The Endocrine System

Chapter 18

Endocrine versus Nervous system

- The nervous system performs short term crisis management
- The endocrine system regulates long term ongoing metabolic processes
- Endocrine communication is carried out by endocrine cells releasing hormones. Hormones are released in one tissue and travel to specific cells in other tissues
- Paracrine communication involves chemical messengers between cells within one tissue

An Overview

- The endocrine system includes all cells and tissues in the body that produce hormones or paracrine factors
- Endocrine cells are glandular secretory cells that release their secretions into extracellular fluids
- Exocrine cells secrete their products onto epithelial surfaces, generally via ducts

Hormone Structure

- Hormones are divided into three groups based on chemical structure
  - Amino Acid Derivatives: relatively small hormones that are structurally similar to amino acids, AKA biogenic amines
  - Peptide Hormones: Amino acid chains, typically produced as prohormones that are later converted to the active hormone, includes small proteins and glycoproteins
  - Lipid Derivatives: includes steroid hormones; derived from cholesterol, and eicosanoids; derived from arachidonic acid, a fatty acid
Mechanisms of Hormone Action
- To affect a target cell, a hormone must first interact with an appropriate receptor
- The presence or absence of specific receptors dictates a cell’s hormonal sensitivities
- Hormone receptors are found either on the cell membrane or inside the cell

First and Second Messengers
- Any hormone that binds to a cell surface receptor is termed a first messenger
- The first messenger causes the appearance or activation of a second messenger in the cytoplasm
- The second messenger functions inside the cells as an enzyme activator, inhibitor, or cofactor, that will change the rates of various metabolic reactions

First and Second Messengers
- Important second messengers include
  - Cyclic-AMP (cAMP)
  - Cyclic-GMP (cGMP)
  - Calcium ions
- The binding of a small number of hormone molecules may lead to the appearance of thousands of second messengers
- This process, known as amplification, magnifies the effect of the hormone on the cell

First and Second Messengers
- The link between the first and second messenger commonly involves a G-protein
- A G-protein is an enzyme complex coupled to a membrane receptor
- When a hormone binds to the receptor, the G-protein is activated

G Proteins and cAMP
- Many G-proteins, when activated, exert their effects by changing the concentration of the second messenger cAMP
- In most cases, cAMP levels increase, and this accelerates metabolic activity in the cell
- The increase is generally short-lived, because the cytoplasm contains phosphodiesterase (PDE) which convert cAMP into AMP
G-Proteins and Ca\(^{2+}\):

- Activated G-proteins can also trigger either the opening of Ca\(^{2+}\) channels or the release of Ca\(^{2+}\) from intercellular stores.
- The Ca\(^{2+}\) serve as messengers, binding to the protein calmodulin.
- Calmodulin then activates specific cytoplasmic enzymes.

Hormones and Intracellular Receptors:

- Steroid hormones are lipid soluble and diffuse across the cell membrane to bind to receptors within the cell.
- The hormone-receptor complex can then activate or deactivate specific genes, typically by altering rates of transcription, or bind to the mitochondria where it increases rates of ATP production (ex. Thyroid hormone).

Control of Endocrine Activity:

- Endocrine reflexes are the counterparts of neural reflexes.
- They can be triggered by:
  - Humoral stimuli (changes in the extracellular fluid)
  - Hormonal stimuli
  - Neural stimuli
- In most cases hormonal reflexes are controlled by negative feedback.

Control of Endocrine Activity:

- The hypothalamus integrates the activity of the nervous and endocrine systems by:
  - Secreting regulatory hormones that control the anterior pituitary gland
  - Releasing hormones directly into the bloodstream at the posterior pituitary gland
  - Exerting direct neural control over the endocrine cells of the adrenal medulla.
The Pituitary Gland

- The pituitary gland, or hypophysis, is a small, oval gland that lies within the sella turcica, a depression in the sphenoid bone
- It is connected to the hypothalamus by the infundibulum a slender stalk lying between the optic chiasma and mamillary bodies
- The pituitary gland can be divided into a posterior and anterior lobe on the basis of function

The Anterior Lobe

- The anterior lobe of the pituitary, or adenohypophysis, is divided into three regions
  - The pars distalis is most anterior
  - The pars tuberalis wraps around the adjacent portion of the infundibulum
  - The pars intermedia forms a narrow band bordering the posterior lobe
- An extensive capillary network radiates through these regions providing easy access to the circulatory system

The Hypophyseal Portal System

- By secreting regulatory hormones, the hypothalamus controls the production of hormones in the anterior lobe of the pituitary
- These hormones enter the bloodstream easily because the endothelial cells lining the capillaries are unusually permeable
- These capillaries are termed fenestrated capillaries and allow large molecules to readily enter or leave the circulatory system

The Hypophyseal Portal System

- Before leaving the hypothalamus, the capillaries unite into a series of larger vessels that pass through the infundibulum to reach the anterior lobe
- There the vessels form a second capillary bed that branches among the endocrine cells of the anterior pituitary
- Blood vessels that link two capillary networks are termed portal vessels, the entire complex is a portal system, thus this system is the hypophyseal portal system
Hypothalamic control of the anterior lobe

- The hypothalamus releases two classes of regulatory hormones
  - Releasing hormones (RH) stimulate the synthesis and secretion of one or more hormones in the anterior lobe
  - Inhibiting hormones (IH) prevent same
- The rate of release of these regulatory hormones is under negative feedback see 18-8 (figure needs some explanation)

Hormones of the anterior lobe

- Thyroid stimulating hormone (TSH)
  - Triggers the release of thyroid hormones
  - Thyrotropin releasing hormone is the regulatory hormone that promotes the release of TSH
- Adrenocorticotropic hormone (ACTH)
  - Stimulates the release of glucocorticoids by the adrenal gland
  - Corticotrophin releasing hormone is the regulatory hormone that causes the secretion of ACTH

Hormones of the anterior lobe

- Follicle stimulating hormone (FSH)
  - Stimulates follicle development and estrogen secretion in females and sperm production in males
- Leutinizing hormone (LH)
  - Causes ovulation and progestin production in females and androgen production in males
- Gonadotropin releasing hormone (GNRH) is the regulatory hormone that promotes the secretion of FSH and LH
Hormones of the anterior lobe

- Prolactin (PH)
  - Stimulates the development of mammary glands and milk production
- Growth hormone (GH or somatotropin)
  - Stimulates cell growth and replication through release of somatomedins or IGF
  - Growth-hormone releasing hormone (GH-RH)
  - Growth-hormone inhibiting hormone (GH-IH)

Melanocyte stimulating hormone (MSH)

- May be secreted by the pars intermedia during fetal development, early childhood, pregnancy or certain diseases
- Stimulates melanocytes to produce melanin

The Posterior Lobe

- The posterior lobe, neurohypophysis, or pars nervosa, contains the axons of the hypothalamic neurons
- Neurons of the supraoptic and paraventricular nuclei manufacture antidiuretic hormone (ADH) and oxytocin respectively.
- These hormones move along the axons, through the infundibulum and into capillaries of the posterior lobe

Hormones of the Posterior Lobe

- Antidiuretic hormone (ADH) is also known as arginine vasopressin (AVP)
  - The primary function of ADH is to decrease the amount of water lost at the kidneys
  - High concentrations of ADH also cause vasoconstriction and accordingly an increase in blood pressure
  - ADH is inhibited by alcohol
  - Diabetes insipidus is a syndrome characterized by high urine volume and excessive thirst, it often develops due to a decrease in ADH production, and is often treated with a vasopressin nasal spray

Hormones of the Posterior Lobe

- Oxytocin (OT) stimulates contraction of the uterus during childbirth.
- After delivery, oxytocin stimulates the ejection of milk from the breasts
- Sensitivity to oxytocin is low until the last stages of pregnancy, and becomes pronounced as delivery begins
The Thyroid Gland

- The thyroid gland curves across the anterior surface of the trachea just below the thyroid cartilage
- The thyroid gland contains numerous thyroid follicles, which release several hormones such as thyroxine (T4) and triiodothyronine (T3)
- The major factor controlling the rate of release of the thyroid hormones is the concentration of TSH circulating in the blood

Thyroid Hormones

- Thyroid hormones affect almost every cell in the body
- Thyroid hormones bound to cytoplasmic receptors are held in storage and released as intracellular levels of the hormones drop
- Thyroid hormones bound to mitochondrial receptors increase ATP production
- Thyroid hormones bound to nuclear receptors activate genes that are involved in metabolism

C-Cells in the Thyroid

- A second population of endocrine cells lies between the cuboidal follicle cells of the thyroid
- These C-cells or parafollicular cells produce the hormone Calcitonin
- Calcitonin inhibits the action of osteoclasts, thus reducing the rate of calcium release from bone and stimulates the removal of calcium by the kidneys

The Parathyroid Glands

- There are normally two pair of parathyroid glands embedded in the posterior surface of the thyroid
- Parathyroid glands have two populations of cells
  - Chief cells produce parathyroid hormone
  - Oxyphils with no known parathyroid function
- Parathyroid hormone increases blood calcium levels through a variety of mechanisms
- In addition, PTH stimulates the secretion of calcitriol at the kidneys, which complements the action of PTH by increasing absorption of Calcium by the digestive tract
The Adrenal Gland

- The adrenal or suprarenal glands sit on the superior border of each kidney
- The adrenal gland is divided into two parts; the superficial adrenal cortex and the inner adrenal medulla

The Adrenal Cortex

- The adrenal cortex produces more than 2 dozen steroid hormones called adrenocortical steroids or corticosteroids
- Corticosteroids are vital, without corticosteroids we die
- Corticosteroids modify gene transcription and thereby modify cellular metabolism

The Adrenal Cortex

- The adrenal cortex is divided into three regions
- The outer zona glomerulosa produces mineralocorticoids, hormones that affect electrolyte balance, principally aldosterone
- The zona fasciculata lies beneath the zona glomerulosa and secretes steroid hormones called glucocorticoids, principally cortisol which accelerate glucose synthesis and glycogen formation (and read 617 Rt hand column on anti-inflammatory properties)
The Adrenal Cortex

- The zona reticularis is the innermost layer of the adrenal cortex
- The zona reticularis produces small amounts of androgens, the male sex hormone
- Some of these androgens are converted to estrogen in the bloodstream
- Neither affects sex characteristics and the role of adrenal sex hormone production is unclear

The Adrenal Medulla

- The adrenal medulla contains two populations of secretory cells
  - One produces epinephrine (adrenalin)
  - One produces norepinephrine (noradrenaline)
- Evidence suggests that the two cell types can be independently controlled
- The hormones are packaged in vesicles and secreted continuously at low levels by exocytosis, sympathetic stimulation increases the rate of release

Epinephrine and Norepinephrine

- Epinephrine and norepinephrine trigger a mobilization of glycogen reserves and accelerate ATP production in skeletal muscle
- In adipose tissue, fats are broken down into fatty acids which are then released into the bloodstream
- In the liver, glycogen is broken down to glucose and the glucose released into the bloodstream
- In the heart, stimulation of the β1 receptor triggers an increase in heart rate and strength of contraction

The Pineal Gland

- The pineal gland lies in the posterior portion of the roof of the third ventricle of the brain
- Its secretory cells, called pinealocytes, synthesize melatonin from the neurotransmitter serotonin
- Melatonin:
  - Inhibits reproductive function (prevents precocious puberty)
  - Protects against free radical damage
  - Sets circadian rhythms

The Pancreas

- The pancreas lies within the abdominopelvic cavity between the stomach and small intestine
- The exocrine pancreas consists of clusters of gland cells, called pancreatic acini, and secretes large quantities of an alkaline, enzyme rich fluid into the lumen of the digestive tract
- The endocrine pancreas consists of small groups of cells, called pancreatic islets, scattered among the exocrine cells
The Pancreatic Islets

- Alpha cells secrete glucagon which raises blood glucose
- Beta cells secrete insulin which lowers blood glucose
- Delta cells secrete GH-IH, a hypothalamic regulatory hormone, which suppresses the activity of other islet cells
- F cells secrete pancreatic polypeptide, which regulates gallbladder contractions

Endocrine Tissue of Other Systems

- Intestines produce hormones important to the coordination of digestive activities
- The Kidneys produce calcitriol and erythropoietin (EPO) and the enzyme rennin
  - Calcitriol stimulates calcium and phosphate ion absorption along the digestive tract
  - EPO stimulates red blood cell production by bone marrow
  - Renin converts angiotensinogen to angiotensin I
  - Angiotensin I converted to angiotensin II in the lungs

Angiotensin II

- Stimulates adrenal production of aldosterone
- Stimulates the pituitary gland to release ADH
- Promotes thirst
- Elevates blood pressure
- Renin is released in response to sympathetic stimulation or a decline in renal bloodflow
- The renin—angiotensinogen system is a regulator of blood pressure and blood volume
Endocrine Tissue of Other Systems

• The endocrine cells in the heart are cardiac muscle cells in the walls of the atria and ventricles
• When blood volume/blood pressure increases the walls of the heart stretch and these cells release natriuretic peptides, which oppose the actions of angiotensin II to reduce blood volume and pressure

Endocrine Tissue of Other Systems

• The thymus produces thymosins, which help develop and maintain normal immune defenses
• Adipose tissue secretes leptin, a feedback control for appetite, produces a feeling of satiation, and resistin, which reduces insulin sensitivity

The Gonads

• Interstitial cells of the testes produce testosterone, which is responsible for libido and secondary sexual characteristics in males
• In females, oocytes develop in follicles
• Follicular cells produce estrogens when stimulated by FSH and LH
• Estrogens support the maturation of the oocytes and stimulate the uterine lining
• After ovulation, the follicle cells form a corpus luteum that releases a mixture of estrogens and progesterone, which prepare the uterus for implantation

Patterns of Hormonal interaction

• Hormones often interact, producing
  – Antagonistic (opposing) effects
  – Synergistic (additive) effects
  – Permissive effects (one hormone is required for the other to produce its effect)
  – Integrative effects (hormones produce different but complimentary results)

Hormones and Growth

• Normal growth requires the interaction of several endocrine organs
• Six hormones are important
  – GH
  – Thyroid hormones
  – Insulin
  – PTH
  – Calcitriol
  – Reproductive hormones

Hormones and Stress

• Stress is any condition that threatens homeostasis
• GAS (General Adaptation Syndrome) is our body’s response to stress-causing factors
• There are three phases to GAS
  – Alarm phase (immediate, fight or flight, directed by the sympathetic nervous system)
  – Resistance phase (dominated by glucocorticoids)
  – Exhaustion phase (breakdown of homeostatic regulation and failure of one or more organ systems)
Hormones and behavior

- Many hormones affect the CNS
- Changes in the normal mixture of hormones significantly alters intellectual capabilities, memory, learning and emotional states