Hormones

The definition of a hormone has been expanded over the last several decades. Hormones secreted by glands such as adrenals, ovaries, parathyroids, pituitary, testes and thyroid were originally considered to represent all of the physiologically relevant hormones. Today, the term hormone refers to any substance in an organism that carries a signal to generate some sort of alteration at the cellular level. Thus **endocrine hormones** represent a class of hormones that arise in one tissue and travel a considerable distance through the circulation to reach a target cell expressing cognate receptors.**Paracrine hormones** arise from a cell and travel a relatively small distance to interact withtheir cognate receptor on another neighboring cell. **Autocrine hormones** are produced by the same cell that functions as the target for that hormone (neighborin g cells may also be targets). Thus we can classify hormones based on their of action.

Often, endocrine hormones that travel long distances to their target cells may be more stable than autocrine hormones that exert their effects over very short distances A diverse array of hormones each with distinctive mechanisms of action and properties of biosynthesis, storage, secretion, transport, and metabolism has evolved to provide homeostatic responses.

Hormone secretion

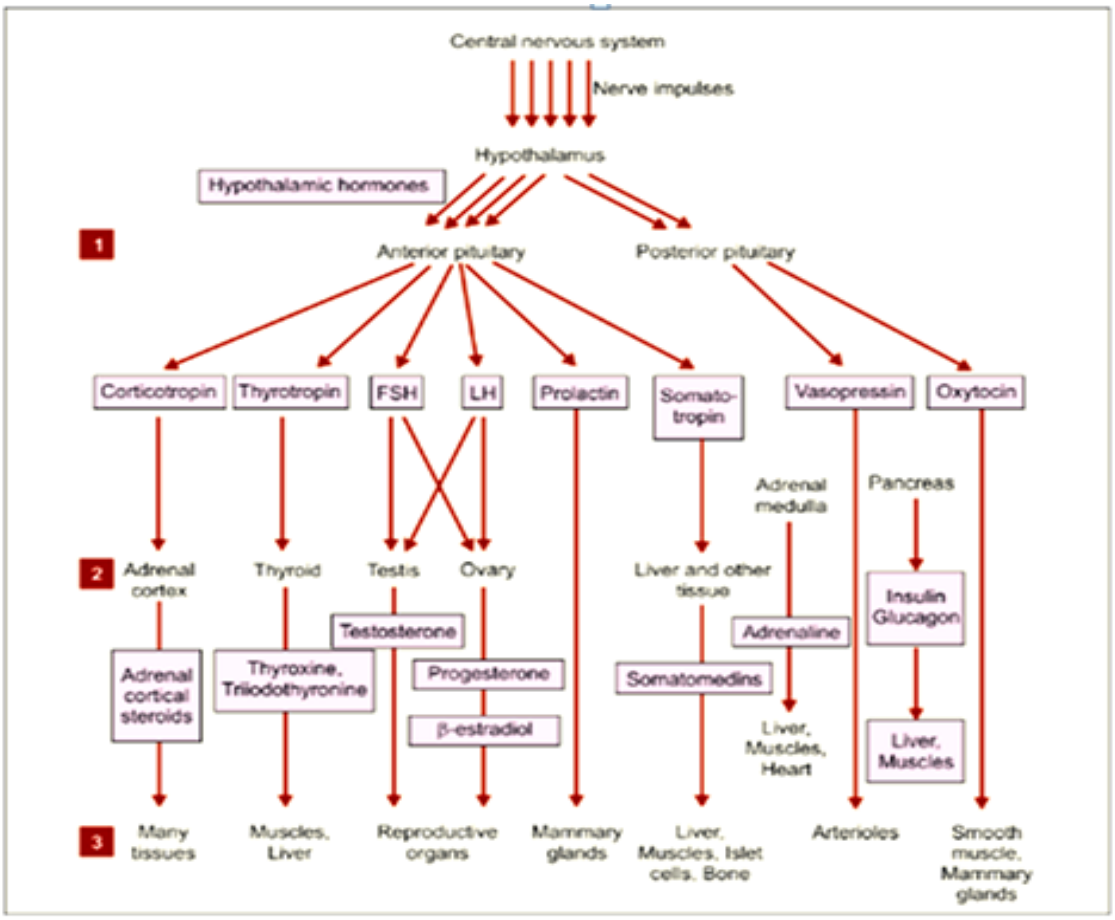
1- Endocrine hormones are secreted directly into the bloodstream.

2- Exocrine hormones are secreted directly into a duct.

Cascade System of hormone

For many hormonal systems in higher animals, the signal pathway origin ates with the brain and culminates with the ultimate target cell. The signa l may be transmitted as an electrical pulse (action potential) or as a chemi cal signal or both. In many cases, but not all, such signals forwarded to th e limbic system and subsequently to the hypothalamus,the pituitary or other gland that secretes the final hormone.

This hormone then affects various target cells to a degree that frequently proportional to the number of cognate receptors



Classification of hormone

Hormones can be classified according to:

•Chemical structure

•Mechanism of hormone action.

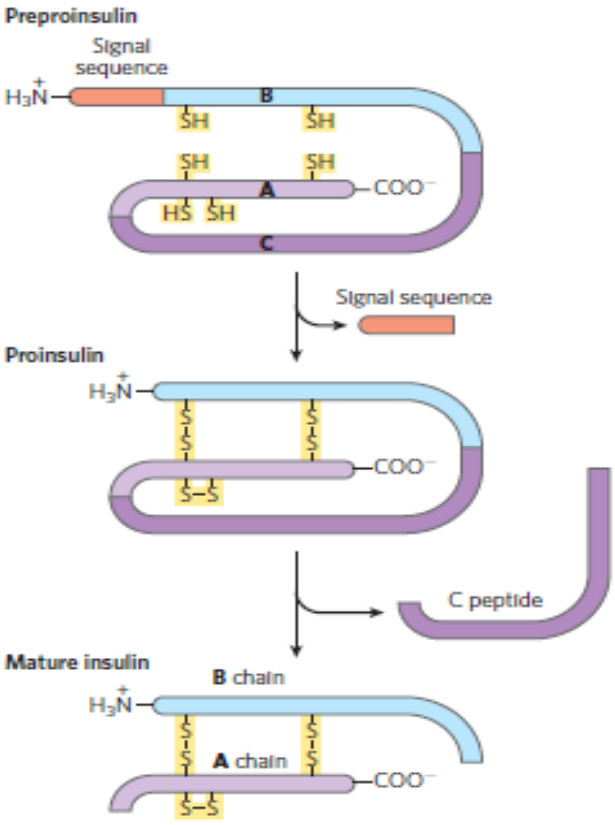
Classification Based on Chemical Structure

Hormones are usually classified into three main groups on the basis of their chemical structure as follows:

1. Peptide or protein hormones.
2. Amine hormones or amino acid derivatives.
3. Steroid hormones.

1-Peptide or Protein Hormones

Most hormones fall into this class. These are water soluble and may have 3 to over 200 amino acid residues, e.g. hormones of the hypothalamus and pituitary. As well as insulin and glucagon of the pancreas. These hormones are synthesized on ribosomes in the form of longer precursor proteins (prohormones), then packaged into secretory vesicles and proteolytically cleaved to form the active peptides. **Insulin** is a small protein (*M*r 5,800) with two polypeptide chains, A and B, joined by two disulfide bonds. It is synthesized in the pancreas as an inactive single-chain precursor, preproinsulin with an amino-terminal "signal sequence" that directs its passage into secretory vesicles. Proteolytic removal of the signal sequence and formation of three disulfide bonds produces proinsulin, which is stored in secretory granules (membrane vesicles filled with protein synthesized in the endoplasmic reticulum) in pancreatic _ cells. When blood glucose is elevated sufficiently to trigger insulin secretion proinsulin is converted to active insulin by specific proteases, which cleave two peptide bonds to form the mature insulin molecule and C peptide, which are released into the blood by exocytosis. as shown in the Figure:



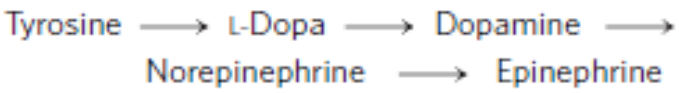
2- Amino Acid Derivatives

These are small, water soluble compounds containing amino groups. For example:

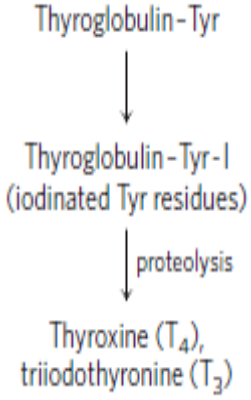
• Adrenaline of the adrenal medulla

• Thyroid hormones.

Catecholamine Hormones The water-soluble compounds epinephrine (adrenaline) and norepinephrine (noradrenaline) are catecholamines, named for the structurally related compound catechol. They are synthesized from tyrosine . Catecholamines produced in the brain and in other neural tissues function as neurotransmitters, but epinephrine and norepinephrine are also hormones, synthesized and secreted by the adrenal glands. Like the peptide hormones, catecholamines are highly concentrated in secretory vesicles and released by exocytosis, and they act through surface receptors to generate intracellular second messengers. They mediate a wide variety of physiological responses to acute stress .



The thyroid hormones T4 (thyroxine) and T3 (triiodothyronine) are synthesized from the precursor protein thyroglobulin (*M*r 660,000). Up to 20 Tyr residues in thyroglobulin are enzymatically iodinated in the thyroid gland, then two iodotyrosine residues condense to form the precursor to thyroxine. When needed, thyroxine is released by proteolysis. Condensation of monoiodotyrosine with diiodothyronine produces T3, which is also an active hormone released by proteolysis.

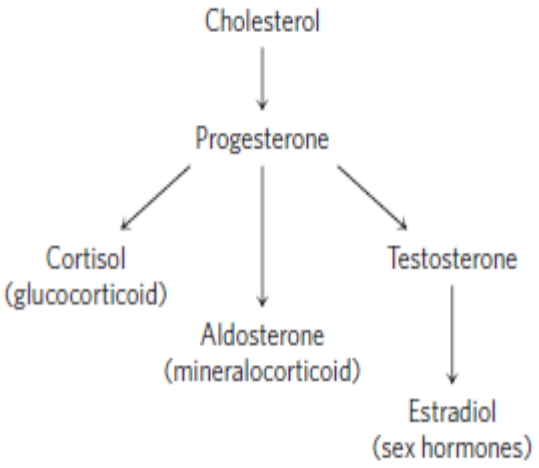


3-Steroid Hormones

These are fat soluble (lipophilic) and all are derivatives of cholesterol.
For example:

- Adrenal cortical hormones
- Androgen (male sex hormones)
- Estrogens (female sex hormones)

Steroid Hormones The steroid hormones (adrenocortical hormones and sex hormones) are synthesized from cholesterol in several endocrine tissues.



They travel to their target cells through the bloodstream, bound to carrier proteins. More than 50 corticosteroid hormones are produced in the adrenal cortex by reactions that remove the side chain from the D ring of cholesterol and introduce oxygen to form keto and hydroxyl groups. Many of these reactions involve cytochrome P-450 enzymes . The corticosteroids are of two general types, defined by their actions. Glucocorticoids (such as cortisol) primarily affect the metabolism of carbohydrates; mineralocorticoids (such as aldosterone) regulate the concentrations of electrolytes (K^{+1}, Na^{+1}, Ca^{+2}, Cl^{-}) in the blood. Androgens (such as testosterone) and estrogens are synthesized in the testes and ovaries. They affect sexual development, sexual behavior, and a variety of other reproductive and nonreproductive functions.

Their synthesis also involves cytochrome P-450 enzymes that cleave the side chain of cholesterol and introduce oxygen atoms. All steroid hormones act through nuclear receptors to change the level of expression of specific genes . They can also have more rapid effects, mediated by receptors in the plasma membrane.

In this Table as shown of classes of Hormones:

Type	Example	Synthetic path	Mode of action
Peptide	Insulin, glucagon	Proteolytic processing of prohormone	Plasma membrane receptors; second messengers
Catecholamine	Epinephrine	From tyrosine	
Eicosanoid	PGE_1	From arachidonate (20:4 fatty acid)	
Steroid	Testosterone	From cholesterol	Nuclear receptors; transcriptional regulation
Vitamin D	1α,25-Dihydroxyvitamin D_3	From cholesterol	
Retinoid	Retinoic acid	From vitamin A	
Thyroid	Triiodothyronine (T_3)	From Tyr in thyroglobulin	
Nitric oxide	Nitric oxide	From arginine + O_2	Cytosolic receptor (guanylyl cyclase) and second messenger (cGMP)

Classification Based on Mechanism of Hormone Action

Hormones can be classified according to mechanism of hormone action to:

1. Group I hormones
2. Group II hormones.

This classification is based on location of the hormone receptors.

1-The hormones of Group I are lipophilic which readily pass through the lipophilic plasma membrane of the target cells and interacts with receptors which are located intracellular in either the cystol or the nucleus. The receptors for the different steroid hormones are found mainly in the cytoplasm and the receptors for the thyroid hormones are found in the nucleus.

2- The hormones of group II are water-soluble . Hormones which do not penetrate lipophilic cell membrane readily. The receptors for such hormones are located on the outer surface of the target cell (cell surface receptors).

Class	*Second messenger or mediator*	*Examples*
Group I Cytosolic or nuclear receptor	Hormone-receptor complex	Androgens Estrogens Glucocorticoids Mineralocorticoids Progesterol Thyroid hormones (T_3 and T_4)
Group II Cell membrane receptor	c-AMP	Epinephrine Norepinephrines Glucagon Parathyroid hormone
	Calcium or phosphatidylinositol or both	Vasopressin Oxytocin

Mechanism of hormone action

The first step of hormone action is binding of hormone to specific receptors of the target cell. Hormone receptor complex activates the hormonal effects. Hormonal receptors are large proteins, which are highly specific for a single hormone. Due to this specificity a particular hormone will act on a particular tissue.

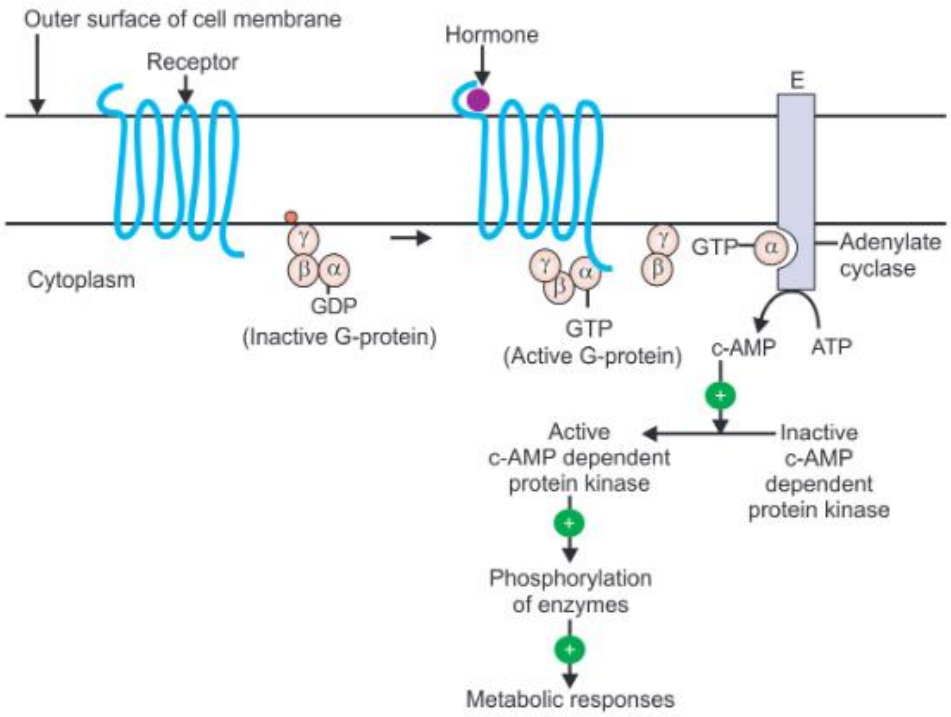
Mechanism of hormone action at Systolic nuclear level

Several hormones, e.g. steroid hormones (adrenal and gonadal) and thyroid hormones bind with receptors inside the cell rather than in the cell membrane. Because these hormones are lipid soluble, they readily cross the cell membrane and interact with receptors in the cytoplasm or nucleus. The receptors for the steroid hormones are found mainly in the cytoplasm and the receptors for the thyroid hormones are found in the nucleus.

Cell membrane receptor of hormone action

The receptors for group II hormones are located on the outer surface of the target cell because these hormones are water soluble which do not enter lipophilic cell membrane. Hormones that bind to surface receptors of the cells communicate their action through intermediary molecules called second messenger (the hormone itself is the first messenger) . On binding of the hormone to the receptor, a conformational change occurs in the receptor, that causes activation of the G-protein that consist of

three subunits α, β, γ. GDP (Inactive G-protein) convert to GTP (active G-Protein) interacts with other intracellular signaling enzymes such as adenylate cyclase which generates c-AMP for many hormones, e.g. epinephrine, glucagon, calcitonin, PTH, etc

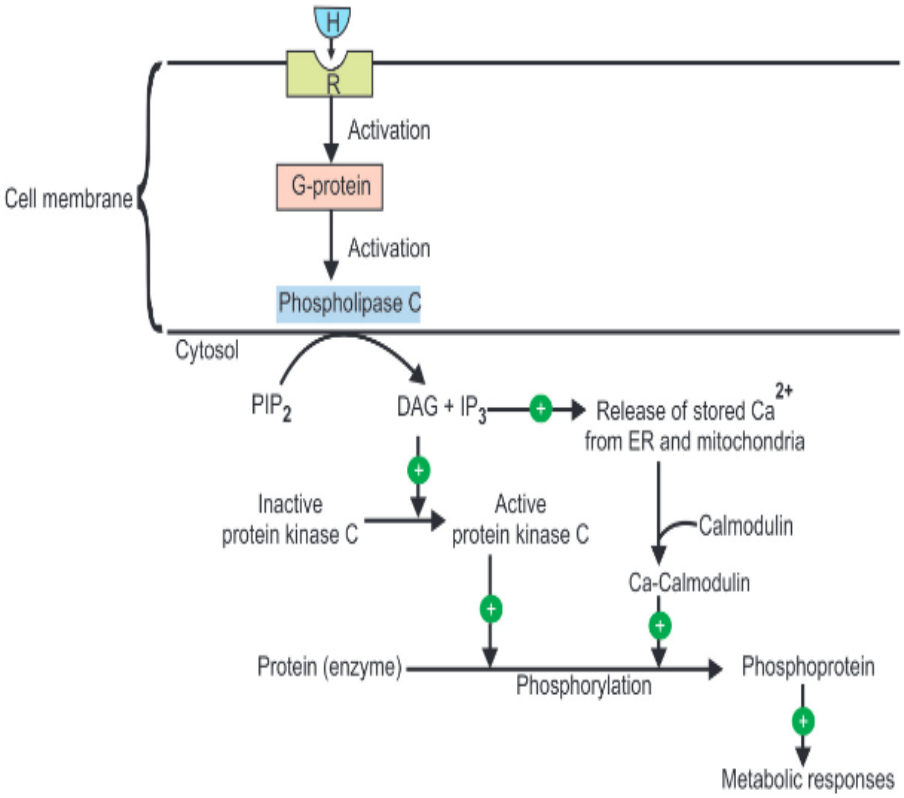


Phosphatidylinositol/calcium second messenger

•Certain hormone-receptor interaction result in the activation of the enzyme phospholipase C through a specific G-protein . Phospholipase C enzyme catalyzes the breakdown of phospholipids in cell membrane especially phosphatidylinositol bisphosphate (PIP 2) into:

1. Inositol triphosphate (IP3): that liberates stored intracellular calcium ions from mitochondria and endoplasmic reticulum. The calcium in turn acts as a third messenger which influences a variety of biochemical processes.

2. Diacylglycerol (DAG): the other second messenger, activates the enzyme kinase C which then alter physiological processes. The hormones thyrotropin releasing hormone (TRH) gastrain, cholecystokinin act through this second messenger.



Gland

A gland is an organ in an animal's body that synthesizes a substance such as hormones for release into the bloodstream (endocrine gland) or into cavities inside the body or its outer surface (exocrine gland). The following glands make up the endocrine system and some of hormone secretion:

- **Pituitary Gland secretion each of :** (growth hormone, prolactin, adrenocorticotropic hormone, thyroid stimulating hormone, luteinizing hormone, oxytosin)
- **Hypothalmus gland secretion each of :**
  - Thyrotrophic-releasing hormone
  - Growth hormone-releasing hormone
  - Corticotrophin-releasing hormone
  - Gonadotropin-releasing hormone
- **Thymus:** this gland secretes hormones that are commonly referred to as humoral factors and are important during puberty. The role of these hormones is to make sure a person develops a healthy immune system.

- **Pineal Gland:** The pineal gland releases melatonin, which helps the body recognize when it is time to go to sleep.
- **Testes:** this gland produces testosterone.
- **Ovaries:** this gland produces both estrogen and progesterone. secreted by the ovarian follicles of the ovaries.
- **Thyroid:** of Thyroid-Stimulating hormone (TSH) with T3 (Triiodothyronine) and T4 (Thyroxine)
- **Adrenal Glands:** norepinephrine, epinephrine, cortisol
- **Parathyroid:** Calcitonin
- **Pancreas:** insulin, glucagon, which secretes digestive enzymes