

Physiology of the Menstrual Cycle

429 OB/GYN Team

Sources: Hacker and Moore's Essentials of obstetrics and gynecology, 428 team notes, wikipedia and Lecture notes

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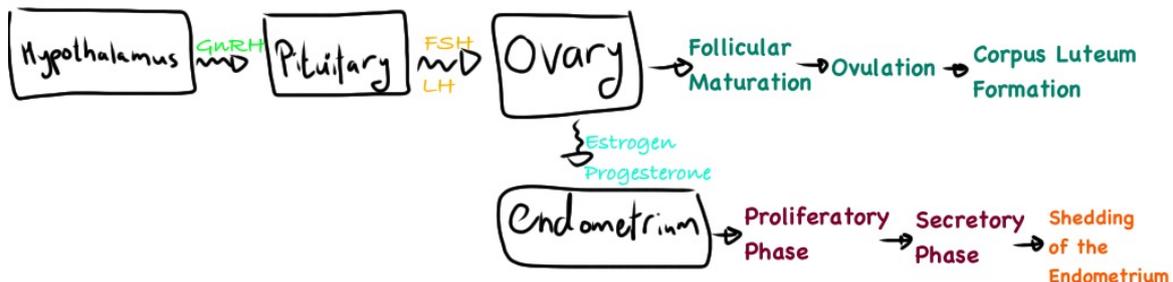


THE MENSTRUAL CYCLE

The menstrual cycle is the scientific term for the physiological changes that can occur in fertile women for the purposes of sexual reproduction and fertilization.

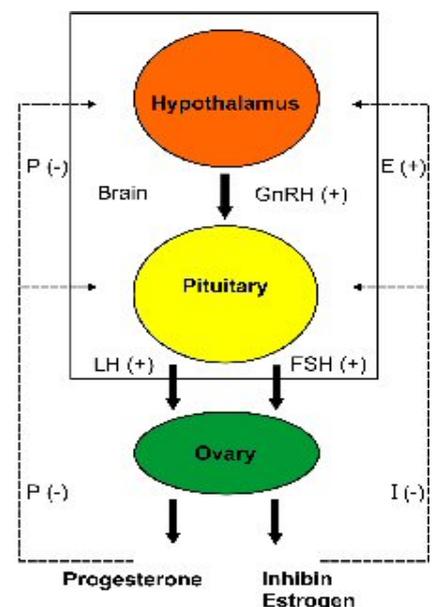
Each menstrual cycle is a complex interaction between the **Hypothalamus**, **Pituitary Gland**, **Ovaries** and **Endometrium**. This, can be summarized by the following *Cyclic Changes*:

- Gonadotropin Releasing Hormone GnRH, produced by the **hypothalamus**, acts on the **pituitary gland**
- Follicular Stimulating Hormone FSH and Luteinizing Hormone LH, produced by **the pituitary gland**, act on the **ovary**; resulting in functional as well as morphological changes.
- Changes in the **ovary** include; follicular maturation, ovulation and corpus luteum formation.
- Changes in the **endometrium** include; proliferation and secretion phases, allowing successful implantation of the developing embryo to happen, or the physiological **endometrial shedding** in absence of fertilization (i.e. menstrual cycle)

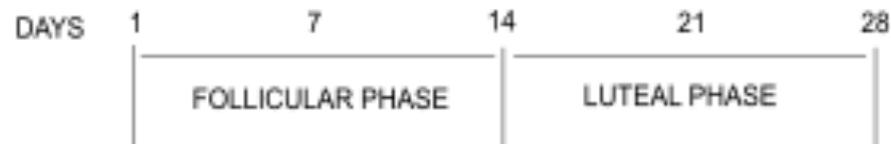


HYPOTHALAMIC-PITUITARY AXIS

- The **hypothalamus** controls the **pituitary gland** by “releasing hormones”.
- GnRH, secreted in a pulsatile fashion, is a **peptide hormone** that is very important in the synthesis and release of the trophic hormones of the **pituitary**
- The Gonadotropins; FSH and LH, which are **glycoproteins** contain alpha and beta subunits.
- The beta subunit is specific to every individual while the alpha subunit is same among all individuals.



MENSTRUATION (Ovarian and Uterine Cycles)



FOLLICULAR PHASE (also called PROLIFERATIVE PHASE):

- Initiated by FSH, resulting in, follicle maturation and endometrial proliferation.
- Since fetal development, the follicles develop into **primordial follicles**, and FSH helps formulate the fully mature **Graafian follicle**:
 - It is an oocyte covered with **Granulosa Cells** and **Theca Cells**
 - Many follicles grow during the follicular phase, but **ONLY ONE** of them continue to differentiate and mature into a fully mature **Ovarian (Graafian) Follicle**
- Estrogen hormone; Estradiol E2:
 - A steroidal hormone produced by the ovary's follicle, in precise the granulosa cells
 - It is the predominant hormone in the **Proliferative** phase.
 - It starts low and peaks right before the LH surge
 - Effects:
 - Stimulates proliferation of the **endometrium** and increases its production of progesterone receptors
 - It causes marked cellular proliferation of the epithelial lining, the endometrial glands and the connective tissue of the stroma
 - Inhibits GnRH by its negative feedback

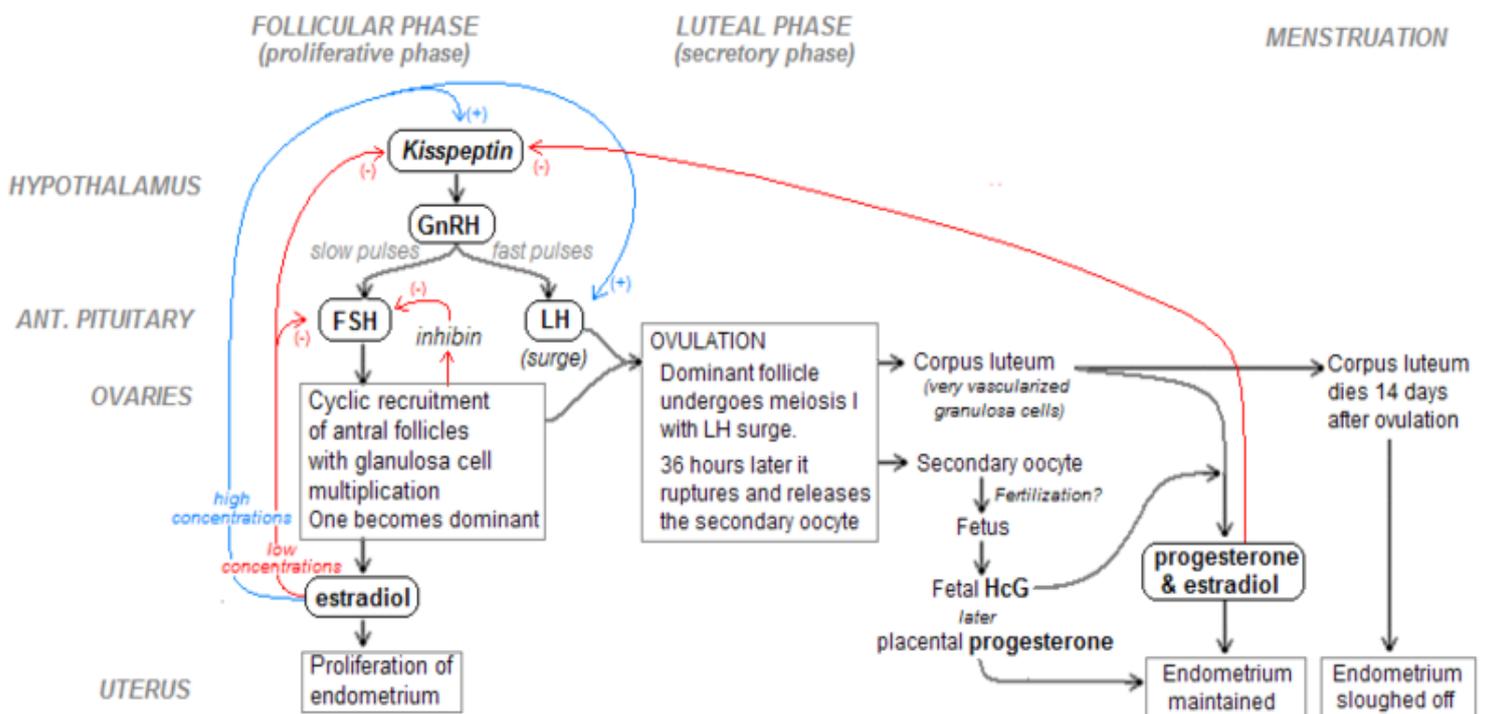
OVULATION (and LH SURGE)

- During the follicular phase, estradiol suppresses production of luteinizing hormone (LH) from the anterior pituitary gland.
 - When the egg has nearly matured and reaches a mean diameter of **18-24**, the levels of estradiol will reach a threshold above, then the negative feedback effect is reversed and estrogen starts to stimulate the production the LH surge.
 - This process, known as the LH surge, starts around day 12 of the average cycle and may last 48 hours.
- The release of LH matures the egg and weakens the wall of the follicle in the ovary, causing the fully developed follicle to release its secondary oocyte.
 - The secondary oocyte promptly matures into an ootid, becomes a mature ovum and then released into the fallopian tubes waiting for fertilization

LUTEAL PHASE (also called SECRETORY PHASE)

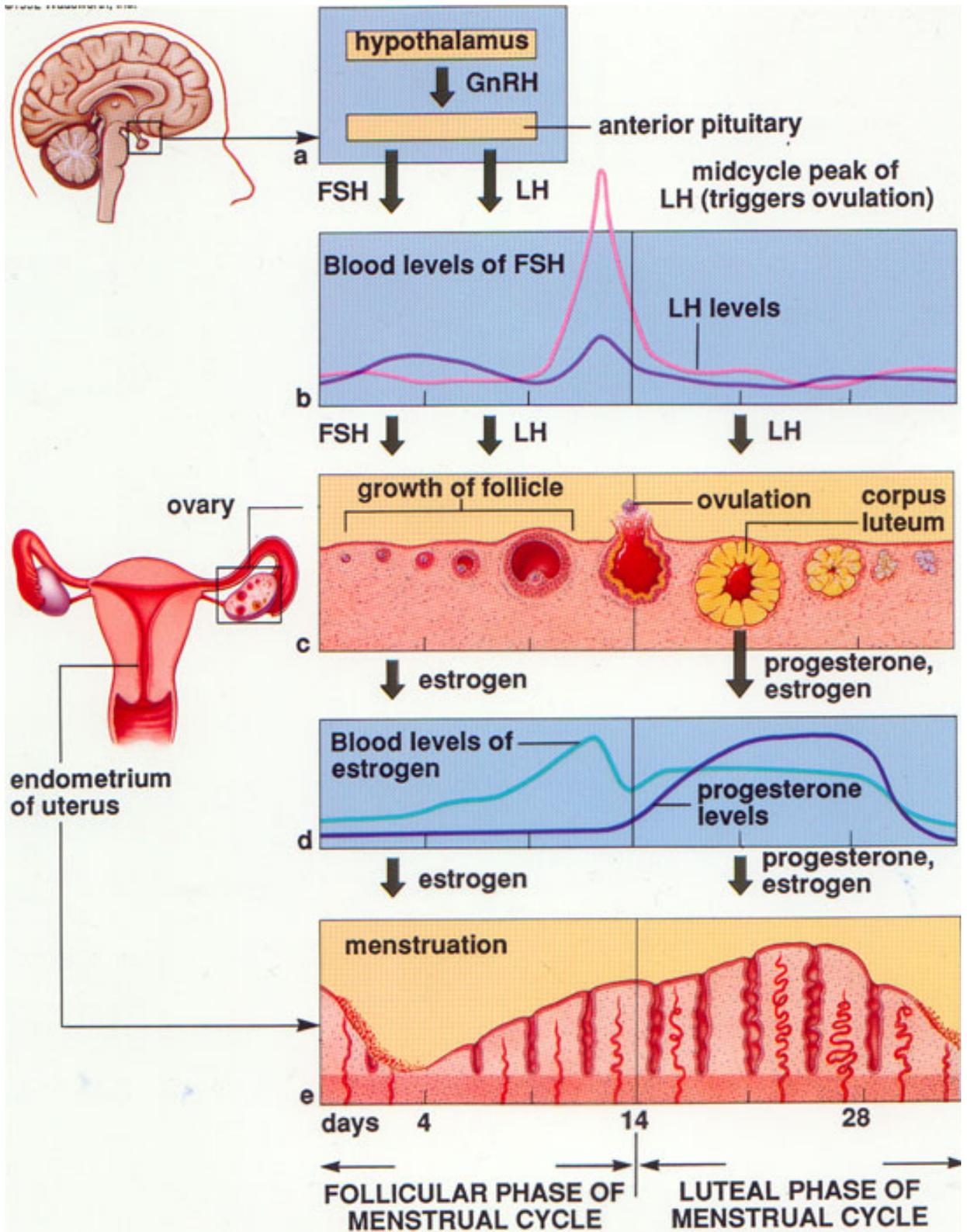
- A **Fixed** period of 14 days
- After ovulation, the pituitary hormones FSH and LH cause the remaining parts of the dominant follicle (The granulosa and the theca cell layers) to transform into the corpus luteum, which produces progesterone.
- Granulosa cells undergo lutenization
- Progesterone Hormone; 17 α -hydroxyprogesterone:
 - A steroidal hormone, produced by the mature ovarian follicle
 - It is the predominant hormone is the **Secretory** phase

- Effects:
 - Stimulates the glandular cells to secrete glycogen, mucus and other substances (thus the naming; secretory phase, or secretory endometrium).
 - The glands become torturous and the lumens are dilated and filled with these substances
 - The stroma becomes edematous
 - The spiral arteries extend into the superficial layer of the endometrium and become convoluted
- The normal life span of the corpus luteum is **10 days** then it regresses and is replaced by an avascular scar called **corpus albicans**.
- If pregnancy doesn't occur by day 23, the corpus luteum regresses, secretion of progesterone and estradiol declines, and the endometrium undergoes involution (shedding of the endometrium → menstrual bleeding)



Kisspeptin:

A human protein formally known as **metastatin**. The KISS1 gene encodes it. Kiss1 was originally identified as a human metastasis suppressor gene that has the ability to suppress melanoma and breast cancer metastasis. It recently became clear that kisspeptin-GPR54 signaling has an important role in initiating secretion of GnRH at puberty



Changing hormone levels during the menstrual cycle.