

Hypothalamo-Pituitary axis and regulatory mechanisms

Objectives:

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

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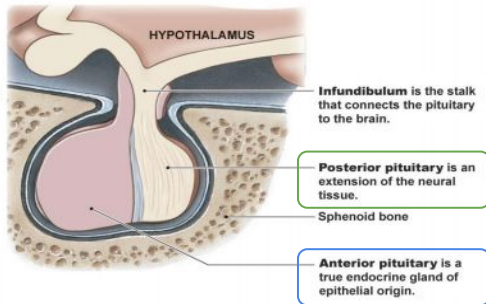
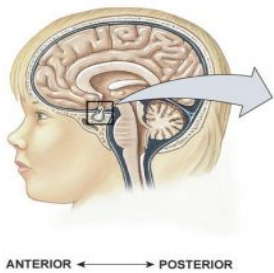
Colour index:

- Important
- Numbers
- Extra

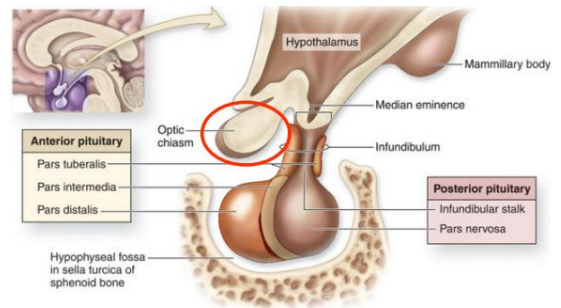
Structure of Pituitary Gland

Pituitary gland consists of two lobes:

- Anterior lobe (Adenohypophysis)
- Posterior lobe (Neurohypophysis)

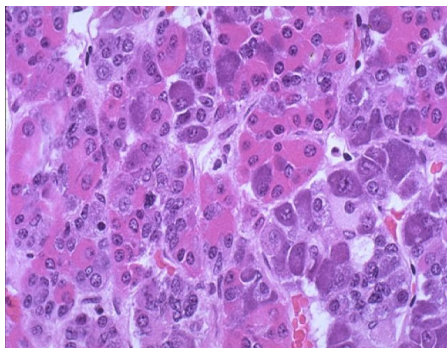
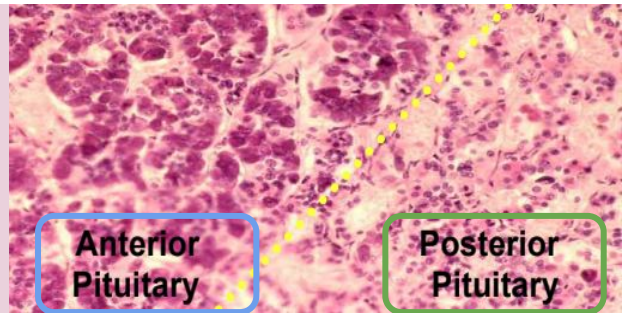


(Relation to Optic Chiasm)



Histology of Pituitary Gland

- Anterior pituitary originates from Rathke's pouch. (Pharyngeal epithelium)
- Posterior pituitary originates from hypothalamus. (glial-type cells)

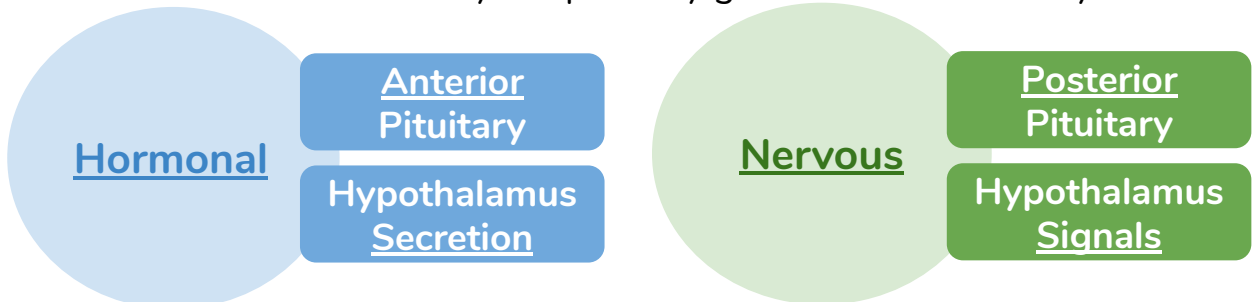


□ Anterior pituitary contains 5 cell types:

- Somatotropes: GH 40%
- Corticotropes: ACTH 20%
- Thyrotropes: TSH
- Gonadotropes: LH & FSH
- Lactotropes: PRL

Hypothalamic Control of Pituitary Secretions

Almost all secretions by the pituitary gland are controlled by either:



- Hormones that are synthesized in the hypothalamus will travel till they reach the posterior pituitary where they will stay there and wait to be released when any stimulation occurs (no neuron in pituitary gland just axons)
- Hormonal secretion reaches the site of action through the pituitary portal system

Control of Anterior Pituitary by Hypothalamus

- Special neurons in the hypothalamus synthesize and secrete the hypothalamic releasing & inhibitory hormones that control secretion of anterior pituitary.
- all hormones secreted by the hypothalamus are peptides **except dopamine which is an amine**.
- Neurons send their nerve fibers to the **median eminence**. (extension of hypothalamic tissue into pituitary stalk)
- Hormones are secreted to the tissue fluids, absorbed into the **hypothalamic-hypophyseal portal system**, and transported to the sinuses of the **anterior pituitary**.

A Portal system consists of blood vessels connecting 2 capillary beds.

Capillary beds:

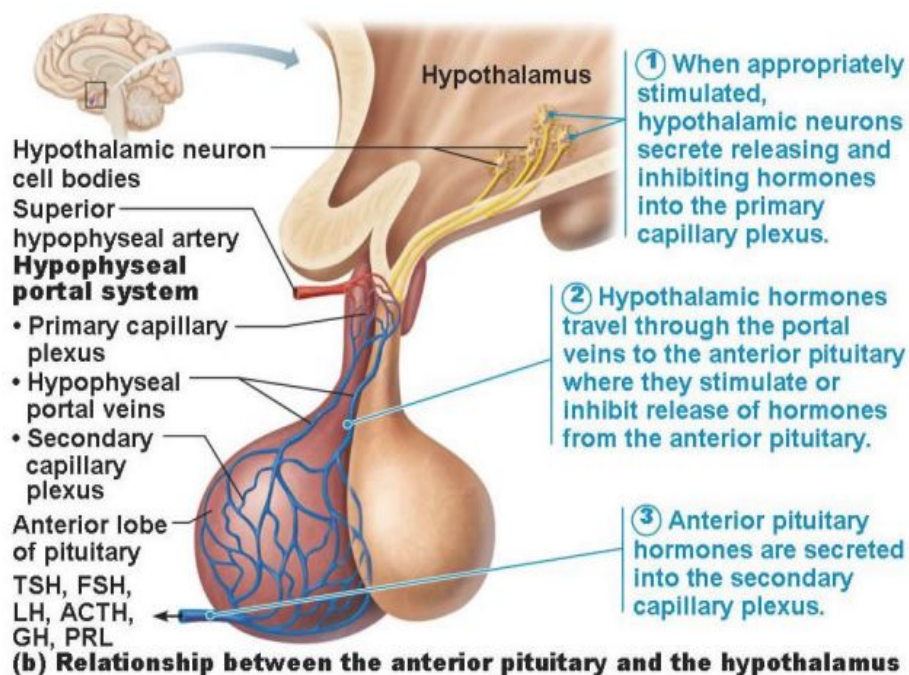
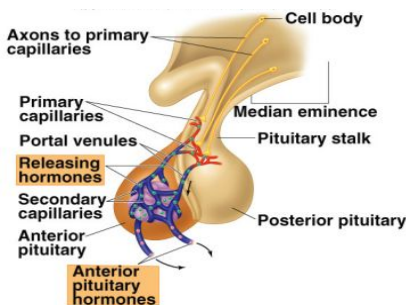
1-primary plexus found near median eminence.

2-secondary plexus found in anterior pituitary.

Adenohypophysis

- Anterior pituitary gland is connected to hypothalamus via the portal system:
 - “Hypothalamic-hypophyseal portal vessels”.

Neurons from the hypothalamus first go to the primary plexus where they will secrete their hormones; and this process is called (neuroendocrine secretion) then they go through the portal venules till they reach anterior pituitary where they will divide and form the secondary plexus



Hypothalamic Releasing and Inhibiting Hormones

- **Growth hormone releasing hormone (GHRH)**

- Stimulates release of growth hormone

- **Growth hormone inhibiting hormone (GHIH) also called Somatostatin**

Somato= body/ statin= stop

- Inhibits release of growth hormone

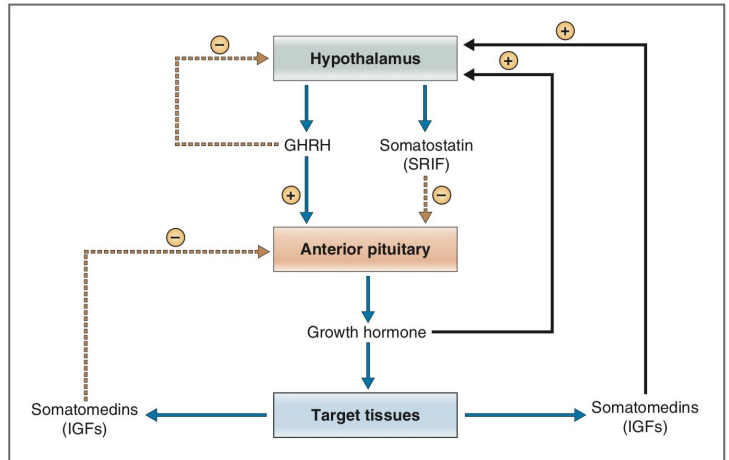
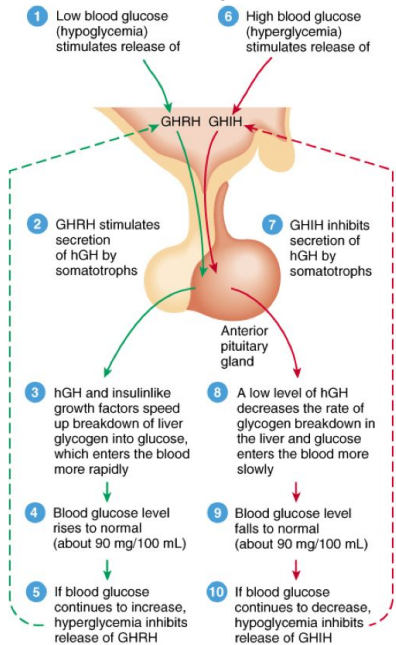
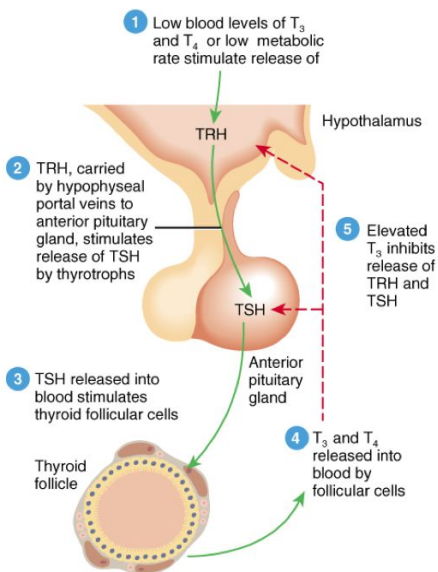


Fig. 9.11 Regulation of growth hormone secretion. *GHRH*, Growth hormone-releasing hormone; *IGF*, insulin-like growth factor; *SRIF*, somatotropin release-inhibiting factor.

-GHRH has an ultra short negative feedback on the hypothalamus.
-GH and IGF potentiate the action of somatostatin which is negative feedback bc it will decrease the secretion of hormone eventually.

- **Thyrotropin-releasing hormone (TRH)**

- Stimulates release of thyroid stimulating hormone (TSH)



Key:

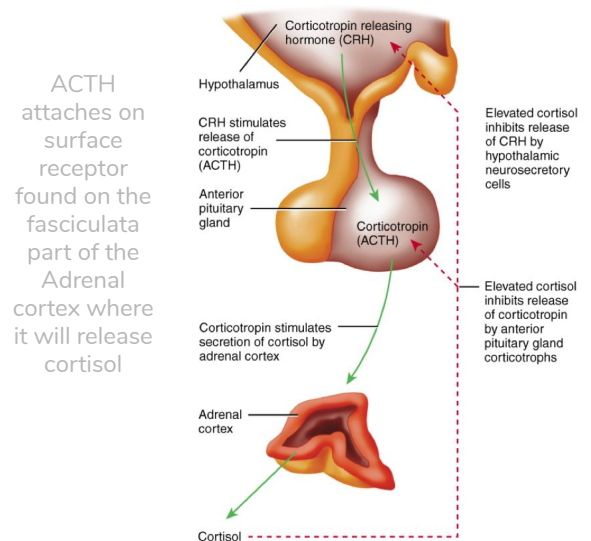
TRH = Thyrotropin releasing hormone
TSH = Thyroid-stimulating hormone
T₃ = Triiodothyronine
T₄ = Thyroxine (Tetraiodothyronine)

T₃ is The Active form of T₄, Thus mediates the inhibition of TRH, TSH

- **Corticotropin-releasing hormone (CRH)**

- Stimulates release of adrenocorticotrophic hormone (ACTH)

Adrenocortico: works on the cortex of the adrenal gland
Tropic: stimulatory



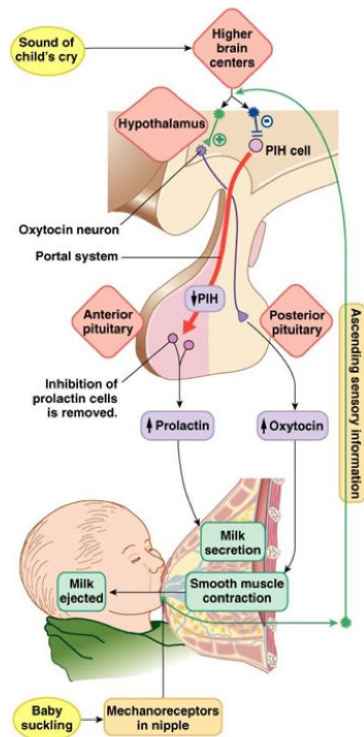
ACTH attaches on surface receptor found on the fasciculate part of the Adrenal cortex where it will release cortisol

Cortisol works as negative feedback on both hypothalamus (long) and pituitary (long) gland

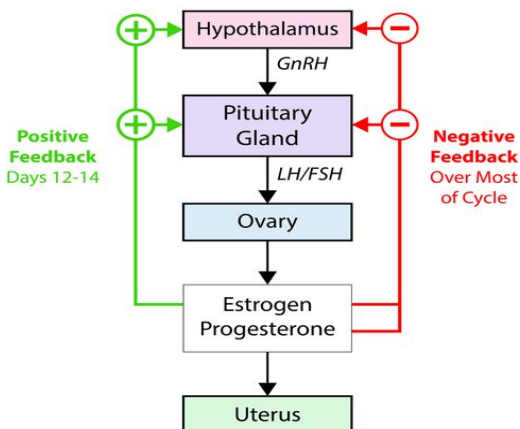
Hypothalamic Releasing and Inhibiting Hormones

- **Prolactin inhibitory hormone (PIH)** also known as **Dopamine**
 - Inhibits prolactin secretion

- Normally prolactin is inhibited all the time, except when breastfeeding.
- The stimulus for PIH inhibition is baby suckling.
- Prolactin is responsible for production of milk.
- Impulses inhibiting PIH also stimulate production of oxytocin, causing ejection of milk and contraction of the uterus, that may present as a stomachache for the mother when breastfeeding.
المغص يحبط عزيمة الأم للإرضاع



- **Gonadotropin releasing hormone (GnRH)** causes release of the 2 gonadotropic hormones:
 - Luteinizing hormone (**LH**)
 - Follicle-stimulating hormone (**FSH**)



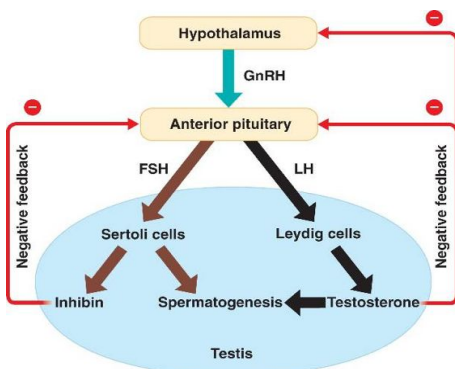
- High levels of estrogen and progesterone inhibit the release of (LH) and (FSH) from the anterior pituitary gland and GnRH from the hypothalamus.

- At a higher levels, estrogen causes a **positive feedback mechanism during mid cycle (days 12-14) "during ovulation"**, causing increased release of GnRH.

- (LH) is important for rupture of the follicle.

- (FSH) responsible for grow of ova /spermatids.

- (Inhibin)+(FSH) inhibits the release of gonadotropins in the anterior pituitary by a negative feedback mechanism.



Clinical Application

Q: What will happen if pituitary gland is removed from its normal position and transplanted to other part of the body?

1. Release of all hormones will stop. **X**
2. Release of some hormones will decrease to very low levels.
3. Release of some hormones will increase. e.g: prolactin.

Prolactin is the only hormone that will not be inhibited and thus increase, the second and third options are correct.

Posterior pituitary gland

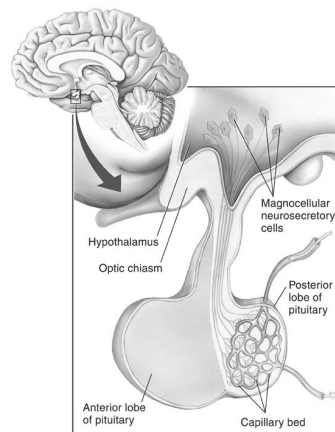
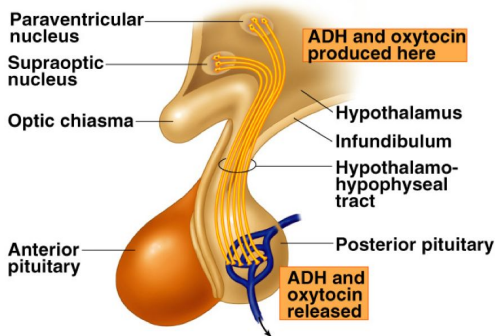
Hypothalamic control of posterior pituitary gland

Hormones synthesized in the **supraoptic** and **paraventricular** nuclei of the hypothalamus and released in the posterior pituitary.

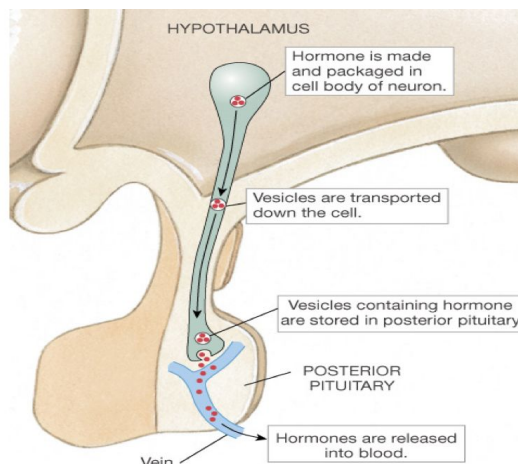
Hormones secreted from posterior pituitary gland don't be confused:
Synthesized = hypothalamus
Secretion = PPG

Magnocellular neurons in paraventricular and supraoptic nuclei secrete **oxytocin** and **vasopressin (ADH)** directly into capillaries in the posterior lobe.

Hypothalamic-pituitary axis is responsible for **Osmoregulation** through ADH



Secretion of posterior pituitary hormones



What do we call
This process?
neuroendocrine

Feedback Mechanisms

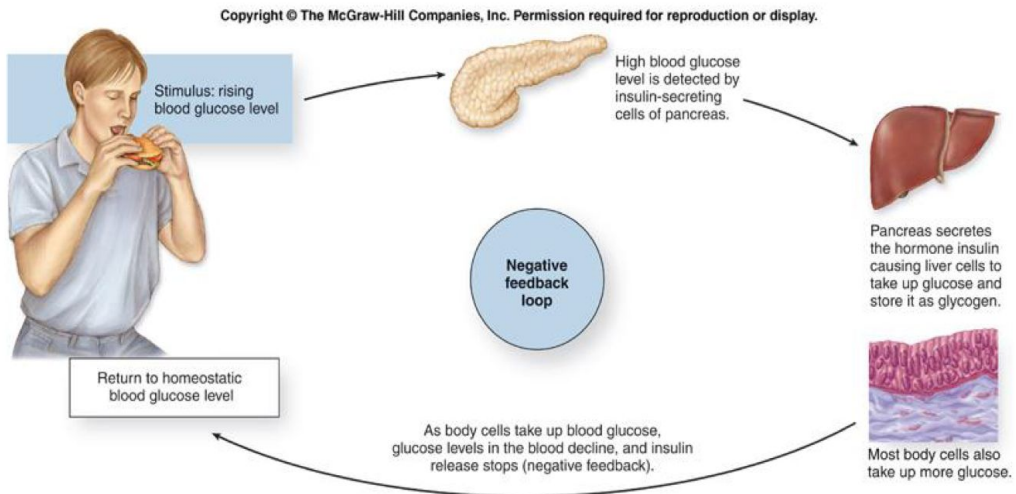
Positive feedback

- Release of **hormone A** stimulates the release of hormone B.
- **Hormone B** stimulates further release of hormone A.

Negative feedback

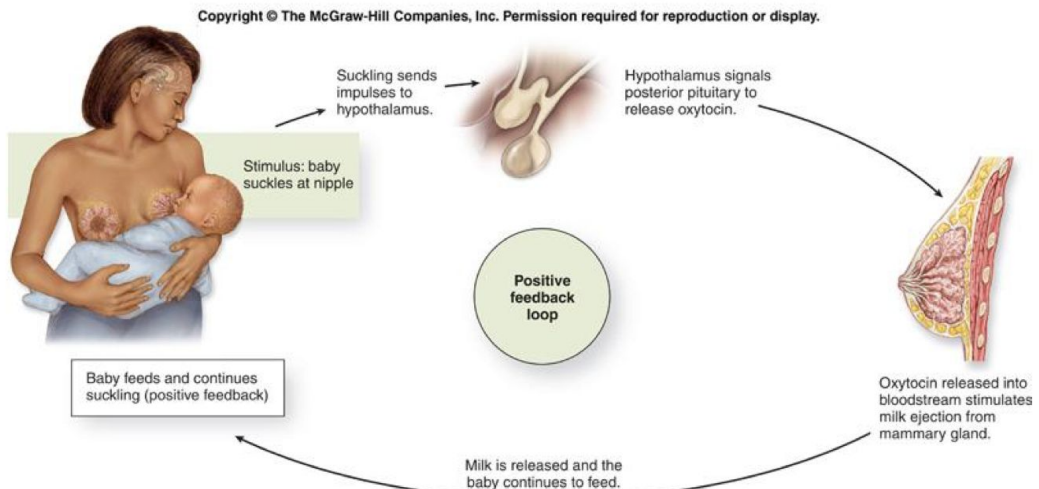
- Release of **hormone A** stimulates the release of hormone B.
- **Hormone B** inhibits the release of hormone A.

NEGATIVE FEEDBACK



(a) Negative feedback

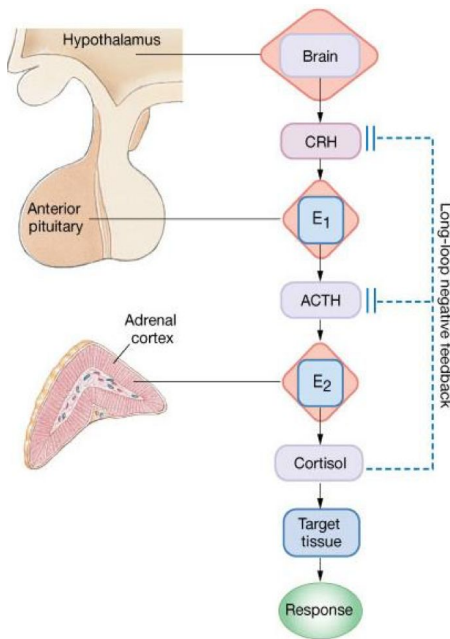
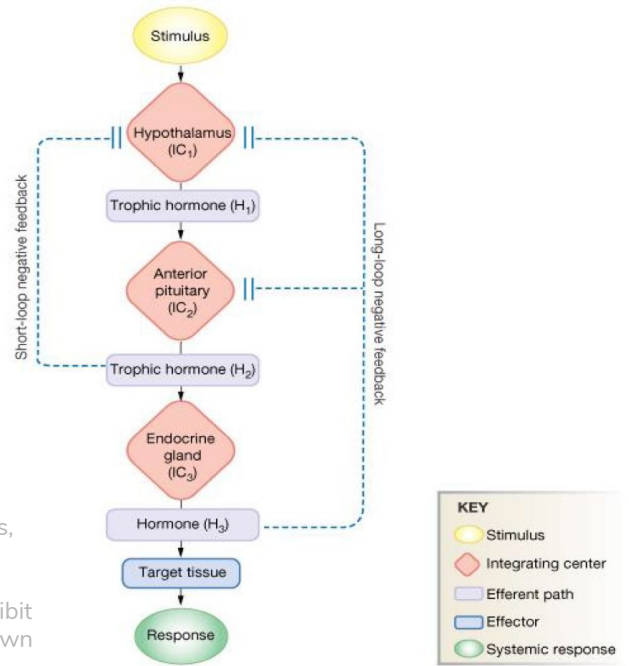
POSITIVE FEEDBACK



(b) Positive feedback

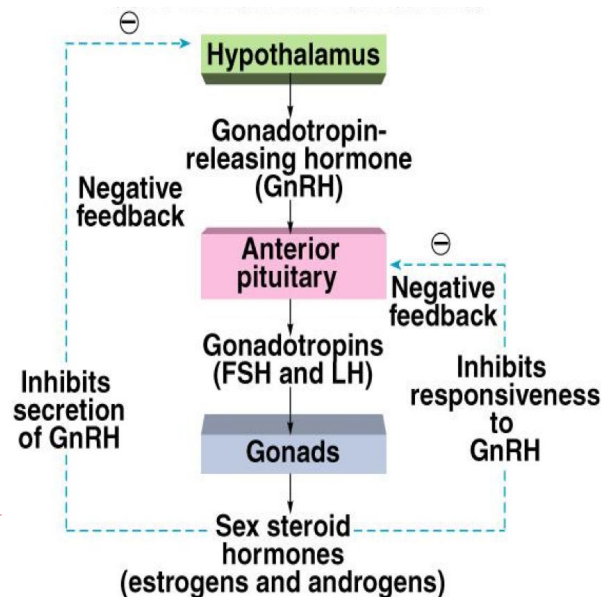
Negative feedback mechanism "Long & Short Loop reflexes"

- When anterior pituitary hormones inhibit the hypothalamus, the process is known as **(short loop negative feedback)**. however, when hormones produced by other pituitary-Dependant endocrine glands, such as thyroid, inhibit the hypothalamus and anterior pituitary, the process is known as **(long loop negative feedback)**.
- (Ultrashort-loop)** is when the hypothalamic hormone inhibits its own secretion (e.g: growth hormone-releasing hormone "GHRH" inhibits GHRH secretion)
- Feedback is considered a short loop only when hormones of anterior pituitary inhibit The hypothalamus.



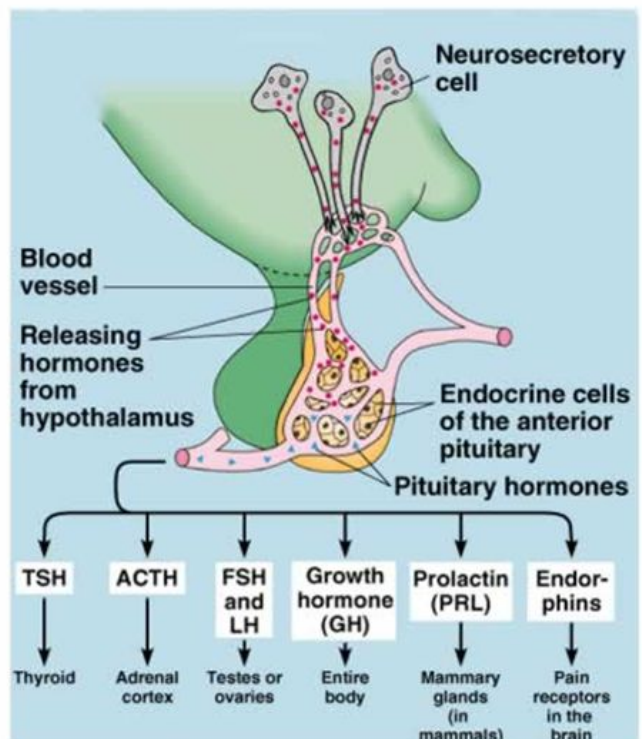
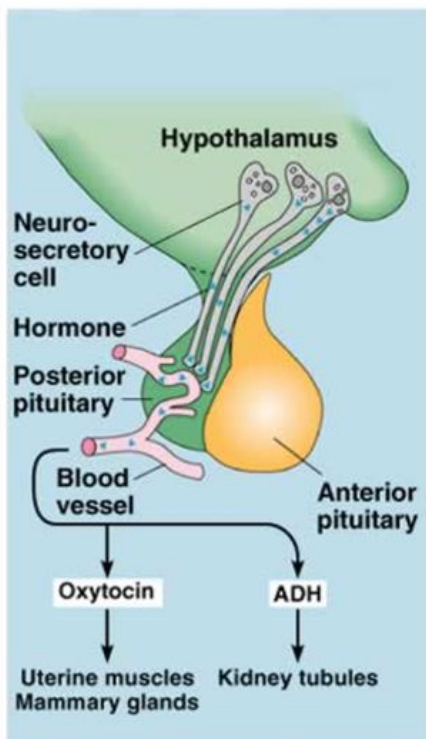
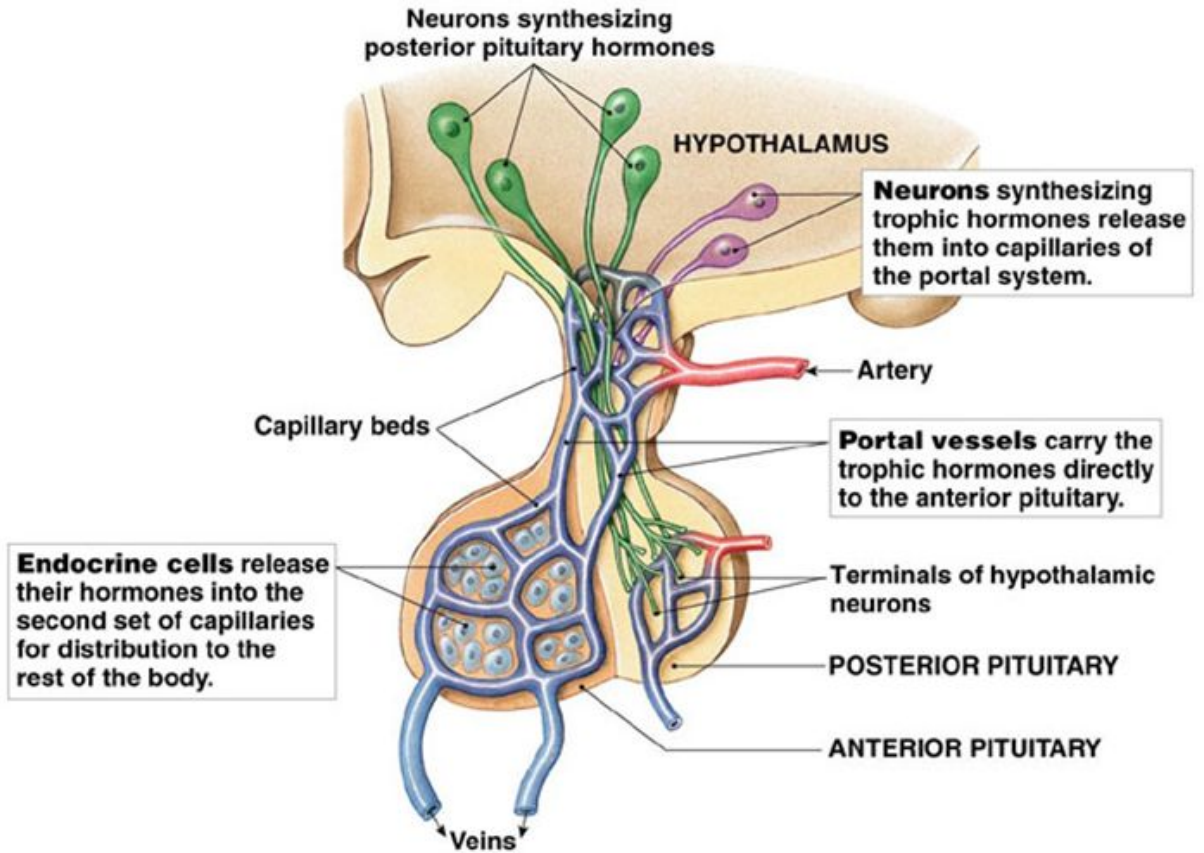
Negative feedback mechanism "cortisol" "long loop"

Negative feedback mechanism "sex steroids" "long loop"



Summary of hypothalamic control of pituitary gland

Purple neurons control the anterior pituitary hormones, whereas green neurons are responsible for the secretion of hormones of the posterior pituitary.



Doctor's Notes:

- 1) The relationship between the hypothalamus and the pituitary gland is **neuronal and endocrine**.
- 2) The Hypothalamus releases **releasing hormones** (have r) which act on the anterior pituitary gland.
 - a) **TRH** (Thyrotropin releasing hormone)
 - b) **CRH** (Corticotropin releasing hormone)
 - c) **GnRH** (Gonadotropin releasing hormone)
 - d) **PIF** (Prolactin Inhibiting Factor)
 - e) **GHRH** (Growth Hormone Releasing Hormone)
- 3) Hypothalamus releases **neuropeptides (paracrine signaling)** which go to the pituitary plexus and stimulate secretion.
- 4) The anterior pituitary gland secretes 6 hormones from 5 types of cells
 - a) Both FSH and LH are released from gonadotrophs
- 5) The posterior pituitary gland secretes:
 - a) **ADH** (responsible for **osmolality** and absorption of water) from Supraoptic Nuclei
 - b) **Oxytocin** from paraventricular nuclei

Hormone	Target
FSH (Follicle Stimulating Hormone)	Gonads
LH (Luteinizing Hormone)	
GH (Growth hormone)	Entire body
Prolactin	Mammary glands
TSH (Thyroid Stimulating Hormone)	Thyroid

MCQs

1/ Negative feedback exerted by target hormones can be directed at:

- A) Only the anterior pituitary .
- B) Only the hypothalamus .
- C) Both the ant pituitary and the hypothalamus .

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

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

3/ The two hormones released from the neurohypophysis are actually manufactured in the:

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

4/Which of the following increases secretion of GH?

- A) Insulin-like growth factor-1 (IGF-1).
- B) Somatostatin.
- C) Hypoglycemia.
- D) Exogenous GH administration.

5/Which of the following hormones originates in the anterior pituitary?

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

6/ Which of the following anterior pituitary hormones plays a major role in the regulation of a nonendocrine target gland?

- A) Adrenocorticotrophic hormone.
- B) Thyroid-stimulating hormone.
- C) Prolactin.
- D) Follicle-stimulating hormone.

7/ Which of the following hormones is both synthesized and stored in the pituitary gland?

- A) Growth hormone.
- B) ADH.
- C) GHRH.
- D) Somatostatin.

8/ Release of which of the following hormones is an example of neuroendocrine secretion?

- A) Cortisol.
- B) Oxytocin.
- C) Prolactin.
- D) Growth Hormone.

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

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

Answers

1. C
2. B
3. D
4. C
5. D
6. C
7. A
8. B
9. C