

# Introduction to Endocrinology

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**Endocrinology** is the study of hormones, their receptors and the intracellular signaling pathways they initiate.

- **Endocrine glands** are ductless and secrete hormones to bloodstream

- **Hormones** are chemical messengers secreted into blood or extracellular fluid by one cell that affect the functioning of other cells.

- The major glands of the endocrine system are the pituitary, pancreas, thyroid, parathyroids, adrenals, pineal, and the reproductive organs (ovaries and testes).

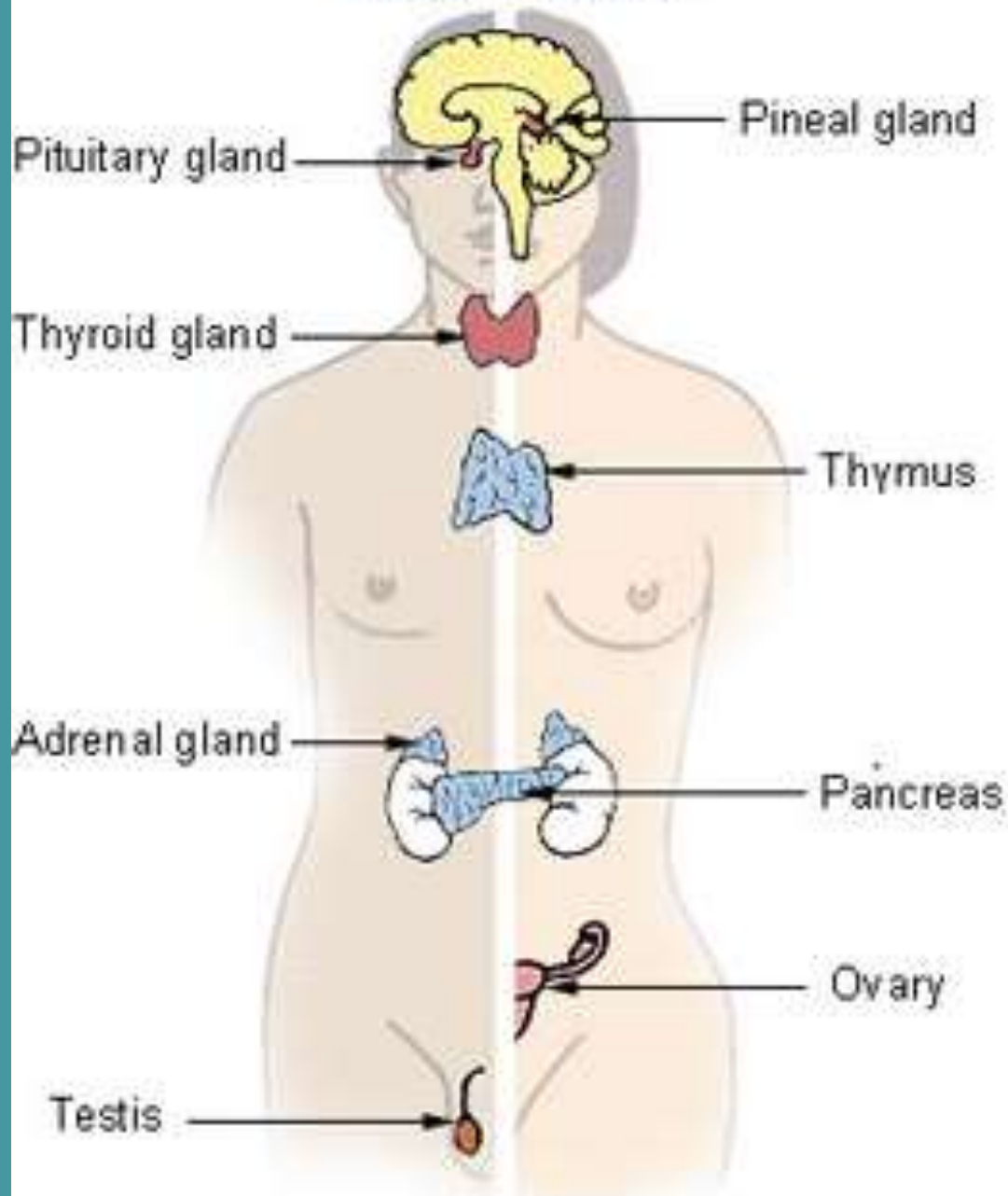
## **Endocrinology is about communications between cells**

- **Hormone functions**: reproduction and sexual differentiation; development and growth; maintenance of the internal environment; and regulation of metabolism and nutrient supply.

- A single hormone may affect more than one of these functions and each function may be controlled by several hormones.

# Major Endocrine Glands

Male Female



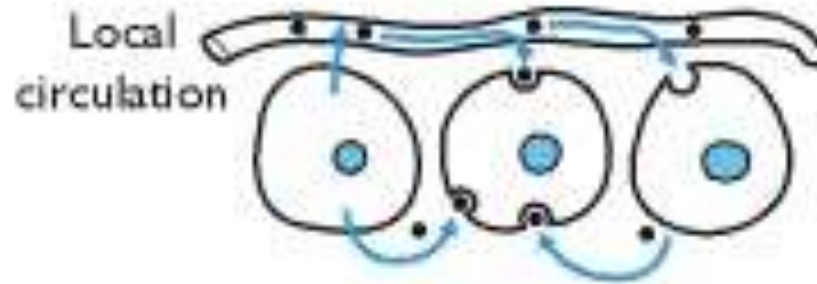
# Chemical signaling

Hormones can be classified depending on the distance between the secreting and target cells into:

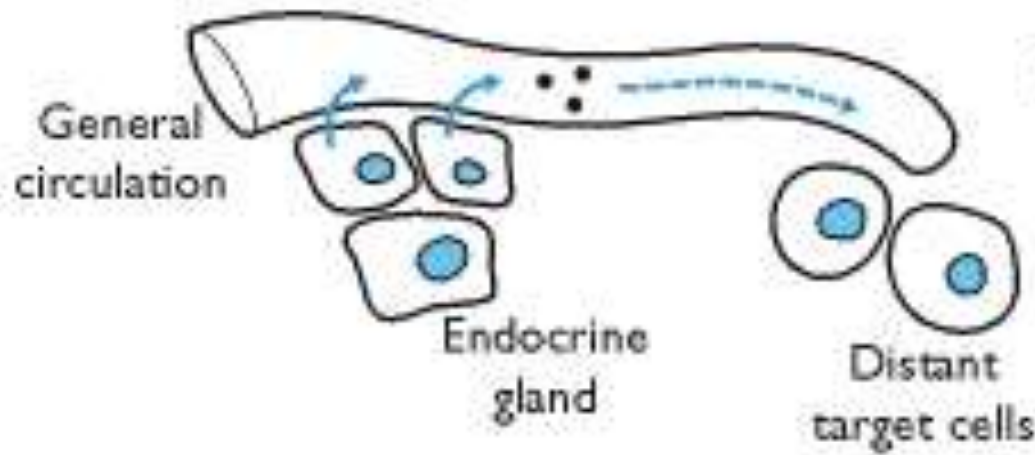
- 1- Endocrine action:** the hormone is distributed in blood and binds to distant target cells. (neuroendocrine: neurons produce both neurotransmitter and hormone (eg. epinephrine))
- 2- Paracrine action:** (Para: near) the hormone acts locally by diffusing from its source to target cells in the neighboring cells within a tissue or organ without entering blood.
- 3- Autocrine action:** the hormone acts on the same cell that produced it.



**Autocrine**



**Paracrine**



**Endocrine**

## Chemical classification of hormones

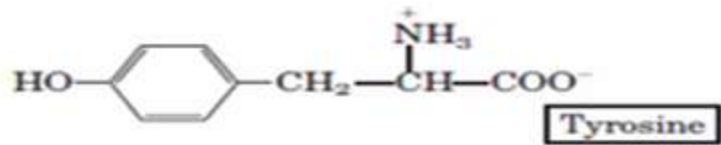
Chemically hormones are grouped into three classes:

**1-Steroid hormones**: are hydrophobic and synthesized from cholesterol and are categorized in the human into six different classes or families that include:

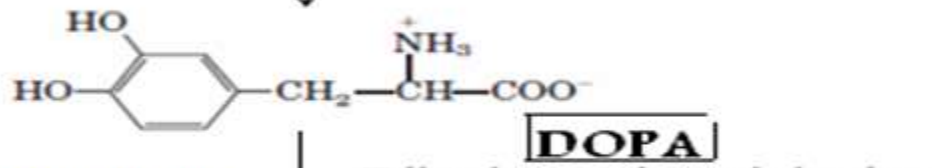
Progestins (C-21) (Progesterone), Glucocorticoids (C-21) (Cortisol), Mineralocorticoids (C-21) (Aldosterone), Androgens (C-19) (Testosterone), Estrogens (C-18) (Estradiol), and vitamin D.

Steroid hormones affect carbohydrate metabolism salt and water balance, and reproductive function.

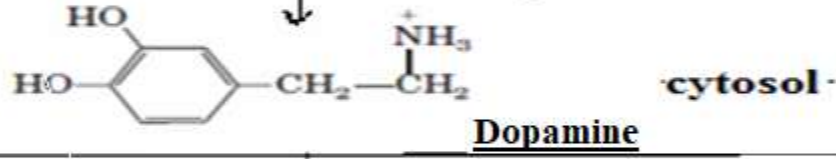
**2-Tyrosine derivatives hormones** including: A. catecholamine hormones (hydrophilic) and B. thyroid hormones (hydrophobic). Catecholamine hormones include epinephrine, norepinephrine and dopamine. Dopamine is a neurotransmitter that can act as hormone is released from median eminence and suppress the secretion of prolactin from anterior pituitary. The thyroid hormones-thyroxin and triiodothyronine-each have two fused molecule of tyrosine. Thyroxin has four iodine atoms attached to the amino rings while triiodothyronine has three iodine atoms.



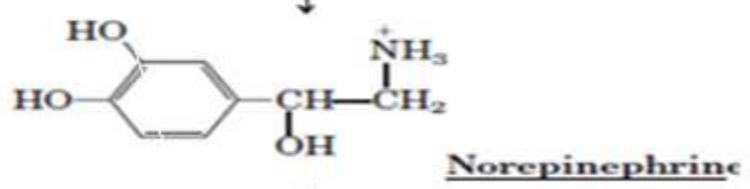
**tyrosine hydroxylase**  
 hydroxylation of tyrosin ring  
 rate limiting step for all catecholamines



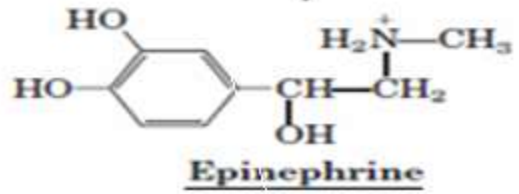
**Aromatic aa decarboxylase**  
 decarboxylation



**dopamine β-hydroxylase**  
 hydroxylation **storage Vesicles**



**phenylethanolamine N-methyltransferase**  
 transfers a methyl group



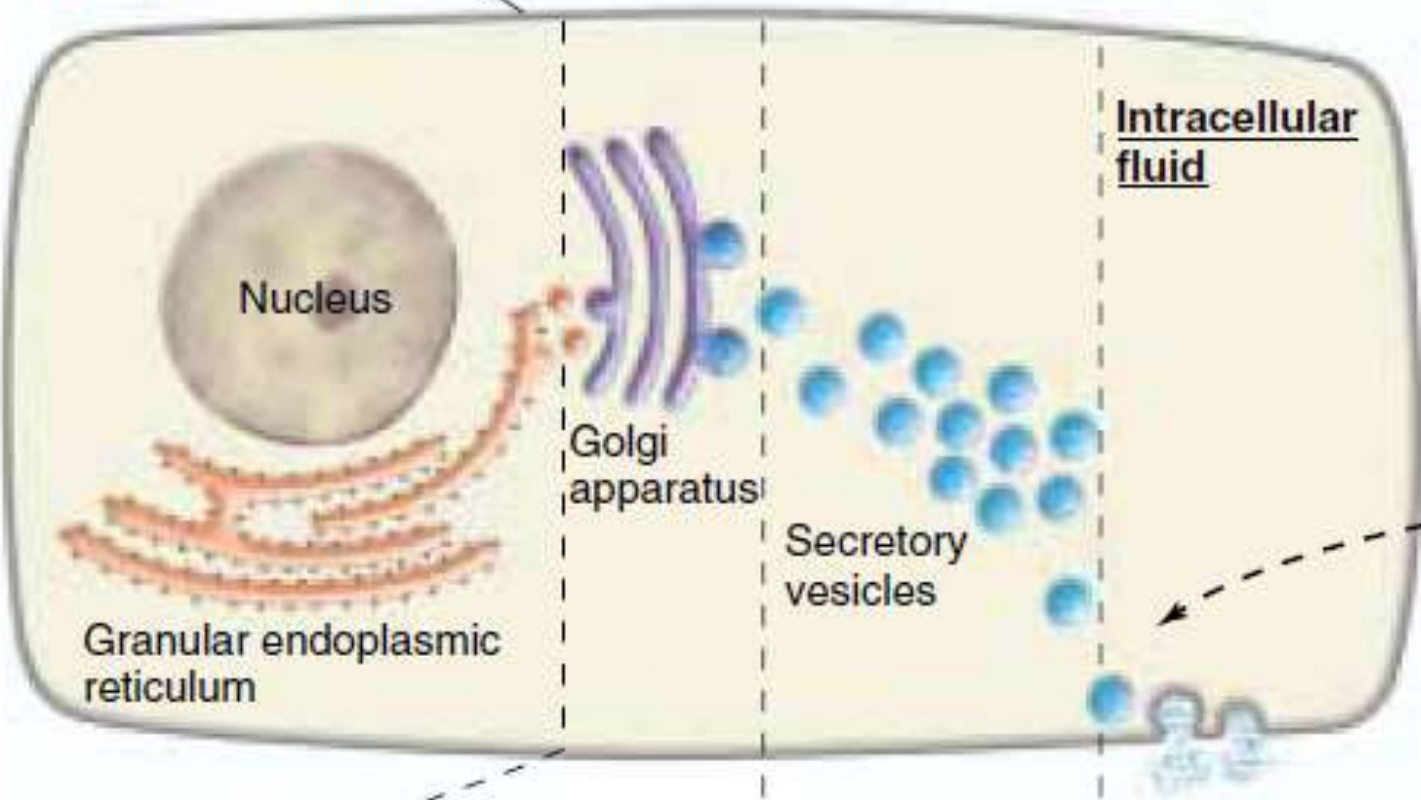
dopamine is mainly synthesized in brain and function as neurotransmitter and in other parts of body it function as a hormone

Norepinephrine and epinephrine are secreted by the adrenal medulla and sympathetic nerve endings and act as hormones and neurotransmitters

**3-Peptides and proteins hormones:** are hydrophilic and the most numerous hormones, they range in size from just three to over 200 amino acids.

- Some hormones, such as insulin which is regarded as a small protein, are made up of two sub-units joined by disulfide bonds between two cysteine molecules whilst the glycoprotein hormones of the anterior pituitary gland are not only made up of two protein sub-units but also have complex sugar moieties attached. Most peptide hormones are water-soluble.
- In peptides and proteins hormones they are synthesized on the ribosomes of the endocrine cells as larger proteins known as preprohormones, which are then cleaved to prohormones by proteolytic enzymes in the granular endoplasmic reticulum. The prohormone is then packaged into secretory vesicles by the Golgi apparatus which is cleaved to active hormone upon activation.

Plasma membrane



Synthesis

Packaging

Storage

Secretion

Preprohormone  
↓  
Prohormone

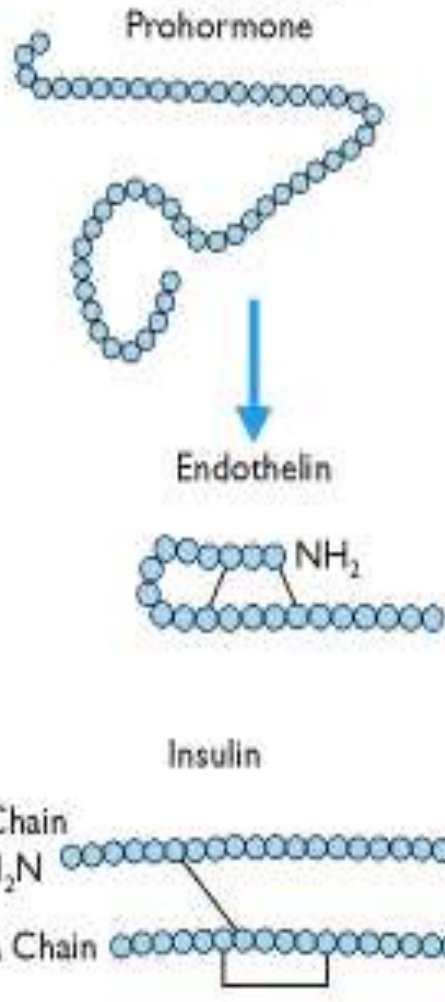
Prohormone  
↓  
Hormone

Hormone

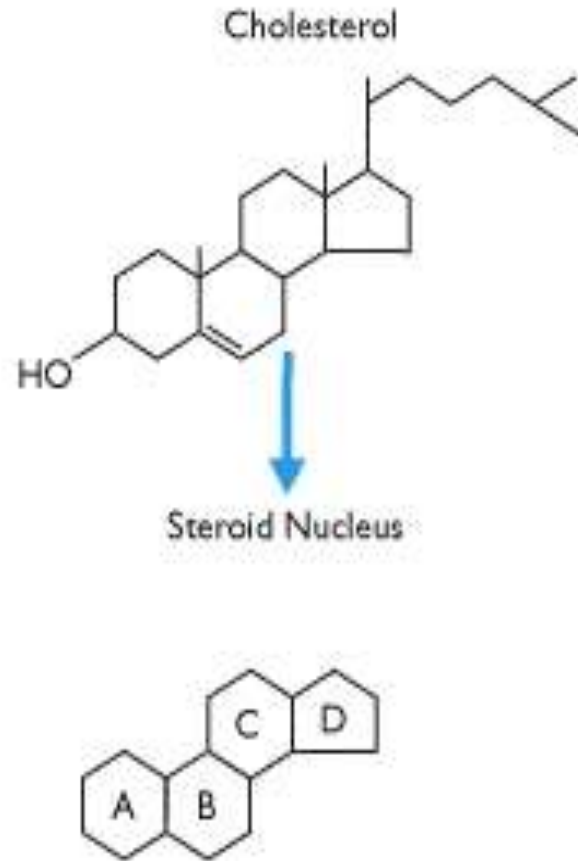
Hormone  
(and any  
"pro" fragments)

Typical synthesis and secretion of peptide hormones. In some cells, the calcium that causes exocytosis is released from the endoplasmic reticulum by action of a second messenger rather than entering from the extracellular fluid

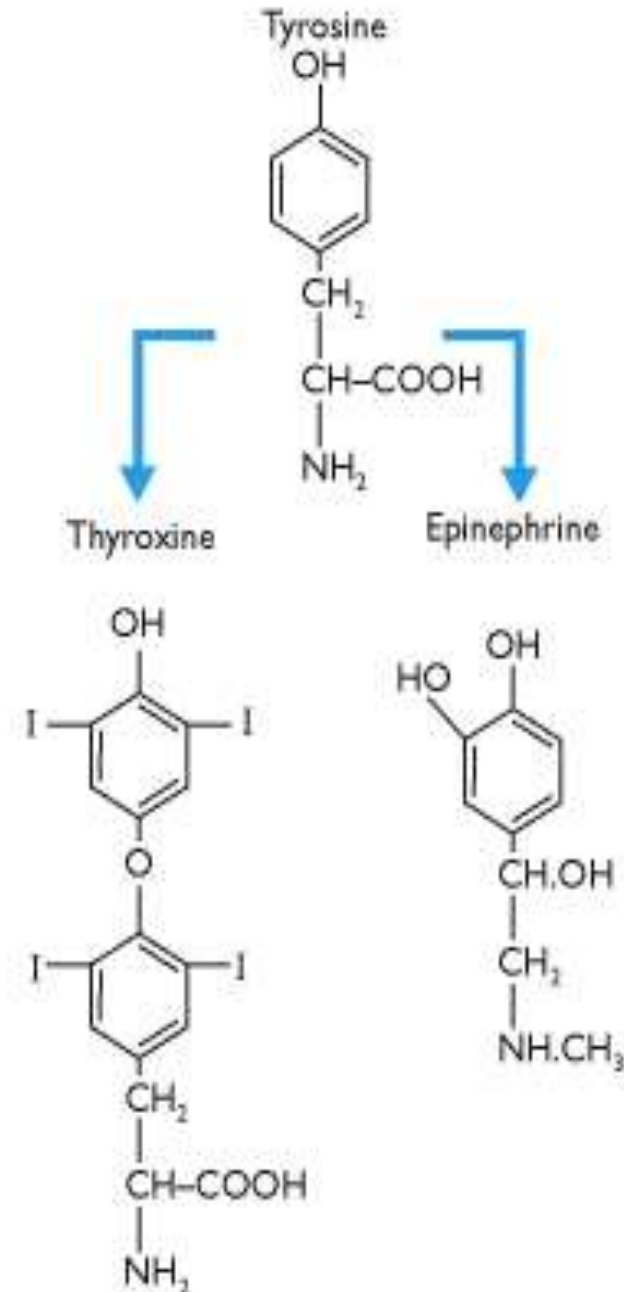
## Protein and Peptide Hormones



## Steroid Hormones



## Tyrosine Derivatives



# Control of Hormone Secretion

## 1. Neural

The adrenal medulla (the inner part of an **adrenal** gland it releases the hormones that initiate the flight or fight response it secret epinephrine and norepinephrine hormones) is directly stimulated by the sympathetic nervous system.

## 2. Hormonal

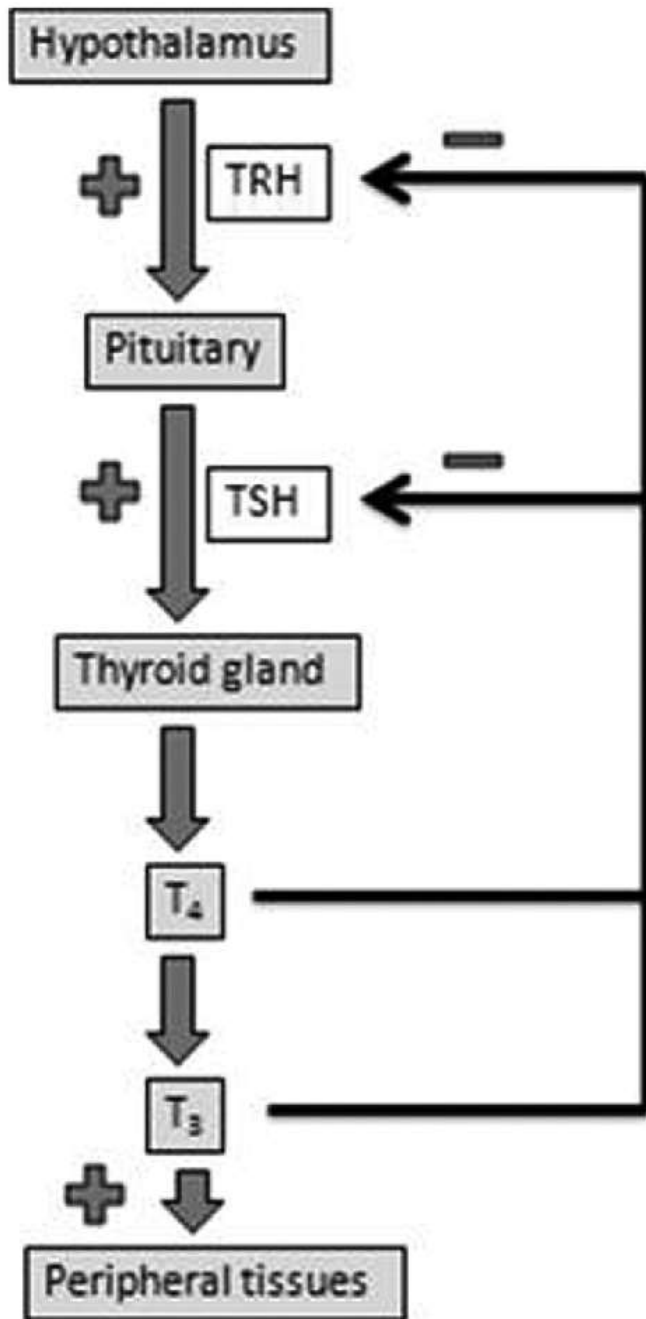
Occurs when hormones from one endocrine gland stimulate the secretion of hormones from another endocrine gland. These routes of secretion are usually controlled in a negative feedback manner.

## 3. Humoral

Occurs when substances other than hormones control the secretion of endocrine glands.

E.g. Insulin secretion by the pancreas is determined by several factors. Rise in glucose and amino acids after a meal triggers insulin secretion.

- **Feedback control**
- For the hormones that are regulated by the pituitary gland, a signal is sent from the hypothalamus to the pituitary gland in the form of a "releasing hormone," which stimulates the pituitary to secrete a "stimulating hormone" into the circulation. The stimulating hormone then signals the target gland to secrete its hormone. As the level of this hormone rises in the circulation, the hypothalamus and the pituitary gland shut down secretion of the releasing hormone and the stimulating hormone, which in turn slows the secretion by the target gland.
- Example: Thyrotropin releasing hormone (TRH) produced by the hypothalamus stimulate the release of thyrotropin-stimulating hormone (TSH produced by anterior pituitary gland) which stimulate the release of thyroid hormones. In turn, high level of thyroid hormones inhibit production and secretion of both TRH and TSH. Decreased production of thyroid hormone results in increased TRH secretion and thus increased thyroid hormone secretion.



**Feedback control** Example: Thyrotropin -Releasing Hormone (TRH) produced by hypothalamus stimulate pituitary gland to secrete Thyrotropin -stimulating hormone (TSH). That stimulate the thyroid gland to release T<sub>4</sub> and T<sub>3</sub>

When T<sub>4</sub> and T<sub>3</sub> levels are high they block the release of TRH and TSH

# • Hormone synthesis, storage, secretion and transport

## 1- Synthesis

A-Most protein and peptide hormones require the transcription of a single gene and then translation on ribosome in the rough endoplasmic reticulum.

B-The synthesis of steroid hormones occurs in the mitochondria and smooth endoplasmic reticulum requires the presence of specific enzymes that convert cholesterol into the appropriate steroid.

- Mitochondria contain the cholesterol side-chain cleavage enzyme, P450<sub>scc</sub>, and its two electron-transfer partners: ferredoxin and ferredoxin reductase. This enzyme system converts cholesterol to pregnenolone (21 carbon atoms)

## 2- Storage

- Protein or peptide hormone-secreting cells store the newly synthesized hormone in small vesicles or secretory granules inside the cell membrane. On the other hand steroid producing hormone cells do not store steroid hormone but synthesis hormone on demand and secreted to blood.

## 3- Secretion

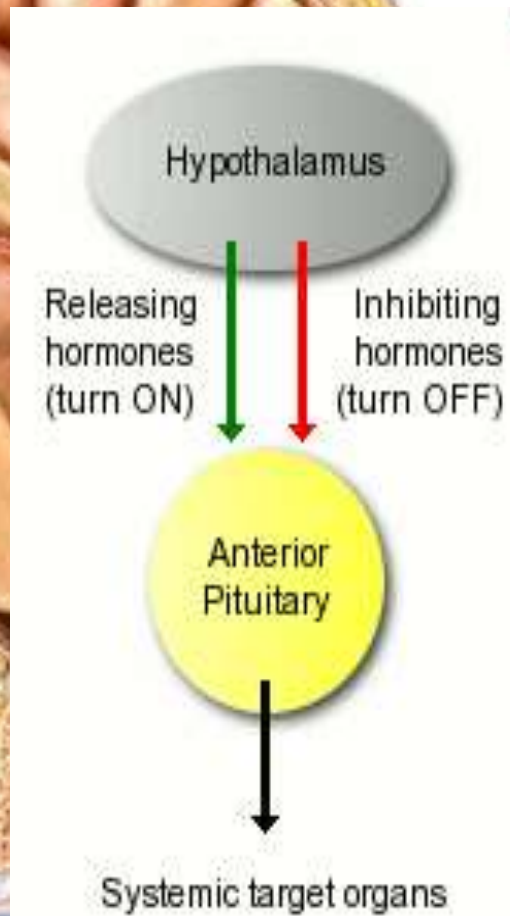
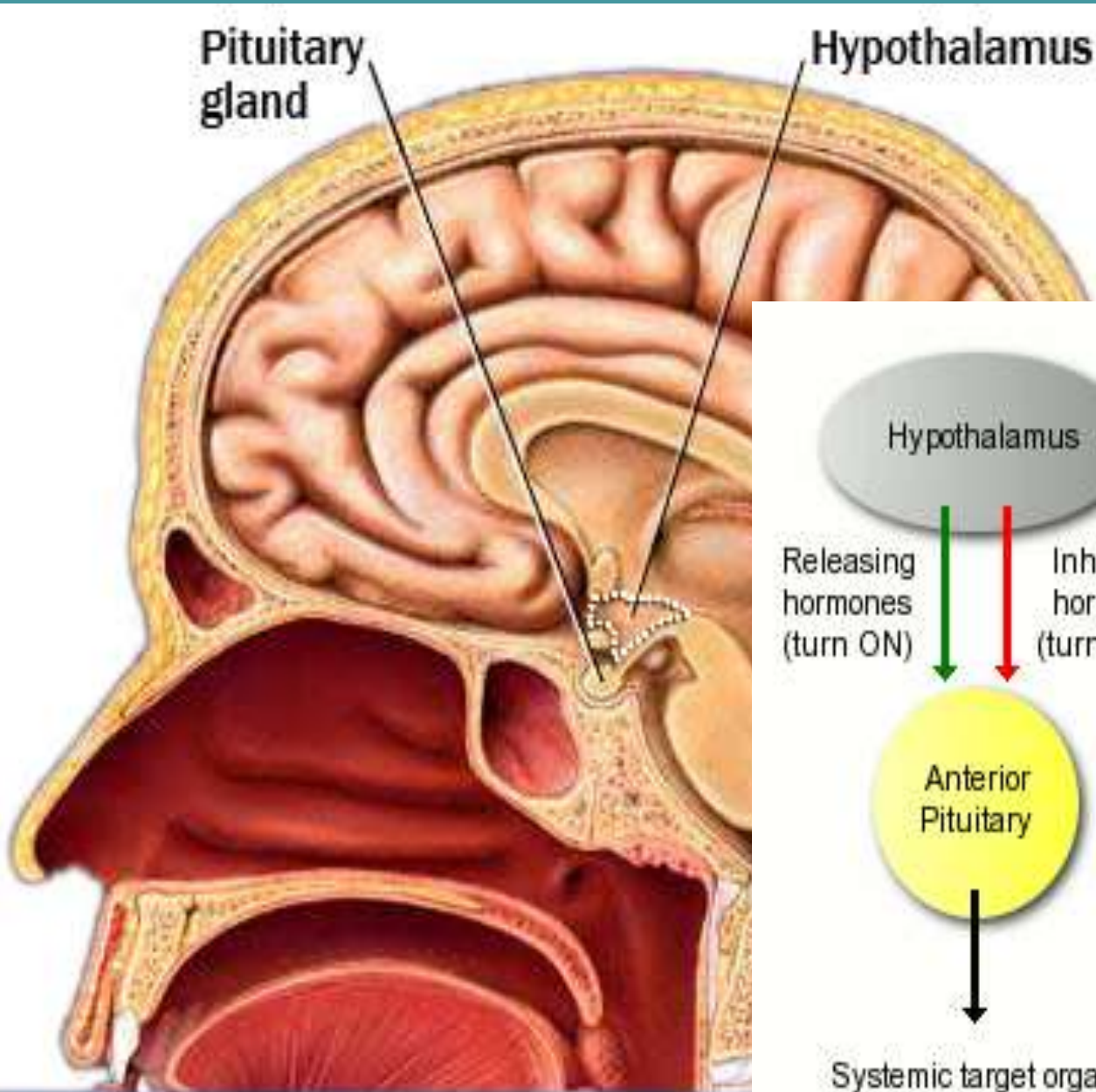
- The cell requires some stimulus before the stored prohormone is activated and released. The stimulation may be hormonal and usually involve a change in permeability of the cell to Ca<sup>2+</sup> ions. The metal ions are required for interaction between the vesicle and plasma membranes and for the activation of enzymes, microfilaments and microtubules. Specific endopeptidases present together with the prohormone in the storage vesicle are activated during the secretory process and produce the active form of the hormone for release from the cell. The mode of secretion from the cell is called exocytosis.

## 4- Transport of hormones in the circulation

- Steroid and thyroid hormones are less soluble in aqueous solution (hydrophobic) than catecholamine hormones and protein and peptide hormones (hydrophilic) and over 90% circulate in blood as complexes bound to specific plasma globulins or albumin and a more specific transport protein, such as steroid hormone binding globulin (SHBG) and thyroid hormone-binding globulin (TBG).
- Free hormone (unbound) is the biologically active and not the bound hormone. Bound hormones are not available for diffusion into cells and thus can't affect the target organ or tissue.
- Bound and free hormones are in equilibrium.
- Therefore, bound hormone act as a storage of free hormone and it regulates the amount of free hormones available for diffusion into tissues.
- it has been suggested that the specific binding globulins may interact with membrane receptors and that hormone binding to the globulins initiates a signal transduction pathway.
- The half life ( $t_{1/2}$ ) of catecholamines and peptide and protein hormones is in the order of seconds to few minutes while it is hours or days for steroid and thyroid hormones.

## Neuroendocrine interactions

- How the endocrine and nervous system linked?
- Hypothalamus connects these two important communication systems. The hypothalamus is a group of tiny nuclei that lie along the base of the brain near the pituitary gland.
- The hypothalamus controls the pituitary gland by secreting hormones which control the secretion of many endocrine glands, and this gives the hypothalamus a great deal of control over many body functions.
- Moreover, all endocrine glands are innervated by autonomic nerves and these may directly control their endocrine function and/or regulate blood flow (and hence function) within the gland. Hormones, in turn, may affect central nervous system functions such as mood, anxiety and behavior.



# Hormones effects

The physiological effects of hormones depend largely on their concentration in blood and extracellular fluid.

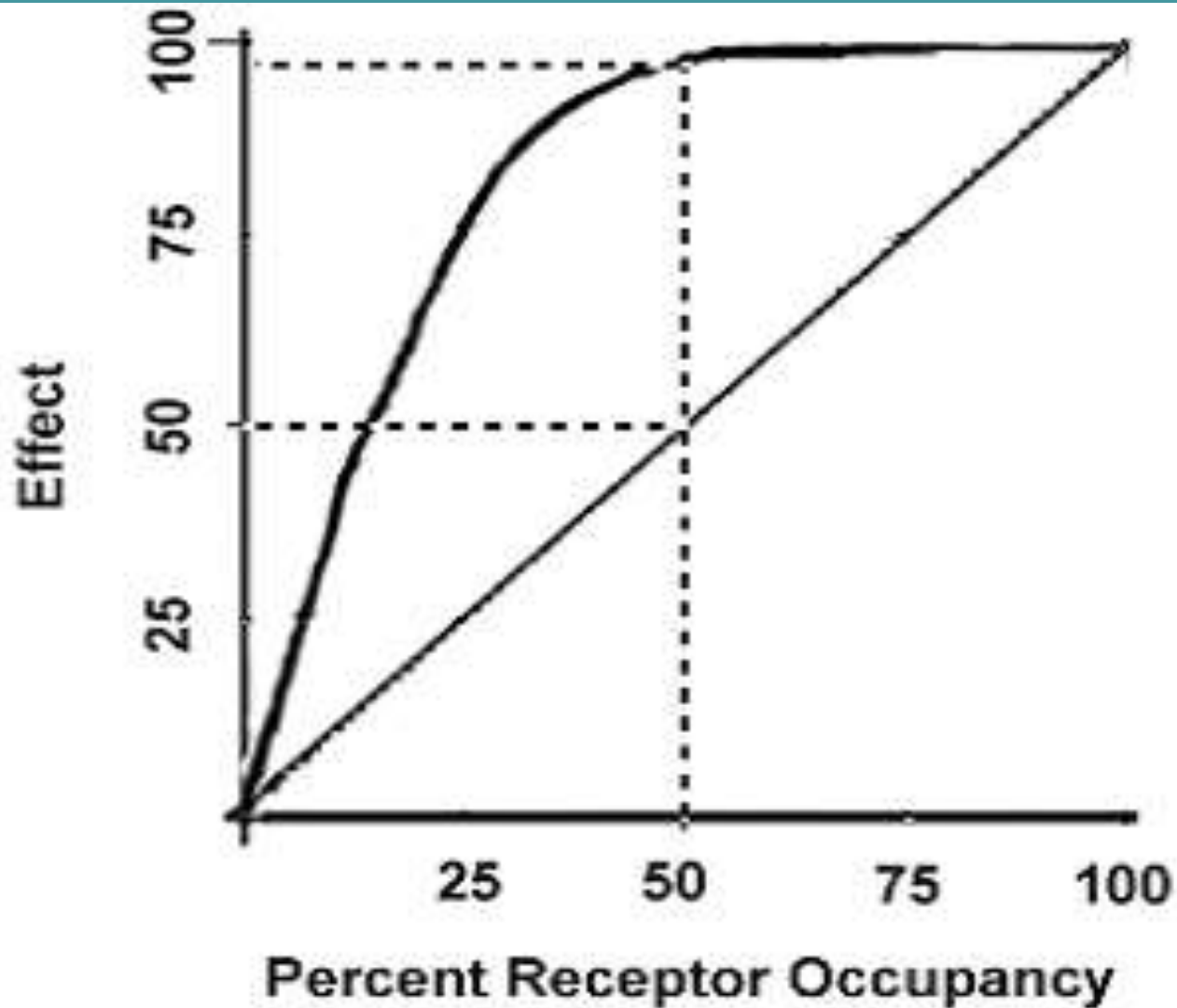
The concentration of hormone is determined by three factors:

- 1- Rate of production: regulated by positive and negative feedback circuits.
- 2- Rate of delivery: An example of this effect is blood flow to a target organ or group of target cells - high blood flow delivers more hormone than low blood flow.
- 3- Rate of degradation and elimination: most of hormone is cleared by liver and kidneys. Only a small fraction is removed by target tissue through enzymatic degradation.

## Spare receptors

- Spare receptors are receptors which exist in excess of those required to produce a full effect therefore a maximum response can be reached with only 2-3% receptor bonded to hormones. The greater the proportion of spare receptors, the more sensitive the target cell to the hormone.
- In most systems the maximum biological response is achieved at concentrations of hormone lower than required to occupy all of the receptors on the cell. For examples insulin stimulates maximum glucose oxidation in adipocytes with only 2-3% of receptors bound. Because hormones are normally present at very low concentrations only small receptors are occupied and it is enough to produce maximum effect. And when hormone is at high concentrations all receptors are occupied but without any extra effect.
- The effectors can be mobile, rapidly moving from one receptor molecule to another so the more receptors the more it can activate. Beside that the hormone has more opportunities to find and activate a receptor.

# Spare receptors



- **Agonists** are molecules that bind the receptor and induce all the post-receptor events that lead to a biologic effect. In other words, they act like the "normal" hormone, although perhaps more or less potently
- **Antagonists** are molecules that bind the receptor but are unable to bring about receptor activation (fail to trigger intracellular signaling events) and block binding of the agonist.