



PHYSIOLOGY

Sheet

Slide

Handout

Number

13

Subject

Female Reproductive Cycle

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- Sheet was written according to section 1 recording with different arrangement.

Female Reproductive Cycle/Menstrual cycle.

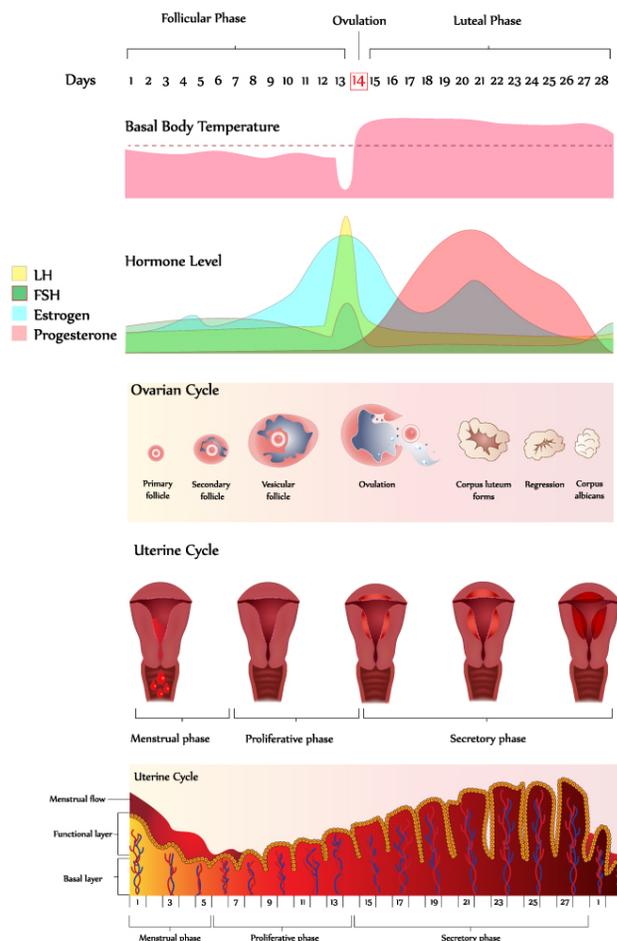
➤ The ovaries are under the control of :

1. Hypothalamic hormones >>> GnRH { Gonadotropin-releasing hormone}.
2. Anterior lobe of the pituitary gland >> FSH and LH.
3. Negative and positive feedback of the estrogen and progesterone.

➤ The menstrual cycle is the regular natural change that occurs in the female reproductive system (specifically the uterus and ovaries) that makes pregnancy possible and is governed by hormonal changes. Each cycle can be divided into three phases based on events in the ovary (ovarian cycle) or in the uterus (uterine cycle)

- ✓ The ovarian cycle is divided into :
 1. Follicular phase { days (0-14)}
 2. Ovulation phase { day14}.
 3. Luteal phase {days 14-28}.
- ✓ The uterine cycle is divided into :
 1. Menstrual phase {0-4}.
 2. Proliferative phase {4-14}.
 3. Secretory phase {14-28}.

✓ If the ovarian cycle doesn't occur then the uterine cycle will be suspended.



➤ Let's discuss each phase in more details ☺ ,,,,

A. **The Ovarian Cycle :**

✓ **The follicular phase :**

1. the level of FSH and LH is low because they are under the negative feedback control of the Estrogen .
2. the level of Estrogen begins to increase at the day 9-10 to reach its maximum at the day 11-13 , this leads to strongly increase of the LH level { this is called Estrogen Induced LH surge } . This occurs under the positive feedback control of the Estrogen on the LH { the only condition during the cycle to have positive feedback } .
3. The doctor said that there is a limit for the level of estrogen which it's exceeded then the positive feedback occurs >>> this the reason behind the Estrogen Induced LH surge.
4. LH matures the egg inside the follicle and causes the follicle to burst, releasing the egg. If no LH surge occurs, ovulation won't take place.
5. So, No Estrogen >>> No LH surge >>> No Ovulation and vice versa.
6. The Activin increase the level of FSH which is also play a role in the ovulation but not as the LH surge effect .

✓ **The Ovulation :**

1. It occurs 14 days before the menses regardless the length of cycle; if the cycle length is 35 days then ovulation occurs at day 22 , if it's 29 then ovulation at day 14 and so on.
2. It's happened as a result of the LH surge in the follicular phase.
3. The hormones { Estrogen , LH and FSH } level decrease !
4. There are some ovarian proteins important for ovulation , they do their jobs in a mechanism which we do not know how but we know they are essential for ovulation and losing them means no ovulation !
 - 1) Progesterone receptors.
 - 2) Cyclooxygenase enzyme { Convert the Arachidonic acid into Prostaglandins } .
 - 3) Transcription factors .
 - 4) Cell cycle regulator.

→ The earliest responses of the ovary to the midcycle LH surge are the release of vasodilatory substances, such as histamine, bradykinin, and prostaglandins, which mediate increased ovarian and follicular blood flow. The highly vascularized dominant follicle becomes hyperemic and edematous and swells.

5.

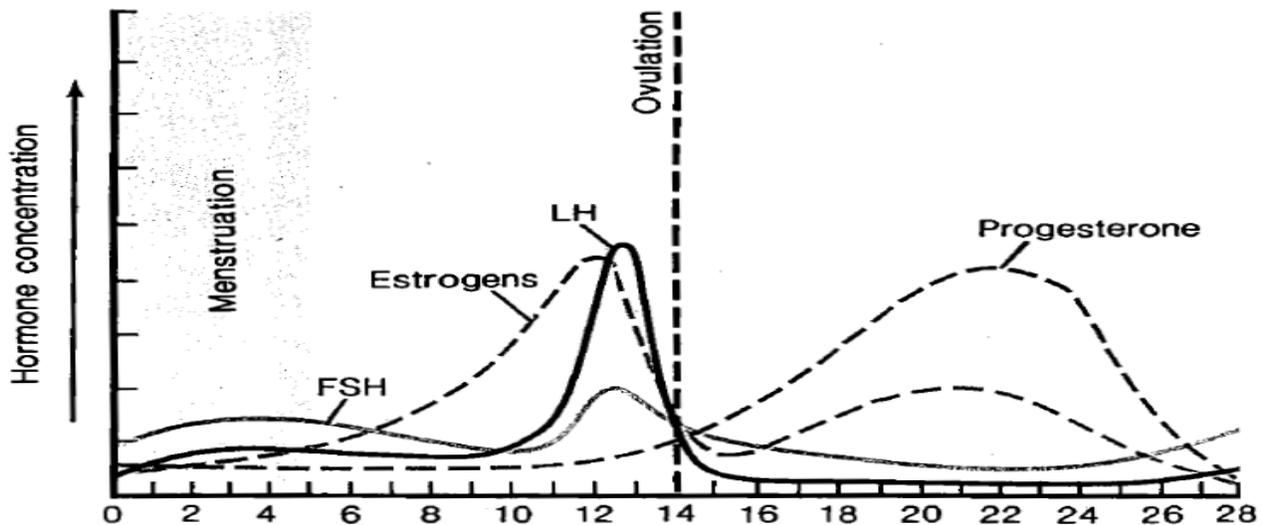
In response to the LH surge, **plasminogen activator** is produced by theca and granulosa cells of the dominant follicle and converts plasminogen to **plasmin**. Plasmin is a proteolytic enzyme that acts directly on the follicular wall and stimulates the production of **collagenase**, an enzyme that digests the connective tissue matrix. *It is believed that prostaglandins cause the release of lysosomal enzymes that digest follicular wall.*

- ✓
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✓ **The Luteal Phase :**

1. **The corpus luteum** is a remnant of the ovarian follicle that has released a mature ovum during a previous ovulation. the corpus luteum is considered as a **temporary endocrine gland** which secret **the Progesterone** { mainly , secreted in high level , it's called pregnancy hormone } and **Estrogen and inhibin** { moderate level, which inhibit the endometrial growth} .
2. The level of Progesterone and Estrogen increase .
3. It's resemble the Secretory phase of the uterine cycle ; the viscosity and secretion activity of endometrium increase.

4. The corpus luteum , in case NO Pregnancy , can survive to 14 days after that the level Progesterone and Estrogen decrease and the menstruation phase start . the corpus luteum becomes corpus albican.
5. In case , there is pregnancy then can survive up to 3 months .



B. The Uterine Cycle :

✓ The Menses :

1. The first phase of the uterine cycle.
2. At the end of the cycle, the estrogen and progesterone levels almost zero then the blood supply of the endometrium will be affected; the capillaries become necrotic then the endometium is sloughed.
3. The range is 1-10 days but usually 4-5 days.
4. Bloodshed is usually 30ml ranging from spots to 80 ml , its affected by the thickness of the endometrium /medication /disease . Above 80 ml is abnormal.

✓ The Proliferative phase :

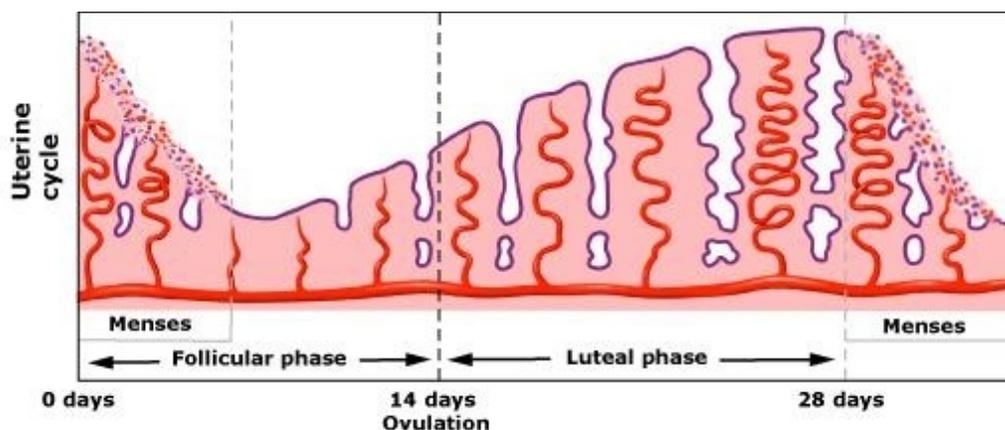
1. The uterus prepare itself to the menstrual cycle.
2. This phase of the uterus begins at the end of menstruation and lasts until ovulation, when the egg is ejected from the ovary.
3. The uterine glands elongate and the spiral arterioles grow for proper blood supply of the new endometrium,
4. High level of estrogen that's why it's called Estrogenic phase.

✓ **The Secretory Phase :**

1. the hormone progesterone is produced by the ovaries. Then it's called Progesteronic phase .
2. Progesterone (as well as estrogen) is secreted by the corpus luteum, (which means yellow body), which develops from the Graafian follicle. Progesterone secreted by the corpus luteum stimulates the further build-up of the cells in the endometrium of the uterus.
3. further thickness of endometrium , marked growth of the coiled arteries and increased complexity of the uterine gland

➤ the withdrawal of estrogen and progesterone just before menses has 2 effects :

1. induces catastrophic degeneration of the endometrium that leads to menstrual bleeding , this period is the menstrual phase of the endometrium cycle (uterine cycle).
2. the fall in estrogen and progesterone levels diminishes the feedback inhibition of the hypothalamus-pituitary system and gonadotropin secretion rises once a day that's the beginning next menstrual cycle . because of the very low level of progesterone and estrogen the menstrual phase begins .



➤ **NOTES :**

- At the end of the cycle progesterone and estrogen level decreases because the pregnancy did not occur . if there is pregnancy progesterone level continues to be almost constant and also estrogen but less than progesterone. But if there is no pregnancy occur corpus luteum regress and estrogen and progesterone level decrease .
- Throughout the life ,90-95% of all follicles are primordial (inactivated follicles), which are stored until they are activated . they may be stored for 50 years or more !
- During the Fetal and childhood life , some primordial follicles can develop all the way to antral stage hormones but they will undergo atresia with different duration { range 3-4 months }
- In vitro Fertilization, we inject FSH or similar exogenous substance then 30 follicles or more are activated but only one follicle will develop and have sufficient blood supply . this follicle is very sensitive to estrogen which suppress the FSH but this FSH level ok it's insufficient for most of follicles but it's sufficient for the dominant follicle that continue to grow until the day of 14 then it's ovulated.
- Why only the dominant follicle continue to grow while others cannot ?!
 1. The FSH level is insufficient for them but sufficient for the Dominant one.
 2. They have insufficient amount of Aromatase enzyme then concentrate the Androgens .
- The number of the ovulatory ovum is species specific and it's affected by genetics, nutritional and environmental factors. In human , usually only one ovum is ovulated and also, affected by genetics, nutritional and environmental factors.
- The ovaries should be exposed to appropriate sequence of hormones; FSH followed by Estrogen then LH surge .

- Removal of Gonads leads to decrease or absence of the sexual activity in both males and females. Although the loss is slow in males of some species.

➤ **General Review:**

- ✓ 1-5 days >>> estrogen and progesterone levels are low because there is no corpus luteum, the endometrium is sloughed, secretion of the FSH and LH are released from the inhibition so increase their concentration.
- ✓ 7-14 days , the dominant follicle is selected, the concentration of the estrogen increase , the endometrium is stimulated for proliferation , LH surge induced by high estrogen.
- ✓ Ovulation mediated by follicular enzymes and prostaglandins.
- ✓ Corpus Luteum , under the influence of the LH. They secrete progesterone and estrogen.

➤ **Anovulatory cycle:**

- ✓ a menstrual cycle characterized by varying degrees of menstrual intervals and the absence of ovulation and a luteal phase. In the absence of ovulation, there will be infertility.
- ✓ These irregular cycles are **short** { 21 days} due to the absence of Progesterone.
- ✓ As there is no progesterone in the anovulatory cycle, bleeding is caused by the inability of estrogen — that needs to be present to stimulate the endometrium in the first place — to support a growing endometrium. Anovulatory bleeding is hence termed *estrogen breakthrough bleeding*.
- ✓ Examples :
 - I. Cycles occur at the Menarche or Menopause.
 - II. Cycles while using contraceptives.

➤ **Characteristics of puberty :**

- ✓ The first sign of puberty in girls is the appearance of breast buds { occurs at a very early stage , average at age of 9}
- ✓ Within 2 years the menarche occurs {the onset of the menstrual cycle}.

- ✓ The growth spurt and closure of the epiphyses typically begins and ends earlier in girls than males. { boys puberty may start at age of 11 which is characterized by the increase of testis size}.
- ✓ The appearance of the axillary and pubic hair precedes the menarche and is dependent on the increased secretion of the adrenal androgen then called Andrenache.

➤ **The Ovarian Hormones :**

1. Estrogens “ Bless Hormone “

- ✓ Estrogens **3** hormones : estradiol , estrone, estriol .
- ✓ The most potent is estradiol then estrone , estriol.
- ✓ Estradiol and estrone are produced directly from the ovaries .
- ✓ estriol is metabolite from these 2 hormones both estradiol produces estriol as well as estrone produces estriol.

✓ Functions :

- I. Against the osteoporosis.
- II. Increase HDL and decrease the LDL.
- III. Increase the steroid binding protein.
- IV. Best performance for the heart and the blood vessels.
- V. For the reproductive organs : increase the uterine ,vaginal ,fallopian tube and breast growth . Also, increase the mucus secretion and the LH receptors.

2. Progesterone :

- ✓ Progesterone and hydroxyprogesterone both have the same potency but the concentration of the Progesterone is higher.
- ✓ Progesterone doesn't play a role during childhood but just during the puberty and above.
- ✓ It's called pregnancy hormone.
- ✓ Functions :
 - I. Increase the lobular development of the breast .
 - II. Increase the endometrial growth and secretion.
 - III. Increase the body temperature; After the ovulation body temperature rises from 0.5-1 because of progesterone .some women measure their body temperature so they are able to control the having or avoidance of the pregnancy .

Relation to Endocrine function

In nonprimate mammals :

1. Removal of the gonads leads eventually to decreased or absent sexual activity in both the male & the female - although the loss is slow to develop in the males of some species
2. Injections of gonadal hormones in castrated animals revive sexual activity .Testosterone in the male & estrogen in the female have the most marked effect.
3. Large doses of testosterone & other androgens in castrated females initiate female behavior and large doses of estrogens in castrated males trigger male mating responses. It is unsettled why responses appropriate to the sex of animal occur when the hormones of the opposite sex are injected.
4. In women , ovariectomy does not necessarily reduce libido (defined in this context as sexual interest and drive) or sexual ability.
5. Postmenopausal women continue to have sexual relations , often without much change in frequency from their premenopausal pattern
6. However , adrenal androgens are still present in these women

Testosterone for example , increases libido in males , and so does estrogen used to treat diseases such as carcinoma of the prostate.

7. The behavioral pattern that was present before treatment is stimulated but not redirected.
8. Thus , administration of testosterone to homosexuals intensifies their homosexual drive but not convert it to a heterosexual drive.

- **Note :** regarding to the point 3 in previous page ; that is wrong bec the testosterone in the ovaries will be converted into estrogen and the estrogen in the testis will be converted into testosterone,
- Gonadotropin release is also suppressed by two mechanisms which affect the hypothalamic Gonadotropin releasing hormones pulse generators { GnRH secretion is pulsatile not continuous}.
 - I. Sex_steroid dependent mechanism that render the pulse generator extremely sensitive to negative feedback by steroid .
 - II. Intrinsic CNS inhibition of the gonadotropin releasing pulse generator : GABA and endogenous opioid peptide in the CNS { Major inhibitors of the GnRh pulse release}.
- That explain why the GnRH and Gonadotropin levels are low during the childhood but activated during puberty.
- During the childhood gonads are inactive then plasma steroid level is low.

" وَأَخِرُ دَعْوَاهُمْ أَنْ الْحَمْدُ لِلَّهِ رَبِّ الْعَالَمِينَ "

بالشغف العظيم بدأنا ... و به سنكمل ...

#دكتور_2014 ... منتصف طريقنا مضى بما حوته الأيام ; حلوها و مرها ...

و بهمة أكبر سنبدأ معاً مرحلتنا القادمة ...

كل الشكر لمن سهر يوماً ليُسَهِّل علينا الصعب ... ليساعد و لو بكلمة ...

تحية لأصدقاء الدرب , تحية من القلب إلى : آية , آلاء , رحمة , رغد , سنال , مجد , مرام , ميساء و ناديا.

شكراً #دكتور_2014 لأنكم أنتم <3 <3

آيات الزغول