Physiology for Medical Students
Endocrinology 1 and 2

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Reference Books

- **Hall, John, E. and Michael E. Hall. Guyton and Hall Textbook of Medical Physiology (14th Edition).**
- Lauralee Sherwood. Human Physiology: From Cells To Systems (9th Edition).
- Gerard J. Tortora and Bryan Derrickson. Principles Of Human Anatomy & Physiology (15th Edition)

Office hours

- **All days from 10:30 to 11:30**
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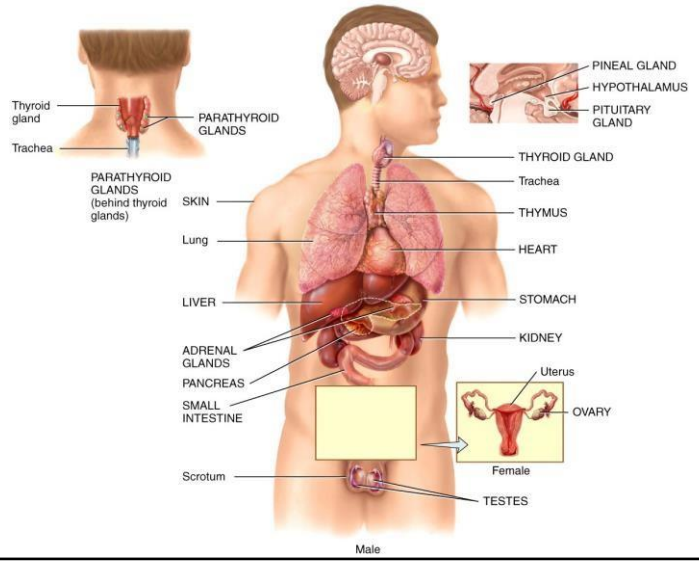
THE ENDOCRINE SYSTEM

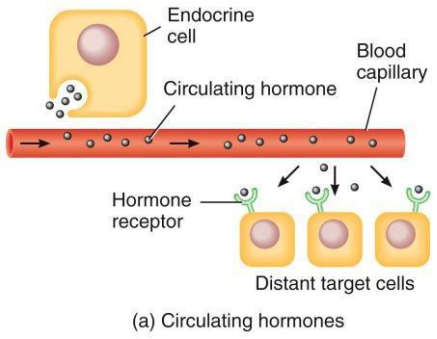


- The nervous and **endocrine systems** coordinate all of the body systems.
- The nervous system does so through the action of neurons, and the neurotransmitters.
- The endocrine system **uses hormones** to produce their effects.
- The nervous system controls homeostasis through nerve impulses and neurotransmitters, which act locally and quickly.
- The endocrine system uses hormones, which act **more slowly in distant parts of the body**.
- The nervous system controls neurons, muscle cells, and glandular cells.
- The endocrine system regulates **virtually all body cells.**
- The endocrine system primarily controls processes that require duration rather than speed, most of which are aimed at **maintaining homeostasis**, such as **regulating nutrient metabolism** and **water and electrolyte balance**; **promoting growth**; and **facilitating reproductive** capacity. Furthermore, the endocrine system works along with the autonomic nervous system to control and **integrate activities of both the circulatory and the digestive systems**

General Principles of Endocrinology

TYPES OF HORMONES

- **Endocrine hormones** are secreted into interstitial fluid and then absorbed into the bloodstream.

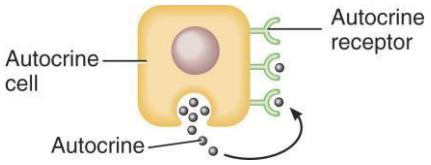


(a) Circulating hormones

- Although a given hormone travels throughout the body in the blood, it affects only specific target cells, since only the target cells for a given hormone have receptors that bind and recognize that hormone.
- **down-regulation (***less sensitive***) Vs. up-regulation (***more sensitive***)**

TYPES OF HORMONES

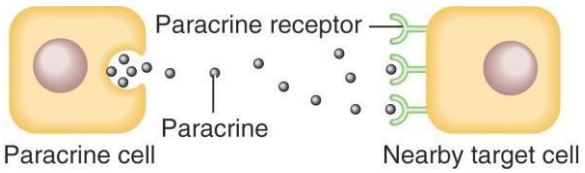
- **Autocrine hormones: are local hormones that are secreted, and bind to the same cell.**



TYPES OF HORMONES

- **Paracrine hormones** are local hormones that are secreted into interstitial fluid and act on nearby cells

- **E.g. nitric oxide (NO).**



CHEMICAL CLASSES OF HORMONES

- Hormones can be divided into two broad **chemical classes.**
- **Water soluble hormones**
- **Lipid soluble hormones**

Water-Soluble Hormones

- **Amine hormones**
- are synthesized by modifying certain **amino acids.**
- The **catecholamines**—epinephrine, norepinephrine, and dopamine—are synthesized by modifying the amino acid **tyrosine.**
- **Histamine** is synthesized from the amino acid **histidine.**
- **Serotonin** and **melatonin** are derived from **tryptophan.**

- **Peptide hormones and protein**
- The smaller peptide hormones consist of chains of **3 to 49 amino acids**
- The larger protein hormones include **50 to 200 amino acids**.
- Peptide hormones are antidiuretic hormone and oxytocin.
- Protein hormones include growth hormone and insulin.

Several of the protein hormones, such as **thyroid-stimulating hormone**, have attached **carbohydrate groups** and thus are glycoprotein hormones.

Lipid-Soluble Hormones

❖ **Steroid hormones**

are derived from cholesterol. Each steroid hormone is unique due to the presence of different chemical groups attached at various sites on the four rings at the core of its structure.

❖ **Thyroid hormones** (T3 and T4)

are synthesized by attaching **iodine** to the **amino acid tyrosine**. The presence of **benzene** ring within a T3 or T4 molecule makes these molecules very **lipid-soluble**.

Water-Soluble Hormone Action

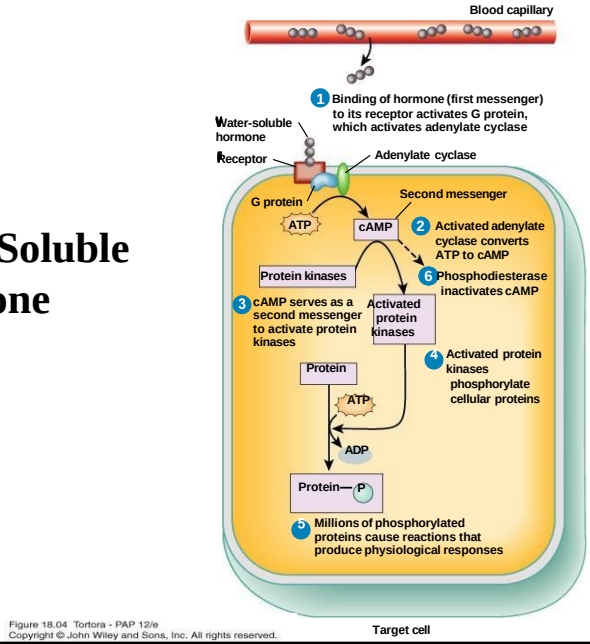
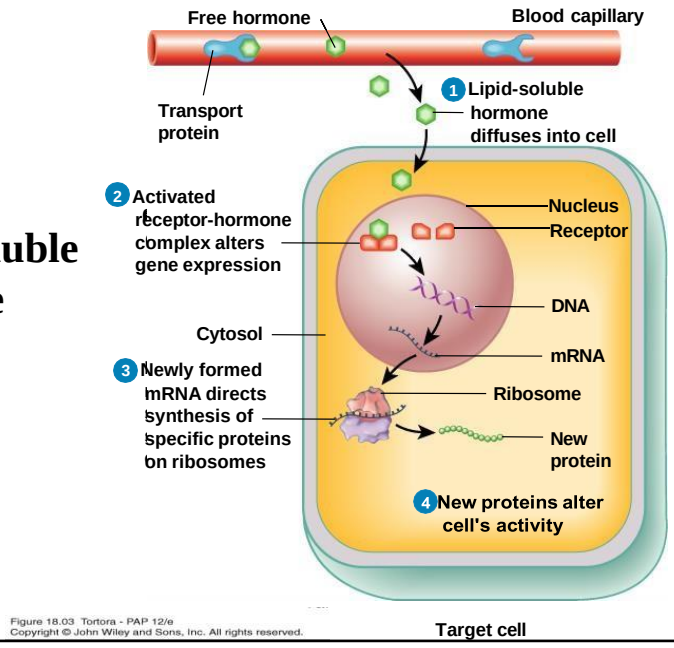


Figure 18.04 Tortora - PAP 12/e

- **Water soluble hormones** are easy to transport in the watery blood. The plasma membrane of target cells, however, is impermeable to them.
- Hydrophilic hormones on binding with surface membrane receptors primarily act through second-messenger systems to alter the activity of preexisting proteins, such as enzymes, within the target cell to produce their physiologic response.

Lipid-Soluble Hormone Action



- lipophilic hormones are largely **bound to plasma protein**
- Lipophilic steroid hormones and thyroid hormone, by contrast, **activate genes on binding with receptors inside the cell**, thus bringing about formation of new proteins in the target cell that carry out the desired response.

TROPIC HORMONES

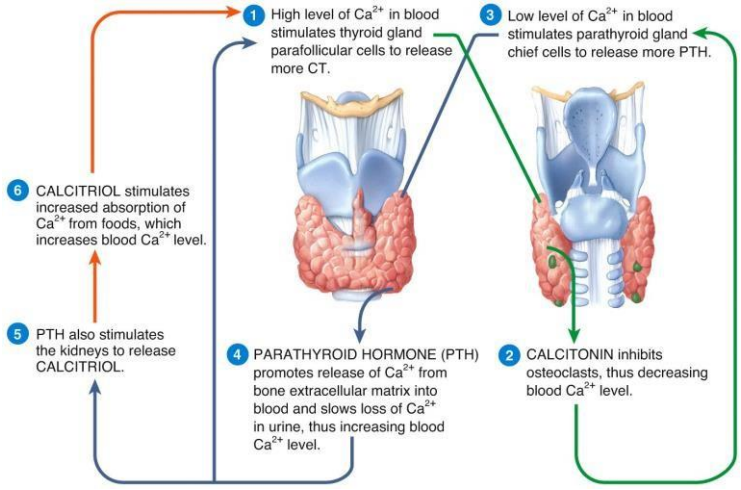
- A hormone that has as its primary function the regulation of hormone secretion of another endocrine gland is classified functionally as a tropic hormone.
- Tropic means “nourishing”.
- For example, thyroid-stimulating hormone (TSH), a tropic hormone stimulates thyroid hormone secretion by the thyroid gland and maintains the structural integrity of this gland. In the absence of TSH, the thyroid gland atrophies (shrinks) and produces very low levels of its hormones.

A tropic hormone’s actions aimed at maintaining the structural integrity of its target gland are specifically known as trophic (growth promoting) actions.

** **down-regulation (***less sensitive***) Vs. up-regulation (***more sensitive***)**
**negative-feedback control, neuroendocrine reflexes, and diurnal (circadian) rhythms.

CONTROL OF HORMONES

- Negative feedback Vs. Positive feedback



**Most hormonal regulatory systems work via negative feedback, but a few operate via positive feedback.

In a **negative feedback system the hormone output reverses a particular stimulus. (Ca/PTH)

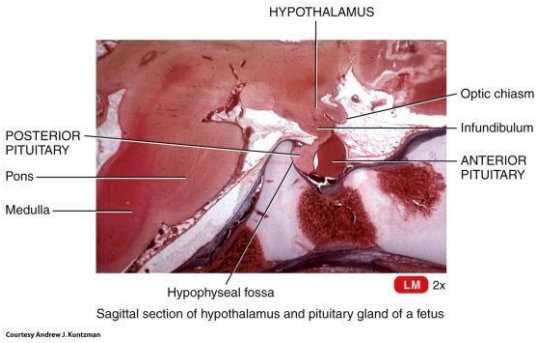
In a **positive feedback system the hormone output reinforces and encourages the stimulus. (oxytocin/childbirth)

Pituitary Hormones and Their Control by the Hypothalamus

Chapter 75

THE HYPOTHALAMUS

- The **hypothalamus** is the major link between the nervous and endocrine systems.

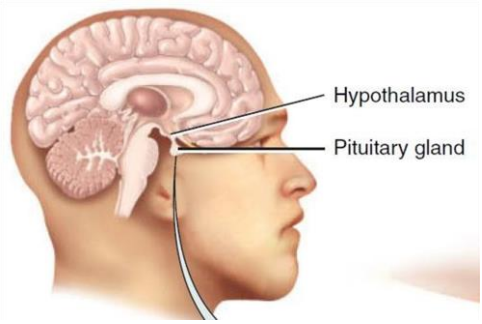


Sagittal section of hypothalamus and pituitary gland of a fetus

Courtesy Andrew J. Kuntzman

The hypothalamus receives signals from many sources in the nervous system. Thus, when a person is exposed to pain, a portion of the pain signal is transmitted into the hypothalamus. Likewise, when a person experiences some powerful depressing or exciting thought, a portion of the signal is transmitted into the hypothalamus. Olfactory stimuli denoting pleasant or unpleasant smells transmit strong signals directly and through the amygdaloid nuclei into the hypothalamus. Even the concentrations of nutrients, electrolytes, water, and various hormones in the blood excite or inhibit various portions of the hypothalamus. **Thus, the hypothalamus is a center for integrating information concerning the internal well-being of the body, and much of this information is used to control secretions of the many globally important pituitary hormones.**

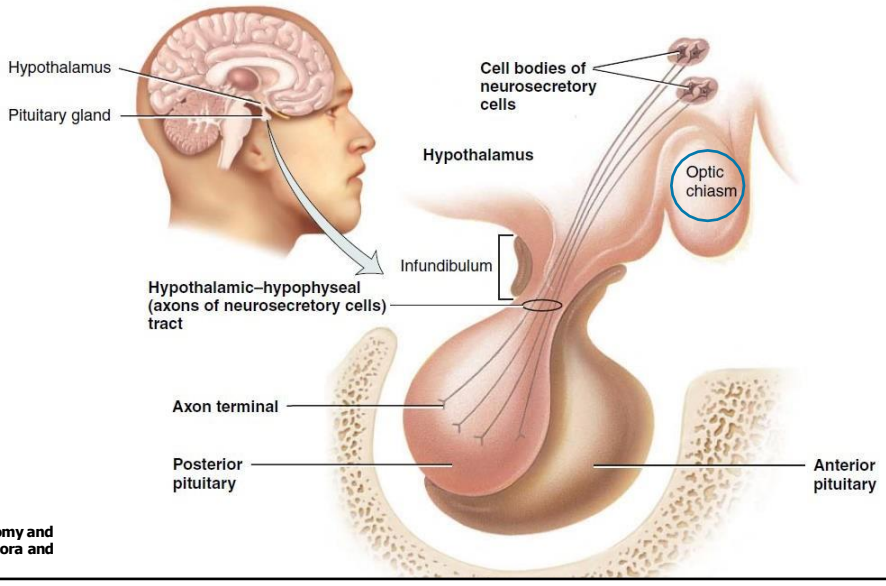
Pituitary Gland (hypophysis)



@Principles of Anatomy and Physiology, G.J. Tortora and B. Derrickson

The pituitary gland, or hypophysis, is a small endocrine gland located in a bony cavity at the base of the brain just below the hypothalamus.
The pituitary is connected to the hypothalamus by a thin connecting stalk.

Pituitary gland



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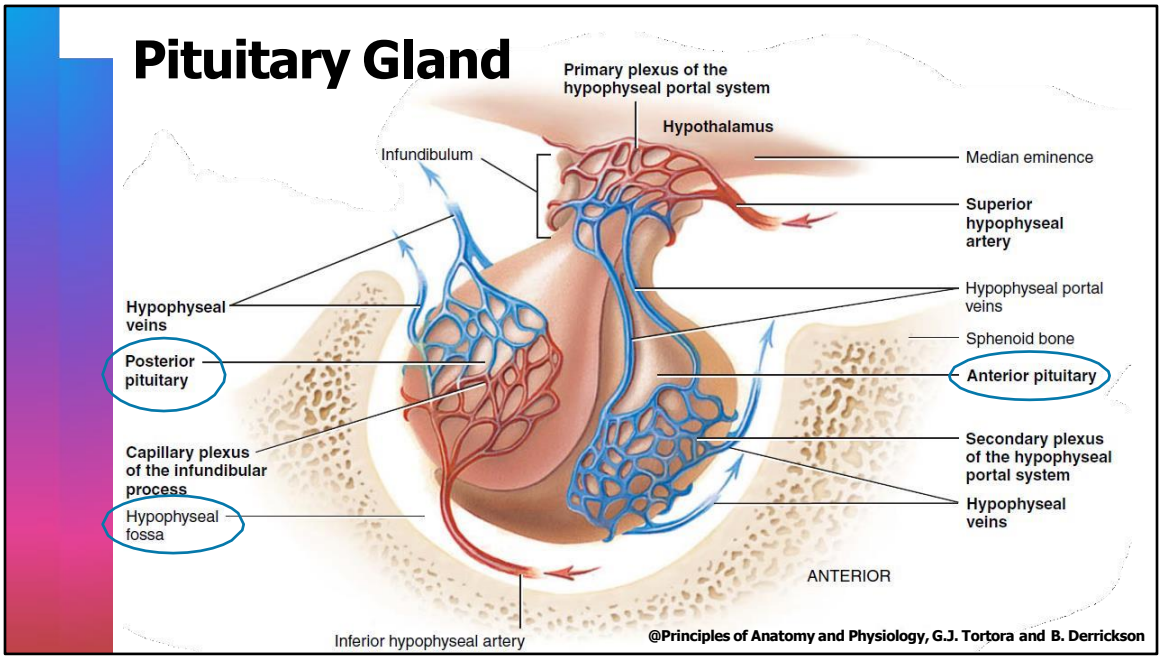


** The pituitary has two anatomically and functionally distinct lobes, the posterior pituitary and the anterior pituitary.

** The **posterior pituitary** is composed of **nervous tissue** and thus is also termed **the neurohypophysis**.

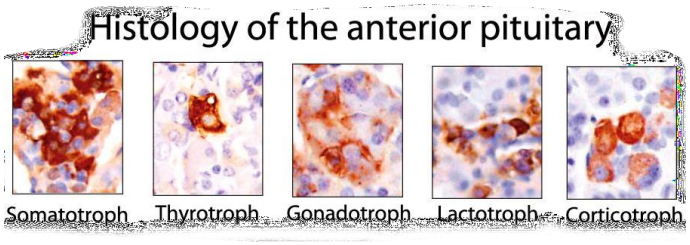
** The anterior pituitary consists of **glandular epithelial** tissue and accordingly is also called the **adenohypophysis**.

** The posterior and anterior pituitary lobes have only their location in common.

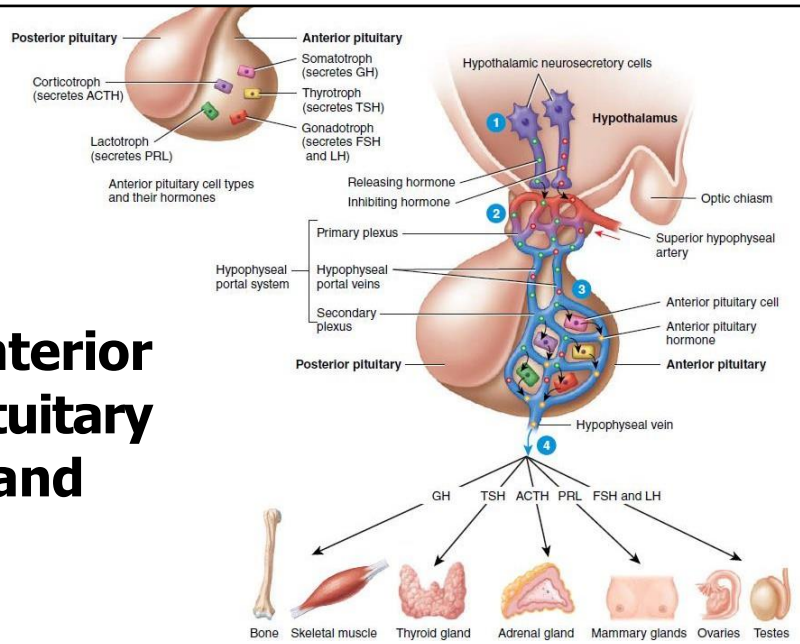
** They arise from different tissues embryonically, serve different functions, and are subject to different control mechanisms

ANTERIOR PITUITARY

- 5 types of anterior pituitary cells secrete six hormones.



Anterior pituitary gland



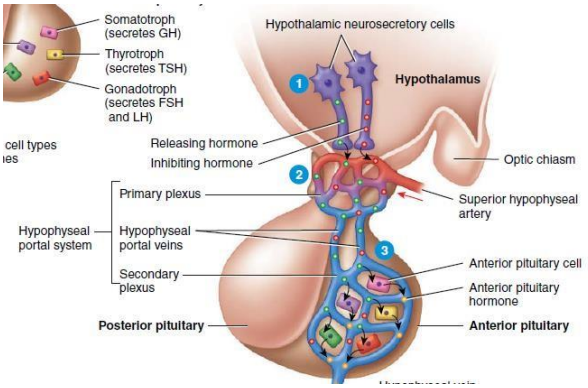
** FSH and LH are collectively referred to as gonadotropins because they control secretion of the sex hormones by the gonads.
** GH, TSH, ACTH, FSH, and LH are all tropic hormones because they each regulate secretion of another specific endocrine gland.
“” Among the anterior pituitary hormones, PRL is the only one that does not stimulate secretion of another hormone. It acts directly on nonendocrine tissue to exert its effects.
** Of the tropic hormones, FSH, LH, and GH exert effects on nonendocrine target cells in addition to stimulating secretion of other hormones.

Anterior pituitary hormones

Cell	Hormone	Chemistry	Physiological Action
Somatotropes	Growth hormone (GH; somatotropin)	Single chain of 191 amino acids	Stimulates body growth; stimulates secretion of IGF-1; stimulates lipolysis; inhibits actions of insulin on carbohydrate and lipid metabolism
Corticotropes	Adrenocorticotropic hormone (ACTH; corticotropin)	Single chain of 39 amino acids	Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculata and zona reticularis of cortex
Thyrotropes	Thyroid-stimulating hormone (TSH; thyrotropin)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids)	Stimulates production of thyroid hormones by thyroid follicular cells; maintains size of follicular cells
Gonadotropes	Follicle-stimulating hormone (FSH) Luteinizing hormone (LH)	Glycoprotein of two subunits, α (89 amino acids) and β (112 amino acids) Glycoprotein of two subunits, α (89 amino acids) and β (115 amino acids)	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis Causes ovulation and formation of the corpus luteum in the ovary; stimulates production of estrogen and progesterone by the ovary; stimulates testosterone production by the testis
Lactotropes Mammotropes	Prolactin (PRL)	Single chain of 198 amino acids	Stimulates milk secretion and production

ANTERIOR PITUITARY

- The anterior pituitary (adenohypophysis) is anatomically and functionally connected to the hypothalamus by blood vessels that form a portal system called the **hypophyseal portal system**



**In a portal system, blood flows from one capillary network into a portal vein, and then into a second capillary network before returning to the heart.

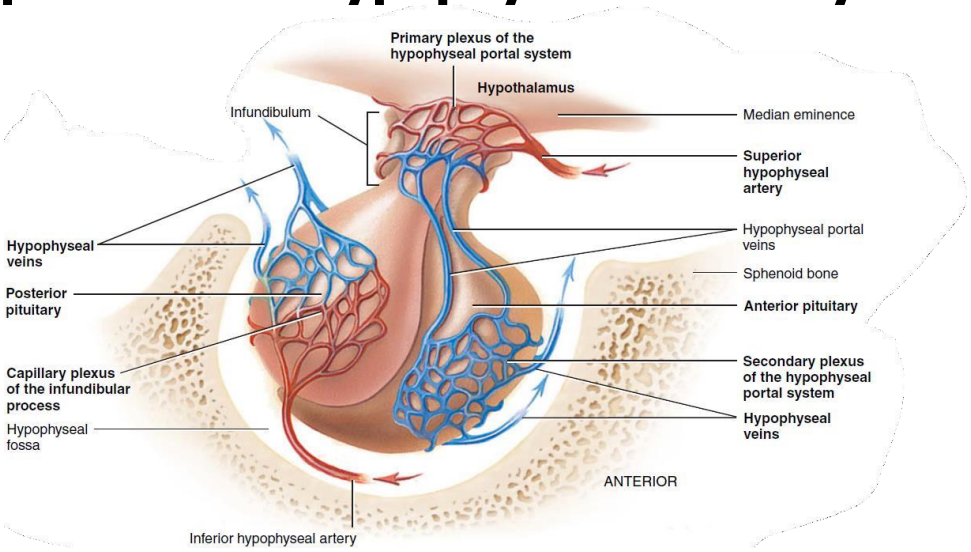
** The name of the portal system indicates the location of the second capillary network. In the **hypophyseal portal system**, blood flows from capillaries in the hypothalamus into portal veins that carry blood to capillaries of the anterior pituitary.

Hypothalamic Releasing and Inhibitory Hormones Control Anterior Pituitary Secretion

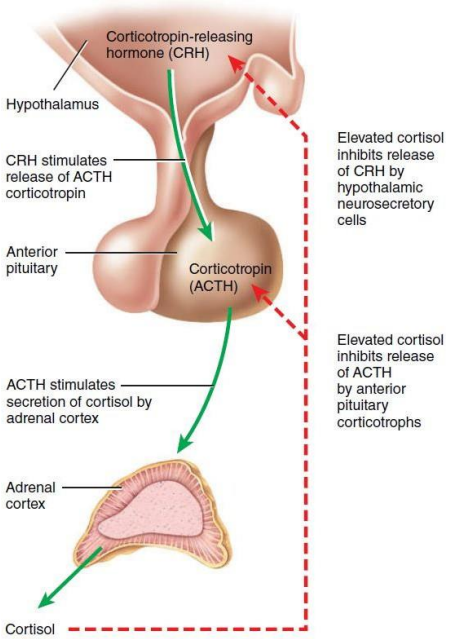
Hormone	Structure	Primary Action on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Peptide of 3 amino acids	Stimulates secretion of TSH by thyrotropes
Gonadotropin-releasing hormone (GnRH)	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes
Growth hormone-releasing hormone (GHRH)	Single chain of 44 amino acids	Stimulates secretion of growth hormone by somatotropes
Growth hormone inhibitory hormone (somatostatin)	Single chain of 14 amino acids	Inhibits secretion of growth hormone by somatotropes
Prolactin-inhibiting hormone (PIH)	Dopamine (a catecholamine)	Inhibits synthesis and secretion of prolactin by lactotropes

** The two most important factors that regulate anterior pituitary hormone secretion are hypothalamic hormones and feedback by target-gland hormones
** For most of the anterior pituitary hormones, it is the releasing hormones that are important, but for prolactin, a hypothalamic inhibitory hormone probably exerts more control.

Hypothalamic-Hypophysial Portal System

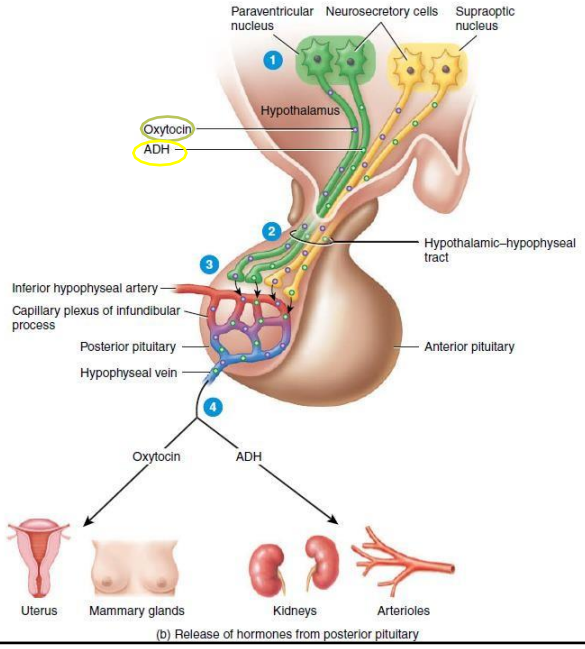


As a result, almost all blood supplied to the anterior pituitary must first pass through the hypothalamus. Because materials can be exchanged between blood and surrounding tissue only at the capillary level, the hypothalamic–hypophyseal portal system provides a "**private" route through which releasing and inhibiting hormones can be picked up at the hypothalamus and delivered immediately and directly to the anterior pituitary at relatively high concentrations, bypassing the general circulation**. If the portal system did not exist, once the hypophysiotropic hormones were picked up in the hypothalamus, they would be returned to the heart through the systemic veins, pumped through the pulmonary circulation, then returned to the heart and finally be pumped into the systemic arteries for delivery throughout the body, including the anterior pituitary. **Not only would this process take much longer, but the hypophysiotropic hormones would be considerably diluted before arriving at the anterior pituitary**



**** This three-hormone sequence is called an endocrine axis, as in the hypothalamus– pituitary–adrenal gland axis.**
**

Posterior pituitary gland



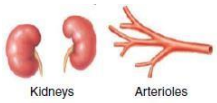
(b) Release of hormones from posterior pituitary

** The posterior pituitary gland, also called the neurohypophysis, is composed mainly of glial-like cells called pituicytes. The pituicytes do not secrete hormones; they act simply as a supporting structure for large numbers of terminal nerve fibers and terminal nerve endings from nerve tracts that originate in the supraoptic and paraventricular nuclei of the hypothalamus.

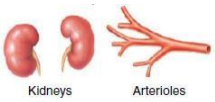
** ADH is formed primarily in the supraoptic nuclei, whereas oxytocin is formed primarily in the paraventricular nuclei. Each of these nuclei can synthesize about one sixth as much of the second hormone as of its primary hormone.

The cell bodies of the neurosecretory cells are in the **paraventricular** and **supraoptic nuclei** of the hypothalamus; their axons form the **hypothalamic-hypophyseal tract**.

This tract begins in the hypothalamus and ends (axon terminals) near blood capillaries in the posterior pituitary.



(Anti Diuretic Hormone ADH)

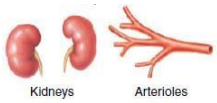


- Targets the collecting ducts in the kidney to **increase reabsorption of water.**

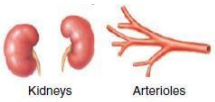
- The major control for hypothalamic-induced release of vasopressin is input from hypothalamic **osmoreceptors**, which increase ADH secretion in response to a **rise in plasma osmolarity.**

** In or near the hypothalamus are modified neuron receptors called osmoreceptors. When **the extracellular fluid becomes too concentrated**, fluid is pulled by osmosis out of the osmoreceptor **cell, decreasing** its size and **initiating** appropriate nerve signals in the hypothalamus to cause **additional ADH secretion**. Conversely, when the extracellular fluid becomes too dilute, water moves by osmosis in the opposite direction, into the cell, which decreases the signal for ADH secretion

** in the absence of ADH, the collecting tubules and ducts become almost **impermeable to water**, which **prevents significant reabsorption** of water and therefore allows **extreme loss of water into the urine**, also causing extreme dilution of the urine, a condition called **central diabetes insipidus**. Conversely, in the presence of high levels of ADH, the permeability of the collecting ducts and tubules to water increases greatly and allows most of the water to be reabsorbed as the tubular fluid passes through these ducts, thereby conserving water in the body and producing very concentrated urine.



(ADH/ VASOPRESSIN)



- Causes contraction of arteriolar smooth muscle.
- A less powerful input from the left atrial volume receptors increases vasopressin secretion in response to **a fall in ECF volume and arterial blood pressure.**

** The **atria have stretch receptors** that are **excited by overfilling**. When excited, they send signals to the brain to inhibit **ADH secretion**. Conversely, when the receptors are unexcited as a result of underfilling, the opposite occurs, with greatly increased ADH secretion.
** Decreased stretch of the baroreceptors of the carotid, aortic, and pulmonary regions also stimulates ADH secretion.

OXYTOCIN

- Targets smooth muscle in the uterus and breasts. In the uterus, oxytocin stimulates **uterine contractions**, and in response to the sucking from an infant, oxytocin stimulates "**milk letdown/milk ejection.** " in the breasts.
- Appropriately, oxytocin secretion is increased by reflexes that originate within the **birth canal during childbirth** and by reflexes that are triggered when the **infant suckles** the breast.
- Oxytocin influences a variety of behaviors (bonding, or attachment).

Hypothalamus Controls Pituitary Secretion

- Almost all secretion by the pituitary is controlled by either hormonal or nervous signals from the hypothalamus.
- The hypothalamus receives signals from many sources in the nervous system :pain, depressing or exciting thoughts, olfactory stimuli, concentrations of nutrients, electrolytes, water.

** All or most of the hypothalamic hormones are secreted at nerve endings in the median eminence before being transported to the anterior pituitary gland. Electrical stimulation of this region excites these nerve endings and, therefore, causes release of essentially all the hypothalamic hormones. However, the neuronal cell bodies that give rise to these median eminence nerve endings are located in other discrete areas of the hypothalamus or in closely related areas of the basal brain.
** when the pituitary gland is removed from its normal position beneath the hypothalamus and transplanted to some other part of the body, its rates of secretion of the different hormones (except for prolactin) fall to very low levels.