

Hypothalamus Pituitary Gonadal Axis

Objectives:

- ❖ Characterize hypothalamic pituitary relationship
 - ❖ Name the hypophysiotropic hormones and outline the effects that each has on anterior pituitary function
 - ❖ Name anterior pituitary gonadotropic hormones and outline the effects that each has on the gonads
 - ❖ Describe the negative and positive feedback mechanisms in the hypothalamic-pituitary-gonadal axis and their importance in the control of reproductive function
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Color index:

- ❖ **Important.**
- ❖ **Girls slide only.**
- ❖ **Boys slide only.**
- ❖ **Dr's note.**
- ❖ **Extra information.**



Editing File

Introduction*

What are hormones?

Chemical substances secreted in a small amount from an endocrine gland directly to the bloodstream in response to stimulus to cause physiological responses at the target tissues.

Second definition provided by dr:

Is a messenger produced by the ductus glands that passes through the circulation to reach the target tissue where they regulate metabolic products.

How hypothalamus controls anterior pituitary?

By the secretion of hypothalamic-releasing and hypothalamic inhibitory hormones into the primary capillary plexus of the hypothalamo-hypophyseal portal system, which travel through portal veins to act on specific receptors on different pituitary cells to secrete their respective hormones.

What are the hormones secreted by anterior pituitary?

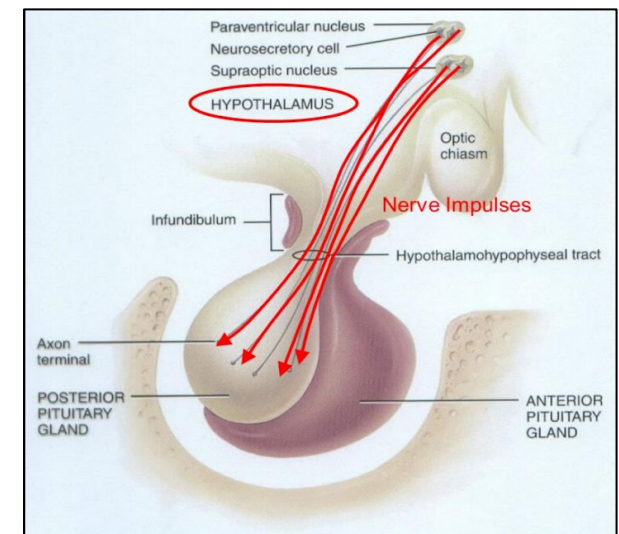
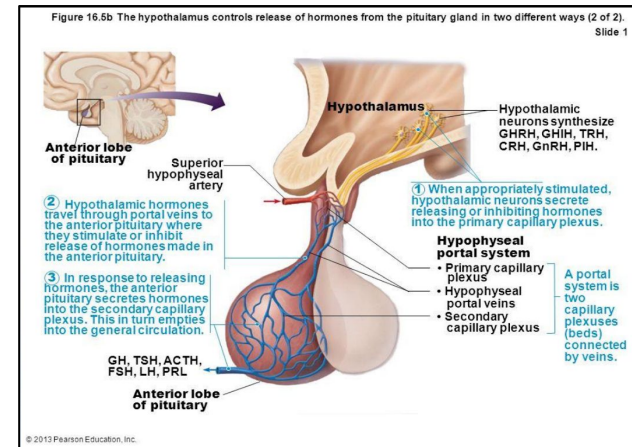
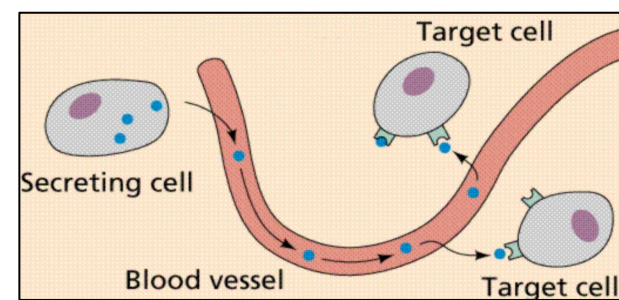
6 main hormones are secreted by the anterior pituitary, main ones are: GH, LH, FSH, TSH, ACTH, Prolactin.

How hypothalamus controls posterior pituitary?

Hypothalamohypophysial tract between the hypothalamic nuclei (supraoptic and paraventricular nuclei) and posterior pituitary gland (neural connection)

What are the hormones secreted by posterior pituitary?

Oxytocin and ADH (also called vasopressin, AVP)

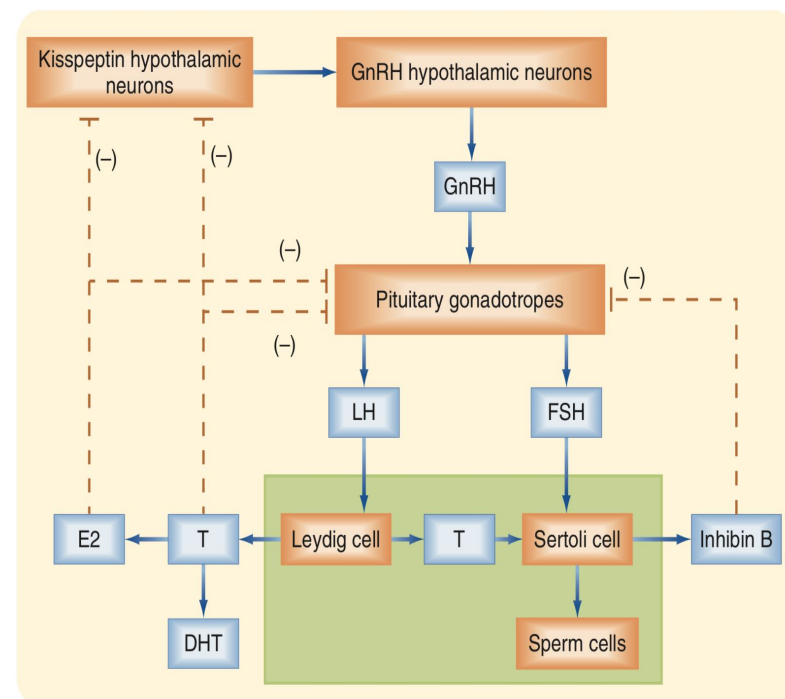


Regulation of Reproduction: General Pathways*

- **Hypothalamus:** Gonadotropin releasing H (GnRH)
- **Anterior Pituitary:** Lutenizing H (LH) and Follicle stimulating H (FSH)
- **Ovary:** Estrogen, progesterone, Inhibin
- **Testis:** testosterone

Testosterone and estradiol have a negative feedback to suppress GnRH (Testosterone and estradiol suppress kisspeptin. so, When we say they suppress the hypothalamus we mean: they suppress GnRH indirectly by suppressing kisspeptin). Its mutation could lead to Hypogonadism.

kisspeptin was first discovered as anti-metastatic & tumor suppression, later it was discovered to be very important for GnRH secretion.



Control of male sexual functions by hypothalamic & anterior pituitary hormones

Gn RH :

(see the picture of testosterone regulation in next slide)

- A peptide secreted by the arcuate nuclei of the hypothalamus
- Released in the median eminence
- Carried via the hypothalamic-hypophyseal portal blood vessels to the anterior pituitary.
- Stimulate anterior pituitary gland to release gonadotropins (**LH** and **FSH**).
- secreted intermittently 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**. (#438: FSH is also affected by GnRH but LH response is more rapid & in higher amount Which is why GnRH is sometimes called LH-releasing factor).

Regulation of Testosterone production by LH

(see the picture of testosterone regulation in next slide).

- **Testosterone** is secreted by leydig cells, in the interstitium of the testis, by **LH** stimulation from the AP and
- Its release is directly proportional to the amount of **LH**.
- Mature leydig cells are found in a child's testis few weeks after birth & then disappear until puberty when it appear again.

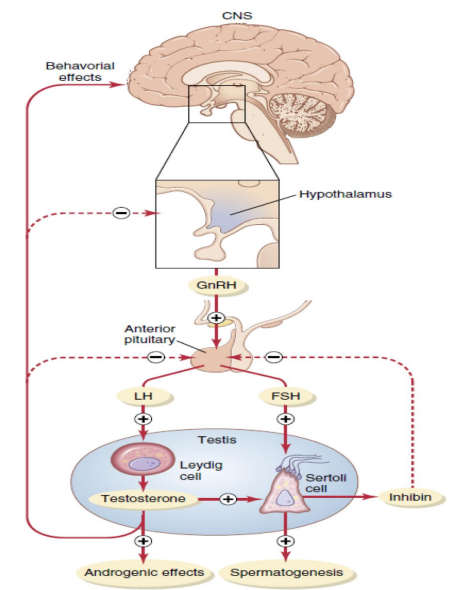
Negative feedback control of testosterone:

LH stimulate **Testosterone** secretion by the testis.

Testosterone inhibit the secretion of **LH**.

Most of the inhibitory effect result from direct inhibition of **GnRH** release from the hypothalamus.

Inhibition of **GnRH** leads to decrease secretion of both **LH** & **FSH**.

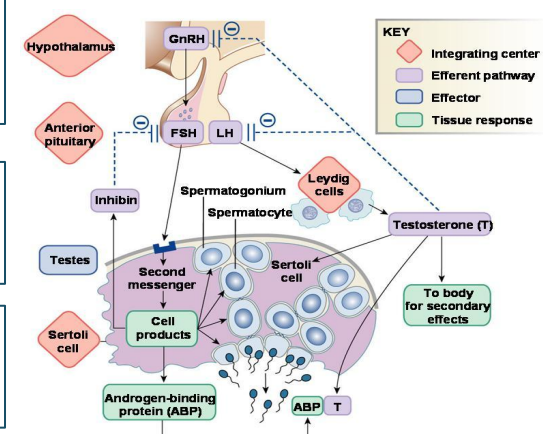


Regulation of spermatogenesis by FSH and testosterone

FSH binds with specific FSH receptors on Sertoli cell (gets activated after puberty by FSH and controls spermatogenesis by releasing inhibin in order to inhibit FSH) in the seminiferous tubules, which causes these cells to grow & secrete spermatogenic substances.

Testosterone & dihydrotestosterone (metabolite of testosterone) diffuse into the seminiferous tubules from Leydig cells which affect spermatogenesis. (concentration of testosterone inside the seminiferous tubule is 100x more than the blood)

Therefore, both **FSH** & **testosterone** are necessary to initiate spermatogenesis.



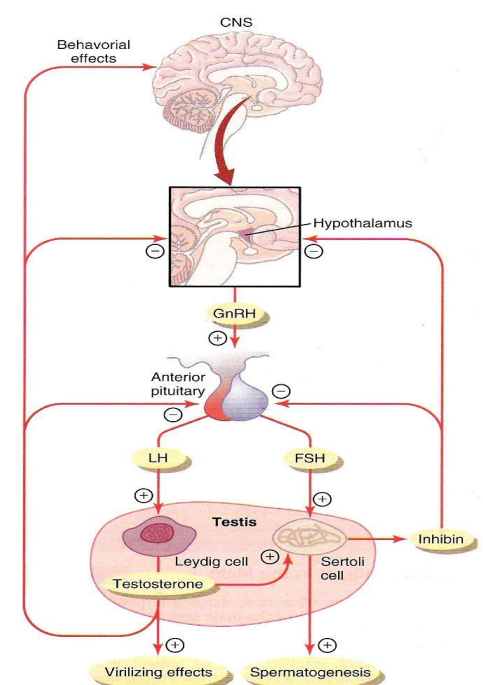
Negative feedback control of seminiferous tubule activity Role of the hormone inhibin:

When the seminiferous tubules fail to produce sperm, the secretion of **FSH** from the AP increases.

Conversely, when spermatogenesis proceeds rapidly pituitary secretion of **FSH** diminishes.

This is due to the secretion of inhibin hormone from the sertoli cells which strongly inhibit the AP- **FSH**

Inhibin has slight inhibitory effect on the hypothalamus to inhibit **GnRH** secretion.



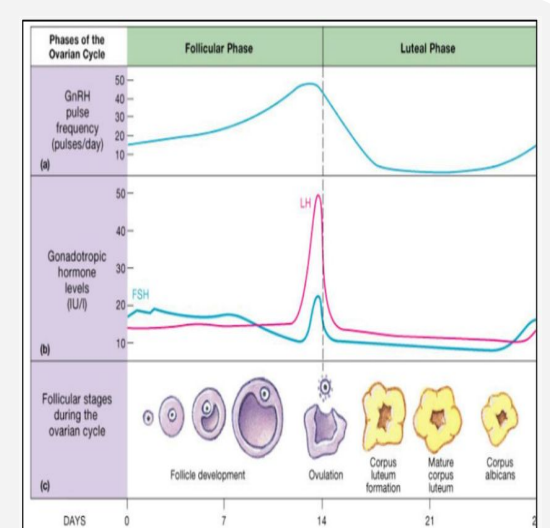
Regulation of the female monthly rhythm Interplay between the ovarian and hypothalamic-pituitary hormones:

Interplay between the ovarian and hypothalamic-pituitary hormones:

- ❖ Secretion of AP hormone is controlled by the hypothalamic GNRH.
- ❖ GNRH released from the arcuate nucleus of the mediobasal hypothalamus that regulate most of the female sexual activity.
- ❖ Intermittent, pulsatile secretion of GNRH by the hypothalamus stimulates intermittent pulsatile release of LH from the AP.

GNRH is secreted in pulses lasting 5 to 25 minutes every 1 to 2 hrs.

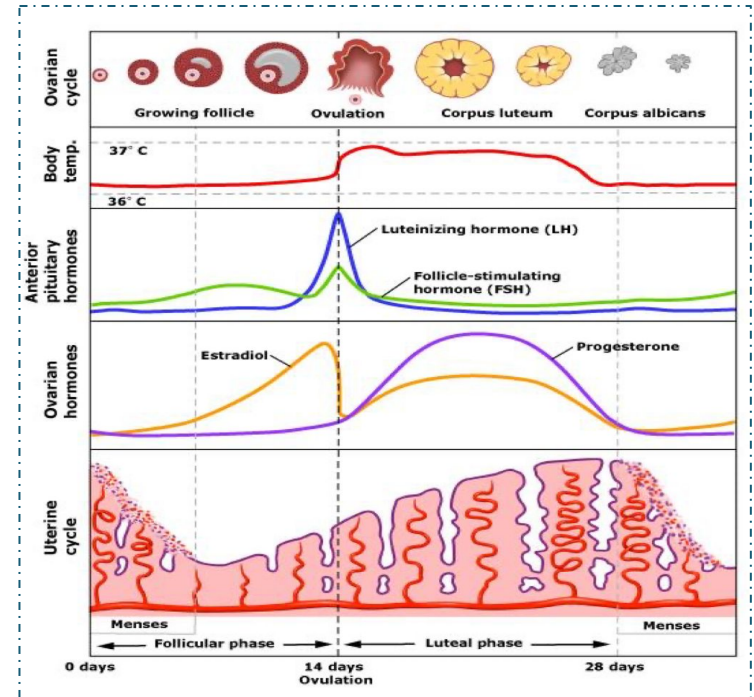
The intermittent pulsatile release of GnRH causes intermittent pulsatile release of LH secretion about every 90 minutes.



Follicular (preovulatory) Phase of the Menstrual Cycle

After menstruation the level of FSH & LH increases

- ❖ Mainly FSH accelerates growth of few follicles (6-12 follicles).
- ❖ The growing follicle secretes increasing amounts of estrogen.
- ❖ **2-3 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 also slightly increased.
- ❖ These hormones causes growth of a new follicle.
- ❖ During the first 11 to 12 days of the follicular growth the rate of secretion of FSH & LH decrease due to the negative feedback effect of estrogen on the AP.



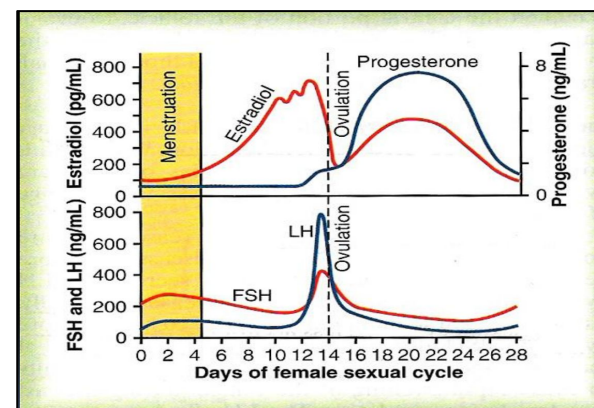
Positive Feedback Effect of Estrogen Before Ovulation – The Preovulatory LH Surge

- ❖ AP secretes increased amount of LH for 1-2 days (at about the 12th day of the cycle) before ovulation.
- ❖ FSH surge is much smaller than LH surge.

❖ The possible causes of LH secretion could be: *Not a place of question*

1 Estrogen has special positive feedback effect of stimulating pituitary secretion of **LH** & to a lesser extent **FSH**.

2 The granulosa cells of the follicle begin to secrete small increasing amount of progesterone about **1 day** before ovulation which stimulate **LH** secretion.



FSH is secreted greater than LH because it is responsible for the follicular growth however, LH is responsible for menstruation.

Postovulatory (after ovulation) Secretion of The Ovarian Hormones And Depression of The Pituitary Gonadotropins

During the postovulatory phase 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)

Negative Feedback Effects of Estrogen and Progesterone

- ❖ 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.

These inhibitory effects are acting more on the AP directly & to lesser extent on the hypothalamus to inhibit the secretion of **GnRH**.

Negative Feedback Effects of Inhibin

- ❖ The hormone **inhibin** secreted by the granulosa cells of the ovarian corpus luteum.

It inhibits the secretion of **FSH** & to lesser extent **LH**.

MCQ & SAQ:

Q1: GnRH is secreted from which of the following nuclei?

- A. Arcuate nuclei
- B. Kisspeptin nuclei
- C. Supra-optic nuclei
- D. IDK

Q3: Which of the following hormones related to the HPG axis in males:

- A. LH
- B. FSH
- C. Estrogen
- D. Cortisol

Q5: During the postovulatory phase the corpus luteum secrete large quantities of:

- A. Progesterone
- B. Estrogen
- C. Inhibin
- D. All of them

Q2: Which of the following is true about Kisspeptin hypothalamic neurons:

- A. Inhibited by low levels of Testosterone
- B. Mutation could lead to Hypogonadism
- C. Inhibited by low levels of Estrogen
- D. Mutation could lead to Hypergonadism

Q4: After menstruation the level of FSH & LH will:

- A. Increase
- B. Decrease
- C. Not Changed
- D. Both A & B

Q6: Estrogen in small amounts has strong effect to inhibit:

- A. FSH
- B. LH
- C. Both
- D. None

6: C
5: D
4: A
3: A
2: B
1: A
key:
answer

1- Explain the regulation between the ovarian and hypothalamic-pituitary hormones:

2- Mention the site of secretion and the function of Inhibin hormone:

A1: Slide 4

A2:

- ❖ The hormone **inhibin** secreted by the granulosa cells of the ovarian corpus luteum.
- ❖ It inhibits the secretion of **FSH** & to lesser extent **LH**.

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