



ENDOCRINE BLOCK

LECTURE 1

INTRODUCTION TO ENDOCRINE SYSTEM



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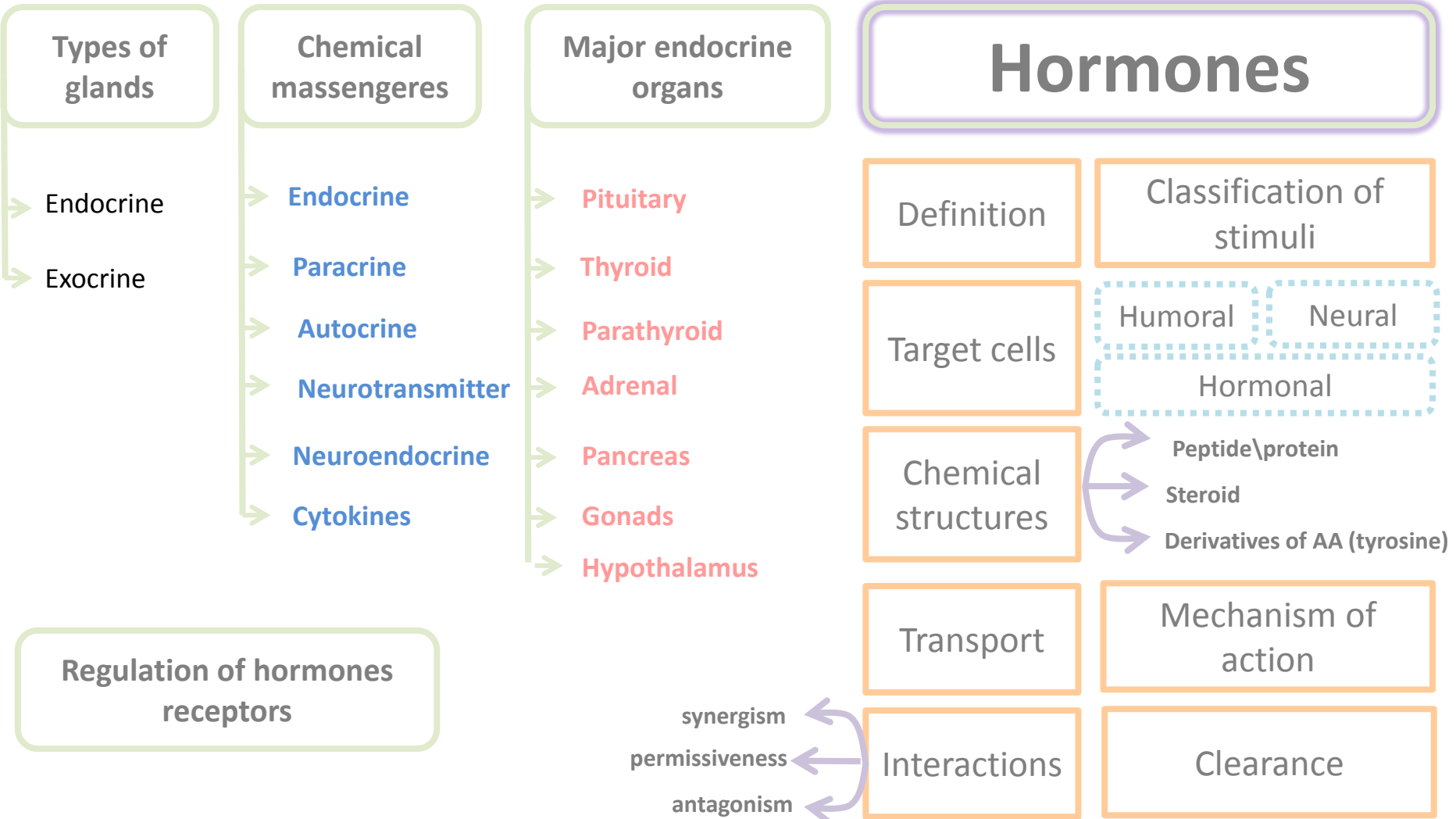
Mohammed Jameel



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



■ Slides

■ Important

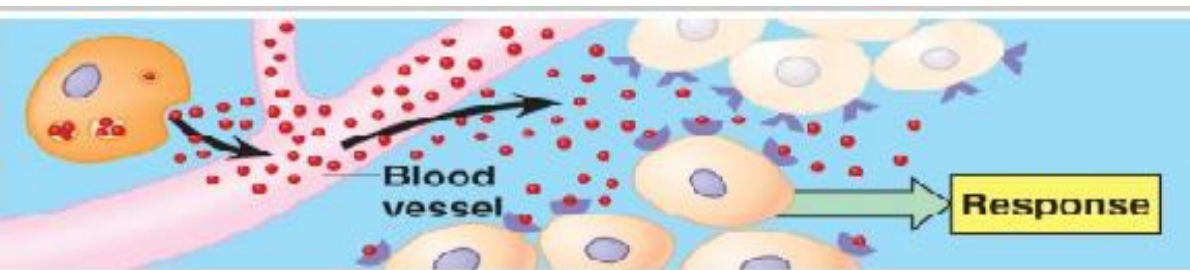
■ Females' Notes

■ Explanation

■ Males' Notes

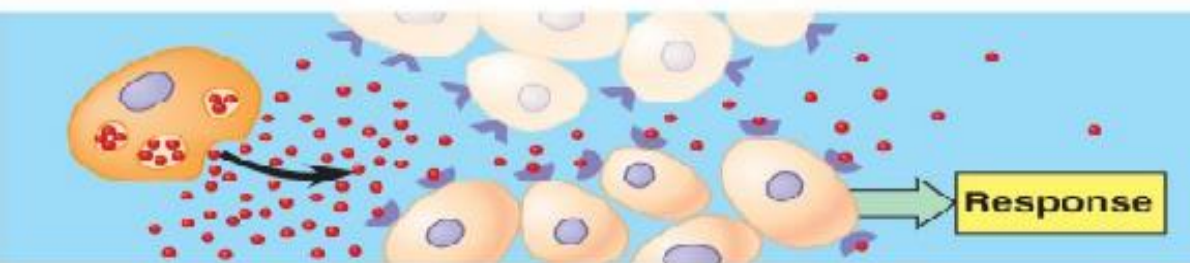
The activities of cells, tissues and organs are coordinated by the interplay of several types of chemical messenger systems:

- Endocrine hormones
- Paracrines
- Autocrines
- Neurotransmitters
- Neuroendocrine hormones
- Cytokines: peptides secreted by cells into ECF and function as autocrines, paracrines, or endocrine hormones and act on other cells (e.g., leptin & interleukins)



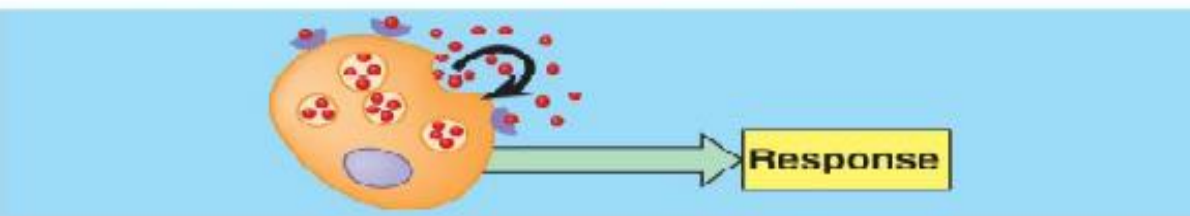
(a) **Endocrine signaling**: Released by glands into blood and influence the function of other cells.

a)-The **endocrine glands** They are **ductless** glands that produce hormones released **directly into the blood**.



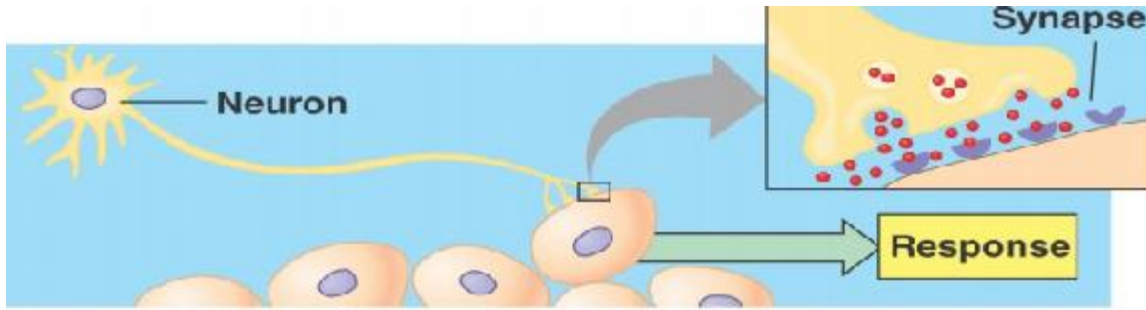
(b) **Paracrine signaling**: Secreted by cells into ECF and affect neighboring cells of a different type.

b)-Secreted by **cells** into ECF and affect **neighboring cells of a different type**.



(c) **Autocrine signaling**: Secreted by cells into ECF and affect the function of the same cells.

c)-Secreted by **cells** into ECF and affect the **function of the same cells**.

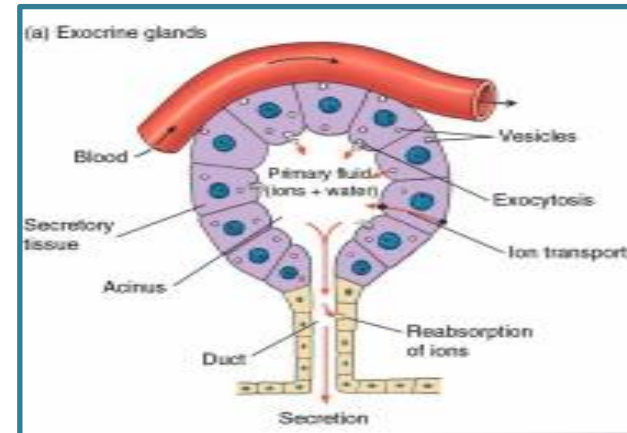


(d) Synaptic signaling (Neurotransmitters): are released by axon terminals of neurons into synaptic junctions and act locally to control nerve cell functions.



(e) Neuroendocrine signaling Secreted by neurons into blood and influence the function of other cells

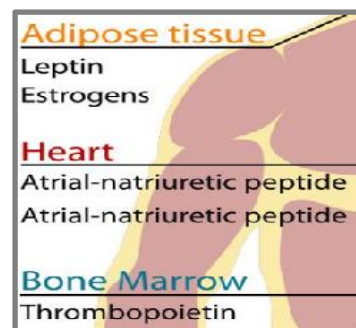
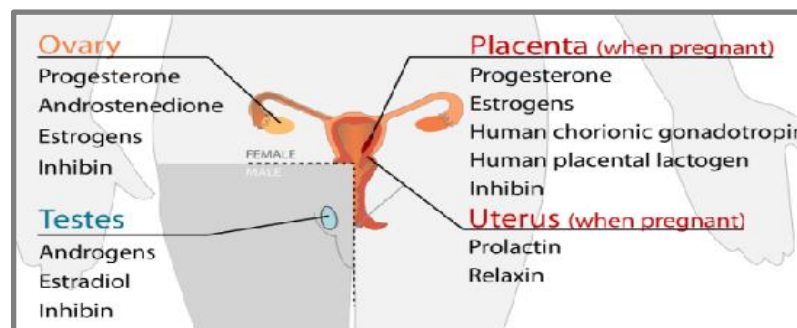
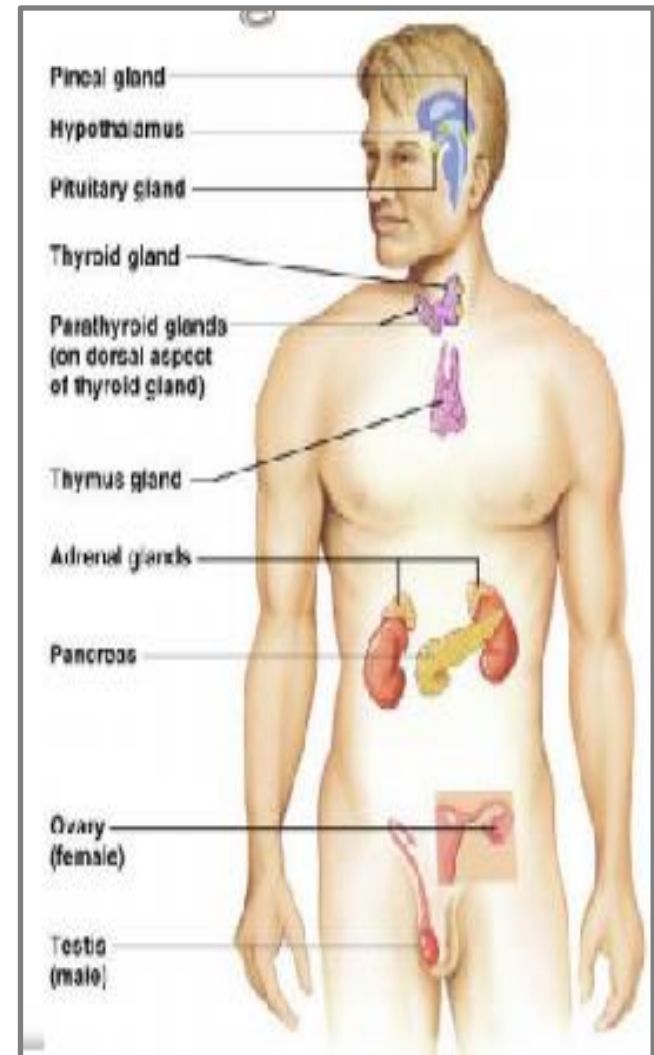
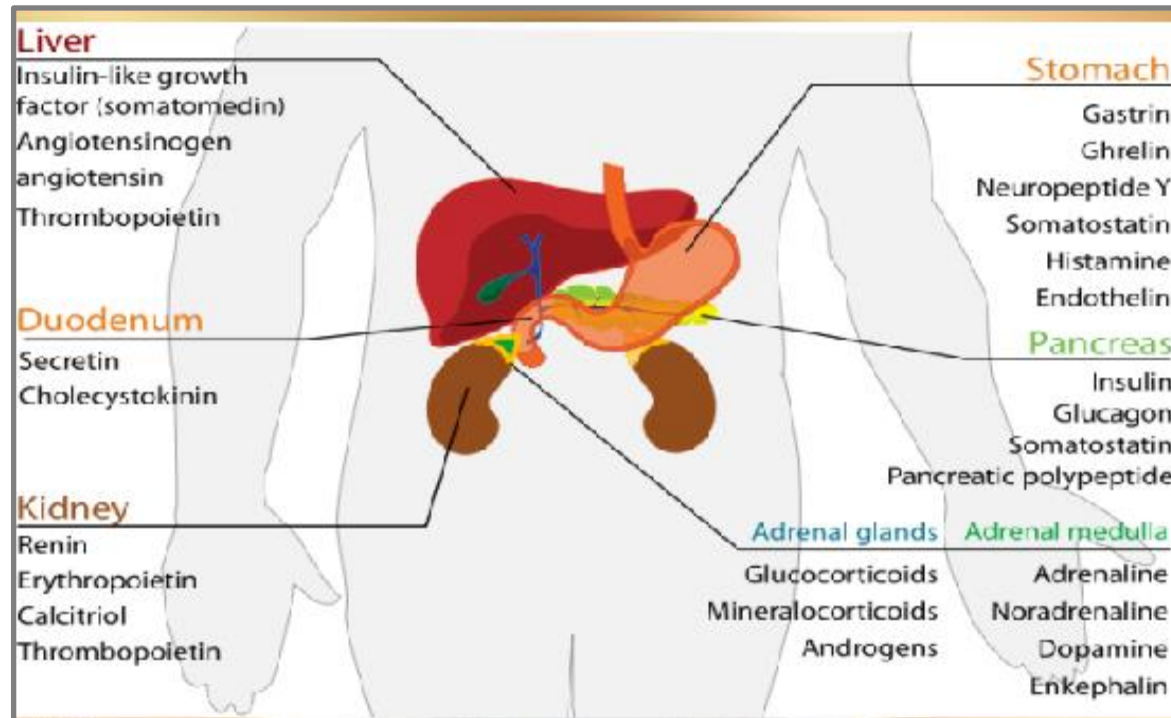
- When it become contact **nerve** with **nerve** called **(neurotransmitter)**
- And if the contact with **nerve** and **vessel** called **(neuroendocrine)**



And don't forget

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

Types of glands and their secretion



■ Slides

■ Important

■ Females' Notes

■ Explanation

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The importance of hormone?

The multiple hormone systems play a key role in regulating almost all body functions:

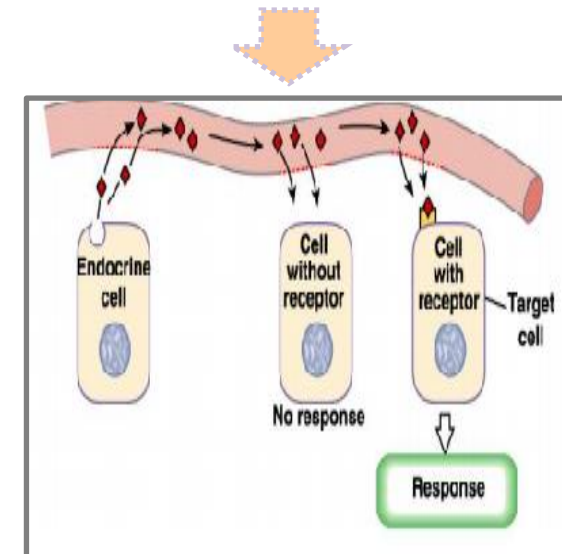
1. Metabolism
2. Growth and development
3. Water and electrolyte balance
4. Reproduction
5. Behavior

What is the hormone?

- 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)

Where their effect?

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

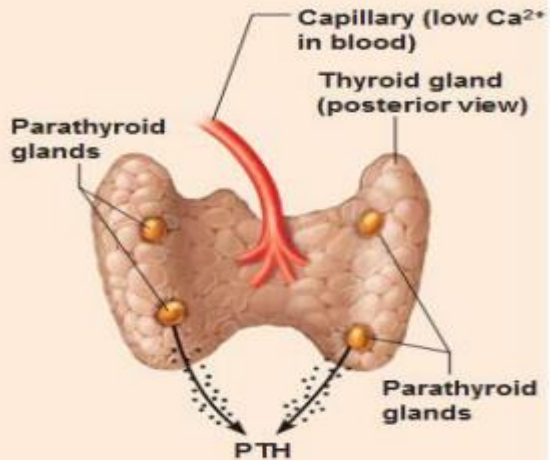




Humoral Stimuli:

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

① Capillary blood contains low concentration of Ca^{2+} , which stimulates...

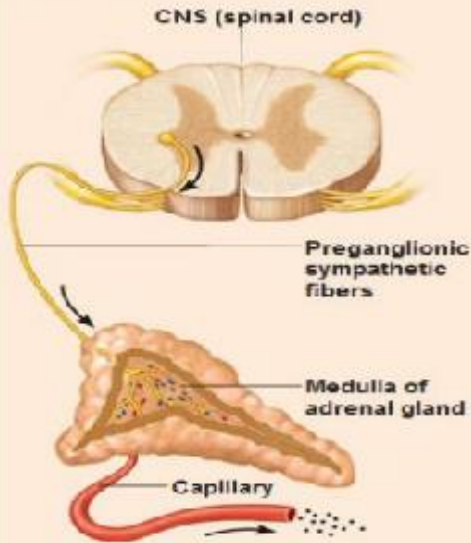


Neural Stimuli:

Nerve fibers stimulate hormone release.

(b) Neural stimulus

① Preganglionic sympathetic fibers stimulate adrenal medulla cells...



② ...to secrete catecholamines (epinephrine and norepinephrine)

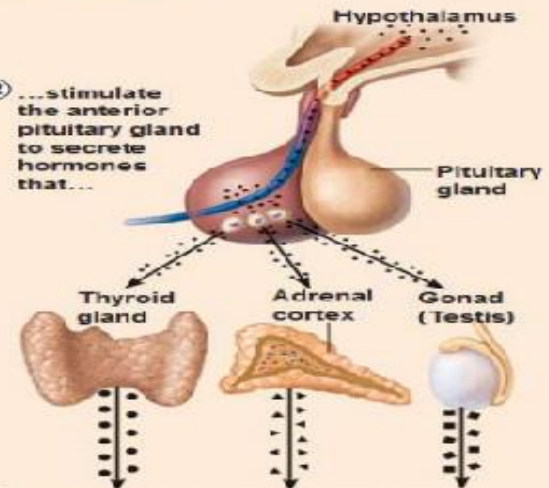
Hormonal Stimuli:

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

(c) Hormonal stimulus

① The hypothalamus secretes hormones that...

② ...stimulate the anterior pituitary gland to secrete hormones that...



③ ...stimulate other endocrine glands to secrete hormones

General classes of hormones

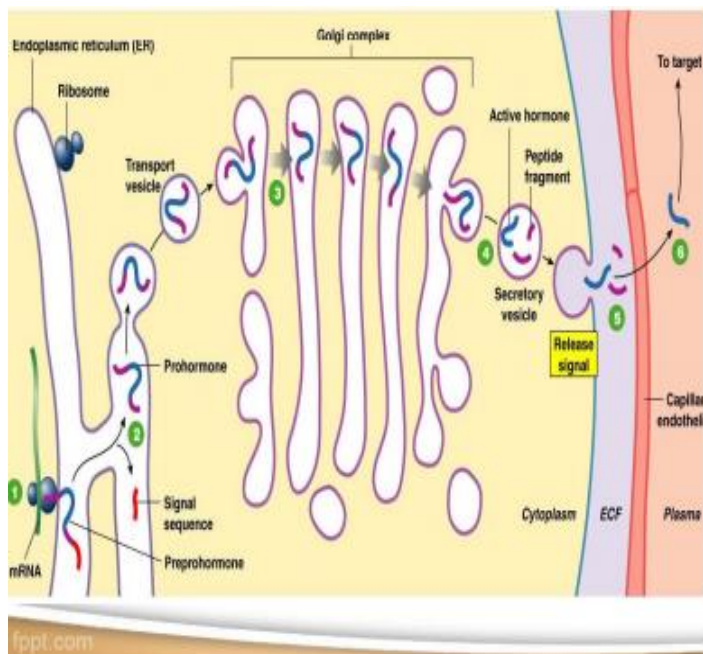
Proteins and polypeptides:
(anterior and posterior pituitary, pancreatic and parathyroid hormones) stored in vesicles until Needed.

Steroids:
(adrenocortical, ovarian and testicular hormones) diffuse across the cell membrane.

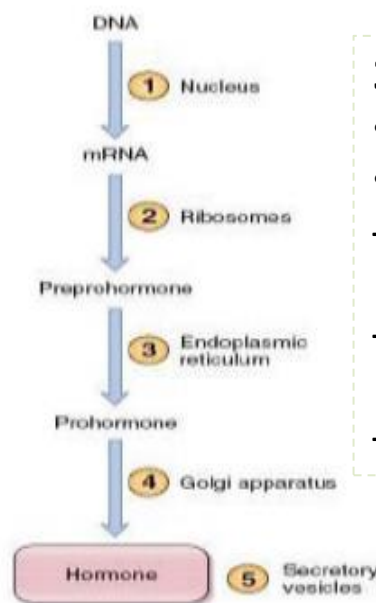
Derivatives of amino acid tyrosine:
(thyroid hormones and catecholamines)

1-Protein and peptide:

- Synthesized as **preprohormone** >> post-translational
- modification to prohormone >> then hormone.
- Example of protein hormone: **insulin**



PEPTIDE HORMONE SYNTHESIS



2-Steroid Hormones

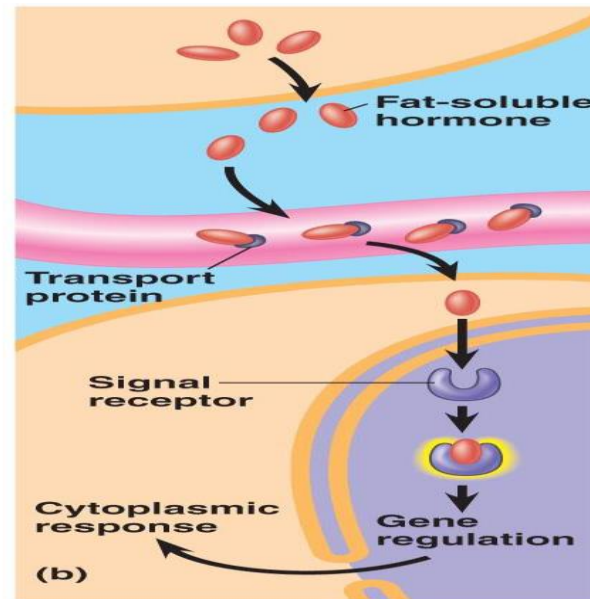
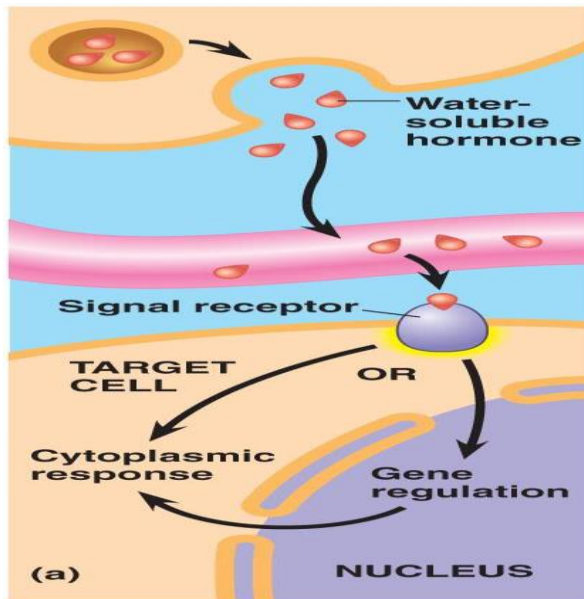
- Derived from cholesterol (**lipophilic**)
- Secreted by **gonads, adrenal cortex, placenta.**
- **On-demand synthesis** (SER).
- Cross membranes (**no storage**).
- Usually **bound to carrier proteins.**

3-Amine hormone

- Derived from tyrosine or tryptophan
- 3 groups
- Tyrosine >> **Catecholamines**
* Behave like peptide hormones
- Tyrosine >> **Thyroid hormones**
* Behave like steroid hormones
- Tryptophan >> **Melatonin**



Water soluble hormones (hydrophilic)	Fat soluble hormones (hydrophobic)
peptides & catecholamines.	Steroids and thyroid hormones.
Dissolved in plasma.	Transported bound to plasma proteins (90%), which helps to: <ul style="list-style-type: none">• Provide reservoirs (brevet loss of Hormones)• Slow hormones clearance





Mechanism of hormone action

For more information you can read Linda physiology book 385-389 , or Guyton Medical Physiology 887-891

In order for a target cell to respond to a hormone, **specific protein receptors** must be present on its **plasma membrane** (peptides & catecholamines) or in its **interior** to which that hormone can attach (Steroids and thyroid hormones), the interior receptors could be in the cytoplasm or in the nucleus.

Only when this binding occurs can the hormone influence the working of the cell:-

- **Hormone-receptor interaction (1st messenger)**
- **Enzyme activation**
- **Release of the second messenger** (the effect of hormones is mediated by the second messenger)
- **Effects on cellular function**

Hormonal receptors: are large proteins ,2000-100,000 receptors/cell

Receptors are highly specific for a single hormone

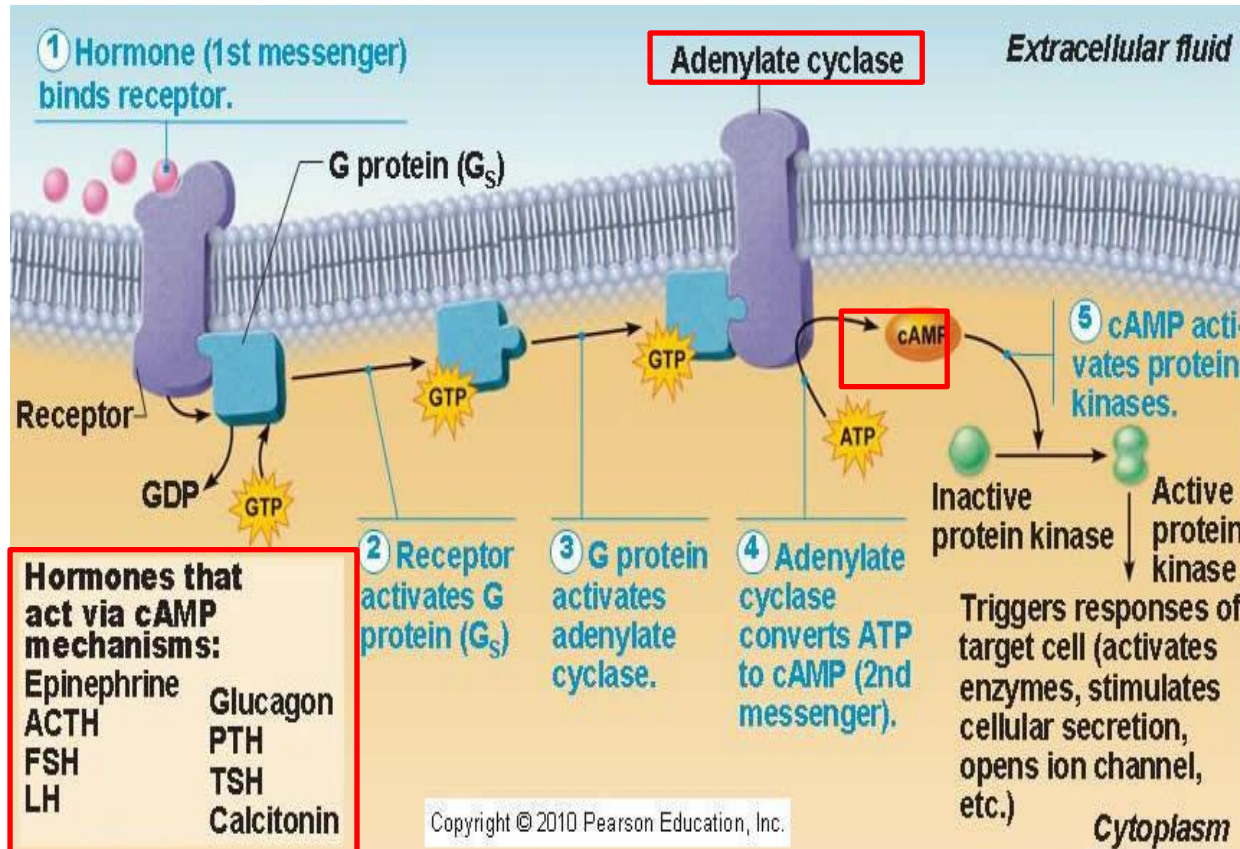
Receptor's location:

- On the **surface of cell membrane** (proteins, peptides and catecholamines)
- In the cell **cytoplasm** (Steroids)
- In the cell **nucleus** (thyroid hormones)



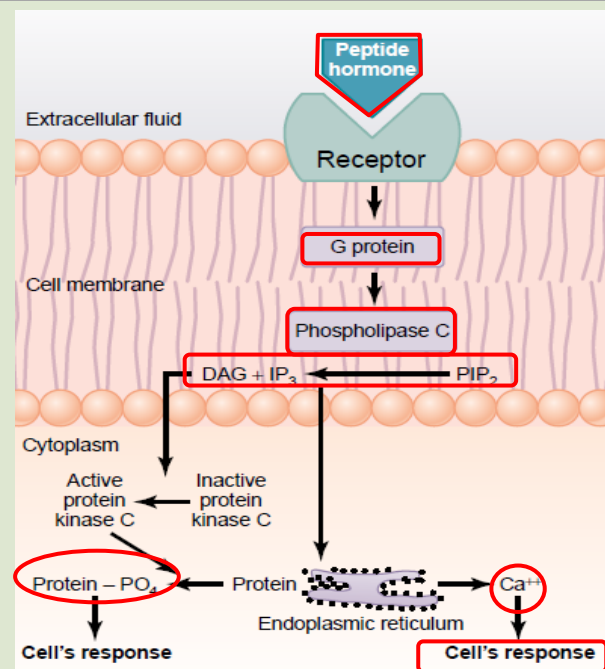
Mechanism of action Protein and peptide hormones

- **Receptor on the cell membrane.** The means by which hormones exert intracellular actions is to stimulate formation of the second messenger inside the cell. **The second messenger does the rest.** (similar like catecholamines)

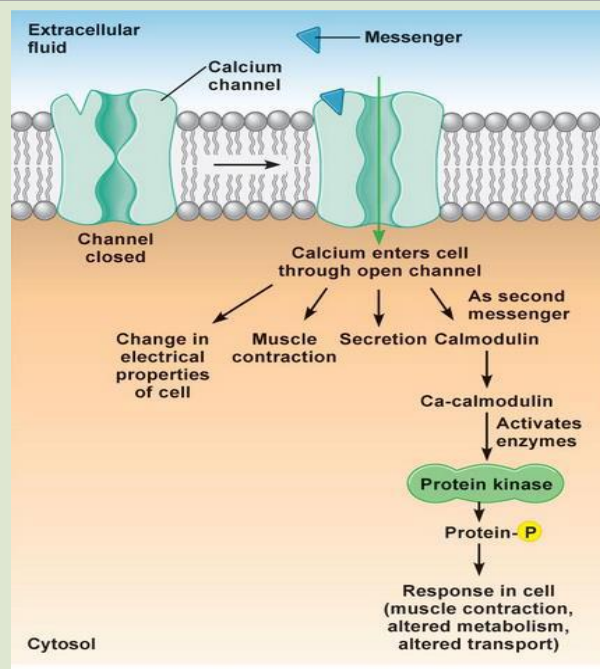


- 1- Non-steroid (other name for protein and peptide) hormones bind to cell membrane receptor (G_s "stimulatory" protein here).
- 2- Activate Adenylate Cyclase which convert ATP to cAMP (2ed Messenger)
- 3- cAMP activate protein kinase and convert inactive enzymes to active form by phosphorylation.
- 4- Production of cellular effect.

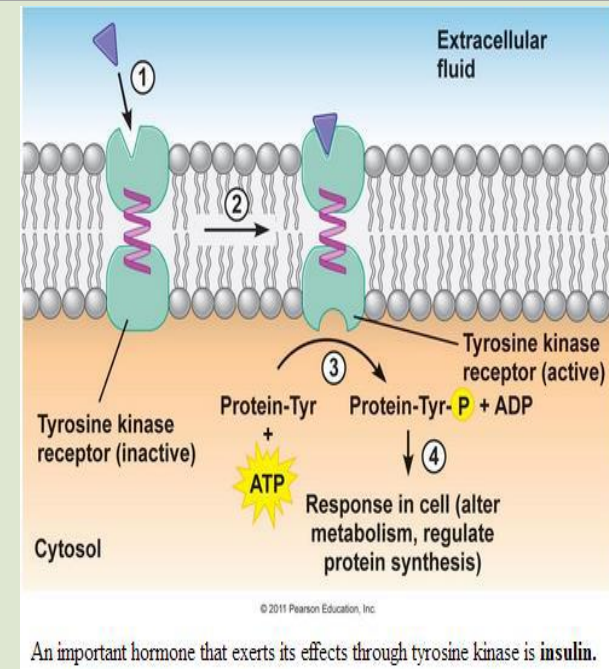
Phospholipase C - IP3 system



Calcium-calmodulin system



Tyrosine Kinase System



Some Hormones that use the phospholipase C second messenger system:

- Angiotensin II (vascular smooth muscle)
- Catecholamines (a receptors)
- Gonadotropin-releasing hormone (GnRH)
- Growth hormone-releasing hormone (GHRH)
- Oxytocin
- Thyroid-releasing hormone (TRH)
- Vasopressin (V1 receptor, vascular smooth muscle)

Second messenger is IP3.

- 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.
- Response happens in the cell.

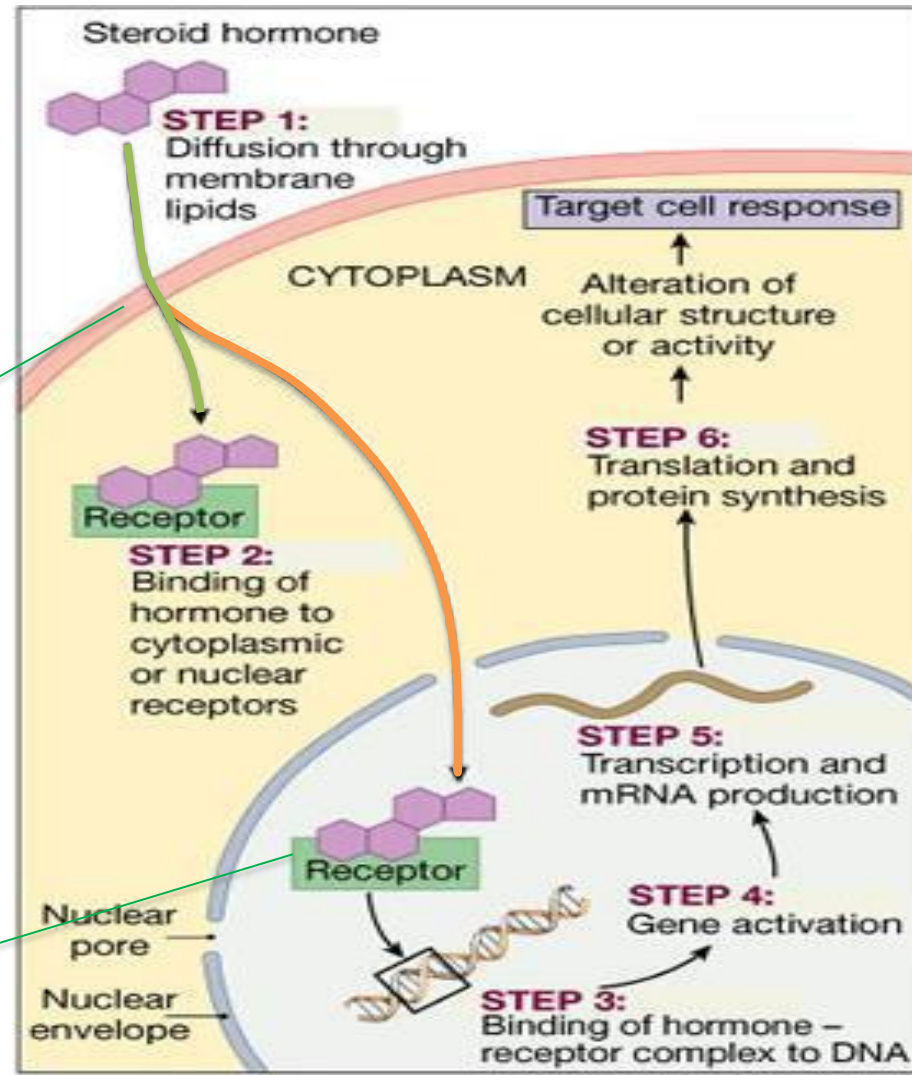
e.g. Insulin

- Activation of tyrosine kinase receptor by attachment of a hormone.
- Activate enzymes by phosphorylation(Kinase=activate)
- Produce effect on the cell.

- Receptor inside the cell:
direct gene activation

Steroid hormones (Gonadal and adrenocortical) Receptors are in the cytoplasm form complex and inter the nucleus.

Thyroid hormones Receptors are inside the nucleus



- **Receptors does not remain constant**

- Inactivated or destroyed
- Reactivated or manufactured
- Dose-response relationship. Depend on concentration of the hormone.
- Sensitivity. Like in some types of diabetes the insulin is normal but the problem is in the sensitivity of the receptor
- Number.
- Affinity.

- **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
- Decrease synthesis.
- Increase degradation.
- Inactivation .
- T3.

- **Up-regulation**

The hormone induces greater than normal formation of a receptor or intracellular signaling proteins (increase of number and sensitivity of a receptor) GH and prolactin

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

Synergism	Permissiveness	Antagonism
<ul style="list-style-type: none"> • Combined action of hormones is more than just additive! • Example: Synergistic effects of glucagon, cortisol and epinephrine on blood glucose levels. 	<ul style="list-style-type: none"> • One hormone allows another hormone to have its <u>full effect</u> • Especially during growth • Example • <u>Thyroid</u> hormone have permissive effect on <u>growth hormone</u> action • Deficiency of thyroid hormone in infants leads to dwarfism. 	<ul style="list-style-type: none"> • Antagonistic hormones have <u>opposing</u> physiological actions • Certain hormone diminishes the effect of other hormone • Example • <u>Glucagon</u> antagonizes the action of <u>insulin</u>
<p>The action in combined hormones is stronger.</p>	<p>One hormone help other hormone to potentiate its action.</p>	<p>Glucagon (increase blood glucose level) , Insulin (Decrease blood glucose level)</p>



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

1. The rate of its secretion.
2. The rate of its **removal** (metabolic clearance).

Each hormone have certain half life time. If the rate of secretion increase and the rate of removal decrease for any reason, the hormone level will increase.

- **Hormones are cleared by:**

- Metabolic destruction by tissues.
- Binding with tissues. **Then loss of there activity.**
- Excretion by the liver into bile.
- Excretion by the kidney into urine.

- **Clearance of protein bound hormones is **slower** than clearance of peptide hormones (**steroid and thyroid**).**



Water soluble hormones (hydrophilic)	Fat soluble hormones (hydrophobic)
peptides & catecholamines.	Steroids and thyroid hormones.
Dissolved in plasma.	Transported bound to plasma proteins (90%), which helps to: <ul style="list-style-type: none"> • Provide reservoirs (brevet loss of Hormones) • Slow hormones clearance
Receptor in the cell membrane.	Receptor for Steroid H in the cytoplasm. Receptor for Thyroid H in the nucleus.
Action production by 2ed messenger	Action production by direct gene activation

- **Regulation of hormonal receptors:**
 - **down regulation** Increase hormone concentration led to decrease receptors.
 - **up regulation** pulsatile secretion which prevents down regulation.
- Multiple hormones can affect a **single** target cell by 3 types of hormone interactions **Synergism, Permissiveness, Antagonism.**
- Clearance of protein bound hormones is **slower** than clearance of peptide hormones.
- Two factors control the concentration of a hormone in the blood: The rate of its **secretion** and **removal**



QUESTIONS

1. where paracrine release their hormone:

- A) Cell membrane
- B) Blood
- C) ECF
- D) Cytoplasm

2. Which of the following hormones has pulsatile secretion :

- A) GH
- B) TSH
- C) prolactin
- D) ACTH

3. Which one of the following hormones has it's receptor in the cytoplasm :

- A) Norepinephrine
- B) Insulin
- C) Testosterone
- D) Oxytocin

4. Peptide and catecholamines hormones produce there action by the :

- A) Binding to intracellular receptor
- B) Transcription
- C) 1st messenger
- D) 2ed messenger

5. Deficiency of which hormone in infants leads to dwarfism:

- A) Oxytocin
- B) Thyroid
- C) Insulin

1	C
2	A
3	C
4	D
5	B

THE END

If there are any Problems or Suggestions,
Feel free to contact us:

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THANK YOU



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