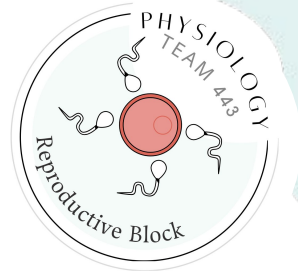


L1-Hypothalamic Pituitary Gonadal Axis

Reproductive physiology



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.

Keywords: **Hypophysiotropic, gonadotropic Hormones, GnRH, FSH, LH, androgens, estrogens**



[Click here](#) for the team channel!



This Lecture was presented by:
Dr.Khalid Alregaiey &Dr.Laila Al Dokhi.



[Editing File](#)

﴿وَلَقَدْ خَلَقْنَا الْإِنْسَانَ وَنَعَلَهُ مَا تَوَسَّوَسُ بِهِ نَفْسَهُ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ (16)﴾

يخبر تعالى، أنه المتفرد بخلق جنس الإنسان، ذكورهم وإناثهم، وأنه يعلم أحواله، وما يسره، ويوسوس في صدره وأنه أقرب إليه من حبل الوريد، الذي هو أقرب شيء إلى الإنسان، وهو العرق المكتنف لشغرة النحر، وهذا مما يدعو الإنسان إلى مراقبة خالقه، المطلع على ضميره وباطنه، القريب منه في جميع أحواله، فيستحي منه أن يراه، حيث نهاه، أو يفقده، حيث أمره، وكذلك ينبغي له أن يجعل الملائكة الكرام الكاتبين منه على بال، فيجلهم ويقرهم، ويحذر أن يفعل أو يقول ما يكتب عنه، مما لا يرضى رب العالمين.

[تيسير الكريم الرحمن، السعدي]

Introduction

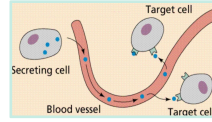
Female slides

What is a hormone? Definition of Hormone?

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.

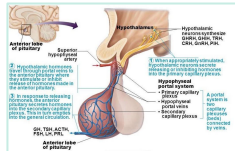
Second definition provided by dr:

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 (Connection between Hypothalamus and anterior pituitary) gland hypothalamic-hypophyseal portal vessels, which travel through portal veins to act on specific receptors on different pituitary cells to secrete their respective hormones.



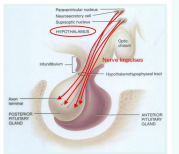
What are the hormones secreted by anterior pituitary?

Six hormones are secreted by the anterior pituitary:

1. Adrenocorticotropic hormone (corticotropin, ACTH)
2. Thyroid-stimulating hormone (thyrotropin, TSH)
3. Growth hormone (GH)
4. Follicle-stimulating hormone (FSH)
5. Luteinizing hormone (LH)
6. Prolactin (PRL)

How hypothalamus controls posterior pituitary? (Connection between the hypothalamus and Posterior pituitary gland):

Hypothalamohypophyseal 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

Male slides



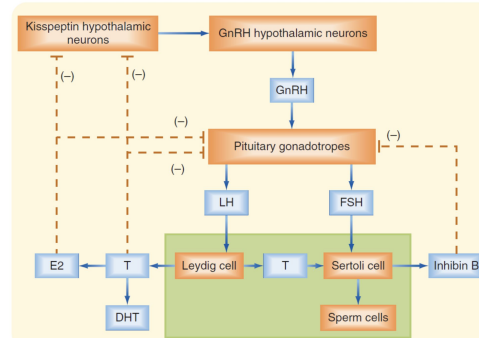
Hypothalamus: Gonadotropin releasing H (GnRH)



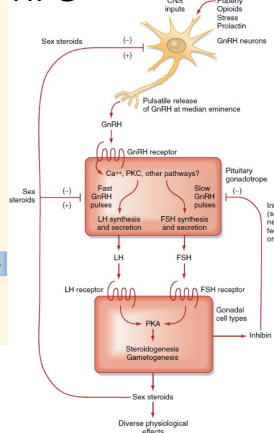
Anterior Pituitary: Luteinizing Hormone (LH) and Follicle stimulating H (FSH)



Ovary: Estrogen, progesterone, Inhibin
Testis: testosterone



HPG



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 :

- 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).

Testosterone

Regulation of Testosterone production by LH

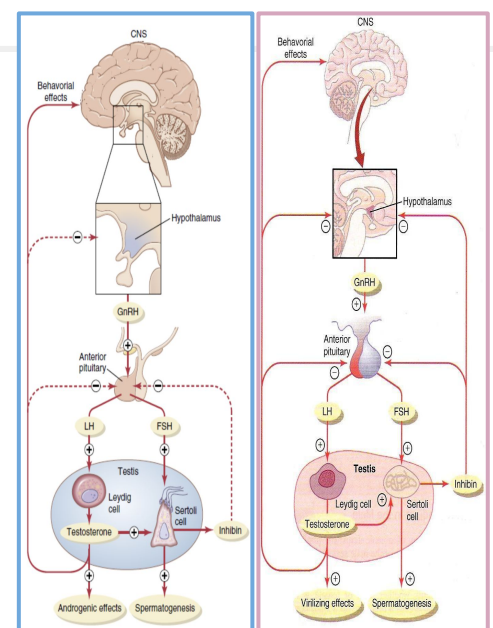
- ▶ Testosterone is secreted by leydig cells, in the interstitium of the testis, by LH stimulation from the AP, and Its release is directly proportional to the amount of LH.
- ▶ **Mature leydig cells are found in a child's testis few weeks after birth & then disappear until puberty when it appear again.**

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. **It's indirect due to the presence of kisseptin**

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



هذه هي الصورة التي يقابلون e14

Testosterone

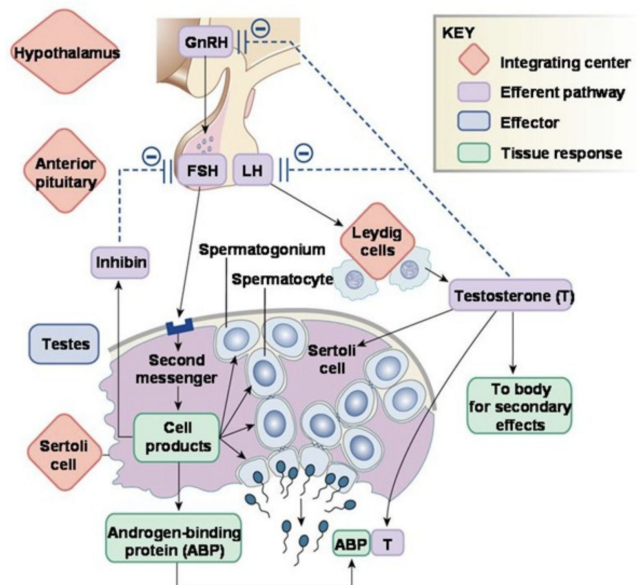
Negative feedback control of testosterone:

Regulation of spermatogenesis by FSH and testosterone

FSH binds with specific FSH receptors **attached to/on Sertoli cell** in the seminiferous tubules, which causes these cells to grow & secrete spermatogenic substances.

Also Testosterone & dihydrotestosterone (metabolite of testosterone) diffuse into the seminiferous tubules from Leydig cells which affect spermatogenesis.

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



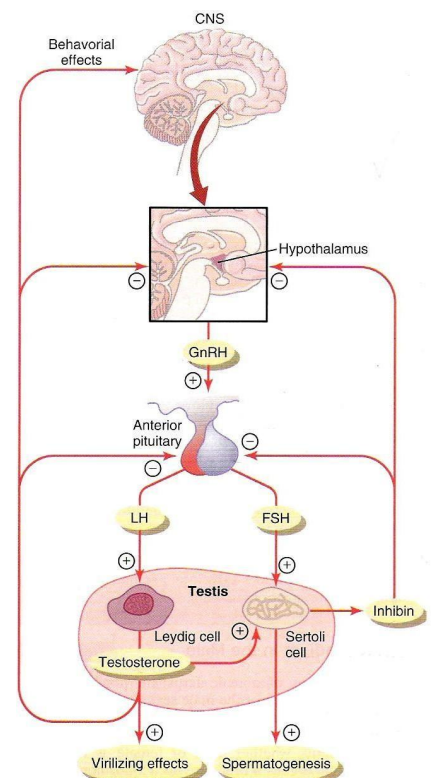
Negative feedback control of seminiferous tubule activity Role of the hormone inhibin:

» 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.



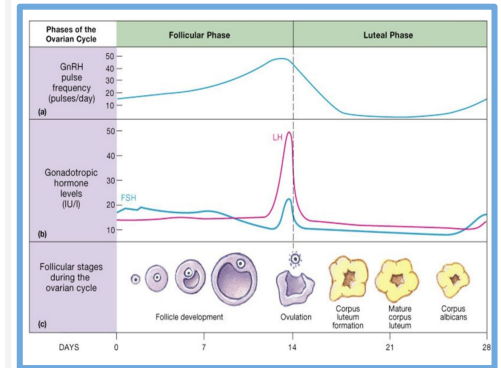
When the seminiferous tubules fail to produce sperm, secretion of FSH by the anterior pituitary gland increases markedly. Conversely, when spermatogenesis proceeds too rapidly, pituitary secretion of FSH diminishes. The cause of this negative feedback effect on the anterior pituitary is believed to be secretion by the Sertoli cells of still another hormone called **inhibin** (see Figure →). This hormone has a strong direct effect on the anterior pituitary gland to inhibit FSH 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 (releasing Hormones.) the hypothalamic GnRH.
- ✧ The neural activity that causes release of GnRH occurs in the (mediobasal hypothalamus), in the arcuate nuclei which regulate most of the female sexual activity.
- ✧ GnRH is secreted in pulses lasting 5 to 25 minutes every 1 to 2 hrs.
- ✧ The pulsatile release of GnRH causes intermittent output of LH secretion about every 90 minutes.



Follicular (preovulatory) Phase of the Menstrual Cycle



From female slides

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.

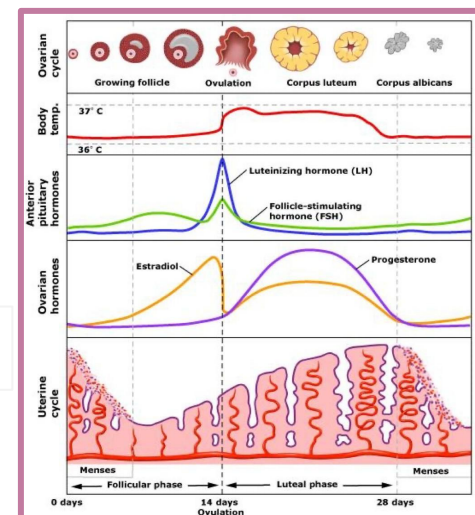
2-3 days before menstruation, **corpus luteum regress** & secretion of **estrogen, progesterone & inhibin decrease**.

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 → LH is highest during ovulation phase.
- ◆ FSH surge is much smaller in the pre-ovulatory than LH surge.
- ◆ This is mediated by kisspeptin neurons in the AVPV.

The possible causes of LH secretion could be:

1

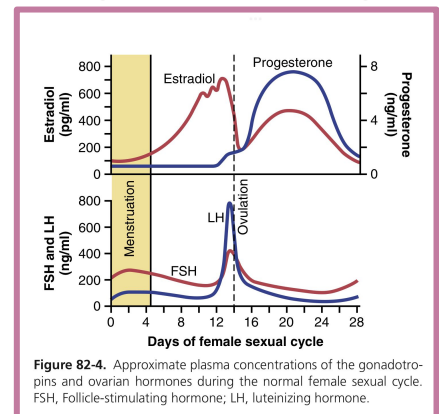
Estrogen has special **positive feedback** effect of stimulating pituitary secretion of LH & to a lesser extent FSH.

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.

يتشوفون القراف هذا مرة ثانية ويتفصيل أكثر



Feedback oscillation of the hypothalamic -pituitary-ovarian system: Postovulatory (after ovulation) Secretion of The Ovarian Hormones And Depression of The Pituitary Gonadotropins/**Negative feedback**

- ◆ During the postovulatory (**luteal**) phase, the corpus luteum secrete large quantities of both progesterone (highest), 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

Negative Feedback Effects of Estrogen and Progesterone

- ➡ Estrogen in **small** amounts has strong effect to **inhibit** the production of LH & FSH. (**kisspeptin mediated in the arcuate nucleus**)
- ➡ This inhibitory effect of estrogen is increased when progesterone is available.
- ➡ This inhibitory affects more on the **AP directly** & to **lesser** extent on the **hypothalamus** to inhibit the secretion of **GnRH**.

Inhibin from the corpus luteum inhibits FSH secretion

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

Spermatogenesis is regulated by a negative feedback control system in which follicle-stimulating hormone (FSH) stimulates the steps in sperm cell formation. What is the negative feedback signal associated with sperm cell production that inhibits pituitary formation of FSH?

Testosterone	Inhibin	Estrogen	Luteinizing hormone
--------------	---------	----------	---------------------

When do progesterone levels rise to their highest point during the female hormonal cycle?

Between ovulation and the beginning of menstruation	Immediately before ovulation	When the blood concentration of luteinizing hormone is at its highest point	When 12 primary follicles are developing to the antral stage
---	------------------------------	---	--

A 20-year-old woman is not having menstrual cycles. Her plasma progesterone concentration is found to be minimal. What is the explanation for the low level of progesterone?

قد يحتاج معلومات من محاضرات قادمة ولكن يعتبر جيد حله قبل دراسة المحاضرات

LH secretion rate is elevated	LH secretion rate is suppressed	FSH secretion rate is suppressed	No corpus luteum is present
-------------------------------	---------------------------------	----------------------------------	-----------------------------

During the first few years after menopause, follicle-stimulating hormone (FSH) levels are normally extremely high. A 56-year-old woman completed menopause 3 years ago. However, she is found to have low levels of FSH in her blood. Which of the following is the best explanation for this finding?

She has been receiving hormone replacement therapy with estrogen and progesterone since she completed menopause	Her adrenal glands continue to produce estrogen	Her ovaries continue to secrete estrogen	She took birth control pills for 20 years before menopause
---	---	--	--

Want Explanation 🤔? [Your Finger HERE!](#)

Leaders

Rafan Alhazzani

Fahad Almughaiseeb



Rate this Lecture [HERE!](#)