Endocrine system

All the physiological activities are regulated by two major systems in the body.

1. Nervous system
2. Endocrine system.

These two systems interact with one another and regulate the body functions. Endocrine system functions by secreting some chemical substances called hormones.

Endocrine glands are the glands which synthesize and release the classical hormones into the blood. The endocrine glands are also called ductless glands because the hormones secreted by them are released directly into blood without any duct.

Coordination of Body Functions by Chemical Messengers

The multiple activities of the cells, tissues, and organs of the body are coordinated by the interplay of several types of chemical messenger systems:

1. Neurotransmitters are released by axon terminals of neurons into the synaptic junctions and act locally to control nerve cell functions.
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.
3. Neuroendocrine hormones are secreted by neurons into the circulating blood and influence the function of cells at another location in the body.
4. Paracrines are secreted by cells into the extracellular fluid and affect neighboring cells of a different type.
5. 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.
6. Cytokines are peptides secreted by cells into the extracellular fluid and can function as autocrines, paracrines, or endocrine hormones. Examples of cytokines include the interleukins and other lymphokines that are secreted by helper cells and act on other cells of the immune system. Cytokine hormones (e.g., leptin) produced by adipocytes are sometimes called adipokines.

Hormone

Hormones are **chemical messengers,** synthesized by endocrine glands. Based on chemical nature, hormones are classified into three types:

1-STEROID HORMONES

Steroid hormones are the hormones synthesized from cholesterol or its derivatives. Steroid hormones are secreted by adrenal cortex, gonads and placenta

2- PROTEIN HORMONES

Protein hormones are large or small peptides. Protein hormones are secreted by pituitary gland, parathyroid glands, pancreas and placenta

3- TYROSINE DERIVATIVES

Two types of hormones, namely thyroid hormones and adrenal medullary hormones are derived from the amino acid tyrosine**.**

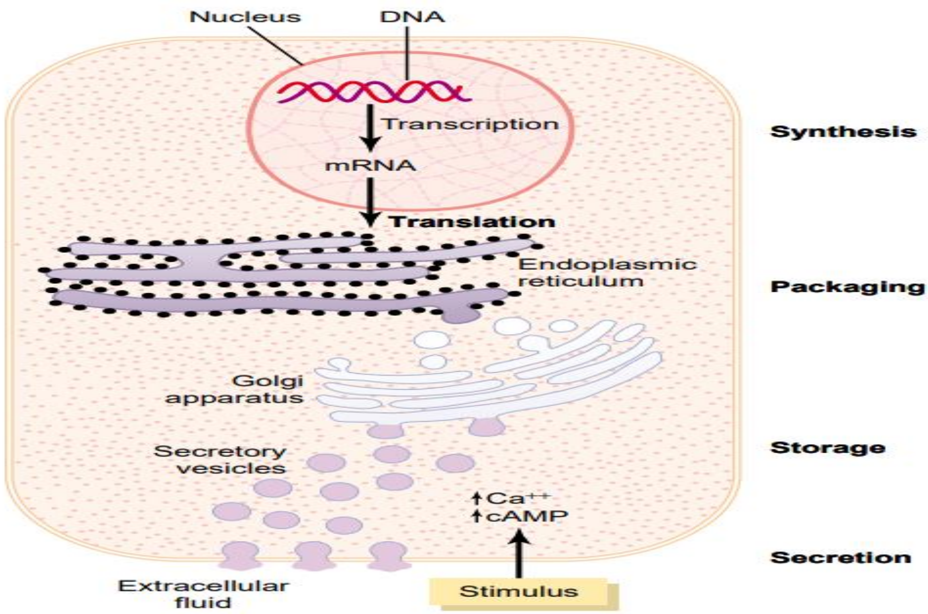
Hormone secretors

Endocrine glands are the glands which synthesize and release the classical hormones into the blood.

Hormones secreted by major endocrine glands

Anterior pituitary	1. Growth hormone (GH) 2. Thyroid stimulating hormone (TSH) 3. Adrenocorticotropic hormone (ACTH) 4. Follicle stimulating hormone (FSH) 5. Luteinizing hormone (LH) 6. Prolactin
Posterior pituitary	1. Antidiuretic hormone (ADH) 2. Oxytocin
Thyroid gland	1. Thyroxine (T_4) 2. Tri-iodothyronine (T_3) 3. Calcitonin
Parathyroid gland	1. Parathormone
Pancreas — islets of Langerhans	1. Insulin 2. Glucagon 3. Somatostatin 4. Pancreatic polypeptide
Adrenal cortex	*Mineralocorticoids* 1. Aldosterone 2. 11 deoxycorticosterone *Glucocorticoids* 1. Cortisol 2. Corticosterone *Sex hormones* 1. Androgens 2. Estrogen 3. Progesterone
Adrenal medulla	*Catecholamines* 1. Adrenaline (Epinephrine) 2. Noradrenaline (Norepinephrine) 3. Dopamine

Polypeptide and Protein Hormones Are Stored in Secretory Vesicles Until Needed. Most of the hormones in the body are polypeptides and proteins. These hormones range in size from small peptides with as few as 3 amino acids (thyrotropin-releasing hormone) to proteins with almost 200 amino acids (growth hormone and prolactin). In general, polypeptides with 100 or more amino acids are called proteins, and those with fewer than 100 amino acids are referred to as peptides. Protein and peptide hormones are synthesized on the rough end of the endoplasmic reticulum of the different endocrine cells, in the same fashion as most other proteins. They are usually synthesized first as larger proteins that are not biologically active (preprohormones) and are cleaved to form smaller prohormones in the endoplasmic reticulum. These are then transferred to the Golgi apparatus for packaging into secretory vesicles. In this process, enzymes in the vesicles cleave the prohormones to produce smaller, biologically active hormones and inactive fragments. The vesicles are stored within the cytoplasm, and many are bound to the cell membrane until their secretion is needed. Secretion of the hormones (as well as the inactive fragments) occurs when the secretory vesicles fuse with the cell membrane and the granular contents are extruded into the interstitial fluid or directly into the blood stream by exocytosis. In many cases, the stimulus for exocytosis is an increase in cytosolic calcium concentration caused by depolarization of the plasma membrane. In other instances, stimulation of an endocrine cell surface receptor causes increased cyclic adenosine monophosphate (cAMP) and subsequently activation of protein kinases that initiate secretion of the hormone. The peptide hormones are water soluble, allowing them to enter the circulatory system easily, where they are carried to their target tissues.



Synthesis and secretion of peptide hormones. The stimulus for hormone secretion often involves changes in intracellular calcium or changes in cyclic adenosine monophosphate (cAMP) in the cell.

HORMONAL ACTION

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Hormone does not act directly on target cells. First it combines with receptor present on the target cells and forms a **hormone-receptor complex.** This hormone receptor complex induces various changes or reactions in the target cells.

HORMONE RECEPTORS

Hormone receptors are the large proteins present in the target cells. Each cell has thousands of receptors. Important characteristic feature of the receptors is that, each receptor is specific for one single hormone, i.e. each receptor can combine with only one hormone. Thus, a hormone can act on a target cell, only if the target cell has the receptor for that particular hormone.

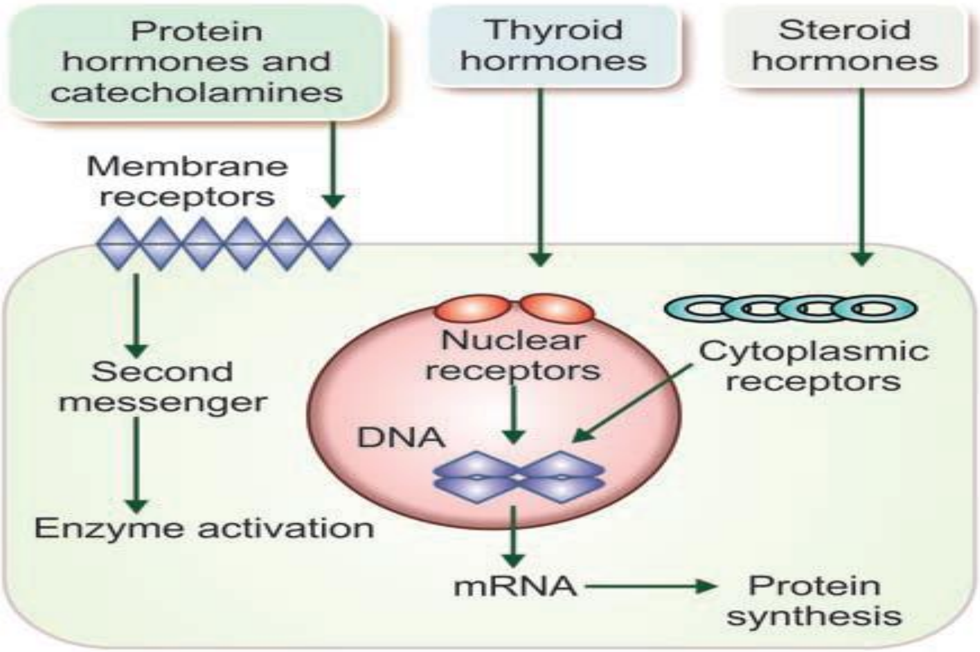
Situation of the Hormone Receptors

Hormone receptors are situated either in cell membrane or cytoplasm or nucleus of the target cells as follows:

1. *Cell membrane:* Receptors of protein hormones and adrenal medullary hormones (catecholamines) are situated in the cell membrane .
2. *Cytoplasm:* Receptors of steroid hormones are situated in the cytoplasm of target cells.
3. *Nucleus:* Receptors of thyroid hormones are in the nucleus of the cell.

Regulation of Hormone Receptors

Receptor proteins are not static components of the cell. Their number increases or decreases in various conditions. Generally, when a hormone is secreted in excess, the number of receptors of that hormone decreases due to binding of hormone with receptors. This process is called **down regulation.** During the deficiency of the hormone, the number of receptor increases, which is called **upregulation**.



Situation of hormonal receptors

MECHANISM OF HORMONAL ACTION

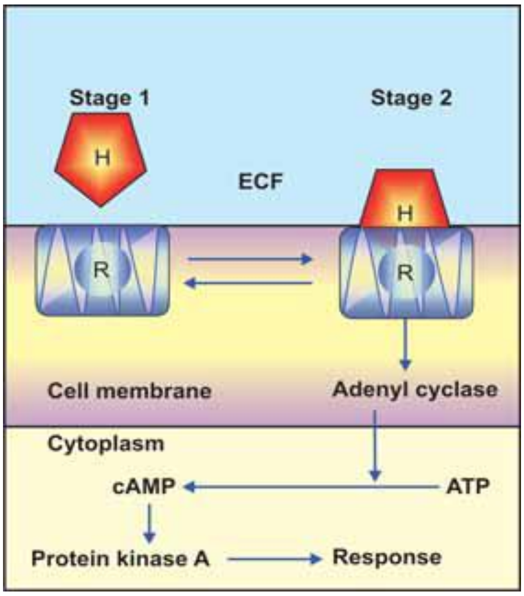
On the target cell, the hormone–receptor complex acts by any one of the following mechanisms:

1. By Altering the Permeability of Cell Membrane

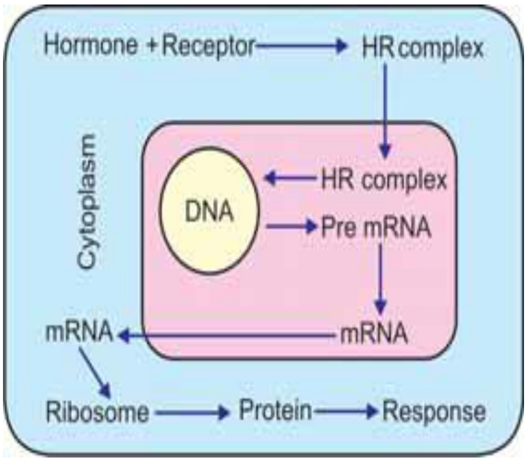
The neurotransmitter substances in a synapse or neuromuscular junction act by changing the permeability of postsynaptic membrane. For example, in a neuromuscular junction, when an impulse (action potential) reaches the axon terminal of the motor nerve, acetylcholine is released from the vesicles. Acetylcholine increases permeability of postsynaptic membrane by opening the ligand gated sodium channels. So, sodium ions enter the neuromuscular junction from ECF through the channels. Sodium ions alter the resting membrane potential so that, endplate potential is developed.

2. By Activating the Intracellular Enzyme

The protein hormones and the catecholamines act by activating the intracellular enzymes. The hormone, which acts on a target cell, is called first messenger or chemical mediator. This hormone, in combination with the receptor forms hormone-receptor complex. This in turn activates the enzymes of the cell and causes the formation of another substance called the second messenger.



Mode of action of protein hormones and catecholamines. H = Hormone, R = Receptor



Mode of action of steroid hormones. Thyroid hormones also act in the similar way. But their receptors are in the nucleus.HR= Hormone-receptor complex

The second messenger produces the effects of the hormone inside the cells. The most common second messenger is adenosine monophosphate (cyclic AMP or cAMP).
Sequence of events in the activation of second messenger:

i. The hormone binds with the receptor in the cell membrane and forms the hormone-receptor complex which activates the enzyme adenyl cyclase
ii. Adenyl cyclase converts the ATP of the cytoplasm into cAMP. Cyclic AMP executes the actions of hormone inside the cell, by stimulating the enzymes like protein kinase A

3. By Acting on Genes
Thyroid and steroid hormones act by activating the genes of the target cells.
Sequence of events during activation of genes:

i. The hormone enters the interior of the cell and binds with receptor in cytoplasm (steroid hormone) or in nucleus (thyroid hormone) and forms hormone-receptor.
ii. This complex bind to DNA and increases transcription of mRNA

iii. The mRNA moves out of nucleus and reaches ribosomes and activates them.
iv. The activated ribosomes produce large quantities of proteins which produce the physiological responses in the target cells.

Onset of Hormone Secretion After a Stimulus, and Duration of Action of Different Hormones.
Some hormones, such as norepinephrine and epinephrine, are secreted within seconds after the gland is stimulated, and they may develop full action within another few seconds to minutes; the actions of other hormones, such as thyroxine or growth hormone, may require months for full effect. Thus, each of the different hormones has its own characteristic onset and duration of action—each tailored to perform its specific control function.

Concentrations of Hormones in the Circulating Blood, and Hormonal Secretion Rates.

The concentrations of hormones required to control most metabolic and endocrine functions are incredibly small. Their concentrations in the blood range from as little as 1 picogram (which is one millionth of one millionth of a gram) in each milliliter of blood up to at most a few micrograms (a few millionths of a gram) per milliliter of blood. Similarly, the rates of secretion of the various hormones are extremely small, usually measured in micrograms or milligrams per day.

Measurement of Hormone Concentrations in the Blood

Most hormones are present in the blood in extremely minute quantities; some concentrations are as low as one billionth of a milligram (1 picogram) per milliliter. Therefore, it was very difficult to measure these concentrations by the usual chemical means. An extremely sensitive method, however, was developed about 40 years ago that revolutionized the measurement of hormones, their precursors, and their metabolic end products. This method is called radioimmunoassay.

Feedback Control of Hormone Secretion Negative Feedback Prevents Overactivity of Hormone Systems.

Although the plasma concentrations of many hormones fluctuate in response to various stimuli that occur throughout the day, all hormones studied thus far appear to be closely controlled. In most instances, this control is exerted through negative feedback mechanisms that ensure a proper level of hormone activity at the target tissue. After a stimulus causes release of the hormone, conditions or products resulting from the action of the hormone tend to suppress its further release.

Surges of Hormones Can Occur with Positive Feedback.

In a few instances, 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. Eventually, LH reaches an appropriate concentration, and typical negative feedback control of hormone secretion is then exerted. Cyclical Variations Occur in Hormone Release.