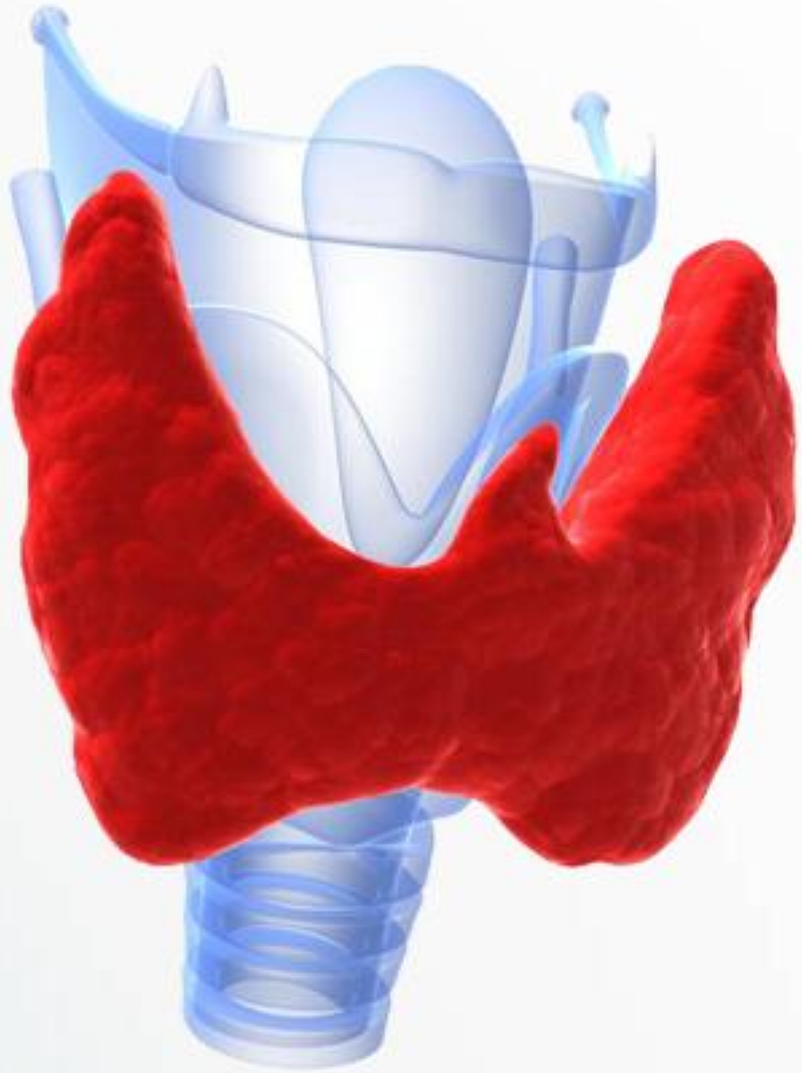
Physiology team



1 Introduction To Endocrine

Sources:
Female slides
BRS Physiology p222-p227

Objectives

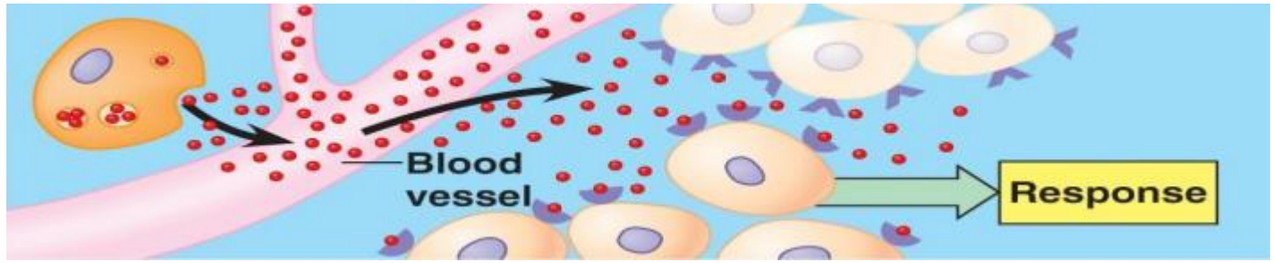
- Difference between endocrine & exocrine glands
- Chemical messengers
- Major endocrine organs
- Hormone
- What is the hormone?
- Types of stimuli
- What are target cells?
- Chemical structure
- Transport
- Mechanism of action
- Receptors, down-regulation & up-regulation
- Intracellular signaling
- Second messenger (cAMP, IP3 & tyrosine kinase)
- Hormones interactions at target cells
- Clearance of hormones

Overview of Chemical substances

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

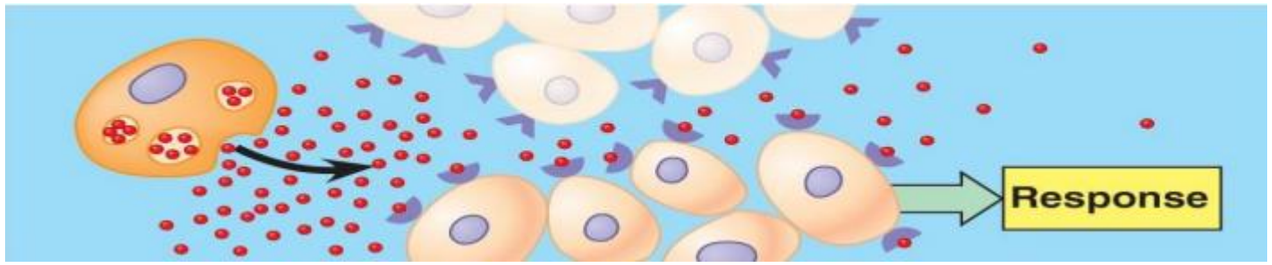
Endocrine glands

They are **ductless** glands that produce hormones released directly into the blood.



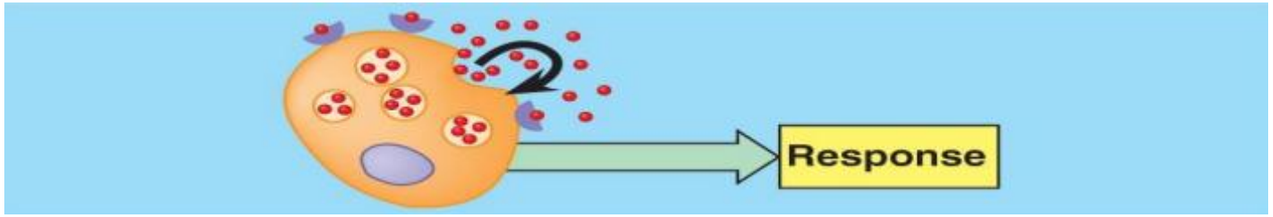
Paracrine glands

Secreted by cells into ECF and affect neighboring cells of a different type



Autocrine glands

Secreted by cells into ECF and affect the function of the same cells.

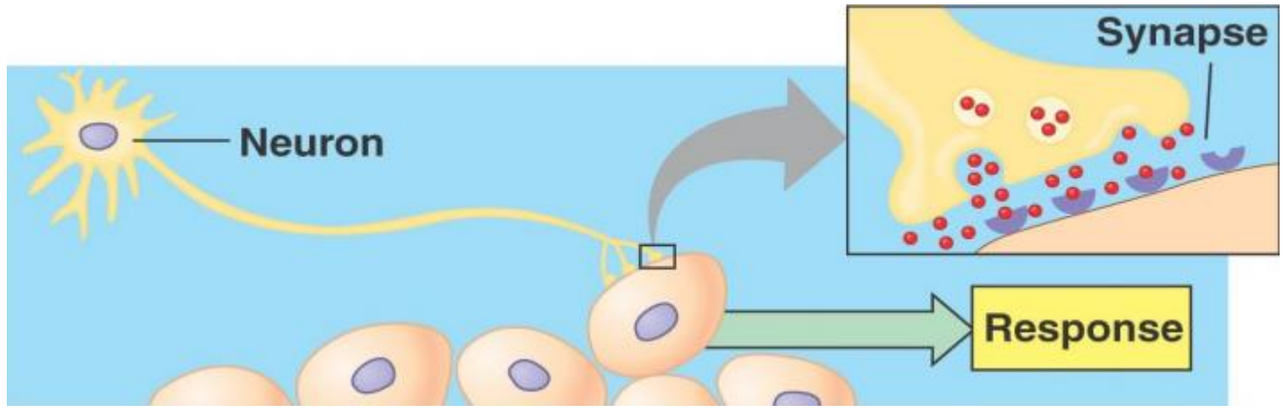


Exocrine glands

Release their products at the body's surface or **into body cavities through ducts.**

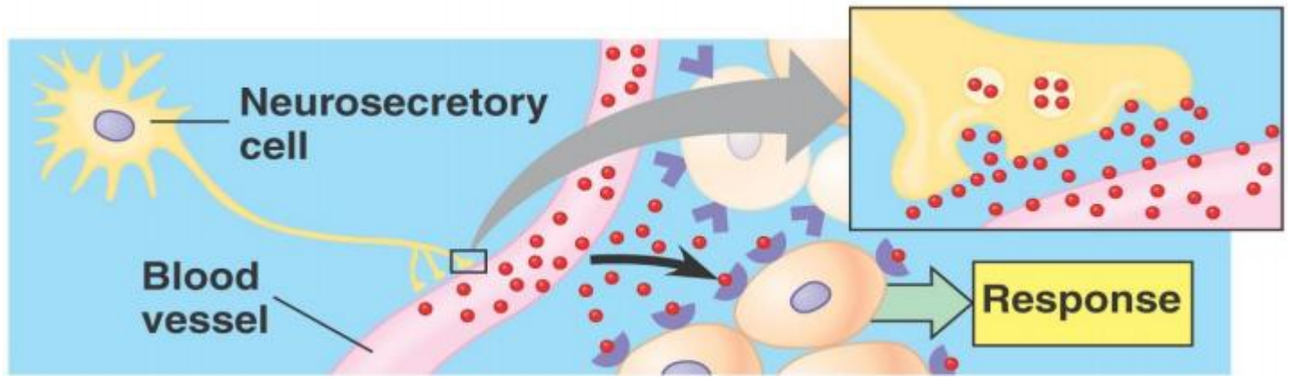
Neurotransmitters

When it become contact nerve with nerve called **neurotransmitter**



Neuroendocrine

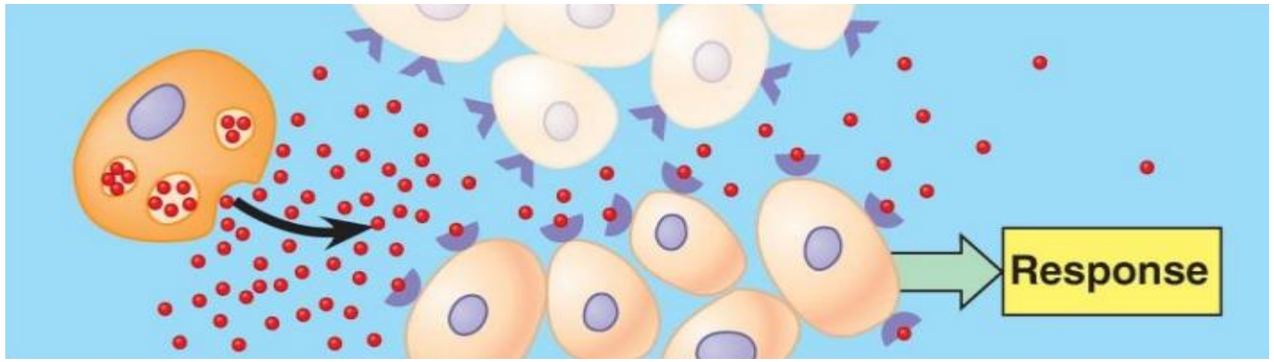
the contact with nerve and vessel called **neuroendocrine**.

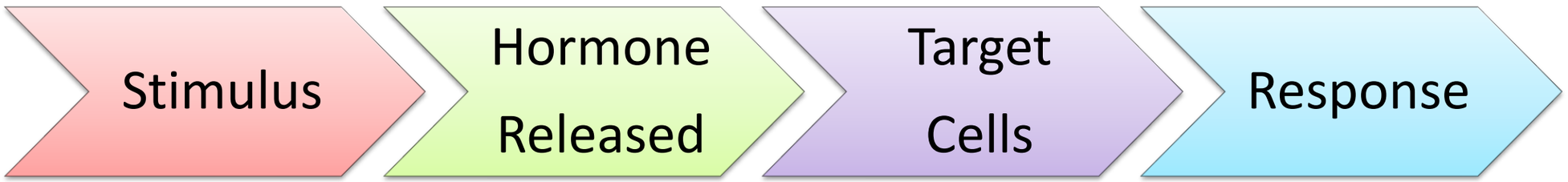


Cytokines

(e.g., leptin & interleukins):

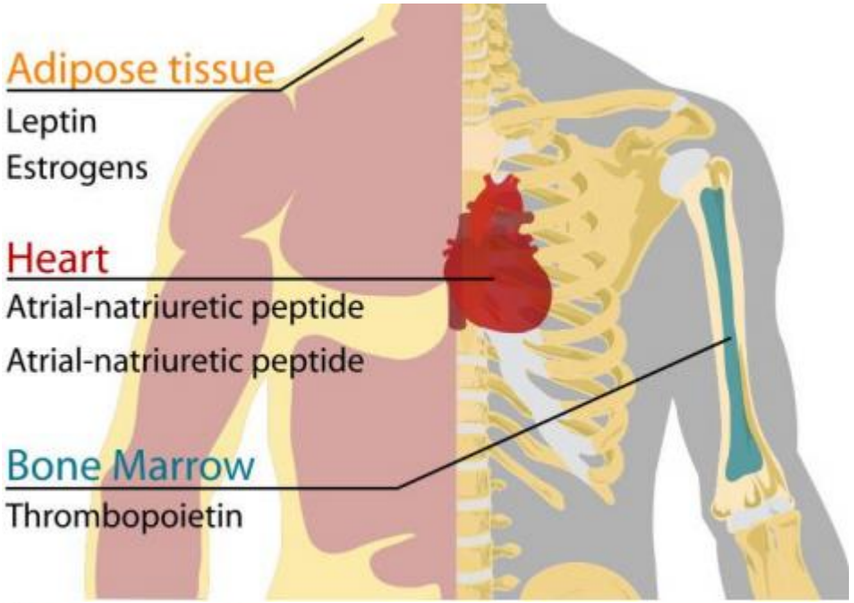
peptides secreted by cells into ECF and function as autocrines, paracrines, or endocrine hormones and act on other cells

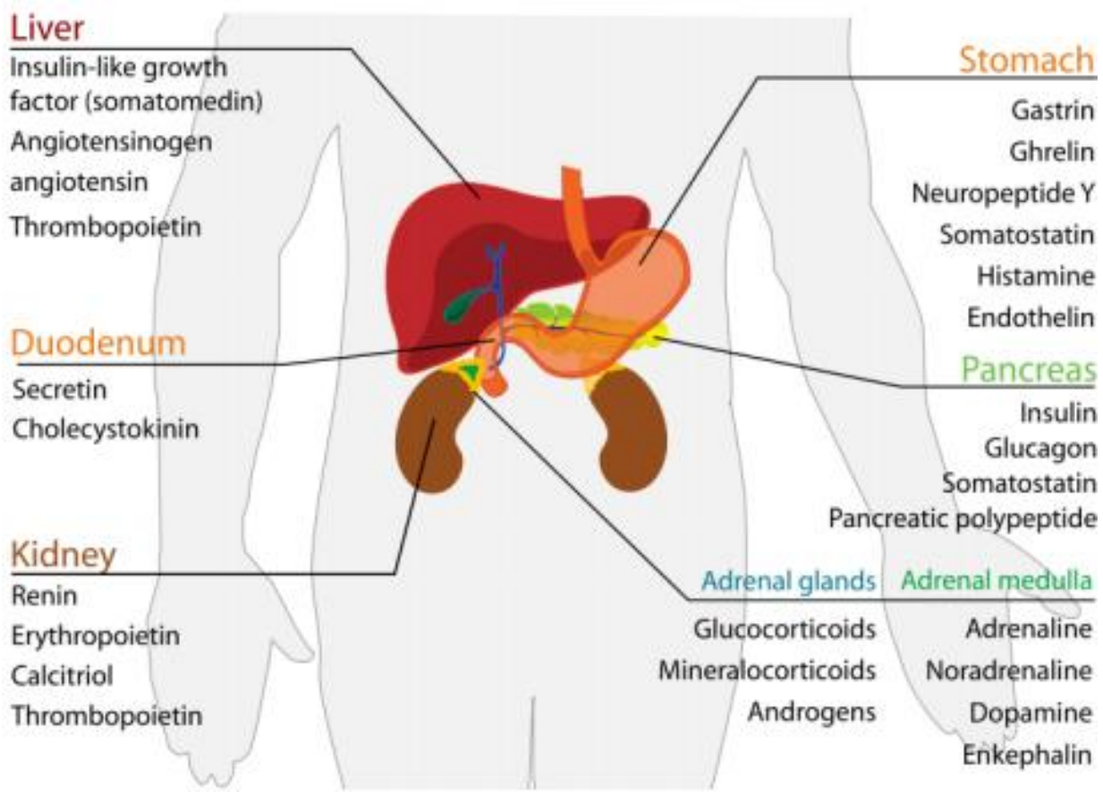


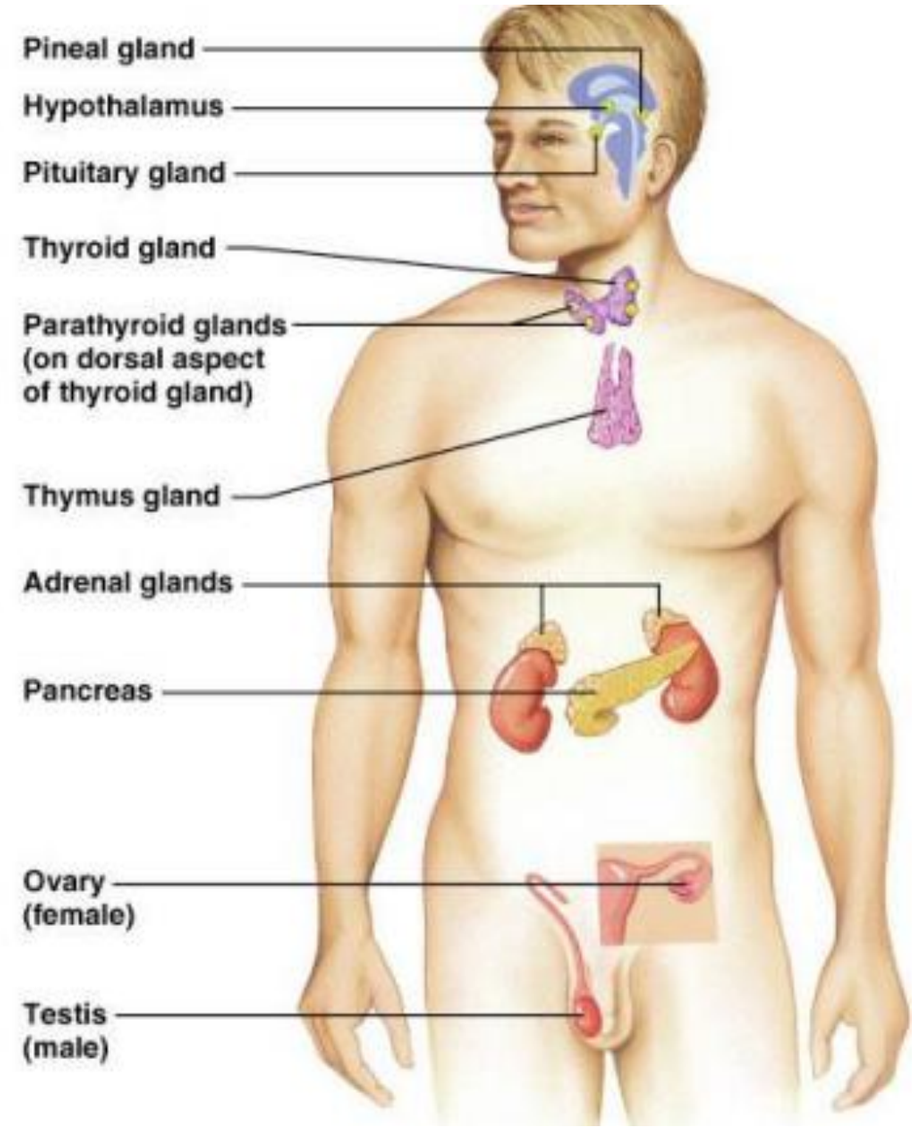


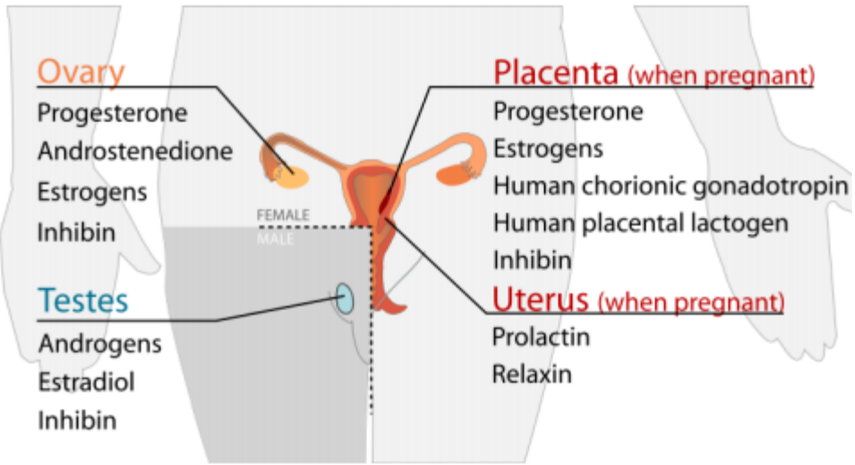
Major Endocrine Organs

o The hypothalamus, which is part of the nervous system, is also considered as a major endocrine organ.







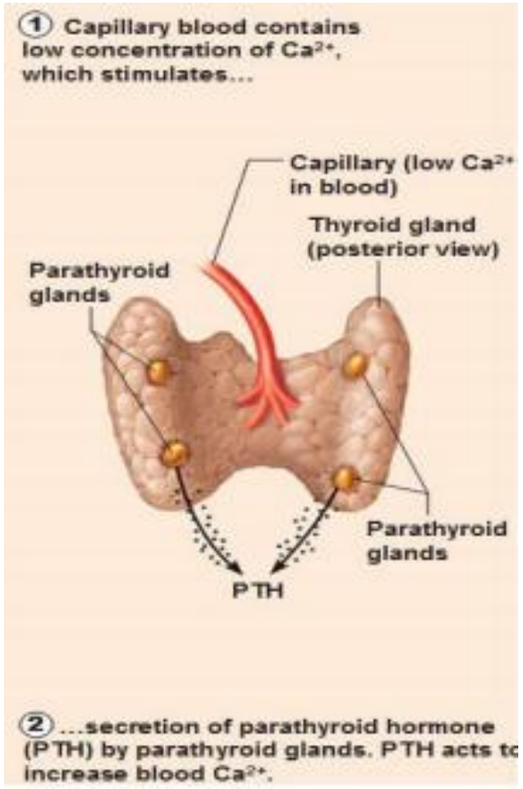


Classification of stimuli

Humoral Stimuli

Secretion of hormones in direct response to **changing in blood levels of ions and Nutrients**

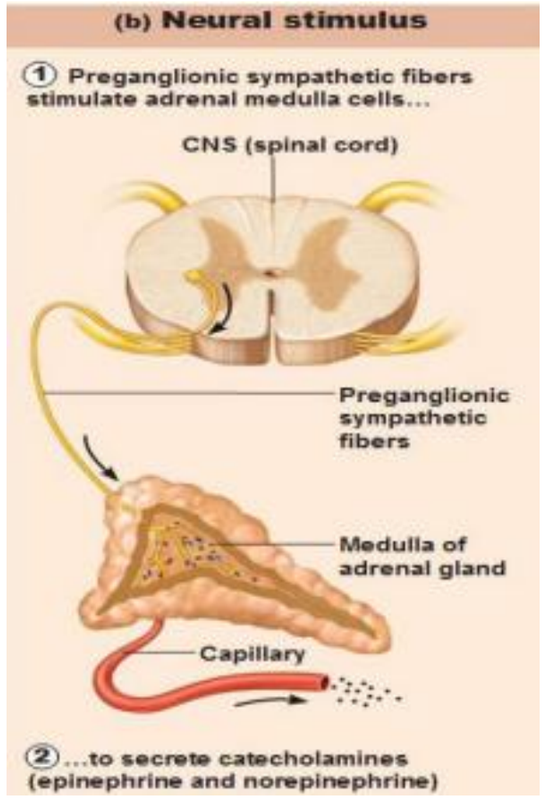
(e.g.: decrease calcium level will lead to produce parathyroid hormone)



Neural Stimuli

Nerve signals stimulate hormone release.

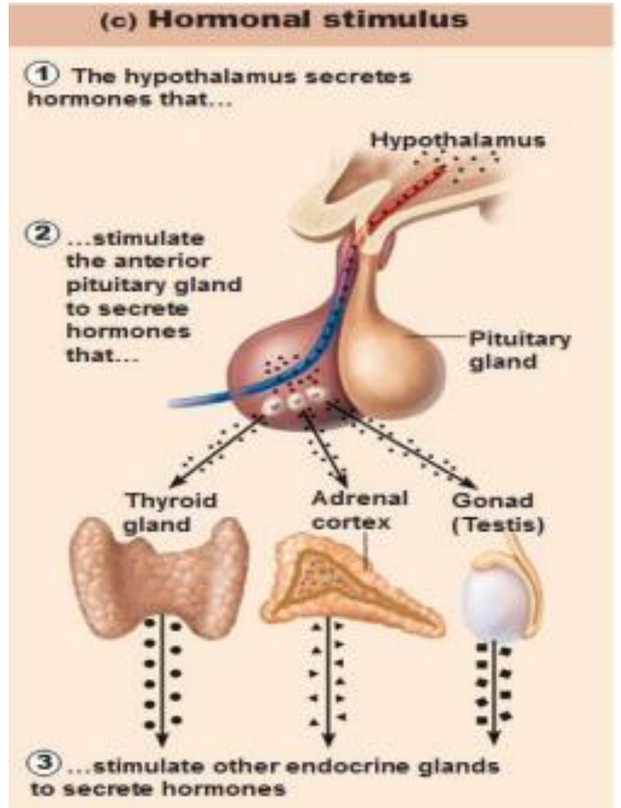
(e.g.: in sympathetic stimulation your body will release epinephrine)



Hormonal Stimuli

Release of **hormones in response to hormones produced by other endocrine gland.**

(e.g.: hypothalamus release hormones to activate releasing other hormones)



Hormones

Definition

Chemical substance secreted in a small amount from endocrine gland directly to the blood stream in response to stimulus to cause physiological responses at other type of cells (target cells).

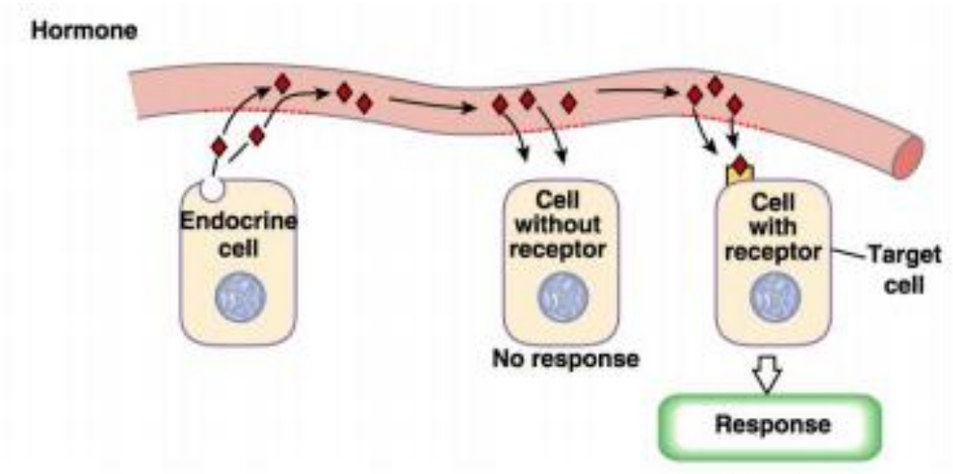
- Hormone can affect many different types of target cells **(e.g. GH and Thyroxin)**
- Hormone can affect only specific target cells **(e.g. ACTH and estrogen)**

Importance of Hormones

The multiple hormone systems play a key role in **regulating almost all body functions**:
(Metabolism - Growth and development - Water and electrolyte balance – Reproduction – Behavior)

What is target cells?

Target cells refer to cells that contain specific receptors (binding sites) for a particular hormone.

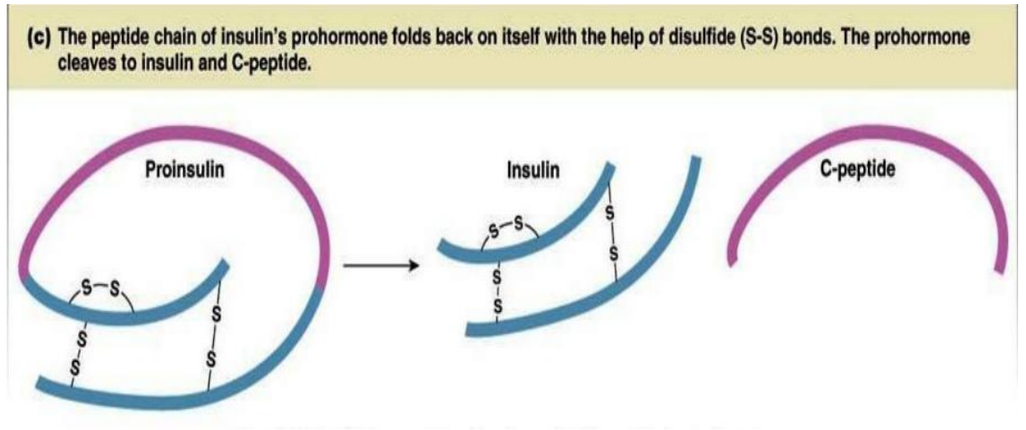


Chemical structure of hormones

1. Proteins and polypeptides: stored in vesicles until needed
2. Steroids: diffuse across the cell membrane
3. Derivatives of amino acid

Proteins and polypeptides hormones

Synthesized as **preprohormone** →
post-translational modification to **prohormone** → hormone
Example of protein hormone:
• **Insulin**



Amine Hormones

• Derived from tyrosine or tryptophan 3 groups:
– **Tyrosine** → **Catecholamines**
Behave like **peptide hormones**
– **Tyrosine** → **Thyroid hormones**
Behave like **steroid hormones**
– **Tryptophan** → **Melatonin**

Steroids

• Derived from cholesterol **(lipophilic)**
• Secreted by gonads, adrenal cortex, placenta
• On-demand synthesis (SER)
• Cross membranes **(no storage)**
• Usually **bound to carrier proteins**

Transport of hormones

• **Water soluble hormones (hydrophilic):**

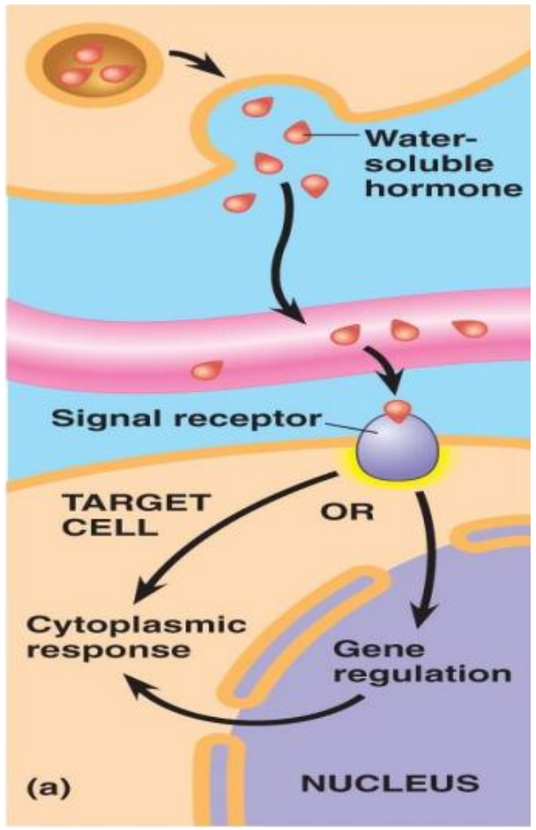
Peptides & catecholamines dissolved in plasma.

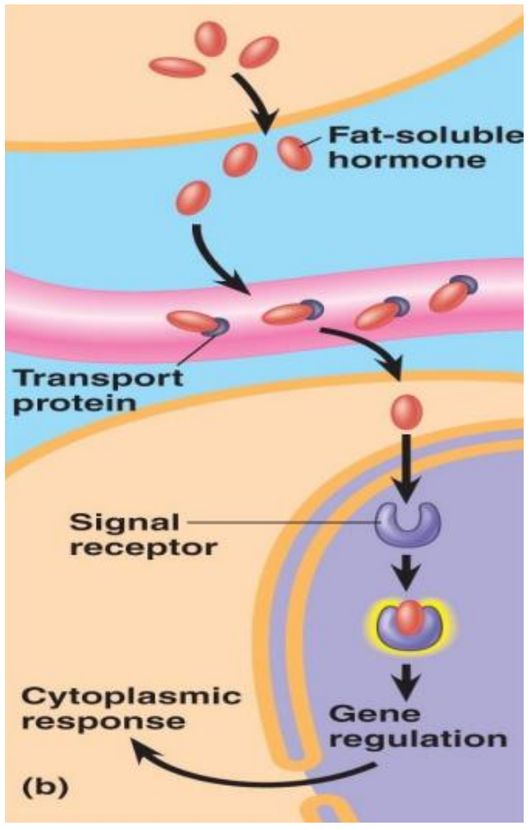
• **Fat soluble hormones (hydrophobic):**

Steroids and thyroid hormones transported bound to **plasma proteins (90%).**

<u>Binding to plasma proteins helps to:</u>

- Provide reservoirs
- Slow hormones clearance **(increase half life)**





Mechanism of hormone action

In order for a **target cell** to respond to a hormone, **specific protein receptors must be present** on its plasma membrane or in its interior to which that hormone can attach.

Hormone receptors

* Hormonal receptors are large proteins
* 2000-100,000 receptors/cell
* Receptors **are highly specific** for a single hormone

*** Receptor's location:**

• On the surface of cell membrane **(Proteins, Peptides hormones and catecholamines)**
• In the cell cytoplasm **(Steroid hormones)**
• In the cell nucleus **(Thyroid hormones)**

Regulation of hormonal receptors

o Receptors does not remain constant

• Inactivated or destroyed
• Reactivated or manufactured
• Dose-response relationship.
• Sensitivity.
• Number.
• Affinity.

o Down-regulation

• **Increase** hormone concentration leads to **decrease** in the number of active receptors
• Most peptide hormones have **pulsatile secretion** which prevents down regulation
- E.g. monthly pulsatile secretion = Ovarian hormone, Daily pulsatile secretion = Growth H

o Up-regulation

• The hormone induces **greater than normal** formation of a receptor or intracellular signaling proteins

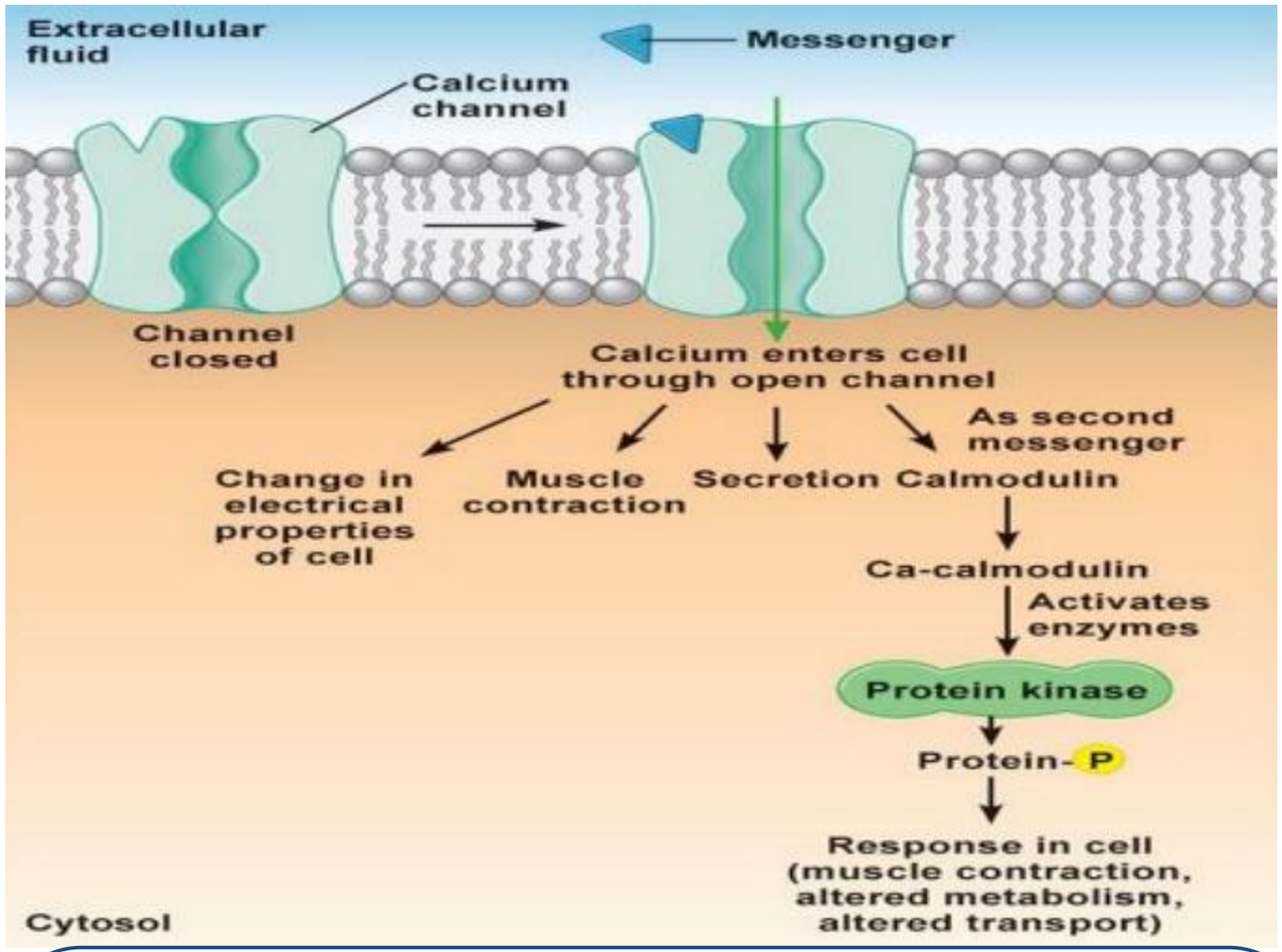
Protein and peptide hormones

Receptor on the cell membrane

The means by which hormones exert intracellular actions is to stimulate **formation of the second messenger inside the cell**.

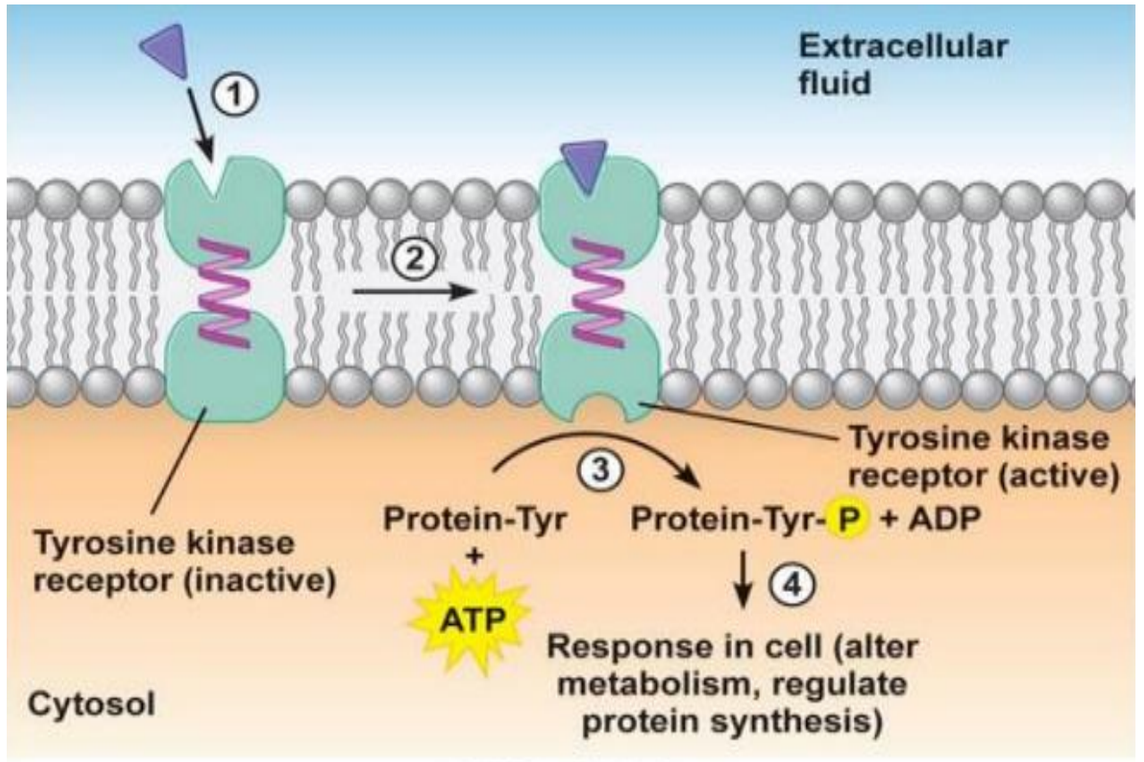
Second Messenger (Phospholipase C - IP3 system)	Second Messenger (Adynylate Cyclase – cAMP system)	Second Messenger (Tyrosine Kinase System)	The second messenger is cGMP	Second Messenger (Calcium-calmodulin system)
- Angiotensin II (vascular smooth muscle) - Catecholamines **(α1 receptors)** - Gonadotropin-releasing hormone (GnRH) - Growth hormone–releasing hormone (GHRH) - Oxytocin - Thyroid-releasing hormone (TRH) - ADH , **Vasopressin (V1 receptor, vascular smooth muscle)**	- Catecholamines **(α2- Adrenergic)** - Catecholamines **(B-Adrenergic)** - ADH **(Renal V2-receptor)** - Ant. Pituitary: ACTH, FSH, LH & TSH - Glucagon - Calcitonin & PTH	-Growth Hormone -Prolactin - Insulin -Erythropoietin	-Atrial natriuretic peptide (ANP) - Nitric oxide	

Second Messenger (Calcium-calmodulin system)



- Attachment of a hormone could change the permeability of cell membrane allowing entry of Ca into the cell .
- Ca binding to Calmodulin (protein in the cytoplasm) and activate protein kinase that phosphorylate certain protein.

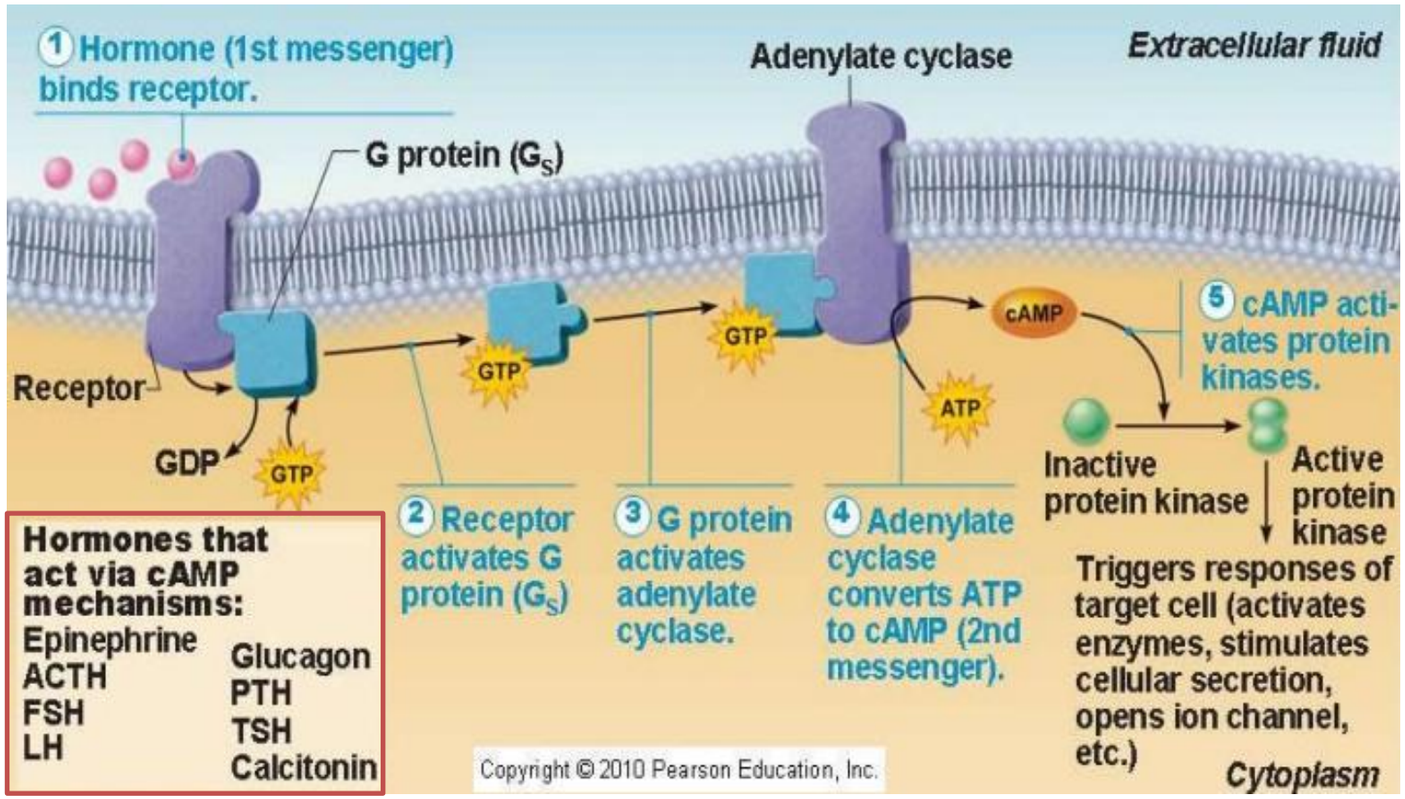
Second Messenger (Tyrosine Kinase System)



An important hormone that exerts its effects through tyrosine kinase is **insulin.**

the tyrosine residue that will be phosphorylated after binding to the insulin)
→ receptor will be active and undergo conformational changes.
o Receptor itself is phosphorylated (autophosphorylation) and gets activated as an enzyme.

Second Messenger
(Adynylate Cyclase – cAMP system)

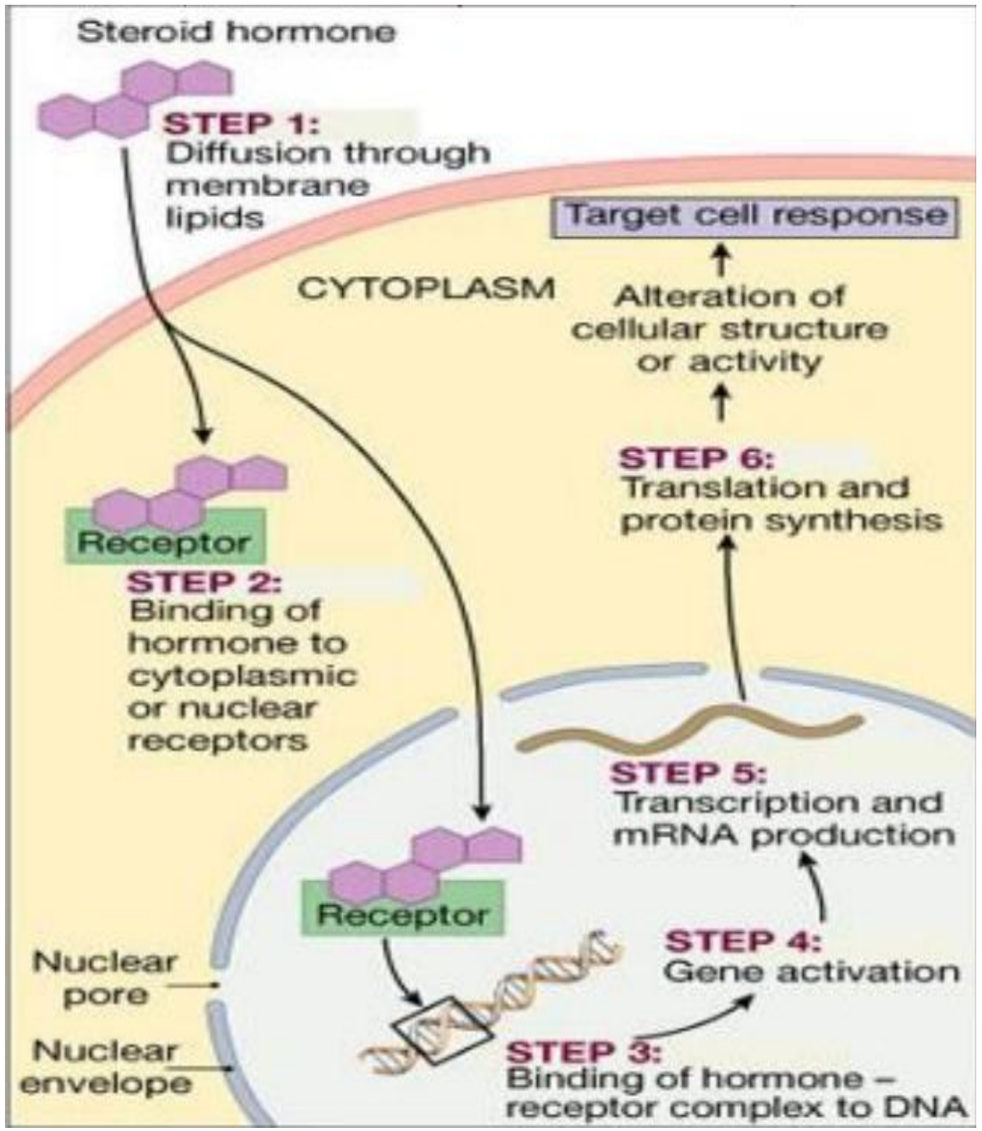


o hormone attaches to its specific receptor on the cell surface, this activates the G-protein subunit to release GDP and attach GTP, and α subunit of the G-protein dissociates and activates adenylyl cyclase.

o Activated adenyly cyclase converts ATP to cAMP , which acts as the second messenger.

o Inactive cAMP-dependent protein kinase A (PKA) is formed of a complex two regulatory and two catalytic subunits. The binding of cAMP to the regulatory subunits of PKA changes its conformation and detaches the catalytic (now active) subunits. the active catalytic subunits phosphorylate target protein substrates to either activate or inhibit them depending on the protein.

Mechanism of action
(Steroid & Thyroid Hormones)



o The hormone pass the cell membrane easily and bind to its receptor to form the hormone receptor complex
(Active form). Then, it passes into the nucleus to bind to the hormone receptor element, which are element on
the DNA → the DNA will undergo conformational change → activation of a promoter region (the site of activate the GENE TRANSCRIPTION). A Promoter region can be enhancer or silencer.

Hormones interactions at target cells

- **Multiple hormones can affect a single target simultaneously**
- **Three types of hormone interactions:**

Synergism

- Combined action of hormones is more than just additive!

- **Example: Synergistic effects of glucagon, cortisol and epinephrine on blood glucose levels.**

Permissiveness

One hormone allows another hormone to have its full effect Especially during growth

- **Example Thyroid hormone have permissive effect on growth hormone action**

Deficiency of thyroid hormone in infants leads to dwarfism.

Antagonism

- Antagonistic hormones have opposing physiological actions – Certain hormone diminishes the effect of other hormone

- **Example**

– Glucagon antagonizes the action of insulin

Clearance of hormones

- **Two factors control the concentration of a hormone in the blood:**

The rate of its secretion and rate of its removal (metabolic clearance)

- **Hormones are cleared by:**

o Metabolic destruction by tissues and Binding with tissues

o Excretion by the liver into bile or the kidney into urine

- **Clearance of protein bound hormones is slower than clearance of peptide hormones**

Summery

B. Hormone synthesis

1. Protein and peptide hormone synthesis

- **Preprohormone** synthesis occurs in the **endoplasmic reticulum** and is directed by a specific mRNA.
- **Signal peptides are cleaved** from the preprohormone, producing a **prohormone,** which is transported to the Golgi apparatus.
- Additional peptide sequences are cleaved in the Golgi apparatus to form the **hormone,** which is packaged in secretory granules for later release.

2. Steroid hormone synthesis

- Steroid hormones are **derivatives of cholesterol** (the biosynthetic pathways are described in V A 1).

3. Amine hormone synthesis

- Amine hormones (thyroid hormones, epinephrine, norepinephrine) are **derivatives of tyrosine** (the biosynthetic pathway for thyroid hormones is described in IV A).

table **7-2** Mechanisms of Hormone Action

cAMP Mechanism	IP_3 Mechanism	Steroid Hormone Mechanism	Other Mechanisms
ACTH	GnRH	Glucocorticoids	**Activation of tyrosine kinase**
LH and FSH	TRH	Estrogen	Insulin
TSH	GHRH	Testosterone	IGF-1
ADH (V_2 receptor)	Angiotensin II	Progesterone	
HCG	ADH (V_1 receptor)	Aldosterone	**cGMP**
MSH	Oxytocin	Vitamin D	ANP
CRH	α_1 Receptors	Thyroid hormone	EDRF
β_1 and β_2 Receptors			Nitric oxide
Calcitonin			
PTH			
Glucagon			

Summery

C. Regulation of hormone secretion

1. Negative feedback

- is the most commonly applied principle for regulating hormone secretion.
- is self-limiting.
- A hormone has biologic actions that, directly or indirectly, inhibit further secretion of the hormone.
- **For example,** insulin is secreted by the pancreatic beta cells in response to an increase in blood glucose. In turn, insulin causes an increase in glucose uptake into cells that results in decreased blood glucose concentration. The decrease in blood glucose concentration then decreases further secretion of insulin.

2. Positive feedback

- is rare.
- is explosive and self-reinforcing.
- A hormone has biologic actions that, directly or indirectly, cause more secretion of the hormone.
- **For example,** the surge of luteinizing hormone (LH) that occurs just before ovulation is a result of positive feedback of estrogen on the anterior pituitary. LH then acts on the ovaries and causes more secretion of estrogen.

D. Regulation of receptors

- Hormones determine the sensitivity of the target tissue by **regulating the number or sensitivity of receptors.**

1. Down-regulation of receptors

- A hormone **decreases the number or affinity of receptors** for itself or for another hormone.
- **For example,** in the uterus, progesterone down-regulates its own receptor and the receptor for estrogen.

2. Up-regulation of receptors

- A hormone **increases the number or affinity of receptors** for itself or for another hormone.
- **For example,** in the ovary, estrogen up-regulates its own receptor and the receptor for LH.

Summery

• Two factors control the concentration of a hormone in the blood:
o The rate of its secretion
o The rate of its removal (metabolic clearance)
• Hormones are cleared by:
o Metabolic destruction by tissues
o Binding with tissues
o Excretion by the liver into bile
o Excretion by the kidney into urine
• Clearance of protein bound hormones is slower than clearance of peptide hormones

MCQs

1- ductless glands that produce hormones released directly into the blood :

A-Paracrine glands
B-Autocrine glands
C-Endocrine glands
D-Exocrine glands

2- which of these organs considered as an endocrine gland :

A-heart
B-lung
C-gall bladder
D-cerebrum

3- the Release of hormones in response to hormones caused by :

A-Humoral Stimuli
B-Neural Stimuli
C-Osmotic stimuli
D-Hormonal Stimuli

4- cells that contain specific receptors for a particular hormone :

A-endocrine cells
B-target cells
C-adenocyte
D-adipocyte

5- the free hormones in plasma are most likely to be :

A-hydrophilic
B-hydrophobic
C-amphipathic
D-A&B

6- which of these hormones have a receptor in the cytoplasm :

A-Steroid hormones
B-Thyroid hormones
C-Peptides hormones
D-catecholamines

7-which of these hormones use Tyrosine Kinase as a second messenger :

A-Nitric oxide
B-Glucagon
C-Oxytocin
D-Insulin

8-"One hormone allows another hormone to have its full effect" is the definition of :

A-Synergism
B-Antagonism
C-Permissiveness
D-hormones Clearance

1- C 2- A 3- D 4- B 5- A 6- A 7- D 8-C

@PhysiologyTeam

Pht433@gmail.com

Physiology team

Done by :

Mojahed Otayf

Revised by:

Rahma Alshehri

Endocrine Block