# Mechanisms of the hormone action

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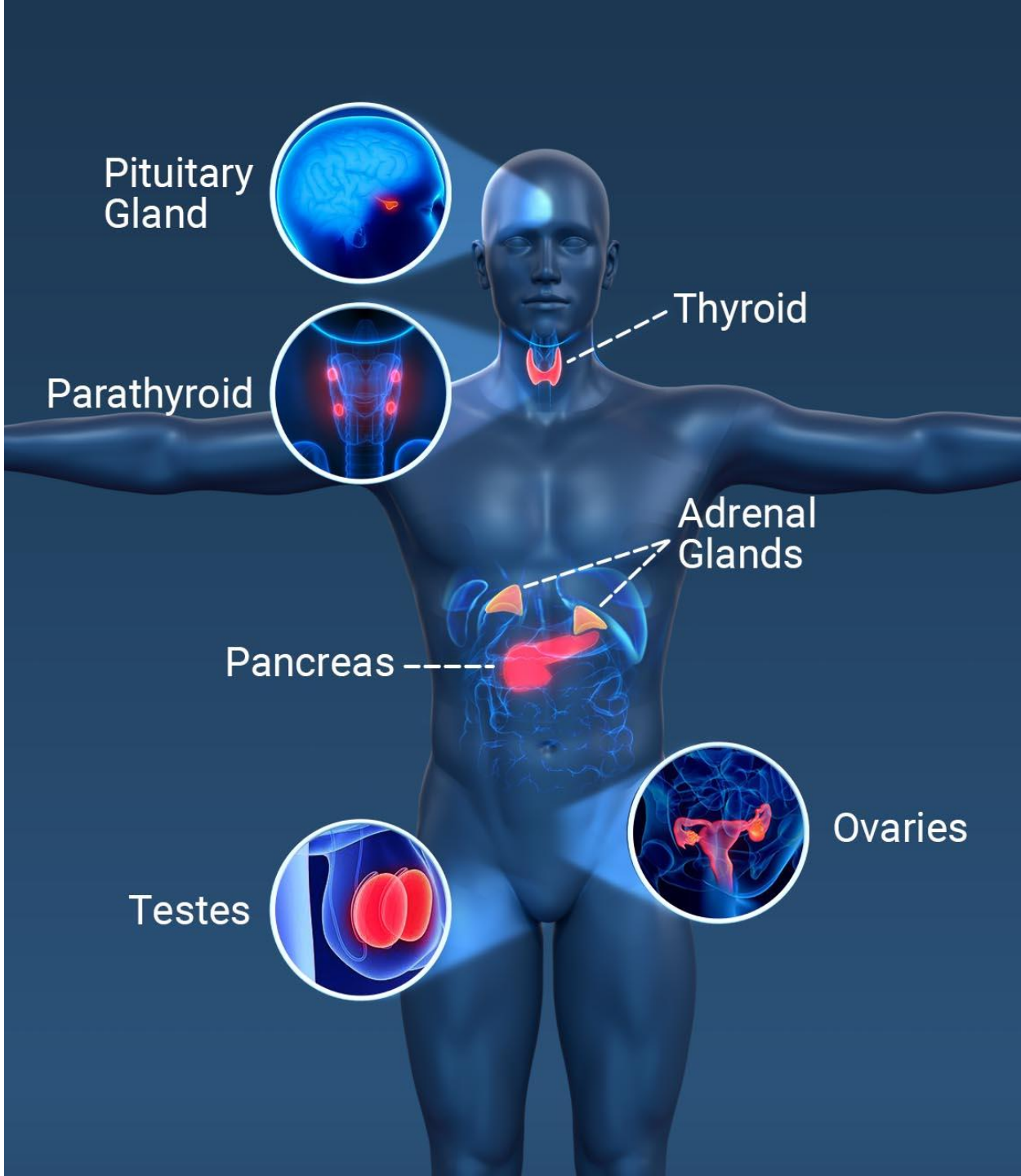


# Outline

- Mechanism of Hormone action
- Location of receptors
- The action of protein hormones (second Messenger action)
- The action of steroid hormones
- Hypothalamus and Pituitary glands

# Objectives

- Understanding the mechanism of action of hormones
- Understanding
- Understanding the process of signal amplification
- Explaining the main hormones of Hypothalamus and pituitary glands

# Mechanisms of the hormone action

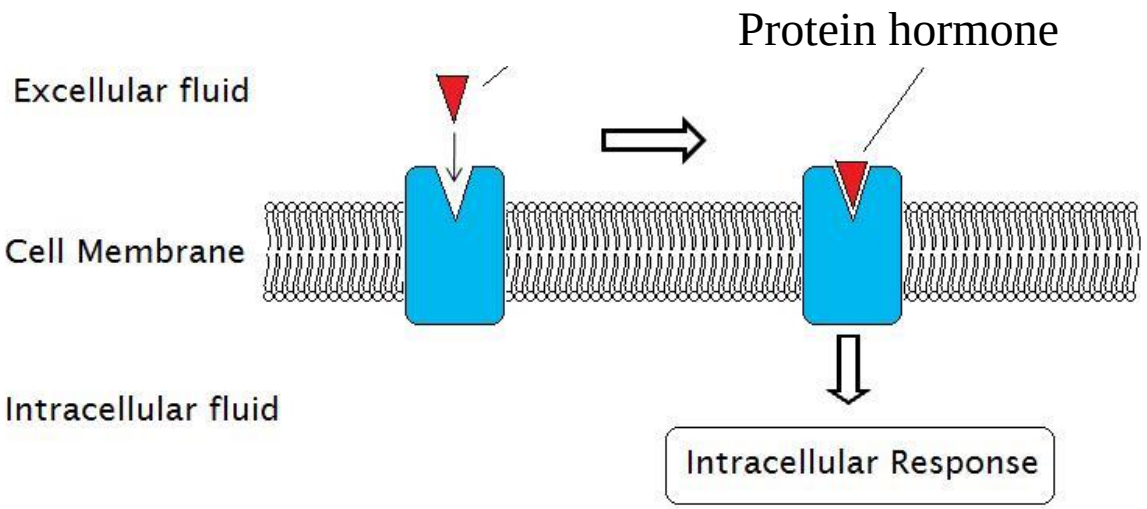
- Each hormone has **target cells**
- **Target cells** are specific cells that have receptors needed to bind hormones and respond to their presence.
- A hormone will affect only those cells that have their specific receptors.
- To initiate changes in target cells, hormones first bind to specific receptor molecules.
- **Receptor** is a molecule inside or on the surface of a cell (target cell) that binds to hormone

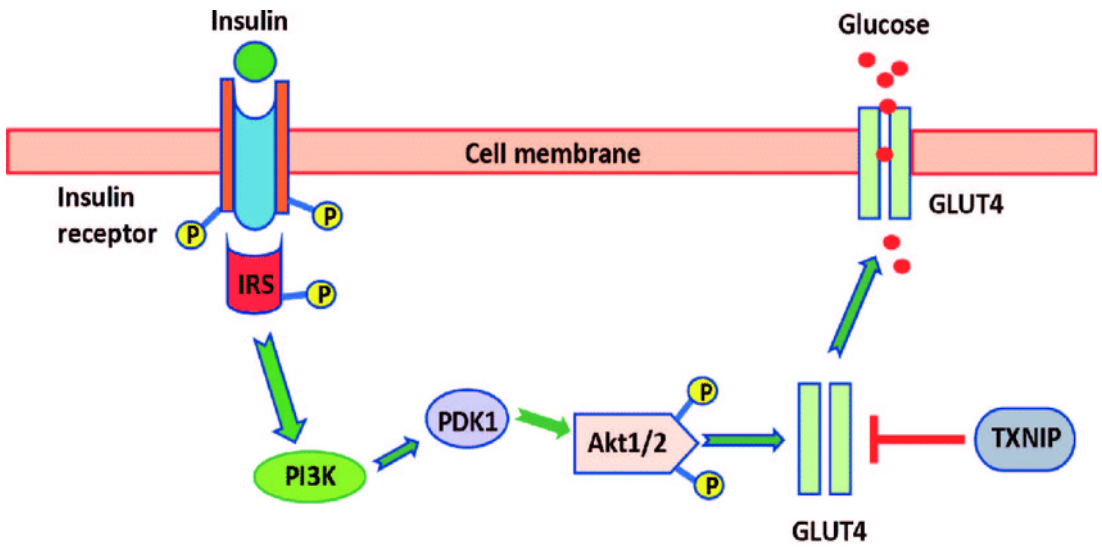
Hormone receptors are classified depending on their **cellular localization** into

1. Cell membrane receptors
2. Intracellular receptors

# Location of receptors for hormone

## 1. Cell membrane receptors

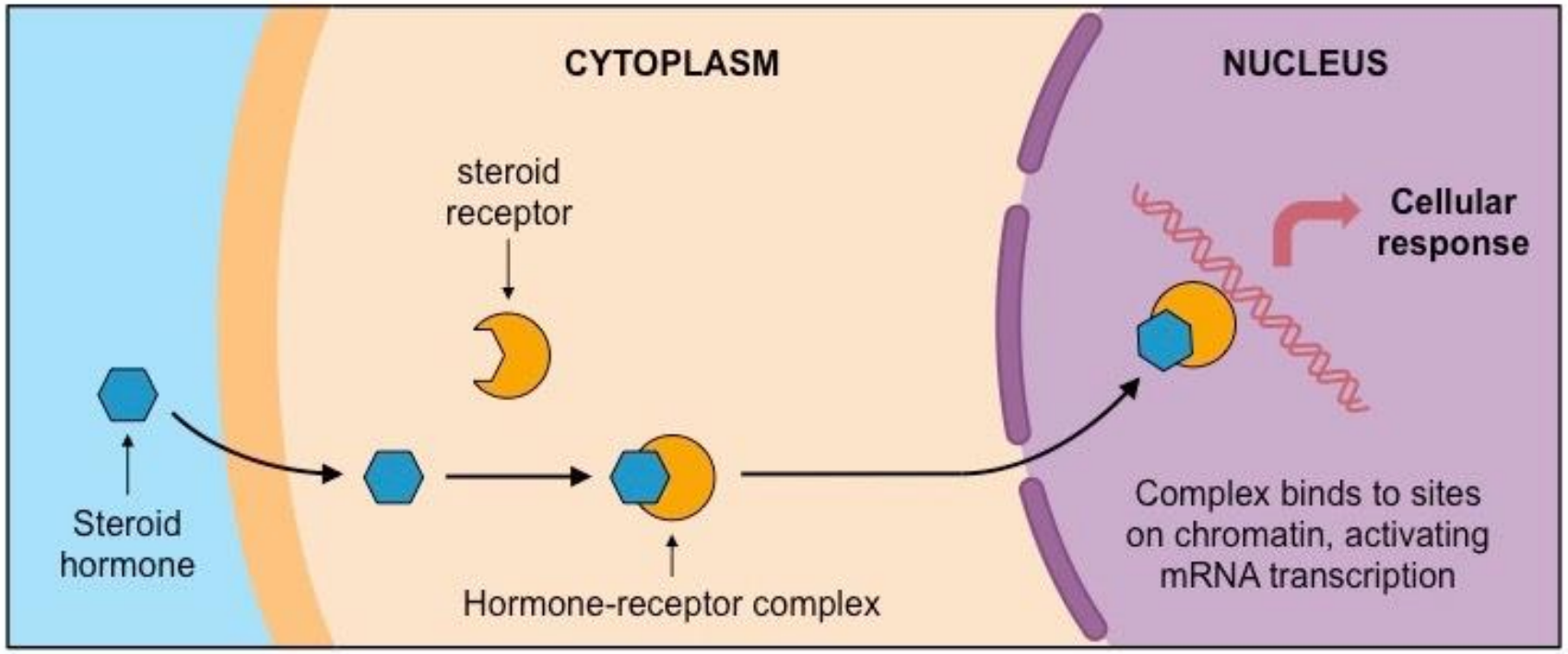



- **Hydrophilic hormones** bind to cell-surface receptors.
- **Protein** and **Peptide hormone** are unable to cross the cell membrane lipid bilayer and in general bind to **cell membrane receptors.**

# Location of receptors for hormone

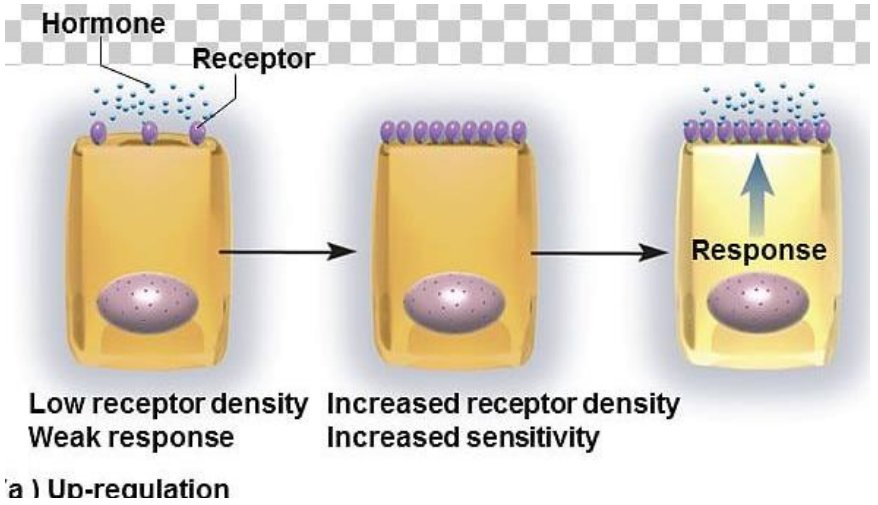
## 2. Intracellular receptors



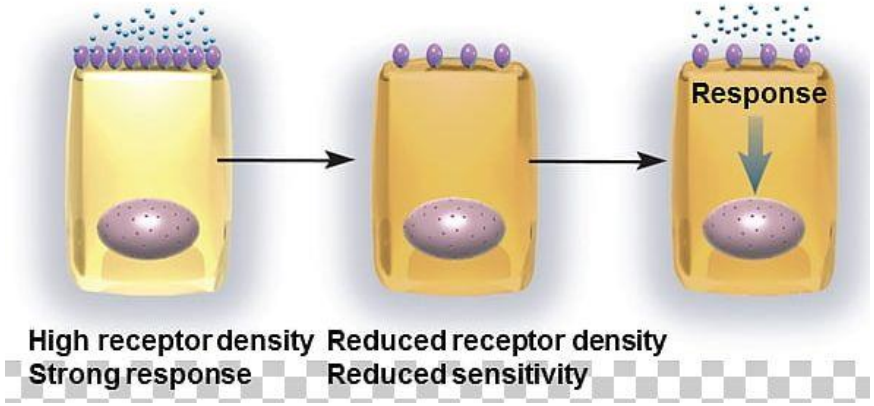

- **Hydrophobic hormones** bind to intracellular receptors
- **Steroid hormones** are lipid soluble, cross the plasma membrane, and bind to **intracellular receptors**.

# Upregulation and downregulation of receptors

**Upregulation** is the process by which a cell increases its response to a substance or signal from outside the cell to carry out a specific function. For example, a cell may increase the number or activity of protein receptors or other molecules on its surface to make it more sensitive to a hormone or drug.




**Receptor downregulation** is characterized by a decrease in total receptor number in the cell due to **endocytosis** and subsequent degradation of the receptors caused by long-term exposure to hormones

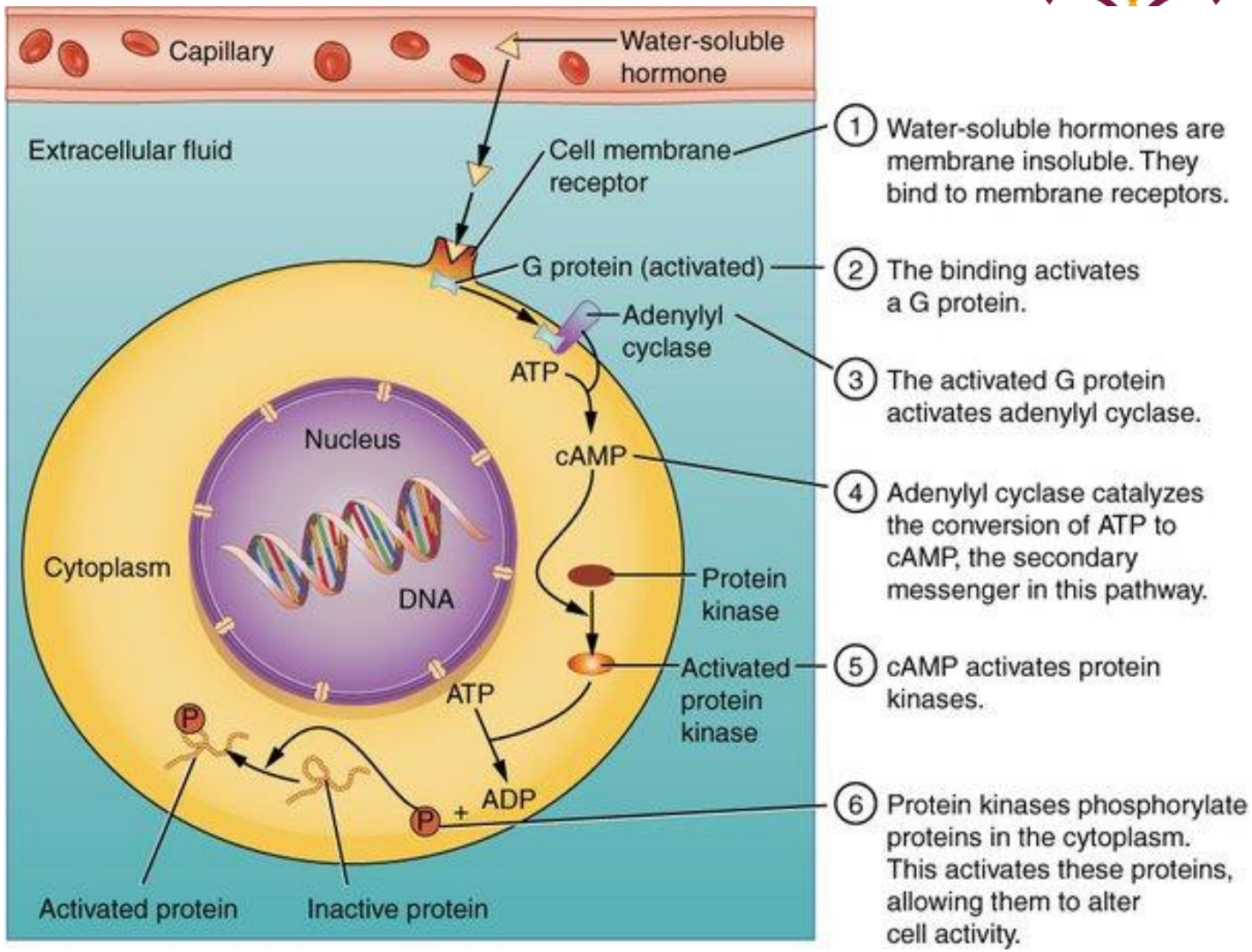


# Mechanisms of the hormone action

- To initiate changes in target cells, hormones first bind to specific receptor molecules.
- Hormone molecules exert their effects **by producing biochemical changes** in target cells
- The hormones exert their effects on their target organs involves **several complex processes**
- Hormones influence **cellular operations** by changing the types, activities, or quantities of key cytoplasmic enzymes.
- **Enzymes** control all **cellular activities** and **metabolic reactions**

# The action of protein hormones (second Messenger action)

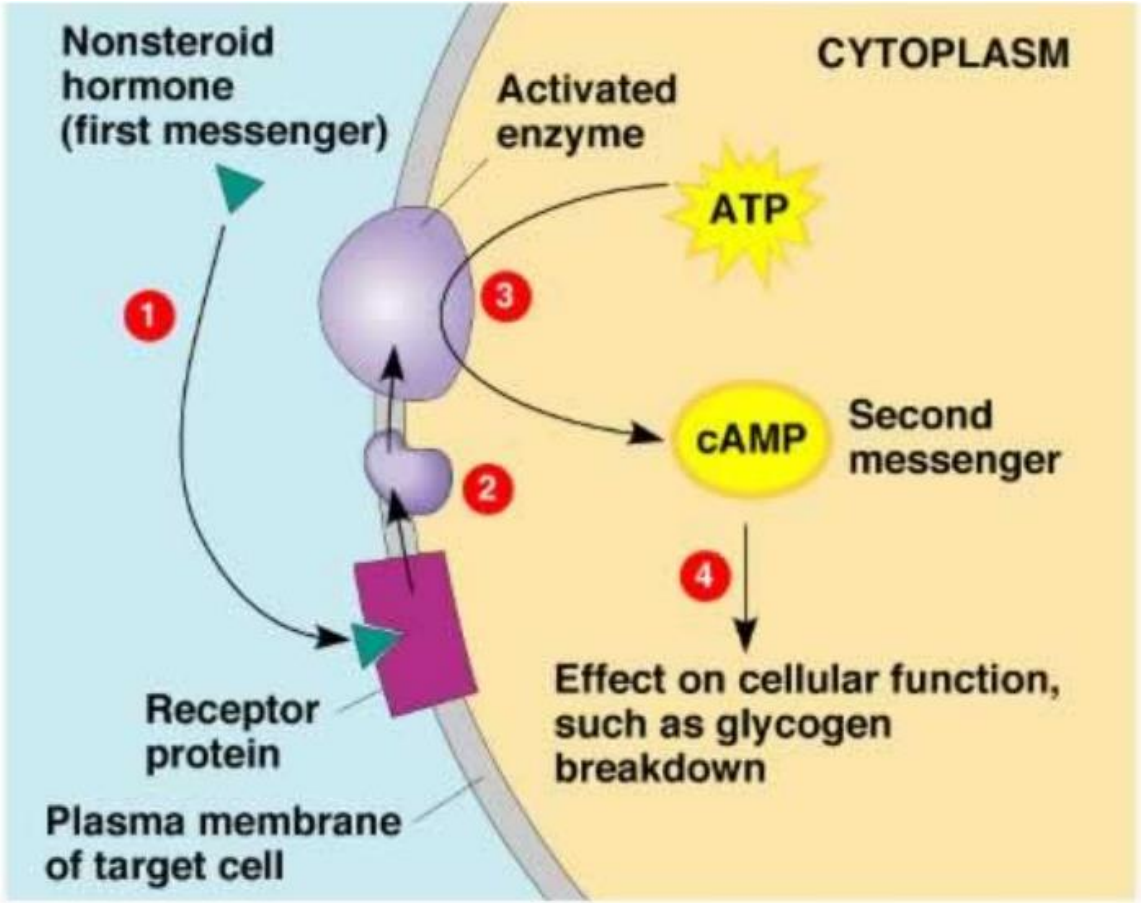
1. Protein and peptide hormones bind to receptors of the cell membrane, and the hormone is called the **first messenger**
2. The binding of membrane insoluble hormones activate **G proteins**
3. The activated G protein activates **adenylate cyclase** in cell membrane
4. Adenylate cyclase synthesizes a substance called **cyclic adenosine monophosphate (cyclic AMP or cAMP)** from **ATP**, and cyclic AMP is the **second messenger**
5. Cyclic AMP activates specific enzymes within the cell, which bring about the cell's characteristic response to the hormone.



# The responses of target cells to hormones include

1. A change in the permeability of the cell membrane to a specific substance,
2. An increase in protein synthesis
3. Activation of other enzymes
4. Or the secretion of a cellular product.

# The second-messenger mechanism–protein hormones




| (a) Signaling pathway | (b) Number of molecules activated |
|---|---|
| RECEPTION<br>Binding of epinephrine to G protein-linked receptor | 1 molecule |
| TRANSDUCTION<br>Inactive G protein → Active G protein | $10^2$ molecules |
| Inactive adenylyl cyclase → Active adenylyl cyclase | $10^2$ molecules |
| ATP → Cyclic AMP | $10^4$ molecules |
| Inactive protein kinase A → Active protein kinase A | $10^4$ molecules |
| Inactive phosphorylase kinase → Active phosphorylase kinase | $10^5$ molecules |
| Inactive glycogen phosphorylase → Active glycogen phosphorylase | $10^6$ molecules |
| RESPONSE<br>Glycogen → Glucose-1-phosphate | $10^8$ molecules |

- **Two other second-messenger** systems begin with one of the phospholipids in the plasma membrane. When activated by certain hormones, the receptor activates a G protein linked to a nearby enzyme, ***phospholipase***, in the plasma membrane. ***Phospholipase*** splits a membrane **phospholipid** into two fragments—a small phosphate-containing piece called **inositol triphosphate (IP3)**, and a larger piece, the triglyceride backbone with two fatty acids still attached, called **diacylglycerol (DAG).**

- **IP3** and **DAG** are the second messengers that go on to activate a wide variety of metabolic changes in the target cells, depending on what cells are involved and what internal signaling pathways they use.

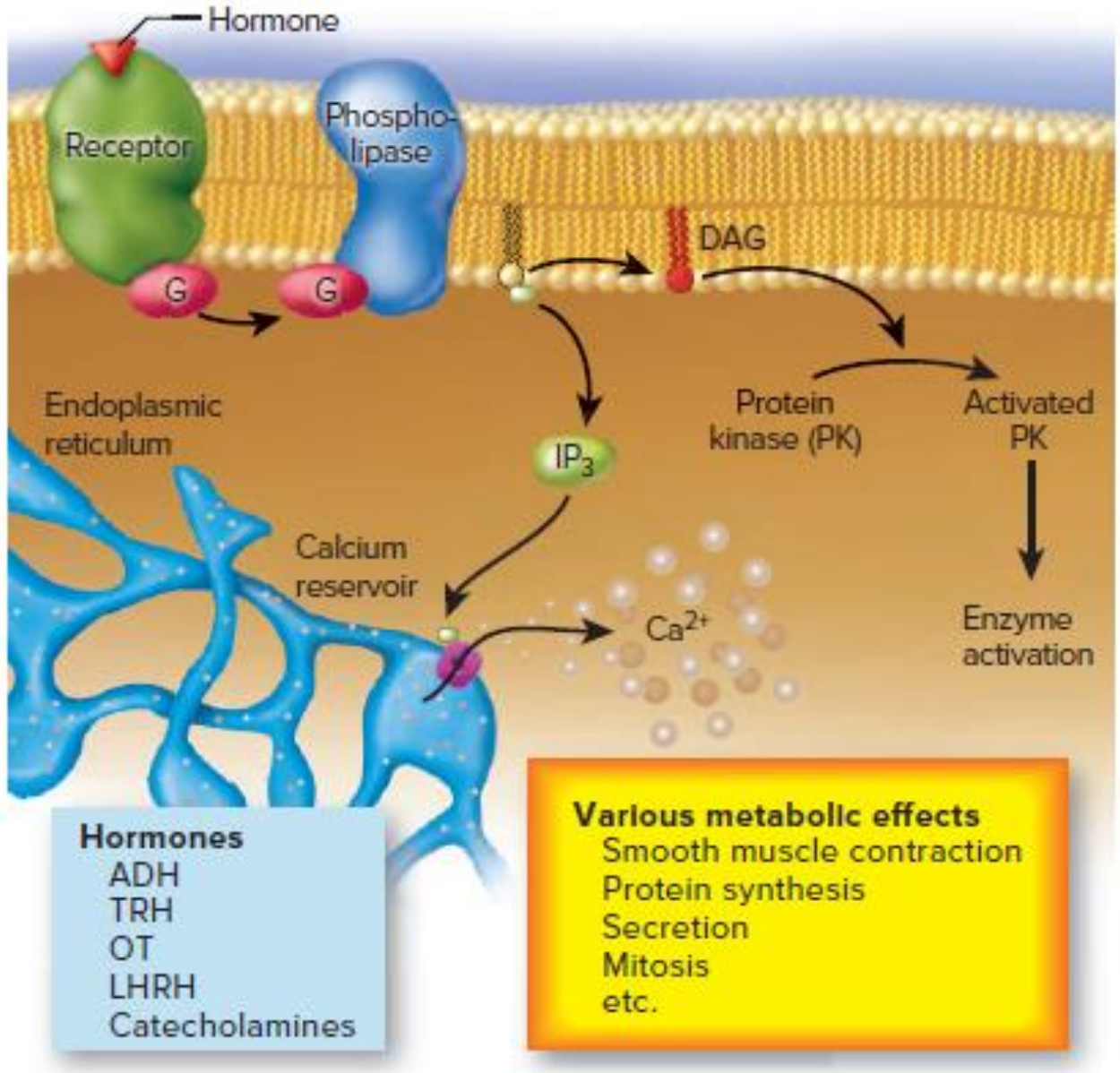
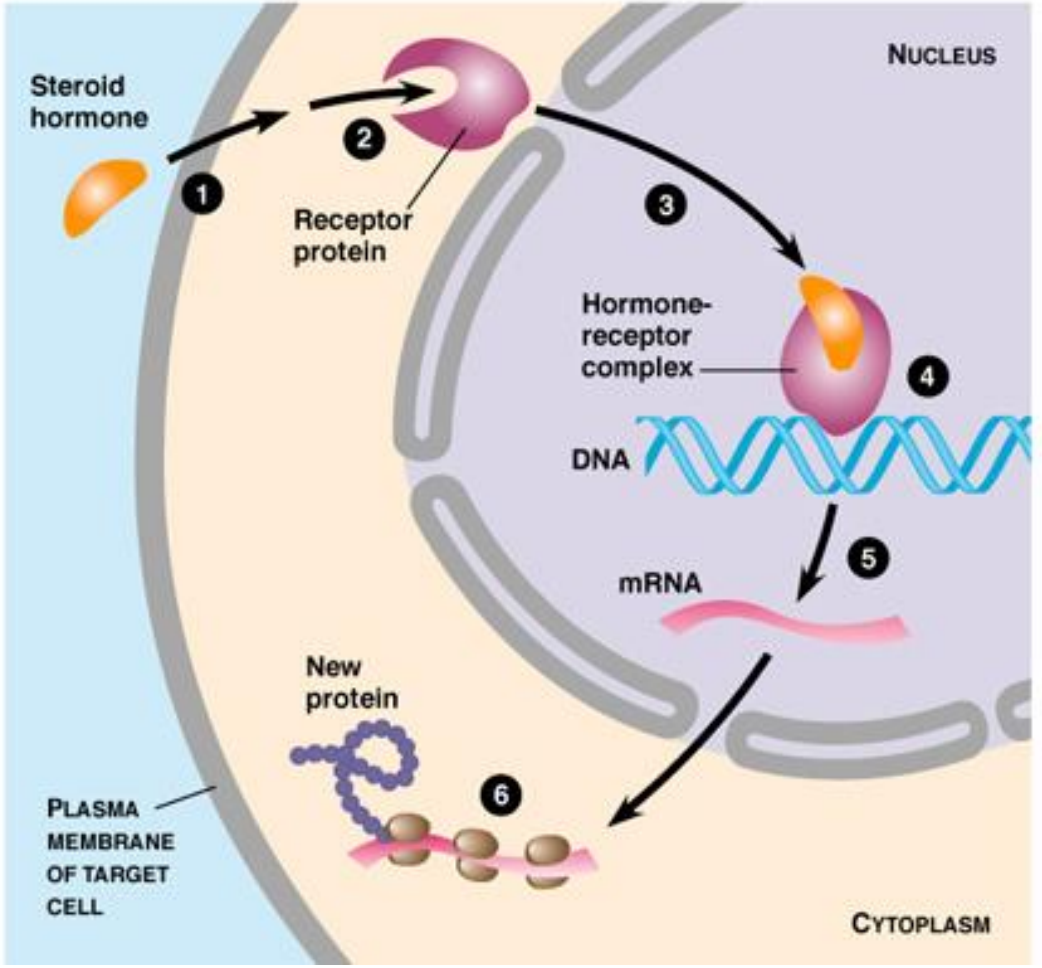



**FIGURE 17.20 Diacylglycerol (DAG) and Inositol Triphosphate ($IP_3$) Second-Messenger System.** These are employed by hormones listed in the blue box.

# The action of steroid hormones

1. Steroid hormones are soluble in the lipids of the cell membrane and diffuse easily into a target cell
2. Once inside the cell, the steroid hormone combines with a protein receptor in the cytoplasm, and
3. This steroid-protein complex enters the nucleus of the cell.
4. Within the nucleus, the steroid-protein complex activates specific genes
5. Which begin the process of mRNA synthesis
6. And then protein synthesis. The enzymes produced bring about the cell's characteristic response to the hormone



# Response time of target cells to hormones

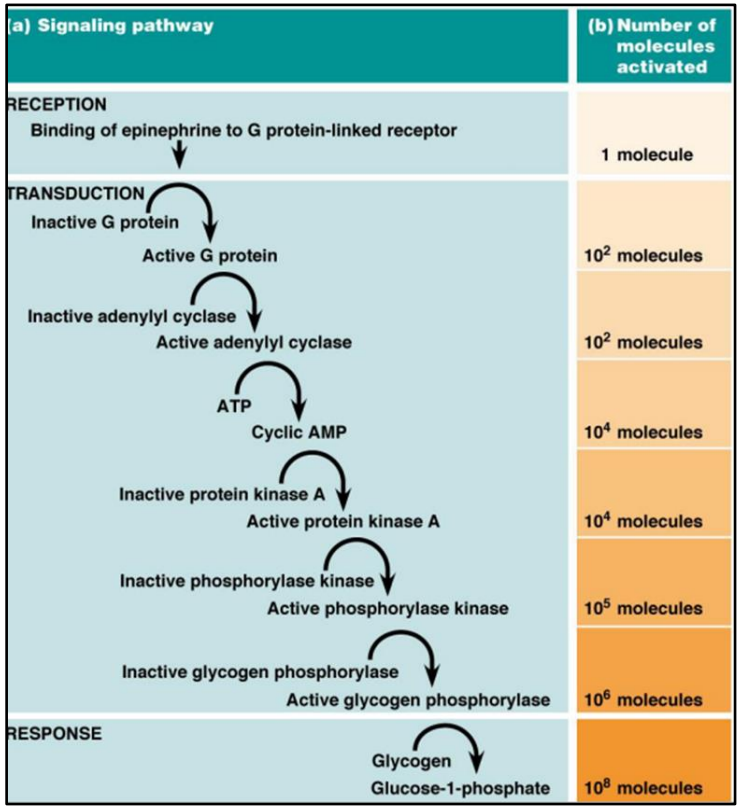
The responses of target cells to hormones occur with a **delay**

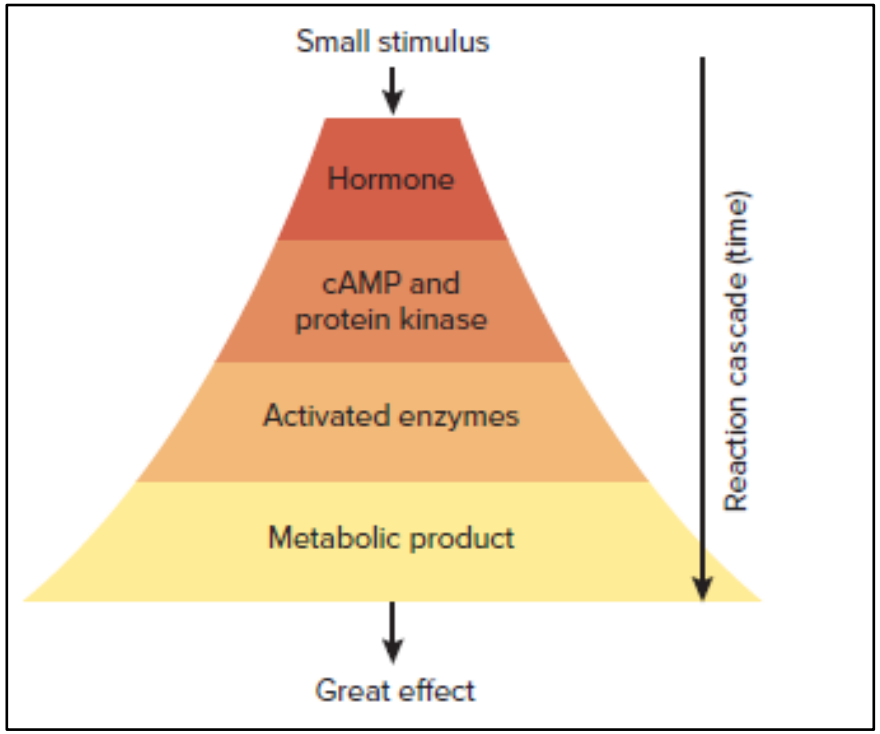
Two main factors contribute to slowed responses to endocrine signals

1. hormones require travel time to reach target cells.
2. Certain hormones control gene transcription and the synthesis of proteins by target cells, so the responses they initiate are exhibited only after a delay, when protein synthesis is accomplished.

# Signal Amplification

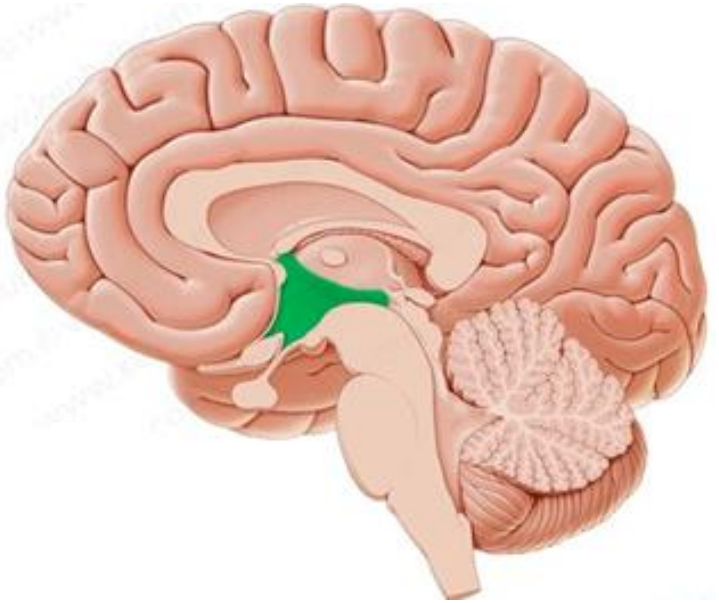
- Hormones are extraordinarily potent chemicals. Through a mechanism called **signal amplification** (or the **cascade effect**), one hormone molecule triggers the synthesis of not just one enzyme molecule but an enormous number



# Hypothalamus

- **The hypothalamus** is a gland in human brain that controls human hormone system. It releases hormones to another part of human brain called the pituitary gland, which sends hormones out to different organs.
- Funnel shaped
- Form wall of third brain ventricle
- Connects the nervous system to the endocrine system



- **Hypothalamus produce nine hormones**
- **Seven** of them, as shown in table, travel through the **portal system** and regulate the activities of the **anterior pituitary**

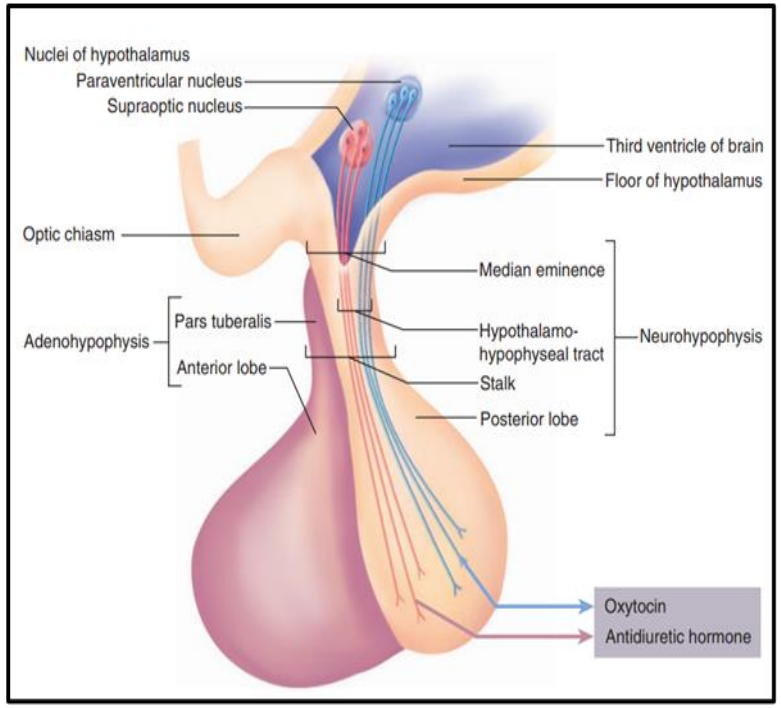
| Hormone | Principal Effects |
|---|---|
| TRH: Thyrotropin-releasing hormone | Promotes TSH and PRL secretion |
| CRH: Corticotropin-releasing hormone | Promotes ACTH secretion |
| GnRH: Gonadotropin-releasing hormone | Promotes FSH and LH secretion |
| PRH: Prolactin-releasing hormone | Promotes PRL secretion |
| PIH: Prolactin-inhibiting hormone | Inhibits PRL secretion |
| GHRH: Growth hormone–releasing hormone | Promotes GH secretion |
| Somatostatin | Inhibits GH and TSH secretion |

- **Gonadotropin-releasing hormone**, however, controls the release of both follicle-stimulating hormone and luteinizing hormone.
- **Somatostatin** is also called growth hormone–inhibiting hormone. Its name derives from **somatotropin**, a synonym for **growth hormone (GH)**.
- The other **two** hypothalamic hormones are secreted by way of the **Posterior pituitary**

**Oxytocin (OT)----------→paraventricular nuclei** of the hypothalamus

**ADH ----------→ supraoptic nuclei.**

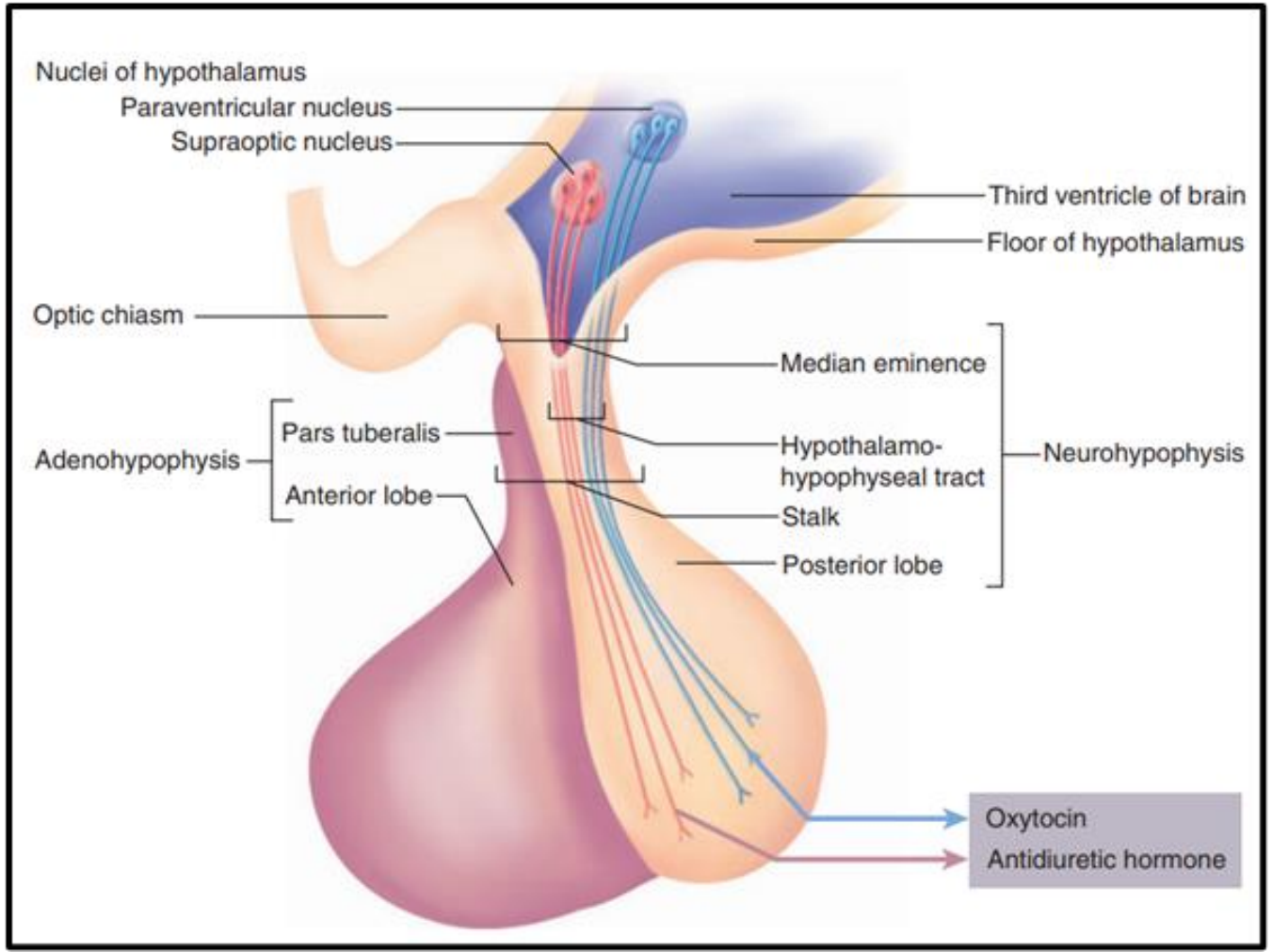
Hypothalamus regulates primitive functions of the body ranging from water balance and thermoregulation to sex drive and childbirth. **Many of its functions are carried out by way of the pituitary gland**, which is closely associated with it both anatomically and physiologically.



## Pituitary gland

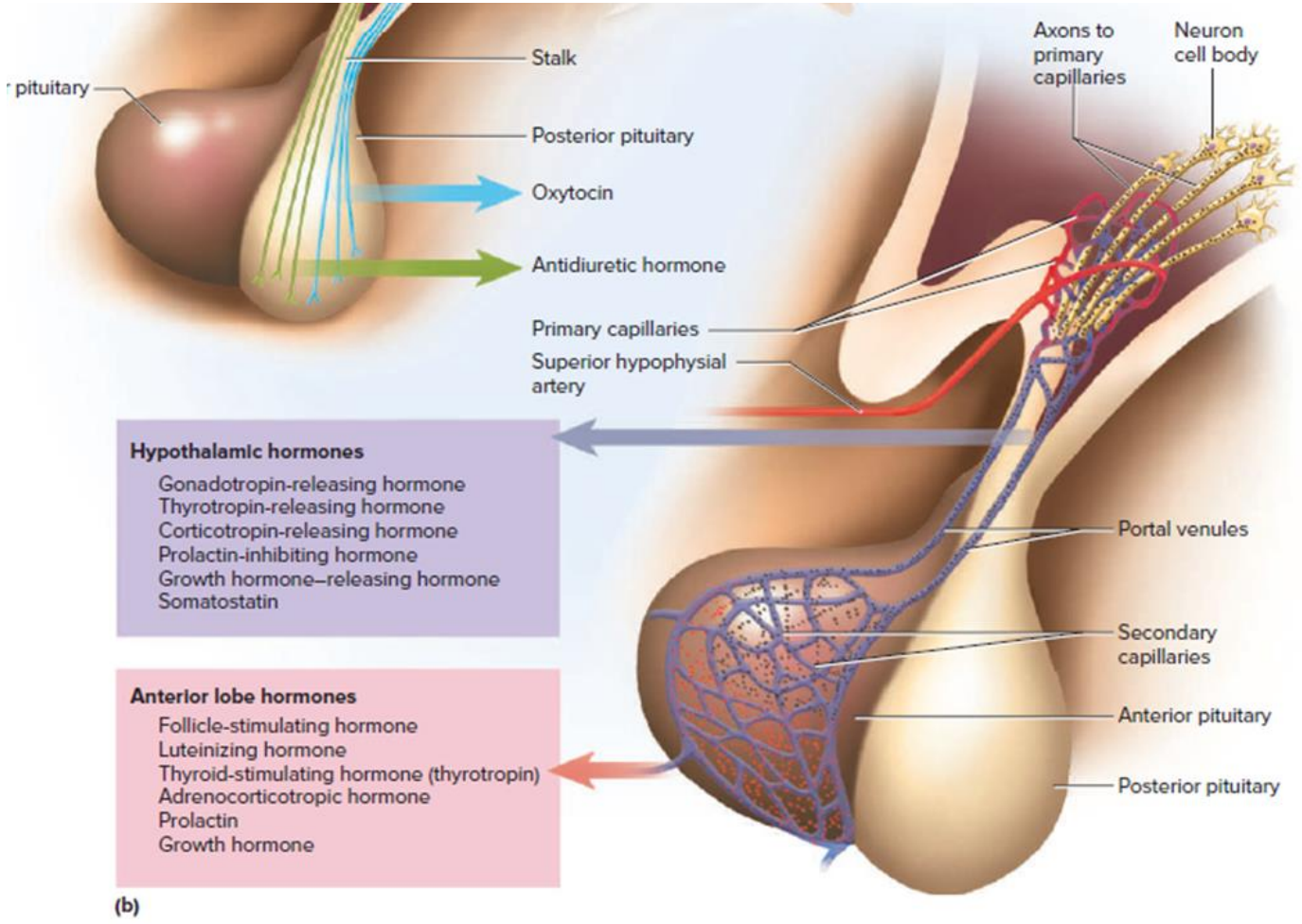
The pituitary gland (hypophysis) is suspended from the floor of the hypothalamus by a stalk (infundibulum) and housed in a depression of the sphenoid bone, the sella turcica

kidney bean; it grows about 50% larger in pregnancy



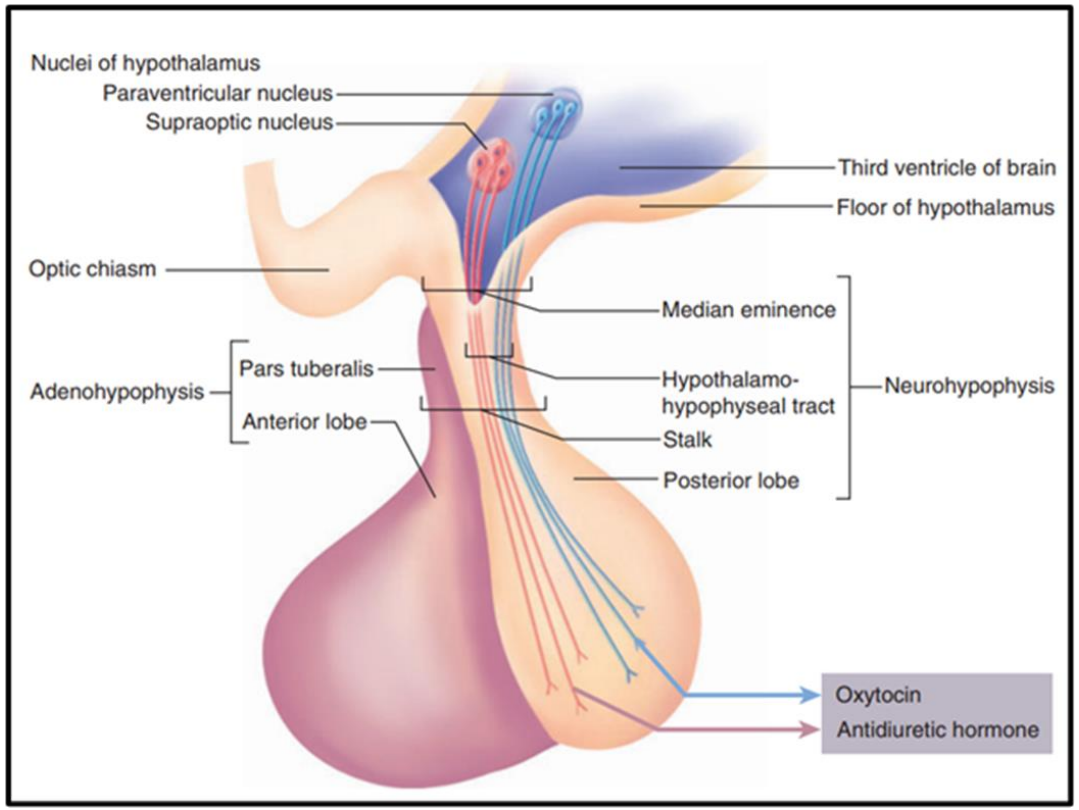
**The anterior pituitary**, also called the **adenohypophysis**

It has no nervous connection to the hypothalamus **hypophysial portal system**



# The posterior pituitary neurohypophysis

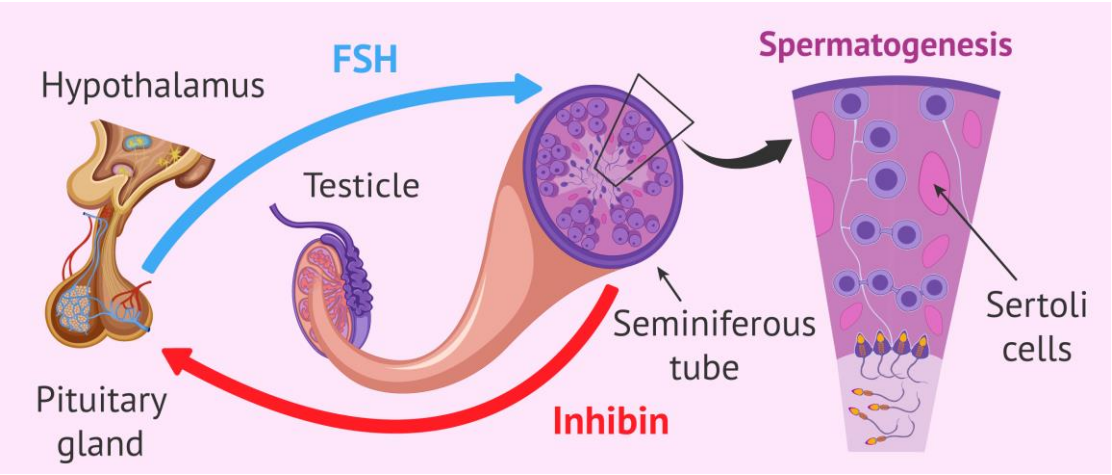
- **The posterior pituitary is nervous tissue**, not a true gland
- Hormones of the posterior pituitary are made by certain neuroendocrine cells in the hypothalamus
- **hypothalamo–hypophysial tract**
- Hormones are stored in the nerve endings until a nerve signal coming down the same axons triggers their release

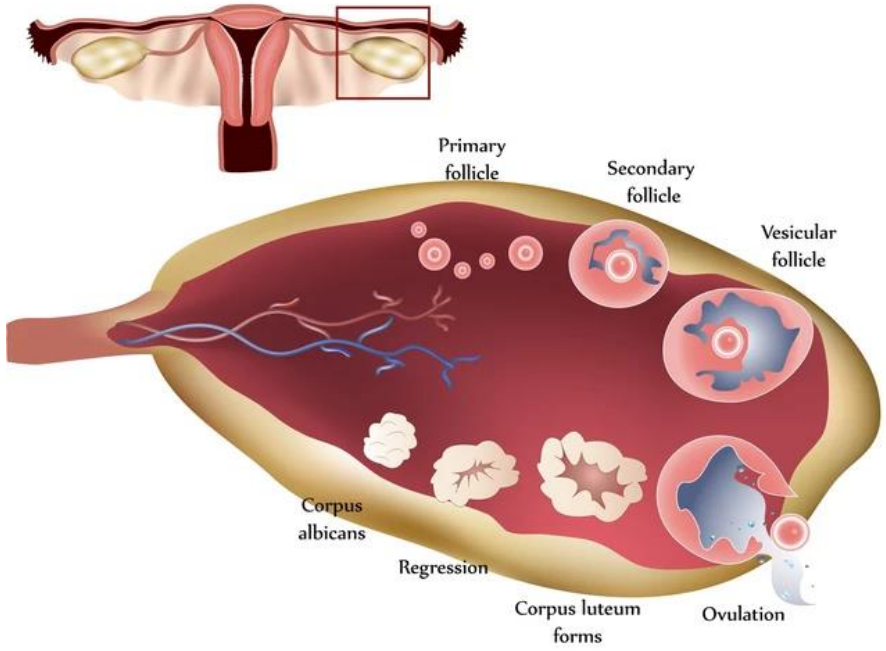


# Anterior pituitary Hormones

## 1. Follicle-stimulating hormone (FSH).

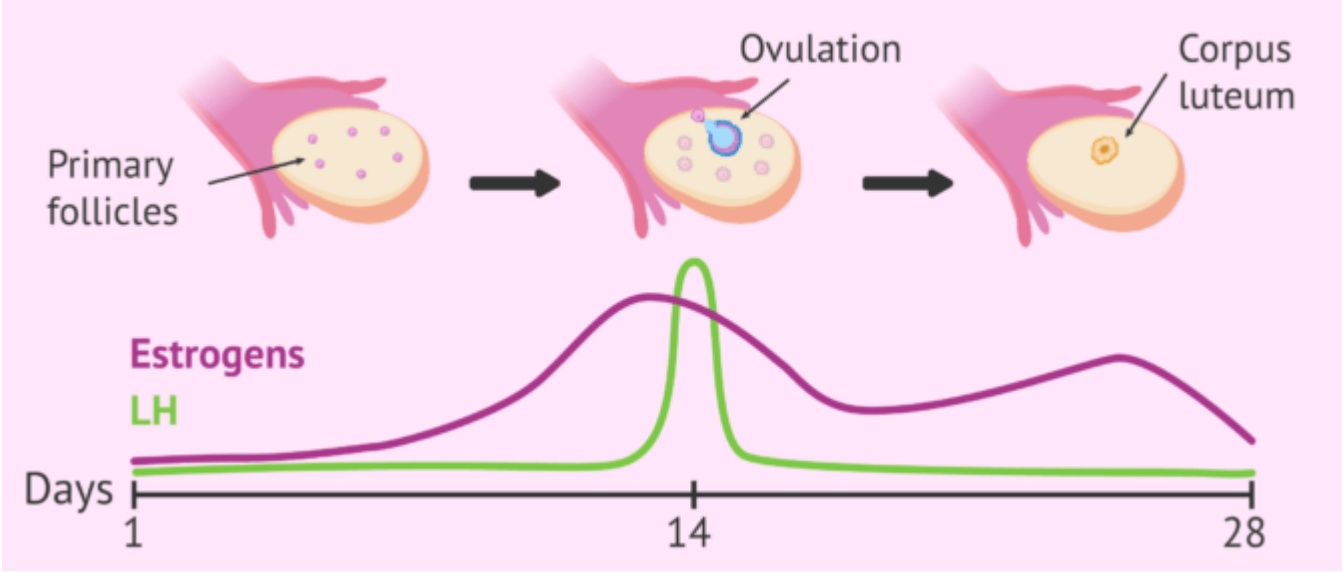
- FSH is secreted by gonadotropic cells. In the ovaries, it stimulates the secretion of ovarian sex hormones and the development of the bubble-like follicles that contain the eggs.
- In the testes, it stimulates sperm production.



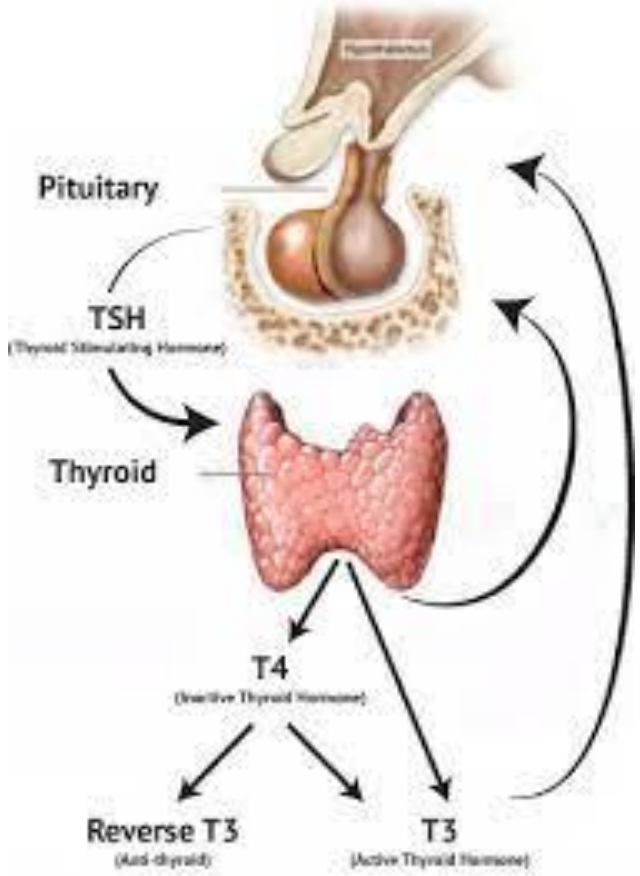
# 2-Luteinizing hormone (LH).

- LH is also secreted by the gonadotropic cells. In females, it **stimulates ovulation** the release of an egg. It is named for the fact that after ovulation, the follicle becomes a yellowish body called the corpus luteum. LH also stimulates the corpus luteum to secrete **progesterone**, a hormone important in pregnancy. In males, LH stimulates the testes to secrete **testosterone**.



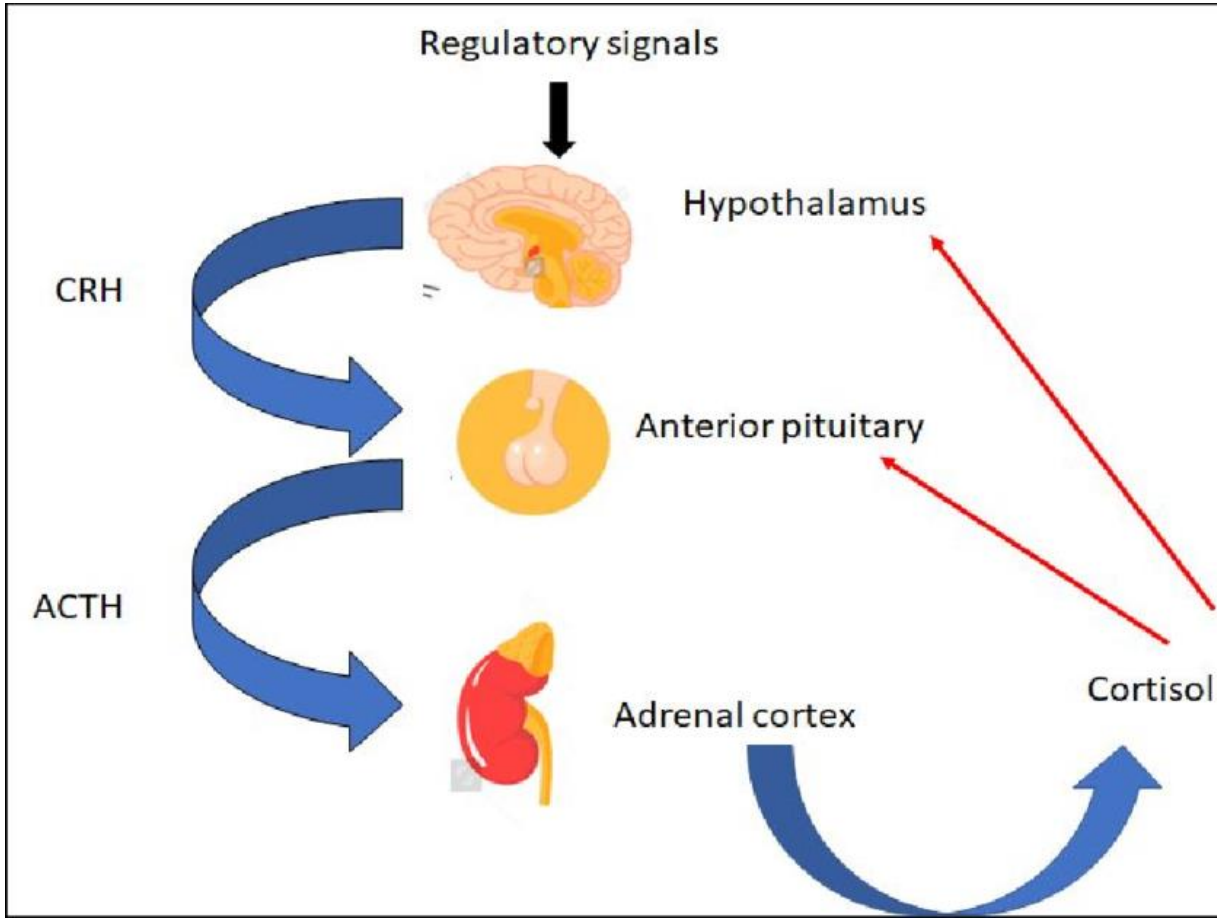
# 3-Thyroid-stimulating hormone (TSH), or thyrotropin.

- TSH is secreted by pituitary cells called *thyrotropic cells*. It stimulates growth of the thyroid gland and the secretion of thyroid hormones (T3 and T4) , which have  widespread effects on metabolic rate, body temperature, and other functions detailed later.
- The secretion of TSH is stimulated by **thyrotropin-releasing hormone (TRH)** from the hypothalamus. When metabolic rate (energy production) decreases, TRH is produced.



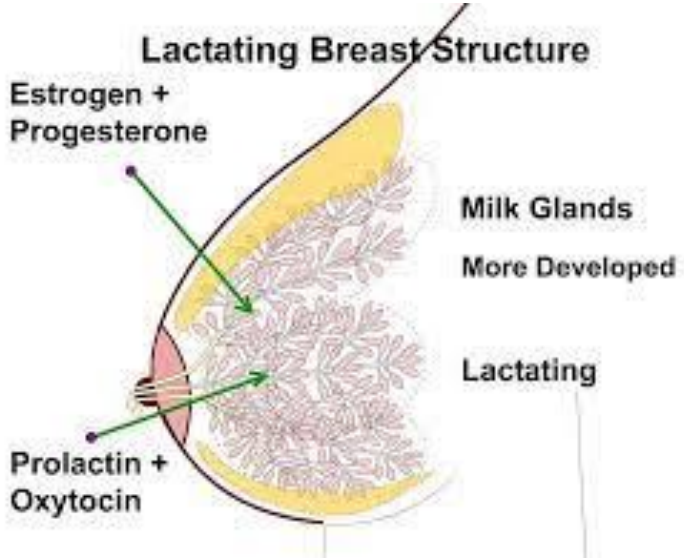
# 4- Adrenocorticotropic hormone (ACTH), or corticotropin.

- **ACTH is secreted by cells called corticotropic cells. Its target organ and the basis for its name is the adrenal cortex. ACTH stimulates the cortex to secrete hormones called glucocorticoids (especially cortisol), which regulate glucose, protein, and fat metabolism and are important in the body' response to stress**



# 5- Prolactin

- As its name suggests, is responsible for **lactation**. More precisely, prolactin initiates and maintains milk production by the **mammary glands**. The regulation of secretion of prolactin is complex, involving both **prolactin-releasing hormone (PRH)** and **prolactin-inhibiting hormone (PIH)** from the hypothalamus. The mammary glands must first be acted upon by other hormones such as **estrogen** and **progesterone**, which are secreted in large amounts by the **placenta during pregnancy**. Then, after delivery of the baby, prolactin secretion increases, and milk is produced. If the mother continues to breast-feed, prolactin levels remain high.



# 6- Growth hormone (GH)

- **Growth hormone (GH)** is also called somatotropin. GH is secreted by somatotropic cells, the most numerous cells of the anterior pituitary. The pituitary produces at least a thousand times as much GH as any other hormone. The general effect of GH is to stimulate mitosis and cellular differentiation and thus to promote tissue growth throughout the body.
- The secretion of GH is regulated by two hormones from the hypothalamus. **Growth hormone-releasing hormone (GHRH),** which increases the secretion of GH, is produced during hypoglycemia and exercise. Another stimulus for GHRH is a high blood level of amino acids; the GH then secreted will ensure the conversion of these amino acids into protein.
- **Somatostatin** may also be called growth hormone inhibiting hormone (GHIH), and, as its name tells us, it decreases the secretion of GH. Somatostatin is produced during hyperglycemia.

# References


- Hall, J. E., & Hall, M. E. (2020). Guyton and Hall Textbook of Medical Physiology. Elsevier.
- Saladin, K. (2020). Anatomy & Physiology: The Unity of Form and Function. McGraw-Hill Education.