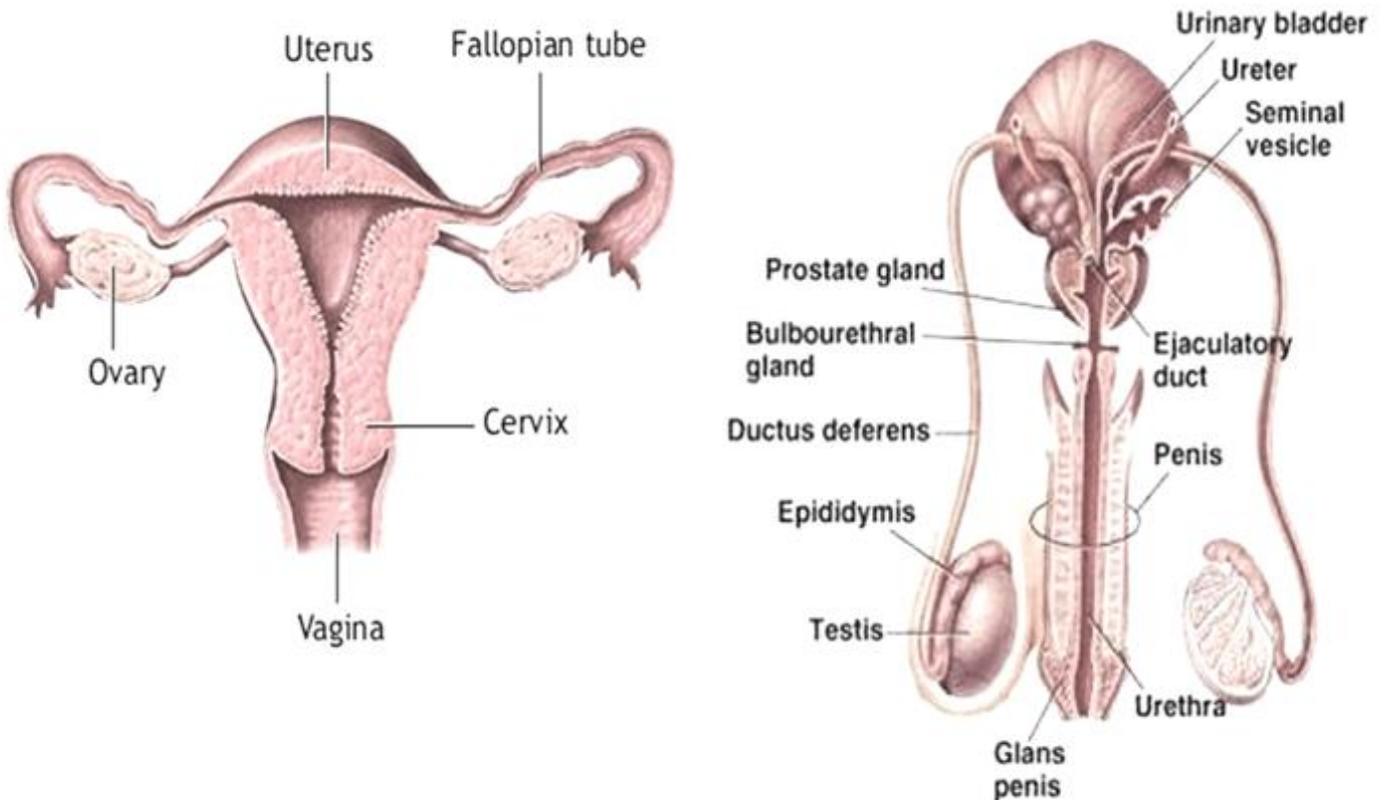


3rd Lecture Uterine Cycle



PHYSIOLOGY TEAM – 430

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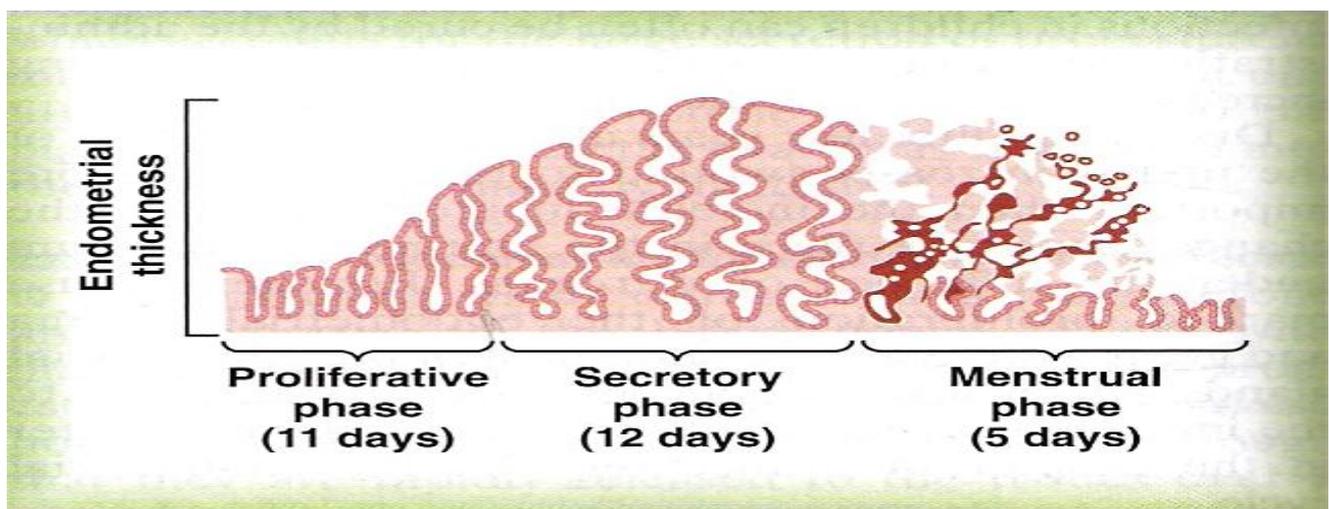
Uterine Cycle

- **Monthly endometrial cycle and menstruation:**

1) Proliferation phase (estrogen phase) of the endometrial cycle, occurring before ovulation:

- 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. Under the influence of estrogen, the stromal cells & epithelial cells proliferate rapidly.
- The endometrial surface re-epithelialized within 4-7 days after the beginning of menstruation. Before ovulation the endometrium thickness increase, due to increase numbers of stromal cells & progressive growth of the glands & new blood vessels.
- At the time of ovulation, the endometrium is 3-5 mm thick. The endometrial glands, cervical region secrete a thin, stringy mucus which help to guide sperm in the proper direction from the vagina into the uterus.

Desquamate: To shed the outer layers of the skin.



2) Secretory phase (progesterone phase) of the endometrial cycle, occurring after ovulation:

- After ovulation, estrogen & progesterone are secreted in the later part of the monthly cycle by the corpus luteum. Estrogen cause slight proliferation in the endometrium & progesterone causes marked swelling & secretory development of the endometrium.
- Stromal cells cytoplasm increase lipid & glycogen deposits in the cells & blood supply to the endometrium increases and become more tortuous. 1 week after ovulation, endometrium thickness is 5-6 mm.
- The secretory changes prepare the endometrium for implantation of the fertilized ovum
- Uterine secretions called “uterine milk” provide nutrition for the diving ovum.
- The trophoblastic cells on the surface of the implanted ovum begin to digest the endometrium & absorb endometrial stored substances.

- **Menstruation:**

- If the ovum is **not fertilized**, about 2 days before the end of the monthly cycle:
 1. The **Corpus Luteum involutes**.
 2. **Estrogens & Progesterone decrease** to low levels of secretion → **decrease stimulation** of the endometrium → **involution of the endometrium** about 65% of its previous thickness.
 3. During the 24 hrs preceding the menstruation, there is **vasospasm** of the tortuous blood vessels & release of **vasoconstrictor prostaglandins**.
- **Vasospasm, decrease nutrients** to the endometrium, and **loss of the hormonal stimulation**, all initiate **necrosis** in the endometrium blood vessels
- There is **gradual necrosis of the outer layer of the endometrium**. All the superficial layers of the endometrium desquamated in the uterine cavity.
- The mass of **desquamated tissue & blood** plus the **contractile effects of prostaglandins** all initiate **contractions** which **expel** the uterine contents.
- 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**.
- Within 4 to 7 days after menstruation, the **loss of blood ceases** & the endometrium become **re-epithelialized**.
- During menstruation, **leukocytes are released** with the necrotic material & blood so the uterus is **highly resistant to infection** during menstruation as protective mechanism.

- **Regulation of the female monthly rhythm, interplay between the ovarian and hypothalamic-pituitary hormones:**

- Secretion of Anterior Pituitary hormone is controlled by "**GnRH**" and transported to the AP gland by the hypothalamic-hypophysial portal system.
- **Intermittent, pulsatile** secretion of GnRH by the hypothalamus stimulates **pulsatile release** of LH from the AP
- GnRH is secreted in pulses lasting **5 to 25 minutes every 1 to 2 hrs**. The pulsatile release of GnRH cause **intermittent** output of LH secretion about every **90 minutes**.
- Hypothalamic centers for release of GnRH:
The neural activity that causes pulsatile release of GnRH occurs in the **mediobasal hypothalamus**, in the **arcuate nuclei** regulate most of the female sexual activity.

- **Negative feedback effects of estrogen and progesterone in decreasing both LH and FSH secretion:**

- **Estrogen in small amounts** has strong effect to **inhibit** the production of LH & FSH. This inhibitory effect of estrogen is increased when **progesterone is available**. This inhibitory affects more on the **Anterior Pituitary directly** & to **lesser extent** on the **hypothalamus** to **inhibit** the secretion of GnRH.
- The hormone **inhibin** secreted by the **granulosa cells** of the ovarian corpus luteum **inhibits** the secretion of FSH & to **lesser extent** LH.

- **Positive feedback effect of estrogen before ovulation - the pre-ovulatory LH surge:**

- AP secretes large amounts of LH 24 to 48 hrs before ovulation. FSH surge is much smaller in the pre-ovulatory than LH surge.
- The possible causes of LH secretion could be:
Estrogen has special positive feedback effect of stimulating pituitary secretion of LH & to a lesser extent FSH

- **Feedback oscillation of the hypothalamic-pituitary-ovarian system:**

- Post - ovulatory secretion of the ovarian hormones, and depression of the pituitary gonadotropins:
- During the post - ovulatory phase (between ovulation & beginning of menstruation) the corpus luteum secrete large quantities of progesterone & estrogen & inhibin which all together cause negative feedback effect on AP & hypothalamus to inhibit both FSH & LH secretion. (lowest level 3-4 days before the onset of menstruation)

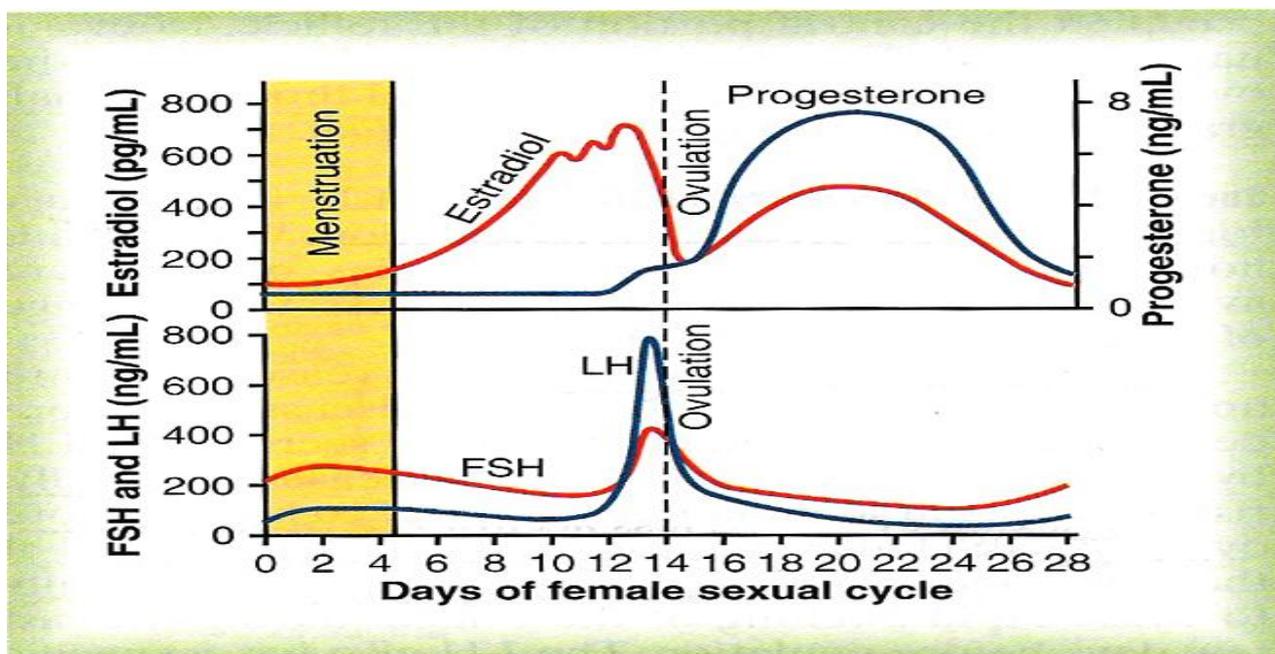
Surge: Any marked ↑ in flow of a substance.

- **Follicular growth phase:**

- 2 to 3 days before menstruation, corpus luteum regress & secretion of estrogen, progesterone & inhibin decrease.
- This decrease removes the negative feedback effect on AP hormones. Therefore a day after menstruation FSH secretion begins to increase (2 folds) while LH secretion is slightly. These hormones cause growth of the follicle. During the first 11 to 12 days of this follicle growth the rate of secretion of FSH & LH decrease slightly because of the negative feedback effect of estrogen on the AP.

- **Pre ovulatory surge of LH & FSH causes ovulation:**

- About 12 days of the monthly cycle, the high secretion of FSH & LH start to increase due to high level of estrogens causes positive feedback on the anterior pituitary which leads to pre-ovulatory LH surge & FSH surge.



- **Menopause:**
 - At the age of 40 to 50 years, the sexual cycle becomes **irregular**, ovulation **fails to occur** & the cycle **ceases**.
 - With advanced age the ovaries become **unresponsive** (decline in the number of primordial follicles) **to gonadotropins**, and their function declines so that sexual cycles **disappear** (menopause). The ovaries **no longer secrete estrogen and progesterone**. The uterus and vagina **atrophy**. Due to removal of the negative feedback effect therefore → **increased secretion of FSH and LH**.

- **The loss of estrogens causes marked physiological changes in the function of the body including:**
 1. “Hot Flashes” characterized by extreme flushing of the skin;
 2. **Psychic sensations and dyspnea**;
 3. **Irritability**;
 4. **Fatigue**;
 5. **Anxiety**;
 6. **Occasionally various psychotic states**
 7. **Decreased strength and calcification of bones throughout the body.**

- **Amenorrhea:**
Is absence of menstrual period, and has two subtypes:
 1. **Primary amenorrhea**
In which menstrual bleeding has **never occurred**.
 2. **Secondary amenorrhea**
Cessation of cycles in a woman with **previously normal periods**, causes:
 - **Pregnancy** (is the most common cause)
 - **Emotional stimuli and changes in the environment.**
 - **Hypothalamic diseases (GnRH pulses)**
 - **Pituitary disorders**
 - **Primary ovarian disorders and various systemic diseases.**

- **Menorrhagia:**
 - Refer to abnormally **profuse flow** during regular periods.

- **Hypomenorrhea:**
 - Refer to **scanty flow**.

- **Dysmenorrhea:**
 - **Painful menstruation** (cramps due to accumulation of prostaglandins in the uterus and treatment with inhibitors of prostaglandin synthesis).