ENDOCRINE MODULE
PHYSIOLOGY (LECTURE 1)
HYPOTHALAMIC PITUITARY RELATIONSHIP

BY

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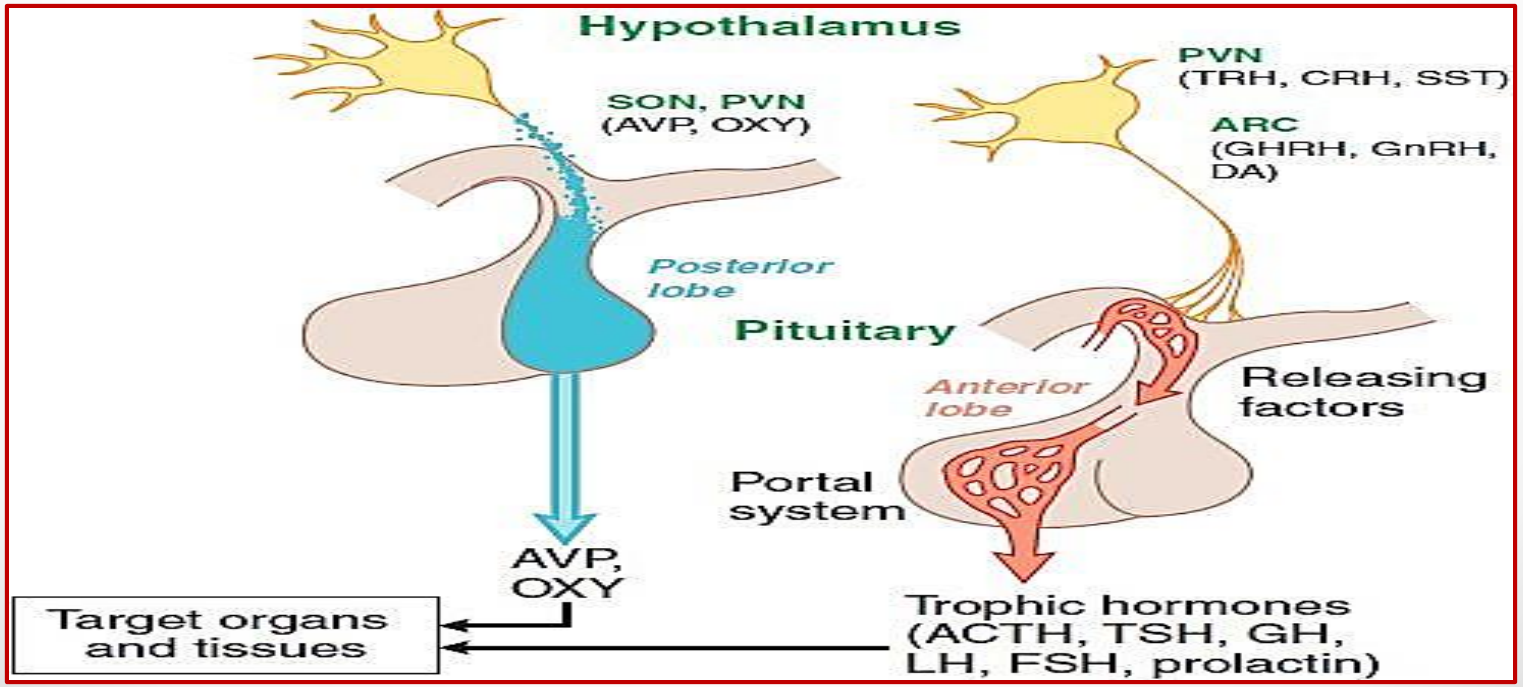


CONTROL SYSTEMS

The different body activities are regulated by two main systems:

- **Nervous system:** which is made up of central nervous system and peripheral nervous system.

The nervous system is a rapid control system. So, its response is **rapid and transient.**

- **Endocrine System:** which is made up of **ductless glands** secreting chemical substances called **hormones** directly into the bloodstream through which they reach other sites (target organs). It is a **slow control system**. So, its **response is slow and prolonged**.

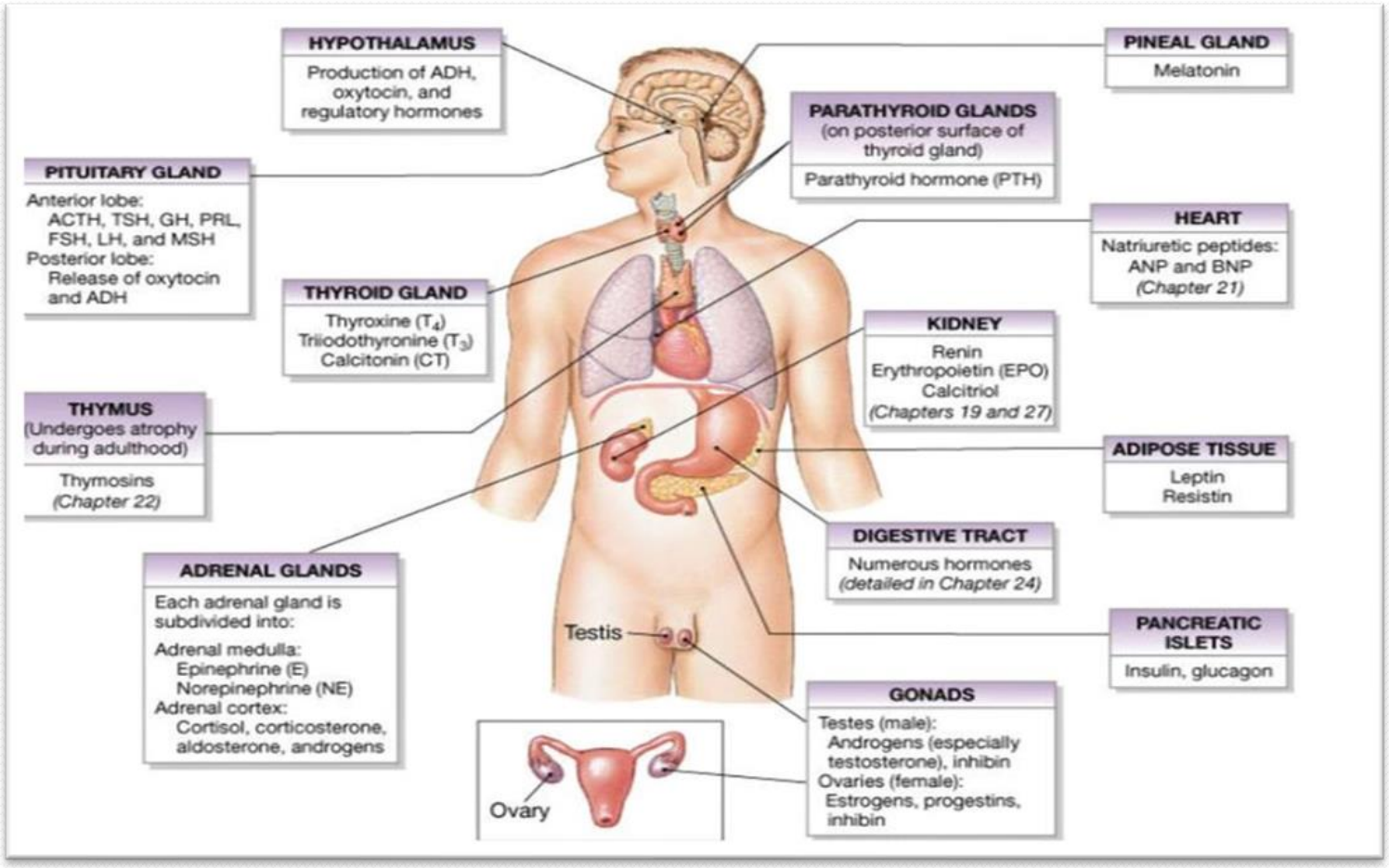
Endocrine glands include:

- Pituitary gland (hypophysis).
- Thyroid gland.
- Parathyroid glands.
- Adrenal (suprarenal) glands (each contains cortex and medulla).
- Gonads (2 testes in males and 2 ovaries in females).
- Islets of Langerhans (in Pancreas).

Hypothalamus

- It is a part of the nervous system that is considered as a link between the two systems.
- It controls the master gland (anterior pituitary) that controls other endocrine glands.

- **Endocrine hormones** are released by endocrine glands into the circulating blood and influence the function of cells at another location in the body.
- **Neuroendocrine hormones:** Are secreted by neurons into the circulating blood & influence the function of target cells at another location in the body. Oxytocin and ADH.
- Paracrines: are secreted by cells into the extracellular fluid and affect neighboring cells.
- Autocrines: are secreted by cells into the extracellular fluid and affect the function of the same cells that produced them by binding to cell surface receptors.


HYPOTHALAMUS
Production of ADH, oxytocin, and regulatory hormones
PINEAL GLAND
Melatonin
PARATHYROID GLANDS
(on posterior surface of thyroid gland)
Parathyroid hormone (PTH)
PITUITARY GLAND
Anterior lobe:
ACTH, TSH, GH, PRL, FSH, LH, and MSH
Posterior lobe:
Release of oxytocin and ADH
HEART
Natriuretic peptides: ANP and BNP
(Chapter 21)
THYROID GLAND
Thyroxine (T_4)
Triiodothyronine (T_3)
Calcitonin (CT)
KIDNEY
Renin
Erythropoietin (EPO)
Calcitriol
(Chapters 19 and 27)
THYMUS
(Undergoes atrophy during adulthood)
Thymosins
(Chapter 22)
ADIPOSE TISSUE
Leptin
Resistin
DIGESTIVE TRACT
Numerous hormones
(detailed in Chapter 24)
ADRENAL GLANDS
Each adrenal gland is subdivided into:
Adrenal medulla:
Epinephrine (E)
Norepinephrine (NE)
Adrenal cortex:
Cortisol, corticosterone, aldosterone, androgens
Testis
PANCREATIC ISLETS
Insulin, glucagon
GONADS
Testes (male):
Androgens (especially testosterone), inhibin
Ovaries (female):
Estrogens, progestins, inhibin
Ovary

What is a hormone ?

It is a chemical substance secreted into the blood stream by endocrine glands to act on distant organs called effector (target) organs.

Properties of hormones:

1. They are secreted in very small amounts that maintain a basal quantity of each hormone in bloodstream and the rate of secretion of a certain hormone depends on the needs of the body to this hormone.
2. They do not act on the organs secreting them (endocrine glands) but act on distant organs (effector organs).
3. Hormones may act on a **specific** effector organ e.g. thyroid stimulating hormone (TSH) of the anterior pituitary acts specifically on the thyroid gland, or hormones may act on the body as a whole (**generalized**) e. g. growth hormone (GH) of the anterior pituitary.

4. In target cells, hormones initiate certain biochemical reactions which often continue for sometime after disappearance of hormones from bloodstream.
5. Stimuli that release a certain hormone inhibit the secretion of other hormones that exert antagonistic effects e.g. hyperglycemia stimulates insulin secretion and inhibits secretion of its antagonists (e.g. glucagon and growth hormone)
6. Many hormones show cyclic variations in their rate of secretion over the 24 hours (= diurnal or circadian rhythm) e.g. ACTH.
7. Most hormones circulate in bloodstream in 2 forms: a very small amount in free (active) form and a much greater amount bound to plasma proteins (reservoir for the hormone).

Hormones can be chemically classified into three groups:

- **Steroids:** Hormones that are lipids synthesized from cholesterol (sex hormones and adrenocortical hormones).
- **Polypeptide and protein (non-steroids):** Hormones that are chains of amino acids(pituitary, pancreatic and parathyroid hormones).
- **Amino acid-derived :** Thyroid hormones (T3 and T4) and Catecholamines. They are derived from **tyrosine**.

Hormonal Receptors

- Hormonal receptors are located either inside the target cells (in the cytoplasm or in the nucleus) or on their membranes. They are chemically protein in nature and are specific (each receptor is specified to bind a certain hormone).
- Their regulation includes:
- Upregulation: a low blood level of a certain hormone leads to an increase in number of its active receptors.
- Downregulation: a high blood level of a certain hormone leads to a decrease in number of its active receptors.

Mechanism of Hormonal Action

(1) *For non - steroidal hormones* (proteins, polypeptides and catecholamines) :

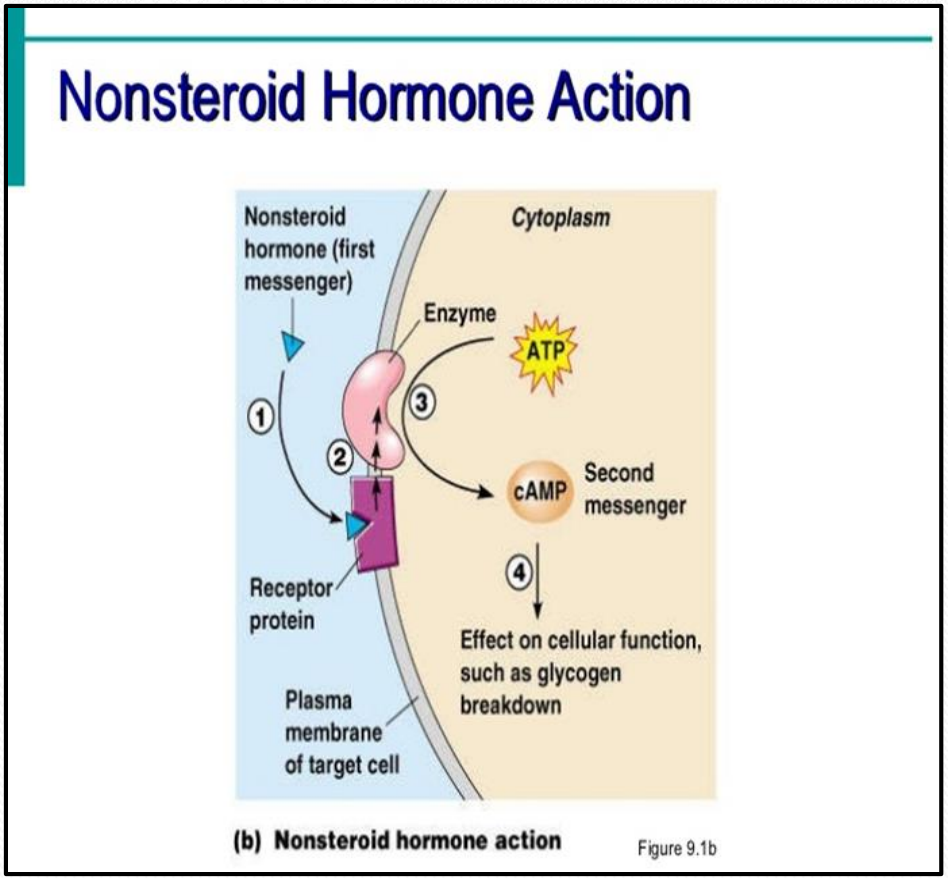
- Hormones are carried by the blood stream to the cells of the effector organ.
- Hormones do not pass the cell membrane to the inside of the cells because they are **lipid insoluble**.
- Therefore, hormones bind to **specific protein receptors on the outer surface of the cell membrane**.
- This binding activates a protein enzyme on the inner surface of the cell membrane as **adenyl cyclase.**
- Adenyl cyclase catalyzes the conversion of: **ATP → cAMP + PPi → ↑ cAMP inside the cells of the effector organ (second messenger to stimulate the enzyme activity).**
- Other second messengers include DAG & IP3, calcium-calmodulin pathway and cGMP.
- They are rapid in action (increase enzyme activity).

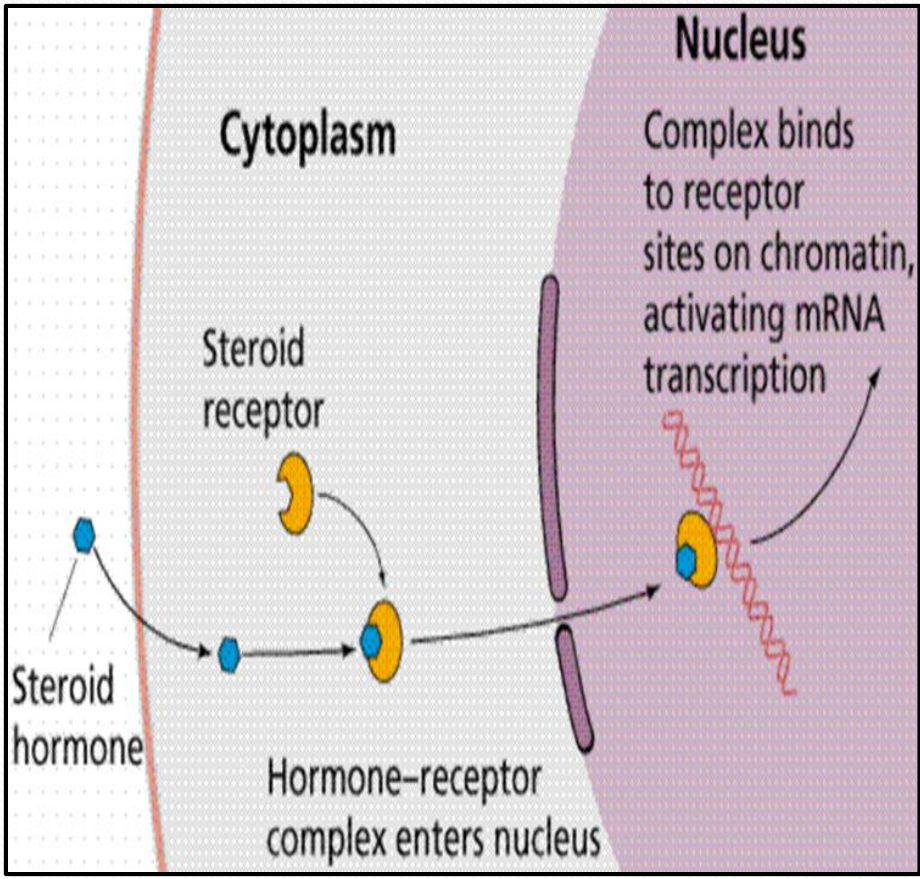
(2) For steroidal and thyroid hormones :

- Hormones are carried by the blood stream to the cells of the effector organ.
- Being **lipid soluble**, they enter the cell and bind to specific receptors inside the cytoplasm forming a complex.
- The hormone-receptor complex moves towards the nucleus and enters through the nuclear membrane.
- ln the nucleus, it accelerates RNA formation from DNA (transcription).
- Newly formed RNA (mRNA) leaves the nucleus to the cytoplasmic ribosomes where the process of protein synthesis is stimulated according to the genetic code carried by mRNA (translation). Thus, the enzyme protein is increased.
- **N.B. Thyroid hormones bind directly to nuclear receptors.**
- **They are slow in action; increase protein synthesis (enzyme formation).**

(A) protein hormones

(B) steroid





THE PITUTARY GLAND (HYPOPHYSIS)

- The pituitary gland is a small gland (0.5-1 gm in weight) lying in a small cavity (sella turcica) at the skull base.
- It is connected to the hypothalamus by the pituitary stalk (infundibulum).
- It is divided into anterior and posterior lobes:
- Adenohypophysis (anterior lobe): made up of glandular tissue.
- Neurohypophysis (posterior lobe): (neural tissue), receives, stores, and releases hormones from the hypothalamus.

HORMONES OF THE PITUITARY GLAND

(1) Anterior Lobe Or Anterior Pituitary Hormones :

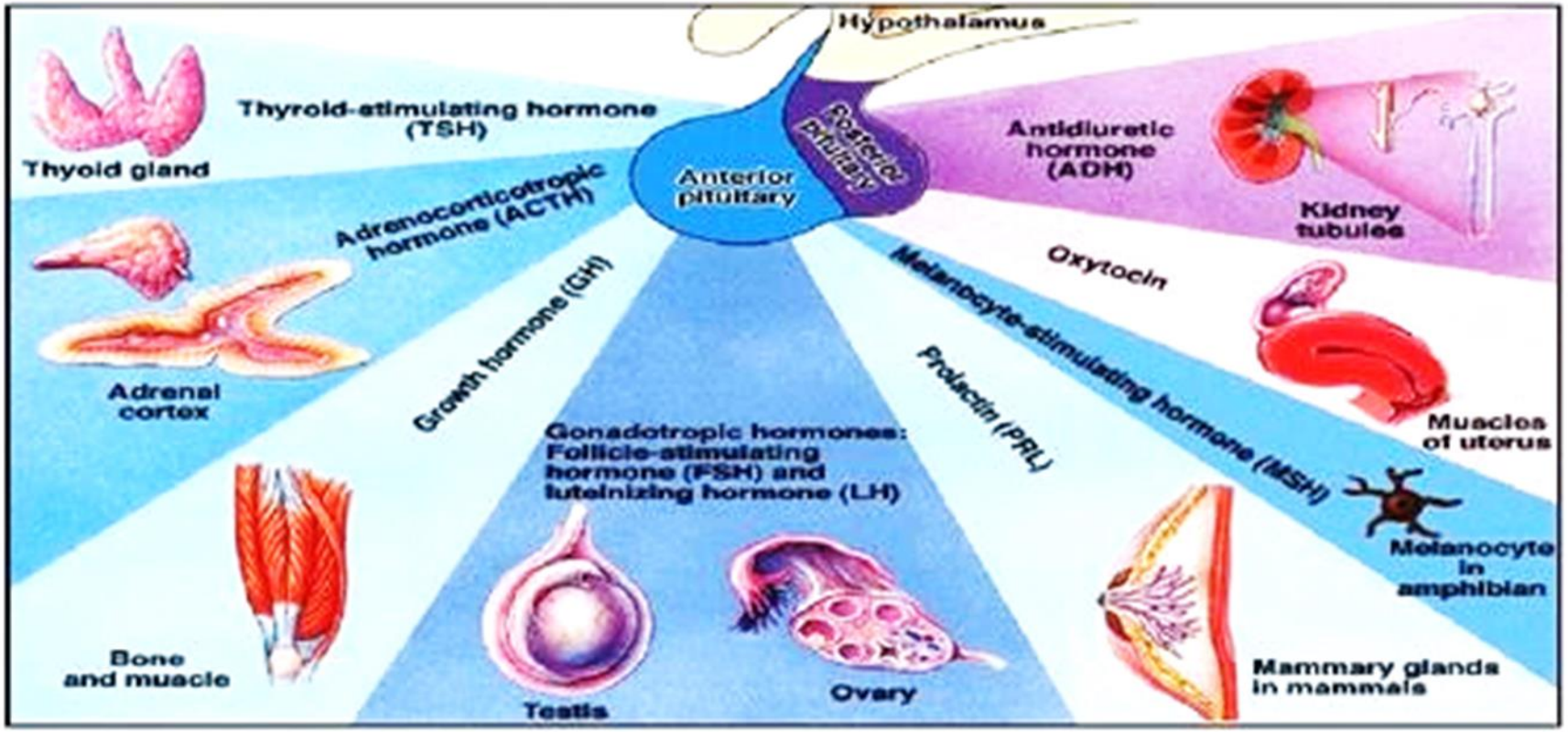
1. Growth Hormone (GH, Somatotropin, or somatotropic hormone; STH).
2. Thyroid Stimulating Hormone (TSH, Thyrotropin).
3. Adrenocorticotrophic Hormone (ACTH, Corticotropin).
4. Follicle Stimulating Hormone (FSH).
5. Luteinizing Hormone or lnterstitial Cell Stimulating Hormone (LH, ICSH). FSH and LH are referred to as gonadotrophic hormones (GnHs).
6. Prolactin (PL), Mammotropin, Lactogenic Hormone (LGH).

- **The anterior pituitary gland** is frequently called the **master gland** because it secrets tropic hormones that control most of the other endocrine glands (ACTH controls the adrenal cortex, TSH controls the thyroid gland, while GnHs control both male and female gonads).
- Tropic hormones stimulate secretion from other endocrine glands except somatotropin (GH) because it is a **systemic hormone** that is not tropic to any specific endocrine gland.

(2) The Posterior Pituitary Hormones :

1. Antidiuretic Hormone (ADH, or Vasopressin).
2. Oxytocin.

- GH, PL and ACTH are polypeptides.
- TSH, FSH and LH are glycoproteins.

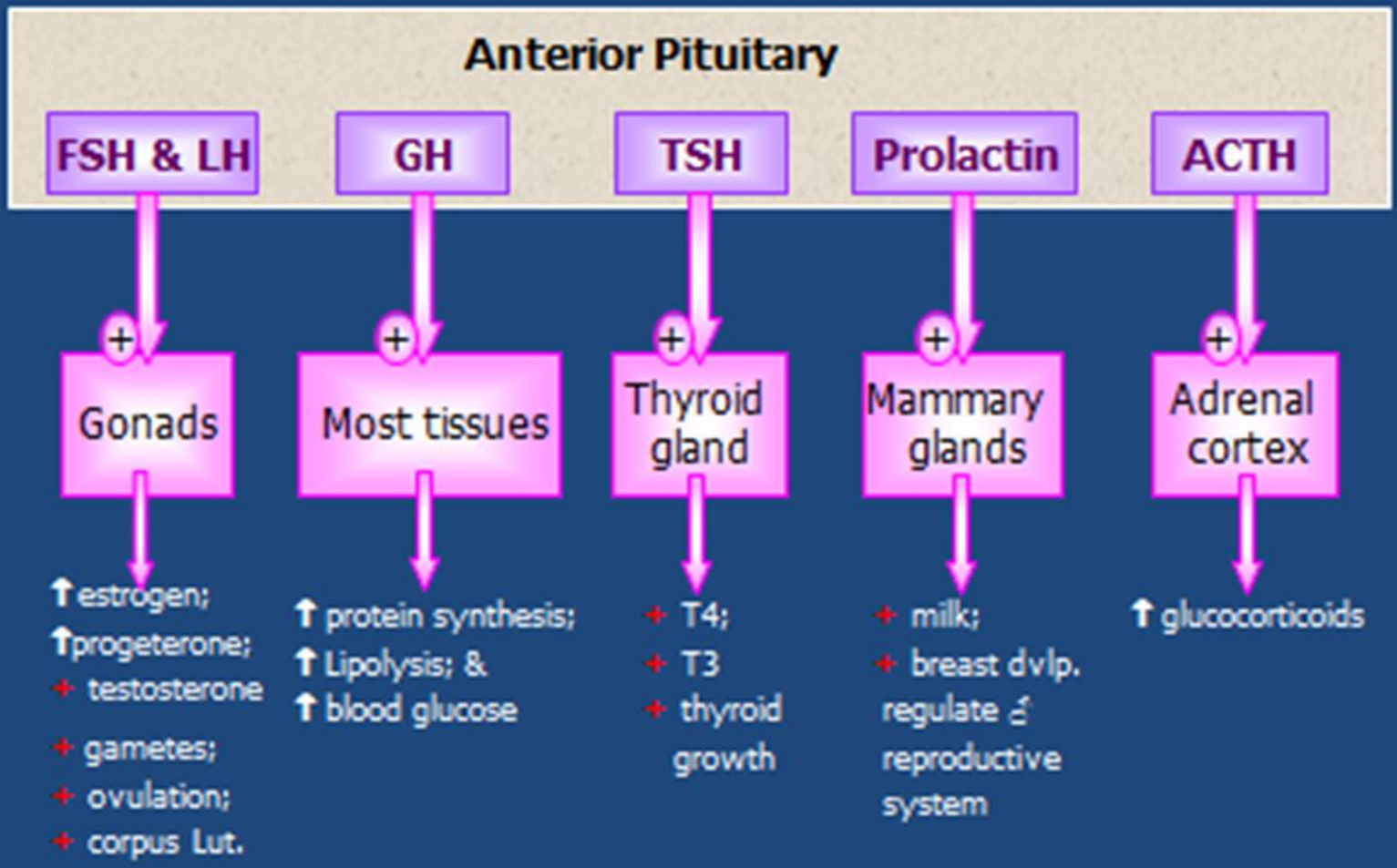


CELL TYPES IN THE ANTERIOR PITUITARY GLAND (ADENOHYPOPHYSIS)

- 5 types of secretory cells were distinguished:

1. Somatotropes, which secrete growth hormone.
2. Lactotropes (also called mammotropes), which secrete prolactin.
3. Thyrotropes, which secrete TSH.
4. Gonadotropes, which secrete both LH and FSH.
5. Corticotropes, which secrete both ACTH and B- Lipotropin.

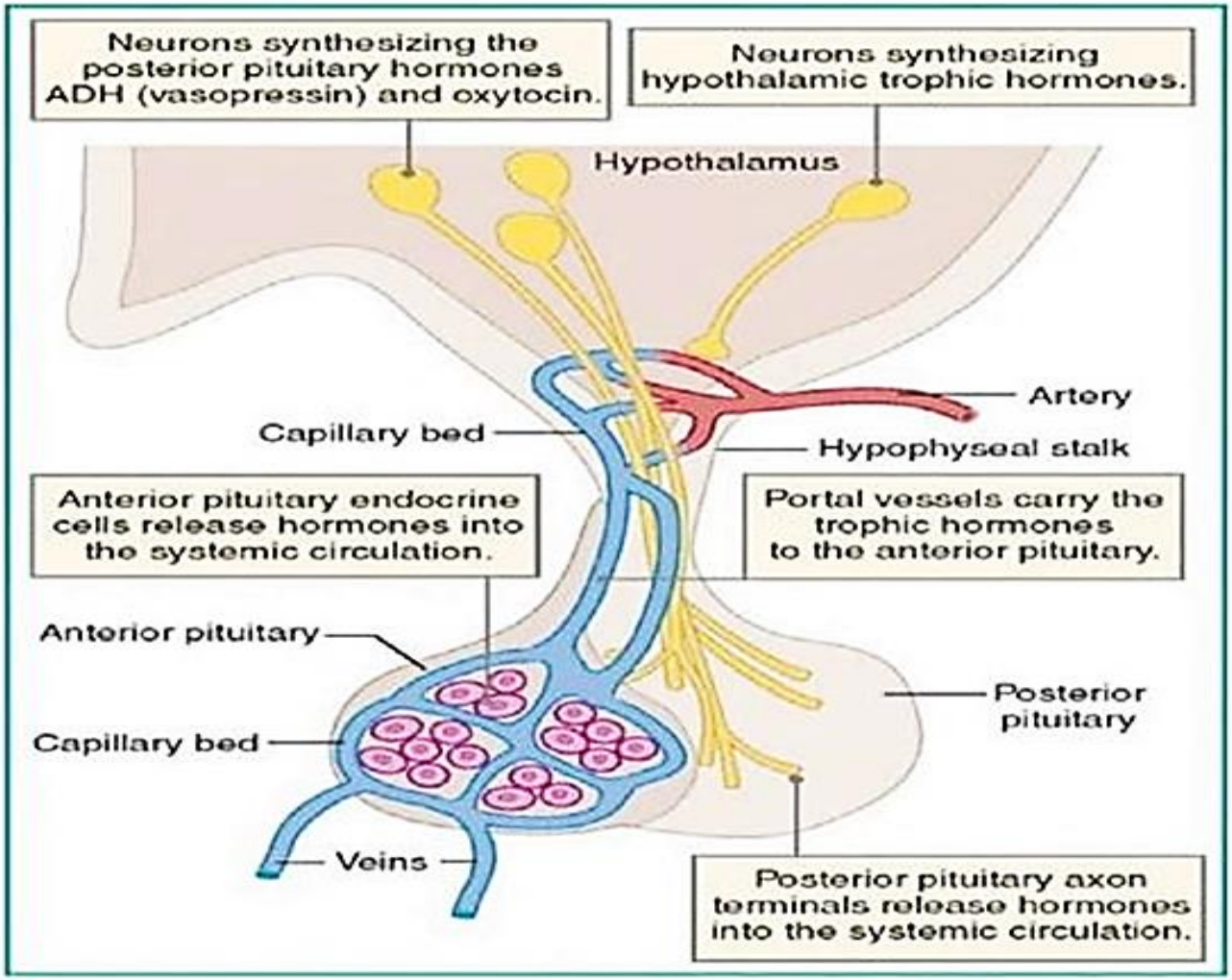
Anterior pituitary hormones



The Hypothalamic Connections with the Pituitary Gland

- There are **2 types of connections** between the hypothalamus and the pituitary gland (which form a link between the nervous system and the gland):
- **A vascular connection between the hypothalamus and the anterior pituitary gland in the form of a hypothalamo-hypophyseal portal circulation**.
- **A nervous connection between the hypothalamus and posterior pituitary gland** in the form of a **hypothalamo-hypophyseal tract**.

HYPOTHALAMO-HYPOPHYSEAL RELATIOSHIP



Through these connections the hypothalamus acts as a control center to the endocrine system as follows:

- The hypothalamus secrets several hormones called **hypophysiotropic hormones**. These hormones are then released from the median eminence into the portal vessels through which they reach the **anterior pituitary gland** where they affect the secretion of its hormones. In this way, **the hypothalamus indirectly controls the activity of most of the endocrine system because the anterior pituitary gland secrets tropic hormones that control most of the other endocrine glands**.
- **The hypothalamus also secrets the 2 hormones of the posterior pituitary** gland, which are transported via the **hypothalamo-hypophyseal tract to the posterior pituitary gland** where they are stored then released when required by signals discharged from the hypothalamus.

Regulation (Control) of Anterior Pituitary Secretion

- The hormonal secretion by the anterior pituitary gland is regulated through 3 mechanisms:

1. The hypothalamic control.
2. Feedback control by the hormones of the effector organs (target glands). This is the **long loop feedback** .
3. Feedback control by the pituitary hormones themselves. This is **the short loop feedback** .

1. The Hypothalamic Control

- The hypothalamus controls the activity of anterior pituitary gland by releasing hormones called hypophysiotropic hormones that reach the gland via the hypothalamo-hypophyseal portal circulation.
- These hypothalamic hormones are polypeptides that act mostly by increasing intracellular cAMP and they either stimulate release of anterior pituitary hormones (= releasing hormones) or inhibit the release of these hormones (= inhibiting hormones) .

The Hypothalamic Hormones (Hypophysiotropic hormones)

- **Releasing hormones:**
  - Growth hormone-releasing hormone (GHR).
  - Prolactin – releasing hormone (PRH).
  - Thyrotropin-releasing hormone (TRH).
  - Corticotropin-releasing hormone (CRH).
  - Gonadotropin-releasing hormone (GnRH).

- **Inhibiting hormones:**
  - Growth hormone-inhibiting hormone (GIH or somatostatin).
  - Prolactin – inhibiting hormone (PIH; dopamine).
- The activity of the anterior pituitary gland is largely controlled by the hypothalamic hypophysiotropic hormones. All anterior pituitary hormones are controlled mainly by their releasing hormones except prolactin which is controlled mainly by PIH.

2. Feed back control by the endocrine target organs (Long Loop Feed Back)

- Feed back control means the effect of the target gland hormones on the secretion of both the hypothalamic hypophysiotropic hormones and pituitary tropic hormones i.e. either at a hypothalamic or pituitary levels.
- If this effect is inhibitory, the feedback is negative (more common).
- If this effect is stimulatory, the feedback is positive.
- **Example:**

Stress stimulates the hypothalamus → Release of CRH → Anterior Pituitary ↑→ ACTH → carried by blood to adrenal cortex → ↑ Cortisol → inhibits hypothalamic CRH. (negative feedback).

3- Feed back control by the pituitary hormones themselves (Short Loop Feed Back)

Portal Circulation

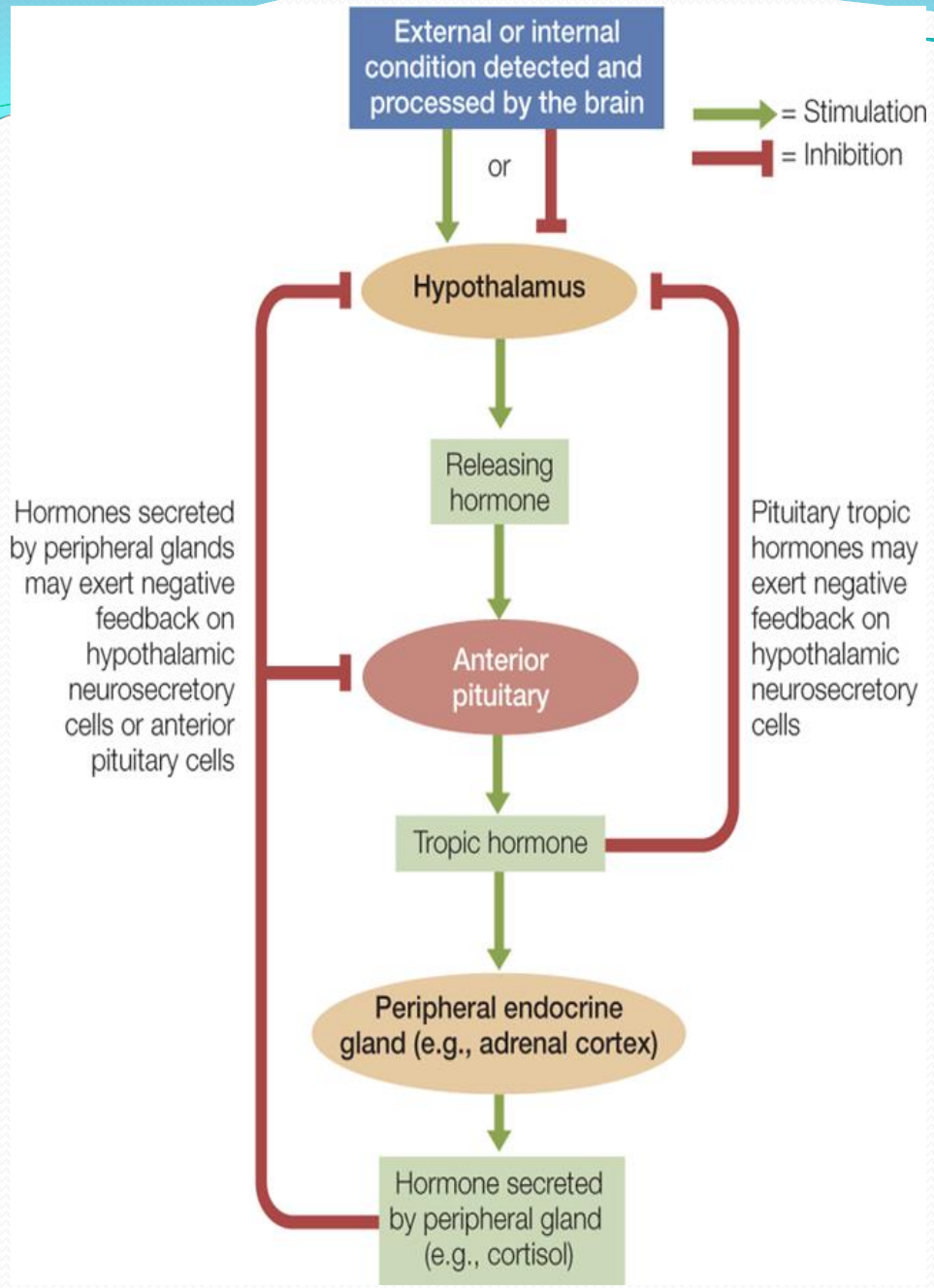
Stimulus → Hypothalamus → Release of neurohormone ----------> Anterior Pituitary.

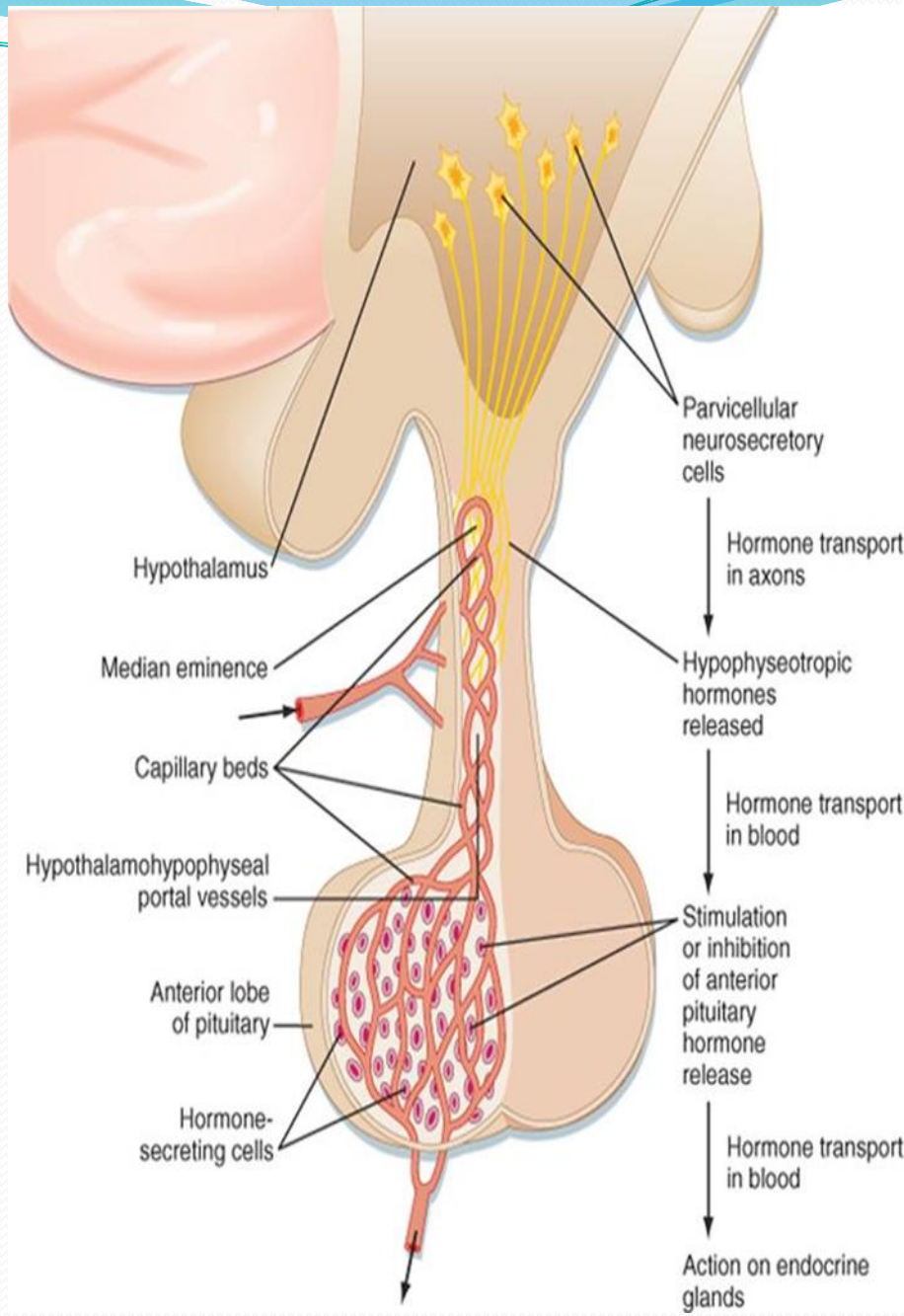
To hypothalamus by blood or back diffusion

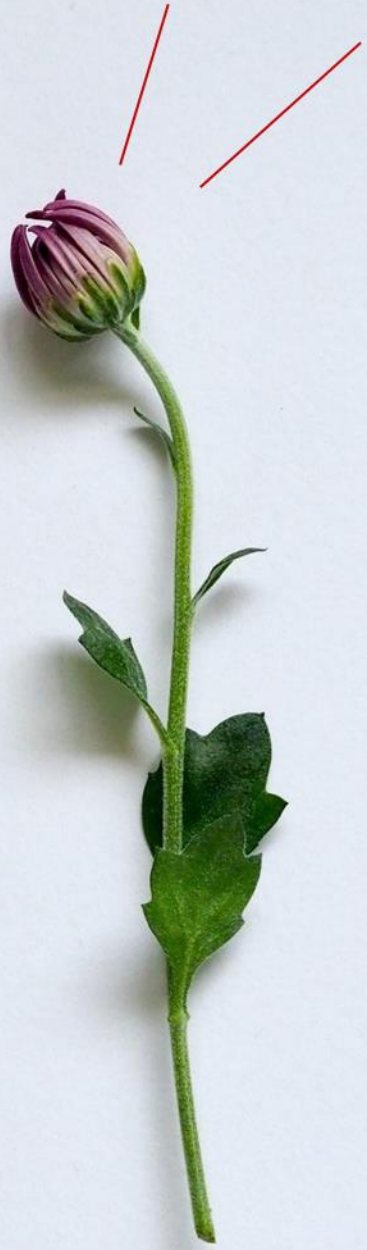
→↑ Anterior Pituitary hormones ----------> inhibit the release of the corresponding releasing hormone.

<u>Importance of the feed back control :</u>

- Maintain the normal level of the target gland hormone in blood.
- Prevent over stimulation of the target gland by the corresponding trophic hormone.
- Adjust the rate of secretion of the target gland hormones according to the body need.


External or internal condition detected and processed by the brain
= Stimulation
= Inhibition
or
Hypothalamus
Releasing hormone
Anterior pituitary
Tropic hormone
Peripheral endocrine gland (e.g., adrenal cortex)
Hormone secreted by peripheral gland (e.g., cortisol)
Hormones secreted by peripheral glands may exert negative feedback on hypothalamic neurosecretory cells or anterior pituitary cells
Pituitary tropic hormones may exert negative feedback on hypothalamic neurosecretory cells


Hypothalamus
Median eminence
Capillary beds
Hypothalamohypophyseal portal vessels
Anterior lobe of pituitary
Hormone-secreting cells
Parvicellular neurosecretory cells
Hormone transport in axons
Hypophyseotropic hormones released
Hormone transport in blood
Stimulation or inhibition of anterior pituitary hormone release
Hormone transport in blood
Action on endocrine glands



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