



Physiology Team 431
Reproductive Block

Lecture 1

Hypothalamic and Pituitary Gonadal Axis

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Hypothalamic and Pituitary Gonadal Axis

Definition of hormone:

Chemical substance (messengers) produced by ductless glands that are transported in the circulation to the target cells where they regulate the metabolic processes.

The connection between the hypothalamus and pituitary gland via:

- Hypothalamohypophysial tract between the posterior pituitary gland, supraoptic and paraventricular nuclei (neural connection).
- Portal hypophysial vessels between the anterior pituitary gland and the hypothalamus.

The anterior pituitary secretes six hormones:

1. Adrenocorticotrophic hormone (corticotrophin, ACTH).
2. Thyroid-stimulating hormone (thyrotropin, TSH).
3. Growth hormone (GH).
4. Follicle-stimulating hormone (FSH).
5. Luteinizing hormone (LH).(affect ovary or testis).
6. Prolactin (PRL).

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** secreted by the **arcuate nuclei** of the **hypothalamus** through the **hypothalamic-hypophysial 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 **pulsatile** secretion of **LH** by the anterior pituitary is also cyclical following the **pulsatile** release of **GnRH**.

Testosterone regulation by LH:

- ✓ LH from anterior pituitary stimulates the secretions of **Testosterone** from **Leydig** cells (in the interstitium of the testis).
- ✓ Its release is **directly proportional to the amount of LH**.
- ✓ **Mature leydig cells are found in neonates' testis few weeks after birth & then disappear until puberty when it appears again.**
Because neonate need it to form epididymis ,vas deferens and seminal vesicle

Inhibition of anterior pituitary secretion of LH and FSH by testosterone – negative feedback control of testosterone secretion:

Testosterone has reciprocal effect of inhibiting the AP secretion of LH.

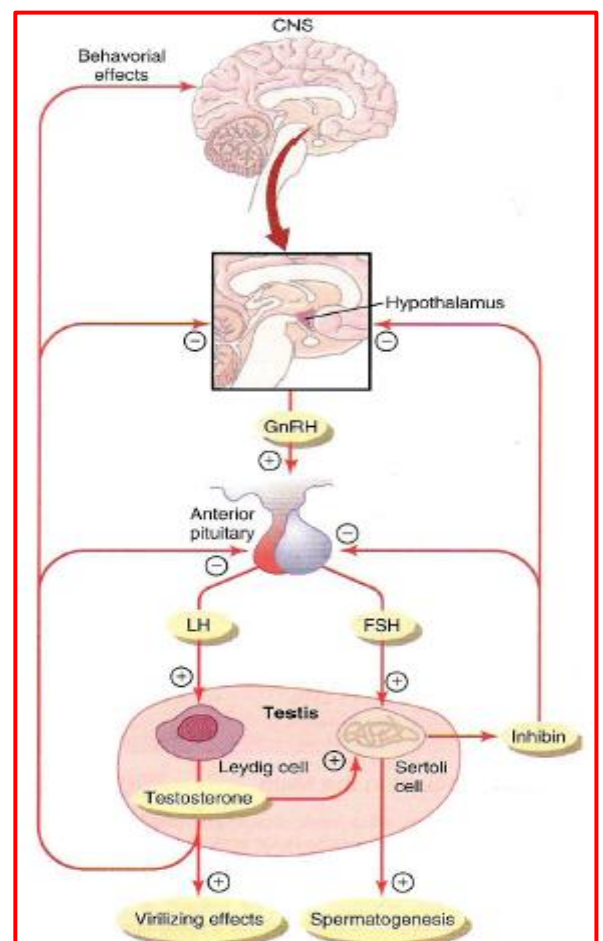
- ✓ **Most of the inhibitory effect results from direct effect of testosterone on the hypothalamus to decrease secretion of GnRH which causes decrease secretion of both LH & FSH.**
- ✓ Also **some inhibitory** effect on anterior pituitary to inhibit LH and FSH.

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

LH: targets leydig cells to produce testosterone which produces virilizing effects (male sexual characteristics and organs).

FSH: acts on Sertoli cells to initiates spermatogenesis.

- FSH alone is not enough to stimulate spermatogenesis.
- It also needs testosterone and dihydrotestosterone to stimulate spermatogenesis.



Spermatogenic substances: androgen-binding protein, inhibin, antimullerian hormone.

Antimullerian hormone: prevents formation of the female sex organs in male fetus.

Regulation of spermatogenesis by FSH and testosterone:

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

Negative feedback control of seminiferous tubule activity –role of the hormone inhibin:

The control of spermatogenesis is through the FSH by inhibin hormone.

- ✓ When **spermatogenesis proceeds rapidly** pituitary secretion of **FSH diminishes**, this is due to the secretion of **inhibin hormone** (polypeptide) from the **sertoli** cells which **strongly inhibit the AP-FSH secretion** and slight inhibitory effect on the hypothalamus to inhibit GnRH secretion.
- ✓ When the **seminiferous tubules fail to produce sperms**, secretion of FSH from the AP **increases**. (**Secretion of inhibin will be inhibited**).

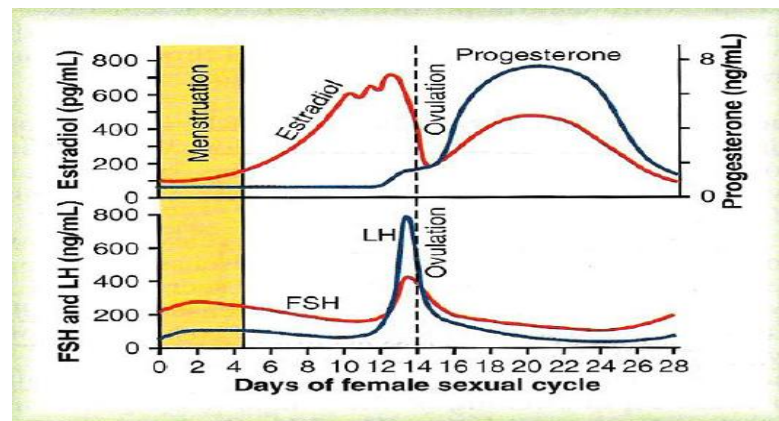
Regulation of the female monthly rhythm, interplay between the ovarian and hypothalamic-pituitary hormones:

- ✓ Releasing hormone (GnRH) formed in the hypothalamus controls the secretion of anterior pituitary hormones (gonadotropins) through the hypothalamic-hypophysial portal system. (as in males).
- ✓ Intermittent, **pulsatile** secretion of **GnRH** by the hypothalamus stimulates **pulsatile** release of **LH** from the anterior pituitary.
- ✓ **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.

The Dr. said, GnRH is secreted in pulses lasting 5-10 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.



Negative feedback effects of estrogen and progesterone in decreasing both LH and FSH secretion:

- ✓ 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 the anterior pituitary directly & to lesser extent on the hypothalamus to inhibit the secretion of GnRH.

Hormone inhibin from the corpus luteum inhibits FSH & LH secretion:

- ✓ The hormone **inhibin** is secreted by the **granulosa cells of the ovarian corpus luteum** inhibit the secretion of FSH & to lesser extent LH.

Corpus luteum: remaining of the follicular growth phase.

Ovulation start at 14 day of menstrual cycle and pass in three phase :-

- 1) Follicular phase :- FSH increase to secrete more estrogen to make uterus more proliferated and thick . form griffin follicle and increase fluid volume in this follicle. It forms a pronounced bulge at the surface of the ovary (blister)
- 2) Ovulation phase : the bulge open and ovum come out to enter fallopian tube and start meiosis I & II
- 3) Luteal phase : at the opening in ovary the corpus luteum made up, the carpus produce estrogen , progesterone (to make uterus ready to respond pregnancy by make uterus more vascular , glandular) and inhibin , these progesterone and estrogen and inhibin have a negative feedback

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

- ✓ Anterior pituitary secretes **increased** amount of **LH for 1 to 2 days before ovulation**. **FSH surge** is much **smaller** in the **pre-ovulatory** than **LH surge**.

Before ovulation, estrogen secreted from secondary follicle because it has positive effect on pituitary to secrete more LH to start the ovulation

Hormone responsible for ovulation is LH.

The possible causes of LH surge could be:

- ✓ Large amount of 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).

We explained that in the top of the page

Follicular growth phase:-

- ✓ 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**.
- ✓ 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 cause **growth of the follicle**.

- 1) By negative feedback of estrogen and progesterone
- 2) Corpus luteum die at the end of ovulation (end of the luteal phase) so negative feedback gone
- 3) the time after menstruation and before the next ovulation , FSH increase to secret estrogen to begin the follicular phase (read the Top of last page)

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**. To secret more LH cause it important in ovulation

Questions

Which one of the following has reciprocal effect of inhibiting the AP secretion of LH

- 1) Testosterone 2) estrogen

Which one of the following is necessary to initiate spermatogenesis

- 1) FSH only 2) testosterone and FSH 3) FSH and LH

Before ovulation the estrogen has :-

- 1) Negative feedback 2) positive feedback

After ovulation estrogen has

- 1) Negative feedback 2) positive feedback

Answers → 1, 2, 2, 1