REBRODUCTIVE BLOCK

Physiology Team

LECTURE 1

Hypothalamic and Pituitary Gonadal Axis

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Believe you can & you're halfway there !
Theodore Roosevelt

OBJECTIVES

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By the end of this lecture, you should be able to:

- **Define** hormones.
- **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.

MIND MAP

The HPG Axis: Hormones of Male Reproduction

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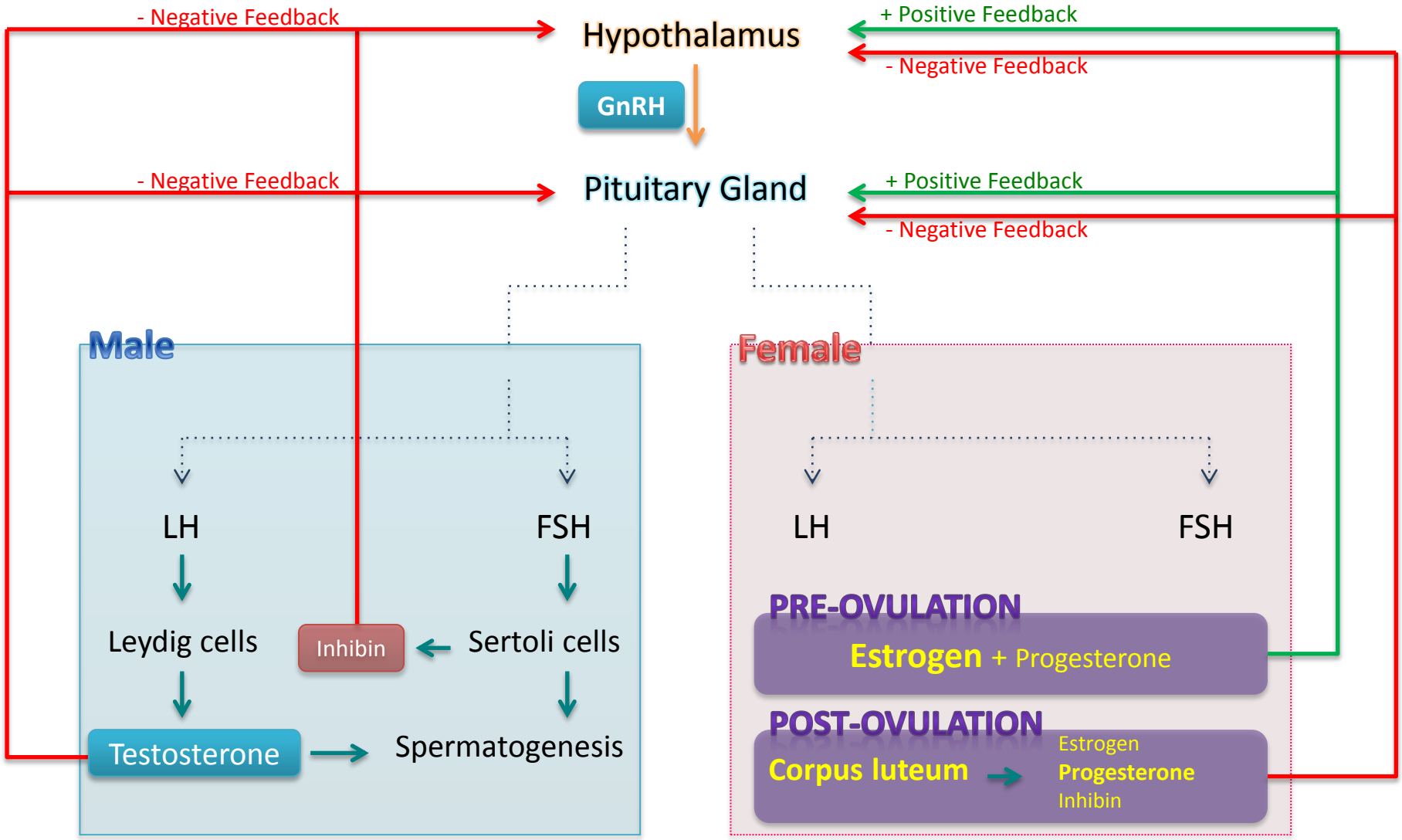

SLIDES | IMPORTANT | FEMALES' NOTES | EXPLANATION | MALES' NOTES

Hormones

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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 & pituitary gland via:

With posterior pituitary gland	With anterior pituitary gland
• Hypothalamohypophysial tract . • supraoptic and paraventricular nuclei. (**neural connection**)	• Hypothalamic hypophysial portal vessels . (**Vascular connection**)

The anterior pituitary secretes six hormones:

- Adrenocorticotropic hormone (corticotrophin, **ACTH**).
- Thyroid-stimulating hormone (thyrotropin, **TSH**).
- Growth hormone (**GH**).
- Follicle-stimulating hormone (**FSH**).
- Luteinizing hormone (**LH**).
- Prolactin (**PRL**).

Control of male sexual functions

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

- GnRH (Gonadotropin releasing hormone) 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).

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- GnRH is secrete intermittently for few minutes every 1 to 3 hrs. **The secretion of LH** by the anterior pituitary is **also cyclical flowing the pulsatile release of GnRH.**

Testosterone

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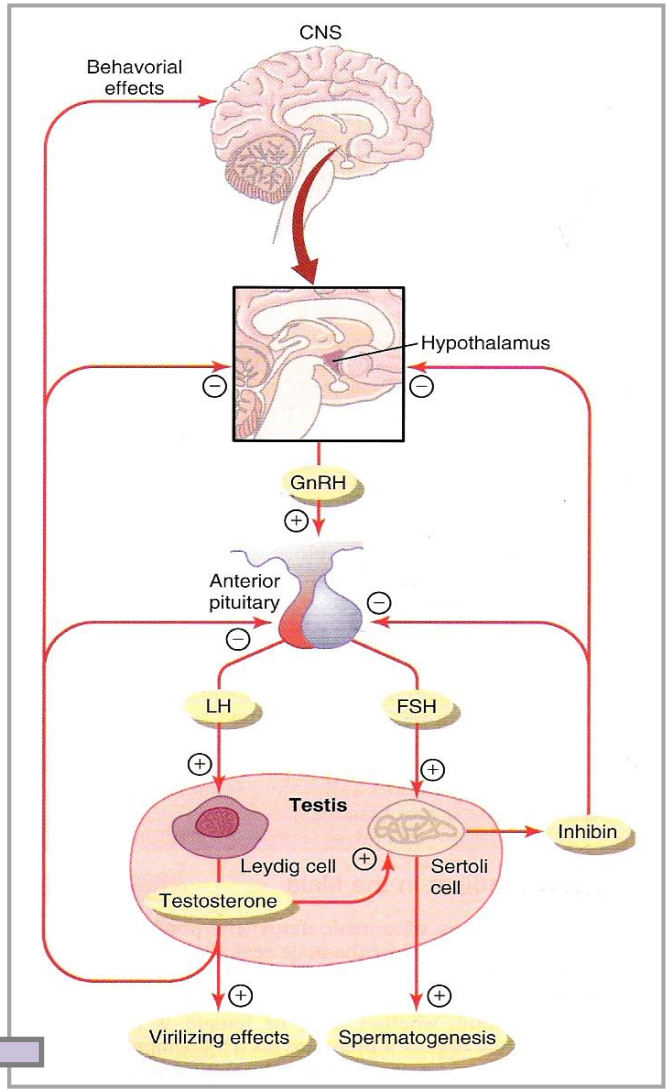
Testosterone regulation of its production by LH:

- 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 infants testis , few weeks after birth & then disappear (in childhood) until puberty when it appear again.

Inhibition of anterior pituitary secretion of LH & FSH by testosterone-negative feedback control of testosterone secretion:

- Testosterone secreted by the testis in response to LH stimulation and has reciprocal effect of inhibiting the AP secretion of LH.
- **Most** of the inhibitory effect result from a direct effect of testosterone in the hypothalamus to decrease secretion of GnRH which causes decrease secretion of **both** LH & FSH.

Testosterone secreted by the testis in response to LH stimulation , but when it exceeds certain limit the testosterone will cause negative feedback on both AP an hypothalamus but mostly on the hypothalamus



Regulation of spermatogenesis by FSH and testosterone:

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

Remember:
LH > **L**eydig cell
F**S**H > **S**ertoli cell

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

- When the seminiferous tubules fail to produce sperm 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 and **slight** inhibitory effect on the hypothalamus to inhibit GnRH secretion.

So ,we have 2 pathways for the negative feedback:
1- Through **testosterone** which inhibit the secretion of GnRH & **LH** (mainly acts on the hypothalamus).
2- Through **inhibin** hormone from sertoli cells which inhibit the secretion of the **FSH** and GnRH (mainly acts on the AP).

Female monthly rhythm

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

- Secretion of AP hormone is controlled by "releasing hormones" formed in the hypothalamus and transported to the AP gland by the hypothalamic-hypophysial portal system.
- 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 min.

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.

Ovulation

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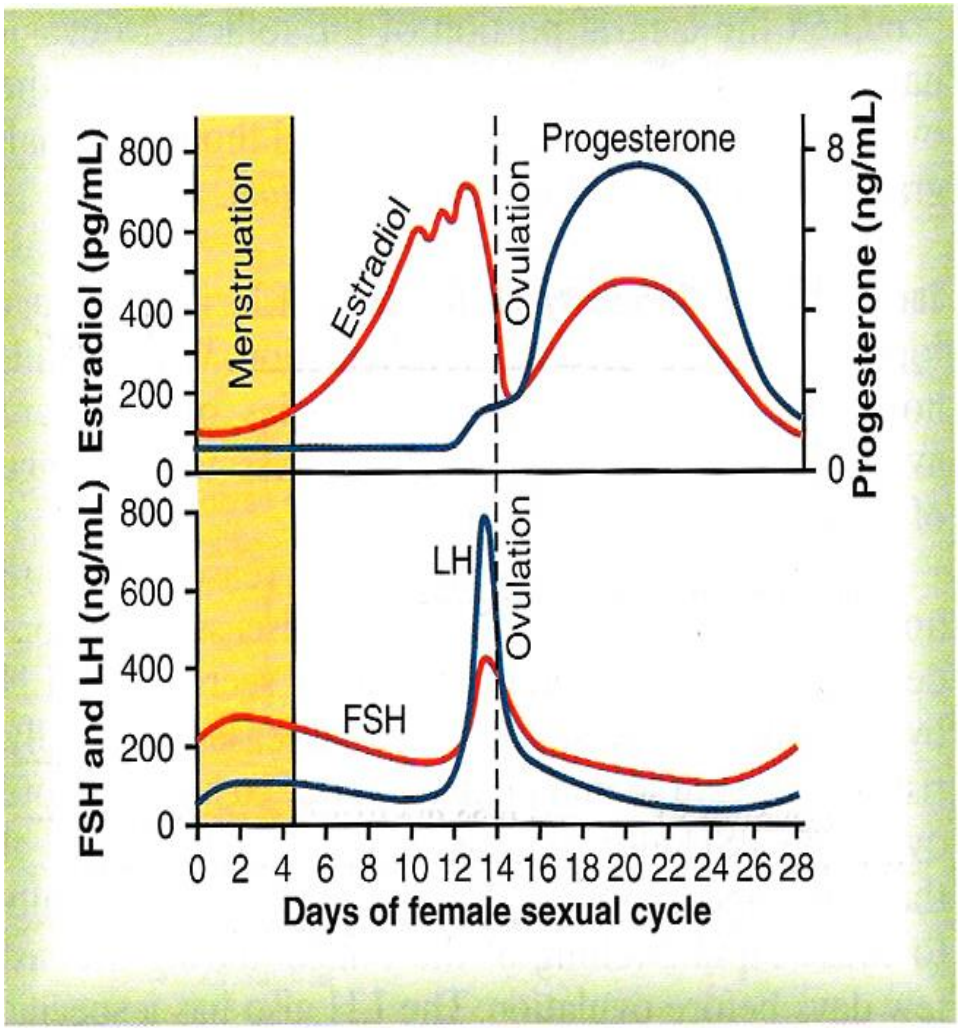
In the first half (pre-ovulation):"positive feedback"

- The predominant is the **estrogen** which will cause the **LH** surge just before the ovulation .
- Also **some progesterone** will be secreted at that time .
- The LH surge is much **higher** than the FSH surge because the effect of the estrogen is stronger on LH than FSH .

In the second half (post-ovulation):"negative feedback"

- The predominant is **progesterone** which secreted from the granulosa cells of the corpus luteum (الجسم الأصفر) .
- The level of the estrogen decreased .
- As a result the levels of the LH & FSH will be deceased .



I advice you to watch this amazing video

Negative Feedback

Important

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Negative feedback effects of estrogen and progesterone in decreasing both LH & 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 effects more on the AP directly & to lesser extent on the hypothalamus to inhibit the secretion of GnRH. (this is the principle of oral contraceptive)

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

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

Female cycle

Important

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

- 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** is higher)

The possible causes of LH secretion could be:

- 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 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)

Female cycle

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Follicular growth phase:

- 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 causes 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.

SUMMARY

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- 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 posterior pituitary gland via Hypothalamohypophysial tract, supraoptic and paraventricular nuclei (neural connection).

- and with anterior pituitary gland via Hypothalamic hypophysial portal vessels (Vascular connection).

- 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).

- GnRH is secrete intermittently for few minutes every 1 to 3 hrs**.** **The secretion of LH** by the anterior pituitary is **also cyclical flowing the pulsatile release of GnRH.**

SUMMARY

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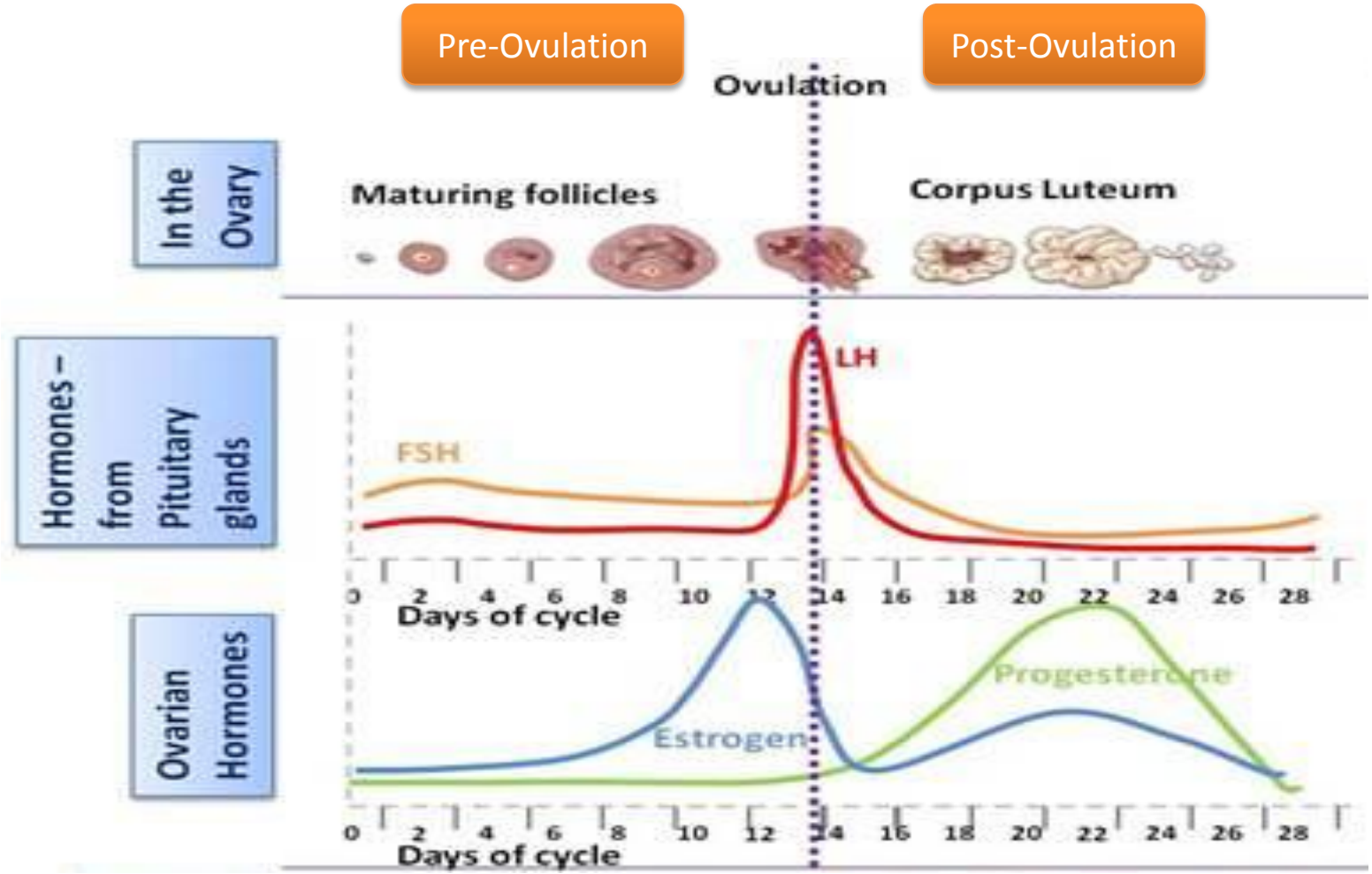
- Testosterone is secreted by leydig cells, in the interstitium of the testis, by LH stimulation.
- Regulation of spermatogenesis by FSH and testosterone.
- FSH binds with specific FSH receptors attached to the sertoli cell in the seminiferous tubule.
- We have 2 pathways for the negative feedback:
  1. Through testosterone which inhibit the secretion of GnRH & LH (mainly acts on the hypothalamus).
  2. Through inhibin hormone from sertoli cells which inhibit the secretion of the FSH and GnRH (mainly acts on the AP)
- Estrogen has positive feedback effect before ovulation.
- During the postovulatory phase 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.


Pre-Ovulation
Post-Ovulation
Ovulation
In the Ovary
Maturing follicles
Corpus Luteum
Hormones – from Pituitary glands
LH
FSH
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days of cycle
Ovarian Hormones
Progesterone
Estrogen
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days of cycle

QUESTIONS

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1. The seminiferous tubules:

A) Are where androgens are produced for the testis.
B) Are where mature sperm are stored.
C) Are the site of the production of sperm.
D) None of the above.

2. The male hormone testesterone is produced by:

A) Leydig cells.
B) Seminiferous tubules.
C) Epididymis.
D) Vas deferens.

3. The process by which the sperms are produced is known as:

A) Ovulation.
B) Spermatogenesis.
C) Oogenesis.
D) Gestation.

4. The hormone secreted by the pituitary to start the ovulation process is:

A) FSH.
B) LH.
C) Estrogen.
D) Progesterone.

5. Progesterone is secreted by:

A) Ovarian follicle.
B) Graffian follicle.
C) Corpus luteum.
D) Corpus albicans.

1	C
2	A
3	B
4	B
5	C

THE END

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If there are any Problems or Suggestions, Feel free to contact us:

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THANK YOU

IF YOU WANT TO SHARE ANY INFORMATION REGARDING PHYSIOLOGY OR ANY OTHER SUBJECT .. YOU CAN MENTION THIS ACCOUNT

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