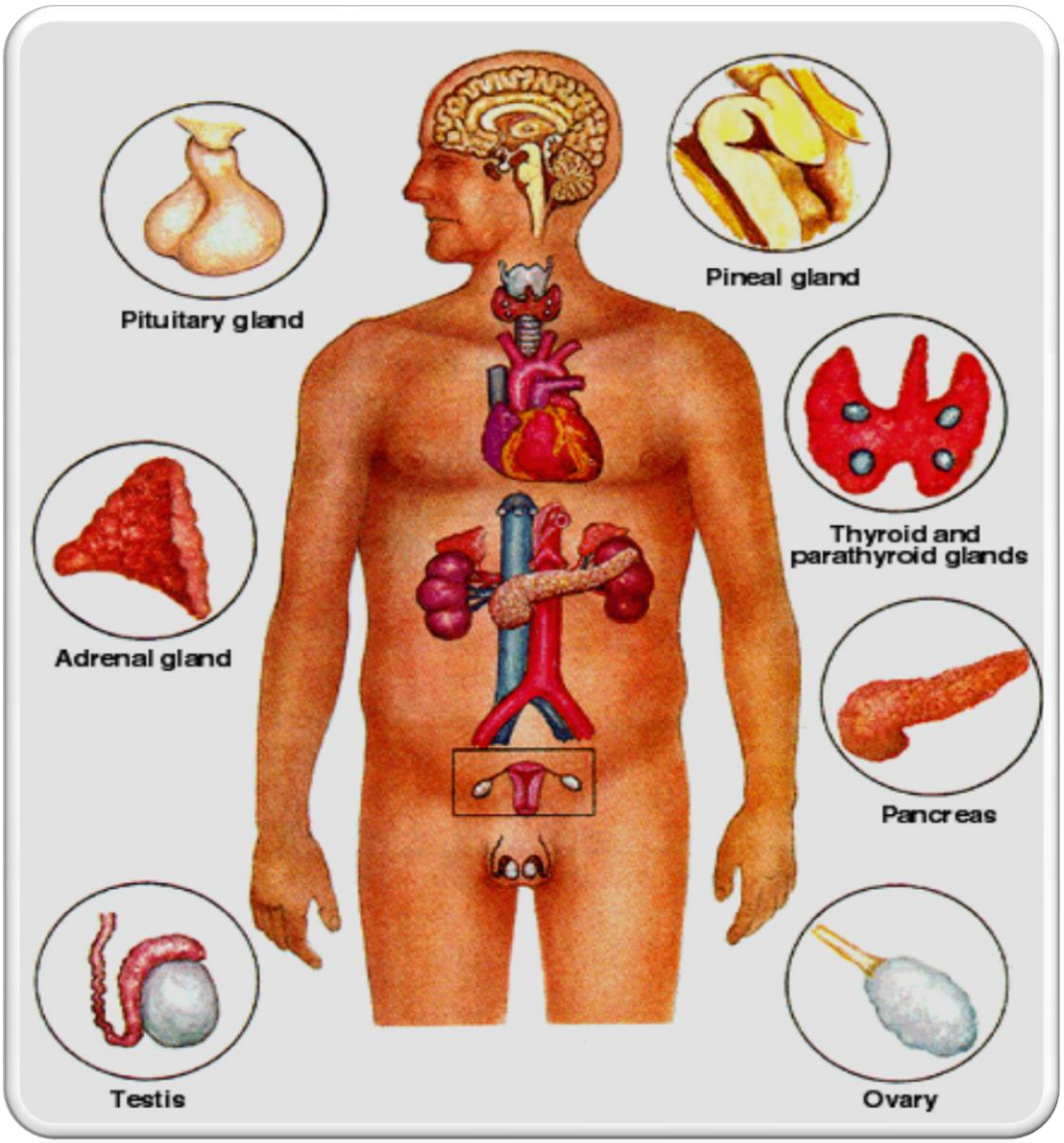
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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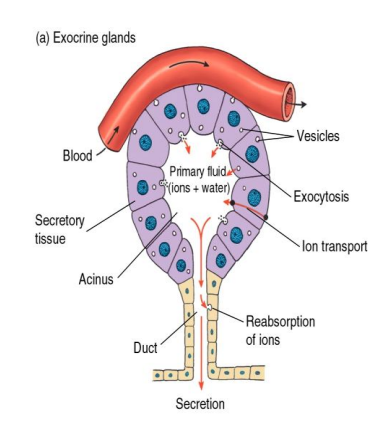
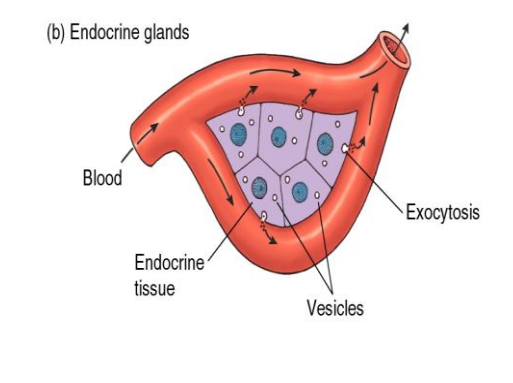
Endocrinology (Introduction)

Learning objectives:

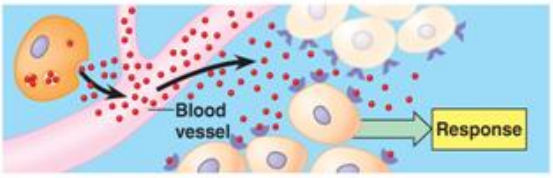
- Endocrine vs exocrine gland
- Chemical messengers
- Hormone
  - Definition
  - Chemical structure
  - Paracrine & autocrine
  - Transport and clearance
- Mechanism of action
  - Receptors, down-regulation and up-regulation
  - Intracellular signaling
  - Second messenger (cAMP, IP3)

Endocrine vs exocrine gland

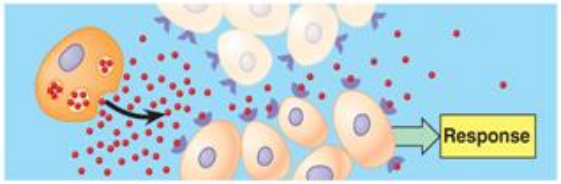
EXOCRINE GLANDS	ENDOCRINE GLANDS
Ducts + lumen and surface Their secretions are released through ducts onto an organ's lumen and surface. 	Chemical messengers + bloodstream Their secretions are released directly into the bloodstream rather than through a duct. 

Endocrine gland :- ductless, classical gland e.g hypothalamus

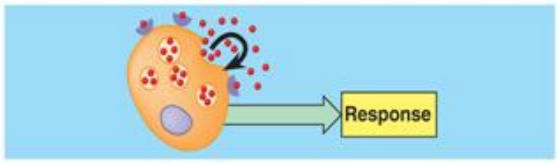
Endocrine tissue :- tissue secreting hormone e.g skin



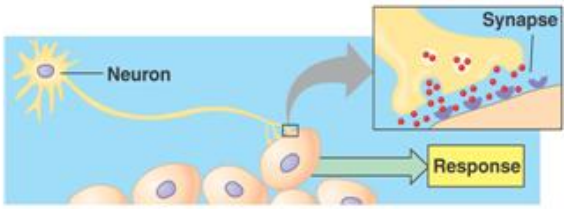
(a) Endocrine signaling



(b) Paracrine signaling



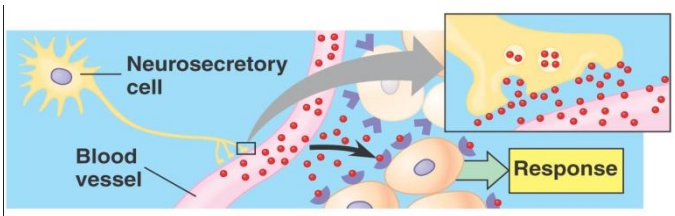
(c) Autocrine signaling



(d) Synaptic signaling

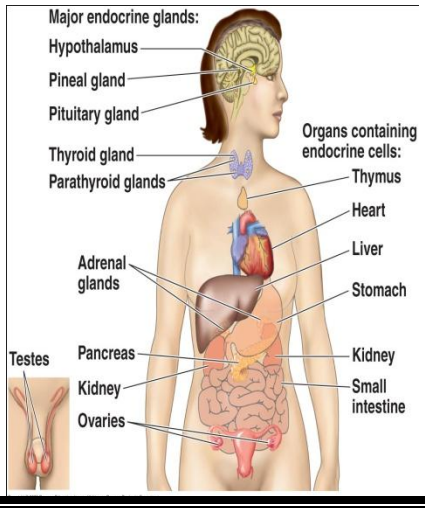
Chemical messengers

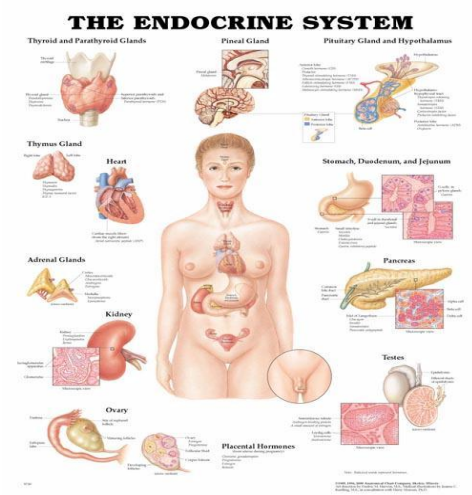
- The activities of cells, tissues and organs are coordinated by chemical messengers
  - Neurotransmitters
  - Endocrine hormones
  - Neuroendocrine hormones
  - Paracrines :-gland produce affect on local tissue
  - Autocrines
  - Cytokines
  - Juxtacrine :- part of hormone receptor on one cell and other part on other cell.



(e) Neuroendocrine signaling

- Endocrine glands:
  - Adrenal
  - Pancreas
  - Ovaries
  - Testes
  - Pituitary
  - Thyroid
  - Parathyroid





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

- Metabolism
- Growth and development
- Water and electrolyte balance
- Reproduction
- Behavior

* Definition:

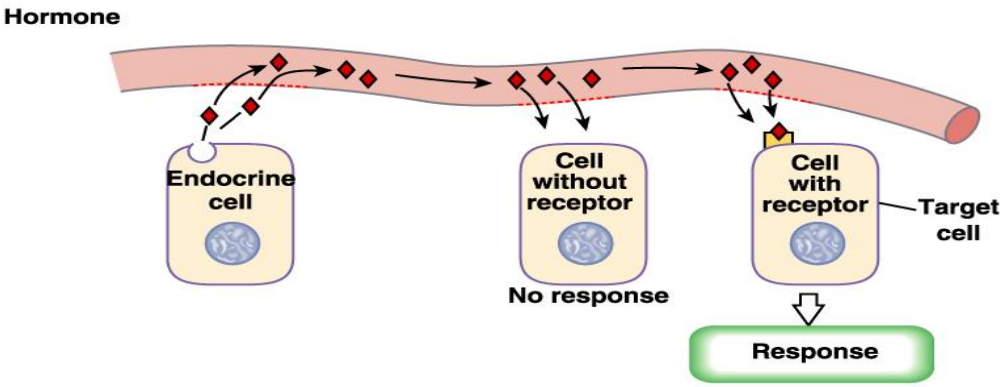
- Hormone is a chemical substance released by group of cells to control the function of other type of cells. (It is secreted directly to the blood stream in response to stimulus to cause physiological response at the target tissues.)

* Types of hormones

- Affect many different types of cells (eg. GH and Thyroxin)
- Affect only specific target cells (eg. ACTH and estrogen)

* What are target cells?

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

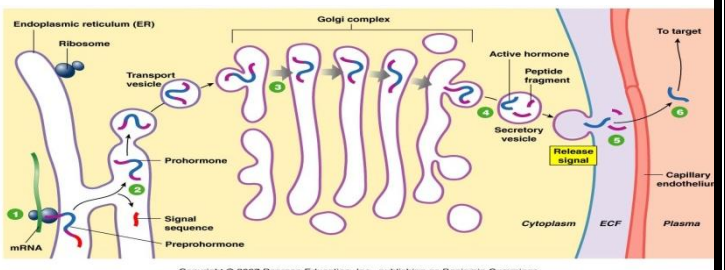


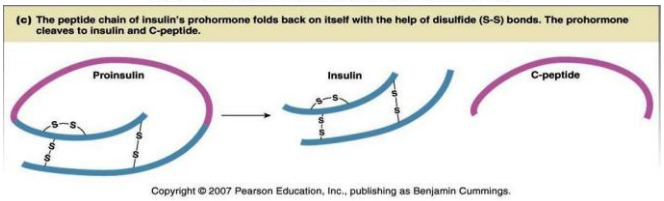
* Chemical structure of hormones

- Three general classes of hormones:
  - Proteins and polypeptides (anterior and posterior pituitary, pancreas and parathyroid hormones) stored in vesicles until needed
  - Steroids (adrenal cortex, ovarian and testicular hormones) diffuse across the cell membrane
  - Derivatives of amino acid tyrosine (thyroid hormones and catecholamines)

Peptide (Protein) Hormones

- **Synthesis as preprohormone → post-translational modification to prohormone → then hormone**



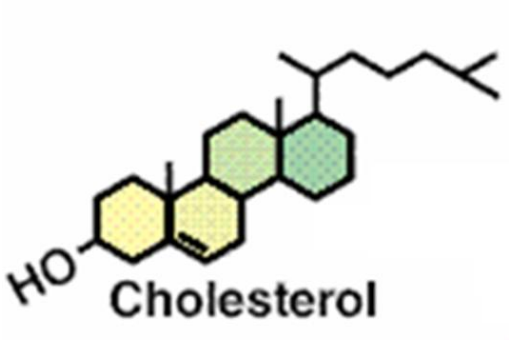


- Example of protein hormone:
  - Insulin
- Polypeptides:
  - Chains of < 100 amino acids in length.
  - – ADH.
- – Protein hormones:
  - Polypeptide chains with > 100 amino acids.
  - -GH

Glycoprotein hormone bind to carbohydrate molecule e.g FSH

Steroid Hormones

- Secreted by gonads, adrenals, placenta
- Derived from cholesterol (lipophilic)
  - Cross membranes (no storage)
- On-demand synthesis (SER)
- Usually Bound to Carrier proteins



Amine Hormones

- **Derived from tyrosine or tryptophan**
- **3 groups**
  - **Tryptophan ⇒ Melatonin**
  - **Tyrosine ⇒ Catecholamines (behave like peptide hormones)**
  - **Tyrosine ⇒ Thyroid hormones (behave like steroid hormones)**

Fatty acid derivatives (for knowledge)

- **Eicosanoids prostaglandins, prostacyclins, leukotrienes and thromboxanes)**

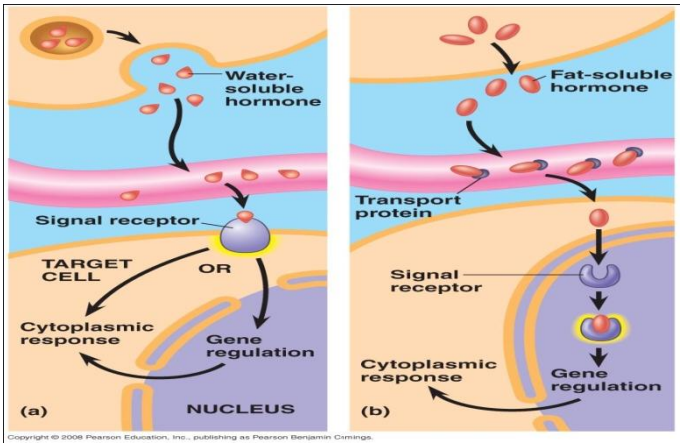
Transport of hormones

- *Water soluble hormones*- hydrophilic (peptides & catecholamines) dissolved in plasma (go to target tissue)

- *Fat soluble hormones* – hydrophobic (Steroids and thyroid hormones*) transported bound to plasma proteins (90%),* (10%) free fraction of hormone that act on receptors.

Binding to proteins helps to:

Provide reservoirs and slow hormones clearance



Mechanism of action of hormones

- **Mechanism of action :**

  Hormone-receptor interaction (1st messenger) → Enzyme activation → Release of the second messenger → Effects on cellular function

- **Receptors:**

  1. Hormonal receptors are large proteins
  2. 2000-100,000 receptors/cell
  3. Receptors are highly specific for a single hormone

- **Receptor's Location:**

  1. On the surface of cell membrane (proteins, peptides and catecholamines)
  2. In the cell cytoplasm (Steroids)
  3. In the cell nucleus (thyroid hormones)

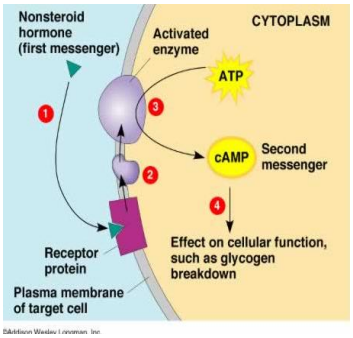
✓ **Hydrophilic hormones:** cannot enter the cell→ hence; they only bind on an outer surface receptor→ resulting in a fast response

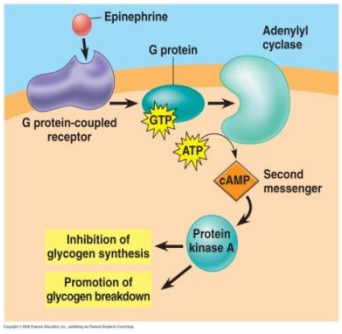
✓ **Lipophilic hormones:** (steroid and thyroid) can enter the cell→ often lead to gene activation→ Therefore; they result in a slower response

Mechanism of action (peptids and protein hormones)

Second messenger could be:

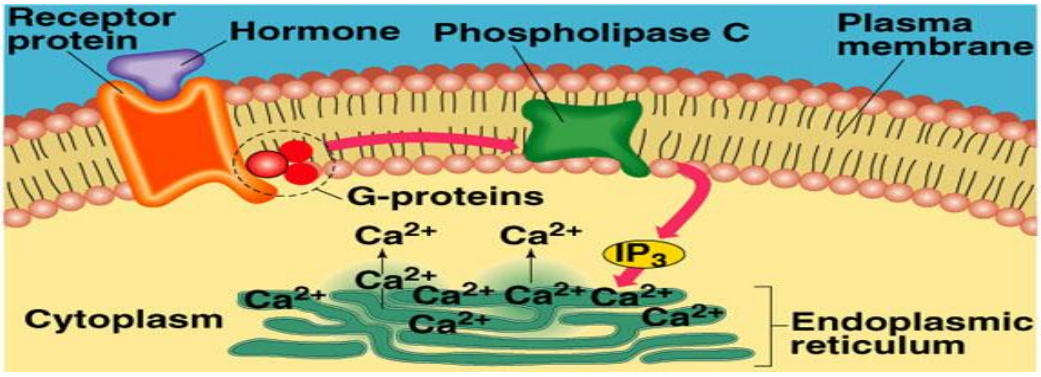
- ✓ Adenylyl cyclase system
- ✓ Phospholipase C system
- ✓ Tyrosine kinase system



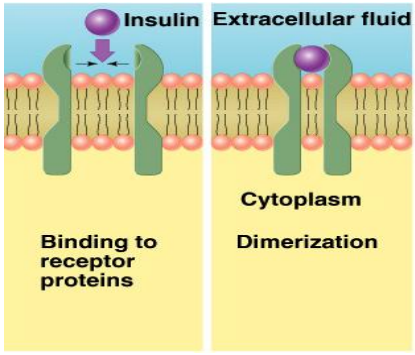


Second messenger (ADYNYLATE CYCLASE-CAMP)

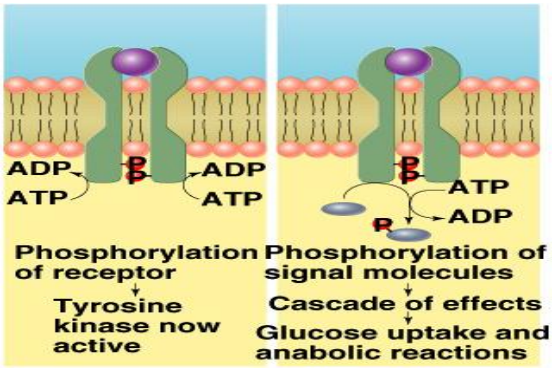
Second messenger (PPOSPHOLIPASE C-ip3)



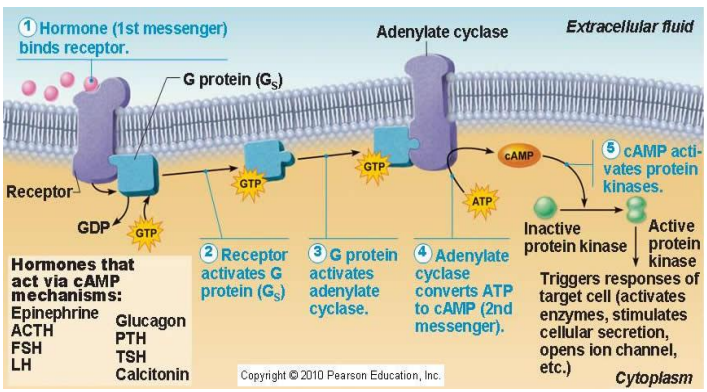
Second Messenger (Tyrosine Kinase System)

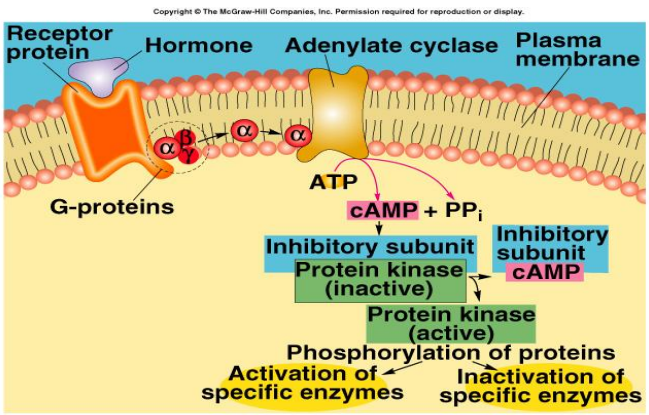


- Is used by insulin & many growth factors to cause cellular effects
- Surface receptor is tyrosine kinase
  - Consists of 2 units that form active dimer when insulin binds

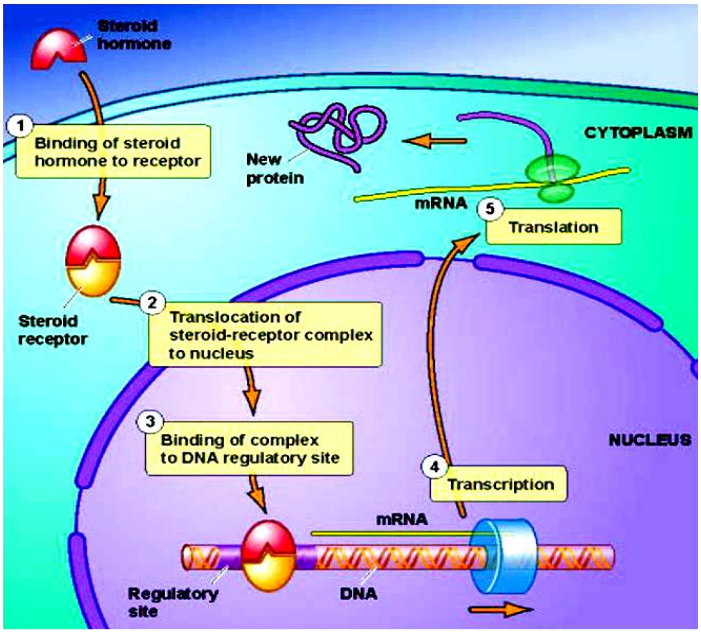


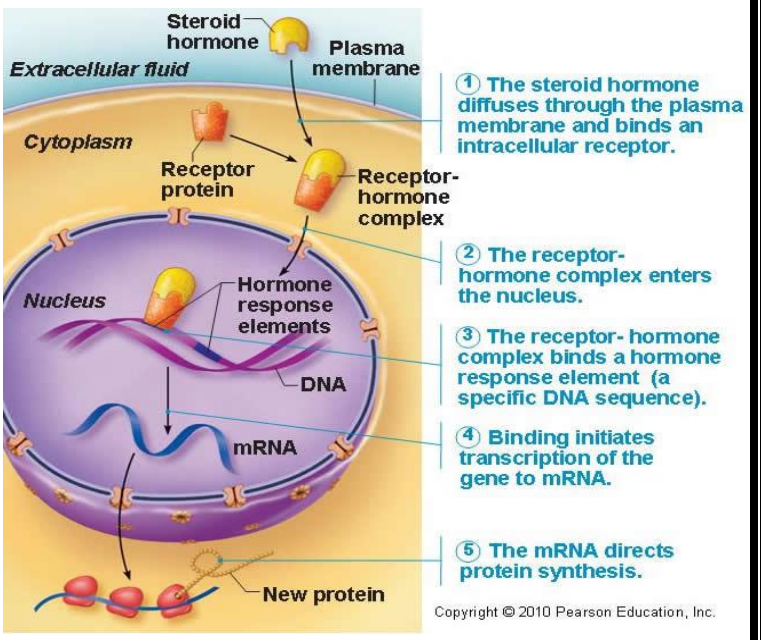
- Activated tyrosine kinase phosphorylates signaling molecules.
- Induction of hormone/growth factor effects.





Mechanism of action (steroid hormones)





Regulation of hormonal receptors

Receptors do not remain constant, either they are **Inactivated/destroyed** or **Reactivated/manufactured**

1. **Dose-response relationship:** the higher the hormone's concentration, the more response from receptors.
2. **Sensitivity:** the hormone concentration that produces 50% of the maximal response. If more hormones are required to produce 50% of response, then there is a decrease in sensitivity, and vice versa.
3. **Number and affinity:** response of receptors can be changed by down-regulation or up-regulation.

- **Downregulation:**
  - Increase hormone concentration leads to decrease in the number of active receptors
  - Most peptide hormones have pulsatile secretion which prevents downregulation
- **Upregulation:**
  - The hormone induces greater than normal formation of a receptor or intracellular signaling proteins

Clearance of hormones

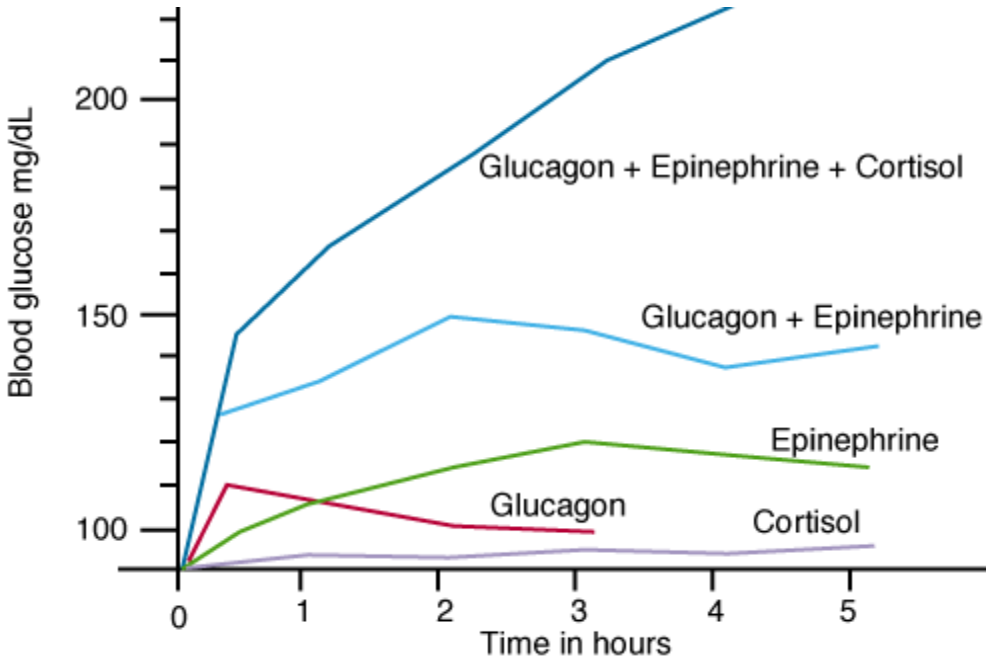
- Two factors control the concentration of a hormone in the blood:
  - The rate of its secretion
  - The rate of its removal (metabolic clearance)
- Hormones are cleared by:
  - Metabolic destruction by tissues
  - Binding with tissues
  - Excretion by the liver into bile
  - Excretion by the kidney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

Hormone Interactions

- Multiple hormones can affect a single target simultaneously
- Three types of hormone interactions*:*
  1. **Synergism**
  2. **Permissiveness**
  3. **Antagonism**

Synergism

- **Combined action of hormones is more than just additive!** **It occurs when more than one hormone produces the same effects in a target cell, and their combined effects are amplified**
- **Example: Blood glucose levels & synergistic effects of glucagon, cortisol and epinephrine**



Permissiveness

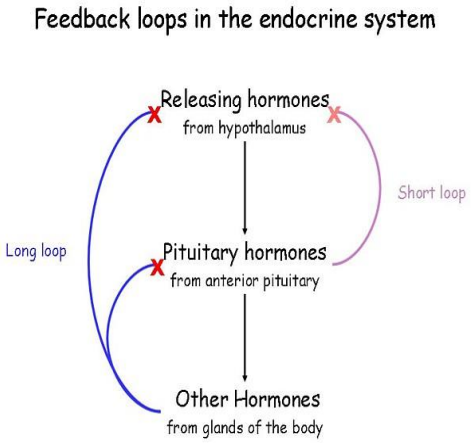
- **One hormone allows another hormone to have its full effect (It occurs especially during growth and development)**
  - **Especially during growth**
- **Example**
  - **Thyroid hormone have permissive effect on growth hormone action**
  - **Deficiency of thyroid hormone in infants leads to dwarfism.**

Antagonism

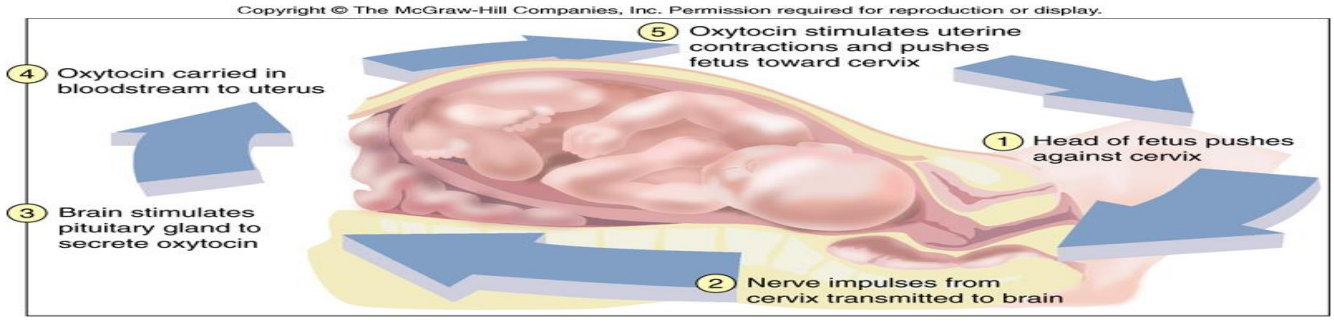
- Antagonistic hormones have opposing physiological actions (It means that one hormone decreases the action of the other).
  - Hormone B diminishes the effect of hormone A
- Example
  - Glucagon antagonizes the action of insulin

FEEDBACK CONTROLS

Short & Long loop Negative.

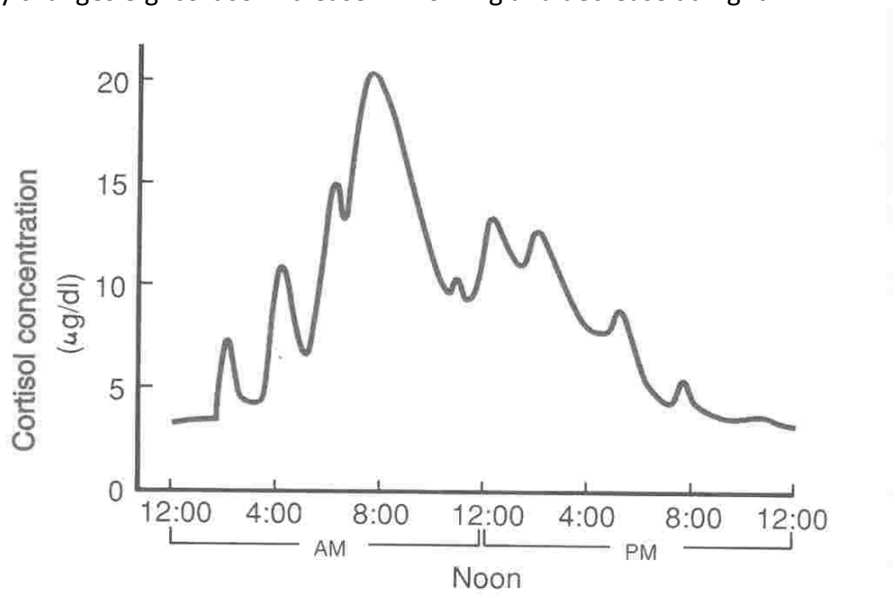


Positive Feedback



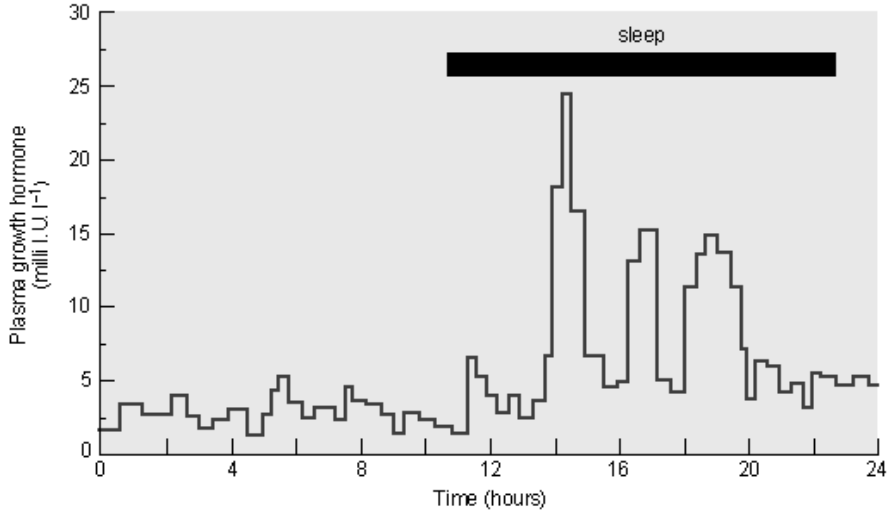
Circadian Rhythm

- Day changes e.g. cortisol increase in morning and decrease at night.



Circhoral Rhythm

- Hour to hour changes. E.g. insulin → increase after male .growth hormone→ increase during sleep.



Extra Info – mentioned in 430 team work:

Hormone concentration in the blood:

- Concentrations of circulating hormone in blood reflect:
  - Rate of release
  - Speed of inactivation and removal from the body
- Two factors control the concentration of a hormone in the blood:
  - The rate of its secretion
  - The rate of its removal (metabolic clearance)
- Hormones are cleared by:
  - Metabolic destruction by tissues
  - Binding with tissues
  - Excretion by the liver into bile
  - Excretion by the kidney into urine
  - Liver enzyme systems and degrading enzymes
- Clearance of protein-bound hormones (lipophilic hormones) is slower than clearance of peptide hormones (hydrophilic hormones)

Summary

- Endocrine glands Their secretions are released directly into the bloodstream rather than through a duct.
- Types of hormones
  - Affect many different types of cells (eg. GH and Thyroxin)
  - Affect only specific target cells (eg. ACTH and estrogen)
- Target cells refer to cells that contain specific receptors (binding sites) for a particular hormone.
- Proteins and polypeptides hormones stored in vesicles until needed.
- Steroids diffuse across the cell membrane.
- Amine Hormones Derived from tyrosine or tryptophan.
- Synergism action of hormones is more than just additive .It occurs when more than one hormone produces the same effects in a target cell, and their combined effects are amplified
- permissiveness One hormone allows another hormone to have its full effect (It occurs especially during growth and development)

Questions

Q1: which one of the following hormones diffuse across the cell membrane

A. protein hormones
B. polypeptide hormones
C. steroid hormones

Q2: example for Circhoral Rhythm

A. GH
B. Insulin
C. A and B

Q3: which one of the following hormones affect many different types of cells

A. Thyroxin
B. ACTH
C. Estrogen

Answers : 1-C 2-C 3-A