The Endocrine System

Endocrine System and Hormone Function

1. Endocrine System
   - affects bodily activities by hormones
   - sends messages to target cells in virtually any part of the body
   - brings about changes in metabolic activities of body tissue
   - hormones can take a long time to bring about their responses
   - Endocrine glands, or ductless glands, release hormones into the blood or lymph
   - (e.g.) pituitary, thyroid, parathyroid, adrenal, pineal, and thymus glands
   - Exocrine glands have ducts through which their nonhormonal products are routed to a membrane surface.
     - Pancreas and the gonads are both endocrine and exocrine glands
     - Hypothalamus is a major endocrine gland
     - Small intestine, stomach, kidney, placenta, and the heart also produce hormones.
     - Some tumor cells also synthesize hormones but uncontrolled
   - Endocrine organs are highly receptive to specific internal signals and release hormones in a predictable fashion.

2. Effects of Hormones
• controls the internal environment by regulating its chemical composition, hence maintaining **homeostasis**
• respond to marked changes in environmental conditions to help the body cope with emergency demands, such as infection, trauma, emotional stress, dehydration, starvation, hemorrhage and temperature changes
• role in the smooth, sequential integration of growth and development
• contributes to basic processes of reproduction
• hormones control and integrate:
  o reproduction
  o growth development
  o mobilization of the body
  o defenses
  o maintain electrolytes
  o water & nutrient balance
  o regulation of blood

3. **Mechanism of Hormone Action**
• Hormones affect target cells by altering cell activity; it may increase or decrease the rate of normal cellular processes.
• Hormones produce the following changes:
  A. changes in plasma membrane permeability (electrical state)
  B. synthesis of protein or certain regulatory molecule within the cell
  C. enzyme activation or deactivation
  D. induction of secretory activity
• **2 systems/mechanisms:**
  0. **Second-messenger system**

⇒ are protein or amino acid based hormones
⇒ steps:

  o hormone (the first messenger) binds to specific plasma membrane receptors
  o increases the synthesis of **cyclic AMP**
    - cyclic AMP is synthesized from ATP, by a process that requires the presence of an enzyme, **adenylate cyclase**, which is on the inner surface of the membrane. The activation of adenylate cyclase, called Cyclic AMP Mechanism, is caused by the attachment of the first messenger (hormone) to the membrane.
    - cyclic AMP then acts as the second messenger and alters cell function according to the message indicated by the hormone (Note: cyclic AMP does not directly produce a given physiological response, as indicated by the hormone; but cyclic AMP activates one or more enzymes collectively known
protein kinases. Each hormone molecule activates the formations of several protein kinases.

1. **Direct gene activation**

⇒ steroid and thyroid hormone both alter cell function by activation of genes.
⇒ steroid hormones are lipid-soluble, therefore can pass easily thru the plasma membrane of the target cell.
⇒ then binds to an intracellular protein receptor site in the cytoplasm
⇒ activating the receptor so that hormone-receptor complex moves into the nucleus
⇒ hormone-receptor complex interacts with specific genes, activates the genes to form the proteins, usually enzymes, necessary to produce the effect of the hormone

4. **Control of Hormone Release**
- The synthesis and release of hormones is regulated by the negative feedback system, however, some such as Oxytocin are regulated by a positive feedback system.
- Hormone secretion is stimulated by an internal / external stimulus and the increasing hormone levels in the blood inhibit the release of the hormone.

**Endocrine Organs and their Function**

1. **The Pituitary Gland (Hypophysis)**
- Although it is a distinct organ it is connected to the hypothalamus.
- has two major lobes:
  - Posterior lobe or neurohypophysis
  - Anterior lobe or adenohypophysis

a) **Pituitary-Hypothalamic Relationships**

- the pituitary gland is connected to the hypothalamus via a nerve bundle called the **hypothalamic-hypophyseal tract**
- hypothalamus synthesizes oxytocin and antidiuretic hormone (neurohormones). These are transported down the length of the axons to the neurohypophysis, where they are stored and released when needed.
- Anterior lobe is formed from epithelial tissue. It has no direct neural connection with the hypothalamus. There is a vascular connection called the **hypophyseal portal system**. Through this system, the releasing and inhibiting hormones circulate directly to the anterior lobe where they regulate the secretory activity of its hormone-producing cells.
2. **Anterior Lobe (Adenohypophyseal) Hormone**
   - also called the "master endocrine gland." It regulates the activity of other endocrine glands.
   - receives an appropriate chemical stimulus from the hypothalamus.
   - **Tropic hormones** - hormones that regulate the hormonal functioning of other endocrine organs. Such as:
     - Thyroid Stimulating Hormone (TSH)
     - Adrenocorticotropic Hormone (ACTH)
     - Follicle Stimulating Hormone (FSH)
     - Luteinizing Hormone (LH)
   - **Adenohypophyseal hormones** - hormones that exert their major effects on non-endocrine targets and effect target cell via second-messenger system. Such as:
     - Growth hormone (GH)
     - Prolactin (PRL)

A. **Growth Hormone**
   - produced by the somatotropic cells
   - major target are the bones and the skeletal muscles
   - anabolic hormone that promotes protein synthesis and encourages the use of fats for cellular respiration, thus conserving glucose.
   - stimulates uptake of amino acids from the blood and the build up of proteins
   - stimulates the uptake of sulfur into cartilage matrix
   - uses the second-messenger system to activate its affect
   - is regulated by:
     - GHRH - Growth hormone releasing hormone
     - GHIH - Growth hormone inhibiting hormone
   - GH secretion has a diurnal cycle; with large amounts released during sleep. Total amount secreted with age.

B. **Thyroid Stimulating Hormone (TSH) or Thyrotropin**
   - stimulates normal development and secretory activity of the thyroid gland
   - released from Thyrotropin cells of anterior lobe
   - triggered by hypothalamic hormone, Thyrotropin-releasing hormone (TRH) and inhibited by the negative feedback system.

C. **Adrenocorticotropic Hormone (ACTH) or Corticotropin**
   - secreted by the corticotropic cells of the anterior lobe
   - stimulates the adrenal cortex to release corticosteriod hormone, glucocorticoid hormones that help the body to resist stressors.
o release is influenced by hypothalamus hormone, Corticotropin-releasing hormone (CRH). CRH has a diurnal rhythm, with high levels in the morning.

D. Gonadotropins

o Follicle Stimulating Hormone (FSH) stimulates gamete production, eggs in females and sperm in males
o Luteinizing Hormone (LH) promotes production of gonadal hormone
o In females FSH and LH work together in the menstrual cycle.
o In males LH stimulates the interstitial cells of the testis to produce testosterone
o both FSH and LH are stimulated by the Gonadotropin-Releasing Hormone (GnRH) from the hypothalamus

o controlled by the negative feedback system

E. Prolactin (PRL)

o similar to the Growth Hormone
o produced by the lactotropic cells
o stimulates the ovaries of some animals, and in humans also stimulates milk production
o controlled by the hypothalamus
o Prolactin-releasing hormone (PRH) causes synthesis and production of PRL
o Prolactin-inhibiting hormone (PRI) prevents prolactin secretion
o in females the PRL levels rise and fall with rise and fall of the estrogen levels
o after birth the infants suckling stimulates PRH release and increases milk production

3. The Posterior Lobe (Neurohypophysis) and the Hypothalamic Hormones

• the posterior lobe is constructed largely of supportive neuroglial cells. It stores the hypothalamic hormones: Oxytocin and Antidiuretic hormone

a. Oxytocin

o stimulates uterine contractions and milk production
o synthesized and released during childbirth and nursing (suckling stimulates Oxytocin release)
  o the stretching of the uterus and cervix sends impulses to the hypothalamus, which then increases the synthesis and release of oxytocin
  o works on the positive feedback system

b. Antidiuretic Hormone (ADH)

o inhibits urine formation (H₂O loss)
  o targets the kidney tubules, to reabsorb H₂O from forming urine and return to the blood
  o Osmoreceptors in the body monitor H₂O levels in the blood (as the solute concentration increases). Decreasing levels stimulate the hypothalamus to synthesis and release
ADH to the posterior lobe of the pituitary gland, where it is released into the blood stream. As the solute concentration decreases, the osmoreceptors stop sending impulses to the hypothalamus.

- Alcoholic beverages inhibit ADH secretion, thus increasing urine output.
- Drinking excessive amounts of H₂O will also inhibit ADH release.
- ADH is also released when there is excessive blood loss (tries to restore blood volume).
- ADH is a vasoconstrictor, hence increases blood pressure; and also increases blood volume.
- **Diabetes insipidus** - imbalance of ADH causing: urine output and intense thirst (some of the symptoms)

4. **The Thyroid Gland**
   - butterfly-shaped thyroid gland is located in the anterior throat
   
   **A. Thyroid Hormone**
   - body's major metabolic hormone
   - two active iodine containing hormones
     - Thyroxine or T₄
     - Triiodothyronine T₃
     - accelerates the rate of cellular metabolism throughout the body; except the adult brain, spleen, testes, uterus and the thyroid gland
     - important regulator of tissue growth and development
     - stimulates enzymes concerned with glucose oxidation. In this way it acts to increase the basal metabolic rate and body heat production; this is known as the hormone’s calorigenic effect.
     - plays an important role in maintaining blood pressure

   **B. Thyrocalcitonin or Calcitonin**
   - produced by the parafollicular cells of the thyroid gland
   - Calcitonin is released in response to increased levels of calcium in the blood.
   - Calcitonin acts on the skeleton (bones) by:
a. inhibiting bone reabsorption and release of ionic calcium from the bone matrix
b. stimulating calcium uptake and incorporation into bone matrix by osteoblasts (bone-forming cells)
c. increasing the excretion of calcium and phosphate ions by the kidneys

5. The Parathyroid Gland
   A. Parathyroid Hormone (PTH) or Parathormone
      • controls the balance of calcium in the blood
      • release by decreasing levels of calcium in the blood and inhibited by the increasing levels of calcium.
      • PTH's target organs:
        o skeleton
        o kidneys
        o intestine
      • action:
        a. release Ca\(^{2+}\) from the bones
        b. enhance Ca\(^{2+}\) reabsorption by the kidney tubules
        c. increase absorption of Ca\(^{2+}\) by intestinal mucosal cells via vitamin D activation

6. The Adrenal Glands:
   A. The Adrenal Cortex
   B. The Adrenal Medulla
   C. The Adrenal Cortex
      1. The Corticosteroids
         0. Mineralocorticosteroids
            • regulate the electrolyte concentration in the extracellular fluid, particularly Na\(^+\) and K\(^+\)
            • Aldosterone
              o accounts for 95% of the mineralocorticoids
- maintains Na\(^+\) balance (excessive Na\(^+\) intake may cause H\(_2\)O retention, thus increasing blood pressure)
- primary target is the distal parts of the kidney tubules
- also regulates K\(^+\), H\(^+\), and Cl\(^-\)
- secretion is stimulated by:
  - K\(^+\) levels
  - ↓ Na\(^+\) levels
  - ↓ in the blood volume and blood pressure

- **Four Mechanism in the regulation of Aldosterone:**
  1. Renin-Angiotensin System
     - major regulator of aldosterone releases, influences both the electrolyte-water balance of the blood and the blood pressure
  2. Plasma concentration of Na\(^+\) and K\(^+\) ions

--- Na\(^+\) and K\(^+\) are stimulatory

3. ACTH (Adrenocortiotropic Hormone)
   - rise in ACTH levels in the blood will effectively step up the secretion of aldosterone release, which will blood volume and blood pressure and ensure adequate supply of nutrients and oxygen during stressful periods.

4. Atrial Natriuretic Factor (ANF)
   - secreted by the heart when blood pressure
   - acts to fine tune blood pressure by modifying the effects of the renin-angiotensin system
   - major effect--inhibitory, it blocks renin and aldosterone
secretion, therefore decreasing blood pressure

1. **Glucocorticoids**
   - influence the metabolism of all cells
   - help with resistance to stressors
   - maintain blood sugar levels
   - maintain blood volume by preventing the shift of H₂O into tissue cells
   - hormones:
     1. Cortisol (Hydrocortisone)
        - cortisol release is promoted by ACTH which is triggered by CRH (hypothalamic releasing hormone)
        - major effect is **gluconogenesis**
        - enhances epinephrine vasoconstrictive effect
     2. Cortisone
     3. Corticosterone
   - regulated by the negative feedback system
   - glucocorticoids levels:
     0. depress cartilage and bone formation
     1. inhibit the inflammatory response by stabilizing lysosomal membranes and preventing vasodilatation
     2. depress the activity of the immune system
     3. promotes changes in the cardiovascular, neural, and gastrointestinal function

2. **Gonadocorticoids (sex hormones or androgens)**
   - amount of sex hormones produced by the adrenal cortex is insignificant compared to the amounts made by the gonads during late puberty and adulthood
   - causes masculinization for the males and virilization for the female

D. **Adrenal Medulla**

   - chromaffin cells are the hormone-producing cells and are directly stimulated by sympathetic preganglionic fibers

   I. two powerful hormones are the **catecholamines**:
      0. epinephrine or adrenaline
      1. norepinephrine or noradrenaline
         - both are similar in structure
         - since norepinephrine is also a neurotransmitter, it is called sympathomimetic amines, in other words, it mimics the effects of the sympathetic nervous system
• the activation of the body's response to "fight-or-flight," which is a short-term stressor or emergence response. The SNS is mobilized by the hypothalamic centers; as a result:
  0. the blood sugar levels rise
  1. heart rate and breathing rates increase
  2. blood is temporarily diverted from the nonessential organs to the brain, heart, and skeletal muscles
  3. at the same time the sympathetic nerve stimulates the adrenal medulla to release the sympathomimetic amines, which reinforce and prolong the stress response

• similarities between epinephrine and norepinephrine:
  0. stimulate the heart
  1. constrict blood vessels within skin and viscera
  2. inhibit visceral muscles
  3. dilate the bronchioles
  4. increase the respiratory rate
  5. promote hyperglycemia
  6. increase the rate of cellular metabolism

• differences between epinephrine and norepinephrine:
  0. epinephrine is more potent stimulator of the heart and metabolic activites
  1. norepinephrine has the greater influence on peripheral vasoconstriction (and blood pressure)

7. The Pancreas
   A. is both endocrine and exocrine gland
   B. acinar cells are enzyme-produced for food digestion
   C. the islets of Langerhans, scattered among the acinar cells, produce the pancreatic hormones. The islets of Langerhans are divided into two types of hormone-producing cells:
     I. glucagon-synthesizing alpha (α) cells
     II. insulin-producing beta (β) cells
     III. somatostatin producing delta (δ) cells, in small amounts (hypothalamus produces it in larger amounts)
   III. Glucagon
      0. hyperglycemic agent
      1. major target is the liver
      2. acts through the cAMP (secondary messenger) to promote:
         • glycogenolysis - conversion of glycogen to glucose
• gluconeogenesis - formation of glucose from fatty acid and amino acid molecules, which the liver releases into the bloodstream

3. secreted by the alpha (α) cell
4. prompted by humoral stimuli

IV. **Insulin**

0. hypoglycemia hormone
1. influences protein and fat metabolism, also enhancing membrane transport of glucose into muscle cells, fat, and other connective tissue
2. mechanism: the only protein hormone that does not use cyclic AMP
3. after entering the target cells:
   • catalyze the oxidation of glucose for ATP production
   • join glucose together to form glycogen
   • converts glucose to fat
4. also induces amino acid uptake and protein synthesis in muscle tissue
5. β (beta) cells are stimulated to secrete insulin in response to increasing blood sugar and increasing levels of amino acid and fatty acids
6. somatostatin depresses insulin release
8. The Gonads
   - gonads produce gonadal sex hormones such as estrogen and progesterone, in females, and testosterone, in males

B. Estrogen
   a. for the maturation of the reproductive organs and the secondary sex characteristics
   b. with progesterone, promotes breast development and cyclic changes in the uterine mucosa
   c. during pregnancy both hormones, estrogen and progesterone, which are produced by the placenta during pregnancy remain high to maintain the pregnancy;

C. Testosterone
   a. produced by the scrotum
   b. initiates maturation of the reproductive organ of the males and the appearance of the secondary sex characteristics and sex drive
   c. is necessary to promote normal sperm production and maintain the reproductive organ in its mature functional state

- the release of gonadal hormones is regulated by Gonadotropins, which are released by the anterior lobe of the pituitary gland