Chapter 18: The Endocrine System

I. Intercellular Communication, p. 591

Objectives
1. Explain the importance of intercellular communication and describe the mechanisms involved.
2. Compare the modes of intercellular communication used by the endocrine and nervous systems.
3. Discuss the functional significance of the differences between the two systems.

• The nervous system cannot regulate such long-term processes as growth, development, or reproduction, which involve or affect metabolic activities in virtually every cell and tissue.

• Regulation is provided by the endocrine system, which uses chemical messengers to relay information and instructions between cells.

• Cellular activities are coordinated by the exchange of ions and molecules between adjacent cells across gap junctions. This direct communication occurs between two cells of the same type, and the cells must be in extensive physical contact. The two cells communicate so closely that they function as a single entity. Direct communication is highly specialized and relatively rare.

• Most communication between cells involves the release and receipt of chemical messages. Paracrine communication involves the use of chemical signals to transfer information from cell to cell within a single tissue.

• Endocrine communication is carried out by endocrine cells releasing chemicals called hormones into the bloodstream, which alters the metabolic activities of many tissues and organs simultaneously. Hormones exert their effects by modifying the activities of target cells: specific cells that possess the receptors needed to bind and “read” the hormonal message.

• A hormone may:
  1. stimulate the synthesis of an enzyme or a structural protein not already present in the cytoplasm by activating appropriate genes in the cell nucleus
  2. increase or decrease the rate of synthesis of a particular enzyme or other protein by changing the rate of transcription or translation
  3. turn an existing enzyme or membrane channel “on” or “off” by changing its shape or structure.

• The endocrine system is totally unable to handle situations requiring split-second responses. Crisis management is the job of the nervous system. Synaptic
communication – release of a neurotransmitter at a synapse very close to target cells that bear the appropriate receptors – is ideal for crisis management.

Table 18–1

- The endocrine system and nervous system are similarly organized. Both systems:
  1. rely on the release of chemicals that bind to specific receptors on their target cells.
  2. share many chemical messengers; for example, norepinephrine and epinephrine are called hormones when released into the bloodstream, but neurotransmitters when released across synapses.
  3. are regulated primarily by negative feedback control mechanisms.
  4. share a common goal: to preserve homeostasis by coordinating and regulating the activities of other cells, tissues, organs, and systems.

II. An Overview of the Endocrine System, p. 593

Objectives
  1. Compare the cellular components of the endocrine system with those of other tissues and systems.
  2. Compare the major structural classes of hormones.
  3. Explain the general mechanisms of hormonal action.
  4. Describe how endocrine organs are controlled.

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

Figure 18–1

Classes of Hormones, p. 593

- Hormones can be divided into three groups: amino acid derivatives; peptide hormones; and lipid derivatives.

Figure 18–2

Amino Acid Derivatives, p. 595

- Amino acid derivatives are relatively small molecules that are structurally related to amino acids. This group of hormones, sometimes known as the biogenic amines, is synthesized from the amino acids tyrosine and tryptophan.
Tyrosine derivatives include:
1. thyroid hormones (produced by the thyroid gland)
2. compounds epinephrine (E), norepinephrine (NE), and dopamine, which are sometimes called catecholamines.

The primary hormone derivative of tryptophan is melatonin, produced by the pineal gland.

*Peptide Hormones, p. 595*

- Peptide hormones are chains of amino acids. They are synthesized as prohormones—inactive molecules that are converted to active hormones either before or after they are secreted.

- Peptide hormones are divided into two groups:
  1. Group 1: Glycoproteins – more than 200 amino acids long, with carbohydrate side chains. Glycoproteins include: thyroid-stimulating hormone (TSH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) from the anterior lobe of the pituitary gland, as well as several hormones produced in other organs.
  2. Group 2: large and diverse, including hormones from short polypeptide chains, such as antidiuretic hormone (ADH) and oxytocin, to small proteins such as growth hormone (GH) and prolactin (PRL). This group includes all the hormones secreted by the hypothalamus, heart, thymus, digestive tract, pancreas, and posterior lobe of the pituitary gland, as well as most of the hormones secreted by the anterior lobe of the pituitary gland.

*Lipid Derivatives, p. 595*

- There are two classes of lipid derivatives:
  1. Eicosanoids: derived from arachidonic acid
  2. Steroid hormones: derived from cholesterol

- Eicosanoids are small molecules with a five-carbon ring at one end. These compounds are important paracrine factors that coordinate cellular activities and affect enzymatic processes in extracellular fluids.

- Leukotrienes are eicosanoids released by activated white blood cells, or leukocytes. Leukotrienes are important in coordinating tissue responses to injury or disease.

- Prostaglandins, a second group of eicosanoids, are produced in most tissues of the body. Prostaglandins are involved primarily in coordinating local cellular
activities. In some tissues, prostaglandins are converted to thromboxanes and prostacyclins, which also have strong paracrine effects.

- **Steroid hormones** are lipids structurally similar to cholesterol. They are released by male and female reproductive organs (androgens by the testes, estrogens and progestins by the ovaries), the adrenal glands (corticosteroids), and the kidneys (calcitriol).

- In the blood, steroid hormones are bound to specific transport proteins in the plasma. They remain in circulation longer than do secreted peptide hormones. The liver gradually absorbs these steroids and converts them to a soluble form that can be excreted in the bile or urine.

*Secretion and Distribution of Hormones, p. 595*

- Hormones may circulate freely, or bound to transport proteins.

- Free hormones remain functional for less than one hour. A free hormone is inactivated when:
  1. it diffuses out of the bloodstream and binds to receptors on target cells
  2. it is absorbed and broken down by cells of the liver or kidneys
  3. it is broken down by enzymes in the plasma or interstitial fluids

- Thyroid hormones and steroid hormones remain in circulation much longer because, when they enter the bloodstream, more than 99% become attached to special transport proteins.

- At any given time, the bloodstream contains a substantial reserve of bound hormones.

*Mechanisms of Hormone Action, p. 595*

- A hormone receptor is a protein molecule to which a particular molecule binds strongly. Each cell has receptors for responding to several different hormones, but cells in different tissues have different combinations of receptors. For every cell, the presence or absence of a specific receptor determines the cells hormonal sensitivities.

- Hormone receptors are located either on the cell membrane or inside the cell.

*Hormones and Cell Membrane Receptors, p. 596*

- Receptors for catecholamines (E, NE, and dopamine), peptide hormones, and eicosanoids are in the cell membranes of target cells. Catecholamines and peptide hormones are not lipid soluble; they are unable to penetrate a cell membrane. Instead, these hormones bind to receptor proteins at the outer surface of the cell
membrane (extracellular receptors). Eicosanoids are lipid soluble and diffuse across the membrane to reach receptor proteins on the inner surface of the membrane (intracellular receptors).

- A hormone that binds to receptors in the cell membrane cannot have a direct effect on the activities under way inside the target cell. The hormone uses an intracellular intermediary to exert its effects. The hormone, or first messenger, does something that leads to the appearance of a second messenger in the cytoplasm. The second messenger may act as an enzyme activator, inhibitor, or cofactor. The result is a change in the rates of various metabolic reactions.

- The most important second messengers are:
  1. cyclic-AMP (cAMP), a derivative of ATP
  2. cyclic-GMP (cGMP), a derivative of GTP
  3. calcium ions

- The binding of a small number of hormone molecules to membrane receptors may lead to the appearance of thousands of second messengers in a cell. This amplification magnifies the effect of a hormone on the target cell.

- The arrival of a single hormone may promote the release of more than one type of second messenger, or a receptor cascade: the production of a linked sequence of enzymatic reactions.

- Down-regulation occurs when the presence of a hormone triggers a decrease in the number of hormone receptors. When levels of a particular hormone are high, cells become less sensitive to it.

- Up-regulation occurs when the absence of a hormone triggers an increase in the number of hormone receptors. When levels of a particular hormone are low, cells become more sensitive to it.

- A link between the first messenger and the second messenger generally involves a G protein, an enzyme complex coupled to a membrane receptor. These proteins bind GTP. A G protein is activated when a hormone binds to its receptor at the membrane surface.

**Figure 18-3 (left panel)**

- Many G proteins, once activated, exert their effects by changing the concentration of second messenger cyclic-AMP (cAMP) within the cell. In most cases the result is an increase in cAMP levels. This accelerates metabolic activity within the cell.
  1. The activated G protein activates the enzyme adenylate cyclase.
  2. Adenylate cyclase converts ATP to the ring-shaped molecule cyclic-AMP.
3. Cyclic-AMP then functions as a second messenger, typically by activating kinase: an enzyme that performs phosphorylation, the attachment of a high-energy phosphate group to another molecule.
4. Generally, the kinase is activated by cyclic-AMP phosphorylate proteins. The effect on the target cell depends on the nature of the proteins affected.

- The hormones calcitonin, parathyroid hormone, ADH, ACTH, epinephrine, FSH, LH, TSH, and glucagon all produce their effects by this mechanism. The increase is usually short-lived, because the cytoplasm contains another enzyme, phosphodiesterase (PDE), which inactivates cyclic-AMP by converting it to AMP.

**Figure 18-3 (center panel)**

- The activation of G proteins can also lower the concentration of cAMP within the cell. The activated G protein stimulates PDE activity and inhibits adenylate cyclase activity. Levels of cAMP then decline, because cAMP breakdown accelerates while cAMP synthesis is prevented.

**Figure 18-3 (right panel)**

- An activated G protein can trigger either the opening of calcium ion channels in the membrane or the release of calcium ions from intracellular stores.
  1. The G protein first activates the enzyme phospholipase C (PLC).
  2. This enzyme triggers a receptor cascade that begins with the production of diacylglycerol (DAG) and inositol triphosphate (IP\(_3\)) from membrane phospholipids. The cascade then proceeds as follows:
    - IP\(_3\) diffuses into the cytoplasm and triggers the release of Ca\(^{2+}\) from intracellular reserves, such as those in the smooth endoplasmic reticulum of many cells.
    - The combination of DAG and intracellular calcium ions activates another membrane protein: protein kinase C (PKC). The activation of PKC leads to the phosphorylation of calcium channel proteins, a process that opens the channels and permits the entry of extracellular Ca\(^{2+}\).
    - The calcium ions themselves serve as messengers, generally in combination with an intracellular protein called calmodulin, which can activate specific cytoplasmic enzymes.

*Hormones and Intracellular Receptors*, p. 598

- Steroid hormones cross the cell membrane and bind to receptors in the cytoplasm or nucleus, activating or inactivating specific genes.

**Figure 18–4a**
• Steroid hormones can alter the rate of DNA transcription in the nucleus and change the patterns of protein synthesis. Alterations in the synthesis of enzymes or structural proteins will directly affect both the metabolic activity and the structure of the target cell.

• Thyroid hormones cross the cell membrane primarily by a transport mechanism. Once in the cytosol, these hormones bind to receptors within the nucleus and on mitochondria, activating specific genes or changing the rate of transcription.

Figure 18–4b

Key
- **Hormones coordinate cell, tissue, and organ activities on a sustained basis.**
- **They circulate in the extracellular fluid and bind to specific receptors on or in target cells.**
- **They then modify cellular activities by altering membrane permeability, activating or inactivating key enzymes, or changing genetic activity.**

Control of Endocrine Activity, p. 599

- **Endocrine reflexes** are the functional counterparts of neural reflexes.

Endocrine Reflexes, p. 599

- Endocrine reflexes can be triggered by:
  1. **humoral stimuli:** changes in the composition of the extracellular fluid
  2. **hormonal stimuli:** the arrival or removal of a specific hormone
  3. **neural stimuli:** the arrival of neurotransmitters at neuroglandular junctions

- In most cases, endocrine reflexes are controlled by negative feedback mechanisms.

- A simple endocrine reflex involves only one hormone. This type of reflex controls hormone secretion by the heart, pancreas, parathyroid gland, and digestive tract.

- More complex endocrine reflexes involve one or more intermediary steps and two or more hormones. The hypothalamus, which provides the highest level of endocrine control, integrates the activities of the nervous and endocrine systems in three ways.

Figure 18–5

1. The hypothalamus secretes **regulatory hormones**, special hormones that control endocrine cells in the pituitary gland. The hypothalamic regulatory hormones control the secretory activities of endocrine cells in the anterior lobe of the pituitary gland, which control the activities of endocrine cells in the thyroid, adrenal cortex, and reproductive organs.
2. The hypothalamus itself acts as an endocrine organ. Hypothalamic neurons synthesize hormones, transport them along axons within the infundibulum, and release them into the circulation at the posterior lobe of the pituitary gland.
3. The hypothalamus contains autonomic centers that exert direct neural control over the endocrine cells of the adrenal medullae. When the sympathetic division is activated, the adrenal medullae release hormones into the bloodstream.

- The hypothalamus secretes regulatory hormones and ADH in response to changes in the composition of the circulating blood. Pathways called neuroendocrine reflexes include both neural and endocrine components.
- In the endocrine system, complex commands are issued by changing the amount of hormone secreted and the pattern of hormone release. The relationship between hormone concentration and target cell response is not always predictable.
- Several hypothalamic and pituitary hormones are released in sudden bursts called pulses, rather than continuously. When hormones arrive in pulses, target cells may vary their response with the frequency of the pulses.
- The most complicated hormonal instructions issued by the hypothalamus involve changes in the frequency of pulses and in the amount secreted in each pulse.

III. The Pituitary Gland, p. 600

Objectives
1. Describe the location and structure of the pituitary gland and explain its structural and functional relationships with the hypothalamus.
2. Identify the hormones produced by the anterior and posterior lobes of the pituitary gland and specify the functions of those hormones.
3. Discuss the results of abnormal levels of pituitary hormone production.

- The pituitary gland, or hypophysis, lies within the sella turcica. It hangs inferior to the hypothalamus, connected by the infundibulum. The diaphragma sellae locks the pituitary gland in position and isolates it from the cranial cavity.

Figure 18-6
- The pituitary gland releases nine important peptide hormones; all bind to membrane receptors and use cyclic-AMP as a second messenger.

The Anterior Lobe, p. 601
- The anterior lobe (adenohypophysis) of the pituitary gland can be subdivided into the pars distalis, the pars intermedia, and the pars tuberalis.
Figure 18–6

*The Hypophyseal Portal System, p. 601*

- At the **median eminence** of the hypothalamus, neurons release regulatory factors into the surrounding interstitial fluids **fenestrated capillaries**.

- The capillary networks in the median eminence are supplied by the **superior hypophyseal artery**.

Figure 18–7

- The vascular arrangement is unusual. The vessels between the median eminence and the anterior lobe carry blood from one capillary network to another. Blood vessels that link two capillary networks are **portal vessels**, which are named for their destinations; the entire complex is a **portal system**.

- The **hypophyseal portal system** ensures that these regulatory factors reach the intended target cells before they enter the general circulation.

*Hypothalamic Control of the Anterior Lobe, p. 602*

- There are two classes of hypothalamic regulatory hormones: **releasing hormones** and **inhibiting hormones**.

- **Releasing hormones** (RH) stimulate the synthesis and secretion of one or more hormones at the anterior lobe.

- **Inhibiting hormones** (IH) prevent the synthesis and secretion of hormones from the anterior lobe.

- The rate at which the hypothalamus secretes regulatory hormones is controlled by negative feedback.

Figure 18–8

*Hormones of the Anterior Lobe, p. 602*

- The **pars distalis** produces six hormones: four regulate the production of hormones by other endocrine glands. The anterior lobe produces hormones that “turn on” endocrine glands or support the functions of other organs.

Figure 18–8a

- **Thyroid-stimulating hormone** (TSH) (thryotropin) triggers the release of thyroid hormones. **Thyrotropin-releasing hormone** (TRH) promotes the secretion of TSH.

- **Adrenocorticotropic hormone** (ACTH) (corticotropin) stimulates the release of steroid hormones by the adrenal cortex. ACTH specifically targets cells that
produce glucocorticoids, hormones that affect glucose metabolism. Corticotropin-releasing hormone (CRH) causes the secretion of ACTH.

- **Gonadotropins** regulate the activities of the **gonads** (testes and ovaries). An abnormally low production of gonadotropins produces hypogonadism. Children with hypogonadism will not undergo sexual maturation; adults cannot produce functional sperm or oocytes. The two gonadotropins are follicle-stimulating hormone and luteinizing hormone.

- **Follicle-stimulating hormone (FSH)** (follitropin) stimulates follicle development and **estrogen** secretion in females. Estradiol is the most important estrogen. In males, FSH stimulates sustentacular cells, which promotes the physical maturation of sperm. FSH production is inhibited by inhibin, a peptide hormone released by cells in the testes and ovaries.

- **Luteinizing hormone (LH)** (lutropin) causes ovulation and progestin production in females, and **androgen** production in males. The most important androgen is testosterone. In males, LH is sometimes called interstitial cell-stimulating hormone (ICSH).

- FSH and LH production is stimulated by **gonadotropin-releasing hormone** (GnRH) from the hypothalamus. GnRH production is inhibited by estrogens, progestins, and androgens.

- **Prolactin (PRL)** (mammotropin), together with other hormones, stimulates both the development of the mammary glands and milk production. Prolactin production is inhibited by prolactin-inhibiting hormone (PIH) – the neurotransmitter dopamine. Circulating PRL stimulates PIH release and inhibits the secretion of prolactin-releasing factors (PRF).

*Figure 18-8b*

- **Growth hormone (GH)**, or somatotropin, stimulates cell growth and replication by accelerating the rate of protein synthesis. Skeletal muscle cells and chondrocytes (cartilage cells) are particularly sensitive to GH. Liver cells respond to the presence of GH by synthesizing and releasing somatomedins or insulin-like growth factors (IGFs).

- The direct actions of GH tend not to appear until after blood glucose and amino acid concentrations have returned to normal levels:
  1. In epithelia and connective tissues GH stimulates stem cell divisions and the differentiation of daughter cells. The growth of these daughter cells will be stimulated by somatomedins.
  2. In adipose tissue GH stimulates the breakdown of stored triglycerides by fat cells, which then release fatty acids into the blood. As circulating fatty acid levels rise, many tissues stop breaking down glucose and start breaking down fatty acids to generate ATP: glucose-sparing effect.
3. In the liver, GH stimulates the breakdown of glycogen reserves by liver cells, which then release glucose into the bloodstream. Blood glucose concentrations begin to climb: diabetogenic effect.

- The production of GH is regulated by growth hormone–releasing hormone (GH–RH) (somatocrinin) and growth hormone–inhibiting hormone (GH–IH) (somatostatin) from the hypothalamus.

- Melanocyte-stimulating hormone (MSH) (melanotropin) may be secreted by the pars intermedia during fetal development, early childhood, pregnancy, or certain diseases. This hormone stimulates melanocytes to produce melanin but its function in normal adults is not known. The release of MSH is inhibited by dopamine.

**Key:**
- The hypothalamus produces regulatory factors that adjust the activities of the anterior lobe of the pituitary gland, which produces seven hormones.
- Most of these hormones control other endocrine organs, including the thyroid gland, adrenal gland, and gonads.
- The anterior lobe also produces growth hormone, which stimulates cell growth and protein synthesis.
- The posterior lobe of the pituitary gland releases two hormones produced in the hypothalamus; ADH restricts water loss and promotes thirst, and oxytocin stimulates smooth muscle contractions in the mammary glands and uterus (in females) and the prostate gland (in males).

**The Posterior Lobe, p. 604**

- The posterior lobe (neurohypophysis) of the pituitary gland contains the unmyelinated axons of hypothalamic neurons. Neurons of the supraoptic and paraventricular nuclei manufacture antidiuretic hormone (ADH) and oxytocin, respectively.

**Antidiuretic Hormone, p. 605**

- Antidiuretic hormone (ADH) decreases the amount of water lost at the kidneys and, in higher concentrations, elevates blood pressure. ADH release is inhibited by alcohol.

**Oxytocin, p. 605**

- In women, oxytocin (OT) stimulates contractile cells in the mammary glands and has a stimulatory effect on smooth muscles in the uterus. Oxytocin secretion and milk ejection are part of a neuroendocrine reflex.

**Summary: The Hormones of the Pituitary Gland, p. 605**
Objectives

1. Describe the location and structure of the thyroid gland.
2. Identify the hormones produced by the thyroid gland, specify the functions of those hormones, and discuss the results of abnormal levels of thyroid hormones.

- The thyroid gland lies anterior to the thyroid cartilage of the larynx and consists of two lobes connected by a narrow isthmus.

Thyroid Follicles and Thyroid Hormones, p. 606

- The thyroid gland contains numerous thyroid follicles: hollow spheres lined by a simple cuboidal epithelium. The follicle cells surround a follicle cavity that holds a viscous colloid: a fluid containing large quantities of dissolved proteins. A network of capillaries surrounds each follicle, delivering nutrients and regulatory hormones and accepting their secretory products and metabolic wastes.

- Follicle cells synthesize thyroglobulin, a globular protein, and secrete it into the colloid of the thyroid follicles. Thyroglobulin molecules contain the amino acid tyrosine.

The formation of thyroid hormones involves the following basic steps:

- The major factor controlling the rate of thyroid hormone release is the concentration of TSH in the circulating blood.
Figure 18-11b

- Under the influence of TSH, the following steps occur:

Figure 18-11a

1. Follicle cells remove thyroglobulin from the follicles by endocytosis.
2. Lysosomal enzymes break the thyroglobulin down, and the amino acids and thyroid hormones enter the cytoplasm. The amino acids are then recycled and used to synthesize more thyroglobulin.
3. The released molecules of T3 and T4 diffuse across the basement membrane and enter the bloodstream.
4. Most T3 and T4 molecules entering the bloodstream become attached to transport proteins called thyroid-binding globulins (TBGs). Most of the rest of the T3 and T4 in the circulation is attached to transthyretin (thyroid-binding prealbumin - TBPA) or to albumin, one of the plasma proteins. Only the small quantities of thyroid hormones that remain unbound are free to diffuse into peripheral tissues.

- When unbound thyroid hormones diffuse out of the bloodstream and into other tissues, the equilibrium is disturbed. The carrier proteins then release additional thyroid hormones until a new equilibrium is reached. The bloodstream normally contains more than a week’s supply of thyroid hormones.

- In the absence of TSH, the thyroid follicles become inactive, and neither synthesis nor secretion occurs. TSH binds to membrane receptors and activates key enzymes involved in thyroid hormone production.

Figure 18-3

Functions of Thyroid Hormones, p. 610

- Thyroid hormones enter target cells by means of an energy dependent transport system, and they affect almost every cell in the body.

- Thyroid hormones bound to cytoplasmic receptors are held in storage until intracellular levels of thyroid hormone decline. Thyroid hormones bound to mitochondria increase ATP production. Thyroid hormones bound to receptors in the nucleus activate genes that control energy utilization.

- The calorigenic effect: the cell consumes more energy resulting in increased heat generation.

- In growing children, thyroid hormones are essential to normal development of the skeletal, muscular, and nervous systems.

- The thyroid gland is primarily responsible for a strong, immediate, and short-lived increase in the rate of cellular metabolism.

Table 18–3
Iodine and Thyroid Hormones, p. 610

- Iodide ions are actively transported into the thyroid follicle cells. The thyroid follicles contain most of the iodide reserves in the body. The active transport mechanism for iodide is stimulated by TSH. The resulting increase in the rate of iodide movement into the cytoplasm accelerates the formation of thyroid hormones. Excess iodine is removed from the blood at the kidneys; a small amount is excreted by the liver into the bile.

The C Cells of the Thyroid Gland and Calcitonin, p. 610

- The C (clear) cells of the thyroid follicles produce calcitonin (CT), which helps regulate concentrations of Ca$^{2+}$ in body fluids, especially during childhood (when it stimulates bone growth and mineral deposition in the skeleton) and pregnancy (to reduce the loss of bone mass).

V. The Parathyroid Glands, p. 611

Objective

1. Describe the location of the parathyroid glands, the functions of the hormone they produce, and the effects of abnormal levels of parathyroid hormone production.

- Four parathyroid glands are embedded in the posterior surface of the thyroid gland. The chief cells produce parathyroid hormone (PTH) in response to lower-than-normal concentrations of Ca$^{2+}$.

Figure 18–12

- Parathyroid hormone has four major effects:
  1. It stimulates osteoclasts, accelerating mineral turnover and the release of Ca$^{2+}$ from bone.
  2. It inhibits osteoblasts, reducing the rate of calcium deposition in bone.
  3. It enhances the reabsorption of Ca$^{2+}$ at the kidneys, reducing urinary losses.
  4. It stimulates the formation and secretion of calcitriol at the kidneys. The effects of calcitriol complement or enhance those of PTH, but one major effect of calcitriol is the enhancement of Ca$^{2+}$ and PO$_4^{3-}$ absorption by the digestive tract.

- The parathyroid glands, aided by calcitriol, are the primary regulators of blood calcium I levels in healthy adults.

Figure 18–13

Table 18–4
Key
- The thyroid gland produces (1) hormones that adjust tissue metabolic rates and (2) a hormone that usually plays a minor role in calcium ion homeostasis by opposing the action of parathyroid hormone.

VI. The Adrenal Glands, p. 613

Objectives
1. Describe the location, structure, and general functions of the adrenal glands.
2. Identify the hormones produced by the adrenal cortex and medulla and specify the functions of each hormone.
3. Discuss the results of abnormal levels of adrenal hormone production.

- One adrenal (suprarenal) gland lies along the superior border of each kidney. The gland is subdivided into the superficial adrenal cortex and the inner adrenal medulla.

Figure 18–14a, b

The Adrenal Cortex, p. 613

- The adrenal cortex stores lipids, especially cholesterol and various fatty acids. The adrenal cortex manufactures steroid hormones called adrenocortical steroids (corticosteroids). Corticosteroids are vital: if the adrenal glands are destroyed or removed, the individual will die unless corticosteroids are administered.

- The cortex can be subdivided into three regions which synthesize specific steroid hormones: (1) the zona glomerulosa, (2) the zona fasciculata, and (3) the zona reticularis.

Figure 18–14c

Table 18–5

The Zona Glomerulosa, p. 613

- The outer region of the adrenal cortex, the zona glomerulosa, produces mineralocorticoids: steroid hormones that affect the electrolyte composition of body fluids. Aldosterone is the principal mineralocorticoid produced by the adrenal cortex.

Figure 18-14c

- Aldosterone secretion stimulates the conservation of sodium ions and the elimination of potassium ions. It causes the retention of sodium ions at the kidneys, sweat glands, salivary glands, and pancreas, preventing Na⁺ loss in urine, sweat, saliva, and digestive secretions. Aldosterone increases the sensitivity of salt receptors in the taste buds of the tongue. Aldosterone secretion occurs in response to a drop in blood Na⁺ content, blood volume, or blood pressure, or to a rise in blood K⁺ concentration.
The Zona Fasciculata, p. 615

- The zona fasciculata produces steroid hormones collectively known as glucocorticoids. The endocrine cells are larger and contain more lipids than those of the zona glomerulosa, and the lipid droplets give the cytoplasm a pale, foamy appearance.

Figure 18-14c

- When stimulated by ACTH from the anterior lobe of the pituitary, the zona fasciculata secretes primarily cortisol (hydrocortisone) along with smaller amounts of the related steroid corticosterone. The liver converts some of the cortisol to cortisone.

- Glucocorticoid secretion is regulated by negative feedback: the glucocorticoids released have an inhibitory effect on the production of corticotropin-releasing hormone (CRH) in the hypothalamus, and of ACTH in the anterior lobe.

Figure 18-8a

- Glucocorticoids accelerate the rate of glucose synthesis and glycogen formation, especially in the liver. Adipose tissue responds by releasing fatty acids into the blood, and other tissues begin to break down fatty acids and proteins instead of glucose.

- Glucocorticoids show anti-inflammatory effects: they inhibit the activities of white blood cells and other components of the immune system.

The Zona Reticularis, p. 615

- The zona reticularis forms a narrow band bordering each adrenal medulla. The endocrine cells of the zona reticularis form a folded, branching network, and fenestrated blood vessels wind among the cells.

Figure 18-14c

- The zona reticularis normally produces small quantities of androgens under stimulation by ACTH. In the bloodstream, some of the androgens are converted to estrogens. Adrenal androgens stimulate the development of pubic hair and, in adult women, promote muscle mass, blood cell formation, and support libido.

The Adrenal Medulla, p. 615

- The secretory activities of the adrenal medullae are controlled by the sympathetic division of the autonomic nervous system.

- The adrenal medulla produces epinephrine (adrenaline) and norepinephrine.
• Activation of the adrenal medullae has the following effects:
  1. In skeletal muscles, epinephrine and norepinephrine trigger a mobilization of glycogen reserves and accelerate the breakdown of glucose to provide ATP. This combination increases both muscular strength and endurance.
  2. In adipose tissue, stored fats are broken down into fatty acids, which are released into the bloodstream for use by other tissues for ATP production.
  3. In the liver, glycogen molecules are broken down. The resulting glucose molecules are released into the bloodstream, primarily for use by neural tissues, which cannot shift to fatty acid metabolism.
  4. In the heart, the stimulation of $\beta_1$ receptors triggers an increase in the rate and force of cardiac muscle contraction.

• The metabolic changes that follow the release of catecholamines such as E and NE are at their peak 30 seconds after adrenal stimulation, and they persist for several minutes.

**Key**

- The adrenal glands produce hormones that adjust metabolic activities at specific sites, affecting either the pattern of nutrient utilization, mineral ion balance, or the rate of energy consumption by active tissues.

**VII. The Pineal Gland, p. 616**

**Objective**

1. Describe the location of the pineal gland and the functions of the hormone that it produces.

• The pineal gland lies in the posterior portion of the roof of the third ventricle. It contains pinealocytes, which synthesize the hormone melatonin.

• Suggested functions include inhibiting reproductive functions, protecting against damage by free radicals, and setting circadian rhythms.

**VIII. The Pancreas, p. 616**

**Objectives**

1. Describe the location and structure of the pancreas.
2. Identify the hormones produced by the pancreas, and specify the functions of those hormones.
3. Discuss the results of abnormal levels of pancreatic hormone production.

• The pancreas lies in the loop formed between the inferior border of the stomach and the proximal portion of the small intestine. It has a lumpy consistency.

*Figures 18-1, 18-15a*
The pancreas contains both exocrine and endocrine cells. Cells of the endocrine pancreas form clusters called pancreatic islets (islets of Langerhans).

**Figure 18–15**

*The Pancreatic Islets, p. 617*

- The pancreatic islets are surrounded by a fenestrated capillary network that carries pancreatic hormones into the bloodstream.

- Each islet contains four types of cells:
  1. **Alpha cells** produce glucagon
  2. **Beta cells** secrete insulin
  3. **Delta cells** produce a peptide hormone identical to growth hormone-inhibiting hormone (GH-IH)
  4. **F cells** secrete pancreatic polypeptide (PP)

**Figure 18–16**

- When blood glucose levels rise, beta cells secrete insulin, which then stimulates the transport of glucose across cell membranes. When blood glucose levels decline, alpha cells secrete glucagons, which stimulates glucose release by the liver.

*Insulin, p. 617*

- **Insulin** is a peptide hormone released by beta cells when glucose concentrations exceed normal levels.

- Insulin receptors are present in most cell membranes, these cells are called insulin dependent. Insulin independent cells (in the brain, kidneys, lining of the digestive tract, and red blood cells) can absorb and utilize glucose without insulin stimulation.

- Insulin effects on its target cells include:
  1. acceleration of glucose uptake
  2. acceleration of glucose utilization and enhanced ATP production
  3. stimulation of glycogen formation (skeletal muscles and liver cells)
  4. stimulation of amino acid absorption and protein synthesis
  5. stimulation of triglyceride formation in adipose tissue

- Insulin is secreted when glucose is abundant; the hormone stimulates glucose utilization to support growth and the establishment of carbohydrate (glycogen) and lipid (triglyceride) reserves. The accelerated use of glucose soon brings circulating glucose to normal limits.

*Glucagon, p. 619*
• When glucose concentrations fall below normal, alpha cells release glucagons and energy reserves are mobilized.

• The primary effects of glucagons are:
  1. stimulates the breakdown of glycogen in skeletal muscle and liver cells
  2. stimulates the breakdown of triglycerides in adipose tissue
  3. stimulates the production of glucose in the liver

• Pancreatic alpha cells and beta cells monitor blood glucose concentrations, and the secretion of glucagons and insulin occur without endocrine or nervous instructions.

• Any hormone that affects blood glucose concentrations will indirectly affect the production of both insulin and glucagon.

**Table 18-6**

**Key**

- The pancreatic islets release insulin and glucagons.
- Insulin is released when blood glucose levels rise, and it stimulates glucose transport into, and utilization by, peripheral tissues.
- Glucagon is released when blood glucose levels decline, and it stimulates glycogen breakdown, glucose synthesis, and fatty acid release.

IX. The Endocrine Tissues of Other Systems, p. 620

**Objective**

1. Describe the functions of the hormones produced by the kidneys, heart, thymus, testes, ovaries, and adipose tissue.

**Table 18-7**

*The Intestines*, p. 621

• The intestines produce hormones important to the coordination of digestive activities.

*The Kidneys*, p. 621

• Endocrine cells in the kidneys produce the hormones **calcitriol** and **erythropoietin** and the enzyme **renin**.

*Calcitriol*, p. 621
• **Calcitriol** stimulates calcium and phosphate ion absorption along the digestive tract.

*Figure 18–17a*

• Calcitriol’s other effects on calcium metabolism include:
  1. stimulating the formation and differentiation of osteoprogenitor cells and osteoclasts
  2. stimulating bone resorption by osteoclasts
  3. stimulating Ca\(^{2+}\) reabsorption at the kidneys
  4. suppressing parathyroid hormone (PTH) production

*Erythropoietin*, p. 621

• **Erythropoietin** (EPO) stimulates red blood cell production by the bone marrow.

• The increased number of red blood cells elevates blood volume.

*Renin*, p. 621

• **Renin** converts angiotensinogen (a plasma protein produced by the liver) to angiotensin I. In the capillaries of the lungs, angiotensin I is converted to angiotensin II, a hormone that:
  1. stimulates the adrenal production of aldosterone
  2. stimulates the pituitary release of ADH
  3. promotes thirst
  4. elevates blood pressure

*Figure 18–17b*

*The Heart*, p. 622

• Endocrine cells of the heart are cardiac muscle cells in the walls of the atria and the ventricles. These cells produce natriuretic peptides (*ANP* and *BNP*) when the blood volume becomes excessive.

• In general, the actions of natriuretic peptides oppose those of angiotensin II. The result is a reduction in both blood volume and blood pressure.

*The Thymus*, p. 623

• The **thymus** produces several hormones, collectively known as **thymosins**, which play a role in developing and maintaining normal immune defenses.

*The Gonads*, p. 623

**Table 18–8**
• The interstitial cells of the testes produce androgens. Testosterone is the most important sex hormone in males.

• Sustentacular cells in the testes support the differentiation and physical maturation of sperm. Under FSH stimulation, these cells secrete the hormone inhibin, which inhibits the secretion of FSH at the anterior lobe.

• In females, oocytes develop in follicles; follicle cells produce estrogens, especially estradiol.

• After ovulation, the remaining follicle cells reorganize into a corpus luteum. Those cells release a mixture of estrogens and progestins, especially progesterone.

Adipose Tissue, p. 624

• Adipose tissue secretes leptin (a feedback control for appetite) and resistin (which reduces insulin sensitivity).

• Leptin must be present for there to be normal levels of GnRH and gonadotropin synthesis.

X. Patterns of Hormonal Interaction, p. 624

Objectives
1. Explain how hormones interact to produce coordinated physiological responses.
2. Identify the hormones of special importance to normal growth and discuss their roles.
3. Define the general adaptation syndrome and compare homeostatic responses with stress responses.
4. Describe the effects of hormones on behavior.

• The hormones of the endocrine system often interact, producing:
  1. antagonistic (opposing) effects
  2. synergistic (additive) effects
  3. permissive effects, in which one hormone is necessary for another to produce its effect
  4. integrative effects, in which hormones produce different, but complementary, results

Role of Hormones in Growth, p. 624

• Normal growth requires the cooperation of several endocrine organs.

• Several hormones are especially important: GH, thyroid hormones, insulin, PTH, calcitriol, and reproductive hormones. The circulation concentrations of these
hormones are regulated independently. Changes produce unique individual
growth patterns.

- **Growth Hormone (GH):** effects are most apparent in children where GH supports
  muscular and skeletal development. In adults GH assists in the maintenance of
  normal blood glucose concentrations and in the mobilization of lipid reserves.

- **Thyroid hormones:** if these hormones are absent during fetal development or for
  the first year after birth, the nervous system will fail to develop normally and
  mental retardation will result. If T4 concentrations decline before puberty, normal
  skeletal development will not continue.

- **Insulin:** without insulin the passage of glucose and amino acids across cell
  membranes will be drastically reduced or eliminated.

- **Parathyroid Hormone (PTH) and Calcitriol:** promote the absorption of calcium
  salts for subsequent deposition in bone. Without adequate levels of both
  hormones, bones will be weak and flexible.

- **Reproductive Hormones:** the sex hormones (androgens in males, estrogens in
  females) stimulate cell growth and differentiation in their target tissues.  
  Differential growth induced by each hormone accounts for gender-related
  differences in skeletal proportions and secondary sex characteristics.

*The Hormonal Response to Stress*, p. 626

- Any condition that threatens homeostasis is a **stress**.

- Our bodies respond to a variety of stress-causing factors through the **general
  adaptation syndrome (GAS)**, or **stress response**.

- The GAS can be divided into three phases:
  1. the alarm phase
  2. the resistance phase
  3. the exhaustion phase

*Figure 18–18*

*The Alarm Phase*, p. 626

- During the **alarm phase**, an immediate response to the stress occurs, directed by
  the autonomous nervous system.

- In the alarm phase:
  1. energy reserves are mobilized, mainly in the form of glucose
  2. the body prepares to deal with the stress by “fight or flight” responses
• Epinephrine is the dominant hormone in the alarm phase.

• Characteristics of the alarm phase include:
  1. increased mental alertness
  2. increased energy consumption
  3. mobilization of energy reserves (glycogen and lipids)
  4. changes in circulation: increased blood flow to skeletal muscles, decreased blood flow to the skin, kidneys, and digestive organs
  5. drastic reduction in digestion and urine production
  6. increased sweat gland secretion
  7. increases in blood pressure, heart rate, and respiratory rate

The Resistance Phase, p. 626

• If a stress lasts longer than a few hours, the individual enters the resistance phase of the GAS.

• Glucocorticoids are the dominant hormones of the resistance phase.

• Energy demands remain higher than normal in the resistance phase. Glycogen reserves are nearly exhausted after several hours of stress.

• The secretions of the resistance phase are coordinated to achieve four integrated results:
  1. mobilization of remaining lipid and protein reserves
  2. conservation of glucose for neural tissues
  3. elevation and stabilization of blood glucose concentrations
  4. conservation of salts and water, and the loss of $K^+$ and $H^+$.

• The body’s lipid reserves are sufficient to maintain the resistance phase for weeks or even months. If starvation is the primary stress, the resistance phase ends when lipid reserves are exhausted and structural proteins become the primary energy source. If another stress is the cause, the resistance phase ends due to complications by hormonal side effects:
  1. glucocorticoids have anti-inflammatory actions that slow wound healing and increase the body’s susceptibility to infection
  2. ADH and aldosterone conserve fluids that over time produce elevated blood volumes and higher-than-normal blood pressures
  3. the adrenal cortex may become unable to produce glucocorticoids, eliminating the ability to maintain acceptable blood glucose concentrations

• Poor nutrition, emotional or physical trauma, chronic illness, and damage to key organs can hasten the end of the resistance phase.

The Exhaustion Phase, p. 628
• The exhaustion phase begins when homeostatic regulation breaks down.

• Unless corrective actions are taken almost immediately, the failure of one or more organ systems will prove fatal.

• Mineral imbalances contribute to the existing problems with major systems.

• The inability to sustain the endocrine and metabolic adjustments of the resistance phase will cause death.

*The Effects of Hormones on Behavior*, p. 628

• Many hormones affect the CNS; changes in the normal mixture of hormones can significantly alter intellectual capabilities, memory, learning, and emotional states.

• The clearest demonstrations of the behavioral effects of specific hormones involve individuals whose endocrine glands are oversecreting or undersecreting.

**XI. Aging and Hormone Production, p. 628**

• The endocrine system undergoes few functional changes with advanced age. The major changes include a decline in the concentration of growth hormone and reproductive hormones.

• Some endocrine tissues become less responsive to stimulation even though circulating hormone levels remain within normal limits.

• Changes in peripheral tissues may make them less responsive to some hormones.

**XII. Integration with Other Systems, p. 628**

• The endocrine system provides long-term regulation and adjustments of homeostatic mechanisms that affect many body functions:
  1. fluid and electrolyte balance
  2. cell and tissue metabolism
  3. growth and development
  4. reproductive functions
  5. assists the nervous system in responding to stressful stimuli through the general adaptation syndrome.

*Figure 18-19*

• Many hormones also serve as neurotransmitters in the brain, spinal cord, and/or enteric nervous system.
• Circulating hormones that cross the blood-brain barrier can have direct and widespread effects on neural and neuroendocrine activities.

Clinical Patterns, p. 628

• Primary disorders result from problems within the endocrine organ. An endocrine organ may malfunction due to a metabolic factor, physical damage that destroys cells or disrupts normal blood supply. Congenital problems may also affect the regulation, production, or release of hormones by endocrine cells.

• Secondary disorders result from problems in other organs or target tissues. Such disorders often involve the hypothalamus or pituitary gland.

• Abnormalities in target cells can affect their sensitivity or responsiveness to a particular hormone.

SUMMARY
In chapter 18 we learned about:
- role of the endocrine system
- paracrine communication
- endocrine communication
- classes of hormones:
  - amino acid derivatives
  - peptide hormones
  - lipid derivatives, including steroid hormones and eicosanoids
- secretion and distribution of hormones
- endocrine reflexes
- hypothalamus regulation of the endocrine system
- the pituitary gland
  - the anterior lobe
  - the posterior lobe
- releasing hormones
- inhibiting hormones
- the thyroid gland
  - thyroid follicles
  - thyroid hormones
- the parathyroid glands
- the adrenal glands
  - the adrenal cortex
  - the adrenal medulla
- the pineal gland
- the pancreas
  - the pancreatic islets
  - insulin and glucagon
- endocrine tissues in other systems
  - the intestines
- the kidneys
- the heart
- the thymus
- the gonads
- adipose tissue

-hormonal interaction
-the role of hormones in growth
-the hormonal response to stress
-the effects of hormones on behavior
-the effects of aging on hormone production