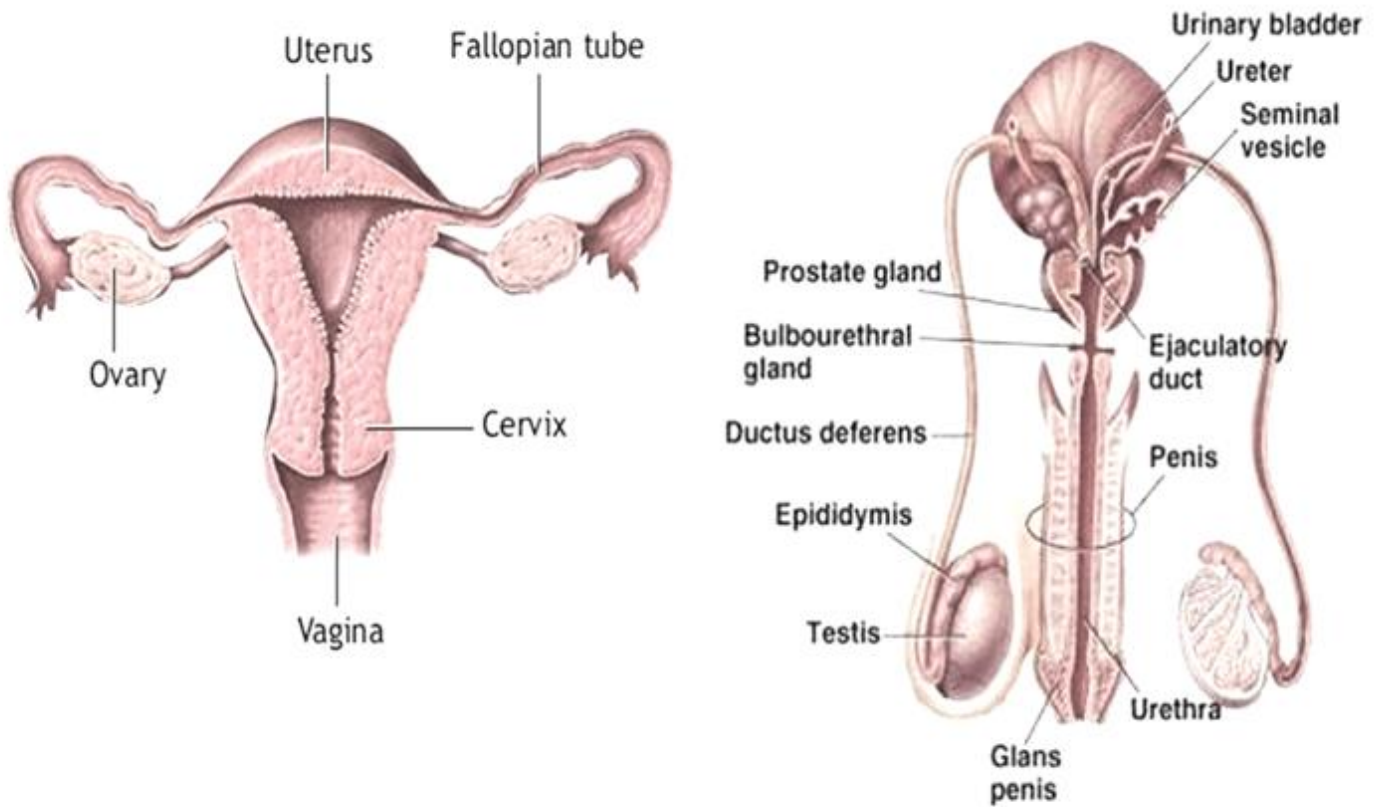


1st Lecture

HPG Axis



PHYSIOLOGY TEAM – 430

This Lecture is done by:

Layan Akkielah

Al-Waleed Al-Johar

Hypothalamic-Pituitary-Gonadal Axis

To make it simple read this before you start:

- The gonads have two functions, secretion of sex steroid hormones and gametogenesis
- Gonads' functions are controlled by the release of gonadotropins from the anterior pituitary.
- There are two gonadotropin hormones : LH (Luteinizing hormone) and FSH (Follicle-stimulating hormone)
- Gonadotropins release is stimulated by the release of GnRH (gonadotropin releasing hormone) from the hypothalamus.
- During puberty , Anterior pituitary will secrete increased amount of gonadotropins which will stimulate the gonads to secrete increased amount of sex hormones , these sex hormones will produce the male's or female's features.
- Sex steroid hormones (androgens especially testosterone and estrogens) have an inhibitory effect on the secretion of gonadotropins.
- There is also a polypeptide hormone secreted from the gonads called Inhibin, it inhibits the anterior pituitary secretion of the FSH without affecting the secretion of the LH.

➤ Control of male sexual functions by hormones from the hypothalamus and anterior pituitary gland:

➤ **GnRH and its effect in increasing the secretion of LH and FSH:**

- GnRH peptide is secreted by the **arcuate nuclei** of the hypothalamus through the **hypothalamic-hypophyseal portal system** to the anterior pituitary gland and **stimulates the release of gonadotropins** (LH and FSH) which will stimulate the release of sex steroid hormones from the gonads.
- GnRH is secreted **intermittently** (not continuous) for few minutes every 1 to 3 hrs.
- The secretion of **LH by the anterior pituitary** is also cyclical following the **pulsatile release of GnRH**.

➤ **Testosterone regulation :**

- LH stimulates the secretion of Testosterone from **leydig cells** (in the interstitium of the testis)
- Its release is **directly proportional to the amount of LH secreted**, so when LH secretion increases, testosterone will increase as well.
- Mature leydig cells are found in an **infant's testis** few weeks after birth & then disappear until puberty then it will appear again.

➤ **Regulation of spermatogenesis by FSH and testosterone:**

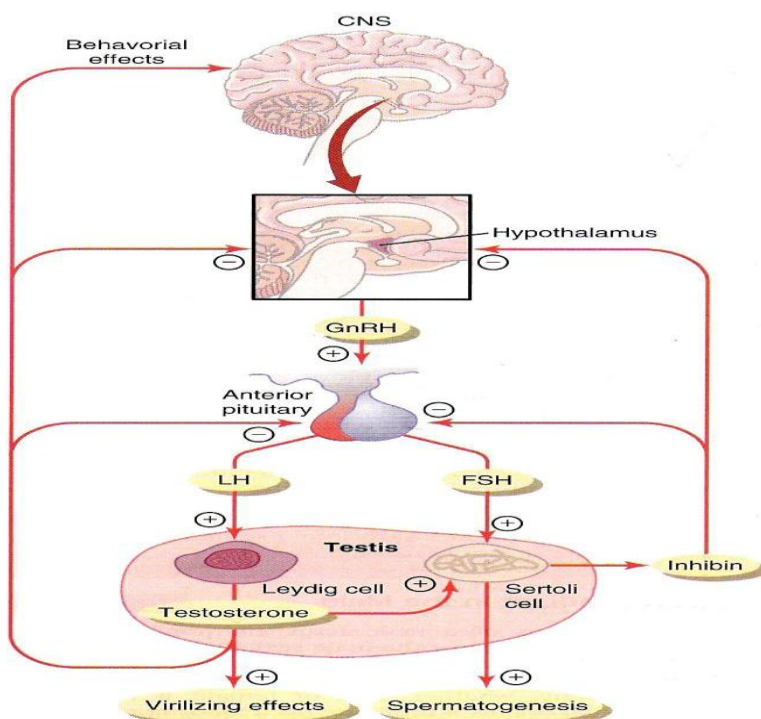
- FSH binds with specific FSH receptors attached to the **sertoli cell** in the seminiferous tubules in the testicles, which causes these **cells to grow & secrete spermatogenic substances**.
- Also the diffusion of testosterone & dihydrotestosterone into the seminiferous tubules from the leydig cells affect the spermatogenesis , so **both FSH & testosterone are necessary to initiate spermatogenesis**

➤ Negative feedback effect of testosterone and inhibin :

- Testosterone has an inhibitory effect on the gonadotropins release by **inhibiting the release of GnRH** from the hypothalamus.
- Testosterone has a direct inhibitory effect on the hypothalamus.
- Inhibin is a polypeptide hormone secreted from **the sertoli cells** in the seminiferous tubules in the testis.
- Inhibin has a slight inhibitory effect of the hypothalamus and **a strong inhibitory effect of the anterior pituitary; it inhibits the secretion of FSH particularly.**
- **Inhibin is released when the spermatogenesis is rapid;** it inhibits FSH production leading to **reduced** testosterone secretion.
- When **spermatogenesis is slow**, secretion of **FSH increases**.

Testosterone → leydig cells, it has an inhibitory effect on the hypothalamus

Inhibin → sertoli cells, It has an inhibitory effect on the anterior pituitary to inhibit FSH.



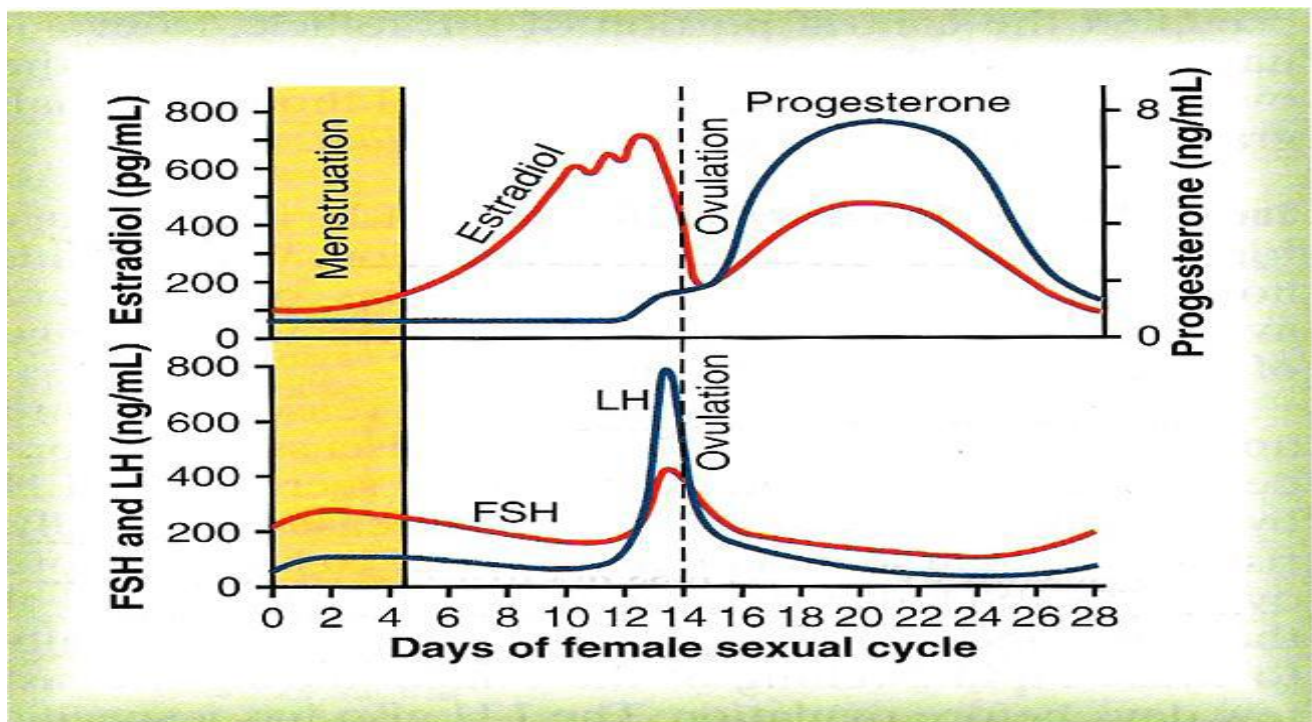
Hypothalamus secretes GnRH which stimulates the anterior pituitary to secrete LH & FSH.

FSH acts on the sertoli cells which initiates spermatogenesis, LH acts on leydig cells to produce testosterone. Testosterone is also necessary to initiate spermatogenesis.

Testosterone has an inhibitory effect mainly on hypothalamus; inhibin has an inhibitory effect on the anterior pituitary to inhibit FSH secretion.

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

- GnRH controls the release of gonadotropins. (Like the males)
- **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.



There is a constant release of FSH and LH at first, but just before ovulation there will be a surge of LH mainly and FSH to a lesser extent, this is due to the high levels of estrogens

➤ **Negative feedback effects of estrogen and progesterone and inhibin:**

- 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** inhibit the secretion of FSH & to lesser extent LH.

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

- The granulosa cells of the follicle begin to **secrete small increasing amount of progesterone** about 1 day before ovulation which **stimulate LH secretion**
- **Estrogen** has **special positive feedback** effect of stimulating pituitary secretion of **LH** & to a lesser extent **FSH**
- AP secretes increased amount of LH for 1 to 2 days before ovulation. FSH surge is much smaller in the pre-ovulatory than LH surge.

LH secretion greatly exceeds FSH secretion before ovulation due to the increasing amount of progesterone secreted from the granulosa cells of the follicles about 1 day before ovulation and also the positive feedback of estrogen on the anterior pituitary which stimulates the secretion of LH and 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)

➤ **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.