

CHAPTER 18

LECTURE OUTLINE

I. COMPARISON of CONTROL by the NERVOUS and ENDOCRINE SYSTEM

- A. Together the nervous and endocrine systems coordinate functions of all body systems.
 - 1. The nervous system controls body actions through nerve impulses and neurotransmitters.
 - 2. The endocrine system controls body activities by releasing mediator molecules called hormones.
 - 3. The nervous and endocrine systems act as a coordinated interlocking supersystem, the neuroendocrine system.
 - 4. Parts of the nervous system stimulate or inhibit the release of hormones.
 - 5. Hormones may promote or inhibit the generation of nerve impulses.
- B. The nervous system causes muscles to contract or glands to secrete. The endocrine system affects virtually all body tissues by altering metabolism, regulating growth and development, and influencing reproductive processes.
 - 1. Table 18.1 compares the characteristics of the nervous and endocrine systems.

II. ENDOCRINE GLANDS

- A. The body contains two kinds of glands: exocrine and endocrine.
 - 1. Exocrine glands secrete their products into ducts, and the ducts carry the secretions to the target site.
 - 2. Endocrine glands secrete their products (hormones) into the interstitial fluid surrounding the secretory cells from which they diffuse into capillaries to be carried away by blood.
 - a. Endocrine glands constitute the endocrine system and include the pituitary, thyroid, parathyroid, adrenal, pancreas, kidneys, gastrointestinal organs, and pineal glands (Figure 18.1).

III. HORMONE ACTIVITY

A. The Role of Hormone Receptors

- 1. Although hormones travel in blood throughout the body, they affect only specific target cells.

- a. Target cells have specific protein or glycoprotein receptors to which hormones bind.
2. Receptors are constantly being synthesized and broken down.
 - a. When a hormone is present in excess, down-regulation, the decrease in the number of receptors, may occur.
 - b. When a hormone is deficient, up-regulation, an increase in the number of receptors, may occur.
 - 1) Clinical Connection: Synthetic hormones that block the receptors for particular naturally occurring hormones are available as drugs.

B. Circulating and Local Hormones

1. Hormones that travel in blood and act on distant target cells are called circulating hormones or endocrines.
2. Hormones that act locally without first entering the blood stream are called local hormones.
 - a. Those that act on neighboring cells are called paracrines.
 - b. Those that act on the same cell that secreted them are termed autocrines.
 - c. Figure 18.2 compares the site of action of circulating and local hormones.

C. Chemical Classes of Hormones

1. Table 18.2 provides a summary of the hormones.
2. **Lipid-soluble hormones**
 - a. Lipid-soluble hormones include the steroids, thyroid hormones, and nitric oxide, which acts as a local hormone in several tissues.
3. **Water-Soluble Hormones**
 - a. Water-soluble hormones include the amines; peptides, proteins, and glycoproteins; and eicosanoids.

D. Hormone Transport in the Blood

1. Most water-soluble hormones circulate in plasma in a free, unattached form.
2. Most lipid-soluble hormones bind to transport proteins to be carried in blood.
 - a. The transport proteins improve the transportability of lipid-soluble hormones by making them temporarily water-soluble, retard passage of the small hormone molecules through the kidney filter thus slowing the rate of hormone loss in urine, and provide a ready reserve of hormone already present in blood.

3. Clinical Connection: Protein and peptide hormones, such as insulin, will be destroyed by digestive enzymes and, therefore, must be given by injection.

IV. MECHANISMS OF HORMONE ACTION

- A. The response to a hormone depends on both the hormone and the target cell; various target cells respond differently to different hormones.

B. Action of Lipid-Soluble Hormone

1. Lipid-soluble hormones bind to and activate receptors within cells.
2. The activated receptors then alter gene expression which results in the formation of new proteins.
3. The new proteins alter the cells activity and result in the physiological responses of those hormones.
4. Figure 18.3 shows this mechanism of action.

C. Action of Water-Soluble Hormones

1. Water-soluble hormones alter cell functions by activating plasma membrane receptors,
2. The water-soluble hormone (first messenger) binds to the cell membrane receptor, which set off a cascade of events inside the cell (Figure 18.4).
3. A second messenger is released inside the cell where hormone stimulated response takes place.
4. A typical mechanism of action of a water-soluble hormone using cyclic AMP as the second messenger is seen in Figure 18.4.
 - a. The hormone binds to the membrane receptor.
 - b. The activated receptor activates a membrane G-protein which turns on adenylate cyclase.
 - c. Adenylate cyclase converts ATP into cyclic AMP which activates protein kinases.
 - d. Protein kinases phosphorylate enzymes which catalyze reactions that produce the physiological response.
 - e. Phosphodiesterase inactivates cAMP
5. Since hormones that bond to plasma membrane receptors initiate a cascade of events, they can induce their effects at very low concentrations.

D. Hormonal Interactions

1. The responsiveness of a target cell to a hormone depends on the hormone's concentration, the abundance of the target cell's hormone receptors, and influences exerted by other hormones.
2. Three hormonal interactions are the permissive effect, the synergistic effect, and the antagonist effect.

V. CONTROL OF HORMONE SECRETIONS

A. Most hormones are released in short bursts, with little or no release between bursts. Regulation of hormone secretion normally maintains homeostasis and prevents overproduction or underproduction of a particular hormone; when these regulating mechanisms do not operate properly, disorders result.

B. Hormone secretion is controlled by stimuli that are:

1. signals from the nervous system
2. chemical changes in the blood
3. other hormones.
4. Most often, negative feedback systems regulate hormonal secretions (Figure 1.3)

VI. HYPOTHALAMUS AND PITUITARY GLAND

- A. The hypothalamus is the major integrating link between the nervous and endocrine systems.
- B. The hypothalamus and the pituitary gland (hypophysis) regulate virtually all aspects of growth, development, metabolism, and homeostasis.
- C. The pituitary gland is located in the sella turcica of the sphenoid bone and is differentiated into the anterior pituitary (adenohypophysis), the posterior pituitary (neurohypophysis), and pars intermedia

D. Anterior Pituitary Gland (Adenohypophysis)

1. Hypothalamic Portal System
 - a. The blood supply to the anterior pituitary is from the superior hypophyseal arteries.(Figure 18.5)
2. Types of Anterior Pituitary Cells and Their Hormones
 - a. Hormones of the anterior pituitary and the cells that produce them are as follows (Figure 18.5)
 - 1) Human growth hormone (hGH) is secreted by somatotrophs.
 - 2) Thyroid-stimulating hormone (TSH) is secreted by thyrotrophs.

- 3) Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are secreted by gonadotrophs.
 - 4) Prolactin (PRL) is secreted by lactotrophs.
 - 5) Adrenocorticotrophic hormone (ACTH) and melanocyte-stimulating hormone (MSH) are secreted by corticotrophs.
 - b. The hormones of the anterior pituitary gland are summarized in Table 18.3.
 - c. Secretion of anterior pituitary gland hormones is regulated by hypothalamic regulating hormones and by negative feedback mechanisms (Figure 18.6, Table 18.3).
3. Human Growth Hormone and Insulin-like Growth Factors
 - a. Human growth hormone (hGH) is the most plentiful anterior pituitary hormone.
 - b. It acts indirectly on tissues by promoting the synthesis and secretion of small protein hormones called insulinlike growth factors (IGFs).
 - c. IGFs stimulate general body growth and regulate various aspects of metabolism.
 - d. Various stimuli promote and inhibit hGH production (Figure 18.7).
 - 1) Clinical Connection: One symptom of excess hGH is hyperglycemia.
4. Thyroid-stimulating hormone (TSH) stimulates the production of Thyroid hormones from thyroid gland activities and is controlled by TFH (thyrotropin releasing hormone).
5. Follicle-Stimulating Hormone (FSH)
 - a. In females, FSH initiates follicle development and secretion of estrogens in the ovaries.
 - b. In males, FSH stimulates sperm production in the testes.
6. Luteinizing Hormone (LH)
 - a. In females, LH stimulates secretion of estrogen by ovarian cells to result in ovulation and stimulates formation of the corpus luteum and secretion of progesterone.
 - b. In males, LH stimulates the interstitial cells of the testes to secrete testosterone.
7. Prolactin (PRL), together with other hormones, initiates and maintains milk secretion by the mammary glands.

8. Adrenocorticotrophic hormone (ACTH) controls the production and secretion of hormones called glucocorticoids by the cortex of the adrenal gland.
9. Melanocyte-stimulating hormone (MSH) increases skin pigmentation although its exact role in humans is unknown.
10. Table 18.4 summarizes the principal actions of the anterior pituitary gland hormones.

E. Posterior Pituitary

1. Although the posterior pituitary gland does not synthesize hormones, it does store and release two hormones that are produced by the neurosecretory cells of the hypothalamus.
2. The neural connection between the hypothalamus and the neurohypophysis is via the hypothalamohypophyseal tract (Figure 18.8).
- 3. Control of Secretion by the Posterior Pituitary**
4. Hormones made by the hypothalamus and stored in the posterior pituitary are oxytocin (OT) and antidiuretic hormone (ADH).
 - a. Oxytocin stimulates contraction of the uterus and ejection (let-down) of milk from the breasts.
 - 1) Clinical Connection: Nursing a baby after delivery stimulates oxytocin release promoting uterine contractions and the expulsion of the placenta. Synthetic OT (Pitocin) may be used to induce birth contractions.
 - b. Antidiuretic hormone stimulates water reabsorption by the kidneys and arteriolar constriction.
 - 1) The effect of ADH is to decrease urine volume and conserve body water.
 - 2) ADH is controlled primarily by osmotic pressure of the blood (Figure 18.9).
5. Table 18.5 lists the posterior pituitary gland hormones and summarizes their principal actions and the control of their secretions.

VII. THYROID GLAND

- A. The thyroid gland is located just below the larynx and has right and left lateral lobes (Figure 18.10).

- B. Histologically, the thyroid consists of the thyroid follicles composed of follicular cells, which secrete the thyroid hormones thyroxine (T4) and triiodothyronine (T3), and parafollicular cells, which secrete calcitonin (CT) (Figure 18.10).
- C. Formation, Storage, and Release of Thyroid Hormones
1. Thyroid hormones are synthesized from iodine and tyrosine within a large glycoprotein molecule called thyroglobulin (TGB) and are transported in the blood by plasma proteins, mostly thyroxine-binding globulin (TBG).
 2. The formation, storage, and release steps include iodide trapping, synthesis of thyroglobulin, oxidation of iodide, iodination of tyrosine, coupling of T1 and T2, pinocytosis and digestion of colloid, secretion of thyroid hormones, and transport in blood (Figure 18.11).
- D. Actions of Thyroid Hormones**
1. Thyroid hormones regulate oxygen use and basal metabolic rate, cellular metabolism, and growth and development.
- E. Control of Thyroid Hormone Secretion**
1. Secretion of thyroid hormone is controlled by the level of iodine in the thyroid gland and by negative feedback systems involving both the hypothalamus and the anterior pituitary gland (Figure 18.12).
- F. Calcitonin**
1. Calcitonin inhibit osteoclast activity and, therefore, lowers the blood level of calcium. Secretion is controlled by calcium levels in the blood.
- G. Table 18.6 summarizes the hormones produced by the thyroid gland, their principal actions, and control of secretion.

VIII. PARATHYROID GLANDS

- A. The parathyroid glands are embedded on the posterior surfaces of the lateral lobes of the thyroid and contain principal cells, which produce parathyroid hormone, and oxyphil cells, whose function is unknown (Figure 18.13a).
- B. Parathyroid hormone (PTH) regulates the homeostasis of calcium and phosphate by increasing blood calcium level and decreasing blood phosphate level.
- C. Control of Secretion of Calcitonin and Parathyroid Hormone**
1. PTH increases the number and activity of osteoclasts, increases the rate of Ca^{+2} and Mg^{+2} from reabsorption from urine and inhibits the reabsorption of HPO_4^{-2} so more

is secreted in the urine, and promotes formation of calcitriol, which increases the absorption of Ca^{+2} , Mg^{+2} , and HPO_4^{-2} from the GI tract.

- a. Blood calcium level directly controls the secretion of calcitonin and parathyroid hormone via negative feedback loops that do not involve the pituitary gland (Figure 18.14).

D. Table 18.7 summarizes the principal actions and control of secretion of parathyroid hormone.

IX. ADRENAL GLANDS

A. The adrenal glands are located superior to the kidneys (Figure 18.15); they consist of an outer cortex and an inner medulla.

B. Adrenal Cortex

1. The adrenal cortex is divided into three zones, each of which secretes different hormones (Figure 18.15).
 - a. The zona glomerulosa (outer zone) secretes mineralocorticoids.
 - b. The zona fasciculata (middle zone) secretes glucocorticoids.
 - c. The zona reticularis (inner zone) secretes androgens.
2. Mineralocorticoids
 - a. Mineralocorticoids (e.g., aldosterone) increase sodium and water reabsorption and decrease potassium reabsorption, helping to regulate sodium and potassium levels in the body.
 - 1) Secretion is controlled by the renin-angiotensin pathway (Figure 18.16) and the blood level of potassium.
3. Glucocorticoids
 - a. Glucocorticoids (e.g., cortisol) promote breakdown of proteins, formation of glucose, lipolysis, resistance to stress, anti-inflammatory effects, and depression of the immune response.
 - b. Secretion is controlled by CRH (corticotropin releasing hormone) and ACTH (adrenocorticotropic hormone) from the anterior pituitary (Figure 18.17).
4. Androgens secreted by the adrenal cortex usually have minimal effects in the male but more pronounced effects in the female.
 - a. Clinical Connection: An absence in the ability to produce Cortisol, from birth, causes Congenital Adrenal Hyperplasia, which results in excessive androgens. This disorder has symptoms of virilism, where individual is masculinized

C. Adrenal Medulla

1. The adrenal medulla consists of hormone-producing cells, called chromaffin cells, which surround large blood-filled sinuses (Figure 18.15)
2. Medullary secretions are epinephrine and norepinephrine (NE), which produce effects similar to sympathetic responses.
3. They are released under stress by direct innervation from the autonomic nervous system. Like the glucocorticoids of the adrenal cortex, these hormones help the body resist stress, but do so over a shorter duration.
4. Table 18.8 summarizes the hormones produced by the adrenal glands, the principal actions, and control of secretion.

X. PANCREATIC ISLETS

- A. The pancreas is a flattened organ located posterior and slightly inferior to the stomach and can be classified as both an endocrine and an exocrine gland (Figure 18.18).
- B. Histologically, it consists of pancreatic islets or islets of Langerhans (Figure 18.18) and clusters of cells (acini) (enzyme-producing exocrine cells).
- C. Cell Types in the Pancreatic Islets
 1. Alpha cells secrete the hormone glucagon which increases blood glucose levels.
 2. Beta cells secrete the hormone insulin which decreases blood glucose levels.
 3. Delta cells secrete growth hormone inhibiting hormone or somatostatin, which acts as a paracrine to inhibit the secretion of insulin and glucagon.
 4. F-cells secrete pancreatic polypeptide, which regulates release of pancreatic digestive enzymes.
- D. Regulation of glucagon and insulin secretion is via negative feedback mechanisms (Figure 18.19).
- E. Table 18.9 summarizes the hormones produced by the pancreas, their principal actions, and control of secretion.

XI. OVARIES AND TESTES

- A. Ovaries are located in the pelvic cavity and produce sex hormones (estrogens and progesterone) related to development and maintenance of female sexual characteristics, reproductive cycle, pregnancy, lactation, and normal reproductive functions. The ovaries also produce inhibin and relaxin.

- B. Testes lie inside the scrotum and produce sex hormones (primarily testosterone) related to the development and maintenance of male sexual characteristics and normal reproductive functions. The testes also produce inhibin.
- C. Table 18.10 summarizes the hormones produced by the ovaries and testes and their principal actions.

XII. PINEAL GLAND and Thymus

- A. The pineal gland (epiphysis cerebri) is attached to the roof of the third ventricle, inside the brain (Figure 18.1).
- B. Histologically, it consists of secretory parenchymal cells called pinealocytes, neuroglia cells, and scattered postganglionic sympathetic fibers. The pineal secretes melatonin in a diurnal rhythm linked to the dark-light cycle.
- C. Clinical Connection: Seasonal affective disorder (SAD), a type of depression that arises during the winter months when day length is short, is thought to be due, in part, to over-production of melatonin. Bright light therapy, repeated doses of several hours exposure to artificial light as bright as sunlight, may provide relief for this disorder and for jet lag.

D. The Thymus

- 1. The thymus gland secretes several hormones related to immunity .
- 2. Thymosin, thymic humoral-factor, thymic factor, and thymopoietin promote the proliferation and maturation of T cells, a type of white blood cell involved in immunity.

XIII. OTHER ENDOCRINE TISSUES AND ORGANS, EICOSANOIDS and GROWTH FACTORS

A. Hormones from Other Endocrine Tissues and Organs

- 1. Several body tissues other than those usually classified as endocrine glands also contain endocrine tissue and thus secrete hormones.
- 2. Table 18.11 summarizes these hormones and their actions.

B. Eicosanoids

- 1. Eicosanoids, (prostaglandins [PGs] and leukotrienes [LTs]) act as paracrines and autocrines in most body tissues by altering the production of second messengers, such as cyclic AMP.
- 2. Prostaglandins have a wide range of biological activity in normal physiology and pathology.

3. Aspirin and related nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and acetaminophen, inhibit a key enzyme in prostaglandin synthesis and are used to treat a wide variety of inflammatory disorders. (Clinical Connection)

C. Growth Factors

1. Growth factors are hormones that stimulate cell growth and division.
2. Examples include epidermal growth factor (EGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), nerve growth factor (NGF), tumor angiogenesis factors (TAFs), insulinlike growth factor (IFG), and cytokines.
3. Table 18.12 presents a summary of sources and actions of six important growth factors.

XIV. THE STRESS RESPONSE

A. Homeostatic mechanisms attempt to counteract the everyday stresses of living. If successful, the internal environment maintains normal physiological limits of chemistry, temperature, and pressure. If a stress is extreme, unusual, or long-lasting, however, the normal mechanisms may not be sufficient, triggering a wide-ranging set of bodily changes called the stress response or general adaptation syndrome (GAS).

1. Unlike the homeostatic mechanisms, this syndrome does not maintain a constant internal environment. It does just the opposite to prepare the body to meet an emergency.
2. Productive stress is termed eustress; whereas, harmful stress is termed distress.
3. The stimuli that produce the general adaptation syndrome are called stressors.
4. Stressors include almost any disturbance: heat or cold, surgical operations, poisons, infections, fever, and strong emotional responses.

B. Fight or Flight Response

1. The alarm reaction is initiated by nerve impulses from the hypothalamus to the sympathetic division of the autonomic nervous system and adrenal medulla (Figure 18.20).
2. Responses are the immediate and brief flight-or-flight reactions that increase circulation, promote catabolism for energy production, and decrease nonessential activities.

C. The Resistance Reaction

1. The resistance reaction is initiated by regulating hormones secreted by the hypothalamus (Figure 18.20).

2. The regulating hormones are CRH (corticotropin releasing hormone), GHRH (growth hormone releasing hormone), and TRH (thyrotropin releasing hormone).
3. CRH stimulates the adenohypophysis (anterior pituitary) to increase its secretion of ACTH (adrenocorticotropic hormone), which in turn stimulates the adrenal cortex to secrete hormones.
4. Resistance reactions are long-term and accelerate catabolism to provide energy to counteract stress.
5. Glucocorticoids are produced in high concentrations during stress. They create many distinct physiological effects.

D. Exhaustion

1. The stage of exhaustion results from dramatic changes during alarm and resistance reactions.
2. Exhaustion is caused mainly by loss of potassium, depletion of adrenal glucocorticoids, and weakened organs. If stress is too great, it may lead to death.

E. Stress and Disease

1. It appears that stress can lead to certain diseases.
2. Among stress-related conditions are gastritis, ulcerative colitis, irritable bowel syndrome, peptic ulcers, hypertension, asthma, rheumatoid arthritis, migraine headaches, anxiety, and depression.
3. It has also been shown that people under stress are at a greater risk of developing chronic disease or of dying prematurely.
4. A very important link between stress and immunity is interleukin-1 (IL-1) produced by macrophages; it stimulates secretion of ACTH.
5. Post-traumatic Stress Disease may be related to the stress reaction and its effects on the endocrine system (Clinical Connection).

XV. DEVELOPMENTAL ANATOMY OF THE ENDOCRINE SYSTEM

- A. The pituitary gland originates from two different regions of the ectoderm.
 1. The anterior pituitary derives from the neurohypophyseal bud, located on the floor of the hypothalamus (Figure 18.21).
 2. The anterior pituitary is derived from an outgrowth of ectoderm from the mouth called the hypophyseal (Rathke's) pouch.

- B. The thyroid gland develops as a midventral outgrowth of endoderm, called the thyroid diverticulum, from the floor of the pharynx at the level of the second pair of pharyngeal pouches.
- C. Parathyroid glands develop from endoderm as outgrowths from the third and fourth pharyngeal pouches.
- D. The adrenal cortex is derived from intermediate mesoderm from the same region that produces the gonads. The adrenal medulla is ectodermal in origin and derives from the neural crest, which also gives rise to sympathetic ganglion and other nervous system structures.
- E. The pancreas develops from the outgrowth of endoderm from the part of the foregut that later becomes the duodenum.
- F. The pineal gland arises as an outgrowth between the thalamus and colliculi from ectoderm associated with the diencephalon.
- G. The thymus gland arises from endoderm of the third pharyngeal pouch.

XVI. AGING AND THE ENDOCRINE SYSTEM

- A. Pituitary gland production of hGH decreases with age, but production of gonadotropins and of TSH increases with age. ACTH levels are unchanged with age.
- B. The thyroid gland decreases its output of thyroxin with age.
- C. The thymus gland begins to atrophy at puberty. Adrenal glands produce less cortisol and aldosterone with age.
- D. The pancreas releases insulin more slowly with age, and receptor sensitivity to glucose declines.
- E. Ovaries reduce in size and no longer respond to gonadotropins. Testosterone production decreases with age but does not present a serious problem.

XVII. FOCUS ON HOMEOSTASIS: THE ENDOCRINE SYSTEM

- A. This exhibit examines the role of the endocrine system in maintaining homeostasis

XVIII. DISORDERS: HOMEOSTATIC IMBALANCES

- A. Pituitary Gland Disorders
 - 1. Pituitary Dwarfism, Giantism, and Acromegaly
 - a. Hyposecretion of hGH results in pituitary dwarfism.
 - b. Hypersecretion of hGH during childhood results in giantism and during adulthood results in acromegaly.

2. A disorder associated with dysfunction of the posterior pituitary is diabetes insipidus. Hyposecretion of ADH causes excretion of large amounts of dilute urine and subsequent dehydration and thirst.

B. Thyroid Gland Disorders

1. Hyposecretion of thyroid hormones during fetal life or infancy results in Congenital Hypothyroidism (cretinism).
2. Hypothyroidism during adult years produces myxedema.
3. The most common form of hyperthyroidism is Graves' disease, an autoimmune disease.
4. A goiter is an enlarged thyroid gland.

C. Parathyroid Gland Disorders

1. Hypoparathyroidism results in muscle tetany.
2. Hyperparathyroidism produces osteitis fibrosa cystica.

D. Adrenal Gland Disorders

1. Cushing's syndrome results from a hypersecretion of cortisol by the adrenal cortex.
2. Hyposecretion of glucocorticoids and aldosterone results in Addison's disease.
3. Pheochromocytomas, benign tumors of the adrenal medulla, cause hypersecretion of medullary hormones and a prolonged fight-or-flight response.

E. Pancreatic Disorders

1. Diabetes Mellitus
 - a. This is a group of disorders caused by an inability to produce or use insulin.
 - b. Type I diabetes or insulin-dependent diabetes mellitus is caused by an absolute deficiency of insulin.
 - c. Type II diabetes or insulin-independent diabetes is caused by a down-regulation of insulin receptors.
 - d. Hyperinsulinism results when too much insulin is present and causes hypoglycemia and possibly insulin shock.
2. Figure 18.22 shows photographs of individuals suffering from various endocrine disorders.