HORMONE MECHANISM & ACTION

- Lecture For MSc Student
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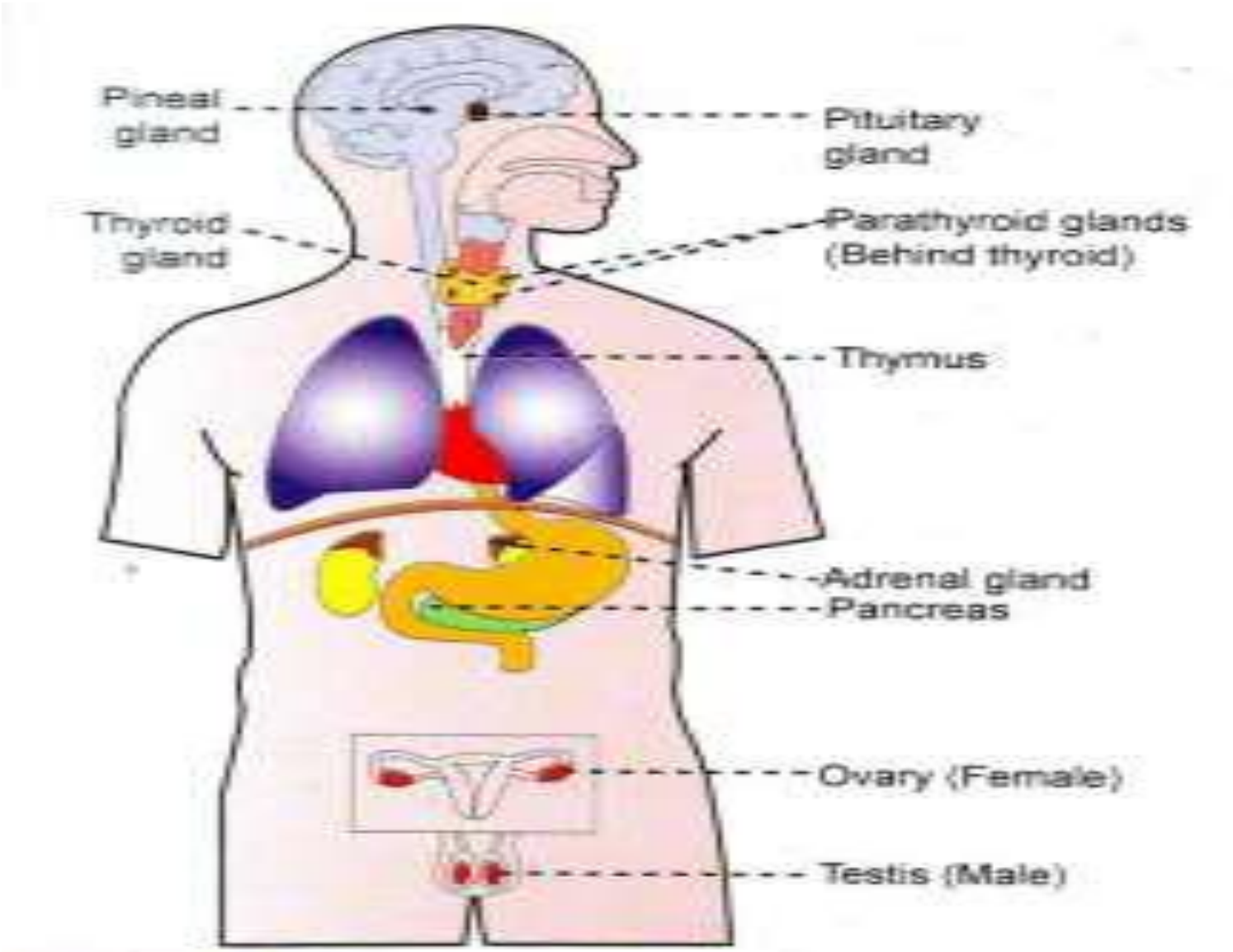


FIGURE 64-1: Diagram showing major endocrine glands

WHAT ARE HORMONES?

- Natural organic substances, that regulate growth, metabolism and other functions of an organism They are simply biochemical messengers They can be classified according to the chemical composition, organs where they work e.g reproductive hormones in the reproductive organs, and if they either act on the same cell producing them i.e. autocrine or paracrine

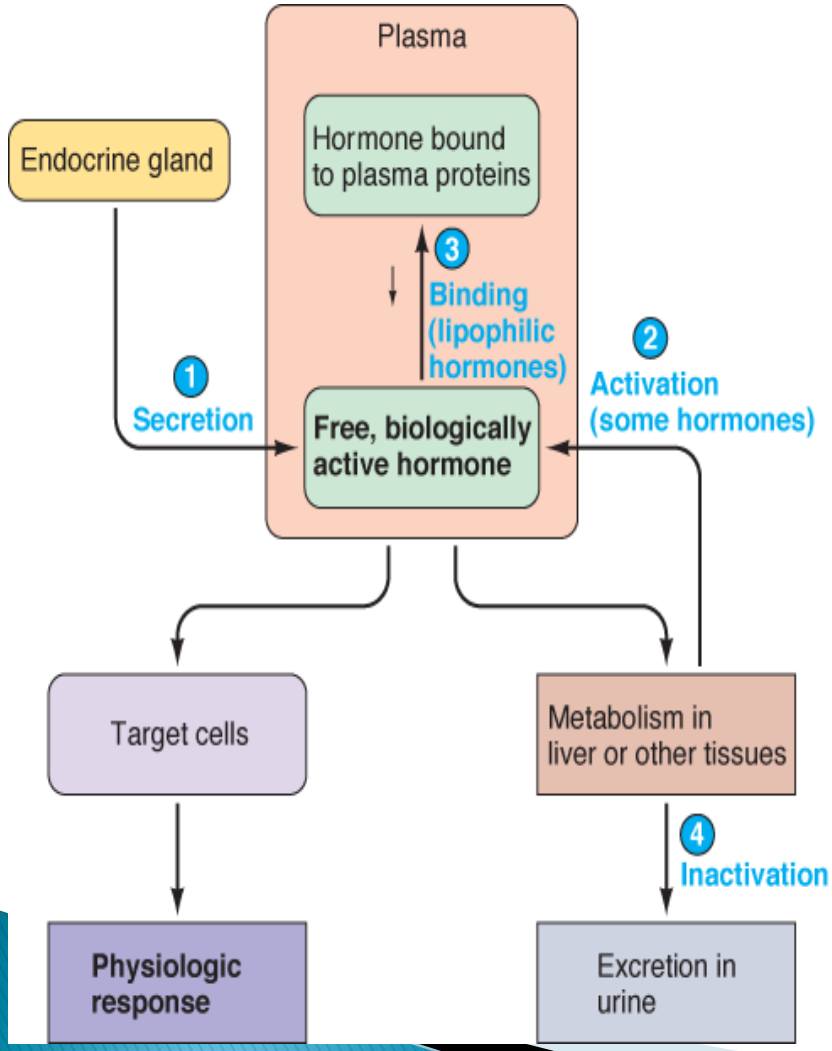
GENERAL PRINCIPLES OF HORMONE ACTION

- Trophic hormone:- A hormone that has its primary function the regulation of hormone secretion by another endocrine gland
- • Synergism-when different hormones work together and have a greater effect than individual hormone action
- • Permissiveness-a small amount of one hormone allows a second hormone to have its full effect on a target cell; i.e. first hormone ‘permits’ the full action of the second hormone

GENERAL PRINCIPLES OF HORMONE ACTION

- • Antagonism-one hormone produces the opposite effect of the other
- The processes involve in both negative and positive feedback. For example, if A>B>C>D, increase in D causes inhibition of A i.e. negative feedback. If D decreases, A production is triggered, i.e. positive feedback

Onset of hormone secretion and action



The plasma concentration of free, biologically active hormone, which can interact with its target cells to produce a physiologic response, depends on

1. the hormone's rate of secretion by the endocrine gland (for all hormones; the major factor)
2. its rate of metabolic activation (for a few hormones)
3. its extent of binding to plasma proteins (for lipophilic hormones)
4. its rate of metabolic inactivation and excretion (for all hormones)

GENERAL CHARACTERISTICS OF HORMONES

- Not secreted at a uniform rate
- Exert their effects in biocatalytic amounts
- Turnover is varied and usually rapid
- Exert multiple actions
- Exhibit high degree of specificity
- Different tissues may respond differently to a given hormone

Mechanism of hormone action

- **The hormones fall into two general classes based on their solubility in water.**

- ・1. Hydrophilic Hormone: **The water soluble hormone.** They are transported simply dissolved in blood
- ・**Examples**: the catecholamines (epinephrine and
- norepinephrine) and peptide/protein hormones.

- **Lipophilic Hormone: They are poorly soluble in water.** So they cannot be dissolved in watery blood. They bind to plasma protein and present in the blood in protein bound form. They are lipid soluble.
- **· Examples:** The lipid soluble hormones include thyroid hormone, steroid hormones and Vitamin D3

Signal Amplification Via 2nd Messenger Pathways

- Initial signal is in the form of hormone which acts as ligand whose concentration is just one/per receptor. The hormonal response has got multiple steps, and each step multiplies the signal (cascading effect) that finally leading to million
- fold amplification, i.e. one hormone molecule mediating its effect through million of molecules. This process is known as **signal amplification**

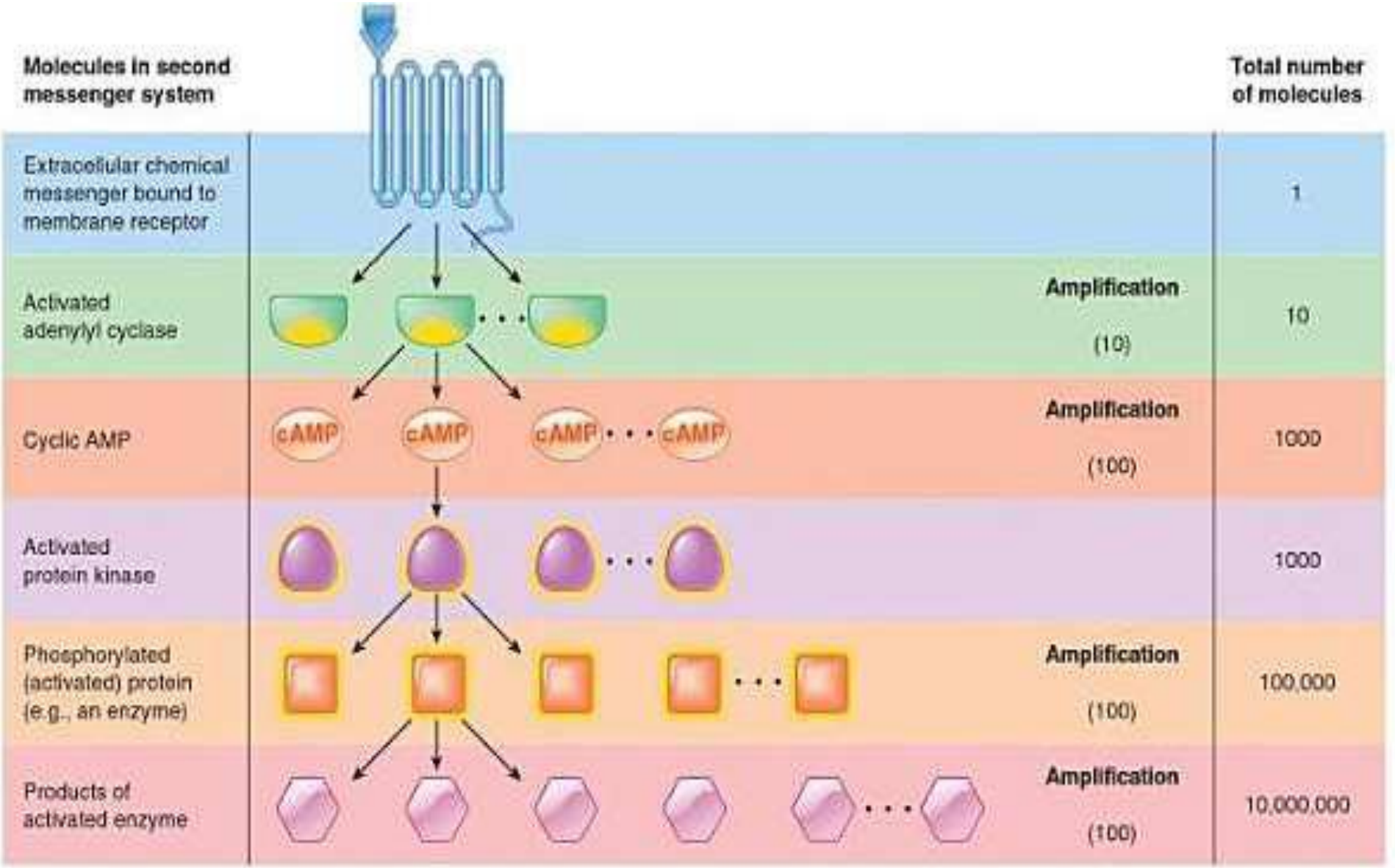


FIGURE 4-26 Amplification of the initial signal by a second-messenger pathway.

TYPES OF RECEPTOR

- **INTERNAL RECEPTOR**

- **1-NUCLEAR**
- **2-CYTOPLASMIC**

- **EXTERNAL RECEPTOR**

- **CELL MEMBRANE**

MEMBRANE RECEPTOR

- Receptors present in or on the surface of the cell membrane
- Types
- **Ion channel-linked receptor**
- **G –protein couple receptor**
- **Enzyme –linked receptor**
- E.g., Proteins, peptides, & catecholamines

CYTOPLASMIC RECEPTOR

- **Receptors present in cell cytoplasm**
- E.g., Steroid hormones

NUCLEAR RECEPTOR

- **Receptors present in nucleus**
- E.g., Thyroid hormones, Retinoid hormones, Vitamin-D

HOW LIPID-SOLUBLE HORMONES WORK?

- Binding to specific cell receptor in the cell membrane and form hormone-cell receptor complex, which diffuses to nucleus
- • The receptor is eventually released for re-use
- • Steroid activates a specific gene to produce mRNA
- • mRNA pass out into the cytoplasm and initiates protein [enzyme] synthesis
- the whole process is called **mobile-receptor hypothesis** in which a steroid hormone is not attached to the plasma membrane, but seem to move freely in the nucleoplasm

HOW LIPID-SOLUBLE HORMONES WORK

- **Step1: Free lipophilic hormone (hormone not bound with its**
- plasma protein carrier) diffuses through the plasma membrane
- of the target cell and binds with the receptor which is
- intracellularly located inside the cytosol/or in the nucleus.
- **Step2. Each receptor has specific binding region with hormone** and another region with binding with DNA. Receptor alone cannot bind to DNA unless it binds to hormone. Once the
- hormone is bound to receptor, the hormone receptor complex
- binds to specific region of DNA known as **Hormone response**
- **element(HRE).**

HOW LIPID–SOLUBLE HORMONES WORK

- **Step3: Transcription of gene**
- **Step4: m RNA transported out of nucleus into the cytoplasm**
- **Step5: Translation at Ribosome**
- **Step6: Protein/enzyme released from ribosome**
- **Step7: protein/enzyme mediate ultimate response**

HOW WATER-SOLUBLE HORMONES WORK

- **●1 A water-soluble hormone (the first messenger)** diffuses from the blood through interstitial fluid and then binds to its receptor at the exterior surface of a target cell's plasma membrane. The hormone– receptor complex activates a membrane protein called a **G protein.** The
- activated G protein in turn activates adenylate cyclase.

- • **●2 Adenylate cyclase converts ATP into cyclic AMP (cAMP).** Because the enzyme's active site is on the inner surface of the plasma membrane, this reaction occurs in the cytosol of the cell.

HOW WATER-SOLUBLE HORMONES WORK

- **●3 Cyclic AMP (the second messenger)** activates one or more protein kinases, which may be free in the cytosol or bound to the plasma membrane. A protein kinase is an enzyme that phosphorylates adds a phosphate group to other cellular proteins (such as enzymes). The donor of the phosphate group is ATP, which is converted to ADP.
- **●4 Activated protein kinases phosphorylate one or more cellular proteins.**
- Phosphorylation activates some of these proteins and inactivates others, rather like turning a switch on or off.

HOW WATER-SOLUBLE HORMONES WORK

- • **●5 Phosphorylated proteins in turn cause reactions that produce physiological responses.**
- Different protein kinases exist within different target cells and within different organelles of the same target cell. Thus, one protein kinase might trigger glycogen synthesis, a second might cause the breakdown of triglyceride, a third may promote protein synthesis, and so forth. As noted in step 4 phosphorylation by a protein kinase can also inhibit certain proteins. For example, some of the kinases unleashed when epinephrine binds to liver cells inactivate an enzyme needed for glycogen synthesis

HOW WATER-SOLUBLE HORMONES WORK

- **6 After a brief period, an enzyme called phosphodiesterase inactivates cAMP.**
- Thus, the cell's response is turned off unless new hormone
- molecules continue to bind to their receptors in the plasma membrane

HOW WATER-SOLUBLE HORMONES WORK

- The whole process above is called **Messenger Mechanisms** In this instance, the first messenger delivers message to fixed receptors in the target cell's plasma membrane. The message then is passed to the cell where second messenger triggers appropriate cellular changes