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LECTURE 3

PHYSIOLOGY OF UTERINE CYCLE

Objectives

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

1. Describe the normal menstrual cycle
2. Discuss the structural changes that occur in the endometrium during the menstrual cycle and explain how these changes are hormonally controlled
3. Describe phases of the menstrual cycle
4. Describe the hormonal control of the menstrual cycle
5. Describe the major disorders of the menstrual cycle
6. Describe the physiology of menopause

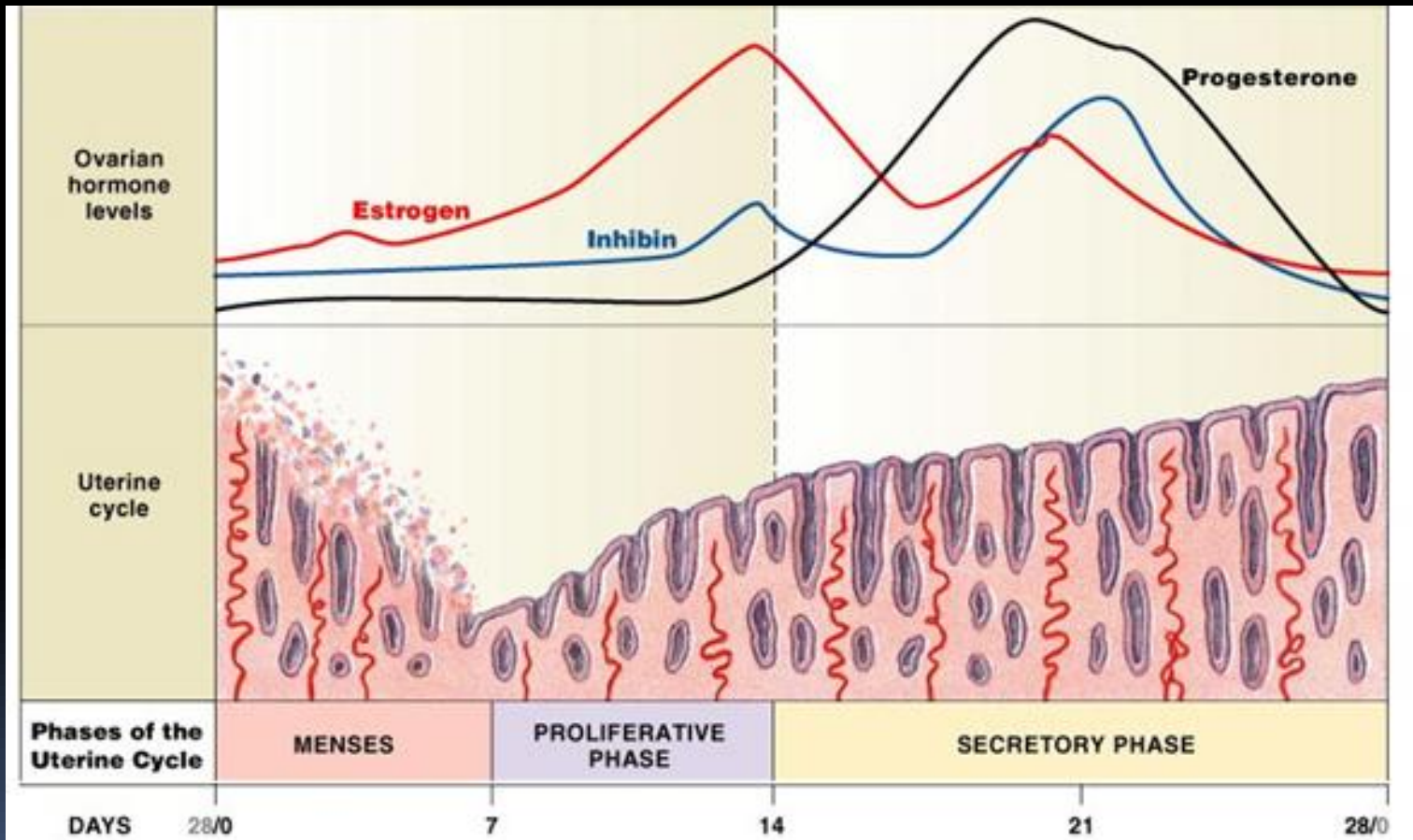
Keywords: proliferative phase, secretory phase, amenorrhea, menorrhagia, menopause

Monthly endometrial cycle and menstruation:

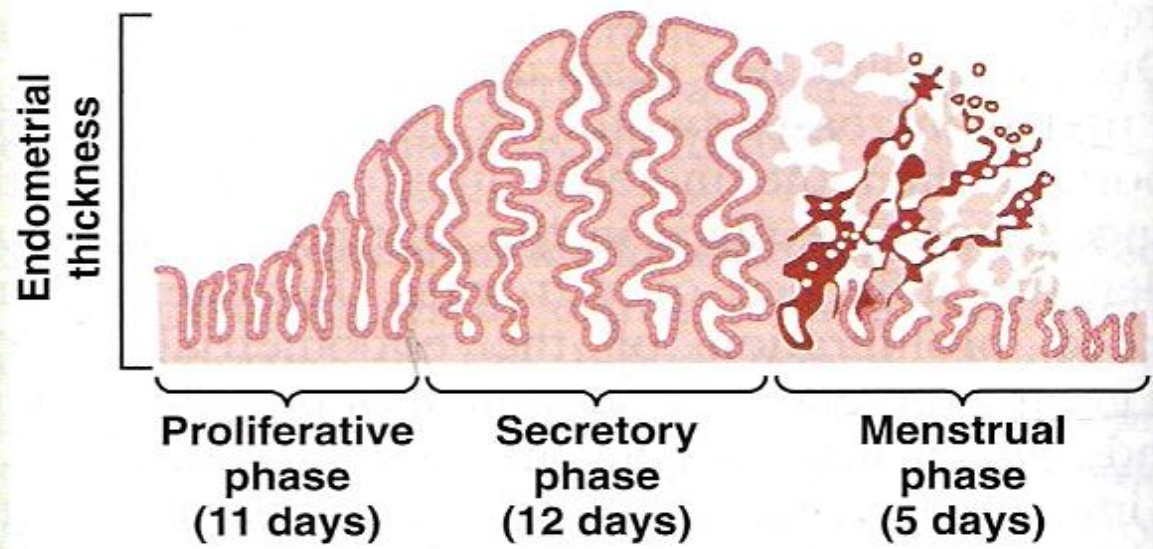
Associated with monthly cyclical production of estrogens & progesterone by the ovaries the endometrial lining of the uterus pass through the following stages.

1- Proliferative 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 & the deeper portions of the glands & crypts of the endometrium under the influence of estrogens, secreted in large quantities by the ovaries, 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.



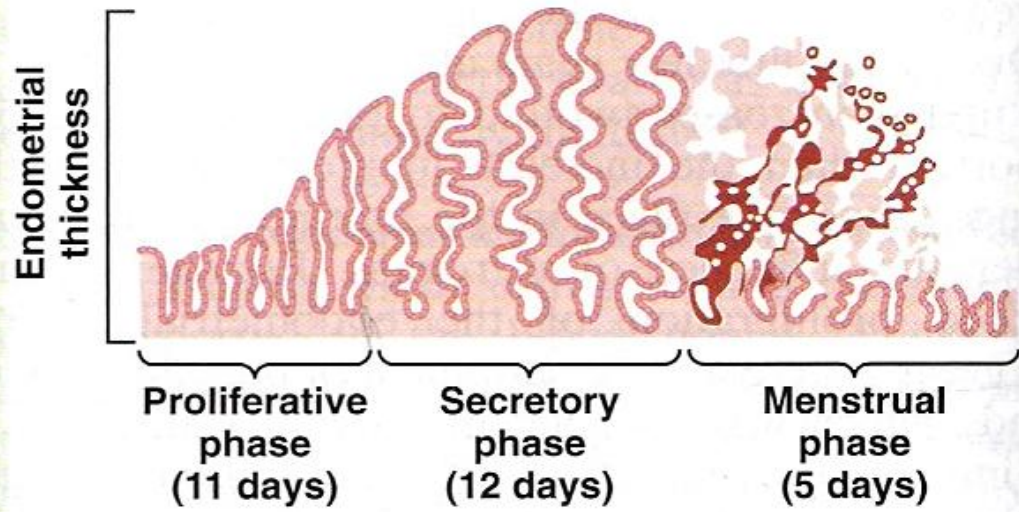
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2- Secretory phase (progestational phase) of the endometrial cycle, occurring after ovulation:

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. The glands increase in tortuosity, excess secretory substances accumulate in the glands.

- 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 prepared the endometrium (stored nutrients) 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 & absorbed endometrial stored substances.



Menstruation:

- 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 of secretion. Due to decrease estrogen & progesterone at the end of the monthly cycle, there is decrease stimulation of the endometrium, followed by involution of the endometrium about 65% of its previous thickness.
- During the 24 hrs preceding the menstruation, there is vasospasm of the tortuous blood vessels & release of vasoconstrictor prostaglandins.

There is ;-

- 1) vasospasm;
 - 2) decrease nutrients to the endometrium
 - 3) loss of the hormonal stimulation, all initiate necrosis in the endometrium blood vessels. There is gradual necrosis of the outer layer of the endometrium separate from the uterus at the site of the hemorrhages within 48 hrs, 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.

Leukorrhea during menstruation:

During menstruation, leukocytes are released with the necrotic material & blood so the uterus is highly resistant to infection during menstruation as protective mechanism.

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

- AP secretes increased amount of LH beginning 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

the granulosa cells of the follicle begin to secrete small increasing amount of progesterone about 1 day before ovulation which stimulate LH secretion

Feedback oscillation of the hypothalamic-pituitary-ovarian system:

Postovulatory secretion of the ovarian hormones, and depression of the pituitary gonadotropins:

During the postovulatory phase (between ovulation & beginning of menstruation) the corpus luteum secrete large quantities of both 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)

Follicular growth phase :-

- 2 to 3 days before menstruation, corpus luteum regress & secretion of estrogen, progesterone & inhibin decrease.
- This decrease remove 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 causes 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 there is increased secretion of FSH and LH.

Definition of menopause:

- The period during which the cycle ceases & the female sex hormones diminish to almost none. When estrogens production falls below the critical value, estrogens no longer inhibit the production of gonadotropins FSH & LH. The production of FSH & LH after menopause in large amount.

The loss of estrogens causes marked physiological changes in the function of the body including:

1. “hot flushes” 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 either

- Primary amenorrhea in which menstrual bleeding has never occurred.
- 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 (\downarrow GnRH pulses)
 - Pituitary disorders
 - Primary ovarian disorders and various systemic disease.

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).