

Obstetrics & Gynecology TEAM



Physiology of menstrual cycle

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◆ very important ◆ mentioned by doctor ◆ team notes ◆ not important

Physiology of menstrual cycle

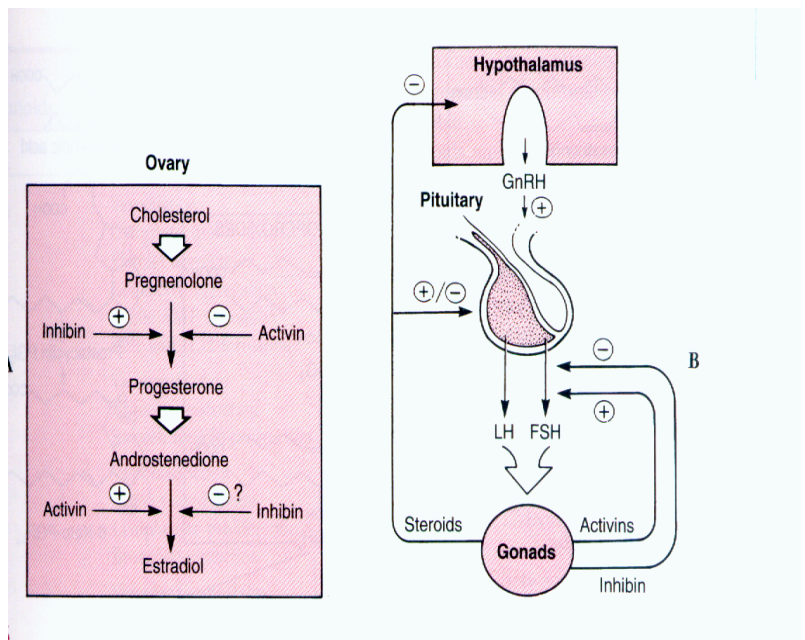
OBJECTIVES

- Definition of the normal menstrual cycle
- Phases of the menstrual cycle
- Control of the menstrual cycle through the hypothalamic pituitary ovarian axis
- Ovulation
- Hormones of the MC
- Two cell theory
- Endometrial changes during the MC

NORMAL MENSTRUAL CYCLE

- What is the mean duration of the MC?
 - ✓ Mean 28 days (only 15% of ♀)
 - ✓ Range 21-35
- What is the average duration of menses?
 - ✓ 3-8 days
- When does ovulation occur?
 - ✓ Usually day 14
 - ✓ 36 hrs after the onset of mid-cycle LH surge
- What regulate the phases of the MC & ovulation?
 - ✓ Interaction between hypothalamus, pituitary & ovaries
- What is the mean age of menarche & menopause?
 - ✓ Menarche 12.7
 - ✓ Menopause 51.4

Gonadotropin releasing hormone is released from the hypothalamus in pulses, to the pituitary which will secrete FSH and LH. FSH and LH will act on the ovaries (gonads). In the ovaries under the effect of the FSH development of the follicles will occur then follicles will secrete estrogen. LH will lead to progesterone secretion after ovulation.



PHASES OF THE MENSTRUAL CYCLE :

The first day of bleeding (menses) is day one of the cycle

- Ovulation divides the MC into two phases:

1-FOLLICULAR PHASE

- ✓ -Begins with menses on day 1 of the menstrual cycle & ends with ovulation

▲ RECRUITMENT (there is a certain number of follicles which will undergo for development and only one or sometimes two will reach ovulation)

FSH ⇒ maturation of a cohort of ovarian follicles “recruitment”

⇒ only one reaches maturity

MATURATION OF THE FOLLICLE (FOLLICULOGENESIS)

♥ FSH ⇒ primordial follicle

(oocyte arrested in the diplotene stage of the 1st meiotic division surrounded by a single layer of granulosa cells)

⇒ ⇒ Primary follicle

(oocyte surrounded by a single layer of granulosa cells basement membrane & theca cells)

⇒ ⇒ 2ry follicle or preantral follicle

(oocyte surrounded by zona pellucida , several layers of granulosa cells & theca cells)

⇒ ⇒ tertiary or antral follicle

2ry follicle accumulate fluid in a cavity “antrum” oocyte is in eccentric position surrounded by granulosa cells “cumulus oophorus”

SELECTION

- Selection of the dominant follicle occurs day 5-7
- It depends on
 - ✓ the intrinsic capacity of the follicle to synthesize estrogen
 - ✓ high est/and ratio in the follicular fluid
- As the follicle mature ⇒ ↑ estrogen ⇒ ↓FSH

“-ve feed back on the pituitary” ⇒ ⇒ the follicle with the highest No. of FSH receptors will continue to thrive (The dominant follicle , the one having highest estrogen , even with FHS being reduced the dominant follicle will continue to grow)

- The other follicles “that were recruited” will become atretic

- ♥ FSH ACTIONS

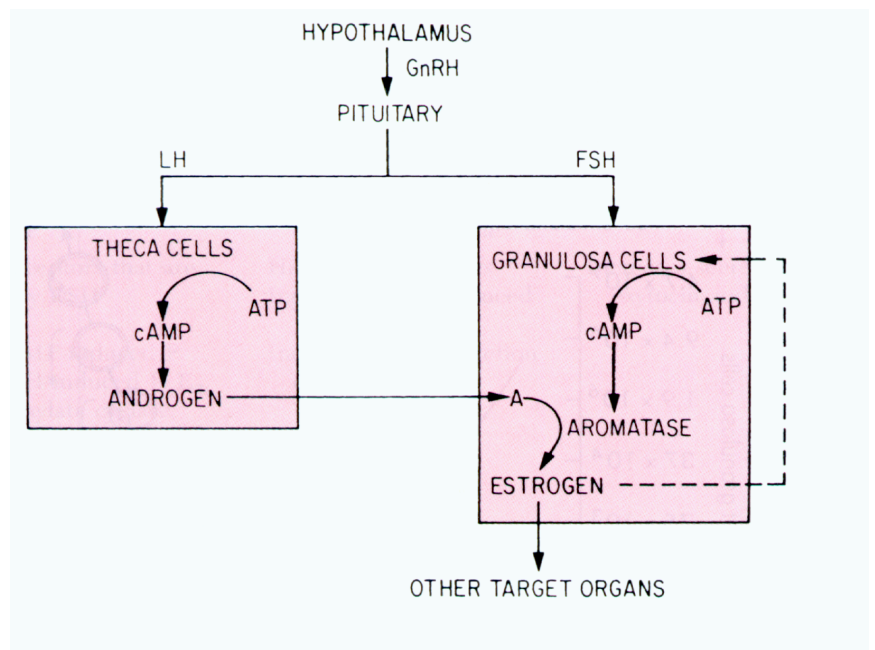
- ✓ -recruitment
- ✓ -mitogenic effect \Rightarrow \uparrow No. of granulosa cells
 - \uparrow FSH receptor
- ✓ -stimulates aromatase activity \Rightarrow conversion of androgens \Rightarrow estrogens “estrone & estradiol”
- ✓ - \uparrow LH receptors

- ♥ ESTROGEN

- ✓ Acts synergistically with FSH to
 - induce LH receptors
 - induce FSH receptors in granulosa & thica cells
- ♥ LH \Rightarrow thica cells \Rightarrow uptake of cholesterol & LDL \Rightarrow androstenedione & testosterone

TWO CELL THEORY

FSH will act on granulosa cells, producing aromatase that will convert the androgen coming from the theca cells formed by LH leading to estrogen formation.



FOLLICULOGENESIS:

OTHER FACTORS THAT PLAY A ROLE IN FOLLICULOGENESIS

-INHIBIN

- Local peptide in the follicular fluid (Not in the blood stream like the other hormones)
- -ve feed back on pituitary FSH secretion
- Locally enhances LH-induced androstenedione production (increase androgen production)

-ACTIVIN

- Found in follicular fluid
- Stimulates FSH induced estrogen production (increase estrogen production)
- ↑ gonadotropin receptors
- ↓ androgen
- No real stimulation of FSH secretion in vivo (bound to protein in serum)

PREOVULATORY PERIOD

♥ NEGATIVE FEEDBACK ON THE PITUITARY

-↑ estradiol & inhibin ⇒ -ve feed back on pituitary ⇒ ↓ FSH

-This mechanism operating since childhood

♥ POSITIVE FEEDBACK ON THE PITUITARY

- ↑ ↑ estradiol (reaching a threshold concentration) ⇒ ⇒ +ve feed back on the pituitary (facilitated by low levels of progesterone) ⇒ ⇒ LH surge ⇒ secretion of progesterone
- Operates after puberty
- +ve feed back on pituitary ⇒ ↑ FSH

♥ LH SURGE

- Lasts for 48 hrs
- Ovulation occurs after 36 hrs of the onset of the LH surge.

When estrogen is increasing it will have a negative feedback suppressing FSH, but when it keeps increasing and reach a certain threshold it will have a positive feedback will result in LH surge.

- Accompanied by rapid fall in estradiol level
- Triggers the resumption of meiosis
- Affects follicular wall \Rightarrow follicular rupture **ovulation**
- Granulosa cells \Rightarrow lutenization \Rightarrow progesterone synthesis

OVULATION

- The dominant follicle protrudes from the ovarian cortex
- Gentle release of the oocyte surrounded by the cumulus granulosa cells
- Mechanism of follicular rupture

1- \uparrow Follicular pressure

Changes in composition of the antral fluid \Rightarrow \uparrow colloid osmotic pressure

2-Enzymatic rupture of the follicular wall

LH & FSH \Rightarrow granulosa cells \Rightarrow production of plasminogen activator
 \Rightarrow \uparrow plasmin \Rightarrow \uparrow fibrinolytic activity \Rightarrow break down of F. wall

LH \Rightarrow \uparrow prostaglandin E \Rightarrow \uparrow plasminogen activator

\Rightarrow \uparrow PG F₂ α \Rightarrow \uparrow lysosomes under follicular wall

LUTEAL PHASE

LASTS 14 days (usually the luteal phase is constant, the variation is in the follicular phase)

FORMATION OF THE CORPUS LUTEUM

- After ovulation the point of rupture in the follicular wall seals
- Vascular capillaries cross the basement membrane & grow into the granulosa cells \Rightarrow \uparrow availability of LDL-cholesterol (from the blood)

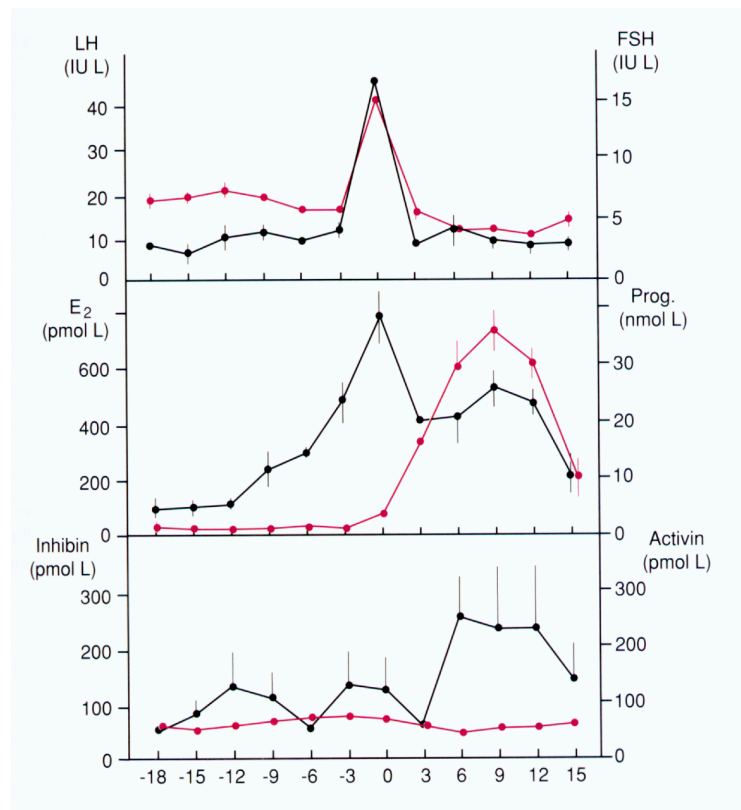
LH \Rightarrow \uparrow LDL binding to receptors

\Rightarrow \uparrow 3 α OH steroid dehydrogenase activity

⇒ ↑ progesterone

- Marked ↑ in progesterone secretion (progesterone only AFTER ovulation while estrogen before and after)
- Progesterone actions:
 - suppress follicular maturation on the ipsilateral ovary
 - thermogenic activity ⇒ ↑ basal body temp
 - endometrial maturation
- Progesterone peak 8 days after ovulation (Day 22 MC) (That's why want to check for ovulation we check progesterone at day 22, it should be the highest level)
- Corpus luteum is sustained by LH
- It loses its sensitivity to gonadotropins ⇒ luteolysis ⇒ ↓ estrogen & progesterone level ⇒ desquamation of the endometrium "menses"
- ↓ estrogen & progesterone ⇒ ↑ FSH & LH (Beginning of the new cycle)
- The new cycle starts with the beginning of menses
- If pregnancy occurs ⇒ hCG secretion ⇒ maintain the corpus luteum

HORMONAL PROFILES DURING THE MENSTRUAL CYCLE



ENDOMETRIAL CHANGES DURING THE MENSTRUAL CYCLE

1-Basal layer of the endometrium

- Adjacent to the myometrium
- Unresponsive to hormonal stimulation
- Remains intact throughout the menstrual cycle

2-Functional layer of the endometrium

Composed of two layers:

- zona compacta ⇒ superficial
- Spongiosum layer

1-Follicular /proliferative phase

Estrogen ⇒ mitotic activity in the glands & stroma ⇒

- ↑ endometrial thickness from 2 to 8 mm
- (from basalis to opposed basalis layer)

2-Luteal /secretory phase

Progesterone ⇒- Mitotic activity is severely restricted

- Endometrial glands produce then secrete glycogen rich vacuoles
- Stromal edema
- Stromal cells enlargement
- Spiral arterioles develop, lengthen & coil

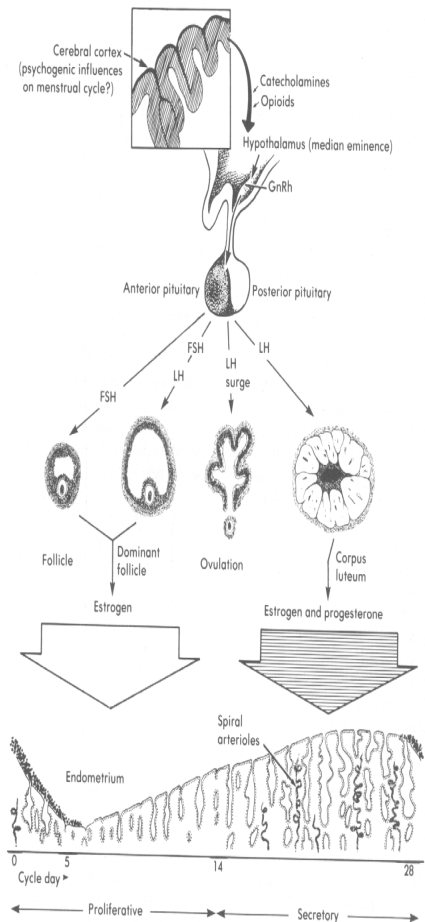


Fig. 15-28. Endocrine and physiologic changes during the menstrual cycle. From: Textbook of Obstetrics and Gynecology, 10th Edition, Williams & Wilkins, Baltimore, MD, 2006, p. 100.

MENSTRUATION

- Periodic desquamation of the endometrium
- The external hallmark of the menstrual cycle
- Just before menses the endometrium is infiltrated with leucocytes
- Prostaglandins are maximal in the endometrium just before menses
- Prostaglandins \Rightarrow constriction of the spiral arterioles \Rightarrow ischemia & desquamation

Followed by arteriolar relaxation, bleeding & tissue breakdown

HYPOTHALAMIC ROLE IN THE MENSTRUAL CYCLE

- The hypothalamus secretes GnRH in a pulsatile fashion (if steady it will suppress the ovaries)
- GnRH activity is first evident at puberty
- Follicular phase GnRH pulses occur hourly
- Luteal phase GnRH pulses occur every 90 minutes
- Loss of pulsatility \Rightarrow down regulation of pituitary receptors \Rightarrow \downarrow secretion of gonadotropins
- Release of GnRH is modulated by –ve feedback by:
 - steroids
 - gonadotropins
- Release of GnRH is modulated by external neural signals

Summary:

