

YU - Medicine

Passion Academic Team

The Urogenital System


Sheet# 9 - Physiology

Lec. Title : Female Reproductive
System (Part 2)

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Female reproductive system, part 2

المحاضرة من الكتاب تبدأ صفحة 473
دعواتكم لنا ولأهل فلسطين و غزة ، كل الحُبّ ...

Regulation of the ovaries

1. Hypothalamic control – GnRH

Pulsatile GnRH activity stimulates the anterior pituitary to secrete FSH and LH.

By hypothalamic-pituitary axis

2. Anterior pituitary gland – FSH and LH

❖ FSH

- Stimulates the **growth of granulosa** cells in primary follicles and stimulates **estradiol synthesis**.
- **Estradiol** then supports the **trophic effect of FSH on follicular cells**.
 - These two effects are **mutually reinforcing**.

❖ LH

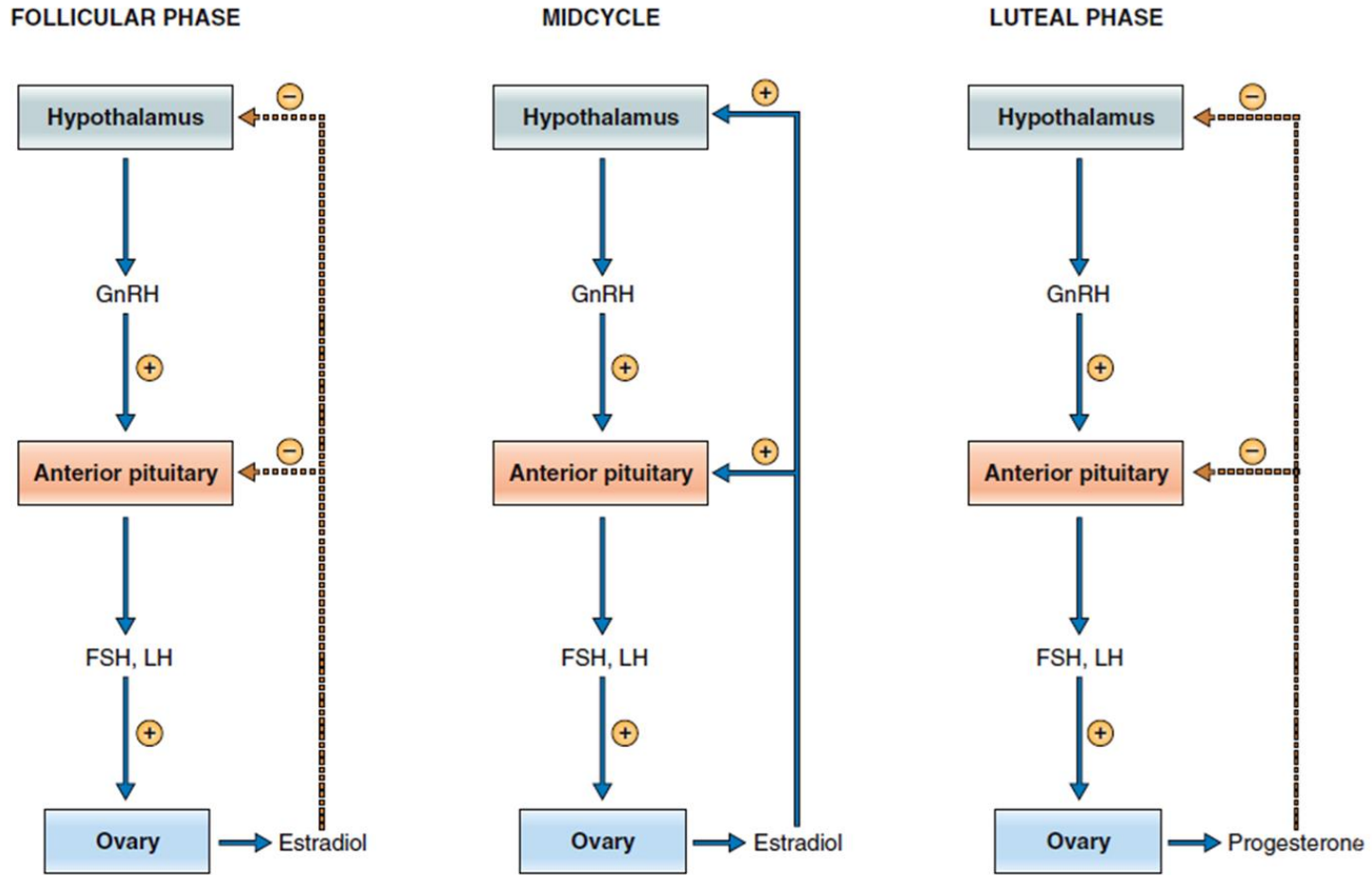
- Initiates ovulation.
 - Just prior to ovulation, the **concentration of LH rises sharply** → **induces** rupture of the dominant follicle → **oocyte release**.
- LH **stimulates** formation of **corpus luteum** (luteinization).
- LH **maintains steroid hormone production** by the corpus luteum during the luteal phase (the last 14 days of the menstrual cycle.)

Negative and positive feedback control - estrogen and progesterone

- ❓ Both feedbacks are depending on the phase of the menstrual cycle.
- ❓ In the **follicular phase** of the menstrual cycle, FSH and LH **stimulate** synthesis and secretion of **estradiol** by follicular cells
 - One action of estradiol is **negative feedback on GnRH** secretion by the hypothalamus and FSH and LH secretion by the anterior pituitary.
- ❓ At **midcycle**, Estradiol levels **rise sharply** as a result of the proliferation of follicular cells and the stimulation of estradiol synthesis that occurred during the follicular phase.
 - When a critical level of estradiol is reached (of at least **200** picograms per milliliter of plasma), estradiol has a **positive feedback effect on GnRH** secretion and **on FSH and LH secretion** (by up-regulating GnRH receptors in the anterior pituitary), thus causing **further secretion** of FSH and LH. This's called **the ovulatory surge of FSH & LH**, then triggers ovulation of the mature oocyte

Negative and positive feedback control - estrogen and progesterone

- ❓ In the **luteal phase**, the major hormonal secretion of the ovaries is **progesterone**.
- One of the actions of progesterone is **negative feedback** on GnRH secretion and FSH and LH secretion.
- ❓ **Inhibin** is produced by ovarian **granulosa** cells. **inhibits FSH secretion**
- ❓ **Activin** is produced by ovarian **granulosa** cells and **stimulates FSH secretion**
- ❓ pregnancy tests check for HCG/LH like hormone.



Actions of estrogen

TABLE 10.2 Actions of Estrogens on Target Tissues

Maturation and maintenance of uterus, fallopian tubes, cervix, and vagina
Responsible at puberty for the development of female secondary sex characteristics
Required for development of the breasts
Responsible for proliferation and development of ovarian granulosa cells
Up-regulation of estrogen, progesterone, and LH receptors
Negative *and* positive feedback effects on FSH and LH secretion
Maintenance of pregnancy
Lowering uterine threshold to contractile stimuli
Stimulation of prolactin secretion
Blocking the action of prolactin on the breast
Decreasing LDL cholesterol
Anti-osteoporosis

FSH, Follicle-stimulating hormone; *LDL*, low-density lipoprotein; *LH*, luteinizing hormone.

Actions of progesterone

TABLE 10.3 Actions of Progesterone on Target Tissues

Maintenance of secretory activity of uterus during luteal phase
Development of the breasts
Negative feedback effects on FSH and LH secretion
Maintenance of pregnancy
Raising uterine threshold to contractile stimuli during pregnancy

FSH, Follicle-stimulating hormone; *LH*, luteinizing hormone.

- ❑ For more details, read the book pages 4/5, 4/6
- ❑ The two ovarian steroid hormones (estrogen & progesterone) function in a **coordinated** fashion to support reproductive activity of the female
- ❑ The highest levels of estrogen and progesterone occur during pregnancy, synthesized in early pregnancy by the corpus luteum and in mid-to-late pregnancy by the placenta.
- ❑ During pregnancy, progesterone increases the uterine threshold to contractile stimuli, thus preserving the pregnancy until the fetus is ready to be delivered.
- ❑ Just before delivery, estrogen decrease the uterine threshold to contractile stimuli facilitating birth process.



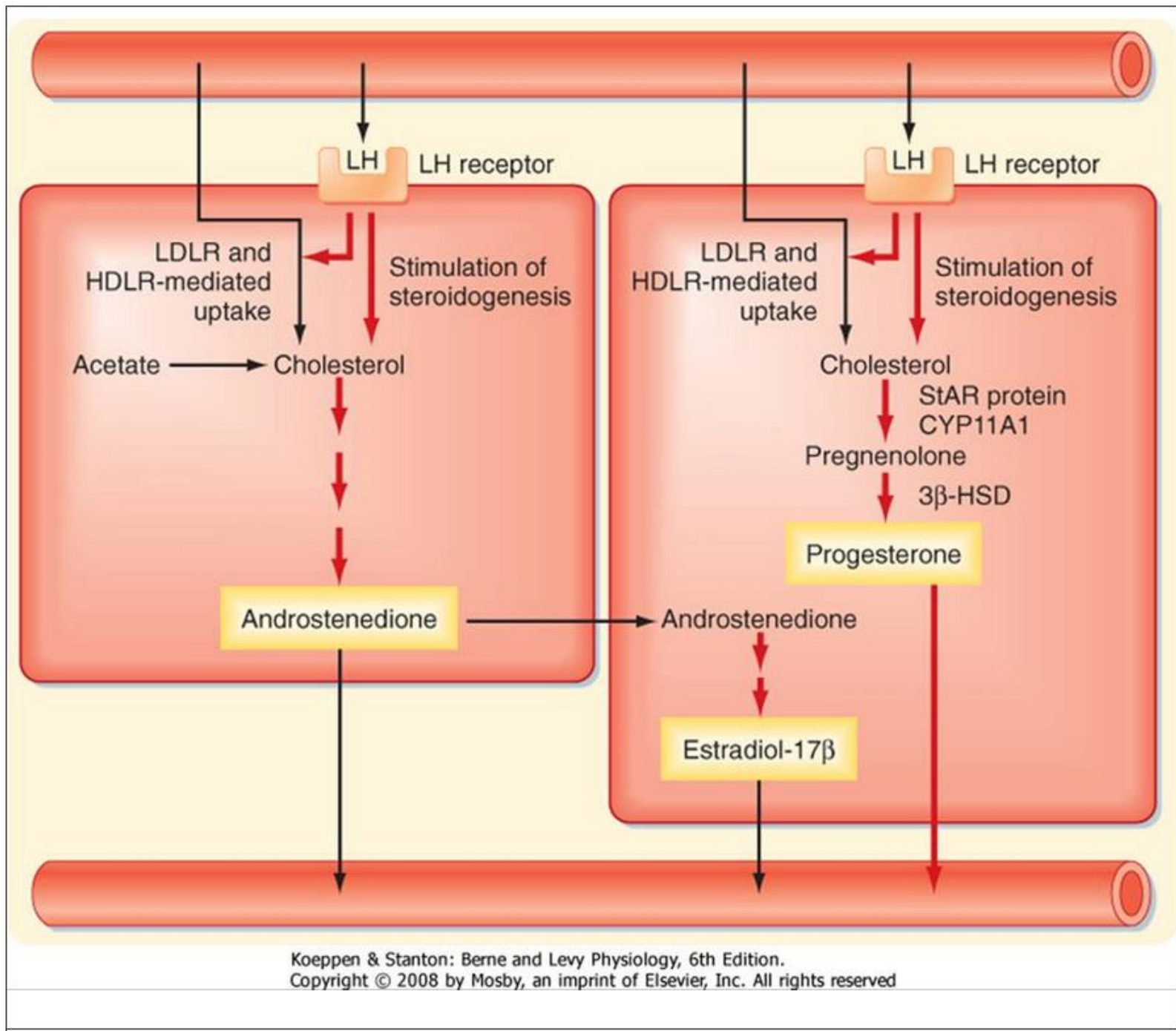
The menstrual cycle

Follicular phase

- ❑ Days 0-14
- ❑ A **primordial follicle develops** to the **graafian stage**, with **atresia** of neighboring follicles. (do u remember he anti Mullerian hormone)
- ❑ the remaining follicle is called the **dominant follicle.**
- ❑ LH and FSH receptors are **up-regulated in theca and granulosa cells.**
- ❑ **Estradiol levels increase** and cause **proliferation endometrial lining of the uterus.**
- ❑ **GnRh & FSH and LH levels are suppressed** by the **negative feedback** effect of estradiol on the anterior pituitary & hypothalamus.
- ❑ **Progesterone levels are low.**

Ovulation

- ❑ Occurs **14 days before menses**, regardless of cycle length.
 - ex: in a 35-day cycle, ovulation occurs on day 21, or 14 days before menses; in a 24-day cycle ovulation occurs on day 10.
- ❑ Follows by **burst of estradiol synthesis** at the end of the follicular phase has a **positive feedback** effect on the secretion of GnRH & FSH and LH (**LH surge**).
- ❑ **Ovulation** occurs as a result of the estrogen-induced LH surge.
- ❑ Estrogen levels decrease just after ovulation (but rise again during the luteal phase).
- ❑ **Cervical mucus increases** in quantity; it becomes **less viscous** and **more penetrable by sperm**.



For more details about this figure please read page 805 from Berne and Levy

Luteal phase

- ❑ Days 14-28
- ❑ The **corpus luteum** begins to develop, and it **synthesizes estrogen and progesterone**.
- ❑ high levels of **progesterone** increases **Vascularity and secretory activity of the endometrium**.
- ❑ **Basal body temperature increases**. (because progesterone increases the hypothalamic temperature set point)
- ❑ If fertilization does not occur, the **corpus luteum regresses** at the end of the luteal phase.
- ❑ As a result, **estradiol** and **progesterone** levels decrease **abruptly**.

Menses

- ❑ Days 0-4
- ❑ Regression of the corpus luteum and the abrupt loss of estradiol and progesterone cause the **endometrial lining and blood to be sloughed** (menses or menstrual bleeding).
- ❑ Typically, menses lasts 4–5 days, **corresponding** to days 0 to 4 or 5 of the next menstrual cycle.
- ❑ During this time, primordial follicles for the **next** cycle are being **recruited** and are beginning to develop.
- ❑ It's a true bleeding with moderate to severe pain, symptoms of hypotension, .Fatigue, Bloating, Bowel issues, Headache & Mood swings... iron deficiency anemia may be developed...

Summary Menstrual cycle

A highly dynamic "conversation" occurs among the ovary, pituitary, and hypothalamus in which the events of the menstrual cycle are orchestrated, beginning with the ovary at the end of the luteal phase of a previous, nonfertile cycle (Fig. 43-24):

- *Event 1:* In the absence of fertilization and implantation, the corpus luteum regresses and dies (called **luteolysis**). This leads to a dramatic decline in levels of progesterone, estrogen, and inhibin A by day 24 of the menstrual cycle.
- *Event 2:* The gonadotrope perceives the end of luteal function as a release from negative feedback. This permits a rise in FSH about 2 days before the onset of menstruation. The basis for the selective increase in FSH is incompletely understood, but it may be due to the slow frequency of GnRH pulses during the luteal phase, which in turn is due to high progesterone levels.
- *Event 3:* The rise in FSH levels recruits a crop of large (2 to 5 mm) antral follicles to begin rapid, highly gonadotropin-dependent growth. These follicles produce low levels of estrogen and inhibin B.
- *Event 4:* The gonadotrope responds to the slowly rising levels of estrogen and inhibin B by decreasing FSH secretion. Loss of high levels of progesterone and estrogen causes an increase in the frequency of GnRH pulses, thereby selectively increasing LH synthesis and secretion by the gonadotrope. Thus, the LH/FSH ratio slowly increases throughout the follicular phase.
- *Event 5:* The ovary's response to declining FSH levels is follicular atresia of all of the recruited follicles, except for one dominant follicle. Thus, the process of selection is driven by an extreme dependency of follicles on FSH in the face of declining FSH secretion. Usually, only the largest follicle with the most FSH receptors and best blood supply can survive. This follicle produces increasing amounts of estradiol-17 β and inhibin B. FSH also induces the expression of LH receptors in the mural granulosa cells of the dominant follicle.
- *Event 6:* Once the dominant follicle causes circulating estrogen levels to exceed 200 pg/mL for about 50 hours in women, estrogen exerts a positive feedback on the gonadotrope to produce the midcycle LH surge. This is enhanced by the small amount of progesterone secreted at midcycle. The exact mechanism of the positive feedback is **unknown**, but it occurs largely at the level of the pituitary. **GnRH receptors** and the sensitivity to GnRH signaling increase dramatically in the gonadotropes. The hypothalamus contributes to the gonadotropin surge by increasing the frequency of GnRH pulses and the secretion of a small amount of progesterone.
- *Event 7:* The LH surge drives meiotic maturation, ovulation, and differentiation of granulosa cells into progesterone-producing cells.
- *Event 8:* Rising levels of progesterone, estrogen, and inhibin A by the mature corpus luteum negatively feed back on the pituitary gonadotrope. Even though estrogen levels exceed the 200-pg/mL threshold for positive feedback, the high progesterone levels block any positive feedback. Consequently, both FSH and LH levels decline to basal levels.
- *Event 9:* Basal levels of LH (but not FSH) are absolutely required for normal corpus luteum function. However, the corpus luteum becomes progressively insensitive to LH signaling and will die unless LH-like activity (i.e., hCG from an implanted embryo) increases. In a nonfertile cycle, the corpus luteum of menstruation will regress in 14 days, and progesterone and estrogen levels will start to decline by about 10 days, thereby cycling back to event 1.

MENSTRUAL CYCLE

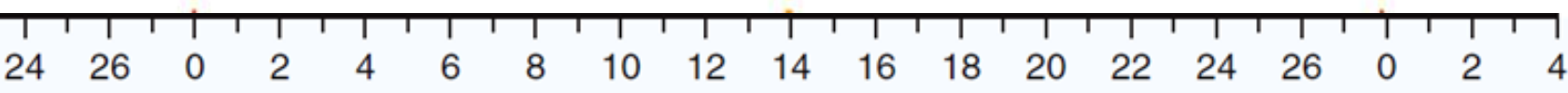
Ovulation



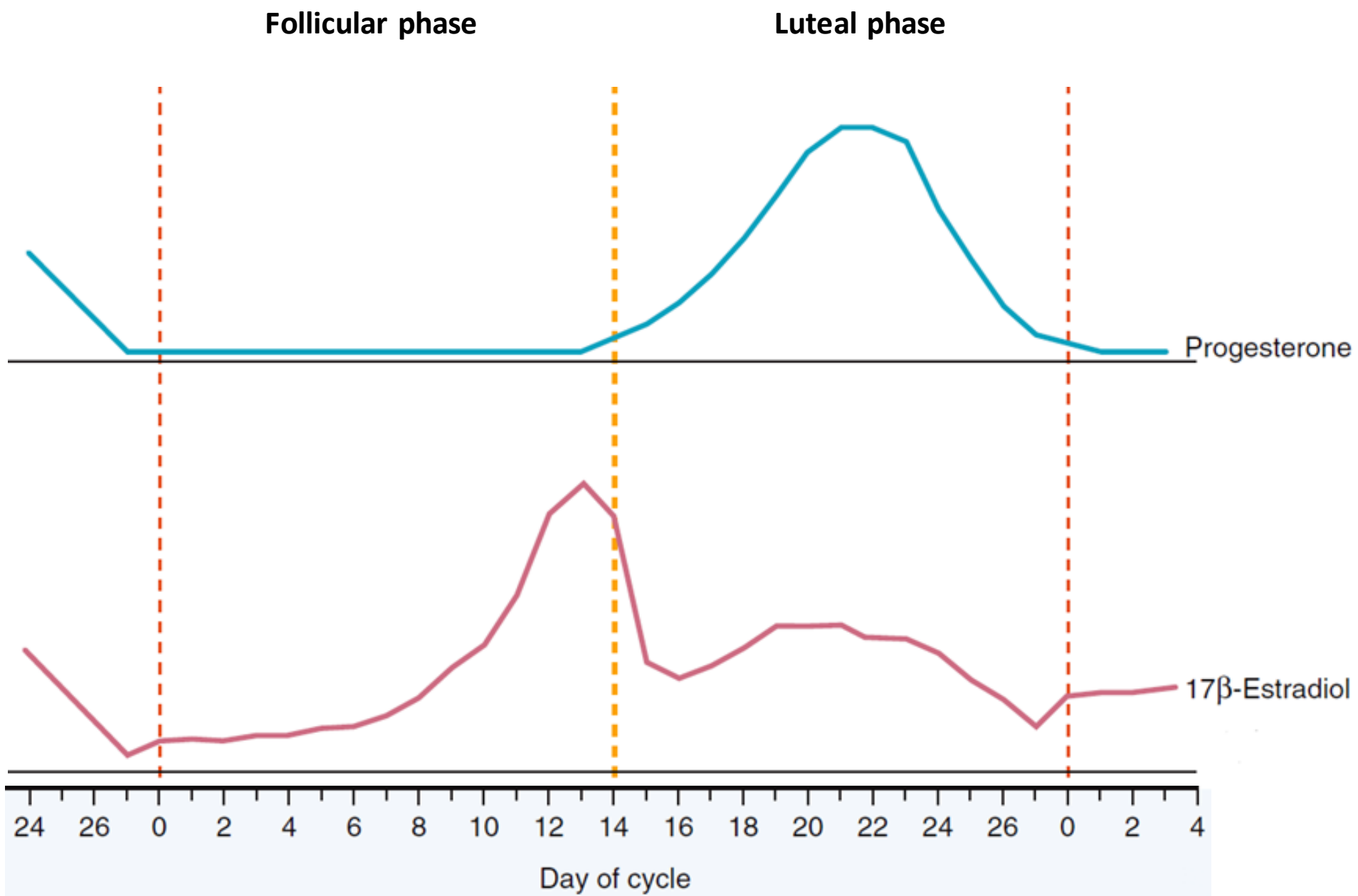
Follicular phase
(proliferative)

Luteal phase
(secretory)

Basal body temperature



Day of cycle



Follicular phase

Luteal phase

