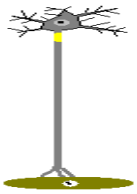
Endocrine Physiology Outlines
Introduction and Overview

- Body functions are regulated by 2 major control systems:

1. Nervous system:
2. Hormonal, or endocrine system:

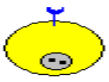
Nervous system

The nervous system exerts point-to-point control through nerves. Nervous control is electrical in nature & it acts through releasing neurotransmitters in response to nervous stimuli. Its target cells are muscles, glands & other neurons, resulting in muscular contraction & glandular secretion. Its action is fast

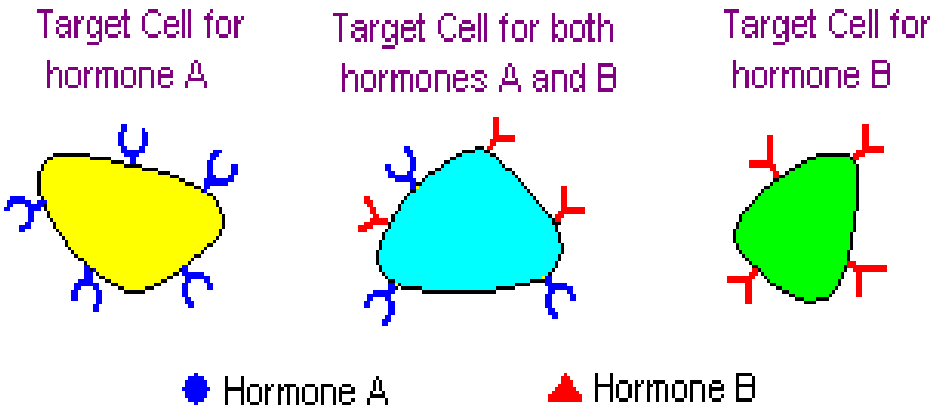


Endocrine system

- A group of glands which have NO ducts.
- Secrete their hormones (chemical messengers) into blood.
- Most hormones circulate in blood, coming into contact with essentially all cells. However, a given hormone usually affects only a limited number of cells, which are called target cells. Resulting in changes in metabolic activities.
- Target cells responds in specific way to a hormone because it bears specific **receptor proteins** for the hormone.



- The distance between hormone producer cell & hormone responder cell may be large, moderate, or small.
- Generally, act slower in onset, more prolonged, & more diffuse than NS.
- Under control of NS.



Hormonal Interactions

- **Synergistic:**
  - Two hormones work together to produce a result.
- **Additive:**
  - Each hormone separately produces response, together at same concentrations stimulate even greater effect.
  - NE & Epi.
- **Complementary:**
  - Each hormone stimulates different step in the process.
  - FSH & testosterone.
- **Permissive effect:**
  - Require previous or simultaneous exposure to two or more hormones.
- **Antagonistic:**
  - Two hormones have opposite effects.

Principal '4' functions of the endocrine system

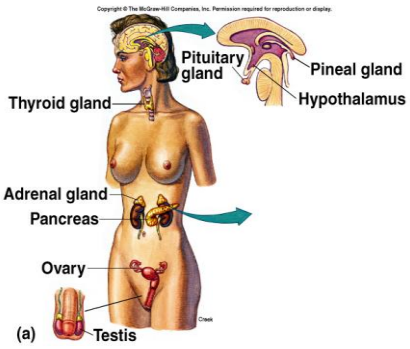
1. Maintenance of internal environment (homeostasis).
   - Regulation total body metabolism.
   - Control of energy production, utilization & storage.
   - Nutrition.
   - Acid base balance
2. Combating stress
   - body's response to environmental stimuli.
   - Infection.
   - Trauma.
   - Shock.
3. Integration & regulation of growth & development.
   - Increase cell size & no.
4. Reproduction
   - Control, & maintenance of sexual reproduction, including hormone secretion, primary sex organs, secondary sexual characteristics, gametogenesis, fertilization, fetal growth & development, & nourishment of the newborn.

Methods of study

- Descriptive (anatomical)
- Chemical:
- Proteins & polypeptides.
- Amino acid derivatives
- Steroids.
- Fatty acid derivatives, etc.
- Immunological
  - Radioactive Immuno Assay (RIA)
  - Enzyme Linked Immuno Sorbent Assay (ELISA)
  - Other techniques
- Experimental studies
- Clinical studies
  - Hypo
  - Hyper

Important endocrine glands & organs

- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid glands
- Adrenal glands
- Endocrine Pancreas (Islets of Langerhans)
- Gonads:
  - Ovaries
  - Testes
- Placenta



- Miscellaneous endocrine glands:
  Hormones & hormone-like substances are also produced by other organs in the body that serve other functions as well; such as:
  Heart → atrial natriuretic peptide (ANP)
  Liver → somatomedins (insulin-like growth factors IGF-1)
  Adipose tissue → leptin
  Kidneys → erythropoietin
  Thymus
  Pineal
  Local hormones

Hormones?

- A hormone is a chemical substance that is secreted into the blood by one cell or a group of cells & exerts a physiological control & regulatory effect on other cells of body.
- Each hormone has its own onset & duration of action; e.g.
  Catecholamine, secreted in sec., & its full action (few sec. to min.)
  Aldosterone, ? takes 1hr to act.
  Thyroxine; GH, ? require months for full effect.

Types of hormones:

I: According to site of action

3 types

1) Local hormones, e.g. Ach; Secretin; Cholecytokinin.
2) General hormones, e.g. Catecholamines; GH; TH.
3) Target tissues hormones, e.g. ACTH; Ovarian hormones; Oxytocin.

II: According to Chemical classification

- **Hormones are categorized into four structural groups, with members of each group having many properties in common:**

- Peptides and proteins
- Amino acid derivatives
- Steroids
- Fatty acid derivatives - Eicosanoids

1. Peptide/protein hormones

- Range from 3 aa to hundreds of aa in size.
- Often produced as larger molecular wt precursors (*preprohormone*) that are proteolytically cleaved to *Prohormone* which is processed to golgi apparatus & cleaved into active form of the hormone and packaged into secretory vesicles**.**
- Secretory vesicles move to plasma membrane where they await a signal. Then they are exocytosed and secreted into blood stream**.**
- Peptide/protein hormones are water soluble.
- Comprise the largest number of hormones, e.g. Anterior & posterior pituitary hormones, Insulin, Glucagon, & Parathormone.
- All protein hormones are synthesized in granular ER.

2. Amine hormones

There are two groups of hormones derived from the amino acid tyrosine

Thyroid hormones and **Catecholamines**

- Water soluble hormones

AA derivatives hormones are formed by enzymatic action in cytoplasm of glandular cells.

- Adrenal medullary hormones are secreted like peptide hormones.
- Thyroid hormones, 1st formed as large protein molecule called thyroglobulin, then stored in large follicles in thyroid gland. When to be secreted, cleaved by specific enzyme systems where thyroid hormones will be released & secreted into the blood.

3. Steroid hormones

- Are all derived from Cholesterol
- Enzymes which produce steroid hormones from cholesterol are located in mitochondria & smooth ER
- Steroids are lipid soluble and thus are freely permeable to membranes so are not stored in cells
- Are not packaged, but synthesized & immediately released

4. Fatty Acid Derivatives – Eicosanoids

- **Arachadonic acid is the most abundant precursor for these hormones** which is stored in membrane lipids & released through the action of various lipases.
- The principal groups of hormones of this class are prostaglandins, prostacyclins, leukotrienes & thromboxanes.
- These hormones are rapidly inactivated by being metabolized & are typically active for only a few seconds.

Stimuli for hormone secretion

- Can be:

1) Chemical, e.g. glucose → insulin.
2) Neural, e.g. Ach → stimulates the release of epinephrine & norepinephrine from the adrenal medulla.
3) Hormonal, e.g. ACTH → adrenal cortex → cortisol.

Hormones share special characteristics

1. Found in small concentrations in blood, …(pgm/ml; µgm/ml)
2. Rates of secretion are extremely small, which is controlled by negative feedback effect from the target organ to the secretory gland.
3. Has specific receptors in target organ.

Hormone receptors?

- Mostly protein in structure.
- **Minute quantities initiate stimulus will lead to powerful & large final effect**
- Each target cell has ≈ 2000 – 100,000 receptors.
- Bind hormone with high affinity.
- Each receptor is highly specific for a single hormone.
- Initiate a cascade of reactions in cell, where each stage of reaction becomes more powerful & active.
- Hormone's concentration in target tissues can be higher than in circulation.

Activation of Hormone receptors:

- Hormone receptors are dynamic in nature & their number respond to physiological & biochemical factors.
- Receptor production is either down or up-regulated:

Down-regulated, when a hormone is present in excess: (↓ no of active receptors, either because of their inactivation or destruction during the course of their fx.)

Up-regulated, when a hormone is low or absent in blood: (↑ no of active receptors, as the stimulating hormone induces their new formation.)

Location of Hormone receptors:

1. **In or on surface of cell membrane**
   specific for protein, peptide, & catecholamine hormones
2. **In cell cytoplasm**
   for steroid hormones
3. **In cell nucleus**
   for metabolic thyroid hormones

Regulation of Hormone secretion:

- Key features of sensing & signaling stimulus response system are:
  - receipt of stimulus
  - synthesis and secretion of hormone
  - delivery of hormone to target cell
  - evoking target cell response
  - degradation of hormone
- The concentration of hormone as seen by target cells is determined by three factors:
  - Rate of production
  - Rate of delivery
  - Rate of degradation & elimination
- Feedback control:
  - Negative feedback is the most common.
  - Positive feedback is less common.

Mechanism of action of hormone?

- Activation of hormonal receptors play a major role in hormonal action
- **3 ways:**

1) Change in Membrane Permeability

When hormone attach to the receptor, conformational changes occur in the receptor protein leading to opening or closing of one or more ions channels, e.g. Na^+; K^+; Ca^{2+}

Example:

- Local hormone (neurotransmitter substances)
- Adrenal medullary secretions (catecholamines

2) Activation of an Intracellular Enzyme

- Hormonal binding to the membrane receptor will activate an enzyme immediately inside the cell membrane, which will act as a second messenger.
- **Second messenger** means that the hormone itself is NOT the only direct institute of the intracellular changes; instead, the 'second messenger' causes these effects.
- **Second messengers are very important:**
  1. Amplify the signal from receptor.
  2. Relay station for chemical reaction to the signal from the receptor.

Second messenger system

- **There are 3 major classes of 2^{nd} messengers:**

1) Cyclic Nucleutides:

a. **cAMP** (cyclic adenosine monophosphate)

- more important, & wide spread.
- when the hormone attach to the receptor on the cell membrane, **G- proteins** (α, β, γ) will be stimulated where (α) will stimulate near by **Adenyl Cyclase** enzyme in the cell membrane. Adenyl Cyclase will stimulate the production of cAMP intracellularly which will lead to introducing physiological intracellular responses & controlling cellular activity:
  1. Activates enzymes such as protein kinase
  2. Alters cell permeability
  3. Causes muscle contraction or relaxation
  4. Causes protein synthesis

b. **cGMP** (Cyclic guanosine monophosphate)

- limited.

2) Inositol Triphosphate (IP_3) & Diacylglycerol (DAG):

- when a hormone attach to the receptor protein in the cell membrane they will stimulate **G- proteins** (α, β, γ) which will stimulate near by **Phospholipase C** enzyme in the cell membrane. The later will lead to break down of membrane phospholipids into 2 parts:

a. Innisitiol triphosphate (**IP3**) which will act as a 2^{nd} messenger and mobilizes Ca^{2+} from both mitochondria & endoplasmic reticulum (ER).

b. **Diacylglycerol (DAG)**: Has biological effects inside the cell & it acts as a second messenger like cAMP & IP_3. It controls intracellular Ca^{2+} concentration.

3) Ca^{2+}:

- when a hormone attach to the receptor protein in the cell membrane they will stimulate C^{2+} gates to open. C^{2+} will enter & attach to

Calmodulin protein intracellularly leading to biological actions by activating a protein kinase:

* causing smooth muscle contraction / myosin kinase
* change secretion by secreting cells
* changes ciliary action

3) Activation of Genes

- **Receptors are located intracellularly.**
  - Receptors for Steroid hormones are located **in the cytoplasm.**
  - Receptors for Thyroid hormones (**T_4 & T_3**) are located **in nucleus itself**.

Endocrinopathies

- **Most endocrine disorders can be attributed to one of the following problems:**

1) Too little hormone, **hyposecretion**.
2) Too much hormone, **hypersecretion**; or
3) Abnormal tissue response to a hormone, end organ **insensitivity** or **resistance**.