

# Reproductive Block

﴿قل سيروا في الأرض  
فانظروا كيف بدأ الخلق﴾  
صدق الله العظيم

- Text
- Only in Females' slide
- Only in Males' slides
- Important
- Numbers
- Doctor notes
- Extra Notes

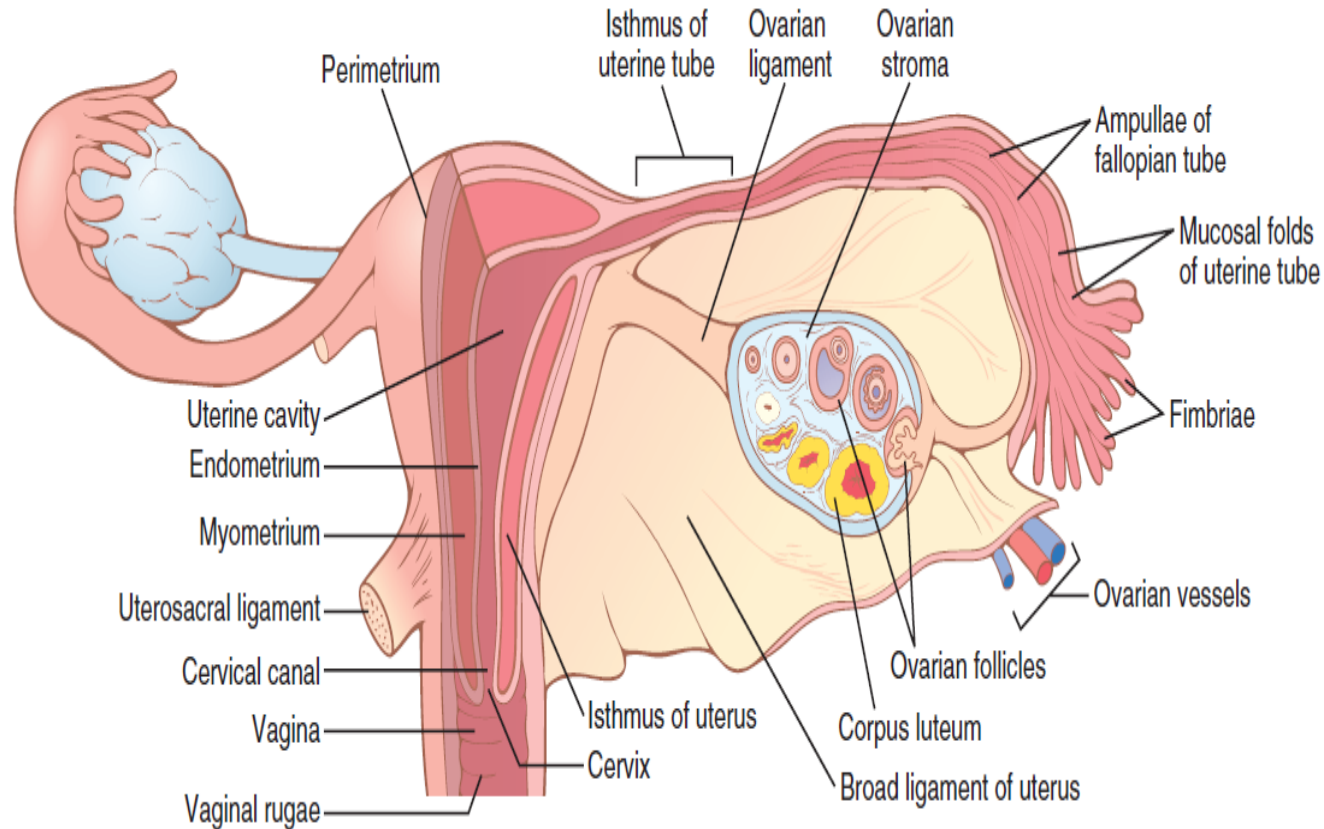


# Menstrual Cycle (Ovarian & Uterine cycles)

By the end of this lecture, students should be able to describe:

1. Recognize the hypothalamic- pituitary-ovarian-axis.
2. Describe the physiological phases of ovarian cycles.
3. Describe the changes that occur in the ovaries leading to ovulation.
4. Describe the development and the fate of corpus luteum.
5. Describe the normal phases of menstrual cycle.
6. Discuss the structural changes that occur in the endometrium during the menstrual cycle and explain how these changes are hormonally controlled.
7. List the hormones of female reproduction and describe their physiological functions.
8. Describe the physiology of menopause and the disorders of menstruation.

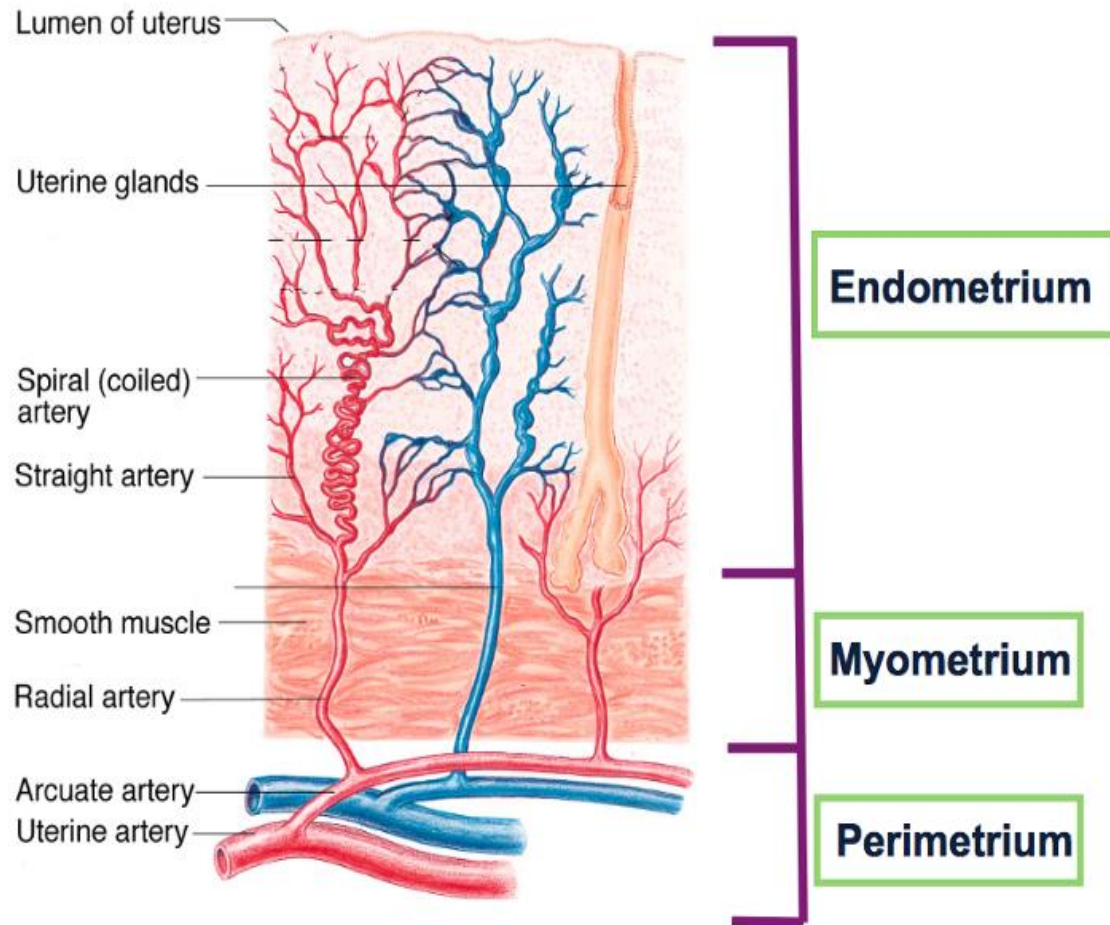
# Physiologic Anatomy of The Female Sexual Organs



- ▶ The picture shows the principal organs of the human female reproductive tract, including the ovaries, fallopian tubes (also called uterine tubes), uterus, and vagina.
- ▶ 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 membrane and eventually into a baby.

Since the vagina is in the middle between the urethra and the rectum, During delivery they put a catheter to evacuate the urinary bladder for easier delivery + enema to expel the rectum contents to facelift the delivery.

# Layers of Uterine Wall



- ▶ Uterine wall, which is made up of three different layers. There's the outer perimetrium, the middle (muscular) myometrium (that's the thickest layer), and the inner endometrium (thinner layer).
- ▶ But only one of these layers undergoes the changes during the uterine cycle, and that's the endometrium.
- ▶ The endometrial tissue itself is also made up of two layers:
  1. Basilar zone, which attaches the endometrium to the underlying myometrium.
  2. Functional zone, which is the part that changes throughout the uterine cycle.

# Introduction of Female Reproductive Physiology

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## ▶ Monthly ovarian cycle:

In normal reproductive years of female there is a monthly rhythmical changes in the rates of secretion of female hormones & corresponding physical changes in the ovaries & other sexual organs (menstrual / sexual cycle).

## ▶ Duration of the cycle:

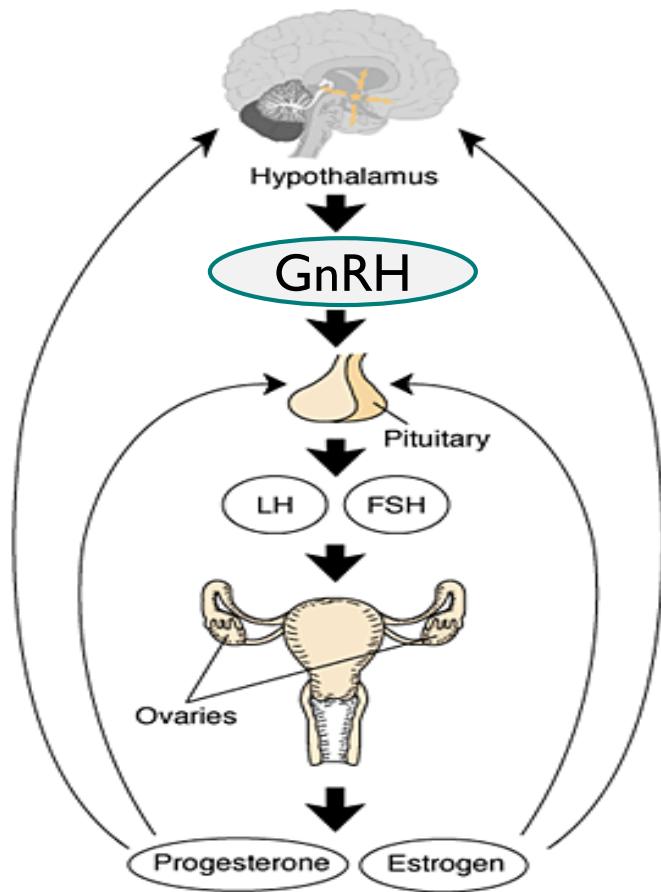
Duration of the menstrual cycle averages 28 days (20 - 45 days).

(menstrual cycle = ovarian cycle + uterine cycle)

## ▶ Results of the female sexual cycle: (important)

1. Single ovum (oocyte) البويضة البدائية is released from the ovaries each month.
2. Uterine endometrium is prepared for implantation of the fertilized ovum (Under the effect of estrogen and secretory changes).

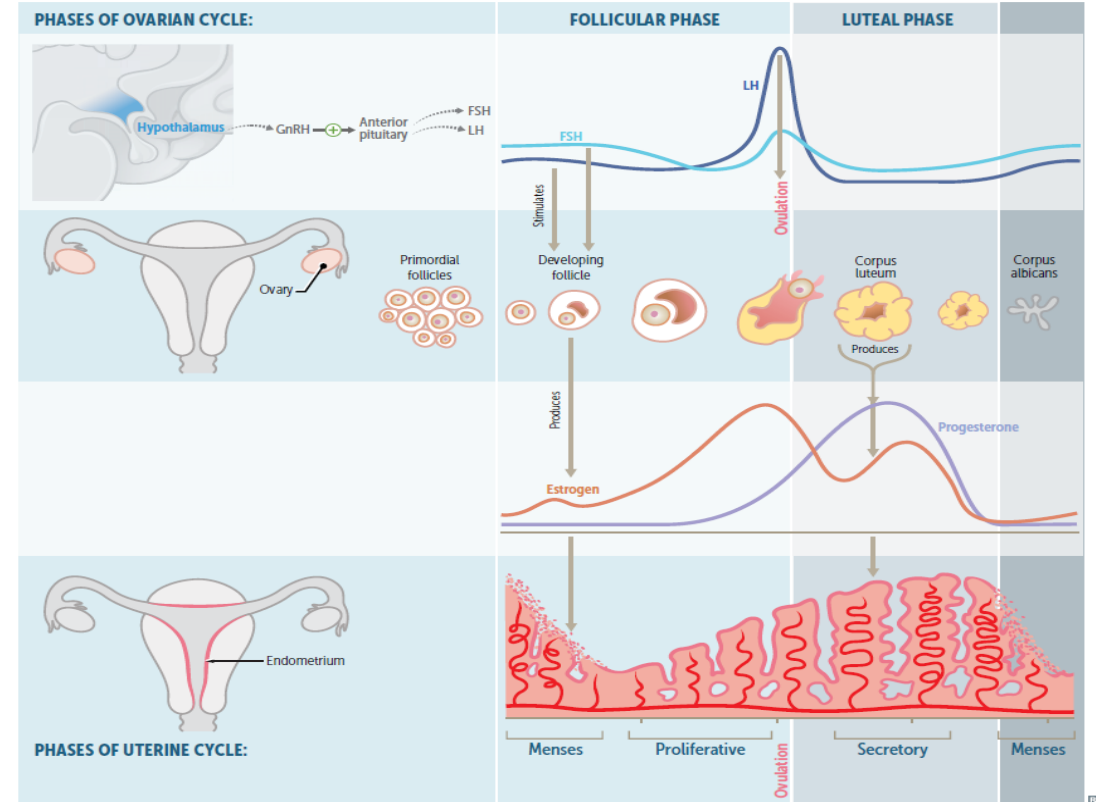
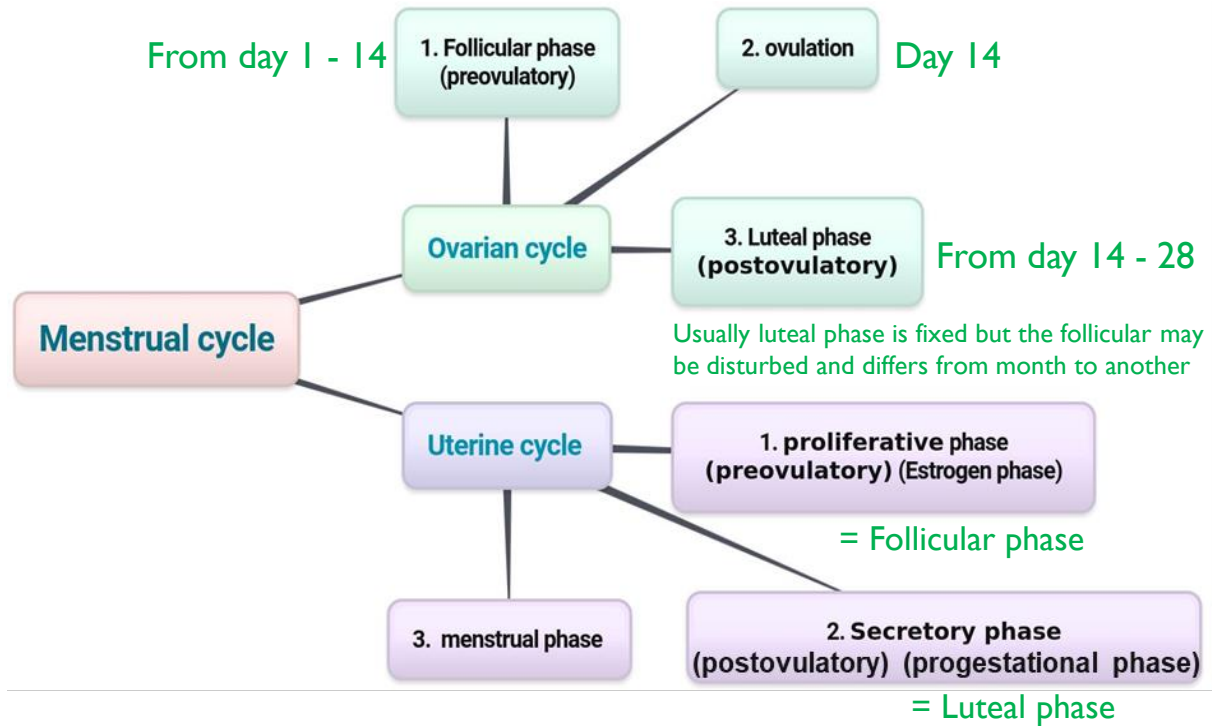
# Gonadotropic Hormones & Their Effects on The Ovaries



- ▶ The ovarian changes during the sexual cycle depend completely on FSH & LH secreted by anterior pituitary, **controlled by negative feedback**.
  - ▶ **In the absence of these hormones, the ovaries remain inactive throughout childhood.**
  - ▶ **At puberty the anterior pituitary starts to secrete FSH & LH which lead to the beginning of monthly reproductive cycles.**
  - ▶ **First menstrual cycle is called menarche.**
  - ▶ Both FSH and LH stimulate their ovarian target cells by combining with highly specific receptors leading to an increase:
    1. Rates of secretion.
    2. Growth & proliferation of the cells.
- 
- ▶ GnRH released at puberty & stimulates the release of FSH and LH which are proteins (peptide hormones) & we cannot measure GnRH from blood because its secretion is pulsatile, not sustained.
  - ▶ in females it will affect ovaries only not endometrium or uterus and in males it will affect testis, then it will stimulate the release of progesterone and estrogen in female and testosterone in male and these are steroid hormones so, it can cross BBB.
  - ▶ Oral contraceptives contain estrogen and progesterone.
  - ▶ All hormones cause -ve feedback except oxytocin and estrogen can cause both -ve feedback & +ve feedback.

# Overview of Menstrual Cycle

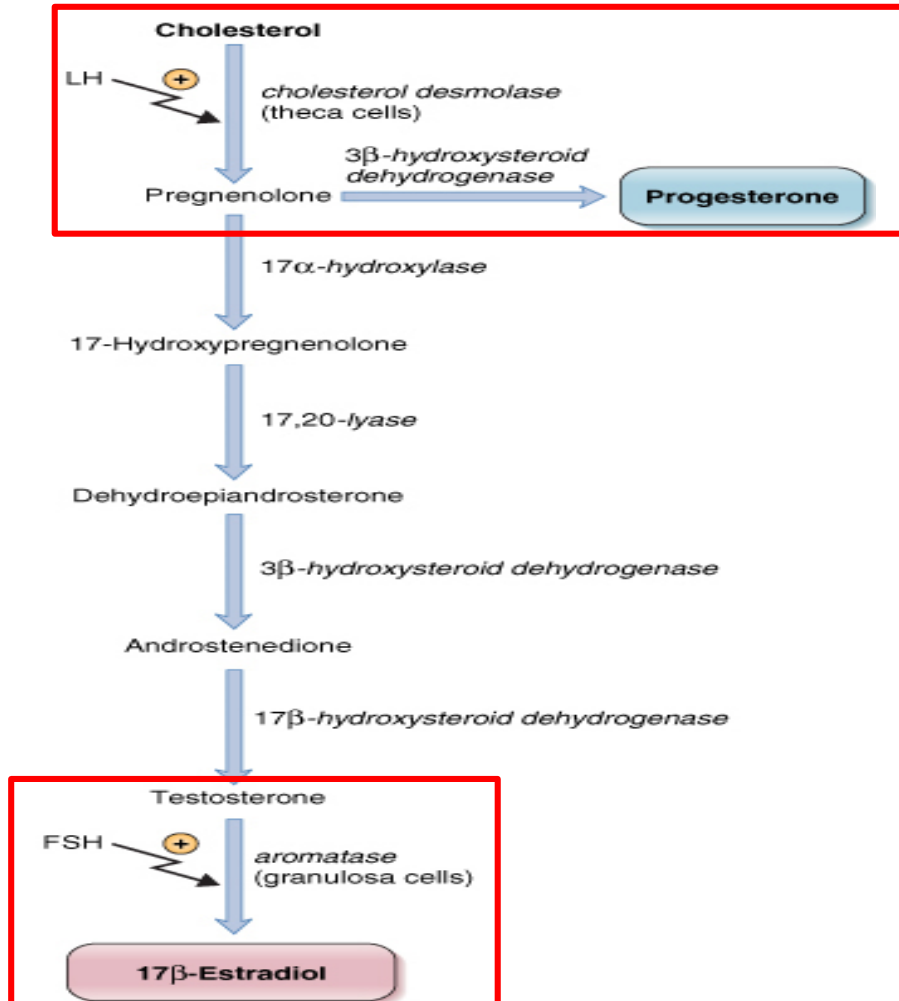
- Mnemonic:**
- ✓ Progesterone → pro- means after or extra, so we correlate its function time being after ovulation.
  - ✓ To memorize the different phases of each cycle remember this sentence: (FOoL Many Protective Sloths) → (Follicular, Ovulatory, Luteal, Menstrual, Proliferative, secretory)



- ✓ When we start to count the days of the cycle? when the bleeding starts.
- ✓ The menstrual cycle الدورة الشهرية composed of two cycles:
  1. The Ovarian cycle which occurs in the ovaries. تغيرات تحدث في المبايض
  2. The Uterine cycle which occurs in the endometrium of the uterus. تغيرات تحدث في الطبقة الداخلية للرحم

خطوا بالكم أن التغيرات والCycles متداخلة وليست جميعها متسلسلة. مثل ماهو موضح بالصورة:  
 ال(Follicular Phase + proliferative phase + menstrual phase) يحدثون بنفس الوقت مع اختلاف أوقات البداية والنهاية، وبعدهم يحدث الOvulation. وبعدها ال(Luteal phase + secretory phase)

# Effect of LH & FSH In Biosynthetic Pathway For Progesterone & 17 $\beta$ -estradiol In The Ovaries

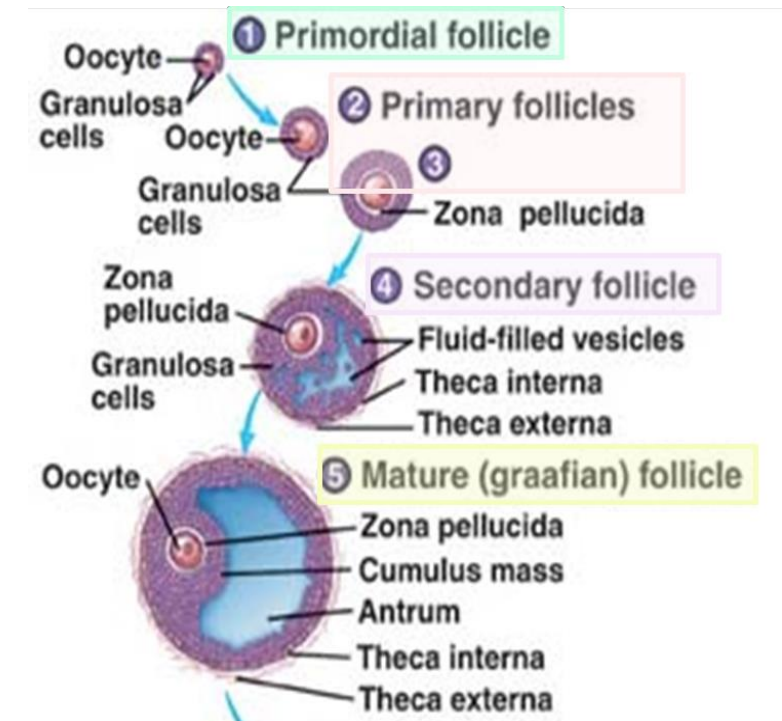
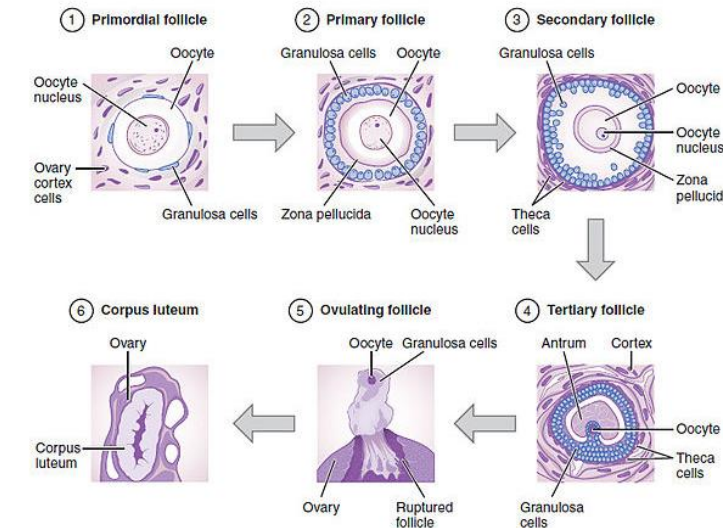
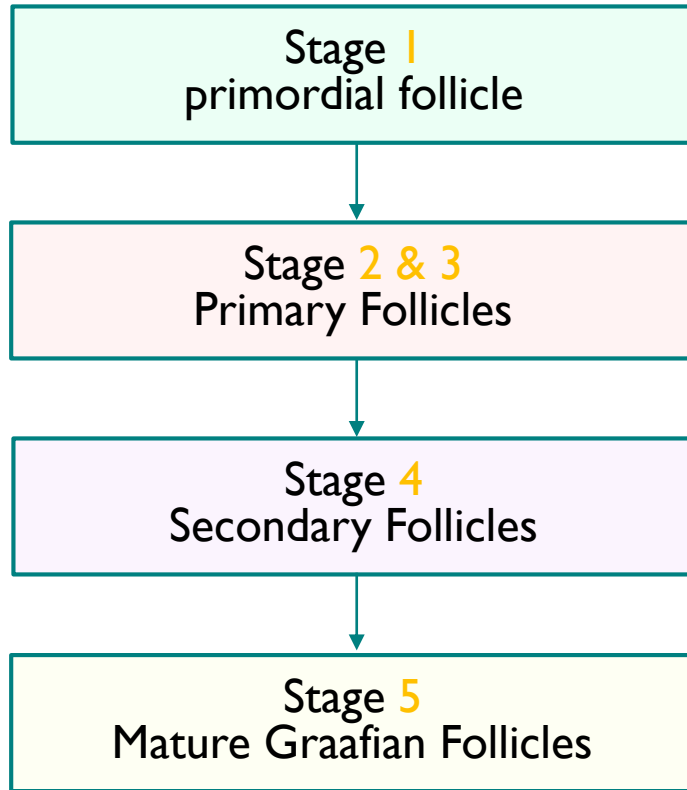


▶ What should I memorize from this diagram?

1. Luteinizing hormone (LH) stimulates cholesterol desmolase enzyme in theca cells. Cholesterol desmolase enzyme is the enzyme that converts cholesterol to pregnenolone which is the first step of steroids hormone synthesis.
2. Pregnenolone will be converted into progesterone by 3 $\beta$ -hydroxysteroid dehydrogenase.
3. Follicle-stimulating hormone (FSH) stimulates aromatase enzyme in granulosa cells. Aromatase enzyme is the enzyme that converts testosterone to the 17 $\beta$ -estradiol.



# “Follicular” Phase of The Ovarian Cycle (Ovarian follicle growth)



When the follicular phase occur?

It occurs **1 - 14** days after the onset of menstruation in **28** days cycle.

# Cont.

## Stage I: Primordial Follicle

- ▶ In female child each ovum (oocyte) is surrounded by single **granulosa cell** sheath called primordial follicle.

Ovum (oocyte) = الصبيغة البدائية للبويضة

- ▶ Functions of granulosa cells during childhood: **(Important)**

1. Provide nourishment الغذاء for the ovum.

2. Secrete oocyte maturation inhibiting factor which keeps the ovum in its primordial state.

- ▶ Embryo female has 7.000.000 primordial follicle (the ova is lined by single layer of follicular cells and layer of granulosa cells).

- ▶ Why is ova inside follicle? Ova has secretions to keep it from drying out.

- ▶ After delivery (fetus female) has 2.000.000 follicle. While In puberty, female has 500.000 follicle.

شرح الكلام:

Primordial Follicle during the childhood هي تكوّن الـ Follicular phase من أول خطوة من الـ Primordial Follicle عبارة عن Ovum (الصبيغة البدائية للبويضة) محاطة بـ granulosa cell زي ما هو موضح بالصورة عالمين، أثناء الطفولة يكون عندنا منها بالملايين ولكنها تكون خاملة وما تكبر ولا يصير لها شيء إلى سن البلوغ (الخطوة الجاية). ليش البويضة تكون محاطة بالـ granulosa cell؟ وظيفة الـ granulosa cell بهذه المرحلة أنها توفر التغذية للـ ovum، وتفرز مثبط نمو للـ ovum حتى تحافظ عليها في حالتها البدائية وما تكمل نموها.



## Cont.

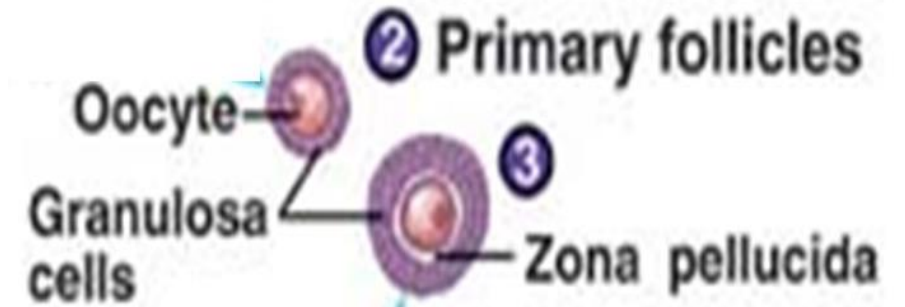
### Stage 2 & 3: Primary Follicles

- ▶ After puberty, anterior pituitary secretes FSH and LH which:

Stimulate the ovaries and result in growth of some follicles. Growth of the follicle begins with increase in size of the ovum & growth of additional layers of granulosa cells of some follicles.

شرح الكلام:

ثاني وثالث خطوة من Follicular phase هي تكوّن ال Primary Follicle after the puberty. بعد البلوغ ال anterior pituitary راح تفرز هرمونين هم: FSH & LH. في هذه المرحلة: راح تتحفز عندنا المبايض عشان يزيد حجم ال ovum وتزيد لنا كمية ال granulosa layers المتكونة من الخطوة السابقة، ونتيجة لذلك راح يزيد عندنا حجم بعض ال follicle. **هذه الخطوات تصير تحت تأثير هرمون ال FSH فقط**، بينما الخطوة الجاية هرمون ال FSH ما يقدر لحاله يستوعب حجم النمو فيحتاج مساعدة هرمون ال LH.



# Cont.

## Stage 4: Secondary Follicles

- ▶ During the first few days of the monthly female reproductive cycle there is increase in secretion of FSH and LH.
- ▶ Increase in FSH is slightly more & earlier than LH which causes the acceleration of growth of many primary follicles each month.
- ▶ There is proliferation of the granulosa cells to many layers. The ovary interstitium collect in several layers outside the granulosa cells to form a second mass of cells called theca.

### This theca is divided into 2 layers: (Important)

1. Theca interna, the cells have epitheloid characteristics and similar to the granulosa cells and secrete sex hormones (estrogen and progesterone).
2. Theca externa, the outer layer, develops into a highly vascular connective tissue capsule of the developing follicle.

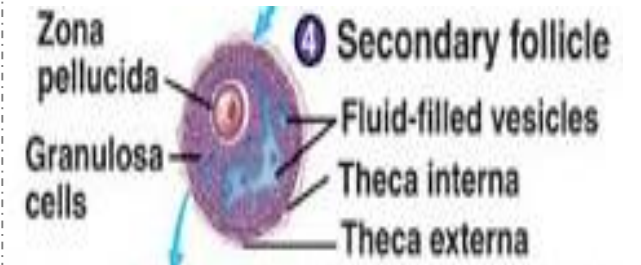
شرح الكلام:

رابع خطوة من الFollicular phase هي تكوّن الSecondary Follicle. يزيد عندنا إفراز هرموني الFSH & LH أثناء الأيام الأولى من الدورة الشهرية، وزي ما قلنا بالاسلايد السابق بداية النمو والتكون تكون تحت تأثير هرمون الFSH، لكن في هذه المرحلة الهرمون لحاله ما يقدر يستوعب الحجم والنمو، فراح يحتاج مساعدة هرمون الLH وهذا راح يسرّع لي نمو كثير من الprimary follicles .

الgranulosa cells تبدأ تكبر ويصير فيها عدة طبقات واحدة منها اسمها theca cells الtheca cells نفسها تنقسم لطبقتين:

Theca interna: الطبقة الداخلية وهي تشبه تشبه للgranulosa cells وتفرز استروجين وبروجسترون.

Theca externa: الطبقة الخارجية، وتكون مليئة الأوعية الدموية (ما تفرز هرمونات فقط طبقة محيطة)



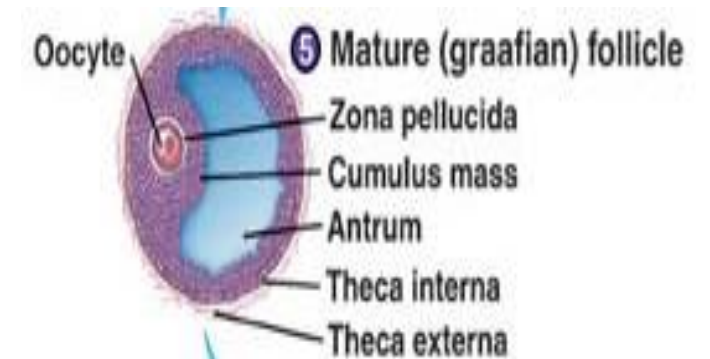
# Cont.

## Stage 5: Mature Graafian Follicles (very large and ready for rupture)

- ▶ Few days after proliferation & growth of the follicles, the granulosa cells secrete follicular fluids **contain high concentration of estrogen**. This fluid accumulate to form antrum within the mass of the granulosa cells.
- ▶ **The early growth of the follicle up to the antral is under FSH stimulation (The follicular cells (granulosa cells) have specific receptor for FSH) Then there is accelerated growth of the follicle to larger follicle called vesicular follicle caused by:**

يعني هذه هي الثلاث خطوات اللي راح تُنتج لي Mature Graafian Follicles

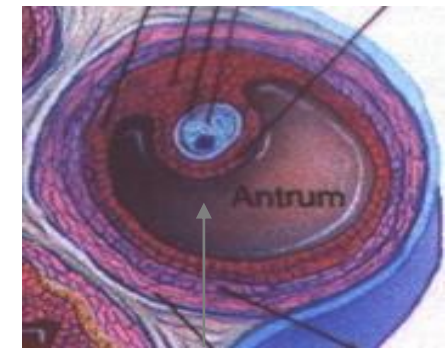
1. Estrogen secreted into the follicle causes the granulosa cells to form increasing number of FSH receptors which causes **positive feedback effect**.
2. Both estrogen & FSH combine to promote LH receptors on the granulosa cells, allowing more increase follicular secretion.
3. The increasing estrogen from the follicle plus increasing LH from the anterior pituitary causes proliferation of the follicular theca cells & increase their secretion.



الشرح بالاسلايد الجاي

# Cont.

- ▶ The antral follicles begin to grow. The ovum enlarges & remain embedded at one pole of the granulosa cells of the follicle.
- ▶ After a week or more of growth (but before ovulation occurs) one of the follicles begins to outgrow all the others, and the remaining 5 to 11 developing follicles involute (a process called atresia). (The cause of the atresia is unknown)
- ▶ **As a result:** (only in females slides)
  1. Rising estrogen levels: Positive feedback locally & Negative feedback centrally.
  2. Rising inhibin levels: Further negative feedback.
  3. Declining FSH levels:
    - Withdraw growth support.
    - Atresia in lesser follicles.



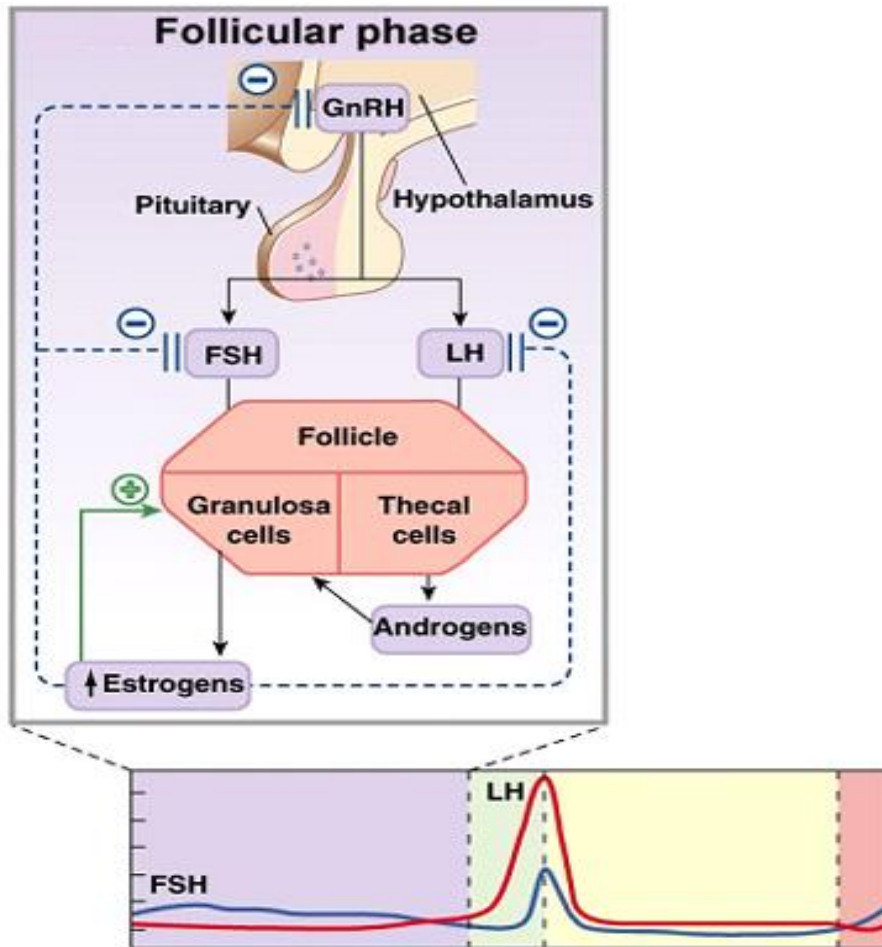
Mainly contains estrogen

- ▶ Once the bleeding starts, FSH secretion start as well, to prepare for the next cycle but its not specific so, it will stimulate from 5-11 follicles only. Each women lose 5-11 ovum monthly
- ▶ The fastest follicle to grow remain in the cycle, while others degenerate because of the low estrogen level.
- ▶ Estrogen has -ve feedback on the FSH while it has two +ve feedback:
  1. paracrine: estrogen and FSH increase LH stores in the follicles.
  2. Endocrine: before the follicle rupture, it sends signals to AP, the signal is "I'm ready to rupture and I need LH".
- ▶ So, estrogen occur in blood and fluctuate (up & down) → LH surge (increase LH) → rupture.
- ▶ What will happen if estrogen level is constant (not fluctuate) → no LH surge → no rupture.

باختصار:

ال granulosa cells راح تنتج كمية كبيرة من follicular fluid اللي يحتوي على كمية كبيرة من الاستروجين وهذا راح يتجمع ويسوي الانtrum تحت تأثير الهرمون FSH. بعد أسبوع، بويضة واحدة من اصل 5-11 بويضة هي اللي بتكبر والباقي راح يتحللون.

# Summary of “Follicular” Phase of The Ovarian Cycle



- ▶ During the first few days of the monthly female sexual cycle there is an increase secretion of FSH, LH.
- ▶ The early growth of the primary follicle up to the antral stage is under FSH stimulation only. Then there is accelerated growth of the follicle to larger follicle called vesicular follicle (Graffian) caused by:
  1. Estrogen  $\uparrow$  FSH receptors (**positive feedback effect**).
  2. Estrogen & FSH combine to promote LH receptors on the original granulosa cells in addition to FSH stimulation.  $\rightarrow$  Proliferation of the follicular theca cells & increase their secretion.
- ▶ From the growth of follicles to the formation of antrum is mainly done by FSH.
- ▶ Antrum is a sac filled with estrogen.
- ▶ At puberty there will only be FSH secretion, since it has target receptors on the follicular cells.
- ▶ During menstruation, FSH secretion is more than LH. LH is insignificant in this phase until the last 2 days (day I-I4), because GnRH is not specific for FSH secretion, so when the AP is stimulated, both FSH & LH will be released.

# “Ovulation” Phase of The Ovarian Cycle



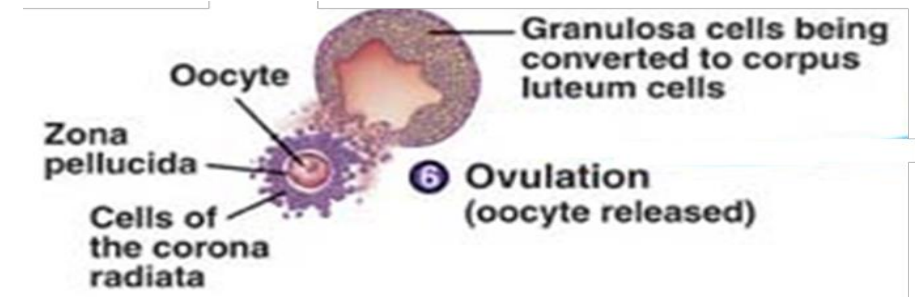
When the ovulation phase occur?

It occurs **14** days after the onset of menstruation in **28** days cycle.

What does that mean? It means it occurs in the half of the period time.

Ex: if the cycle is 28 days the ovulation will be in the 14<sup>th</sup> day.

If the cycle is 35 days the ovulation will be in the 21<sup>th</sup> day. (because if there is menstrual imbalance mostly the problem will be in the follicular phase)



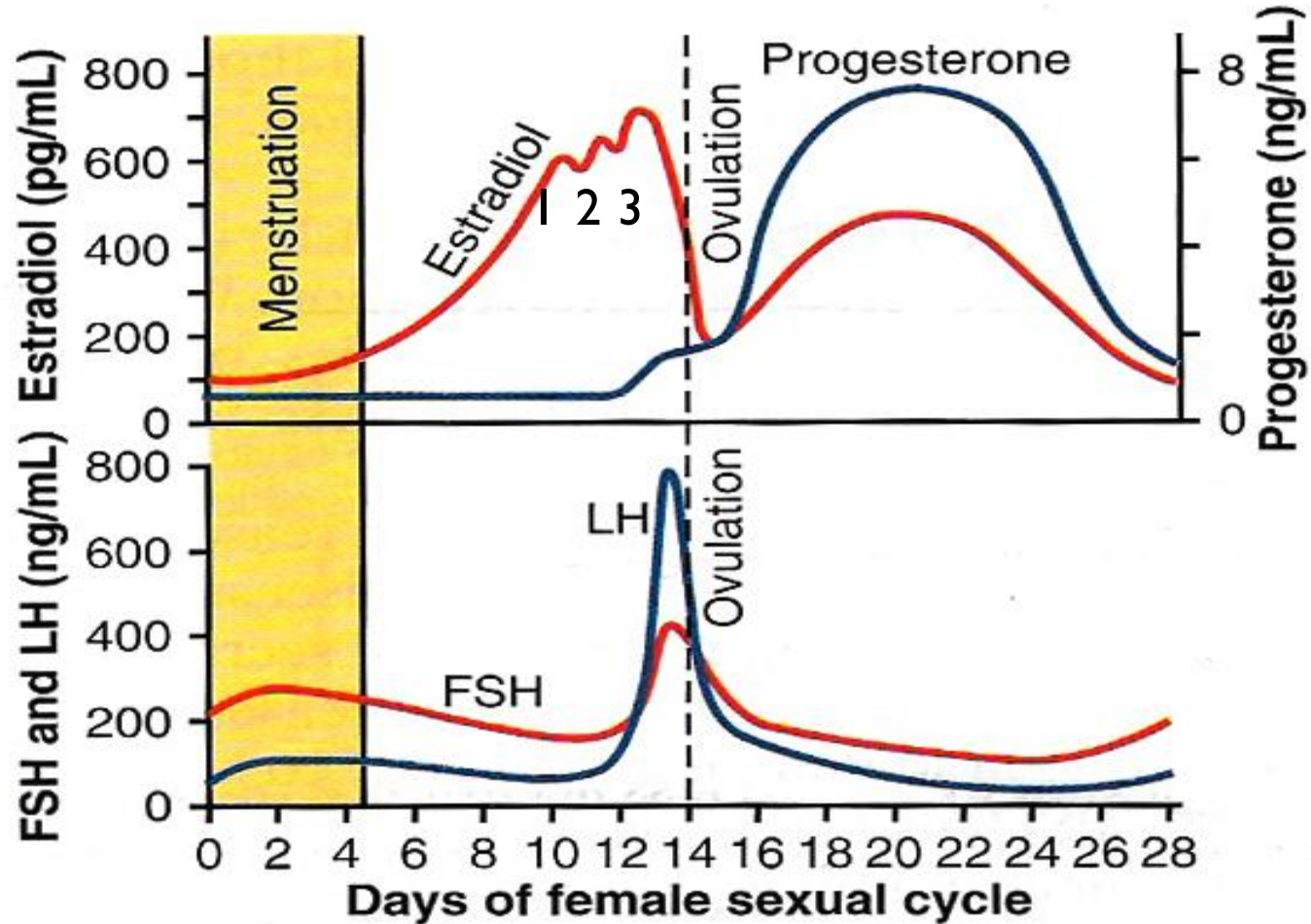
Before ovulation:

- ▶ **2** Days before ovulation, **the rate of LH secretion from the anterior pituitary increase markedly** to **6-16** fold & peak about **16** hours before ovulation. FSH also increases to **2** to **3** folds & acts synergistically with LH to cause swelling of the follicle before ovulation.
- ▶ LH surge is necessary for ovulation (**without LH hormone, ovulation will not occur**): LH has specific effect on the granulosa cells & theca cells converting them to progesterone secreting cells (**these cells are important in maintaining and protecting the embryo from abortion**) so the rate of estrogen secretion begins to fall about **1** day before ovulation while progesterone secretion begin to increase.
- ▶ **Ovulation can be detected by hormonal analysis & increase in body temperature due to the effect of progesterone.**

شرح الكلام:  
قبل التبويض بيومين نسبة الـ LH & FSH بتزيد وتؤدي الى انتفاخ البويضة. لو ماكان عندنا LH كثير مارح يتم التبويض لانه هو الي يخلي الـ granulosa & theca cells تنتج بروجسترون.



## Cont.



- ▶ In day 13 or 14 the follicle is ready so, it will secrete the estrogen (which is stored in the antrum) as signals to the brain.
- ▶ After multiple signals (3 times) the estrogen activate the anterior pituitary gland to secrete LH, then rupture happen

# Cont.

## Starting of ovulation (initiating):

- ▶ Large quantity of **LH** secreted by the anterior pituitary causes rapid secretion of **progesterone** from the follicle within a few hours.
- ▶ 2 events occur which are necessary for ovulation: **(Important)**
  1. The theca externa begins to secrete proteolytic enzymes & causes weakening of the wall result in swelling of the follicle & degeneration of the stigma.
  2. Rapid growth of new blood vessels into the follicle wall & prostaglandins are secreted into the follicular tissue.

Those two changes causes swelling of the follicle, plasma transudation into the follicle & degeneration of the stigma with discharge of the ovum.

شرح الكلام:

theca externa تفرز انزيمات تضعف جدار follicle وتؤدي الى انتفاخها. اوعية دموية تبدأ تنمو داخل ال follicle وتفرز prostaglandins. كل هذي الاحداث تتسبب في التبويض.

# Cont.

## During Ovulation:

- ▶ Small area in the center of the follicle called stigma protrude & fluids ooze from the follicle.
- ▶ The stigma ruptures allowing more viscous fluid outward carrying with it the ovum surrounded by mass of granulosa cells called corona radiata (**Corona radiata= granulosa cells**).
- ▶ In this stage, the ova has layer of follicular cells (corona radiata) and zona pellucida (protective layer that a sperm should penetrate).

شرح الكلام:  
في منطقة بالfollicle اسمها stigma تصير بارزة ويبدأ السائل يتسرب منها  
ومع السائل تطلع البويضة وتكون حولينها corona radiata.

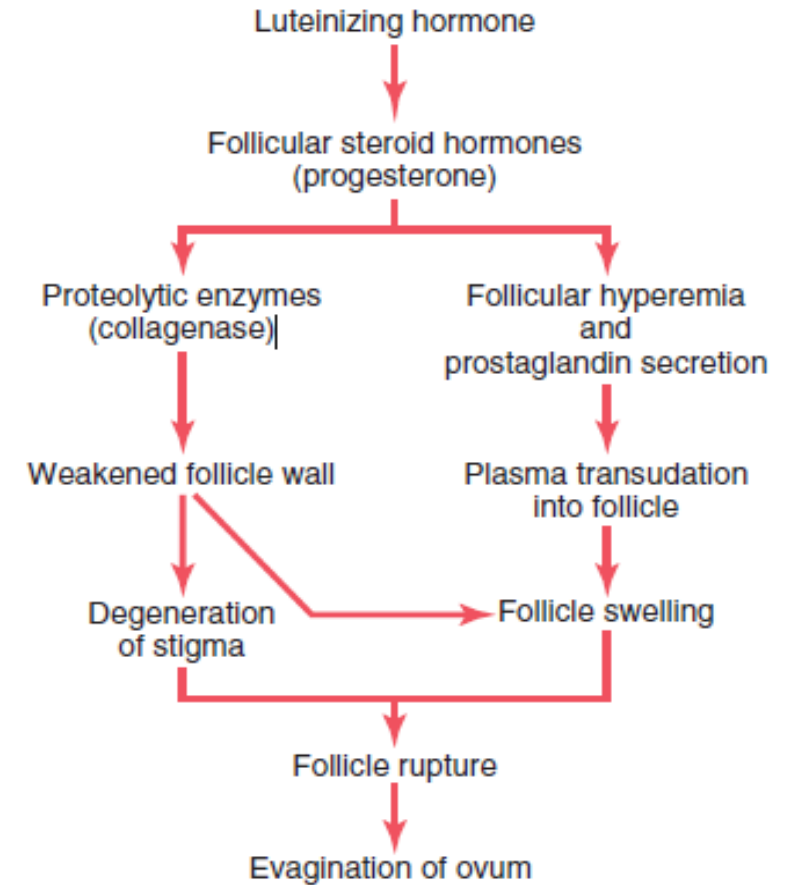
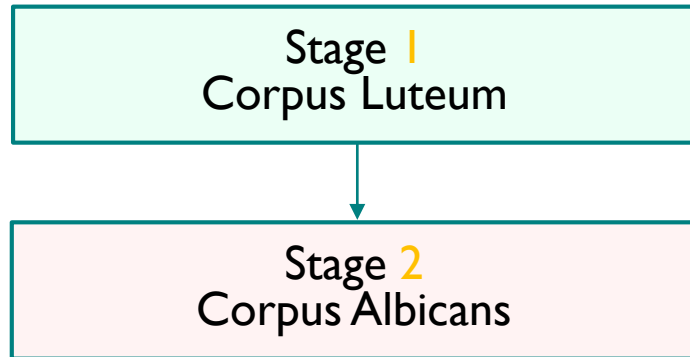


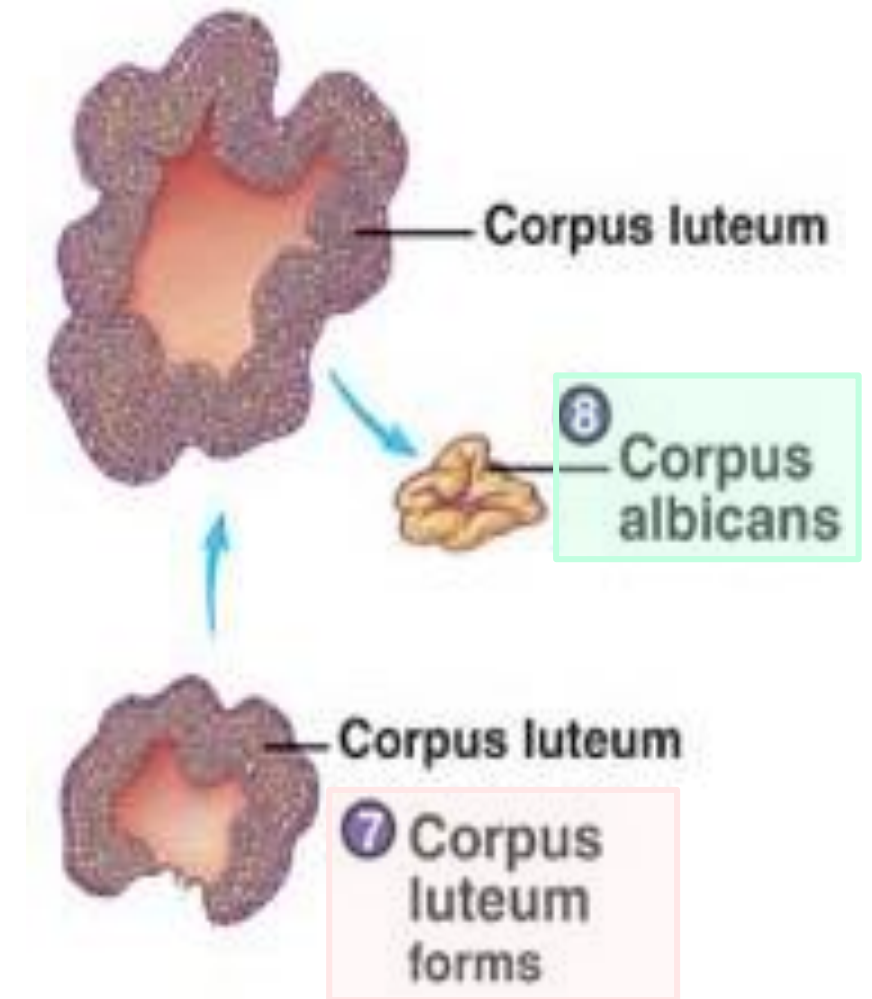
Figure 82-6. The postulated mechanism of ovulation.

# “Luteal” Phase of The Ovarian Cycle



- ▶ When the luteal phase occur?

It occurs 14 – 28 days after the onset of menstruation in 28 days cycle.



# Cont.

From ovulation until bleeding phase LH is the dominant hormone only.

## Stage I: Corpus luteum (الجسم الأصفر)

- ▶ After expulsion of the ovum from the follicle, the remaining granulosa & theca interna cells change to lutein cells & become filled with lipid inclusions giving them yellowish appearance.
- ▶ The granulosa cells with the theca cells called corpus luteum.
- ▶ The functions granulosa cells: develop extensive intracellular endoplasmic reticula & form **large amount of progesterone** & few estrogen.
- ▶ The theca functions cells: form mainly androgens which are converted by granulosa cells into female hormones (by aromatase; the adipose tissue contain this enzyme, so obese males will have high amounts of estrogen in the blood stream → female characteristics) and small amount can appear in plasma. Androgen are not diffused to blood from day 1–14 (follicular phase) because it diffuse from the theca cells to the follicular cells. While the estrogen is diffused to blood and stored in the antrum.
- ▶ The corpus luteum grow to about 1.5 cm in diameter, at about 7 to 8 days after ovulation. Then begins to involute & losses its secretory function & its yellowish characteristic about 12 days after ovulation & becomes **corpus albicans** & replaced by connective tissue & absorbed.

شرح الكلام:

بعد خروج البويضة من follicle، المتبقي من granulosa & theca interna cells راح يتحولون الى lutein cells ويصيرون ممتلئين بالدهون وهذا اللي يعطي اللون الأصفر، ولهذا السبب نسمي corpus luteum بالجسيم الأصفر.

ال corpus luteum هي عبارة عن granulosa & theca cells وتبدأ تتكون بعد 7-8 أيام بعد التبويض

• وظيفة granulosa cells: نمو ال endoplasmic reticulum وكمية كبيرة من الاستروجين البروجسترون.

• وظيفة theca cells تكون لنا الهرمونات الذكورية (androgens) اللي جزء منها راح يتحول الى هرمونات أنثوية بواسطة انزيم aromatase

ال corpus luteum تبدأ تتحلل وتخسر خواصها بعد 12 يوم من التبويض وهنا تسمى corpus albican

# Cont.

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## Luteinizing Function of LH:

- ▶ A local hormone in the follicular fluid called luteinization – inhibiting factor hold the luteinization process until after ovulation.
- ▶ After extrusion of the ovum from the follicle the following changes occur:
  1. Conversion of granulosa and theca interna cells into lutein cells.
  2. Maintains secretion of progesterone & estrogen from the corpus luteum.
  3. Causes ovulation.

Very important : Lutein cells = found in corpus luteum, second half of female sexual cycle and secret progesterone.

## If pregnancy occurs:

- ▶ The chorionic gonadotropin (hCG) (هرمون الحمل) from the placenta (Trophoblast) act on the corpus luteum to prolong its life for 2 to 4 months of pregnancy. (الدكتور قال بنرجع ناخذها بالتفصيل في محاضرة الحمل، بس اعرفوها بشكل سطحي الحين)
- ▶ The ova inside primordial follicle moves to fallopian tube and fertilization occurs in ampulla → form zygote which is covered by a layer of trophoblast cells secreting hCG. If there is no pregnancy, corpus luteum convert to corpus albican → it will die.

(The hCG is almost biochemically identical to LH, it does it's same functions primarily by maintaining the corpus luteum)

# Cont.

Important

- Q1) What are the dominant hormone in the follicular phase?  
**Estrogen**
- Q2) What are the dominant hormone in the luteal phase?  
**Progesterone**

## Stage 2: Corpus albicans الجسم الأبيض (Involution of the corpus luteum and onset of the next ovarian cycle)

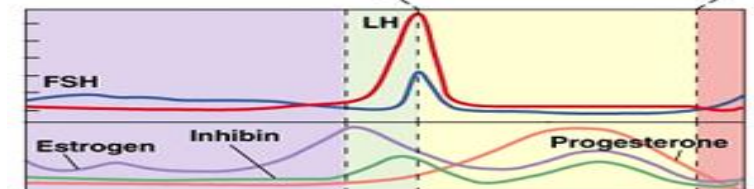
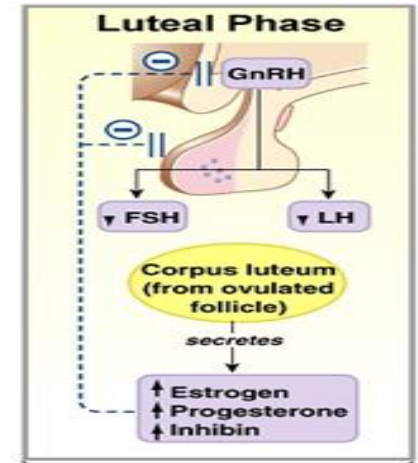
- Lutein cells of the corpus luteum secrete both progesterone & estrogen & inhibin which all together will inhibit both FSH & LH by causing negative feedback on the anterior pituitary.

(The corpus luteum needs LH to survive, so by inhibiting it's release from the AP its killing itself)

- Low levels of both FSH & LH & causes the corpus luteum to degenerate completely, called involution of the corpus luteum.

- Around 26<sup>th</sup> days of normal sexual cycle & after involution of corpus luteum (because there is no LH), sudden cessation of estrogen, progesterone & inhibin removes the negative feedback inhibition of the anterior pituitary & allowing ↑ secretion of FSH & LH again.

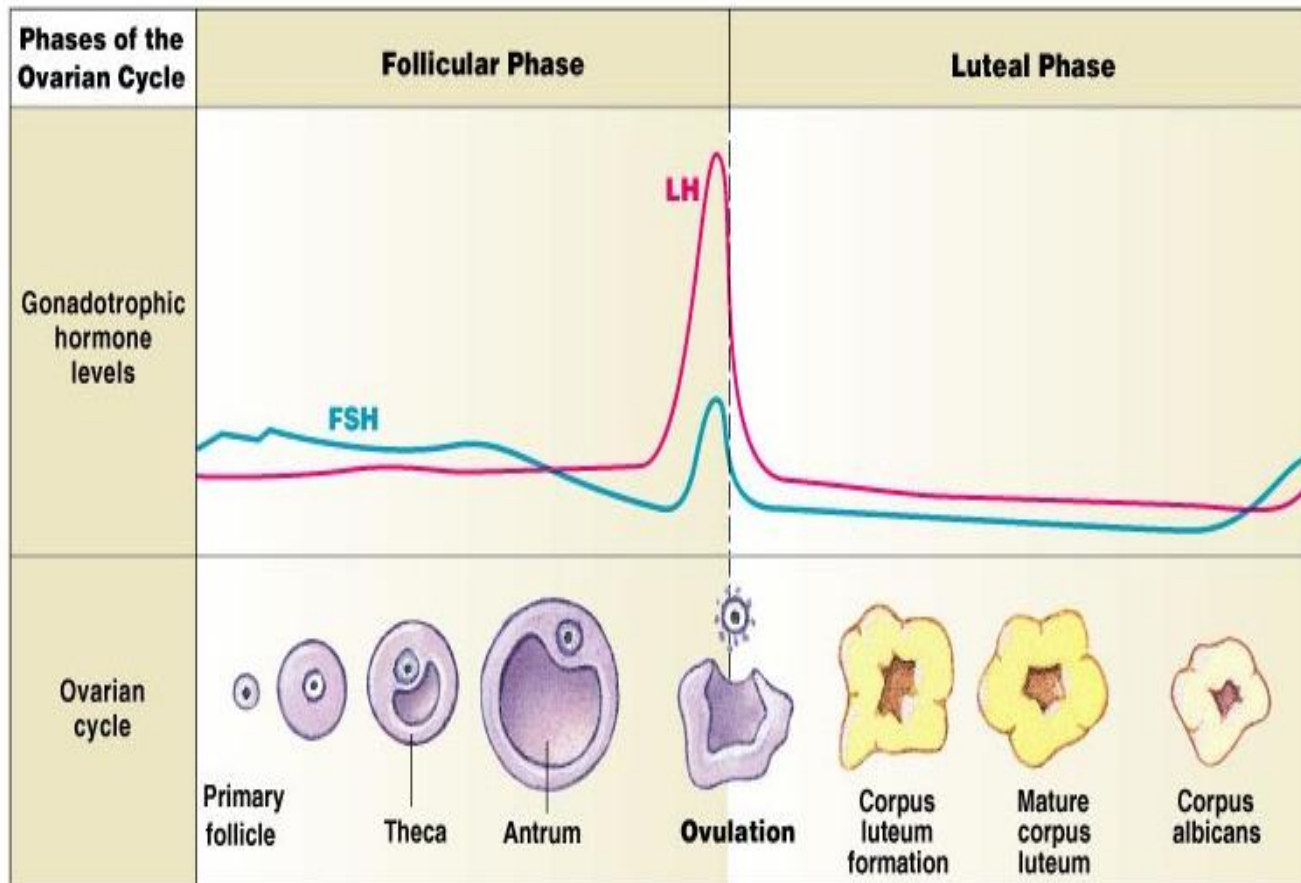
- FSH & LH initiate the growth of new follicles, beginning a new ovarian cycle.



شرح الكلام:

الـ lutein cells تفرز بروجسترون و استروجين وهم اللي راح يثبطون إفراز الـ FSH & LH. لما الـ FSH & LH يكونون نازلين (مثبتين) راح يؤدون الى تحلل الـ corpus luteum ويصير اسمه .corpus albican.

# The End of The Ovarian Cycle



At the end of the cycle when the corpus luteum degenerates, there is no negative feedback on the anterior pituitary anymore, FSH & LH are released again to initiate the beginning of a new cycle.



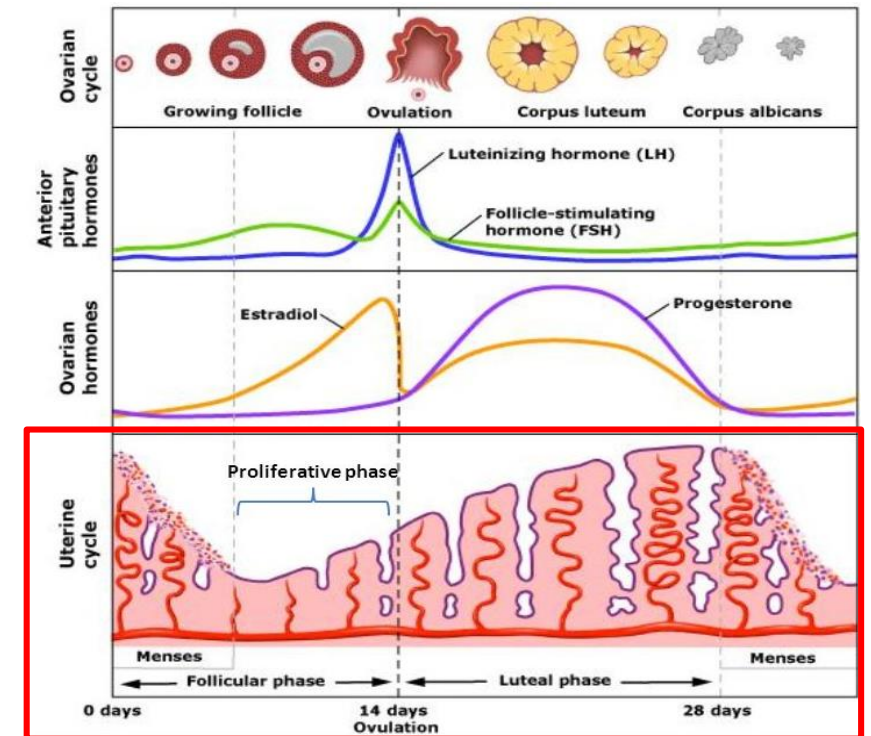
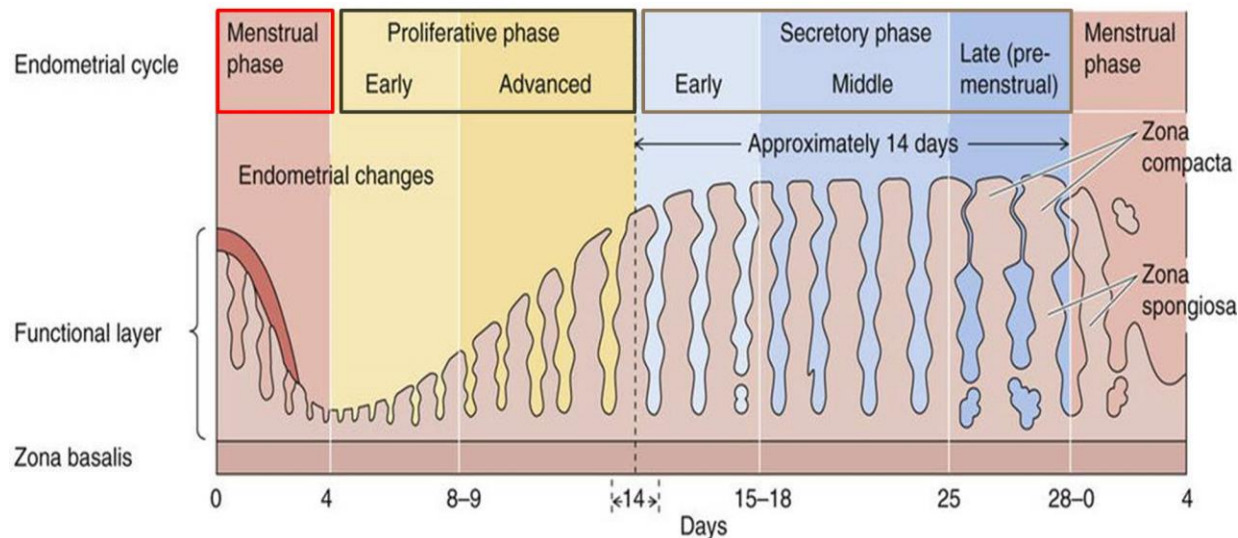
# Uterine Cycle (Endometrial Cycle)

- ▶ Monthly endometrial cycle and menstruation is associated with the monthly cyclical production of estrogens & progesterone by the ovaries in the lining of the uterus.

- ▶ The Uterine cycle occurs in the endometrium of the uterus.

LH and FSH affect the ovaries → so, they secrete estrogen and progesterone → affect the uterus endometrium.

- ▶ Phases:



# Dr. Alotaibi's Explanation For The Upcoming Slides

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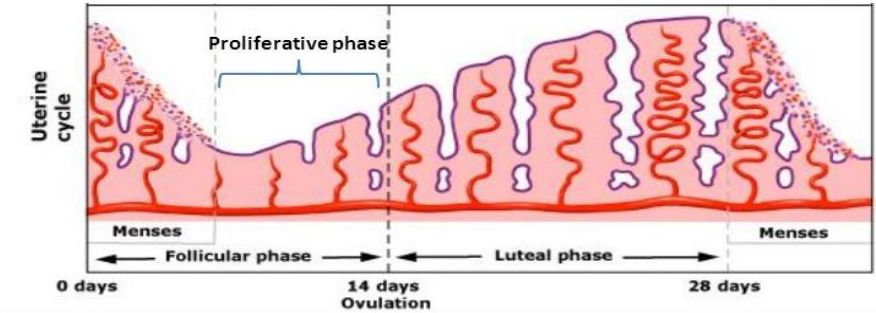
- ▶ The functioning layer of the endometrium is the one which will be renewed monthly.
- ▶ The Basal layer will remain from previous period at day 5, when menstruation stops under the influence of estrogen; the endometrium will proliferate and increase the cell and blood supply.
- ▶ Estrogen has two effects: working on the endometrium and cervix.
- ▶ At the end of day 14 or 15 the thickness is from 3-5 mm (it was in an exam two year ago).
- ▶ Until now it's not ready yet for pregnancy!
- ▶ The other action of estrogen before ovulation by 2 days the estrogen at the highest level, she will have secretion from the cervix, and under microscope there will be channels or holes, that direct the sperm into the fallopian tube.
- ▶ The other half of the cycle is controlled by progesterone from day 15-28, it will make the secretion very thick so the sperm can't penetrate the cervix (because the brain think that pregnancy is happening, so it must protect the embryo from other sperms), the progesterone every month will prepare the endometrium for the pregnancy by increasing the secretion and implantation.
- ▶ How the embryo live its first three months? by uterine milk.

# Proliferative Phase (Estrogen Phase)

▶ When the Proliferative Phase occur? = follicular phase

Occurring before ovulation & it lasts for 11 days.

▶ Stages: Controlled by estrogen



1. At the beginning of each cycle, most of the endometrium has been desquamated by menstruation. After menstruation only thin layer of the endometrial stroma remains & the deeper portions of the glands & crypts of the endometrium.
2. Under the influence of estrogens, secreted in large quantities by the ovaries, the stromal cells & epithelial cells proliferate rapidly.
3. The endometrial surface re-epithelialized within 4-7 days after the beginning of menstruation. Before ovulation the endometrium thickness increases, due to increase numbers of stromal cells & progressive growth of the glands & new blood vessels.
4. At the time of ovulation, the endometrium is 3-5 mm thick. The endometrial glands, cervical region secrete a thin, stringy mucus (due to high estrogen level) which helps to guide sperm in the proper direction from the vagina into the uterus.

شرح الكلام:  
بعد Menstruation تكون بطانة الرحم رقيقة.  
بعد ما تفرز المبايض كميات كبيرة من الاستروجين ترجع البطانة تنمو وتصير سميكه، بهذه المرحله يفرز الرحم مادة مخاطية لتسهيل دخول sperm لها.

# Secretory Phase (Progestational Phase)

- ▶ When the Secretory Phase occur? = luteal phase

Occurring after ovulation & it lasts for 12 days.

- ▶ Stages: Controlled by progesterone

I. After ovulation, estrogen & progesterone are secreted in the later part of the monthly cycle by the corpus luteum (large amounts of progesterone and small amount estrogen).

- ▶ What are The effects of estrogen & progesterone?

- Estrogen: cause slight proliferation in the endometrium.
- Progesterone:
  1. Marked swelling & secretory development of the endometrium.
  2. The glands increase in tortuosity, excess secretory substances accumulate in the glands.
  3. Increase the blood supply to the endometrium & the blood vessels become highly tortuous.
  4. Increase lipids and glycogen deposits in stromal cells cytoplasm

مهم نعرف الفرق بين دور البروجسترون والاستروجين في هذه المرحلة

The estrogens cause slight increase cellular proliferation in the endometrium during this phase of the cycle, while progesterone causes marked swelling and secretory development of the endometrium.

# Cont.

2. **1 week** after ovulation, endometrium thickness is **5-6 mm**.
3. The secretory changes prepare the endometrium (stored nutrients) for implantation of the fertilized ovum .
3. Uterine secretions called “uterine milk” (هنا تبدأ تتكون البلاسينتا ويصير الامبلانتيشن) provide nutrition for the diving ovum.
4. The trophoblastic cells on the surface of the implanted ovum begin to digest the endometrium & absorb endometrial stored substances.

- ✓ No proliferation.
- ✓ Secretions = endometrial glands + blood supply = these secretion **NOURISH** the zygote until the placenta develops.
- ✓ No progesterone = zygote dies.
- ✓ Progesterone relaxes the myometrium = no abortion.

في هذه المرحلة يتم إفراز هرمون الأستروجين وكميات كبيرة من هرمون البروجسترون الضروريين لزيادة كثافة الجدار الداخلي المبطن للرحم واستقبال البيضة الملقحة.



# Menstruation Phase

## ▶ When the Menstruation Phase occur?

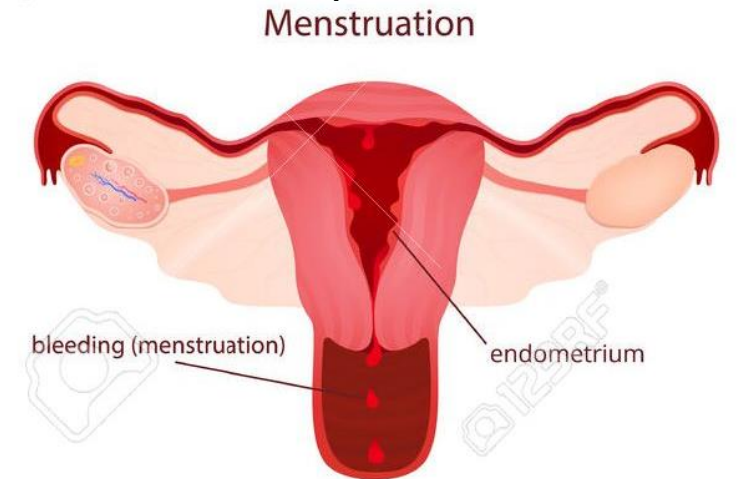
Occurring If the ovum is not fertilized, about **2 days** before the end of the monthly cycle& it lasts **in average 5 days**.

## ▶ Stages: How does the menstruation occur?

1. If the ovum is not fertilized, about **2 days** before the end of the monthly cycle, the corpus luteum involutes & estrogens & progesterone decrease to low levels.
2. Due to decrease estrogen & progesterone there is decrease stimulation of the endometrium, followed by involution of the endometrium to about **65%** of its previous thickness.

الendometrium دائما تحتاج تحفيز هرمون الاستروجين والبروجستيرون.  
في هذه المرحلة عندنا نقص في هذه الهرمونات، بالتالي الendometrium راح تضعف و  
تتكسر ولما تتكسر راح تضعف وتتكسر الarteries اللي داخلها بالتالي يحدث الbleeding.

مشروحة أكثر بالاسلايدات الجاية



# Cont.

3. During the **24 hours** preceding the menstruation, there is vasospasm of the tortuous blood vessels due to release of vasoconstrictor (prostaglandins). There is:

A. Vasospasm.

B. Decrease nutrients to the endometrium.

C. Loss of hormonal stimulation.

All initiate necrosis in the endometrial blood vessels.

No estrogen + no progesterone = degeneration of lutein layer = necrosis

## What will happen during this phase?

1. Gradual necrosis of the outer layer of the endometrium leads to separation from the uterus at the site of the hemorrhages.

2. Within **48 hours**, all the superficial layers of the endometrium desquamated in the uterine cavity.

3. The mass of desquamated tissue & blood plus the contractile effects of prostaglandins initiate contractions which expel the uterine contents.

✓ This blood is rich with prostaglandin A2 causes contractions and spasms when it reaches the myometrium (has prostaglandin receptors).

✓ In each spasm endometrium will rupture and blood supply will tear = pain.



# Menstruation Phase

## What will happen during this phase?

- ▶ In normal menstruation, about 40 ml of blood + 35 ml of serous fluid are lost.
- ▶ The menstrual blood is normally non-clotting due to the presence of fibrinolysin.
- ▶ Leukorrhea during menstruation: During menstruation, leukocytes are released

with the necrotic material & blood so the uterus is highly resistant to infection (protective mechanism).

## Why do females' feel pain during this phase? 😞

- ▶ As we said before, shedding of the endometrium is due to spasm of the blood vessels which lead to necrosis of the endometrium and thus casting it of.
- ▶ The blood released from the ruptured blood vessels contains high amounts of prostaglandin's, the prostaglandin's have binds to receptors in the myometrium (the middle muscular layer) & and this binding will lead to very strong contraction.

## What will happen after this phase?

Within 4 to 7 days after menstruation, the loss of blood ceases & the endometrium become re-epithelialized.

شرح الكلام:

لو مر يومين بدون لا يحصل تلقيح للبويضة، الجسم الأصفر يتحلل ومستوى الاستروجين والبروجسترون ينزل، بالتالي يقل التحفيز لبطانة الرحم وتبدأ سماكتها تقل بنسبة ٦٥٪ عن قبل، سبب قلة السماكة هو ان ال blood vessels يصير لها vasoconstriction وبالتالي necrosis فتبدأ الطبقة السطحية من البطانة بالتساقط على هيئة دم ويخرج من الجسم بسبب انقباضات الرحم.



# Functions of Estrogens Vs Progesterone

Functions of Estrogens Vs Progesterone	
Estrogens	Progesterone
<ul style="list-style-type: none"><li>✓ Estrogens increase the size of ovaries, fallopian tubes, uterus, and external genitalia.</li><li>✓ Estrogens cause marked proliferation of the endometrial stroma and greatly increased development of the endometrial glands.</li><li>✓ Estrogens cause:<ol style="list-style-type: none"><li>1. Development of the stromal tissues of the breasts.</li><li>2. Growth of an extensive ductile system.</li><li>3. Deposition of fat in the breasts.</li></ol></li><li>✓ Estrogens stimulate bone growth and slightly increase protein deposition.</li><li>✓ Estrogens increase body metabolism and fat deposition.</li><li>✓ Estrogens cause sodium and water retention by the kidney tubules.</li></ul>	<ul style="list-style-type: none"><li>✓ Progesterone promotes the secretory changes in the uterine endometrium.</li><li>✓ Progesterone promotes increased secretion by the mucosal lining of the fallopian tubes.</li><li>✓ Progesterone promotes development of the lobules and alveoli of the breasts, causing the alveolar cells to proliferate, enlarge, and become secretory.</li><li>✓ Progesterone decreases the frequency and intensity of uterine contractions.</li></ul>

# Menopause سن اليأس

## ▶ Definition of Menopause:

The period during which the cycle ceases & the female sex hormones diminish to almost none.

## ▶ When the menopause phase occur?

It occurs at the age of 40 to 50 years.

## ▶ When the menopause phase occur?

With advanced age the ovaries become unresponsive to gonadotropins (decline in the number of primordial follicles), and their function declines so that reproductive cycles disappear (menopause).

✓ Menopause women have:

1. No more follicles = no estrogen, no progesterone.
2. High blood levels of LH & FSH because no negative feed back by estradiol and progesterone.

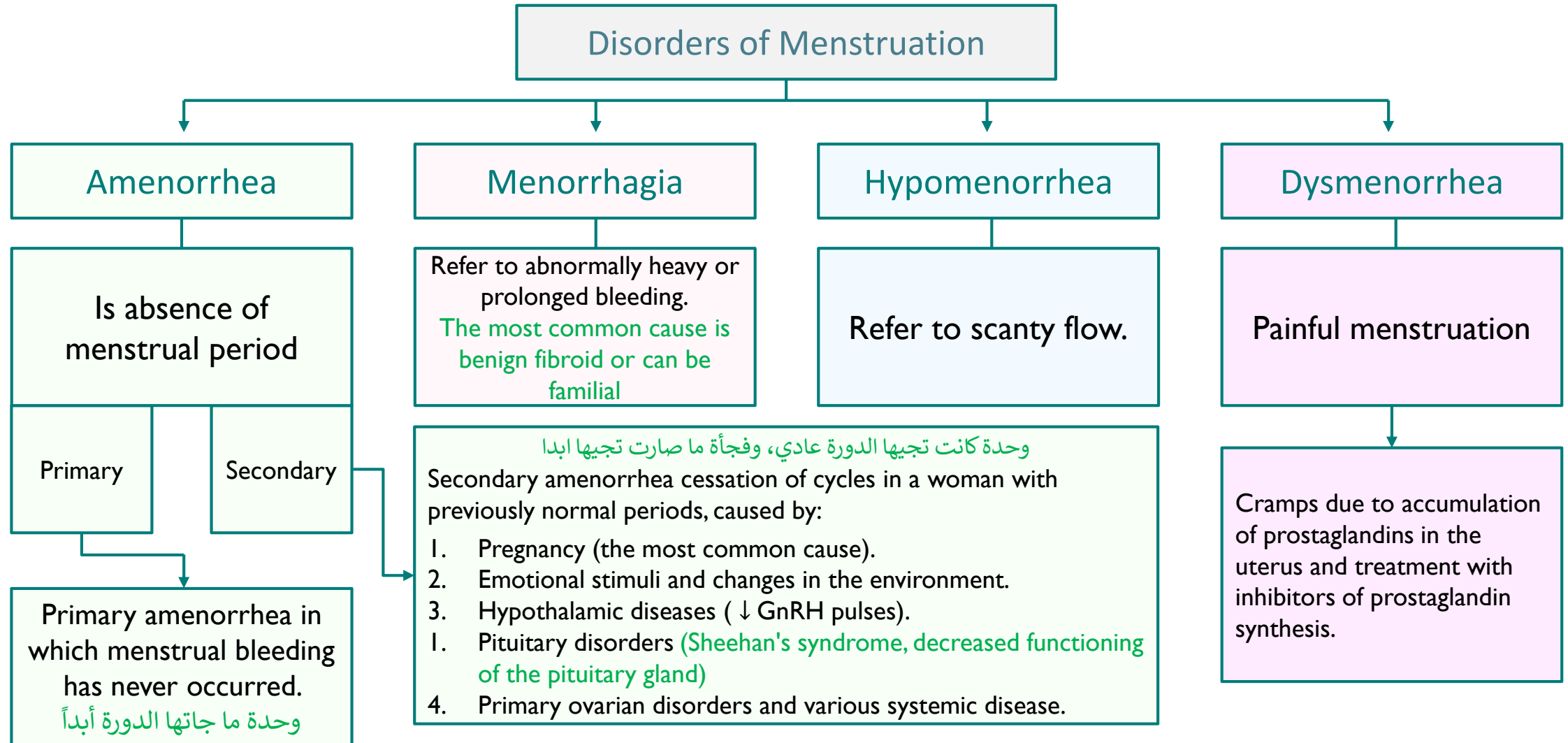
## ▶ What happen during menopause?

1. When estrogens production falls below the critical value, estrogens no longer inhibit the production of gonadotropins (FSH & LH) so, there is no negative feedback effect → increased secretion of FSH and LH.
2. The ovaries no longer secrete estrogen and progesterone → The uterus and vagina atrophy.
3. Ovulation fails to occur & the cycle ceases.

## ▶ What is the Physiological changes due to loss of estrogens?

1. The reproductive cycle becomes irregular.
2. "Hot flushes" characterized by extreme flushing of the skin.
3. Psychic sensations and dyspnea.
4. Irritability.
5. Fatigue.
6. Anxiety.
7. Occasionally various psychotic states.
8. Decreased strength and calcification of bones throughout the body.

# Disorders of Menstruation



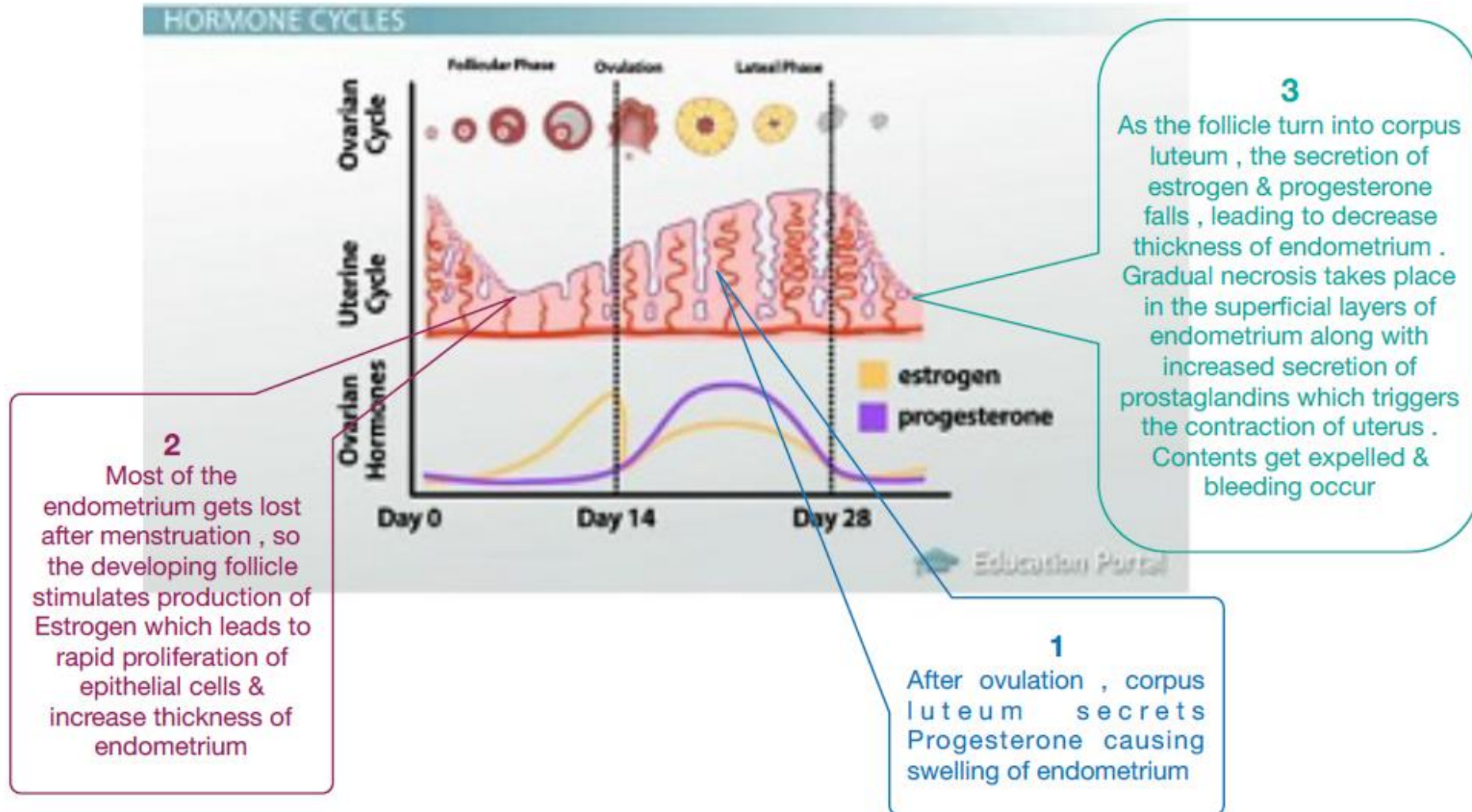
# SUMMARY of ovarian cycle

Location	Ovary during puberty	
Hormones	FSH and LH (very essential to activate ovaries)	
Main goal	Causing growth and maturation of Primordial follicles.	

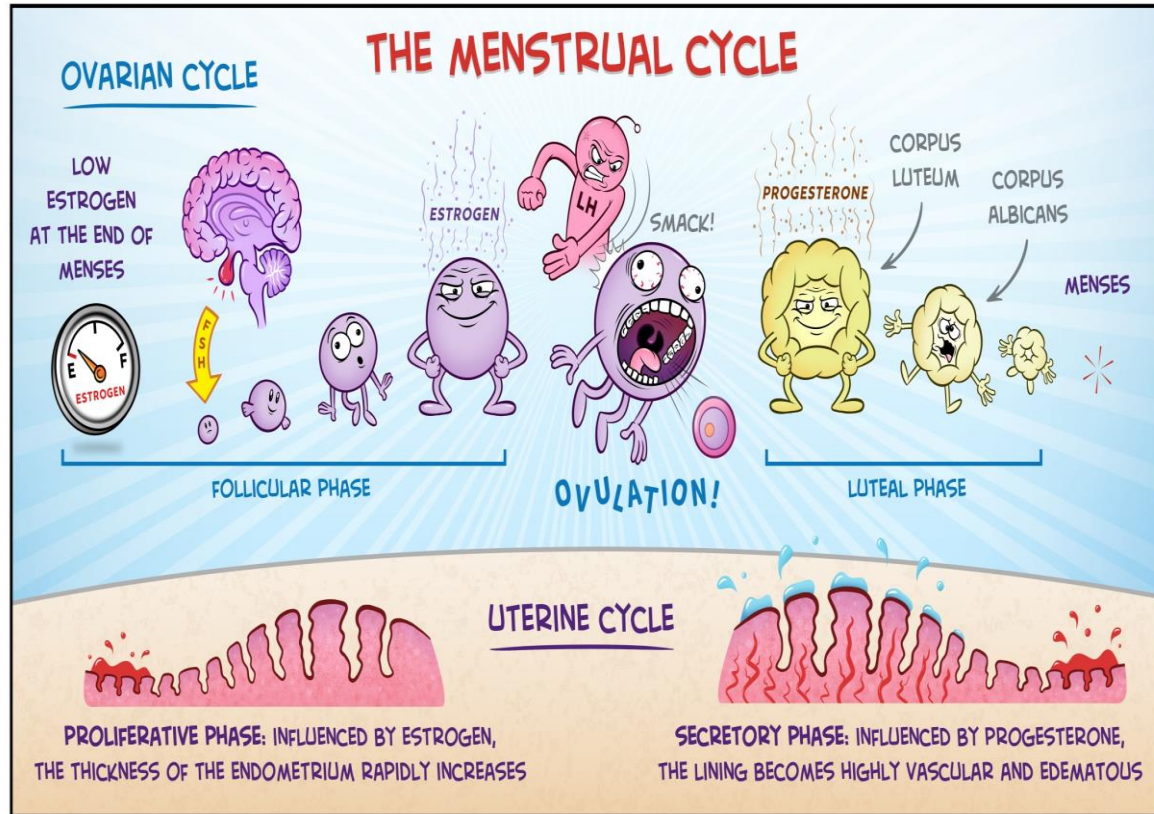
## Events of ovarian cycle

Follicular Phase	<p>Primordial Follicle [single granulosa cell layer] → Puberty [Release of FSH and LH] → Primary Follicle [Increase in size of ovum + growth of additional layers of granulosa cells] → ↑secretion of FSH and LH [FSH is higher] → Acceleration of growth of many primary follicles also proliferation of granulosa cells to many layers → Ovary interstitium collect in several layers outside the granulosa cells → Theca [has two layers; Interna which produces ANDROGENS, Externa which is a vascular capsule][It surrounds the granulosa cell layers] → Granulosa cells starts to secrete follicular fluids [High cont. of Estrogen] → Accumulation of fluid → Antrum formation → High levels of Estrogen causes positive feedback on AP to release FSH and both will stimulate AP to secrete more LH. Estrogen from follicles and LH from AP will cause proliferation of the Theca cells along with their secretion → Vesicular Follicle [Graffian] → Antral follicles start to grow and ovum enlarges and remain in embedded at one pole of the granulosa cells → One week or more before Ovulation → one follicle begins to outgrow and the rest will undergo Atresia.</p>
Ovulation	<p>Swelling of the follicle prior to ovulation by two days due to high secretion of LH and FSH [LH is higher] → During ovulation the stigma will rupture and fluid ooze from follicle → Release of Ovum surrounded by mass of granulosa cells called Corona Rdiata.</p>
Luteal Phase	<p>Corpus Luteum formation [Lipid filled lutein cells originating from remaining granulosa and theca interna cells under influence of LH] → Fate of Corpus Luteum depends on pregnancy if it occurs or not.</p>

# Summary of Uterine Cycle

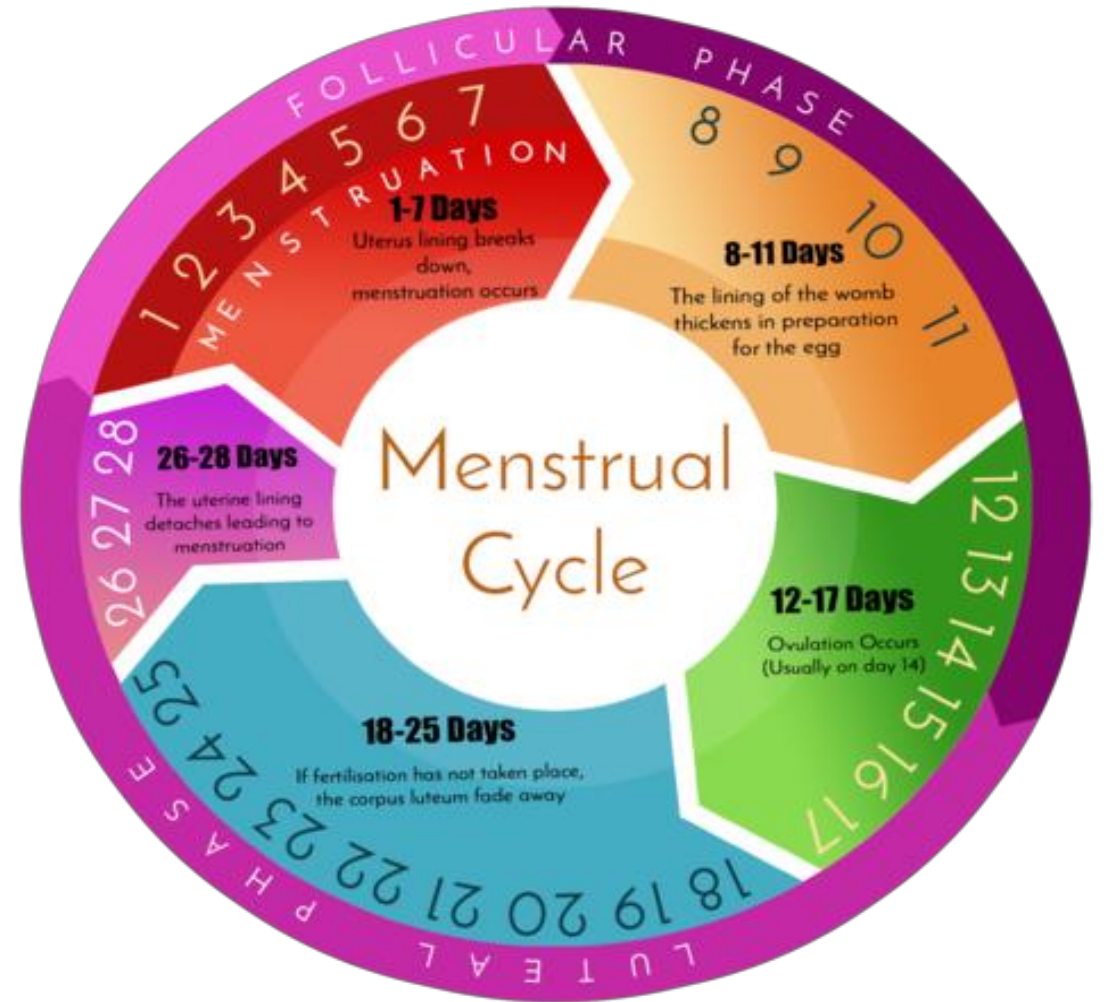


# Summary Of Menstrual Cycle



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# MCQ's

1. LH & FSH in female will stimulate which of the following organ:

- A. Uterus.
- B. Ovaries.
- C. Fallopian tube.
- D. Both A&B.

2. Ovulation occurs approximately at which day over the 28 days of ovarian cycle?

- A. 7
- B. 20
- C. 14
- D. 10

3. The stimulation of the early growth of the primary follicle up to the antral stage is under which one of the following?

- A. estrogen only
- B. estrogen and progesterone
- C. FSH only
- D. FSH and LH

4. How many days after the onset of menstruation does the ovulation occur in a woman who has a normal 28-day female sexual cycle?

- A. 13
- B. 14
- C. 15
- D. 16

5. What is the predominant hormone in the luteal phase?

- A. Estrogen.
- B. progesterone.
- C. testosterone.
- D. chorionic gonadotropin.

6. Which of the following hormones are secreted to maintain the corpus luteum during pregnancy?

- A. LH
- B. FSH
- C. hCG
- D. estrogen

# MCQ's

1. Which of the following is correct about the uterine cycle?

- A. The proliferative phase is known as the progestational phase
- B. The secretory phase is known as the preovulatory
- C. The secretory phase is known as postovulatory
- D. The secretory phase is known as the estrogen phase

2. How thick is the endometrium AT the time of ovulation?

- A. 2-4mm thick
- B. 3-5mm thick
- C. 4-6mm thick
- D. 5-7mmthick

3. which of the following is a function of Estrogen?

- A. increase body metabolism and fat deposition.
- B. promotes increased secretion by the mucosal lining of the fallopian tubes.
- C. decreases the frequency and intensity of uterine contractions.
- D. promotes the secretory changes in the uterine endometrium.

4. progesterone is used to increase the frequency and intensity of uterine contractions in pregnant female.

- A. TRUE
- B. FALSE



# Thank you for checking our work!



اعمل لترسم بسمة، اعمل لتمسح دمة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

قادة الفريق:

ليلى مذكور & محمد نصر

خالص الشكر لأعضاء الفريق الكرام:

ندى الدخيل

لمى التميمي

حمد الخضيرى

لين التميمي

خالد القحطاني

دعاء ماهر

عبد الرحمن الراشد

شذا الغيهب

فارس الجعفر

شروق الصومالي

نواف الخضيرى

أسيل بادخن



Please check our editing file to know if there are any additions, changes or corrections.



[https://www.youtube.com/watch?v=vXrQ\\_FhZmos](https://www.youtube.com/watch?v=vXrQ_FhZmos)



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