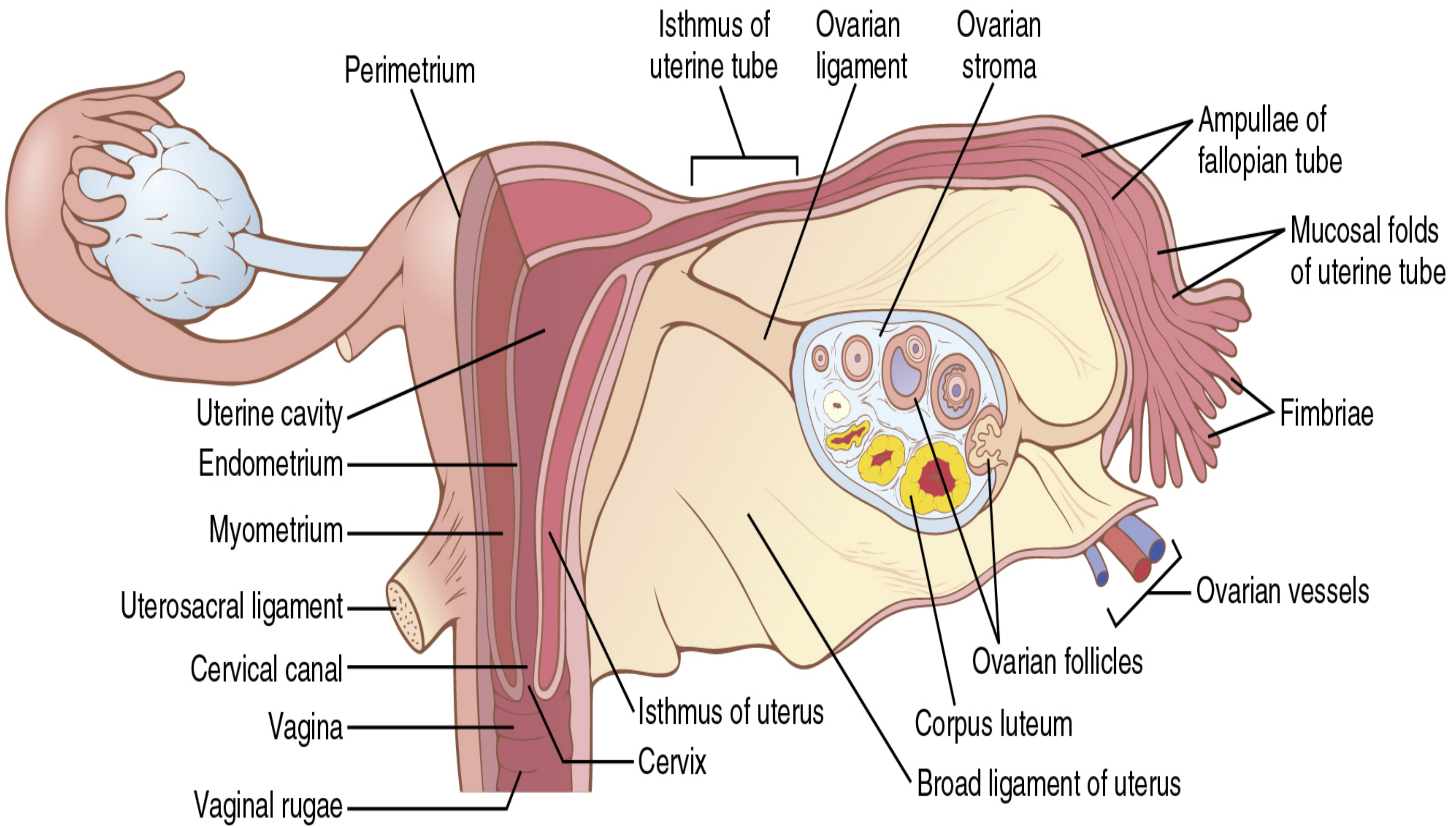


(a) Sagittal section

Quick recap from the anatomy, the parts of the female reproductive system: It starts with the **ovaries** in both sides of the body, then the **fallopian tubes** that are connecting the ovaries to the uterus, then the **uterus** : (fundus, body ,cervix) and beneath is the **vagina** and **the outer parts**, plus the **mammary glands**.

So the mammary glands are considered as a part of the reproductive system in the female.

Relationship of the uterine tubes to the ovaries, uterus, and associated structures

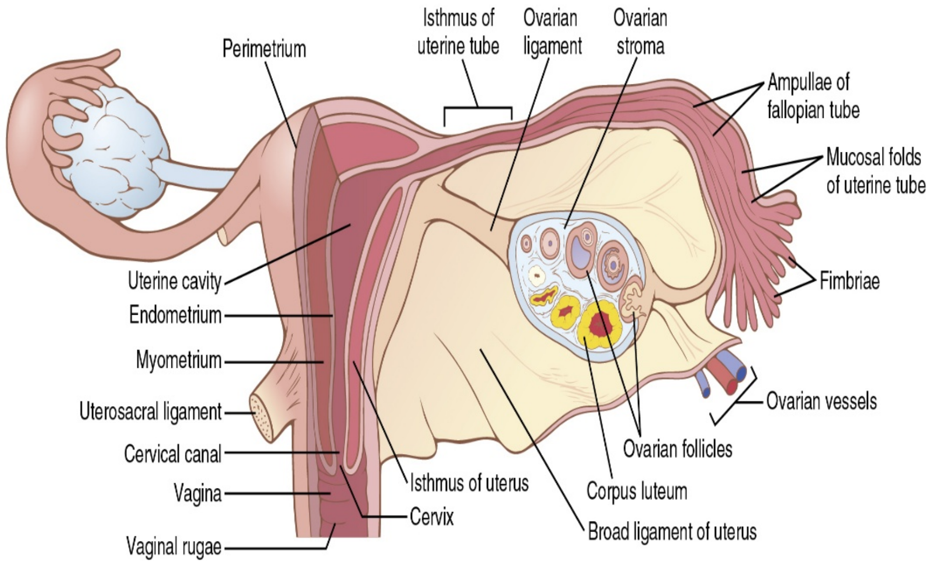


NOTES

Reproduction begins with the development of ova in the ovaries. In the middle of each monthly sexual cycle, a single ovum is expelled from an ovarian follicle into the abdominal cavity near the open fimbriated ends of the two fallopian tubes. This ovum then passes through one of the fallopian tubes into the uterus; if it has been fertilized by a sperm, it implants in the uterus, where it develops into a fetus, a placenta, and fetal membranes—and eventually into a baby.

- Here is another interior view for the female reproductive system, which is composed of :

1- both ovaries in both sides of the body, left side and right side. 2- We have the fallopian tubes. 3- The fallopian tube has the fimbria at the side of the ovary to increase the percentage or the probability of catching the ovum after it's ovulated from the ovaries. The ampulla of the fallopian tube, which is most of the time the area where the fertilization of the oocyte with the sperm will happen. And then we have the isthmus, where the fallopian tube will enter the uterus. And 4- the uterus

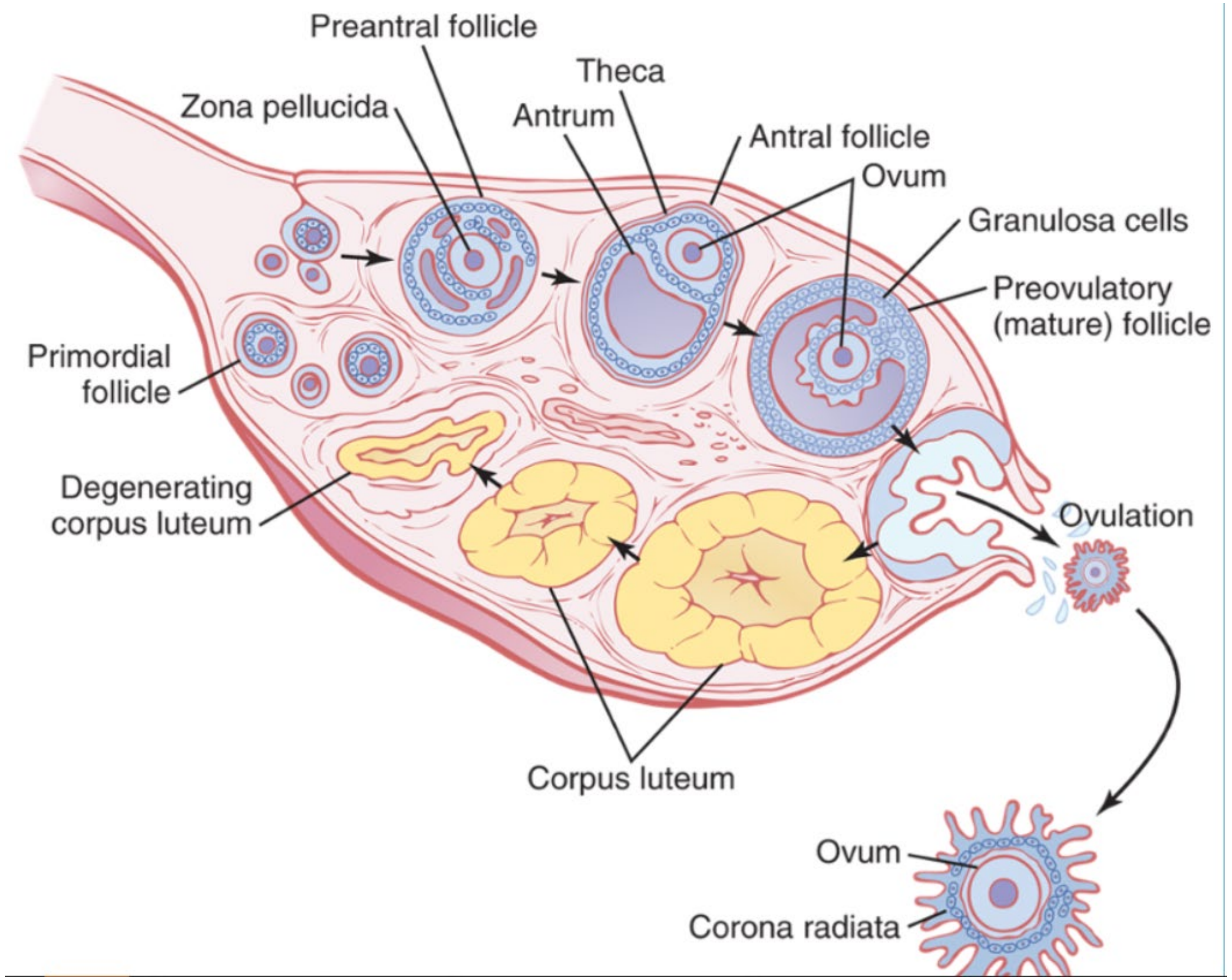


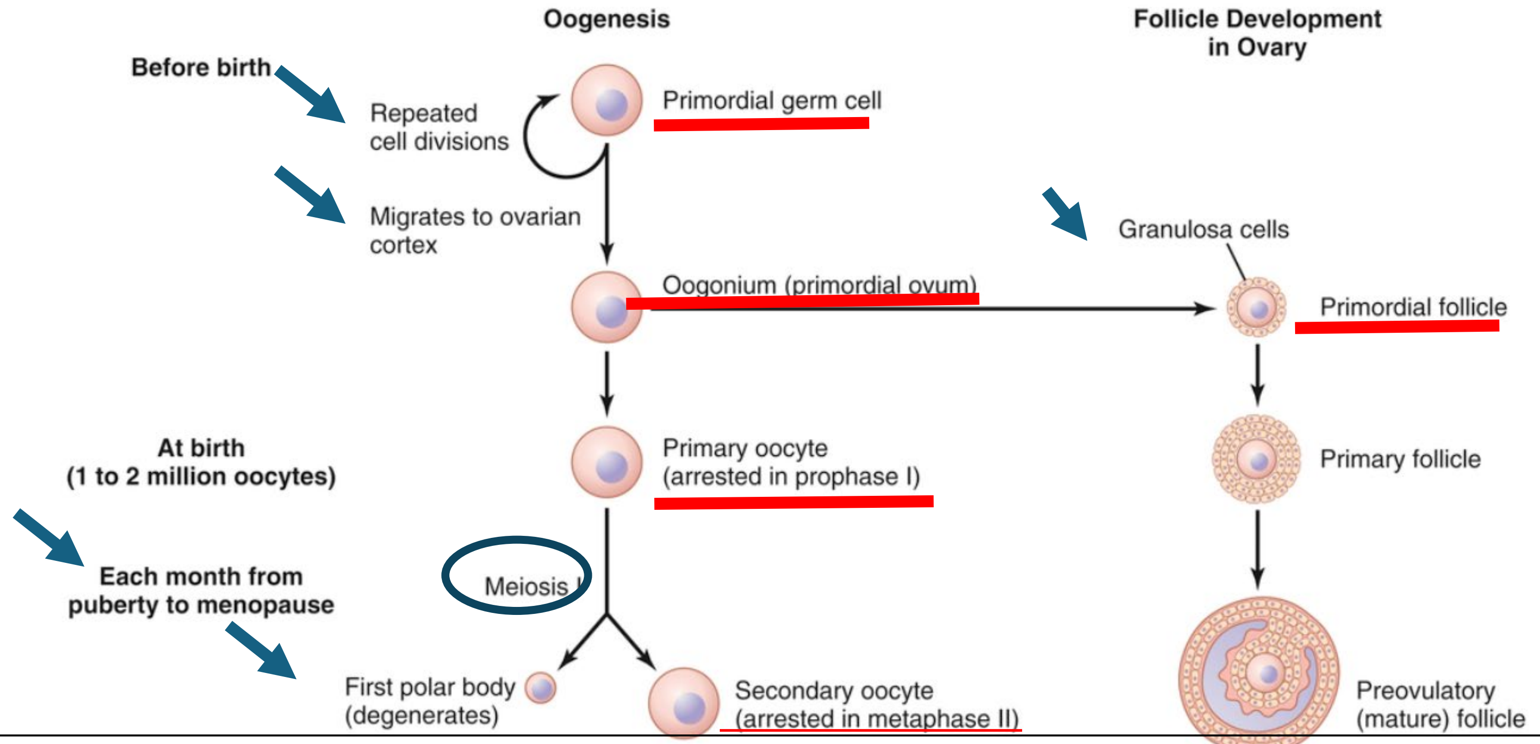
- When we learn about reproduction in the female body, we are talking about **two pathways**. One of them will happen in the ovaries. And synchronizing to that, at the same time, parallelly, there are some changes happening in the uterus.So the **ovaries are preparing the ovum** to be ovulated. Then the ovum will be waiting for sperm here to be fertilized. At the same time, the **uterus will prepare itself**. Then if this ovum will be fertilized by the sperm, then the uterus will be the place where the zygote will be implanted and the conception and the pregnancy will take place . So we will talk about in this lecture about the ovarian cycle, which is composed of three phases, and as well as the endometrial cycle, which is three phases, we will talk about in the next lecture, Inshallah.

Oogenesis

- So we will start talking about the oogenesis.
- What do we mean by oogenesis? oocyte generation.
- Oocyte=ovum=egg. They all have the same meaning, which is البويضة

- So talking about the oogenesis, looking at or zooming in into the ovary, the ovary is composed of different parts. Looking at the ovaries, it's telling us there are some stages that will take place in the ovary and end up with the ovulation, and after the ovulation, there are some stages that are taking place in the ovaries. What will happen is that we have something that we call primordial follicles in the ovaries. Where do these primordial follicles come from?

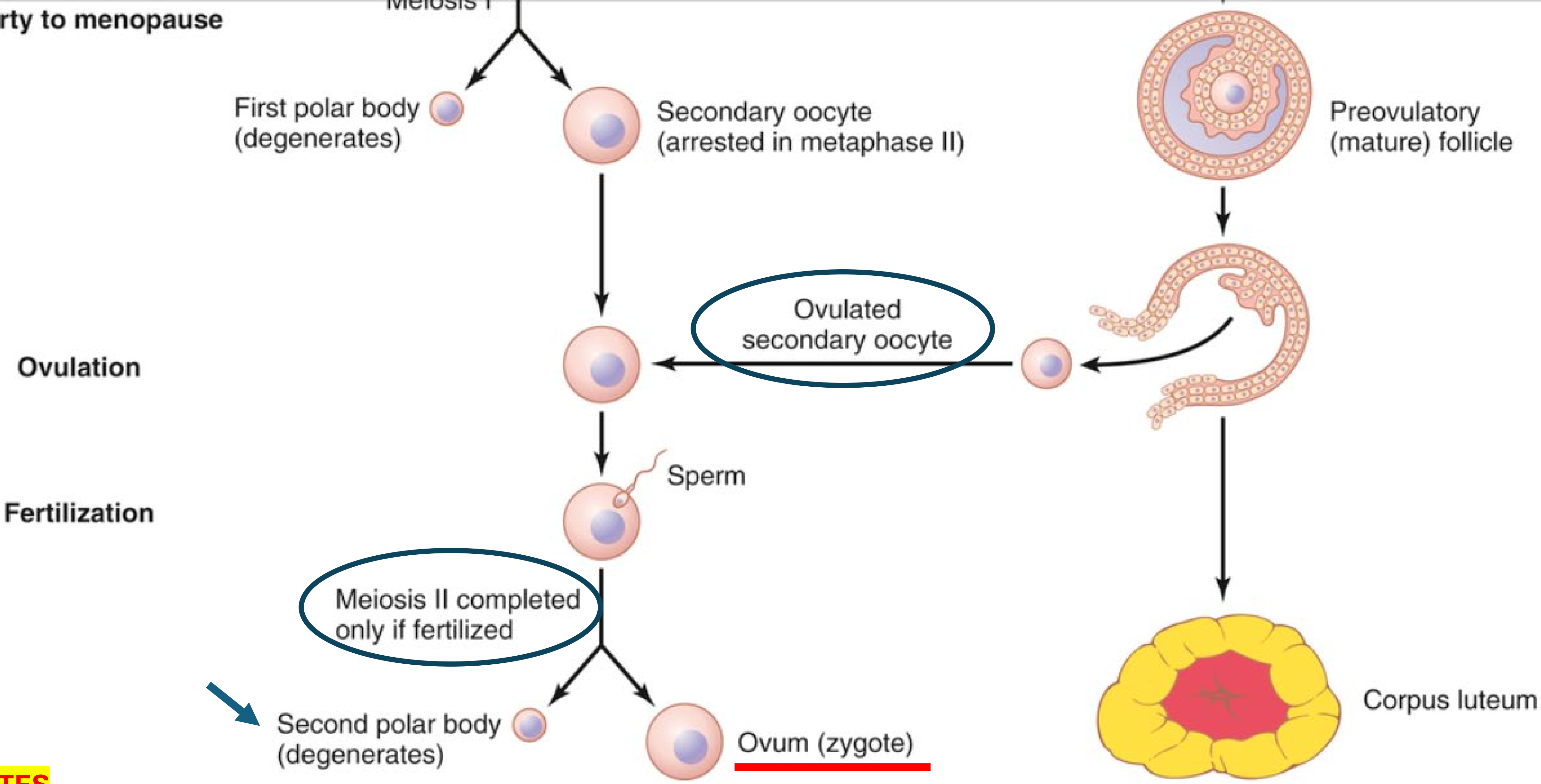




NOTES

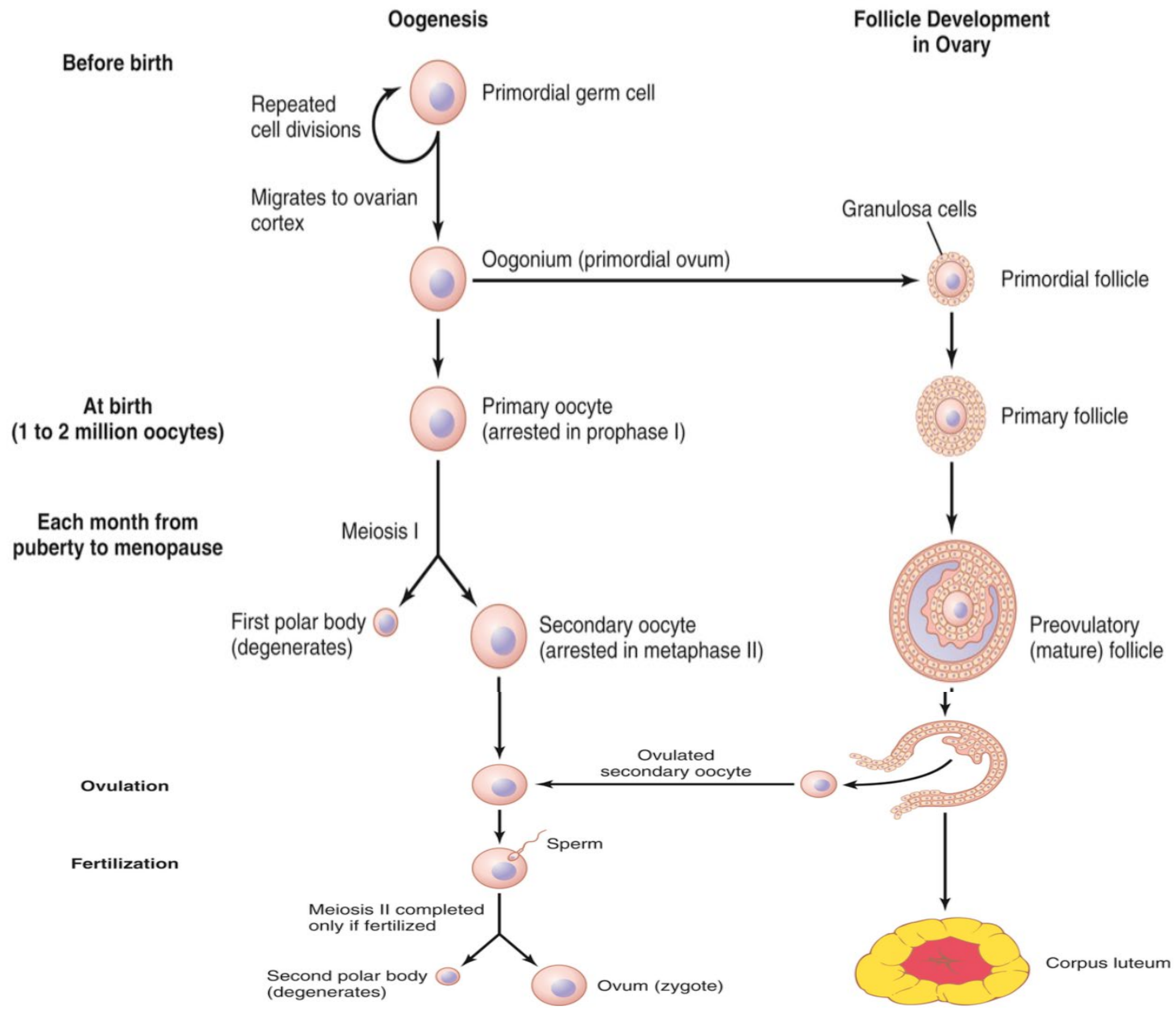
During early embryonic development, **primordial germ cells migrate to the outer surface of the ovary, which is covered by a germinal epithelium.
During this migration, the germ **cells divide repeatedly.
Once these primordial germ cells reach the germinal epithelium, they migrate into the substance of the ovarian cortex and become **oogonia or primordial ova.
Each primordial ovum then collects around it a layer of spindle cells from the **ovarian stroma (the supporting tissue of the ovary) and causes them to take on epithelioid characteristics; these epithelioid-like cells are then called **granulosa cells**. The ovum surrounded by a single layer of granulosa cells is called a **primordial follicle**. At this stage, the ovum is still immature and is called a **primary oocyte.**
The first meiotic division of the oocyte is completed **after puberty. Each oocyte divides into two cells, a large ovum (secondary oocyte) and a small first polar body. Each of these cells contains 23 duplicated chromosomes.

puberty to menopause



NOTES

**The ovum undergoes a second meiotic division, and after the sister chromatids separate, there is a pause in meiosis. If the ovum is fertilized, the final step in meiosis occurs and the sister chromatids in the ovum go to separate cells.



- This figure will be explained in detail over the next three slides, so don't panic — it's simple, just go through it step by step.

Now, the **oogenesis**, which is the **ovum production** or the **oocyte generation**, starts in the female body **before birth**.What does "before birth" mean? It means **in the prenatal period**, when the female baby is in her mother's womb.There is **organogenesis** in the first **three months of pregnancy**. During that time, before birth, there are **germ cells** in the female body, which are called **primordial germ cells**.These cells will be **migrating into the ovarian cortex**. So, the organs inside her body are forming and developing — one of these organs is the **ovary**. The **primordial germ cells**, once they reach the **ovarian cortex**, will undergo **repeated cell divisions**. At this point, they are transformed into what we call the **primordial ovum** or **oogonium**.This **primordial ovum**, when it reaches the ovarian cortex, will have **stroma** around it and becomes **epitheloid**. It will start changing its characteristics and become surrounded by **epithelial cells**, which we call **granulosa cells**.So now, the **primordial ovum**, surrounded by **one layer of granulosa cells**, is called a **primordial follicle**.

These are the **primordial follicles** that are present in the ovaries.Now, during pregnancy and by the time of **birth**, this **primordial follicle** will develop into what we call a **primary oocyte**, which will be **arrested in prophase I**.

So no more division will occur at this point. We know that cell division goes through: **prophase, metaphase, anaphase, telophase** — and here, the primary oocyte is arrested at **prophase**.At some point around **birth**, this **primary oocyte** will be surrounded by **several layers of granulosa cells**, and that is what we call a **primary follicle**.Now, there are some resources that say the female will be born with **primordial follicles** in her ovaries.

Some say she will be born with **primary follicles**, and others say she has **both**.

We will go with the **primordial follicle** resources.

So, the female will be born with **primordial follicles** in her ovaries.

So at birth female will has 1-2 millions of primary oocyte as primodial folicle in here ovaries.

Females continue at birth into childhood. During childhood, there is **no development or change** that happens to the **primary follicle**, the **primordial follicle**, or the **primary oocyte — mainly the primary oocyte**.Nothing will happen during this stage. But at **puberty**, around the age of **11 or 12**, and **until menopause**, the reproductive system becomes active. This period — from **puberty until menopause** — is called the **reproductive age**. During this time, the **primary oocyte** will undergo the **first meiotic division (meiosis I)**, and it will be transformed into a **secondary oocyte**. The **primary oocyte** will divide and produce **two cells**The **secondary oocyte ,** The **first polar body**.Why does it divide into two cells? Because the **number of chromosomes is reduced by half** — from **46 chromosomes** to **23 chromosomes**. This is important because the **secondary oocyte** needs to have only **one set of chromosomes** (23), so that when it's **fertilized by a sperm** (which also has 23 chromosomes), the resulting cell will have the **full human chromosome number**, which is **46**. The **first polar body** is not functional and will be **degenerated inside the ovary**.So, again: the **primary oocyte** undergoes the **first meiosis**, and this whole process happens **inside the follicle**. The **oocyte** inside the ovary is stored **within the follicle** and is surrounded by **granulosa cells**.What is the importance of these **granulosa cells**? They serve as a **source of nourishment** for the oocyte. We have said that in **childhood**, there is **no change or development** in the **primary oocytes**.Why is that?
Because during **childhood**, there are **no hormones** to stimulate this process.Now, this whole process of **oocyte development** is under the control of **anterior pituitary hormones**.We have the **hypothalamus gland**, which produces the **gonadotropin-releasing hormone (GnRH)**.This hormone will go to the **anterior pituitary** and stimulate the release of: **Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH)** During **childhood**, this **hormonal axis** (hypothalamus–pituitary–gonadal axis) is **not active**.

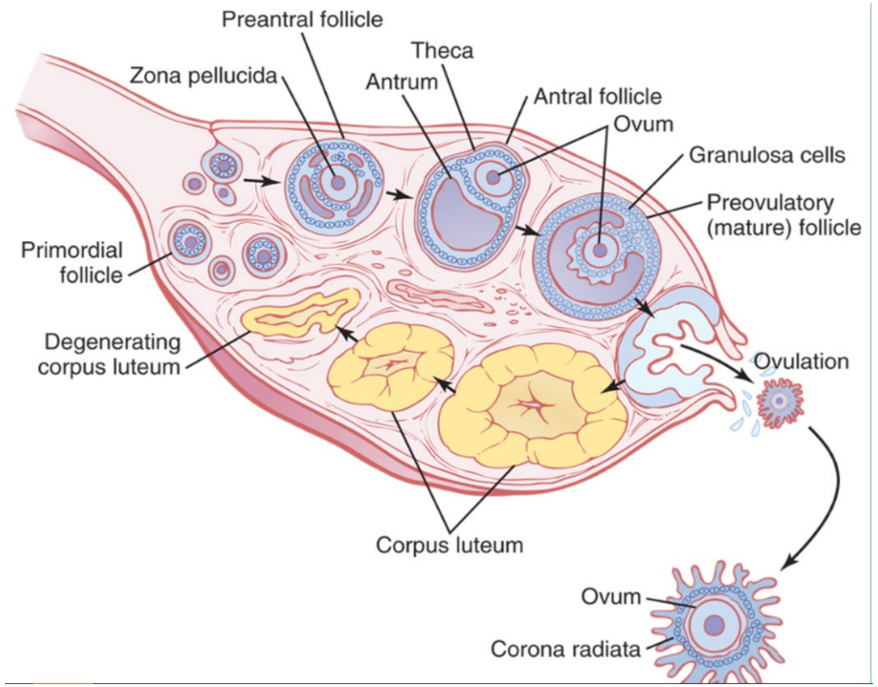
So, in the female during childhood, there are **no hormones** to stimulate the development of the oocyte.
In addition, the **granulosa cells** surrounding the oocytes will produce what we call the **oocyte maturation inhibiting factor**.This substance keeps the **primary oocytes arrested in prophase I**, and prevents any further division during childhood. But once the female reaches **puberty**, the **anterior pituitary** will gradually start producing its hormones — **FSH and LH**.Then, the oocyte development process will begin.
The **secondary oocyte** will be **ovulated** from the **pre-ovulatory follicle**, which we call the **mature follicle**.
This mature follicle contains:**Several layers of granulosa cells,Another type of stromal cells called theca cell, antrum** (a fluid-filled cavity) that is filled with **estrogen**, which is secreted by the granulosa cells.
When this **mature follicle** is ready to rupture and release the secondary oocyte, this process is called **ovulation**.So, the **pre-ovulatory (mature) follicle** will rupture, and the **secondary oocyte** will be released out of the ovary, becoming ready to be **fertilized**.Now, when the secondary oocyte **meets with a sperm**, the **second meiotic division (meiosis II)** will take place.
Let's recall: The **primary oocyte** was arrested in **prophase I**. The **secondary oocyte** is arrested in **metaphase II** — meaning it also hasn't completed its division yet.So, **when will meiosis II be completed? Only after fertilization** — when the **sperm** meets the **secondary oocyte**. At that moment, the secondary oocyte will **complete meiosis II**, and produce: One **fertilized ovum (zygote),**
What will happen to the **pre-ovulatory (mature) follicle** after it ruptures?It will **stay in the ovary**, and it will begin to **accumulate cholesterol** inside it. Because of this cholesterol accumulation, it will develop a **yellow appearance**, and we call it the **corpus luteum** (which means "yellow body").The **corpus luteum** is **very important** during: The **second phase of the ovarian cycle** (called the luteal phase) And it's also **very important during pregnancy**, especially in its early stages

Now, if we look at a figure of this process, things become clearer.

•The **ovary** is originally filled with **primordial follicles**. A female will be **born** with approximately **1 to 2 million primordial follicles** in **both ovaries**.

•But… **Will all these 1 to 2 million follicles remain until puberty?No.**This number will be **dramatically reduced** during childhood. Some books say it may drop to around **40,000** follicles by the time of puberty. Other books say around **400,000** may remain. Either way, it's still a huge number.**Why does this happen?**

Because as the female body grows, many of these primordial follicles: Are **not strong enough** , Will **not mature properly ,** So they will undergo **degeneration** This explains why we **start with a very large number**, and it keeps getting reduced **during childhood**, until puberty. Then, by the time the female reaches **puberty**, the ovary is still filled with many **primordial follicles** and **with hormonal stimulation**, the process of **follicle maturation and ovulation** begins. And this is what we've been talking about



NOTE!!

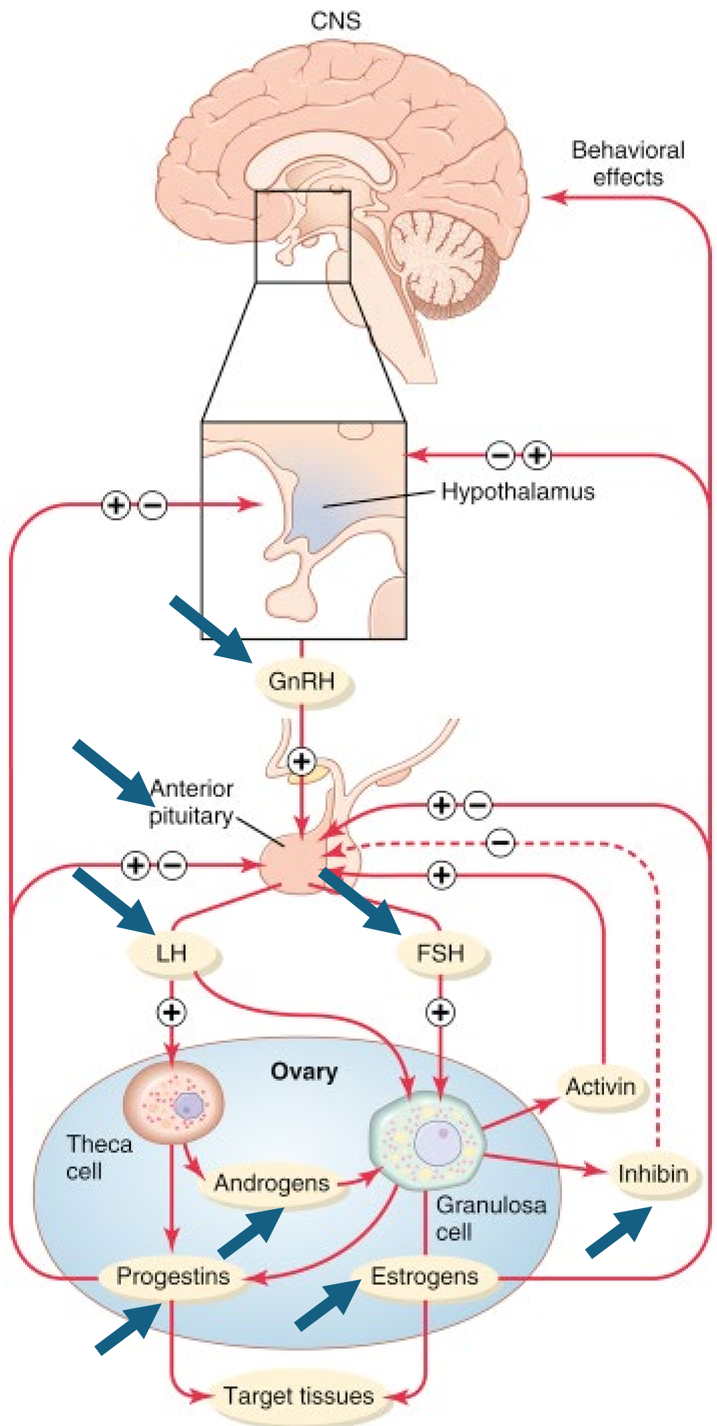
- The oogonia in the embryonic ovary complete mitotic replication, and the first stage of meiosis starts by the **fifth month of fetal development**.
- The germ cell mitosis then ceases and **no additional oocytes are formed**.
- At birth the ovary contains about 1 to 2 million primary oocytes.

NOTE!!

- At puberty, only about 300,000 oocytes remain in the ovaries, and only a small percentage of these oocytes become mature.

- During all the reproductive years of adult life, between about 13 and 46 years of age on average, only 400 to 500 of the primordial follicles develop enough to expel their ova, one each month; the remainder degenerate (i.e., become atretic).

- At the end of reproductive capability (at menopause), only a few primordial follicles remain in the ovaries, and even these follicles degenerate soon thereafter.



Female Hormonal System

Now we will start talking about the **female hormonal system**. At **puberty**, the female body—specifically the **hypothalamus**—will start to produce **gonadotropin-releasing hormone (GnRH)**. This hormone travels to the **anterior pituitary** and stimulates it to produce **luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH)**. This process begins gradually between the ages of **9 and approximately 12 years**. By the age of **11**, when puberty officially starts, these hormones will begin to be secreted regularly every month in a specific pattern. **FSH** and **LH** then travel through the blood to their target tissue, which is the **ovaries**. **FSH**, as the name suggests, stimulates the **primordial follicles** to begin maturing, and it also stimulates the **granulosa cells** to produce **estrogen**. Later in the cycle, **LH** is produced and stimulates the **theca cells** to produce **androgens** and **progesterone**. **LH** is also the hormone responsible for triggering **ovulation**. Once this occurs, the hormone **inhibin** is secreted by the **granulosa cells** in the ovary, and its role is to **inhibit the release of FSH** from the anterior pituitary.

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*.

As we said before, the female reaches **puberty** with around **400,000** (or **40,000**) **primordial follicles**. Still, this number is considered very high. During her **reproductive life**, a female normally goes through a **sexual or menstrual cycle** once each month, producing **one oocyte per cycle**. What we should know is that during each sexual cycle, **only one ovary** produces one ovum.

•So, if the **right ovary** produces an ovum this month, the **left ovary** will be responsible for **ovulation** the following month, while the right one will be at rest. In other words, the **ovaries alternate**—producing **one oocyte per month**.

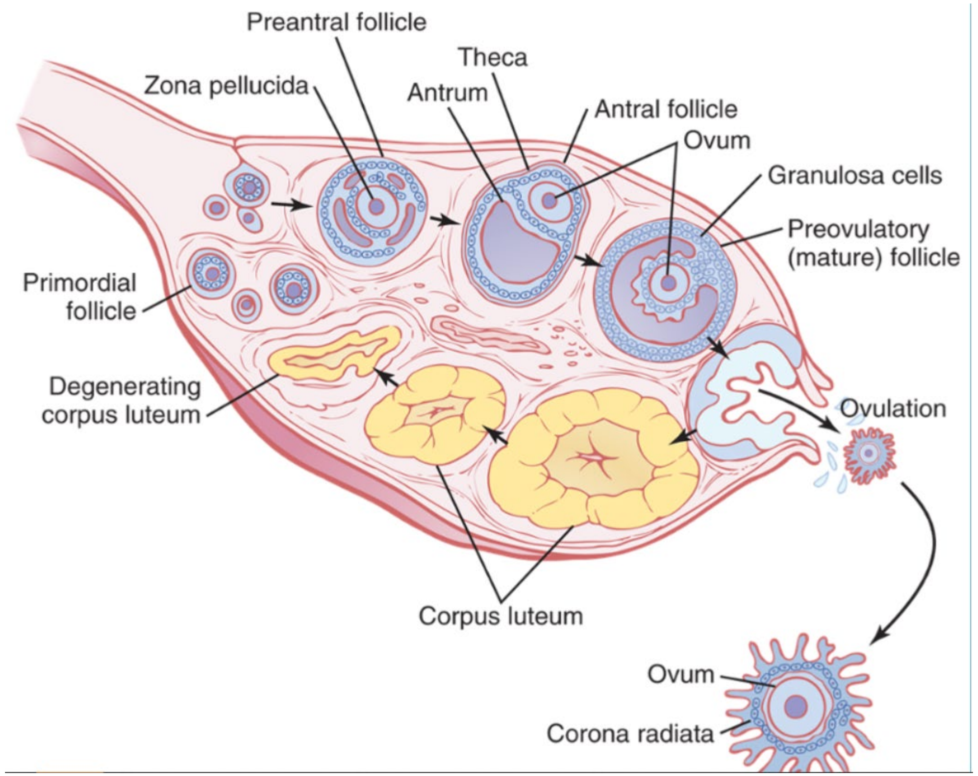
•Throughout her reproductive life, a woman will use approximately **400 to 500** of these follicles. The **remaining follicles are not used**. When the female reaches **menopause**, the remaining follicles will **degenerate**, because the **hormonal system** we talked about earlier becomes **inhibited**.

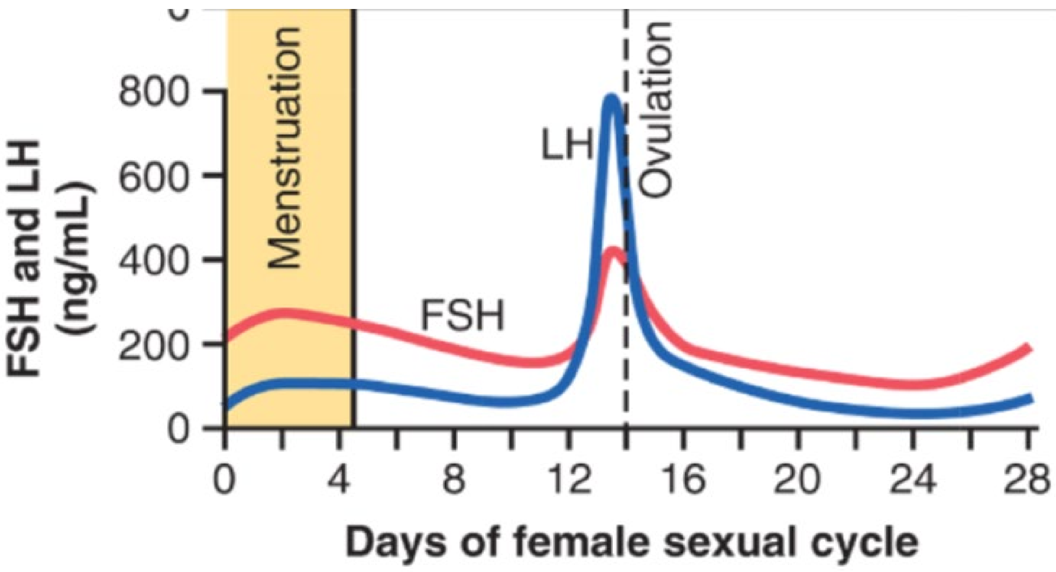
•After menopause, the secretion of **FSH** and **LH** is affected. We will talk later about how **FSH and LH** are secreted in a **specific pattern** during the **female sexual cycle**. However, **GnRH** does not follow that same pattern. **GnRH** is secreted **continuously in bursts** every **90 minutes** throughout life, while **FSH and LH** follow a **monthly cyclical pattern**.

Follicular Developments

In the ovary, there are primordial follicles. Under the stimulation of **follicle-stimulating hormone (FSH)** from the **anterior pituitary gland**, several primordial follicles begin to mature. Typically, around 6 to 12 follicles start developing at the same time, competing with each other to reach full maturity. However, only one of these follicles will fully mature and become ready to release the ovum (or secondary oocyte) during ovulation.

This phase in the ovary is called the **follicular stage** (also known as the **pre-ovulatory stage**), because it is responsible for the maturation of follicles. The **ovulatory stage** represents the critical point or the "dividing line" ((الحد الفاصل where ovulation occurs. After this stage comes the **post-ovulatory stage**, also known as the **luteal phase**, during which the corpus luteum plays the main role in the ovary.





This figure illustrates how the levels of **FSH (follicle-stimulating hormone)** and **LH (luteinizing hormone)**, both secreted by the **anterior pituitary gland**, fluctuate throughout the 28-day **female sexual cycle**, also known as the **menstrual cycle**. On average, this cycle lasts 28 days, though it may vary among individuals (e.g., 28, 32, or 35 days).

The first part of the **ovarian cycle**, which occurs **before ovulation**, is called the **follicular phase** (or **pre-ovulatory phase**). In this phase, the anterior pituitary secretes **FSH in higher amounts than LH**, because FSH plays a key role in **stimulating the development and maturation of ovarian follicles**.

Therefore, **FSH is the primary hormone responsible for the growth and maturation of the follicle** during this stage. LH is present at lower levels but begins to increase as ovulation approaches.

NOTES

These various hormones are secreted at drastically differing rates during different parts of the female monthly sexual cycle.

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 secreted by the anterior pituitary gland 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.

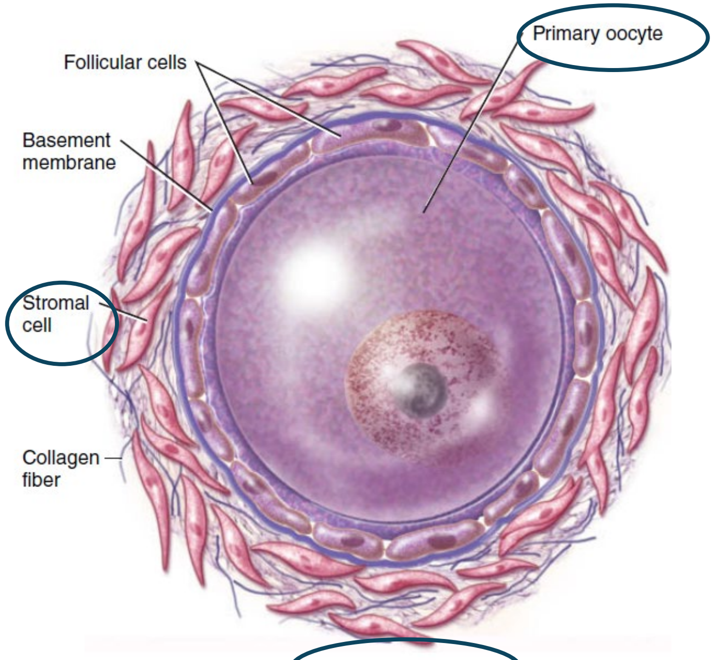
Types of follicles

1. Primordial follicle

- When a **female child is born**, each ovum is surrounded by a single layer of granulosa cells; the ovum, with this granulosa cell sheath, is called a **primordial follicle**.

- **Throughout childhood,** the granulosa cells are believed to provide **nourishment** for the ovum and to secrete an ***oocyte maturation-inhibiting factor*** that keeps the ovum suspended in its primordial state in the prophase stage of meiotic division.

- There is a **basement membrane** surrounded by **stromal cells**, which, under the influence of **luteinizing hormone (LH)**, will differentiate into **theca cells**.



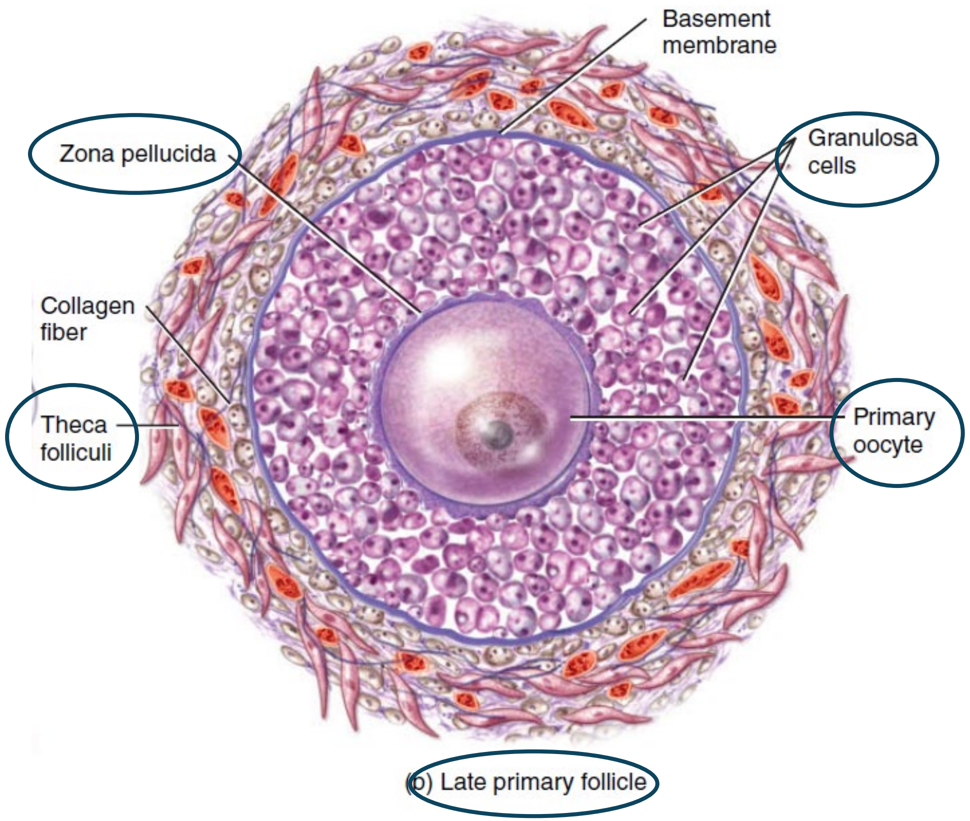
(a) Primordial follicle

2. Primary follicle

- Then, after puberty, when FSH and LH are secreted in significant quantities, the ovaries (together with some of the follicles within them) begin to grow.

- Consists of a primary oocyte that is surrounded by

1. **several layers** of cuboidal and low columnar **granulosa cells.**
2. Zona pellucida, a clear glycoprotein layer
3. Stromal cells surrounding the basement membrane begin to form (The **stromal cells** will begin developing into the **theca folliculi**, and later on, these folliculi will become the **theca cells**).

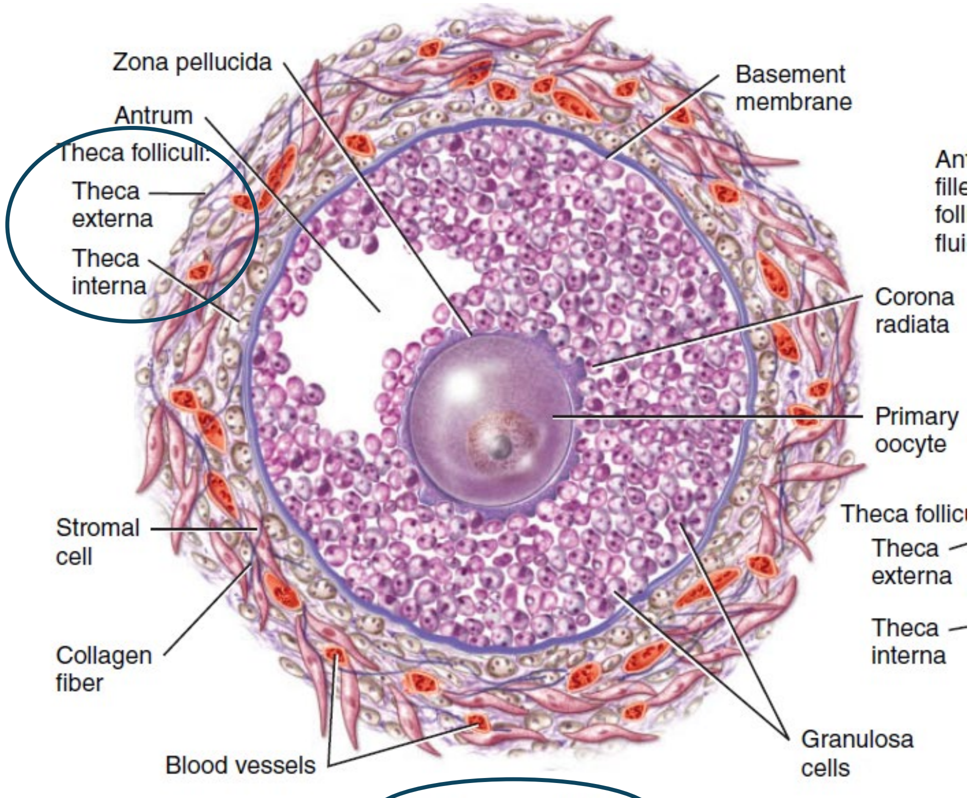


3. Secondary follicle

<u>The theca differentiates into two layers:</u>

1) <u>**Theca interna**,</u> epithelioid characteristics, <u>secrete additional steroid sex hormones.</u>

2) <u>**The theca externa,** develops into a highly vascular connective tissue capsule.</u>

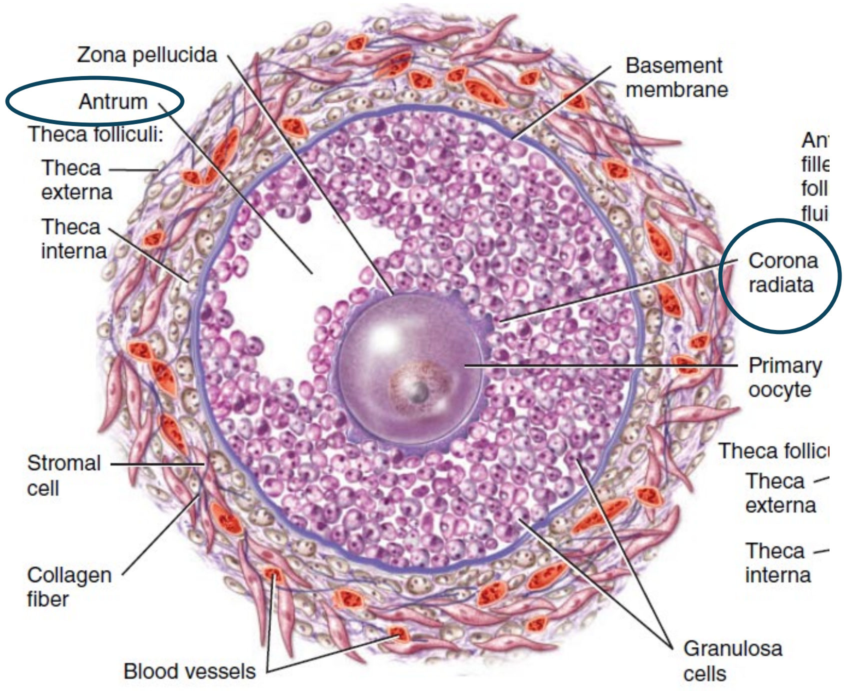


(c) Secondary follicle

Secondary follicle/Antral stage

- <u>The granulosa cells begin to secrete follicular fluid, which builds up in a cavity called the **antrum (high concentration of estrogen).**</u>

- The innermost layer of granulosa cells becomes firmly attached to the zona pellucida and is now called the **corona radiata.**



(c) Secondary follicle

- The **granulosa cells** begin producing **estrogen** under the influence of **follicle-stimulating hormone (FSH)**. At this point of the menstrual cycle, there is a **high concentration of FSH** and a **high concentration of estrogen**. When these two hormones are present together **without progesterone**, they create a **positive internal feedback loop**. How does this happen?

- FSH stimulates the granulosa cells to produce more estrogen. This increasing level of estrogen **upregulates FSH receptors** on granulosa cells, making them more sensitive to even **low levels of FSH**. As a result, estrogen production increases even more.

- At the same time, the combination of high FSH and high estrogen also leads to an **increase in LH receptors** on the granulosa cells, making them more responsive to **low concentrations of luteinizing hormone (LH)**—the key hormone required for ovulation. This prepares the follicle for the upcoming **ovulatory process**.

- Although 6 to 12 follicles begin developing at the same time, only **one follicle** will eventually achieve all the necessary conditions: the highest sensitivity to FSH and LH, and the **highest level of estrogen production**.

- The **estrogen** and **FSH** produced by this dominant follicle will exert **negative feedback** on the anterior pituitary, **inhibiting further FSH secretion**. This drop in FSH levels prevents the other developing follicles from maturing, leading to their **degeneration (atresia)**.

- Thus, only **one follicle**—the **largest**, **strongest**, and **most hormonally active**—reaches the final stage and becomes the **dominant follicle**, ready for ovulation, while the others are lost.

Explained above

Vesicular follicle

- The early growth of the primary follicle up to the antral stage is stimulated mainly **by FSH alone**.
- Greatly **accelerated growth** then occurs, leading to still larger follicles called vesicular follicles and this due to :

- 1. **Estrogen** is secreted into the follicle and causes the **granulosa cells** to form increasing numbers of **FSH receptors**, which causes a **positive feedback effect** because it makes the granulosa cells even more sensitive to FSH.

Explained above

Vesicular follicles

- 2. The pituitary **FSH and the estrogens** combine to promote **LH receptors** on the original granulosa cells, thus allowing LH stimulation to occur in addition to FSH stimulation and creating an **even more rapid increase in follicular secretion.**

- 3. The increasing **estrogens** from the follicle plus the **increasing LH** from the anterior pituitary gland act together to cause proliferation of the follicular **thecal cells** and increase their secretion.

Only One Follicle Fully Matures Each Month, and the Remainder Undergo Atresia.

- Before ovulation occurs, one of the follicles begins to outgrow all the others; the remaining 5 to 11 developing follicles involute (a process called *atresia)*
- The large amounts of estrogen from the most rapidly growing follicle → the hypothalamus to depress further enhancement of FSH secretion →in this way blocking further growth of the less well developed follicles.
- → <u>The largest follicle continues to grow because of its intrinsic positive feedback effects, while all the other follicles stop growing and actually involute.</u>
- This process of atresia is important because it normally allows only one of the follicles to grow large enough each month to ovulate.

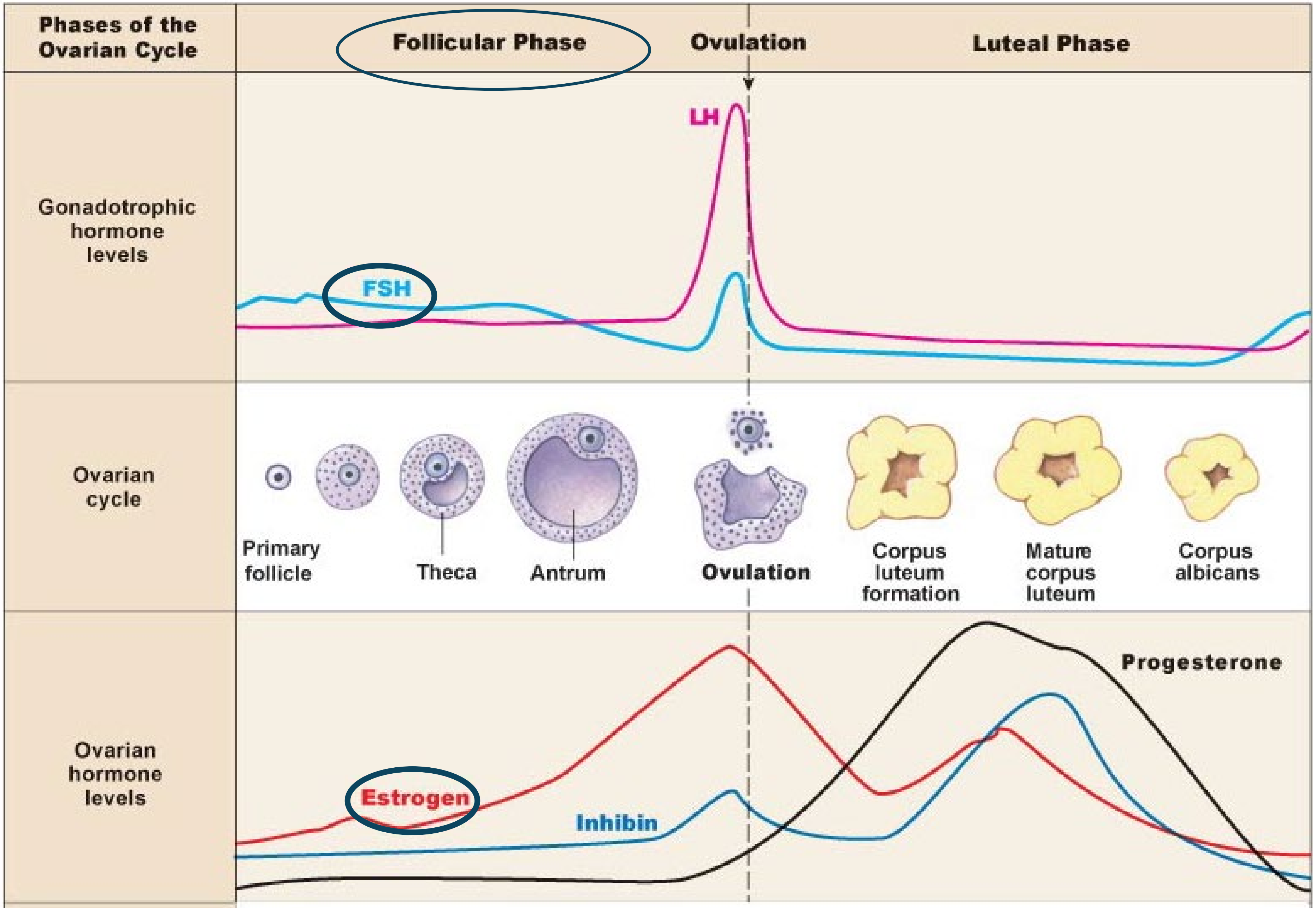
NOTES

About every 28 days, gonadotropic hormones from the anterior pituitary gland cause 8 to 12 new follicles to begin to grow in the ovaries.

One of these follicles finally becomes "mature" and ovulates on the 14th day of the cycle.

NOTES

The early growth of the primary follicle up to the antral stage is stimulated mainly by FSH alone.



- At the beginning of the menstrual cycle, **follicle-stimulating hormone (FSH)** is secreted in high levels by the **anterior pituitary gland**, under the control of **gonadotropin-releasing hormone (GnRH)** from the hypothalamus. During this early phase, the anterior pituitary produces **more FSH than luteinizing hormone (LH).**

- FSH acts on the **ovaries** to stimulate the **maturation of ovarian follicles**, which is why it is named accordingly. Typically, **6 to 12 follicles** begin developing, but only **one follicle** will progress through the stages of development to become dominant. This follicle reaches the **antral stage**, then matures into the **Graafian follicle** (also known as the **vesicular** or **mature follicle**). This follicle becomes ready for **ovulation**, and its **antrum** becomes filled with **estrogen**.

- This part of the ovarian cycle is referred to as the **follicular phase**, also called the **pre-ovulatory phase**. As the dominant follicle matures, it produces increasing amounts of estrogen, which causes a **slight decrease in FSH levels**. This reduction in FSH causes the other developing follicles to **undergo atresia (degeneration)**, leaving only one dominant follicle to continue to ovulation.

- When the dominant follicle is fully mature, it sends signals (via rising estrogen levels) to the anterior pituitary, indicating it is ready for ovulation. In response, the anterior pituitary secretes a **surge of LH**, increasing its concentration up to **10 times** its baseline. FSH also rises slightly (about **2–3 times**), but the **LH** is the **key hormonal event responsible for triggering ovulation.**

• There is **LH surge** which is a sudden high increase in LH level at about 24 hours before the ovulation, the exact mechanism behind the LH surge is **not fully understood**, but two main theories have been proposed:

1. The mature follicle may send a signal to the anterior pituitary that it's ready to ovulate, which triggers the **LH surge** and increased estrogen production.

2. Estrogen has a peculair effect (abnoraml effect), when present at **moderate levels**, exerts **negative feedback** on the anterior pituitary to reduce FSH and LH secretion. However, when estrogen reaches **very high levels** and is accompanied by FSH, this combination exerts a **positive feedback** effect. This leads to increased secretion of **GnRH**, **FSH**, and **LH**.

- Once the LH surge occurs, LH acts on the granulosa cells and theca cells of the mature follicle, stimulating them to shift hormone production from estrogen to progesterone. This transition is critical for preparing the follicle for ovulation and for the luteal phase that follows.

- **Another theory proposes** that the drop in estrogen and the rise in progesterone trigger the LH surge by signaling the anterior pituitary that ovulation should occur.

Ovulation

A Surge of Luteinizing Hormone Is Necessary for Ovulation

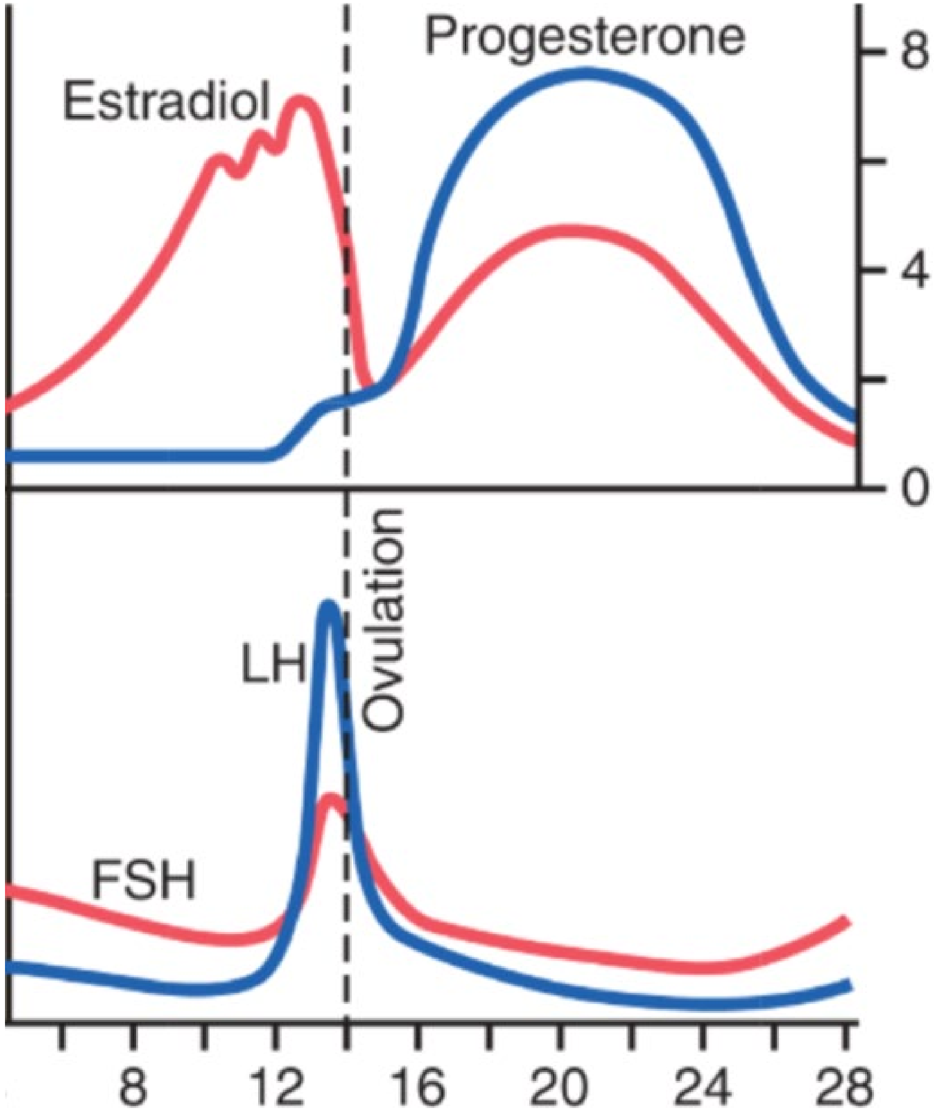
- LH is **necessary** for **final follicular growth** and **ovulation**.
- **Without** this hormone, even when large quantities of FSH are available, the **follicle will not progress to the ovulation** stage.
- FSH and LH act **synergistically** to cause **rapid swelling** of the follicle during the last few days before ovulation.
- The LH also has a specific effect on **the granulosa and theca cells**, converting them **mainly** to **progesterone-secreting cells**.
- Therefore, the rate of **estrogen** secretion begins to **fall** about 1 day before ovulation, while increasing amounts of **progesterone begin** to be secreted.

A Surge of Luteinizing Hormone Is Necessary for Ovulation

What are the actions that occur during ovulation or lead to it?

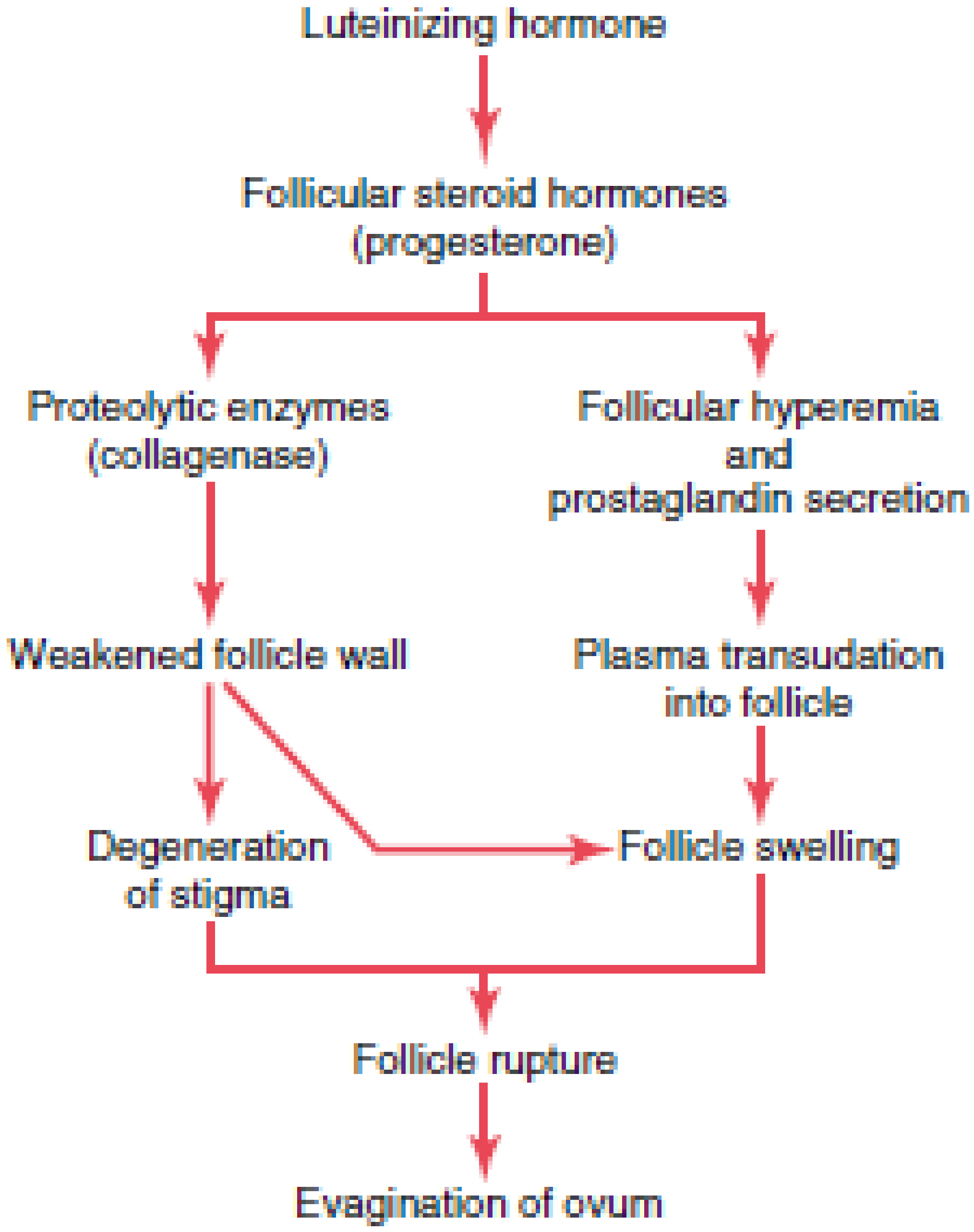
(1) <u>rapid growth of the follicle</u>
(2) <u>preovulatory surge of LH</u>
(3) <u>initiation of secretion of progesterone.</u>
(4) <u>diminishing estrogen secretion after a prolonged phase of excessive estrogen secretion.</u>

- → **ovulation occurs.**



Mechanism of Ovulation!

- LH surge
- Theca Externa release enzymes
- Rapid growth of new blood vessels into follicular wall
- Follicle swelling and degeneration of the stigma
- Follicle rupture
- Ovum discharge



• At the level of the follicle, when luteinizing hormone (LH) is released, two types of cells — **granulosa cells** and **theca cells** — begin to produce steroid hormones from **cholesterol**. These hormones include **estrogen**, **progesterone**, and **androgens**, all of which are synthesized from the precursor **cholesterol**. Under the influence of LH, both granulosa and theca cells convert cholesterol into progesterone, which is always the first steroid hormone produced.

• When **FSH** increases, it stimulates **granulosa cells** to convert progesterone and androgens into **estrogen** through the enzyme **aromatase**, which is activated by FSH. Therefore, during the **early follicular phase**, when FSH levels are high, most of the available progesterone and androgens are converted into **estrogen**. As a result, estrogen levels rise significantly during this phase. However, as ovulation approaches, the LH surge occurs and FSH levels decrease. Due to the reduced FSH, less progesterone is converted to estrogen, so **estrogen levels decline**, and **progesterone secretion increases**. Additionally, **theca cells** convert some progesterone into **androgens**, leading to a rise in both **progesterone and androgen** levels during the **luteal phase** (the second half of the menstrual cycle).

• Progesterone plays a crucial role in preparing the follicle for rupture:

1. It stimulates the production of enzymes within lysosomes, such as proteases and collagenases, which degrade and weaken the follicular wall.

2. It also promotes the secretion of prostaglandins, which increase vascular permeability and vasodilation, allowing more fluid to enter the follicle.

- **This leads to follicular swelling** and **eventually to the degeneration of the stigma** (the weakest point in the follicular wall), **resulting in the rupture of the mature follicle,** a process known as **ovulation.**

- **After ovulation:**

1. The secondary oocyte is released into the fallopian tube, where it awaits potential fertilization by a sperm.

2. The ruptured follicle remains within the ovary and transforms into the corpus luteum, which continues to secrete hormones to support early pregnancy if fertilization occurs.

NOTES

Explained above

- LH causes rapid secretion of follicular steroid hormones that contain progesterone. Within a few hours, two events occur, both of which are necessary for ovulation:

1) The theca externa (the capsule of the follicle) begins to release proteolytic enzymes from lysosomes, and these cause dissolution of the follicular capsular wall and consequent weakening of the wall, resulting in further swelling of the entire follicle and degeneration of the stigma.

(2) Simultaneously there is rapid growth of new blood vessels into the follicle wall, and at the same time, prostaglandins (local hormones that cause vasodilation) are secreted into the follicular tissues. These two effects cause plasma transudation into the follicle, which contributes to follicle swelling. Finally, the combination of follicle swelling and simultaneous degeneration of the stigma causes follicle rupture, with discharge of the ovum.

Positive Feedback Effect of Estrogen Before Ovulation—The Preovulatory Luteinizing Hormone Surge

- Experiments have shown that estrogen infusion into a female **above** a **critical rate** for 2 to 3 days during **the latter part of the first half** of the ovarian cycle will cause rapidly accelerating growth of the ovarian follicles, as well as rapidly accelerating secretion of ovarian estrogens.

- During this period, secretions of FSH and LH by the anterior pituitary gland are at first **slightly suppressed**.

- Secretion of **LH** then **increases** abruptly 6-fold to 8-fold, and secretion of **FSH** increases about 2-fold.

Causes of LH surge

- The cause of this abrupt surge in LH secretion is not known. However, the following explanations are possible:

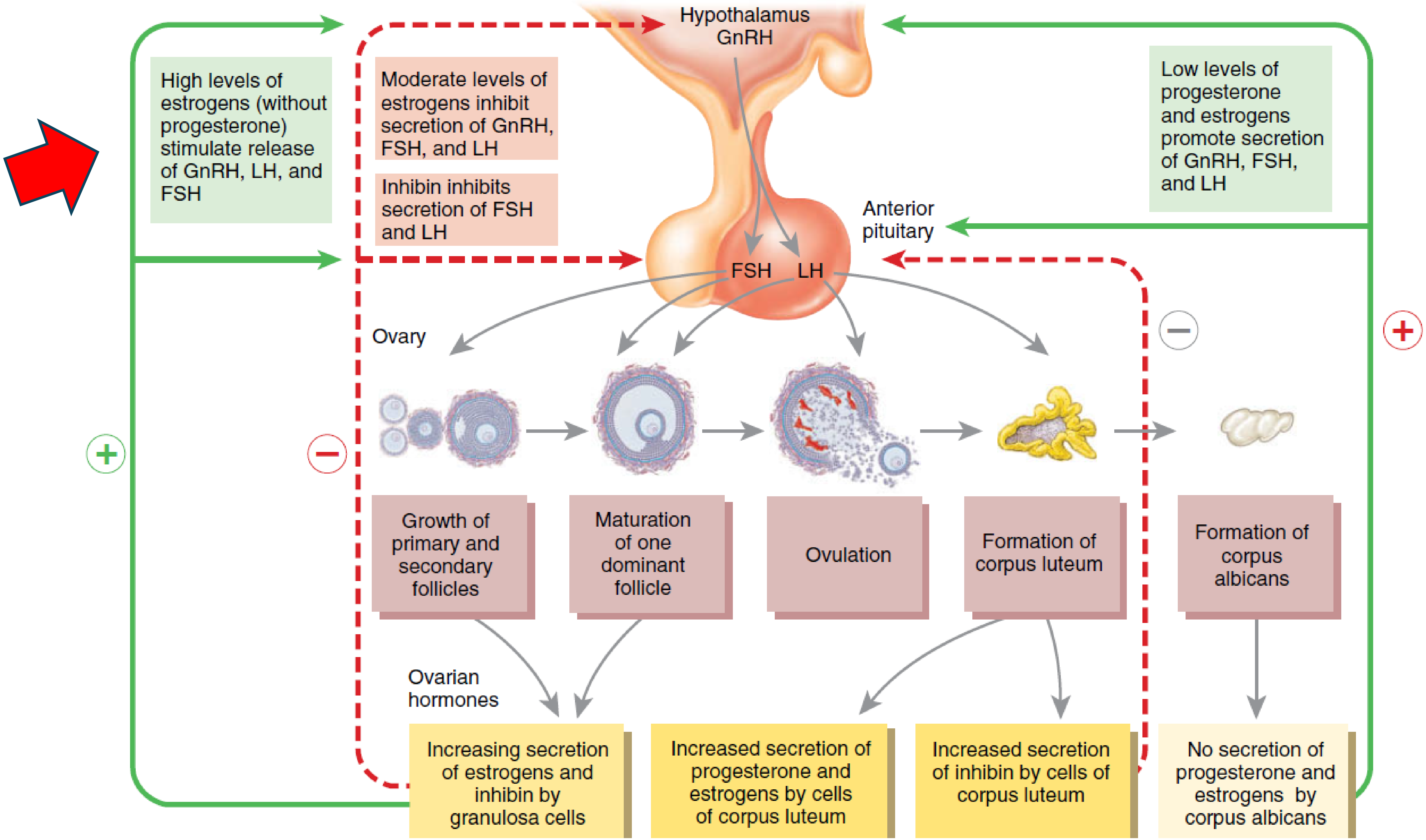
- 1. It has been suggested that at this point in the cycle, **estrogen (high level)** has a **peculiar positive feedback** effect of stimulating pituitary secretion of LH and, to a lesser extent, FSH. which is in sharp contrast to the normal negative feedback effect of estrogen that occurs during the remainder of the female monthly cycle.

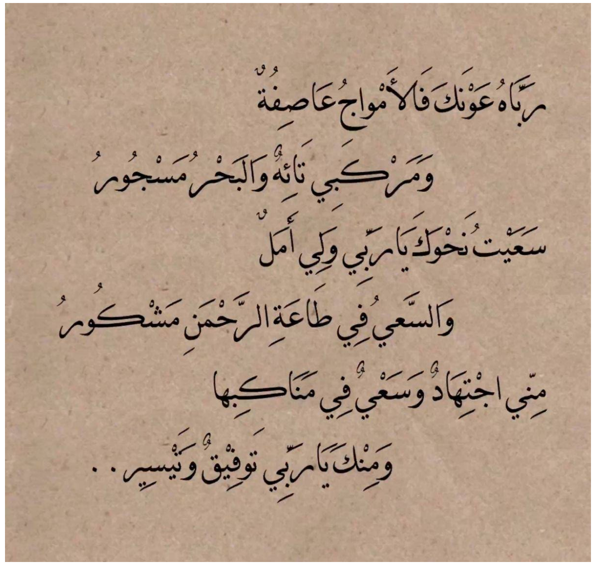
NOTES

When estradiol is high enough, the negative feedback on LH that normally occurs by estrogen is shut off, and it has a positive feedback on LH secretion

- 2. The granulosa cells of the follicles begin to secrete small but **increasing quantities of progesterone** a day or so before the preovulatory LH surge, and it has been suggested that this secretion might be the factor that stimulates the excess LH secretion.

Summary


Hypothalamus
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



رَبَّاهُ عَوْنَكَ فَالأَمْوَاجُ عَاصِفَةٌ
وَمَرْكَبِي تَائِهٌ وَالبَحْرُ مَسْجُورُ
سَعَيْتُ نَحْوَكَ يَا رَبِّي وَلِي أَمَلٌ
وَالسَّعْيُ فِي طَاعَةِ الرَّحْمَنِ مَشْكُورُ
مِنِّي اجْتِهَادٌ وَسَعْيٌ فِي مَنَاكِبِهَا
وَمِنْكَ يَا رَبِّي تَوفِيقٌ وَتَيْسِيرُ ..

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	42	Follicle	Oocyte
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!