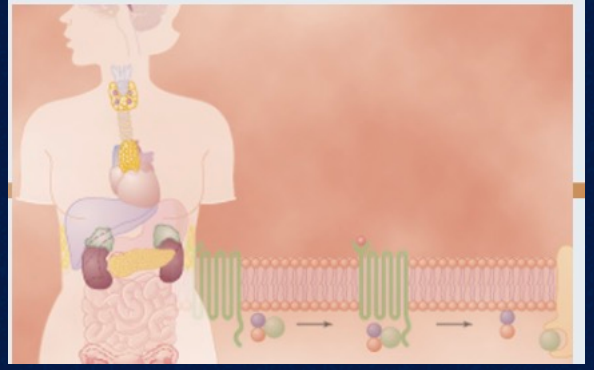
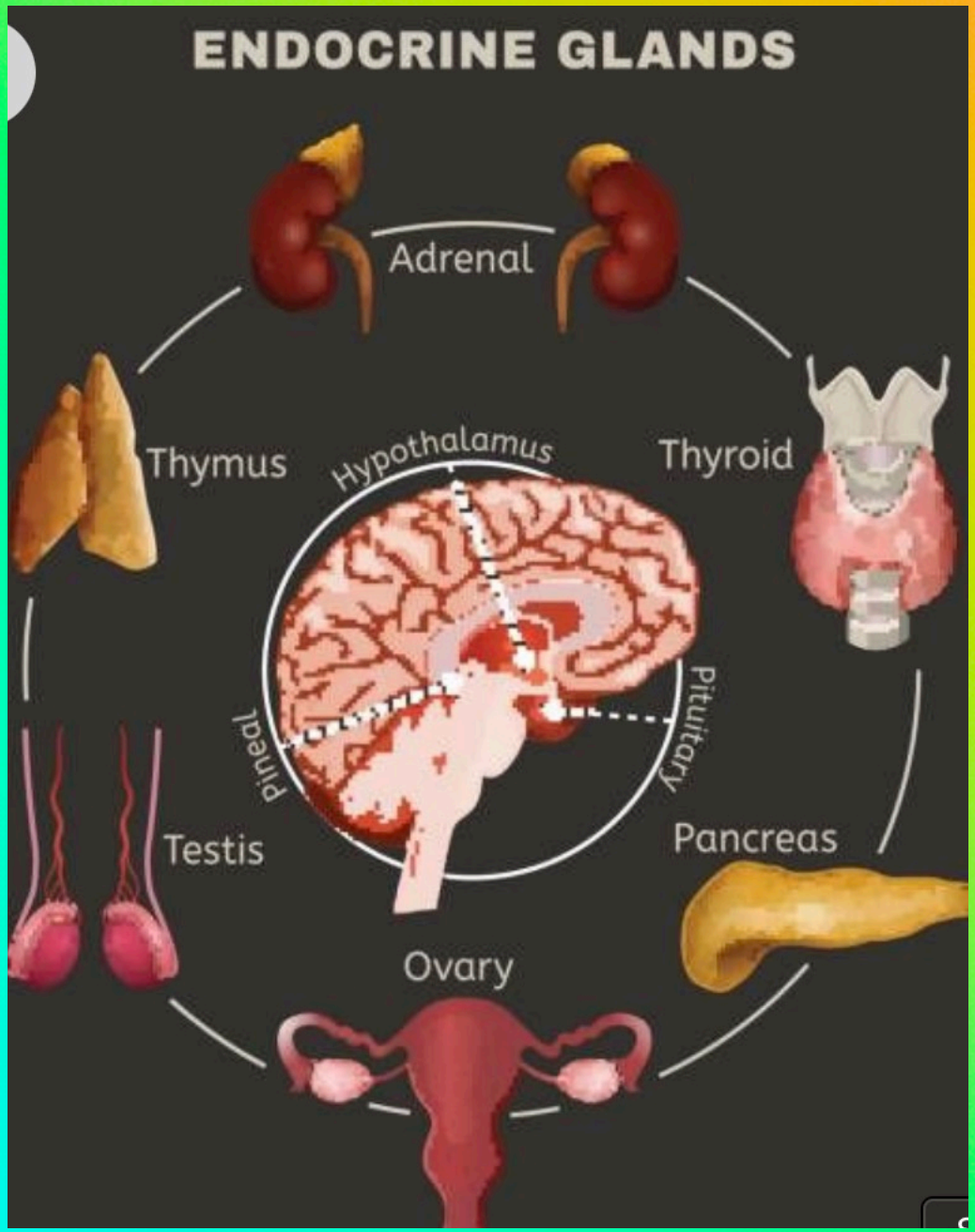


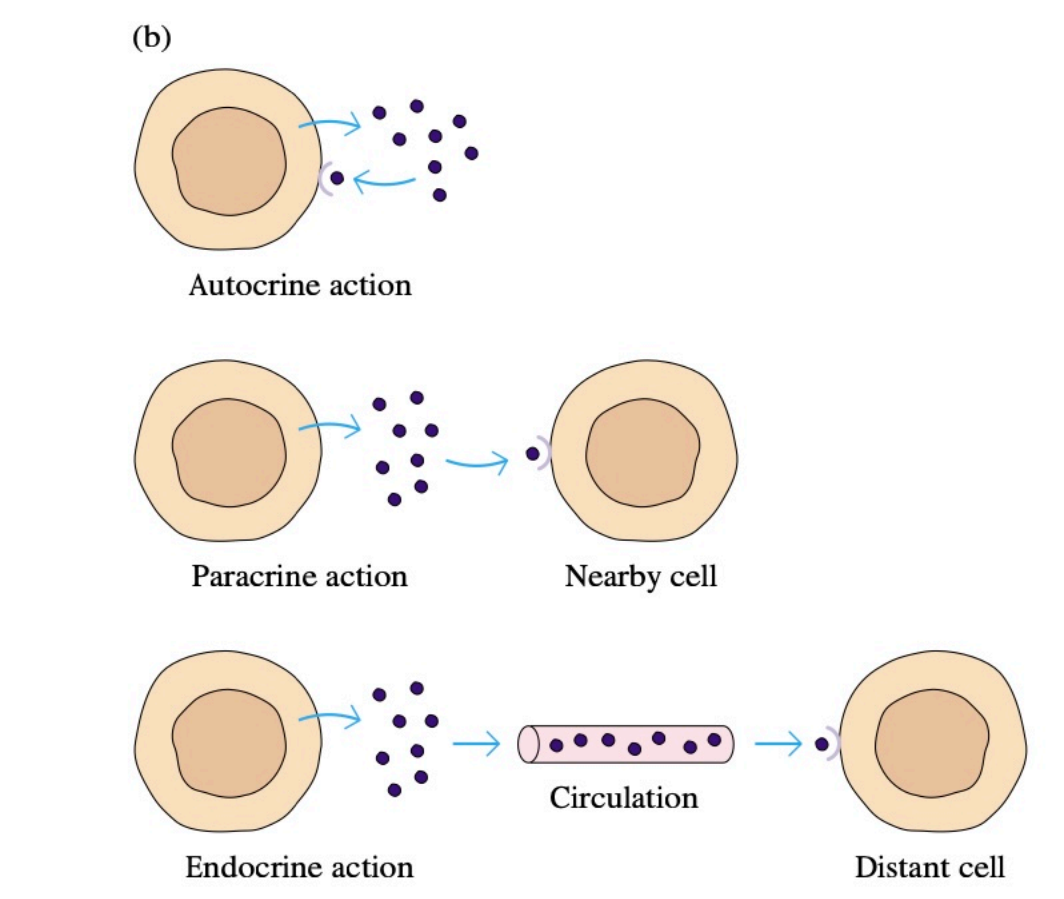
Endocrine System

Slides by Prof. Dr. Abbas Saabbr


ENDOCRINE GLANDS
Adrenal
Thymus
Hypothalamus
Thyroid
Pineal
Pituitary
Testis
Pancreas
Ovary

Forms of hormonal communication (chemical messenger systems):

1. ***Neurotransmitters*** are released by axon terminals of neurons into the synaptic junctions and act locally (eg. Epinephrine)
2. ***Endocrine hormones*** are released by glands or specialized cells into the circulating blood and influence the function of cells at another location in the body. (eg. Pituitary hormones).
3. ***Neuroendocrine hormones*** are secreted by neurons into the circulating blood and influence the function of cells at another location in the body. (ADH and oxytocin)
4. ***Paracrine*** is secreted by cells into the extracellular fluid and affects neighboring cells of a different type (eg. Somatostatin, estrogen, and testosterone).
5. ***Autocrine*** 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 (eg. prostaglandins and interleukin-1).
6. ***Cytokines*** are peptides secreted by cells into the extracellular fluid and can function as autocrine, paracrine, or endocrine hormones (eg. interleukins).



Overview of the hormonal action; most hormomes exhibt endocrine action, fewer are exhibt paracrine and autocrine action.

Chemical structures of hormones

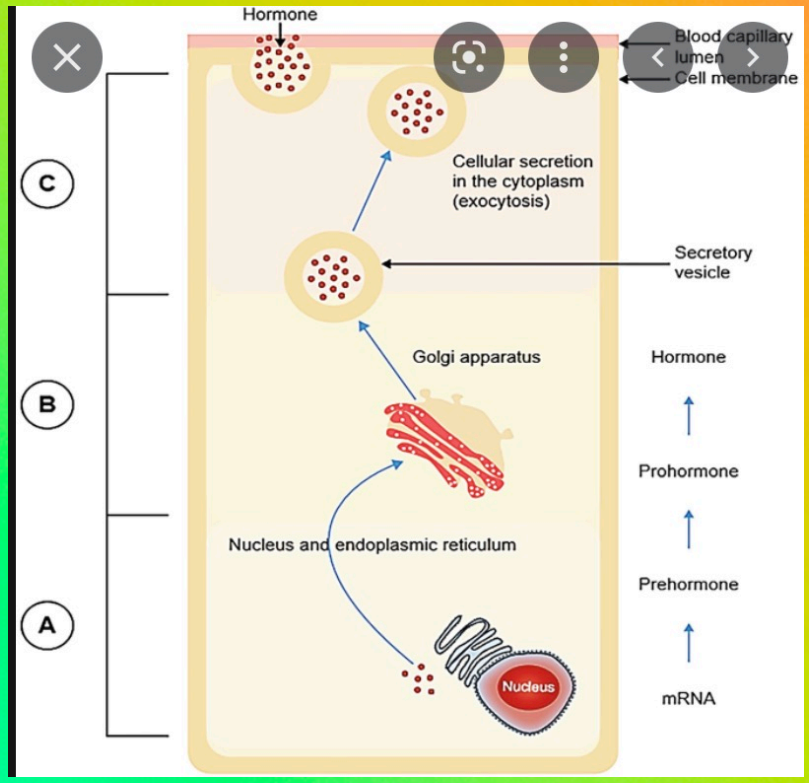
There are three general classes of hormones:

1. ***Proteins and polypeptides***, including hormones secreted by the anterior and posterior pituitary gland, the pancreas (insulin and glucagon), the parathyroid gland (parathyroid hormone), and many others.
2. ***Steroids*** secreted by the adrenal cortex (cortisol and aldosterone), the ovaries (estrogen and progesterone), the testes (testosterone), and the placenta (estrogen and progesterone).
3. ***Derivatives of the amino acid tyrosine***, secreted by the thyroid (thyroxine and triiodothyronine) and the adrenal medullae (epinephrine and norepinephrine).

Synthesis of Hormones

Protein Hormones

- Synthesized first as larger proteins that are not biologically active (*preprohormones*) and are cleaved to form smaller *prohormones* in the endoplasmic reticulum and *Stored in Secretory Vesicles Until Needed*.



- The hormone stored is secreted to The interstitial fluid or directly into the bloodstream by ***exocytosis***.

Steroid hormones

- Steroid Hormones Are Synthesized from Cholesterol and Are Not Stored.
- Because the steroids are highly lipid soluble, once they are synthesized, they simply diffuse across the cell membrane and enter the interstitial fluid and then the blood.

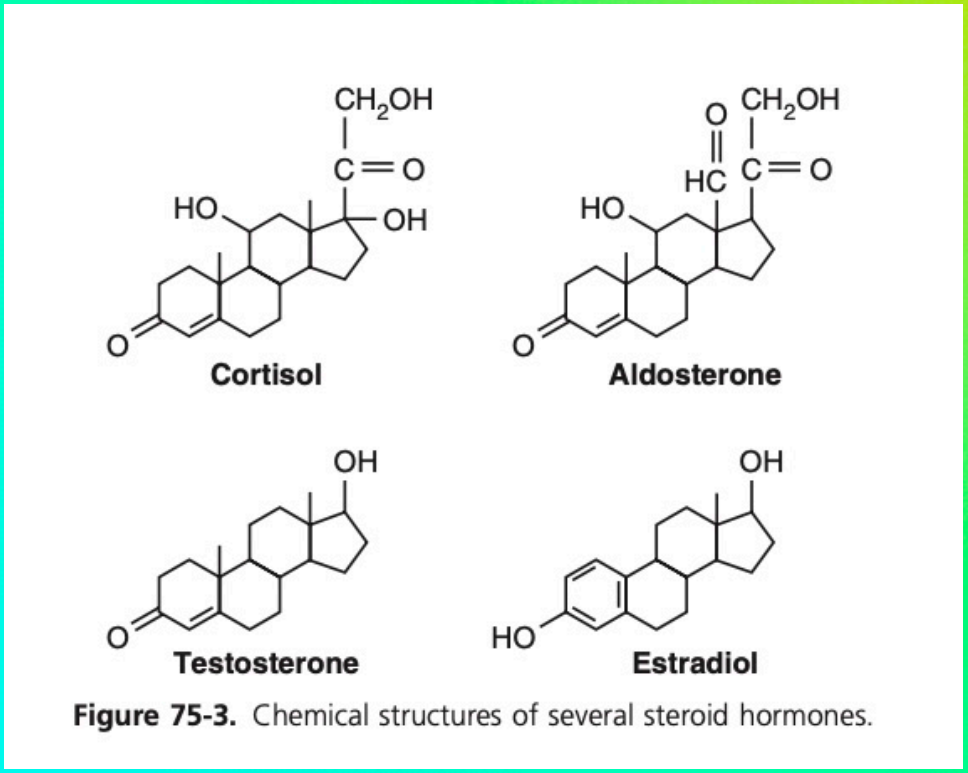


Figure 75-3. Chemical structures of several steroid hormones.

Amine Hormones

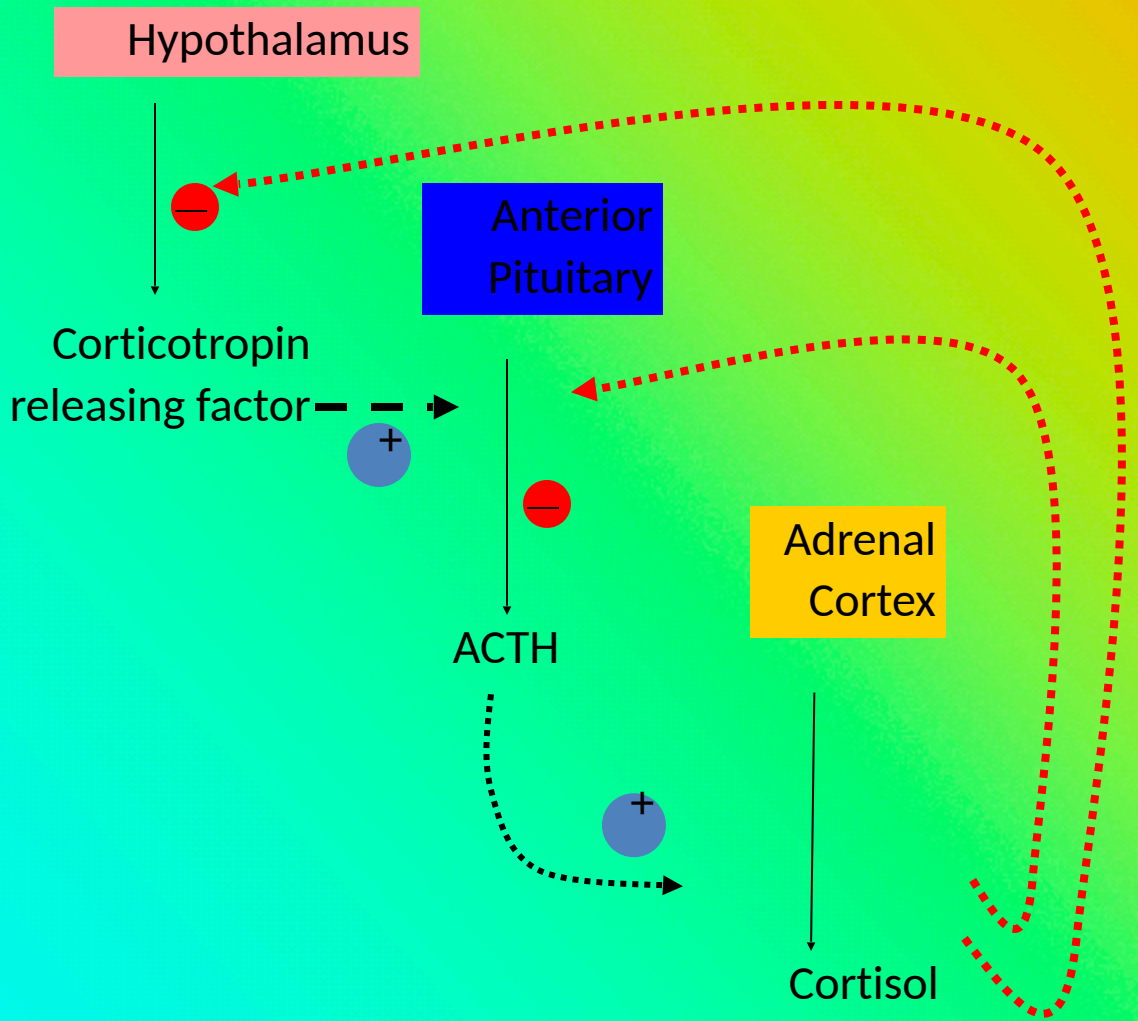
- The two groups of hormones derived from tyrosine, the thyroid and the adrenal medullary hormones, are formed by the actions of enzymes in the cytoplasmic compartments of the glandular cells.
- ***The thyroid hormones*** are synthesized and stored in the thyroid gland and incorporated into macromolecules of the protein ***thyroglobulin***, which is stored in large follicles within the thyroid gland.
- ***Epinephrine and norepinephrine*** (***catecholamines***) are formed in the adrenal medulla, Similar to the protein hormones stored in secretory granules, ***catecholamines*** are also released from adrenal medullary cells by exocytosis.

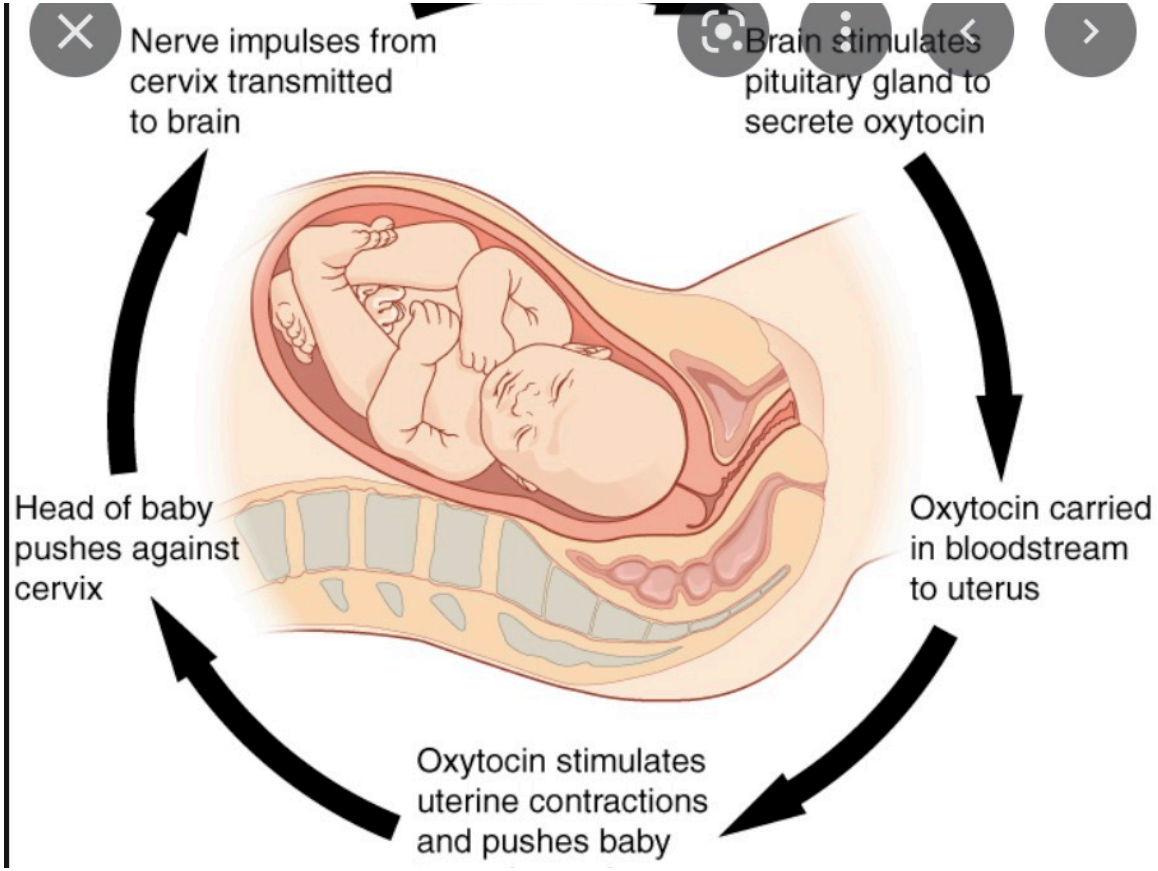
Feedback Control of Hormone Secretion

- ***Negative feedback mechanisms:*** the hormone has a negative feedback effect to prevent oversecretion of the hormone or overactivity at the target tissue and is very important mechanism for regulation of hormone secretion.

- ***positive feedback occurs*** when the biological action of the hormone causes additional secretion of the hormone. One example of this is the surge of ***luteinizing hormone (LH)*** that occurs as a result of the stimulatory effect of estrogen on the anterior pituitary before ovulation. The secreted LH then acts on the ovaries to stimulate additional secretion of estrogen, which in turn causes more secretion of LH.

Negative Feedback Loops





Positive Feedback Mechanism

Childbirth

Transport of Hormones in the Blood

Water-soluble hormones (peptides and catecholamines) are dissolved in the plasma and transported from their sites of synthesis to target tissues, where they diffuse out of the capillaries, into the interstitial fluid, and ultimately to target cells. They are degraded by enzymes in the blood and tissues and rapidly excreted by the kidneys and liver, thus remaining in the blood for only a short time.

Steroid and thyroid hormones, in contrast, circulate in the blood mainly bound to plasma proteins. For example, more than 99 per cent of the thyroxine in the blood is bound to plasma proteins. However, protein-bound hormones cannot easily diffuse across the capillaries and gain access to their target cells and are therefore biologically inactive until they dissociate from plasma proteins. They are cleared from the blood at much slower rates and may remain in the circulation for several hours or even days.

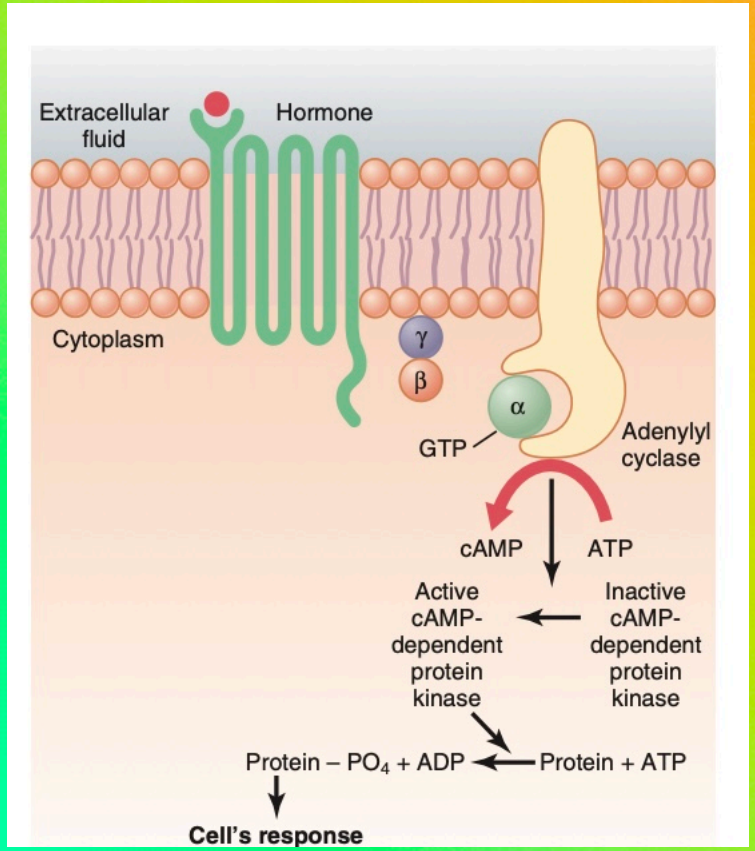
Mechanisms of Action of Hormones

- The first step of a hormone's action is to bind to specific ***receptors*** at the target cell.
- ***Hormonal receptors*** are large proteins. Cells that lack receptors for the hormones do not respond.
- When the hormone combines with its receptor, initiates a cascade of reactions in the cell, with each stage becoming more powerfully activated so that even small concentration of the hormone can have a large effect.
- The locations hormone receptors are generally the following:

1. ***In or on the surface of the cell membrane***. The membrane receptors are specific mostly for the protein, peptide, and catecholamine hormones.
2. ***In the cell cytoplasm***. The receptors for steroid hormones are found in the cytoplasm.
3. ***In the cell nucleus***. The receptors for the thyroid hormones are found in the nucleus and are believed to be located in direct association with one or more of the chromosomes.

Second Messenger Mechanisms for Mediating Intracellular Hormonal Functions

1. Adenylyl Cyclase–cAMP Second Messenger System

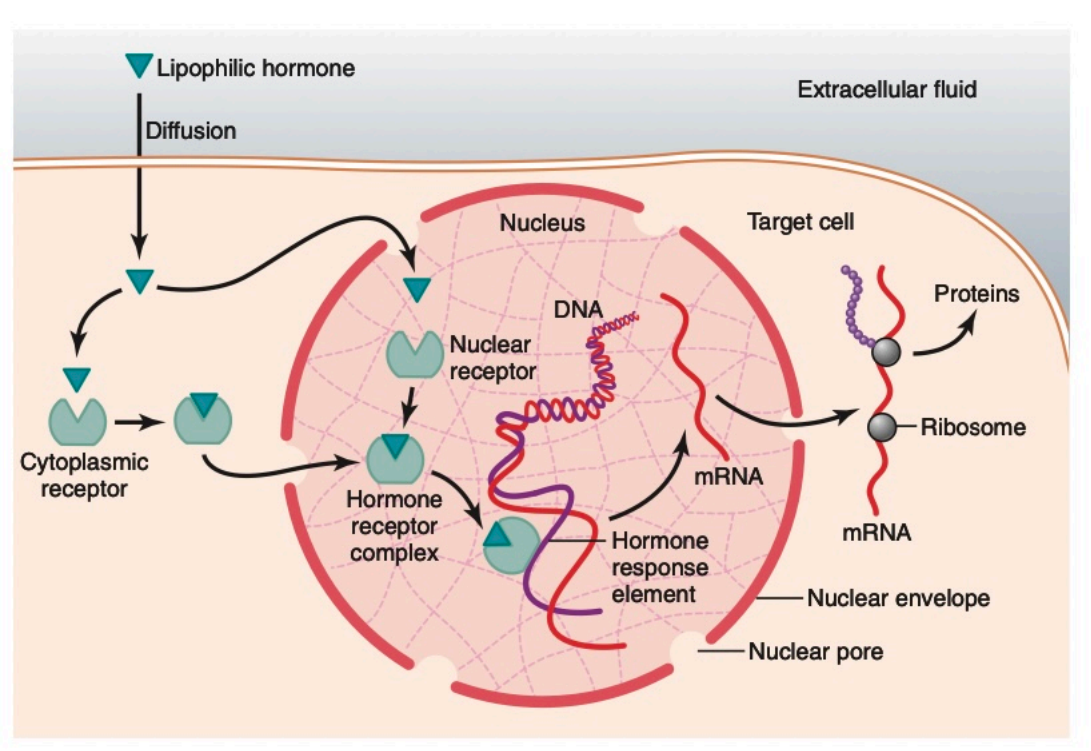


- Binding of the hormones with the receptor allows coupling of the receptor to a ***G protein***
- ***G protein*** stimulates the adenylyl cyclase–cAMP system, a membrane-Bound enzyme.
- ***Adenylyl cyclase*** catalyzes the conversion of (ATP) into cAMP then activates *cAMP-dependent protein kinase* which phosphorylates specific proteins in the cell, triggering biochemical reactions that ultimately lead to the cell's response to the hormone.

Hormones That Use the Adenylyl Cyclase–cAMP Second Messenger System

Adrenocorticotropic hormone (ACTH)
Angiotensin II (epithelial cells)
Calcitonin
Catecholamines (beta receptors)
Corticotropin-releasing hormone (CRH)
Follicle-stimulating hormone (FSH)
Glucagon
Growth hormone–releasing hormone (GHRH)
Human chorionic gonadotropin (hCG)
Luteinizing hormone (LH)
Parathyroid hormone (PTH)
Secretin
Somatostatin
Thyroid-stimulating hormone (TSH)
Vasopressin (V_2 receptor, epithelial cells)

Mechanisms of interaction of steroid hormones

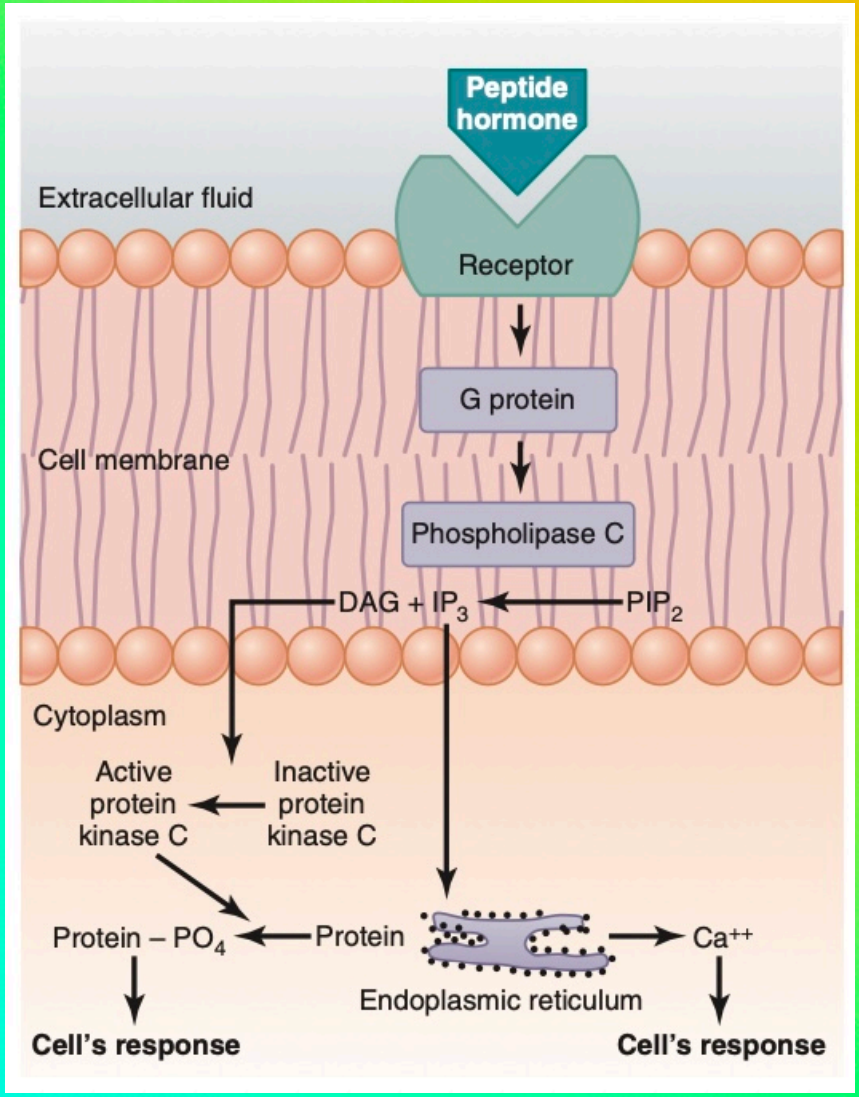


After the hormone binds to the receptor in the cytoplasm or in the nucleus, the hormone-receptor complex binds to the hormone response element (promoter) on the DNA. This either activates or inhibits gene transcription, formation of messenger RNA (mRNA), and protein synthesis

2. The Cell Membrane Phospholipid Second Messenger System

Some hormones activate transmembrane receptors that activate the enzyme *phospholipase C* attached to the inside projections of the receptors . This enzyme catalyzes the breakdown of phospholipids in the cell membrane ***phosphatidylinositol biphosphate (PIP2),*** into two different second messenger products: ***inositol triphosphate (IP3)*** and *diacylglycerol (DAG)*.

- The IP3 mobilizes calcium ions from mitochondria and the endoplasmic reticulum, and the calcium ions then have their own second messenger effects, such as smooth muscle contraction and changes in cell secretion.
- DAG, the other lipid second messenger, activates the enzyme *protein kinase C (PKC)*, which then phosphorylates a large number of proteins, leading to the cell's response



The cell membrane phospholipid second messenger system by which some hormones exert their control of cell function.

Hormones That Use the Phospholipase C Second Messenger System

Angiotensin II (vascular smooth muscle)
Catecholamines (α receptors)
Gonadotropin-releasing hormone (GnRH)
Growth hormone–releasing hormone (GHRH)
Parathyroid hormone (PTH)
Oxytocin
Thyrotropin-releasing hormone (TRH)
Vasopressin (V_1 receptor, vascular smooth muscle)

3. Calcium-Calmodulin Second Messenger System

Another second messenger system operates in response to the entry of calcium into the cells. Calcium entry may be initiated by (1) changes in membrane potential that open calcium channels or (2) a hormone interacting with membrane receptors that open calcium channels.

On entering a cell, calcium ions bind with the protein ***calmodulin***. This protein has four calcium sites, and when three or four of these sites have bound with calcium, the calmodulin changes its shape and initiates multiple effects inside the cell, including activation or inhibition of protein kinases. Activation of calmodulin -dependent protein kinases causes, via phosphorylation, activation or inhibition of proteins involved in the cell's response to the hormone

Calcium-Calmodulin as 2nd Messenger