MEDICINE 438's

ENDOCRINE PHYSIOLOGY

LECTURE II: Hypothalamo-Pituitary Axis and Regulatory Mechanisms

EDITING FILE

IMPORTANT | MALE SLIDES | EXTRA | FEMALE SLIDES | LECTURER'S NOTES

1 HYPOTHALAMO-PITUITARY AXIS AND REGULATORY MECHANISMS

Lecture Two

OBJECTIVES

- Structure of pituitary gland:
  - Anterior pituitary cell types and hormones.
  - Posterior pituitary cell types and hormones.
- Hypothalamic control of pituitary gland:
  - Hypothalamo-hypophysial portal system.
  - Hypothalamo-hypophysial tract.
- Feedback mechanisms:
  - Positive feedback.
  - Negative feedback.

Structure of Pituitary Gland

Pituitary gland is a 1cm gland that weigh 0.5-1g controlled by Hypothalamus and consist of two lobes:

- Anterior (Adenohypophysis) lobe that originates from Rathke's pouch (pharyngeal epithelium).
- Posterior (Neurohypophysis) lobe that originates from hypothalamus (Which explains the presence of glial-type cells).
- Infundibulum.

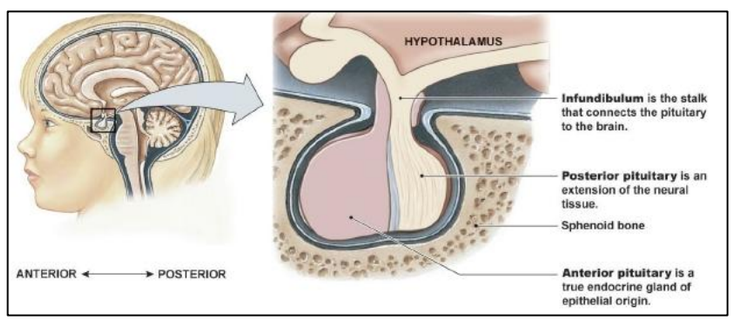

Figure 2-1

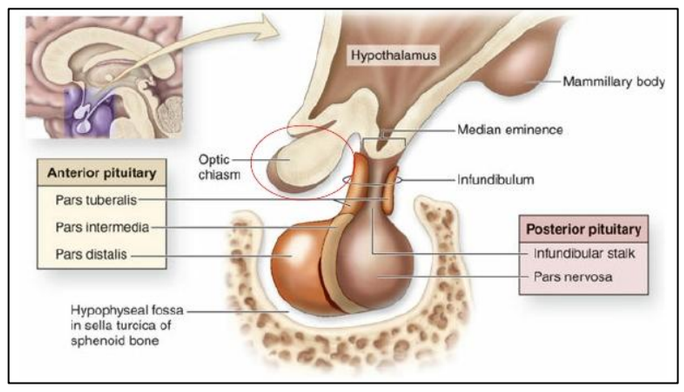

Figure 2-2 shows relation with optic chiasm

Anterior pituitary contains 5 cell types:

- **Somatotrops** produce Growth Hormone (GH) and represent 40% of anterior pituitary lobe cells.
- **Corticotrops** produce Adrenocorticotropic Hormone (ACTH) and represent 20% of anterior pituitary lobe cells.
- **Thyrotropes** produce Thyroid Stimulating Hormone (TSH).
- **Gonadotropes** produce Luteinizing Hormone (LH) & Follicle Stimulating Hormone (FSH).
- **Lactotrops** produce Prolactin (PRL).

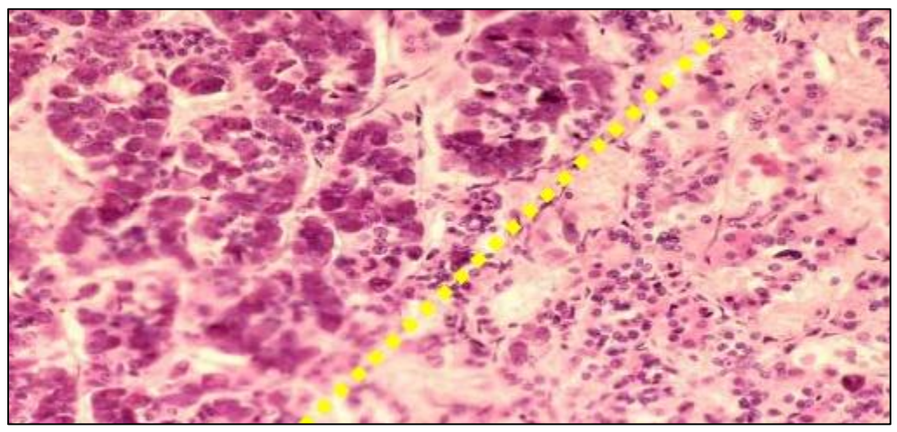

Figure 2-3

Dark Area on the left shows more vascularity (anterior pituitary).

Light area on the right shows less vascularity and have more nerves (posterior pituitary).

Hypothalamic Control of Pituitary Secretions

Almost all secretions by the pituitary are controlled by either:

- Hormonal secretion of hypothalamus (Anterior pituitary).
- Nervous signals from hypothalamus (Posterior pituitary).

Hypothalamic-Pituitary Axis coordinate Thyroid gland, adrenal gland & reproductive gland. It also control growth, milk production and osmoregulation.

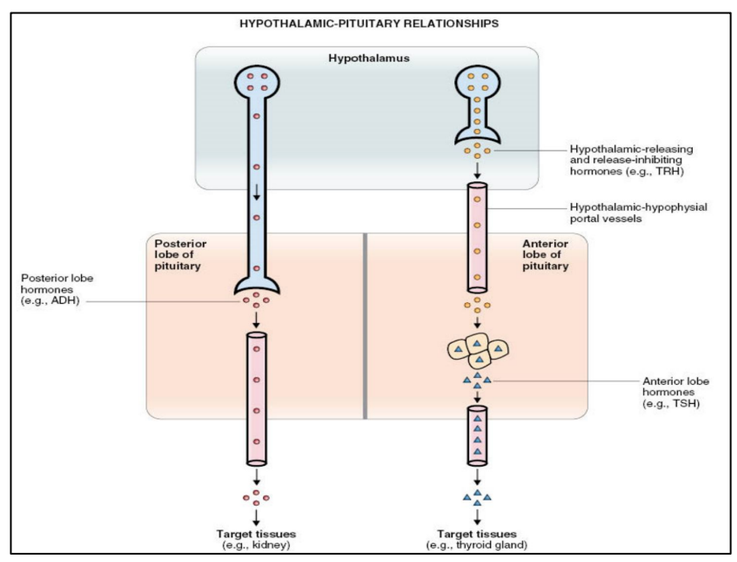

Figure 2-4

Feedback Mechanism

Negative feedback[1]: Release of hormone A stimulates the release of hormone B. Hormone B inhibits the release of hormone A.

Positive feedback[2] : Release of hormone A stimulates the release of hormone B. Hormone B stimulates further release of hormone A.

FOOTNOTES

1. Negative feedback is usually the predominant controlling mechanism, that is, conditions or products resulting from action of hormone on target tissue tend to inhibit further secretion of the hormone to prevent oversecretion. For example, GH causes release of somatomedins from liver that inhibit further release of GH to maintain homeostasis.
2. In few cases, the conditions or products resulting from the action of hormone on target tissues results in further release of hormone, but eventually, all positive feedback reverts to negative feedback to maintain homeostasis, like in Figure 2-16.

2 HYPOTHALAMO-PITUITARY AXIS AND REGULATORY MECHANISMS

Lecture Two

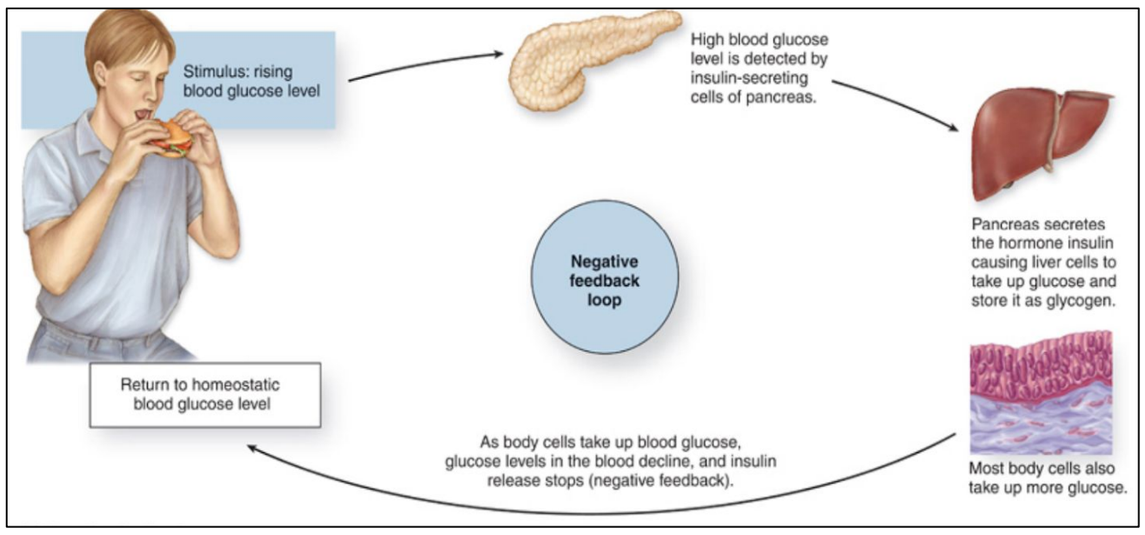

Figure 2-5

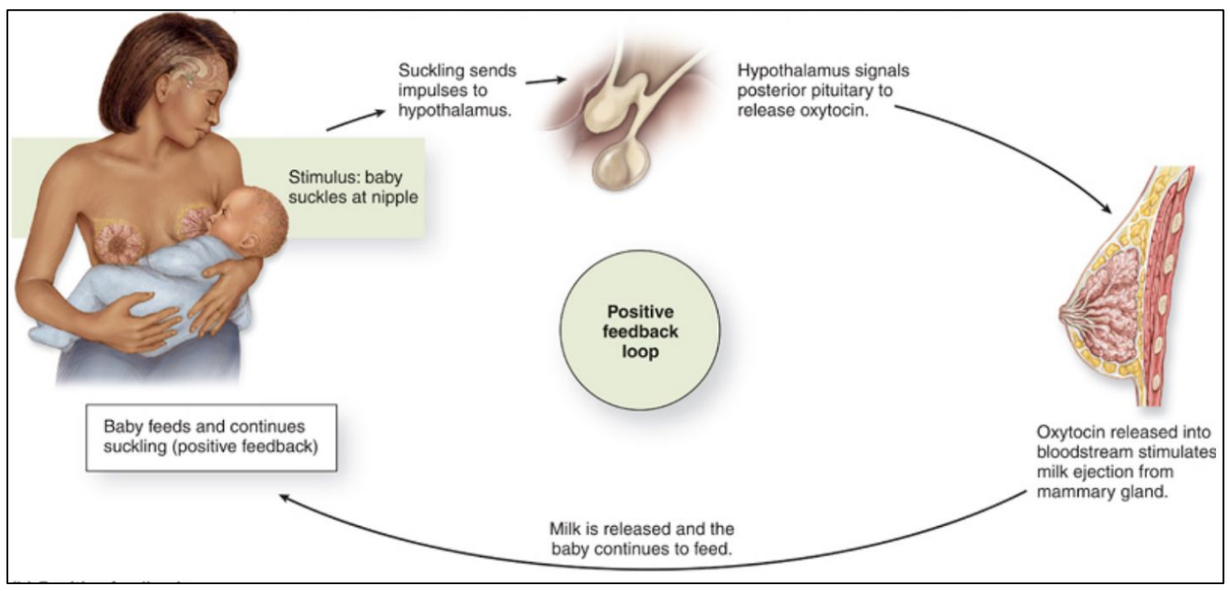

Figure 2-6

Negative Feedback Mechanism (Long And Short Loop Reflexes)

- **Long-loop feedback** means that the hormone feeds back all the way to the hypothalamo-pituitary axis.
- **Short-loop feedback** means that the anterior pituitary hormone feeds back on the hypothalamus to inhibit secretion of hypothalamic-releasing hormone.
- **Ultrashort-loop feedback** in which the hypothalamic hormone inhibits its own secretion.

Note: Feedback is considered a short loop only when hormones of anterior pituitary inhibit the hypothalamus.

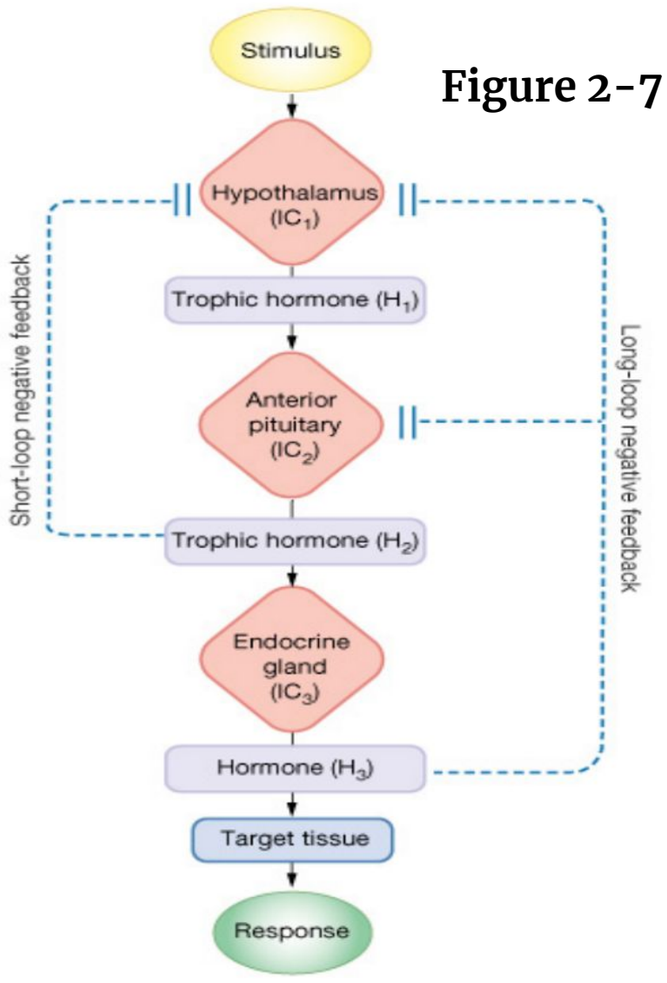

Figure 2-7

Control of Anterior Pituitary (Adenohypophysis) By Hypothalamus

- **Special neurons** in the hypothalamus synthesize and secrete the hypothalamic releasing and inhibitory hormones that control secretion of anterior pituitary.
- Neurons send their nerve fibers to the median eminence (extension of hypothalamic tissue into the pituitary stalk).
- Hormones are secreted to the tissue fluids, absorbed into the Hypothalamic-Hypophysial Portal System and transported to the sinuses of the anterior pituitary.

Anterior pituitary gland is connected to hypothalamus by portal system called (Hypothalamic-Hypophysial Portal Vessels)

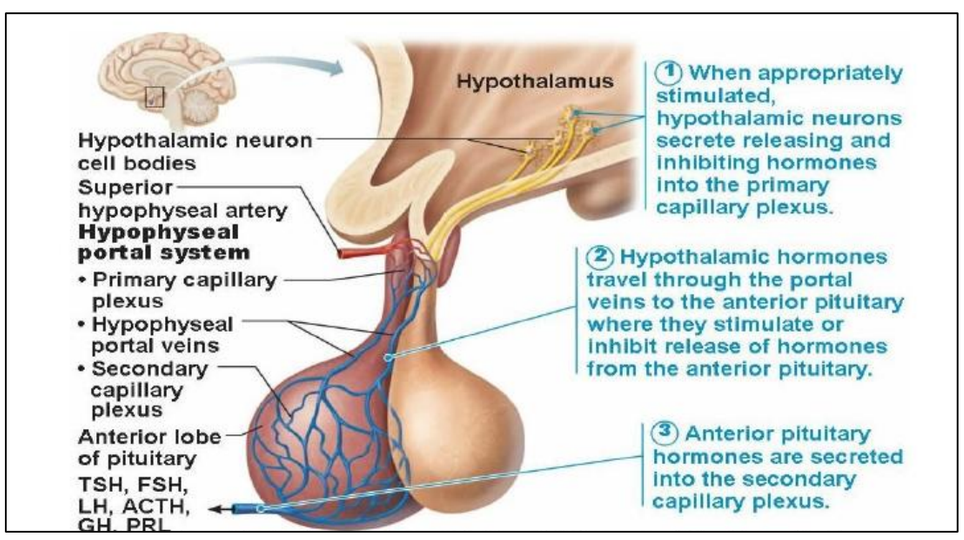

Figure 2-8 4th step is the release to circulation.

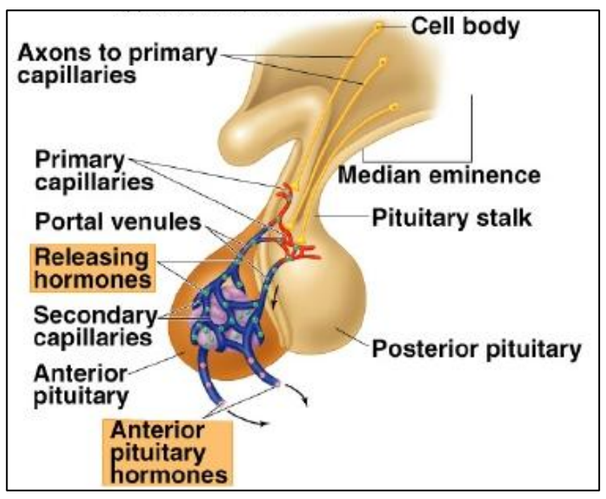

Figure 2-9 What type of secretion is it? neuroendocrine

Hypothalamic Releasing And Inhibiting Hormones

- Growth hormone releasing hormone (GHRH)
- Growth hormone inhibiting hormone (GHIH)
- Thyrotropin-releasing hormone (TRH)
- Corticotropin-releasing hormone (CRH)
- Gonadotropin -releasing hormone (GnRH)
- Prolactin inhibitory hormone (PIH)

- GHRH Stimulates release of **Growth Hormone.**
- GHIH inhibit release of **Growth Hormone.**

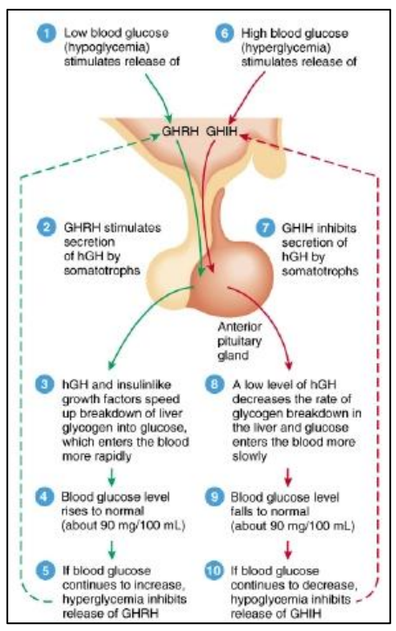

Figure 2-10

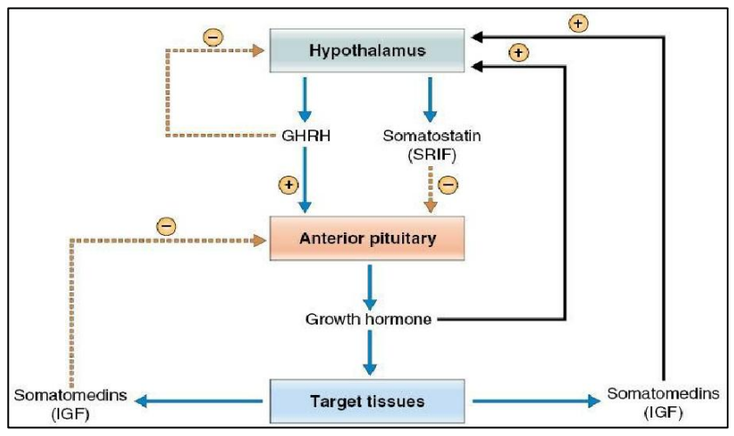

Figure 2-11 Growth hormone secretion is regulated by negative feedback (see Fig 2-7). Three feedback loops including both long and short loops are involved.
(1) GHRH inhibits its own secretion from the hypothalamus via an ultrashort-loop feedback.
(2) Somatomedins, which are byproducts of the growth hormone action on target tissues, inhibit secretion of growth hormone by the anterior pituitary.
(3) Both growth hormone and somatomedins stimulate the secretion of somatostatin by the hypothalamus.
The overall effect of this third loop is inhibitory (i.e., negative feedback) because somatostatin inhibits growth hormone secretion by the anterior pituitary.

Hypothalamic Releasing And Inhibiting Hormones

- Growth hormone releasing hormone (GHRH)
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- Thyrotropin-releasing hormone (TRH)
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- Gonadotropin -releasing hormone (GnRH)
- Prolactin inhibitory hormone (PIH)

- Stimulates release of **Thyroid Stimulating Hormone (TSH)**.

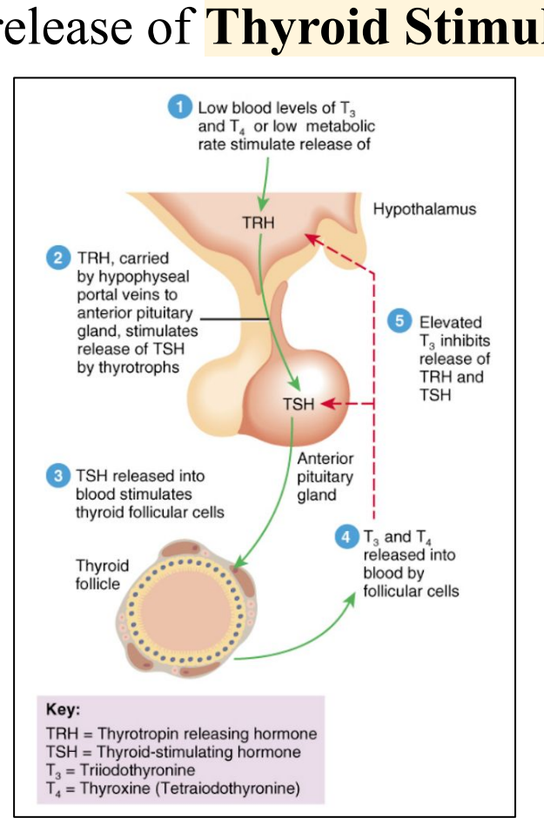

Figure 2-12 T3 is The active form of T4, Thus it mediates the inhibition of TRH & TSH.

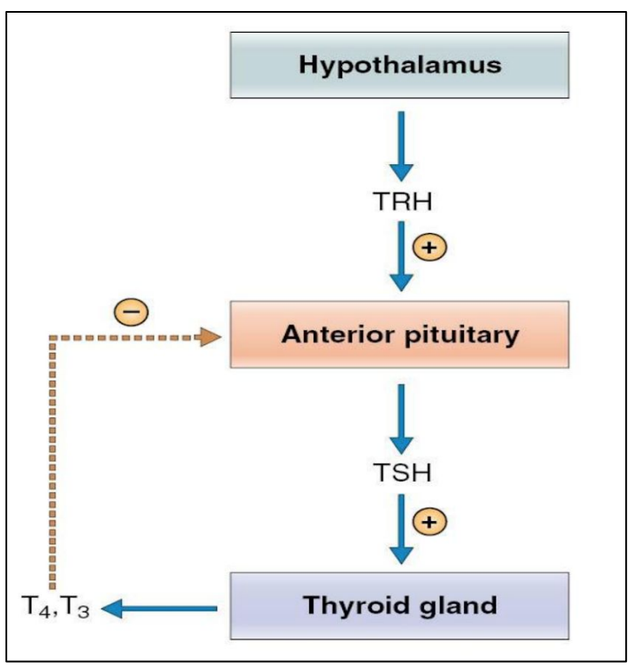

Figure 2-13
TRH is secreted by the hypothalamus and acts on the thyrotrophs of the anterior pituitary to cause secretion of TSH. TSH then acts on the thyroid gland to stimulate the synthesis and secretion of thyroid hormones.
The thyroid hormones secretion will cause a negative feedback on the anterior pituitary to inhibit further secretion of TSH.

4 HYPOTHALAMO-PITUITARY AXIS AND REGULATORY MECHANISMS

Lecture Two

Hypothalamic Releasing And Inhibiting Hormones

- Growth hormone releasing hormone (GHRH)
- Growth hormone inhibiting hormone (GHIH)
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- Corticotropin-releasing hormone (CRH)
- Gonadotropin -releasing hormone (GnRH)
- Prolactin inhibitory hormone (PIH)

➔ Stimulates release of **Adrenocorticotropin Hormone (ACTH)**.

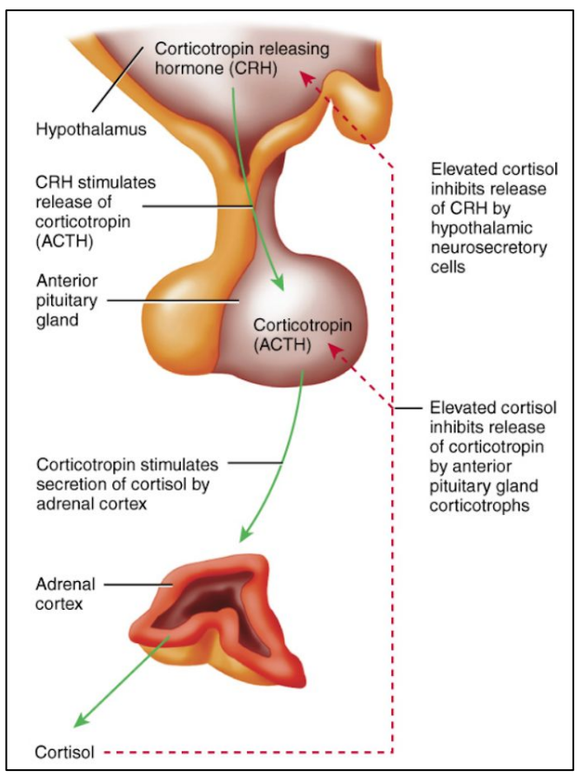

Figure 2-14

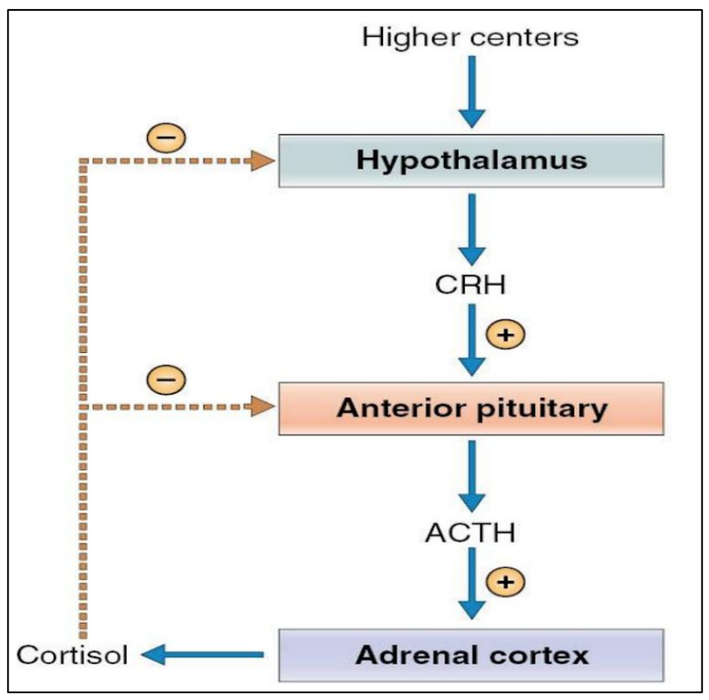

Figure 2-15
CRH is secreted by the hypothalamus and acts on the corticotrophs of the anterior pituitary to cause secretion of ACTH. In turn, ACTH acts on the cells of the adrenal cortex to stimulate the synthesis and secretion of adrenocortical hormones.
It's a long loop negative feedback.

Hypothalamic Releasing And Inhibiting Hormones

- Growth hormone releasing hormone (GHRH)
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- Corticotropin-releasing hormone (CRH)
- Gonadotropin -releasing hormone (GnRH)
- Prolactin inhibitory hormone (PIH)

➔ causes release of two gonadotropic hormones:

★ **Luteinizing (LH)**.

★ **Follicle-stimulating hormone (FSH)**

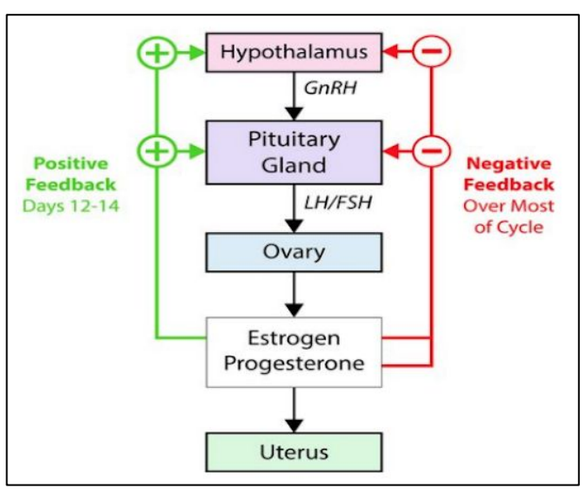

Figure 2-16 why does estrogen at times cause GnRH to be increased in day 12-14 of ovulation as opposed to negative feedback in the remaining days? Simply in these days there is gonna be a higher estrogen concentration which will cause a switch in the feedback mechanism from negative to positive, the reasons for this are not clear.

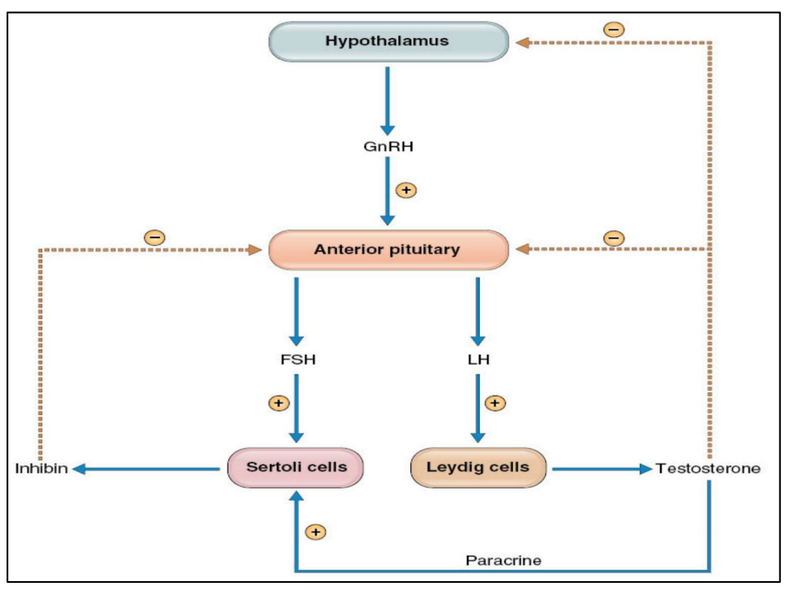

Figure 2-17 Sertoli and leydig are types of cells present in testis

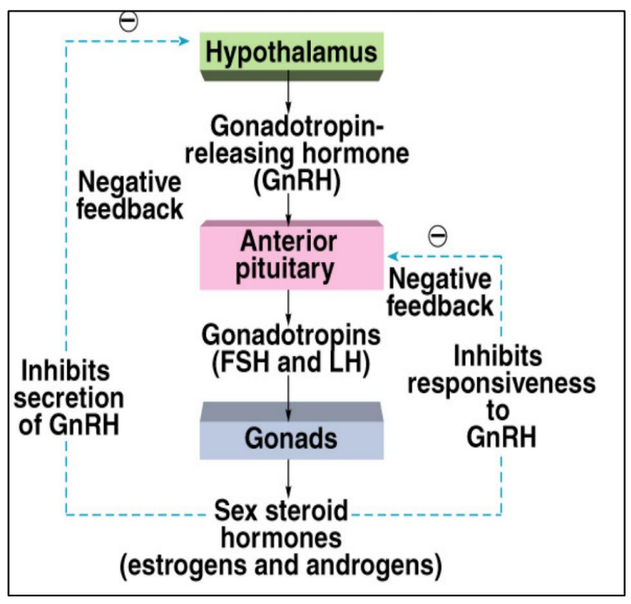

Figure 2-18 Long loop negative feedback mechanism "sex steroids"

Hypothalamic Releasing And Inhibiting Hormones

- Growth hormone releasing hormone (GHRH)
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- Prolactin inhibitory hormone (PIH)

➔ Also called **Dopamine**.

➔ Inhibit secretion of **Prolactin**.

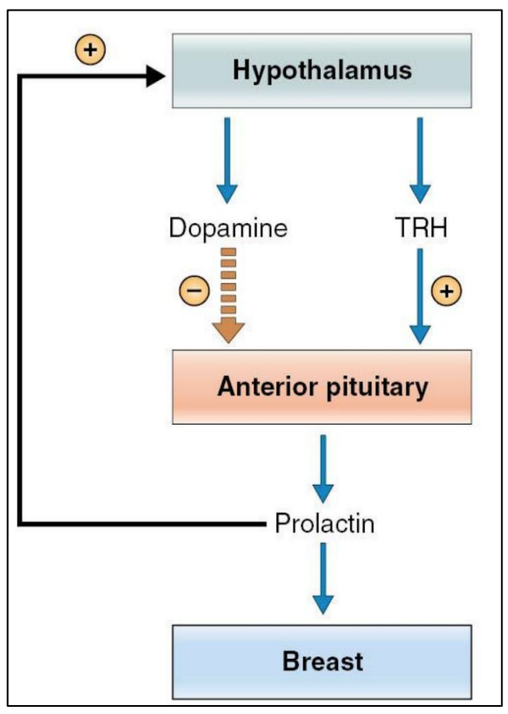

Figure 2-19 There are two regulatory pathways from the hypothalamus, one inhibitory (via dopamine, which acts by decreasing cAMP levels) and the other stimulatory (via TRH). In persons who are not pregnant or lactating, prolactin secretion is tonically inhibited by dopamine (prolactin-inhibiting factor [PIF]) from the hypothalamus. In other words, the inhibitory effect of dopamine dominates and overrides the stimulatory effect of TRH in normal conditions.

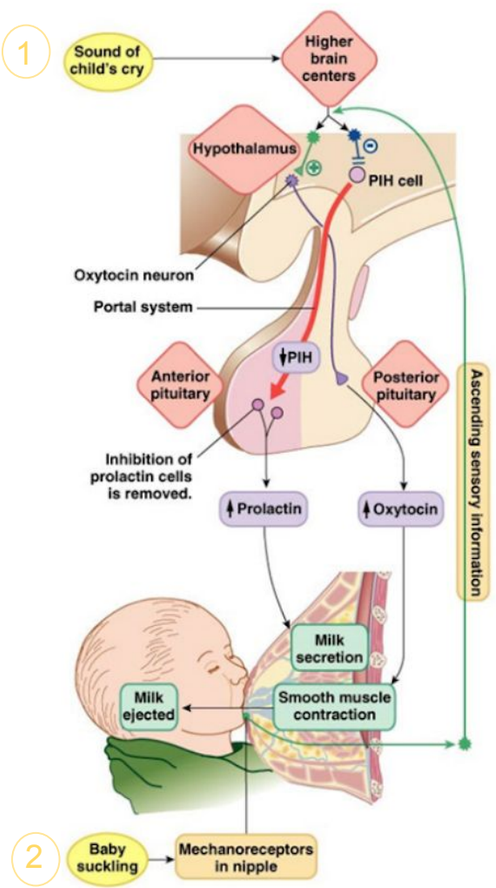

Figure 2-20

Control of Posterior Pituitary (Neurohypophysis) By Hypothalamus

Hormones synthesized in the **supraoptic nuclei (Antidiuretic hormone, ADH)** it synthesizes (1\6 of total oxytocin) and paraventricular secretes (1\6 of ADH) and **paraventricular nuclei** (**Oxytocin)** of the hypothalamus and released in posterior pituitary.

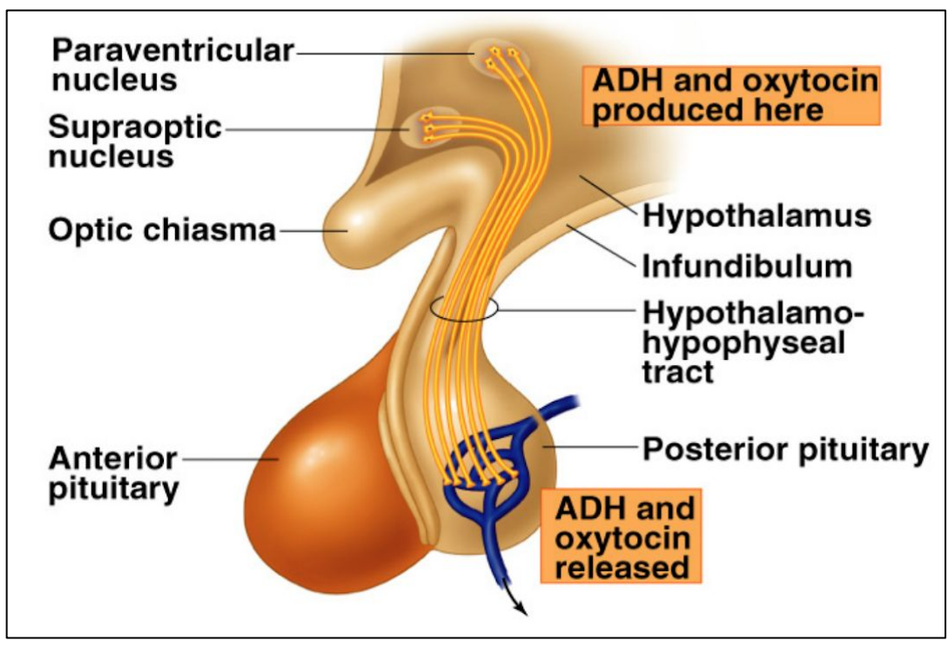

Figure 2-21

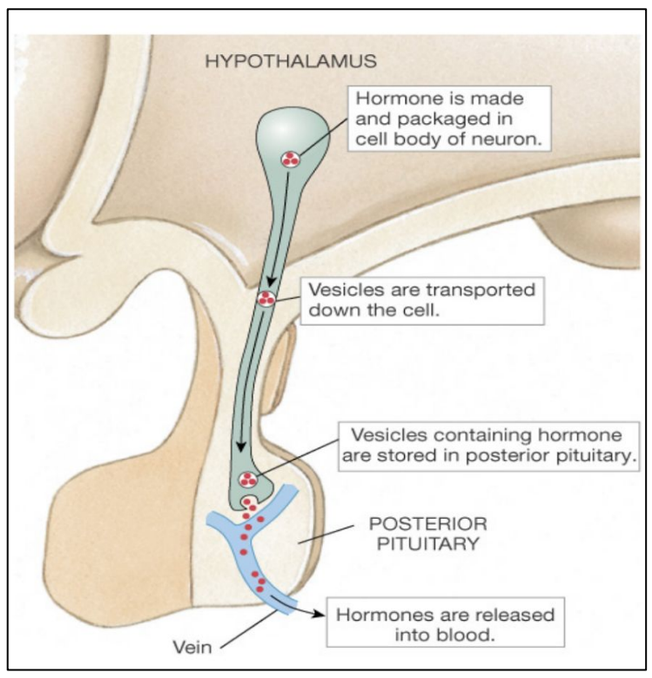

Figure 2-22

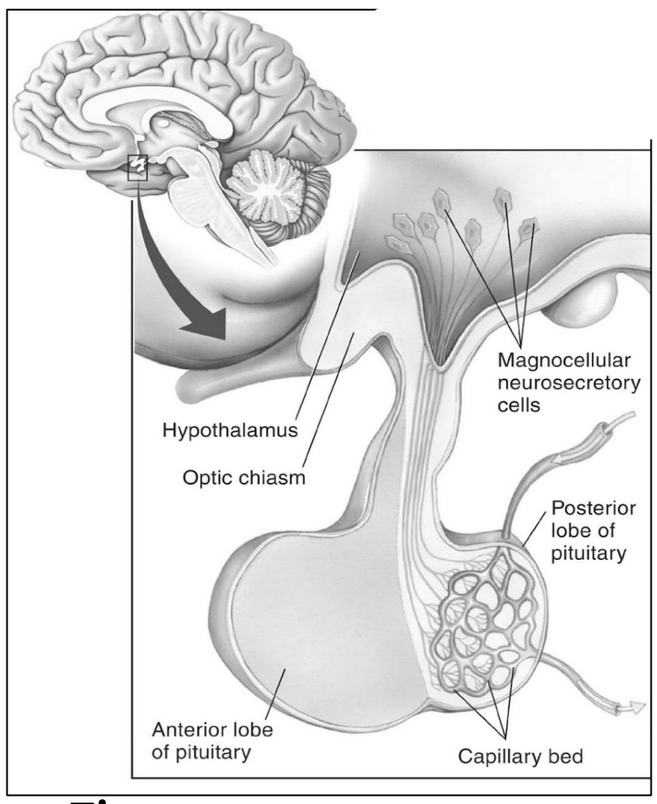

Figure 2-23 Magnocellular neurons in paraventricular and supraoptic nuclei secrete oxytocin and vasopressin directly into capillaries in the posterior lobe.

Clinical Application

- What will happen if pituitary gland is removed from its normal position and transplanted to other part of the body?
- Release of all hormones will stop.
- Release of some hormones will decrease to very low levels.
- Release of some hormones will increase.

Answer: both the 2nd and 3rd answer are correct, Prolactin is the only hormone that will not be inhibited and thus it'll increase.

Summary of Hypothalamic Control of Pituitary Gland

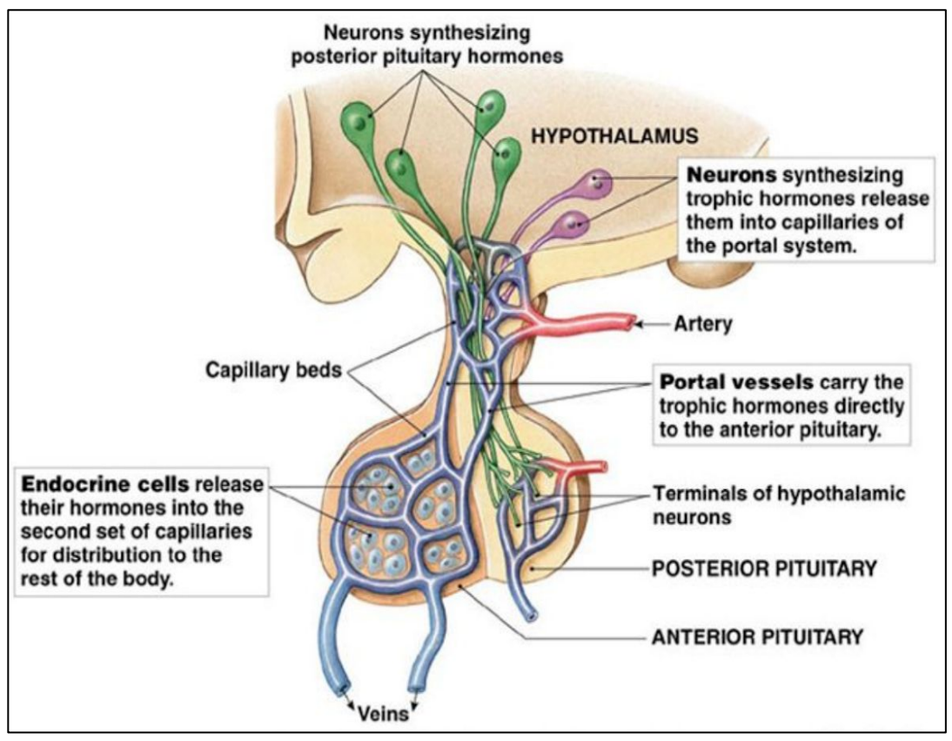

Figure 2-24

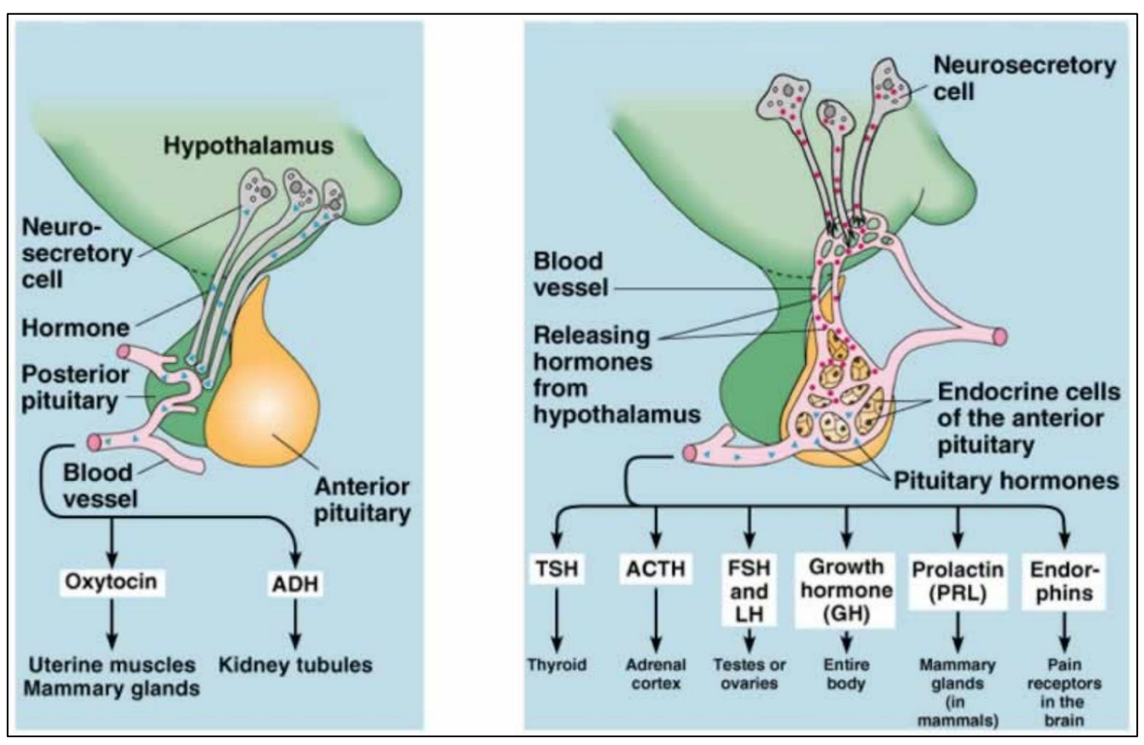

Figure 2-25

Summary of Anterior Pituitary Hormones

Hormone	Target Tissue	Principal Actions	Regulation Of Secretion
ACH (Adrenocorticotropic Hormone)	Adrenal cortex	Stimulate secretion of glucocorticoids	Stimulated by CRH (corticotropin-releasing hormone) Inhibited by glucocorticoids
TSH(thyroid-stimulating Hormone)	Thyroid gland	Stimulate secretion of thyroid hormones	Stimulated by TRH (thyrotropin-releasing hormone) inhibited by thyroid hormone
GH(Growth Hormone)	Most tissues	Promotes protein synthesis and growth , lipolysis and increased blood glucose	Inhibited by somatostatin Stimulated by growth hormone-releasing hormone
FSH(follicle-stimulating Hormone)	Gonads	Promotes gamete production and stimulates estrogen production in females	Stimulated by GnRH(gonadotropin-releasing hormone) inhibited by sex steroids and inhibin
PRL(prolactin)	Mammary glands and other sex accessory organs	Promote milk production in lactating females , additional actions in other organs	Inhibited by PIH(prolactin-inhibiting Hormone)
LH(luteinizing Hormone)	Gonads	Stimulates sex hormone secretion , ovulation and corpus luteum formation in females , stimulation of testosterone secretion in males.	Stimulated by GnRH , Inhibited by sex steroids

QUIZ

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1. Which of the following hormones originates in the anterior pituitary?

A) Growth hormone-releasing hormone.
B) Somatostatin.
C) Oxytocin.
D) Thyroid-stimulating hormone.

2. The two hormones released from the neurohypophysis are actually manufactured in which of the following?

A) Paraventricular and supraoptic nuclei of the hypothalamus.
B) Hypophyseal portal vein.
C) Pars intermedia.
D) Adenophysis.

3. When the anterior pituitary hormone feeds back on the hypothalamus to inhibit secretion of hypothalamic-releasing hormone this called:

A) Positive feedback.
B) Short-loop feedback.
C) Long-loop feedback.
D) Ultra-short feedback.

4. In males which hormone stimulates Sertoli cells to produce androgen binding globulin (ABG)?

A) Oxytocin.
B) FSH.
C) LH.
D) GnRH.

5. For milk to pass from the nipple of the mother into the mouth of the nursing infant, what must occur?

A) Oxytocin secretion from the posterior pituitary must take place.
B) The baby's mouth must develop a strong negative pressure over the nipple.
C) Myoepithelial cells must relax.
D) Prolactin levels must fall.

ANSWER KEY: D, A, B, B, A

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REFERENCES

- Guyton and Hall Textbook of Medical Physiology
- Ganong's Review of Medical Physiology