Biochemistry of Hormones and Their Recepters

University Of Fallujah
College Of Medicine

Lecture : First

Stage : 2nd

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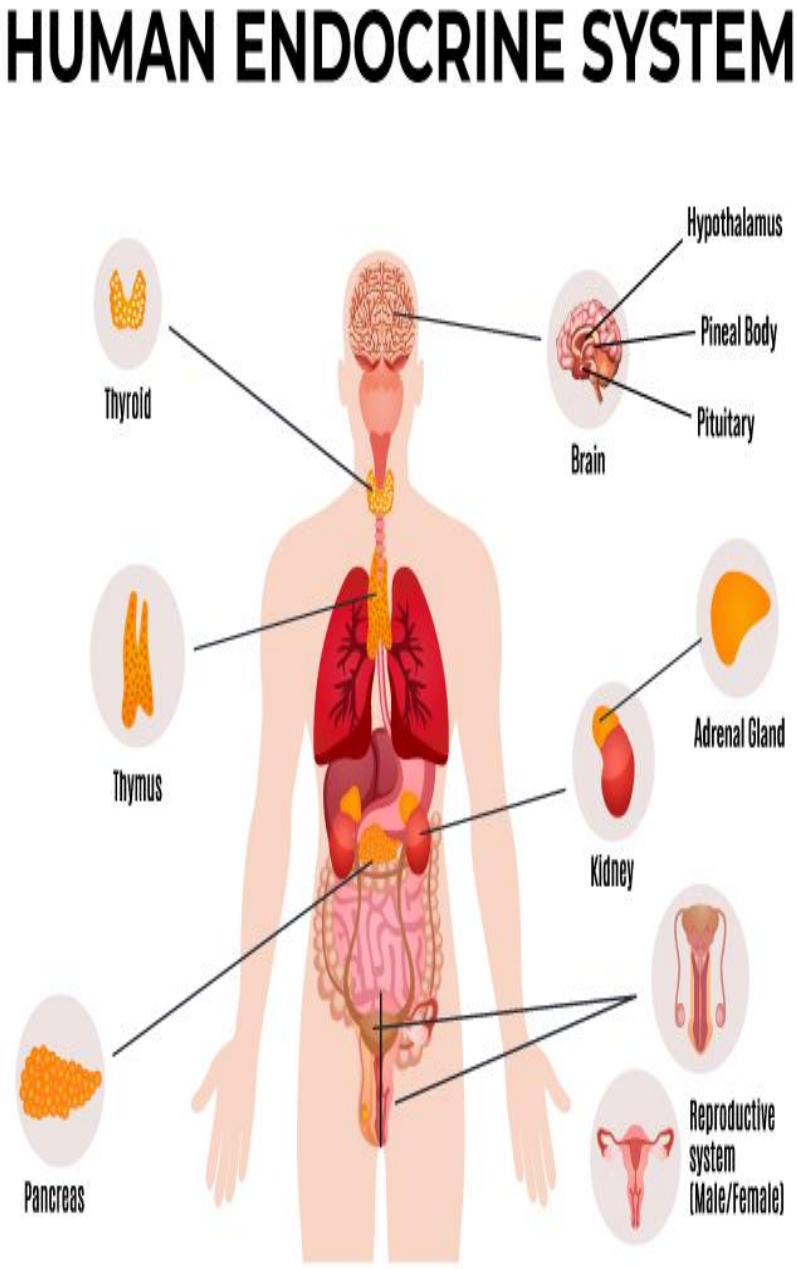
Objectives

- To Understand the biochemical nature and diversity of hormones and their classification .
- To understand the role and nature of receptors on target cells .
- To understand the mechanism of regulation of hormones,

- The endocrine system is one of the two coordinating and integrating system of the body .
- It acts through chemical messengers – hormones- carried in the circulation .

- See figure

Human endocrine system



- **Endocrinology:**
- **Core Focus: The study of:**

- ✓ Hormones
- ✓ Their Receptors
- ✓ The Intracellular Signaling Pathways they trigger.

- **Distribution of Hormone-Secreting Tissues**

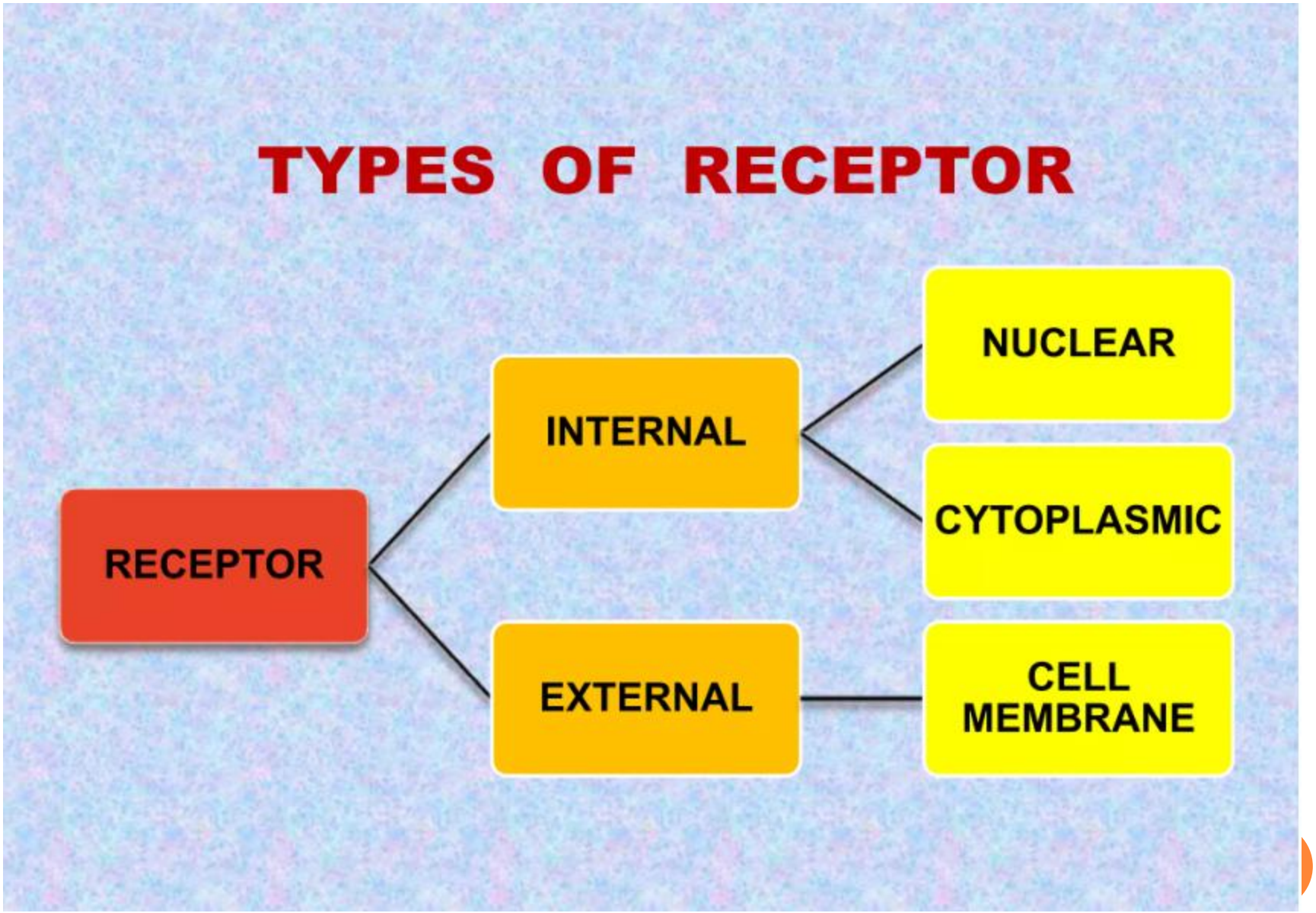
- Classical Endocrine Organs: Discrete glands (e.g., pancreas, thyroid) that are primarily devoted to hormone secretion.
- Non-Classical Sources: Various other cells and tissues throughout the body also possess the capability to produce and secrete hormones.

Definition

- **Hormone** : Are chemical substances (Messengers) produced by specific ductless glands (Endocrine Glands) .
- They are transported directly into the circulation affecting specific responsive tissues (The Target Tissues) where they regulate the metabolic processes.

General functions of hormones:

1. **Regulation of metabolism:**
2. **Growth**
3. **Homeostasis**
4. **Behavior**
5. **Reproduction**


TYPES OF RECEPTOR
RECEPTOR
INTERNAL
EXTERNAL
NUCLEAR
CYTOPLASMIC
CELL MEMBRANE

Hormone receptors

- A protein molecule that binds to a specific hormone, triggering a biological response in a target cell.
- A cell can only respond to a hormone if it has the correct receptor for it.

Two Main Types:

1. Cell Surface Receptors (Membrane-Bound)

- **For:** Water-soluble hormones (e.g., Insulin, Adrenaline, Growth Hormone).
- **Mechanism:** Hormone binds outside the cell → activates internal **second messengers** (like cAMP) → fast, short-term effects (seconds/minutes).

2. Intracellular Receptors

- **For:** Lipid-soluble hormones (e.g., Cortisol, Estrogen, Thyroid Hormones).
- **Mechanism:** Hormone enters cell → binds receptor inside (cytoplasm/nucleus) → complex acts on **DNA** → slow, long-term effects (hours/days) by making new proteins.

- **Hormone receptors** : are Molecules within or on the surface of target cells that bind hormones with high affinity and specificity.
- All receptors have at least two functional domains:

I. recognition domain binds the hormone (sometime the hormone is called ligand) and

II. Coupling domain - generates signal that couples hormone recognition to some intracellular function.

- **Target cells** : Hormones will only produce the response in cells that express the receptors for this particular hormone these cells are called (target cells) **ONLY** target cells respond to hormone.
- While the cells that do not have receptors for the hormone "ignore" the hormone.

- Hormones may be secreted into blood and affect cells at distant sites.
- Some hormones known to act and affect neighboring cells or even have effects on the same cells that secreted the hormone.
- . Three actions are defined:
- **Endocrine** action: the hormone is distributed in blood and binds to distant target cells.
- **Paracrine action**: the hormone acts locally by diffusing from its source to target cells in the neighborhood.
- **Autocrine action**: the hormone acts on the same cell that produced it

- **Two important terms are used to refer to molecules that bind to the**
- hormone-binding sites of receptors:

- **Agonists** are molecules that bind the receptor and induce all the postreceptor 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 and block binding of the agonist, but fail to trigger intracellular signaling events.
- Hormone antagonists are widely used as drugs.

Mechanisms action of Hormone

1. By influencing the rate of synthesis of enzymes and other proteins.

- This is the primary mode of action for **lipid-soluble hormones** (steroids, thyroid hormones). The hormone-receptor complex acts as a transcription factor, binding to specific regions of DNA called **Hormone Response Elements (HREs)**. (e.g cortisol , testosterone and T3)

2. By affecting the rate of enzymatic catalysis.

- This is a primary mode of action for **water-soluble hormones**. They work by rapidly activating or inhibiting existing enzymes through **post-translational modification**, most commonly **phosphorylation**.(e.g **Adrenaline** activates glycogen phosphorylase)

3. By altering the cell membrane permeability.

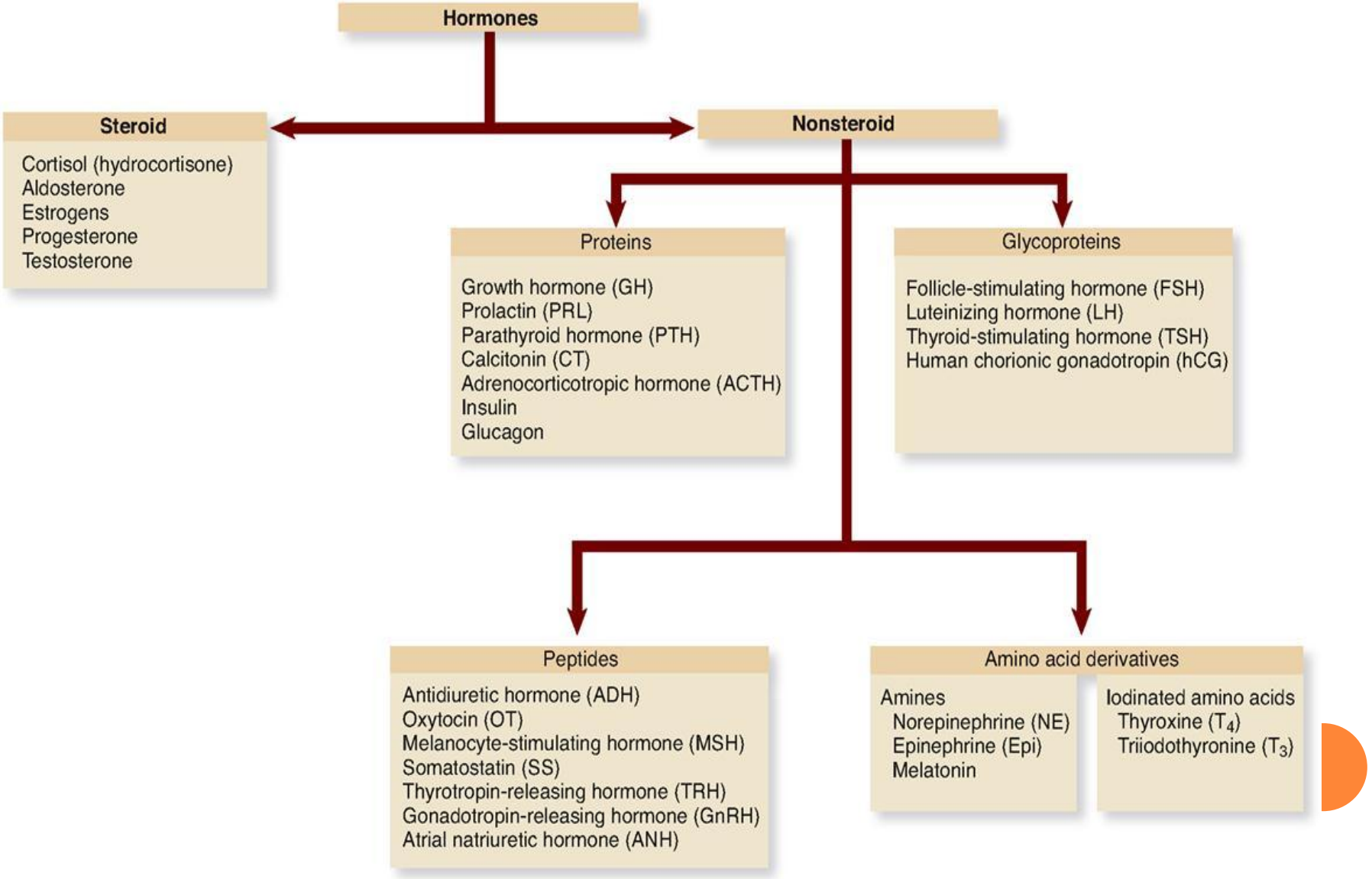
- This involves the rapid opening or closing of **ion channels** in the plasma membrane.(e.g Insulin with **GLUT4 transporters)**

Characteristic features of hormone classes

	Group I	Group II
1- Solubility	lipophilic	hydrophilic
2- Type	Steroids(iodothyronin, T3, T4)	Polypeptide, proteins, glycoproteins (catecholamines).
3- Transport protein	yes	No
4- Plasma half life t1/2	long(hours,days)	Short(minutes).
5-Receptor	Intracellular	plasma membrane
6- Mediator	Receptor hormone complex	cAMP, Ca, phosphatidylinositol.

Classification of Hormones

- **A: According to chemical composition:-**



❑ CLASSLFLCATLON OF HORMONES

- **B: According to the location of hormone receptors and the nature of the signal used to mediate hormone action :**
- **Group I** : Hormones that bind to intracellular receptors :-
- Examples: Sex hormones: Estrogens, Progestins
- Adrenal steroids: Glucocorticoids, Mineralocorticoids.
- Thyroid hormones: (T4 and T3) , Calcitriol.

- **Group II** : Hormones that bind to cell surface receptors :-
- This group is subdivided into 4 subgroups according to the nature of intracellular messenger (Second Messenger):

- **A: The 2nd messenger is cAMP :-**
- Examples:
- Alpha 2 -Adrenergic catecholamines
- Beta -Adrenergic catecholamines
- ACTH (Adrenocorticotropic hormone)
- TSH (Thyroid – Stimulating hormone)
- FSH (Follicle –Stimulating hormone)
- LH (Luteinizing Hormone)
- LPH (Lipotropin)
- MSH (Melanocyte –Stimulating hormone)
- PTH (Parathyroid hormone)
- Calcitonin

- **B: The 2nd messenger is cGMP**:-
- **Examples:**
- ANP (Atrial natriuretic factor)
- NO (Nitric oxide)
- C: **The 2nd messenger is Calcium , Phosphatidyl inositol or both**:-
- **Examples:**
- Alpha 1- adrenergic catecholamines
- Oxytocin
- TRH (Thyroytopin releasing hormone)
- GnRH (Gonadotropin releasing hormone)
- ADH
- Oxytocin

- D: **The 2nd messenger is a kinase or phosphatase cascade**:-
- Examples:
- GH
- Insulin
- PRL
- Erythropoietin
- Chorionic somatomammotropin (CS)
- Insulin like growth factors (IGF-I, IGF-II)

Regulation of hormone secretion

1**) Feedback control**

a. Negative

b. Positive

- **Negative Feedback** ; means that the increases in one hormone leads to the decrease in the secretion of other hormone (it is a common regulatory mechanism in the endocrine system) ex. thyroid hormone inhibits secretion of TRH and TSH
- **Positive feedback ;** means that the increase in one hormone leads to increase the secretion of another hormone

2) Neural control(as visual, olfactory)

Neural input to hypothalamus stimulates synthesis and secretion of hypothalamic releasing factors which stimulate pituitary hormone production and release

3) Chronotropic Control as Diurnal rhythms,), Sleep-wake cycle; seasonal rhythm,

Transport of Hormones in the Circulation

- Hormones circulate in the blood in two main ways, determined by their solubility:

1. Lipid-Soluble Hormones (Steroids, Thyroid Hormones)

Property: Hydrophobic (not water-soluble).

- **Transport:** Over 90% are bound to specific plasma transport proteins (e.g., SHBG, TBG, Albumin).
- **Function of Binding:**
  - **Solves Solubility:** Allows transport in aqueous blood.
  - **Creates a Reservoir:** The bound pool acts as a storage supply.
  - **Prolongs Half-Life:** Bound hormones are protected from degradation, leading to long half-lives (hours).

2. Water-Soluble Hormones (Proteins, Peptides, Catecholamines)

- **Property:** Hydrophilic (freely soluble in plasma).
- **Transport:** Circulate freely in their active form without needing transport proteins.
- **Consequence:** They are rapidly metabolized, resulting in very short half-lives (seconds to minutes).
- **The Critical Concept: Free vs. Bound Hormone**
- **Biologically Active Form:** Only the **free (unbound) hormone** can diffuse into cells and act on target tissues.

Thank you for listening