The Endocrine System

YOUR GOALS
After completing this chapter, you will have a working knowledge of the functions of the endocrine system and will have mastered the objectives listed below.

FUNCTION PREVIEW
- The endocrine system maintains homeostasis by releasing chemicals called hormones, and it controls prolonged or continuous processes such as growth and development, reproduction, and metabolism.

OBJECTIVE CHECKLIST

The Endocrine System and Hormone Function—An Overview
(pp. 310–313)
- Define hormone and target organ.
- Describe how hormones bring about their effects in the body.
- Explain how various endocrine glands are stimulated to release their hormonal products.
- Define negative feedback, and describe its role in regulating blood levels of the various hormones.

The Major Endocrine Organs  (pp. 313–332)
- Describe the difference between endocrine and exocrine glands.
- On an appropriate diagram, identify the major endocrine glands and tissues.
You don’t have to watch CSI to experience action-packed drama. Your body cells have dynamic adventures on microscopic levels all the time. For instance, when insulin molecules, carried passively along in the blood, leave the blood and bind tightly to protein receptors of nearby cells, the response is dramatic: bloodborne glucose molecules begin to disappear into the cells, and cellular activity accelerates. Such is the power of the second great controlling system of the body, the endocrine system. Along with the nervous system, it coordinates and directs the activity of the body’s cells. However, the speed of control in these two great regulating systems is very different. The nervous system is “built for speed.” It uses nerve impulses to prod the muscles and glands into immediate action so that rapid adjustments can be made in response to changes occurring both inside and outside the body. By contrast, the more slowly acting endocrine system uses chemical messengers called hormones, which are released into the blood to be transported leisurely throughout the body.

Although hormones have widespread effects, the major processes they control are reproduction; growth and development; mobilizing body defenses against stressors; maintaining electrolyte, water, and nutrient balance of the blood; and regulating cellular metabolism and energy balance. As you can see, the endocrine system regulates processes that go on for relatively long periods and, in some cases, continuously. The scientific study of hormones and endocrine organs is called endocrinology.

The Endocrine System and Hormone Function—An Overview

Compared to other organs of the body, the organs of the endocrine system are small and unimpressive. Indeed, to collect 1 kg (about 2.2 pounds) of hormone-producing tissue, you would need to collect all the endocrine tissue from eight or nine adults! The endocrine system also lacks the structural or anatomical continuity typical of most organ systems. Instead, bits and pieces of endocrine tissue are tucked away in widely separated regions of the body (see Figure 9.3, p. 314). However, functionally the endocrine organs are very impressive, and when their role in maintaining body homeostasis is considered, they are true giants.

The Chemistry of Hormones

The key to the incredible power of the endocrine glands is the hormones they produce and secrete. Hormones may be defined as chemical substances that are secreted by endocrine cells into the extracellular fluids and regulate the metabolic activity of other cells in the body. Although many different hormones are produced, nearly all of them can be classified chemically as either amino acid-based molecules (including proteins, peptides, and amines) or steroids. Steroid hormones (made from cholesterol) include the sex hormones made by the gonads (ovaries and testes) and the hormones produced by
the adrenal cortex. All others are nonsteroidal amino acid derivatives. If we also consider the local hormones called prostaglandins (prosˈtā-gländˈinz), described later in the chapter (see Table 9.2, p. 333), we must add a third chemical class, because the prostaglandins are made from highly active lipids released from nearly all cell membranes.

**Mechanisms of Hormone Action**

Although the bloodborne hormones circulate to all the organs of the body, a given hormone affects only certain tissue cells or organs, referred to as its **target cells** or **target organs**. For a target cell to respond to a hormone, specific protein receptors must be present on its plasma membrane or in its interior to which *that* hormone can attach. Only when this binding occurs can the hormone influence the workings of a cell.

The term *hormone* comes from a Greek word meaning “to arouse.” In fact, the body’s hormones do just that. They “arouse,” or bring about their effects on the body’s cells primarily by altering cellular activity—that is, by increasing or decreasing the rate of a normal, or usual, metabolic process rather than by stimulating a new one. The precise changes that follow hormone binding depend on the specific hormone and the target cell type, but typically one or more of the following occurs:

1. Changes in plasma membrane permeability or electrical state
2. Synthesis of proteins or certain regulatory molecules (such as enzymes) in the cell
3. Activation or inactivation of enzymes
4. Stimulation of mitosis
5. Promotion of secretory activity

**Direct Gene Activation**

Despite the huge variety of hormones, there are really only two mechanisms by which hormones trigger changes in cells. Steroidal hormones (and, strangely, thyroid hormone) use the mechanism shown in Figure 9.1a. Being lipid-soluble molecules, the steroid hormones can (1) diffuse through the plasma membranes of their target cells. Once inside, the steroid hormone (2) enters the nucleus and (3) binds to a specific receptor protein there. The hormone-receptor complex then (4) binds to specific sites on the cell’s DNA, (5) activating certain genes to transcribe messenger RNA (mRNA). The mRNA then (6) is translated in the cytoplasm, resulting in the synthesis of new proteins.

**Second-Messenger System**

Water-soluble, nonsteroidal hormones—protein and peptide hormones—are unable to enter the target cells. Instead they bind to receptors situated on the target cell’s plasma membrane and utilize a **second-messenger system**. In these cases (Figure 9.1b), (1) the hormone binds to the membrane receptor and (2) the activated receptor sets off a series of reactions (a cascade) that activates an enzyme. In turn, (3) the enzyme, catalyzes reactions that produce second-messenger molecules (in this case, cyclic AMP, also known as cAMP or cyclic adenine monophosphate) that (4) oversee additional intracellular changes that promote the typical response of the target cell to the hormone. As you might guess, there is a variety of possible second messengers (including cyclic guanosine monophosphate (cGMP) and calcium ions) and many possible target cell responses to the same hormone, depending on the tissue type stimulated.

**Control of Hormone Release**

Now that we’ve discussed how hormones work, the next question is, “What prompts the endocrine glands to release or not release their hormones?” Let’s take a look.

**Negative feedback mechanisms** are the chief means of regulating blood levels of nearly all hormones (see Chapter 1, p. 13). In such systems, hormone secretion is triggered by some internal or external stimulus; then rising hormone levels inhibit further hormone release (even while promoting responses in their target organs). As a result, blood levels of many hormones vary only within a very narrow range.

**Endocrine Gland Stimuli**

The stimuli that activate the endocrine organs fall into three major categories—hormonal, humoral, and neural (Figure 9.2).

**Hormonal Stimuli** The most common stimulus is a hormonal stimulus, in which endocrine organs are prodded into action by other hormones. For example, hypothalamic hormones stimulate the anterior
pituitary gland to secrete its hormones, and many anterior pituitary hormones stimulate other endocrine organs to release their hormones into the blood (Figure 9.2a). As the hormones produced by the final target glands increase in the blood, they "feed back" to inhibit the release of anterior pituitary hormones and thus their own release. Hormone release promoted by this mechanism tends to be rhythmic, with hormone blood levels rising and falling again and again.

**Humoral Stimuli** Changing blood levels of certain ions and nutrients may also stimulate hormone release. Such stimuli are referred to as humoral (hyoo-mor'al) stimuli to distinguish them from hormonal stimuli, which are also bloodborne chemicals. The term humoral refers to the ancient use of the word humor to indicate the various body fluids (blood, bile, and others). For example, the release of parathyroid hormone (PTH) by cells of the parathyroid glands is prompted by decreasing blood calcium levels. Because PTH acts by several routes to reverse that decline, blood Ca\(^{2+}\) levels soon rise, ending the stimulus for PTH release (Figure 9.2b). Other hormones released in response to humoral stimuli include calcitonin, released by the thyroid gland, and insulin, produced by the pancreas.

**Neural Stimuli** In isolated cases, nerve fibers stimulate hormone release, and the target cells are said to respond to neural stimuli. The classic example is sympathetic nervous system stimulation of the adrenal medulla to release norepinephrine and epinephrine during periods of stress (Figure 9.2c). Although these three mechanisms typify most systems that control hormone release, they by no means explain all of them, and some endocrine organs respond to many different stimuli.
**FIGURE 9.2** Endocrine gland stimuli. (a) Hormonal stimulus. In this example, hormones released by the hypothalamus stimulate the anterior pituitary to release hormones that stimulate other endocrine organs to secrete hormones. (b) Humoral stimulus. Low blood calcium levels trigger parathyroid hormone (PTH) release from the parathyroid glands. PTH causes blood calcium levels to rise by stimulating release of Ca^{2+} from bone. Consequently, the stimulus for PTH secretion ends. (c) Neural stimulus. The stimulation of adrenal medullary cells by sympathetic nervous system (SNS) fibers triggers the release of catecholamines (epinephrine and norepinephrine) to the blood.

**DID YOU GET IT?**

1. Walking barefoot, you step on a piece of broken glass and immediately pull your foot back. Why is it important that the signal triggering this motion come from the nervous system and not from the endocrine system?

2. What is a hormone? What does target organ mean?

3. Why is cAMP called a second messenger?

4. What are three ways in which endocrine glands are stimulated to secrete their hormones?

For answers, see Appendix D.

**The Major Endocrine Organs**

The major endocrine organs of the body include the **pituitary**, **thyroid**, **parathyroid**, **adrenal**, **pineal**, and **thymus glands**, the **pancreas**, and the gonads (**ovaries** and **testes**) (Figure 9.3). The **hypothalamus**, which is part of the nervous system, is also recognized as a major endocrine organ because it produces several hormones. Although the function of some hormone-producing glands (the anterior pituitary, thyroid, adrenals,
and parathyroids) is purely endocrine, the function of others (pancreas and gonads) is mixed—both endocrine and exocrine. Both types of glands are formed from epithelial tissue, but the endocrine glands are ductless glands that produce hormones that they release into the blood or lymph. (As you might expect, the endocrine glands have a very rich blood supply.) Conversely, the exocrine glands release their products at the body’s surface or into body cavities through ducts. The formation of and differences and similarities between these two types of glands have already been discussed in Chapter 3. Here we will direct our attention to the endocrine glands only.

Besides the more detailed descriptions of the endocrine organs provided next, a summary of their hormones’ main actions and regulatory factors appears in Table 9.1 (pp. 330–331).

**Pituitary Gland**

The **pituitary** (pi-tu’i-tär’e) **gland** is approximately the size of a pea. It hangs by a stalk from the inferior surface of the hypothalamus of the brain, where it is snugly surrounded by the “Turk’s saddle” of the sphenoid bone. It has two functional lobes—the anterior pituitary (glandular tissue) and the posterior pituitary (nervous tissue).

**Hormones of the Anterior Pituitary**

As shown in Figure 9.4, there are several anterior pituitary hormones that affect many body organs. Two of the six anterior pituitary hormones indicated—growth hormone and prolactin—exert their major effects on nonendocrine targets. The remaining four—thyrotropic hormone, adrenocorticotropic hormone, and the two gonadotrophic hormones—are all **tropic** (tro’pik = turn on) **hormones**. Tropic hormones stimulate their target organs, which are also endocrine glands, to secrete their hormones, which in turn exert their effects on other body organs and tissues. All anterior pituitary hormones (1) are proteins (or peptides), (2) act through second-messenger systems, and (3) are regulated by hormonal stimuli and, in most cases, negative feedback.

**Growth hormone (GH)** is a general metabolic hormone. However, its major effects are directed to the growth of skeletal muscles and long bones of the body, and thus it plays an important role in determining final body size. GH is a proteinsparing and anabolic hormone that causes amino acids to be built into proteins and stimulates most target cells to grow in size and divide. At the same time, it causes fats to be broken down and used for energy while it spares glucose, helping to maintain blood sugar homeostasis.

**Homeostatic Imbalance**

If untreated, both deficits and excesses of GH may result in structural abnormalities. Hyposecretion of GH during childhood leads to **pituitary dwarfism** (Figure 9.5). Body proportions are fairly normal, but the person as a whole is a living miniature (with a maximum adult height of 4 feet). Hypersecretion during childhood results in **gigantism**. The individual becomes extremely tall; 8 to 9 feet is common. Again,
body proportions are fairly normal. If hypersecretion occurs after long-bone growth has ended, acromegaly (ak’ro-meg’ah-le) results. The facial bones, particularly the lower jaw and the bony ridges underlying the eyebrows, enlarge tremendously, as do the feet and hands. Thickening of soft tissues leads to coarse or malformed facial features. Most cases of hypersecretion by endocrine organs (the pituitary and the other endocrine organs) result from tumors of the affected gland. The tumor cells act in much the same way as the normal glandular cells do; that is, they produce the hormones normally made by that gland. The use of pharmacological doses of GH to reverse some of the effects of aging is highlighted in the “A Closer Look” box on pp. 317–318. ▲

**Prolactin (PRL)** is a protein hormone structurally similar to growth hormone. Its only known target in humans is the breast (pro = for; lact = milk). After childbirth, it stimulates and maintains milk production by the mother’s breasts. Its function in men is not known.

**Adrenocorticotropic** (ad-re”no-kor”ti-kotro’pi-k) **hormone (ACTH)** regulates the endocrine activity of the cortex portion of the adrenal gland. **Thyroid-stimulating hormone (TSH)**, also called **thyrotropic hormone (TH)**,
influences the growth and activity of the thyroid gland.

The gonadotropic (gon'ús-do-trop'ík) hormones regulate the hormonal activity of the gonads (ovaries and testes). In women, the gonadotropin follicle-stimulating hormone (FSH) stimulates follicle development in the ovaries. As the follicles mature, they produce estrogen, and eggs are readied for ovulation. In men, FSH stimulates sperm development by the testes. Luteinizing (lu'te-in-iz'íng) hormone (LH) triggers ovulation of an egg from the ovary and causes the ruptured follicle to produce progesterone and some estrogen. In men, LH stimulates testosterone production by the interstitial cells of the testes.

**Figure 9.5** Disorders of pituitary growth hormone. (a) Prolonged overproduction of human growth hormone during development, which usually is due to a benign tumor within the pituitary gland, causes gigantism, while normal production of GH during childhood results in an adult of normal height. (b) Underproduction of GH during development causes dwarfism.

The same time rather than the usual single ovulation each month) are fairly common after their use. ▲

**Pituitary-Hypothalamus Relationship**

Despite its insignificant size, the anterior pituitary gland controls the activity of so many other endocrine glands that it has often been called the “master endocrine gland.” Its removal or destruction has a dramatic effect on the body. The adrenal and thyroid glands and the gonads atrophy, and results of hyposecretion by those glands quickly become obvious. However, the anterior pituitary is not as all-powerful in its control as it might appear because the release of each of its hormones is controlled by releasing and inhibiting hormones produced by the hypothalamus. The hypothalamus liberates these regulatory hormones into the blood of the portal circulation, which connects the blood supply of the hypothalamus with that of the anterior pituitary. (In a portal circulation, two capillary beds are connected by vein(s); in this case, the capillaries of the hypothalamus are drained by veins that empty into the capillaries of the anterior pituitary.)
POTENTIAL USES FOR GROWTH HORMONE

Growth hormone (GH) has been used for pharmaceutical purposes (that is, as a drug) since its discovery in the 1950s. Originally obtained from the pituitary glands of cadavers, it is now biosynthesized and administered by injection. Although GH is widely used in clinical trials, its use as a prescription drug is restricted until its helpful and harmful effects—many of which are very intriguing—can be fully documented.

GH is administered legally to children who do not produce it naturally to allow these children to grow to near-normal heights. Unfortunately, some physicians succumb to parental pressures to prescribe GH to children who do produce it but are extremely short.

When GH is administered to adults with a growth-hormone deficiency, body fat decreases and lean body mass, bone density, and muscle mass increase. It also appears to increase the performance and muscle mass of the heart, decreases blood cholesterol, boosts the immune system, and perhaps improves one's psychological outlook. Such effects (particularly those involving increased muscle mass and decreased body fat) have led to abuse of GH by bodybuilders and athletes, which is one reason why this substance remains restricted.

Because GH may also reverse some effects of aging, anti-aging clinics using GH injections to delay aging have sprung up. Many people naturally stop producing GH after age 60, and this may explain why their ratio of lean-to-fat mass declines and their skin thins. GH already is the drug treatment of choice for many aging Hollywood stars who dread the loss of their youth and vitality. Administration of GH to older patients reverses these declines. However, clinical studies reveal that the administered GH does not increase strength or exercise tolerance in older patients, and a careful study of very sick patients in intensive care units (where GH is routinely given to restore nitrogen balance) found that high doses of GH are associated with increased mortality. For these reasons, earlier media claims that GH is a "youth potion" have proven to be dangerously misleading, and GH should not be administered to the very old or the critically ill.

GH may help AIDS patients. Because of improved antibiotics, fewer AIDS patients are dying from opportunistic infections. The other side of this picture is that more die from the weight loss called "wasting." It has been shown that injections of GH can actually reverse wasting during AIDS, leading to a gain of lean muscle and weight gain. In 1996, the U.S. Food and Drug Administration approved the use of GH to treat such wasting.

GH is not a wonder drug, even in cases where it is clearly beneficial.

"Media claims that GH is a ‘youth potion’ have proven to be dangerously misleading.”

Can growth hormone help older patients?
A CLOSER LOOK Potential Uses for Growth Hormone (continued)

GH treatment is expensive and has undesirable side effects. It can lead to fluid retention and edema, joint and muscle pain, high blood sugar, glucose intolerance, and gynecomastia (breast enlargement in men). Hypertension, heart enlargement, diabetes, and cancer of the colon are other possible results of high doses of GH, and edema and headaches accompany even the lowest doses. Carefully tailored dosages can avoid most of these side effects, however.

Intensive research into the potential benefits of GH is ongoing and should keep this hormone in the public eye for years to come. Let’s hope its unbridled use does not become a public health problem.

The hypothalamus also makes two additional hormones, oxytocin and antidiuretic hormone, which are transported along the axons of the hypothalamic neurosecretory cells to the posterior pituitary for storage (Figure 9.6). They are later released into the blood in response to nerve impulses from the hypothalamus.

**Hormones of the Posterior Pituitary**

The posterior pituitary is not an endocrine gland in the strict sense because it does not make the peptide hormones it releases. Instead, as mentioned above, it simply acts as a storage area for hormones made by hypothalamic neurons.

**Oxytocin** (ok`se-to'sin) is released in significant amounts only during childbirth and in nursing women. It stimulates powerful contractions of the uterine muscle during labor, during sexual relations, and during breastfeeding. It also causes milk ejection (the let-down reflex) in a nursing woman. Both natural and synthetic oxytocic drugs (Pitocin and others) are used to induce labor or to hasten labor that is progressing normally but at a slow pace. Less frequently, oxytocics are used to stop postpartum bleeding (by causing constriction of the ruptured blood vessels at the placental site) and to stimulate the milk ejection reflex.

The second hormone released by the posterior pituitary is antidiuretic (an"ti-dy"u-ret'ik) hormone (ADH). *Diuresis* is urine production. Thus, an antidiuretic is a chemical that inhibits or prevents urine production. ADH causes the kidneys to reabsorb more water from the forming urine; as a result, urine volume decreases and blood volume increases. In larger amounts, ADH also increases blood pressure by causing constriction of the arterioles (small

**Figure 9.6** Hormones released by the posterior lobe of the pituitary and the target organs of such hormones. Neurosecretory cells in the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH) and transport them down their axons to the posterior pituitary. There, the hormones are stored until their release is triggered by nerve impulses from the hypothalamus.
arteries). For this reason, it is sometimes referred to as **vasopressin** (vas’o-pres’in).

Drinking alcoholic beverages inhibits ADH secretion and results in output of large amounts of urine. The dry mouth and intense thirst experienced “the morning after” reflect this dehydrating effect of alcohol. Certain drugs, classed together as **diuretics**, antagonize the effects of ADH, causing water to be flushed from the body. These drugs are used to manage the edema (water retention in tissues) typical of congestive heart failure.

**HOMEOSTATIC IMBALANCE**

Hyposecretion of ADH leads to a condition of excessive urine output called **diabetes insipidus** (di’ah-be’tez in-sip’i-dus). People with this problem are continually thirsty and drink huge amounts of water.

**DID YOU GET IT?**

5. Both the anterior pituitary and the posterior pituitary release hormones, but the posterior pituitary is not an endocrine gland. What is it?

6. What are two important differences between endocrine and exocrine glands?

7. What are tropic hormones?

8. Barry is excreting huge amounts of urine. He has an endocrine system problem, but it is not diabetes mellitus, which has a similar sign. What is his possible problem?

For answers, see Appendix D.

**Thyroid Gland**

The **thyroid gland** is a hormone-producing gland that is familiar to most people primarily because many obese individuals blame their overweight condition on their “glands” (meaning the thyroid). Actually, the effect of thyroid hormones on body weight is not as great as many believe it to be.

The thyroid gland is located at the base of the throat, just inferior to the Adam’s apple, where it is easily palpated during a physical examination. It is a fairly large gland consisting of two lobes joined by a central mass, or isthmus (Figure 9.7). The thyroid gland makes two hormones, one called **thyroid hormone**, the other called **calcitonin**. Internally, the thyroid gland is composed of hollow structures called **follicles**, which store a sticky colloidal material (Figure 9.7b). Thyroid hormone is derived from this colloid.

**Thyroid hormone**, often referred to as the body’s major metabolic hormone, is actually two active iodine-containing hormones, **thyroxine** (thi-rok’sin), or $T_4$, and **triiodothyronine** (tri’i-o-do-thi’ro-nén), or $T_3$. Thyroxine is the major hormone secreted by the thyroid follicles. Most triiodothyronine is formed at the target tissues by conversion of thyroxine to triiodothyronine. These two hormones are very much alike. Each is constructed from two tyrosine amino acids linked together, but thyroxine has four bound iodine atoms, whereas triiodothyronine has three (thus, $T_4$ and $T_3$, respectively).

Thyroid hormone controls the rate at which glucose is “burned,” or oxidized, and converted to body heat and chemical energy. Because all body cells depend on a continuous supply of chemical energy to power their activities, every cell in the body is a target. Thyroid hormone is also important for normal tissue growth and development, especially in the reproductive and nervous systems.

**HOMEOSTATIC IMBALANCE**

Without iodine, functional hormones cannot be made. The source of iodine is our diet, and the foods richest in iodine are seafoods. Years ago many people who lived in the Midwest, in areas with iodine-deficient soil that were far from the seashore (and a supply of fresh seafood), developed **goiters** (go’terz). That region of the country came to be known as the “goiter belt.” A goiter is an enlargement of the thyroid gland (Figure 9.8) that results when the diet is deficient in iodine. TSH keeps “calling” for thyroxine, and the thyroid gland enlarges, but without iodine the thyroid makes only the peptide part of the molecule, which is nonfunctional and thus fails to provide negative feedback to inhibit TSH release. Simple goiter is uncommon in the United States today because most of our salt is iodized, but it is still a problem in some other areas of the world.

Hyposecretion of thyroxine may indicate problems other than iodine deficiency, such as lack of stimulation by TSH. If it occurs in early childhood, the result is **cretinism** (kre’tin-izm). Cretinism results in dwarfism in which adult body proportions remain childhood. Together the head and trunk are about 1½ times the length of the legs rather than approximately the same length, as in normal adults. Untreated cretins are mentally retarded. Their hair is scanty, and their skin is dry. If discovered
early, hormone replacement will prevent mental retardation and other signs and symptoms of the deficiency. Hypothyroidism occurring in adults results in myxedema (mik"se-de'mah), which is characterized by both physical and mental sluggishness (however, mental retardation does not occur). Other signs are puffiness of the face, fatigue, poor muscle tone, low body temperature (the person is always cold), obesity, and dry skin. Oral thyroxine is prescribed to treat this condition.

Hyperthyroidism generally results from a tumor of the thyroid gland. Extreme overproduction of thyroxine results in a high basal metabolic rate, intolerance of heat, rapid heartbeat, weight loss, nervous and agitated behavior, and a general inability to relax. Graves' disease is one form of hyperthyroidism. In addition to the symptoms of hyperthyroidism given earlier, the thyroid gland enlarges and the eyes may bulge, or protrude anteriorly (a condition called exophthalmos [ek"sof-thal'mos] (Figure 9.9). Hyperthyroidism may be treated surgically by removal of part of the thyroid (and/or a tumor if present) or chemically by administering thyroid-blocking drugs or radioactive iodine, which destroy some of the thyroid cells. ▲

The second important hormone produced by the thyroid gland, calcitonin, decreases blood calcium levels by causing calcium to be deposited in the bones. It acts antagonistically to parathyroid hormone, the hormone produced by the parathyroid glands. Whereas thyroxine is made and stored in follicles before it is released to the blood, calcitonin is made by the so-called parafollicular cells found in the connective tissue between the follicles (Figure 9.7b). It is released directly to the blood in
response to increasing levels of blood calcium. Few effects of hypo- or hypersecretion of calcitonin are known, and calcitonin production is meager or ceases entirely in adults. This may help to explain (at least in part) the progressive decalcification of bones that accompanies aging.

**Parathyroid Glands**

The **parathyroid glands** are tiny masses of glandular tissue most often found on the posterior surface of the thyroid gland (see Figure 9.3). Typically, there are two parathyroid glands on each thyroid lobe; that is, a total of four parathyroids; but as many as eight have been reported, and some may be in other regions of the neck or even in the thorax. The parathyroids secrete **parathyroid hormone (PTH)**, or **parathormone** (par"ah-thor’mən), which is the most important regulator of calcium ion (Ca\(^{2+}\)) homeostasis of the blood. When blood calcium levels drop below a certain level, the parathyroids release PTH, which stimulates bone destruction cells (osteoclasts) to break down bone matrix and release calcium into the blood. Thus, PTH is a **hypercalcemic** hormone (that is, it acts to increase blood levels of calcium), whereas calcitonin is a **hypocalcemic** hormone. The negative feedback interaction between these two hormones as they control blood calcium level during youth is illustrated in Figure 9.10. Although the skeleton is the major PTH target, PTH also stimulates the kidneys and intestine to absorb more calcium (from urinary filtrate and foodstuffs, respectively).

**HOMEOSTATIC IMBALANCE**

If blood calcium levels fall too low, neurons become extremely irritable and overactive. They deliver impulses to the muscles at such a rapid rate that the muscles go into uncontrollable spasms (tetany), which may be fatal. Before surgeons knew the importance of the tiny parathyroid glands on the backside of the thyroid, they would remove a hyperthyroid patient's gland entirely. Many times this resulted in death. Once it was revealed that the parathyroids are functionally very different from the thyroid gland, surgeons began to leave at least some parathyroid-containing tissue (if at all possible) to take care of blood calcium homeostasis.

Severe hyperparathyroidism causes massive bone destruction—an X-ray examination of the bones shows large punched-out holes in the bony matrix. The bones become very fragile, and spontaneous fractures begin to occur. ▲

**DID YOU GET IT?**

9. How are the thyroid and parathyroid glands linked anatomically?

10. What hormone increases blood calcium levels, and which endocrine gland produces this hormone?

11. What hormone reduces blood calcium levels, and which endocrine gland produces this hormone?

12. Why is iodine important for proper thyroid gland function?

For answers, see Appendix D.
What effect would removal of the parathyroid glands have on blood calcium levels?

**FIGURE 9.10** Hormonal controls of ionic calcium levels in the blood. PTH and calcitonin operate in negative feedback control systems that influence each other.

**Adrenal Glands**

As illustrated in Figure 9.3, the two bean-shaped adrenal glands curve over the top of the kidneys. Although the adrenal gland looks like a single organ, it is structurally and functionally two endocrine organs in one. Much like the pituitary gland, it has glandular (cortex) and neural tissue (medulla) parts. The central medulla region is enclosed by the adrenal cortex, which contains three separate layers of cells (Figure 9.11).

**Hormones of the Adrenal Cortex**

The adrenal cortex produces three major groups of steroid hormones, which are collectively called corticosteroids (kor’i-sté-o-röldz)—mineralocorticoids, glucocorticoids, and sex hormones.

The mineralocorticoids, mainly aldosterone (al’dos-ter’ön), are produced by the outermost adrenal cortex cell layer. As their name suggests, the mineralocorticoids are important in regulating the mineral (or salt) content of the blood,
FIGURE 9.11 Microscopic structure of the adrenal gland.
Diagram of the three regions of the adrenal cortex and part of the adrenal medulla (200X).

particularly the concentrations of sodium and potassium ions. Their target is the kidney tubules that selectively reabsorb the minerals or allow them to be flushed out of the body in urine. When blood levels of aldosterone rise, the kidney tubule cells reclaim increasing amounts of sodium ions and secrete more potassium ions into the urine. When sodium is reabsorbed, water follows. Thus, the mineralocorticoids help regulate both water and electrolyte balance in body fluids. As shown in Figure 9.12, the release of aldosterone is stimulated by humoral factors, such as fewer sodium ions or more potassium ions in the blood (and by ACTH to a lesser degree). Renin, an enzyme produced by the kidneys when blood pressure drops, also causes the release of aldosterone by triggering a series of reactions that form angiotensin II, a potent stimulator of aldosterone release. A hormone released by the heart, atrial natriuretic (na"tre-u-ret'ik) peptide (ANP), prevents aldosterone release, its goal being to reduce blood volume and blood pressure.

The middle cortical layer mainly produces glucocorticoids, which include cortisone and cortisol. Glucocorticoids promote normal cell metabolism and help the body to resist long-term stressors, primarily by increasing blood glucose levels. When blood levels of glucocorticoids are high, fats and even proteins are broken down by body cells and converted to glucose, which is released to the blood. For this reason, glucocorticoids are said to be hyperglycemic hormones. Glucocorticoids also seem to control the more unpleasant effects of inflammation by decreasing edema, and they reduce pain by inhibiting some pain-causing molecules called prostaglandins (see Table 9.2, p. 333). Because of their anti-inflammatory properties, glucocorticoids are often prescribed as drugs to suppress inflammation for patients with rheumatoid arthritis. Glucocorticoids are released
Although the bulk of the sex hormones produced by the innermost cortex layer are **androgens** (male sex hormones), some **estrogens** (female sex hormones) are also formed.

**HOMEOSTATIC IMBALANCE**

A generalized hyposecretion of all the adrenal cortex hormones leads to **Addison's disease**, characterized by a peculiar bronze tone of the skin. Because aldosterone levels are low, sodium and water are lost from the body, which leads to problems with electrolyte and water balance. This, in turn, causes the muscles to become weak, and shock is a possibility. Other signs and symptoms of Addison's disease result from deficient levels of glucocorticoids, such as hypoglycemia, a lessened ability to cope with stress (burnout), and suppression of the immune system (and thereby increased susceptibility to infection). A complete lack of glucocorticoids is incompatible with life.

Hypersecretion problems may result from an ACTH-releasing tumor, and the resulting condition depends on the cortical area involved. Hyperactivity of the outermost cortical area results in **hyperaldosteronism** (hi"per-ald-os-ter-on-izm). Excessive water and sodium are retained, leading to high blood pressure and edema, and potassium is lost to such an extent that the activity of the heart and nervous system may be disrupted. When the tumor is in the middle cortical area or the client has been receiving pharmacological doses (amounts higher than those released in the body) of glucocorticoids to counteract inflammatory disease, **Cushing's syndrome** occurs. Excessive glucocorticoids result in a swollen "moon face" and the appearance of a "buffalo hump" of fat on the upper back. Other common and undesirable effects include high blood pressure, hyperglycemia (steroid diabetes), weakening of the bones (as protein is withdrawn to be converted to glucose), and severe depression of the immune system.

Hypersecretion of the sex hormones leads to **masculinization**, regardless of sex. In adult males these effects may be masked, but in females the results are often dramatic. A beard develops, and a masculine pattern of body hair distribution occurs, among other effects. ▲

**Hormones of the Adrenal Medulla**

The **adrenal medulla**, like the posterior pituitary, develops from a knot of nervous tissue. When the medulla is stimulated by sympathetic nervous system
neurons, its cells release two similar hormones, **epinephrine** (ep′ī-nef′rin), also called **adrenaline**, and **norepinephrine** (noradrenaline), into the bloodstream. Collectively, these hormones are referred to as **catecholamines** (kat′ē-kol-ah′menz). Because some sympathetic neurons also release norepinephrine as a neurotransmitter, the adrenal medulla is often thought of as a "misplaced sympathetic nervous system ganglion."

When you are (or feel) threatened physically or emotionally, your sympathetic nervous system brings about the "fight-or-flight" response to help you cope with the stressful situation. One of the organs it stimulates is the adrenal medulla, which literally pumps its hormones into the bloodstream to enhance and prolong the effects of the neurotransmitters of the sympathetic nervous system. Basically, the catecholamines increase heart rate, blood pressure, and blood glucose levels and dilate the small passageways of the lungs. These events result in more oxygen and glucose in the blood and a faster circulation of blood to the body organs (most importantly, to the brain, muscles, and heart). Thus, the body is better able to deal with a short-term stressor, whether the job at hand is to fight, begin the inflammatory process, or alert you so you think more clearly (Figure 9.13).

The catecholamines of the adrenal medulla prepare the body to cope with a brief or short-term stressful situation and cause the so-called **alarm**
stage of the stress response. Glucocorticoids, by contrast, are produced by the adrenal cortex and are more important in helping the body to cope with prolonged or continuing stressors, such as dealing with the death of a family member or having a major operation. Glucocorticoids operate primarily during the resistance stage of the stress response. If they are successful in protecting the body, the problem will eventually be resolved without lasting damage to the body. When the stress continues on and on, the adrenal cortex may simply “burn out,” which is usually fatal. The roles of glucocorticoids in the stress response are also shown in Figure 9.13.

**HOMEOSTATIC IMBALANCE**

Damage or destruction of the adrenal medulla has no major effects as long as the sympathetic nervous system neurons continue to function normally. However, hypersecretion of catecholamines leads to symptoms typical of excessive sympathetic nervous system activity—a rapidly beating heart, high blood pressure, and a tendency to perspire and be very irritable. Surgical removal of the catecholamine-secreting cells corrects this condition.

### Pancreatic Islets

The **pancreas**, located close to the stomach in the abdominal cavity (see Figure 9.3), is a mixed gland. Probably the best-hidden endocrine glands in the body are the **pancreatic islets**, also called the **islets of Langerhans** (lahng’er-hanz). These little masses of hormone-producing tissue are scattered among the enzyme-producing acinar tissue of the pancreas. The exocrine (enzymeproducing) part of the pancreas, which acts as part of the digestive system, will be discussed later; only the pancreatic islets will be considered here.

Although there are more than a million islets, separated by exocrine cells, each of these tiny clumps of cells busily manufactures its hormones and works like an organ within an organ. Two important hormones produced by the islet cells are **insulin** and **glucagon** (gloo’kah-gon). The islets also produce small amounts of other hormones, but those will not be discussed here.

Islet cells act as fuel sensors, secreting insulin and glucagon appropriately during fed and fasting states. High levels of glucose in the blood stimulate the release of insulin from the **beta** (ba’ tah) cells (Figure 9.14) of the islets. Insulin acts on just about all body cells and increases their ability to transport glucose across their plasma membranes. Once inside the cells, glucose is oxidized for energy or converted to glycogen or fat for storage. These activities are also speeded up by insulin. Because insulin sweeps the glucose out of the blood, its effect is said to be **hypoglycemic**. As blood glucose levels fall, the stimulus for insulin release ends—another classic case of negative feedback control. Many hormones have hyperglycemic effects (glucagon, glucocorticoids, and epinephrine, to name a few), but insulin is the only hormone that decreases blood glucose levels. Insulin is absolutely necessary for the use of glucose by the body cells. Without it, essentially no glucose can get into the cells to be used.

**HOMEOSTATIC IMBALANCE**

Without insulin, blood levels of glucose (which normally range from 80 to 120 mg/100 ml of blood) rise to dramatically high levels (for example, 600 mg/100 ml of blood). In such instances, glucose begins to spill into the urine because the kidney tubule cells cannot reabsorb it fast enough. As glucose flushes from the body, water follows, leading to dehydration. The clinical name for this condition is **diabetes mellitus** (mi-l” tus), which literally means that something sweet (mel = honey) is passing through or siphoning (diabetes = Greek “siphon”) from the body. Because cells cannot use glucose, fats and even proteins are broken down and used to meet the energy requirements of the body. As a result, body weight begins to decline. Loss of body proteins leads to a decreased ability to fight infections, so diabetics must be careful with their hygiene and in caring for even small cuts and bruises. When large amounts of fats (instead of sugars) are used for energy, the blood becomes very acidic (acidosis [as”-i-do’ sis]) as ketones (intermediate products of fat breakdown) appear in the blood. On the basis of cause, this condition of acidosis (as”-i-do’ sis) is referred to as **ketosis**. Unless corrected, coma and death result. The three cardinal signs of diabetes mellitus are (1) **polyuria** (pol” u-ri’ a)—excessive urination to flush out the glucose and ketones; (2) **polydipsia** (pol” di’ p’si-ah)—excessive thirst resulting from water loss; and (3) **polyphagia** (pol” faj’ e-ah)—hunger due to inability to use sugars and the loss of fat and proteins from the body.

Those with mild cases of diabetes mellitus (most cases of type 2, or adult-onset, diabetes) produce insulin, but for some reason their insulin receptors are unable to
responsive to it, a situation called **insulin resistance**. Type 2 diabetics are treated with special diets or oral hypoglycemic medications that prod the sluggish islets into action and increase the sensitivity of the target tissues to insulin and of beta cells to the stimulating effects of glucose. To regulate blood glucose levels in the more severe type 1 (juvenile, or brittle) diabetic, insulin is infused continuously by an insulin pump worn externally, or a regimen of carefully planned insulin injections is administered throughout the day.

Glucagon acts as an antagonist of insulin; that is, it helps to regulate blood glucose levels but in a way opposite that of insulin (Figure 9.15). Its release by the **alpha (α) cells** (see Figure 9.14c) of the islets is stimulated by low blood levels of glucose. Its action is basically hyperglycemic. Its primary target organ is the liver, which it stimulates to break down stored glycogen to glucose and to release the glucose into the blood. No

**FIGURE 9.14** **Pancreatic tissue.**
(a) Location of pancreas relative to the stomach and small intestine. (b) Photomicrograph of pancreas with exocrine and endocrine (islets) areas clearly visible (110×). (c) Diagrammatic view of a pancreatic islet. Beta cells produce insulin, which aids cells in taking up glucose from the blood. Alpha cells produce glucagon, which stimulates liver cells to release glucose to the blood.

**DID YOU GET IT?**

13. What hormone stimulates the kidneys to reabsorb more sodium?

14. Mrs. Bellamy’s husband has suffered a heart attack and is hospitalized. Would you expect her blood glucose levels to be elevated, normal, or lower than normal? Why?

15. Which group of hormones produced by the adrenal cortex has some of the same effects as the ovaries and the testes?

16. Insulin and glucagon are both pancreatic hormones. Which stimulates cellular uptake of glucose?

For answers, see Appendix D.
What happens to the liver’s ability to synthesize and store glycogen when glucagon blood levels rise?

**Stimulus:**
- Rising blood glucose levels (e.g., after eating four jelly doughnuts)
- Elevated blood sugar levels

**Imbalance**
- Uptake of glucose from blood is enhanced in most body cells
- Blood glucose levels decline to set point; stimulus for insulin release diminishes

**Homeostasis:** Normal blood glucose levels (90 mg/100ml)

**Imbalance**
- Liver takes up glucose and stores it as glycogen
- Low blood sugar levels

**Stimulus:**
- Declining blood glucose levels (e.g., after skipping a meal)
- Glucagon-releasing cells of pancreas activated; release glucagon into blood; target is the liver

**Imbalance**
- Liver breaks down glycogen stores and releases glucose to the blood
- Glucagon inhibits these activities in the liver so the liver’s ability to perform them decreases as glycogen levels rise.

**FIGURE 9.15** Regulation of blood glucose levels by a negative feedback mechanism involving pancreatic hormones.
**Pineal Gland**

The *pineal* (pin’ē-əl) gland, also called the *pineal body*, is a small, cone-shaped gland that hangs from the roof of the third ventricle of the brain (see Figure 9.3). The endocrine function of this tiny gland is still somewhat of a mystery. Although many chemical substances have been identified in the pineal gland, only the hormone **melatonin** (mel’ə-hō’to-nin) appears to be secreted in substantial amounts. The levels of melatonin rise and fall during the course of the day and night. Peak levels occur at night and make us drowsy; the lowest levels occur during daylight around noon. Melatonin is believed to be a “sleep trigger” that plays an important role in establishing the body’s day-night cycle. In some animals, melatonin also helps regulate mating behavior and rhythms. In humans, it is believed to coordinate the hormones of fertility and to inhibit the reproductive system (especially the ovaries of females) so that sexual maturation is prevented from occurring before adult body size has been reached.

**Thymus Gland**

The *thymus gland* is located in the upper thorax, posterior to the sternum. Large in infants and children, it decreases in size throughout adulthood. By old age, it is composed mostly of fibrous connective tissue and fat. The thymus produces a hormone called thymosin (thi’mō-sin) and others that appear to be essential for normal development of a special group of white blood cells (T lymphocytes, or T cells) and the immune response. The role of the thymus (and its hormones) in immunity is described in Chapter 12.

**Gonads**

The female and male gonads (see Figure 9.3) produce sex hormones that are identical to those produced by adrenal cortex cells. The major differences are the source and relative amounts produced.

**Hormones of the Ovaries**

The female *gonads* (go’nadz), or *ovaries*, are paired, almond-sized organs located in the pelvic cavity. Besides producing female sex cells (ova, or eggs), ovaries produce two groups of steroid hormones, **estrogens** and **progesterone**.

Alone, the estrogens are responsible for the development of sex characteristics in women (primarily growth and maturation of the reproductive organs) and the appearance of secondary sex characteristics (hair in the pubic and axillary regions) at puberty. Acting with progesterone, estrogens promote breast development and cyclic changes in the uterine lining (the *menstrual cycle*).

Progestrone (pro-jes’to-rōn), as already noted, acts with estrogen to bring about the menstrual cycle. During pregnancy, it quiets the muscles of the uterus so that an implanted embryo will not be aborted and helps prepare breast tissue for lactation.

Ovaries are stimulated to release their estrogens and progesterone in a cyclic way by the anterior pituitary gonadotrophic hormones. More detail on this feedback cycle and on the structure, function, and controls of the ovaries is given in Chapter 16, but it should be obvious that hyposecretion of the ovarian hormones severely hampers the ability of a woman to conceive and bear children.

**Hormones of the Testes**

The paired oval *testes* of the male are suspended in a sac, the *scrotum*, outside the pelvic cavity. In addition to male sex cells, or *sperm*, the testes also produce male sex hormones, or *androgens*, of which **testosterone** (tes-tos’to-rōn) is the most important. At puberty, testosterone promotes the growth and maturation of the reproductive system organs to prepare the young man for reproduction. It also causes the male’s secondary sex characteristics (growth of facial hair, development of heavy bones and muscles, and lowering of the voice) to appear and stimulates the male sex drive.

In adults, testosterone is necessary for continuous production of sperm. In cases of hyposecretion, the man becomes sterile; such cases are usually treated by testosterone injections. The release of gonadal hormones is controlled by anterior pituitary gonadotropins, as described earlier. Testosterone production is specifically stimulated by LH. Chapter 16, which deals with the reproductive system, contains more information on the structure and exocrine function of the testes.

Table 9.1 summarizes the major endocrine glands and some of their hormones.
<table>
<thead>
<tr>
<th>Gland</th>
<th>Hormone</th>
<th>Chemical class</th>
<th>Representative actions</th>
<th>Regulated by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineal body</td>
<td>Melatonin</td>
<td>Amine</td>
<td>Involved in biological rhythms (daily and seasonal)</td>
<td>Light/dark cycles</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Hormones released by the posterior pituitary; releasing and inhibiting hormones that regulate the anterior pituitary (see below)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>Oxytocin</td>
<td>Peptide</td>
<td>Stimulates contraction of uterus and the milk “let-down” reflex</td>
<td>Nervous system (hypothalamus) in response to uterine stretching and/or suckling of a baby</td>
</tr>
<tr>
<td></td>
<td>Antidiuretic hormone (ADH)</td>
<td>Peptide</td>
<td>Promotes retention of water by kidneys</td>
<td>Hypothalamus in response to water/salt imbalance</td>
</tr>
<tr>
<td></td>
<td>Growth hormone (GH)</td>
<td>Protein</td>
<td>Stimulates growth (especially of bones and muscles) and metabolism</td>
<td>Hypothalamic releasing and inhibiting hormones</td>
</tr>
<tr>
<td></td>
<td>Prolactin (PRL)</td>
<td>Protein</td>
<td>Stimulates milk production</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Protein</td>
<td>Stimulates production of ova and sperm</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td>Thyroid lobe</td>
<td>Luteinizing hormone (LH)</td>
<td>Protein</td>
<td>Stimulates ovaries and testes</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Thyroid-stimulating hormone (TSH)</td>
<td>Protein</td>
<td>Stimulates thyroid gland</td>
<td>Thyroxine in blood; hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>Protein</td>
<td>Stimulates adrenal cortex to secrete glucocorticoids</td>
<td>Glucocorticoids; hypothalamic hormones</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Thyroxine (T$_4$) and triiodothyronine (T$_3$)</td>
<td>Amine</td>
<td>Stimulates metabolism</td>
<td>TSH</td>
</tr>
<tr>
<td>Gland</td>
<td>Hormone</td>
<td>Chemical class</td>
<td>Representative actions</td>
<td>Regulated by</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------</td>
<td>----------------</td>
<td>-------------------------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Calcitonin</td>
<td>Peptide</td>
<td>Reduces blood calcium level</td>
<td>Calcium level in blood</td>
</tr>
<tr>
<td>Parathyroid glands</td>
<td>Parathyroid hormone (PTH)</td>
<td>Peptide</td>
<td>Raises blood calcium level</td>
<td>Calcium level in blood</td>
</tr>
<tr>
<td>Thymus gland</td>
<td>Thymosin</td>
<td>Peptide</td>
<td>“Programs” T lymphocytes</td>
<td>Not known</td>
</tr>
<tr>
<td>Adrenal glands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Adrenal medulla</td>
<td>Epinephrine and norepinephrine</td>
<td>Amines</td>
<td>Raise blood glucose level; increase rate of metabolism; constrict certain blood vessels</td>
<td>Nervous system (sympathetic division)</td>
</tr>
<tr>
<td>• Adrenal cortex</td>
<td>Glucocorticoids</td>
<td>Steroids</td>
<td>Increase blood glucose</td>
<td>ACTH</td>
</tr>
<tr>
<td></td>
<td>Mineralocorticoids</td>
<td>Steroids</td>
<td>Promote reabsorption of Na⁺ and excretion of K⁺ in kidneys</td>
<td>Changes in blood volume or blood pressure; K⁺ (potassium) or Na⁺ levels in blood</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Insulin</td>
<td>Protein</td>
<td>Reduces blood glucose</td>
<td>Glucose level in blood</td>
</tr>
<tr>
<td></td>
<td>Glucagon</td>
<td>Protein</td>
<td>Raises blood glucose</td>
<td>Glucose level in blood</td>
</tr>
<tr>
<td>Gonads</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Testes</td>
<td>Androgens</td>
<td>Steroids</td>
<td>Support sperm formation; development and maintenance of male secondary sex characteristics</td>
<td>FSH and LH</td>
</tr>
<tr>
<td>• Ovaries</td>
<td>Estrogens</td>
<td>Steroids</td>
<td>Stimulate uterine lining growth; development and maintenance of female secondary sex characteristics</td>
<td>FSH and LH</td>
</tr>
<tr>
<td></td>
<td>Progesterone</td>
<td>Steroids</td>
<td>Promotes growth of uterine lining</td>
<td>FSH and LH</td>
</tr>
</tbody>
</table>
DID YOU GET IT?

17. What hormone is called the sleep hormone, and which endocrine organ produces it?
18. How do thymosin and other thymus hormones help to protect the body?
19. Which gonadal hormone causes a young girl’s body to develop feminine characteristics at puberty—estrogen or progesterone?

For answers, see Appendix D.

Other Hormone-Producing Tissues and Organs

Besides the major endocrine organs, pockets of hormone-producing cells are found in fatty tissue and in the walls of the small intestine, stomach, kidneys, and heart—organs whose chief functions have little to do with hormone production. Because most of these hormones are described in later chapters, their chief characteristics are only summarized in Table 9.2. Only the placental hormones are considered further here.

Placenta

The placenta (plah-sen’thah) is a remarkable organ formed temporarily in the uterus of pregnant women. In addition to its roles as the respiratory, excretory, and nutrition-delivery systems for the fetus, it also produces several protein and steroid hormones that help to maintain the pregnancy and pave the way for delivery of the baby. During very early pregnancy, a hormone called human chorionic (ko’ri-ôn’ik) gonadotropin (hCG) is produced by the developing embryo and then by the fetal part of the placenta. Similar to LH (luteinizing hormone), hCG stimulates the ovaries to continue producing estrogen and progesterone so that the lining of the uterus is not sloughed off in menses. (The home pregnancy tests sold over the counter test for the presence of hCG in the woman’s urine.) In the third month, the placenta assumes the job of producing estrogen and progesterone, and the ovaries become inactive for the rest of the pregnancy. The high estrogen and progesterone blood levels maintain the lining of the uterus (thus, the pregnancy) and prepare the breasts for producing milk. Human placental lactogen (hPL) works cooperatively with estrogen and progesterone in preparing the breasts for lactation. Relaxin, another placental hormone, causes the mother’s pelvic ligaments and the pubic symphysis to relax and become more flexible, which eases birth passage.

Developmental Aspects of the Endocrine System

The embryonic development of the endocrine glands varies. The pituitary gland is derived from epithelium of the oral cavity and a neural tissue projection of the hypothalamus. The pineal body is entirely neural tissue. Most strictly epithelial glands develop as little saclike outpocketings of the mucosa of the digestive tract. These are the thyroid, thymus, and pancreas. Formation of the gonads and the adrenal and parathyroid glands is much more complex and is not considered here.

Barring outright malfunctions of the endocrine glands, most endocrine organs seem to operate smoothly until old age. In late middle age, the efficiency of the ovaries begins to decline, causing menopause (commonly called “the change of life”). During this period, a woman’s reproductive organs begin to atrophy, and the ability to bear children ends. Problems associated with estrogen deficiency begin to occur, such as arteriosclerosis, osteoporosis, decreased skin elasticity, and changes in the operation of the sympathetic nervous system that result in “hot flashes.” In addition, fatigue, nervousness, and mood changes such as depression are common. No such dramatic changes seem to happen in men. In fact, many men remain fertile throughout their life span, indicating that testosterone is still being produced in adequate amounts.

The efficiency of the endocrine system as a whole gradually declines in old age. Striking changes in aging women are due to decreasing levels of female hormones, and there is no question that growth hormone output by the anterior pituitary declines, which partially explains muscle atrophy in old age. Elderly persons are less able to resist stress and infection. This decreased resistance may result from overproduction or underproduction of the defensive hormones, because both
# TABLE 9.2 Hormones Produced by Organs Other Than the Major Endocrine Organs

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Chemical composition</th>
<th>Source</th>
<th>Stimulus for secretion</th>
<th>Target organ/Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostaglandins (PGs); several groups indicated by letters A–I (PGA–PGI)</td>
<td>Derived from fatty acid molecules</td>
<td>Plasma membranes of virtually all body cells</td>
<td>Various (local irritation, hormones, etc.)</td>
<td>Have many targets, but act locally at site of release. Examples of effects include: increase blood pressure by acting as vasoconstrictors; cause constriction of respiratory passageways; stimulate muscle of the uterus, promoting labor; enhance blood clotting; promote inflammation and pain; increase output of digestive secretions by stomach; cause fever.</td>
</tr>
<tr>
<td>Gastrin</td>
<td>Peptide</td>
<td>Stomach</td>
<td>Food</td>
<td>Stomach: stimulates glands to release hydrochloric acid (HCl).</td>
</tr>
<tr>
<td>Intestinal gastrin</td>
<td>Peptide</td>
<td>Duodenum of small intestine</td>
<td>Food, especially fats</td>
<td>Stomach: inhibits HCI secretion and gastrointestinal tract mobility.</td>
</tr>
<tr>
<td>Cholecystokinin (CCK)</td>
<td>Peptide</td>
<td>Duodenum</td>
<td>Food</td>
<td>Pancreas: stimulates release of enzyme-rich juice. Gallbladder: stimulates expulsion of stored bile. Duodenal papilla: causes sphincter to relax, allowing bile and pancreatic juice to enter duodenum.</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Glycoprotein</td>
<td>Kidney</td>
<td>Hypoxia</td>
<td>Bone marrow: stimulates production of red blood cells.</td>
</tr>
<tr>
<td>Active vitamin D₃</td>
<td>Steroid</td>
<td>Kidney (activates provitamin D made by epidermal cells)</td>
<td>PTH</td>
<td>Intestine: stimulates active transport of dietary calcium across intestinal cell membranes.</td>
</tr>
<tr>
<td>Atrial natriuretic peptide (ANP)</td>
<td>Peptide</td>
<td>Heart</td>
<td>Stretching of atria of heart</td>
<td>Kidney: inhibits sodium ion reabsorption and renin release. Adrenal cortex: inhibits secretion of aldosterone, thereby decreasing blood volume and blood pressure.</td>
</tr>
<tr>
<td>Leptin</td>
<td>Peptide</td>
<td>Adipose tissue</td>
<td>Fatty foods</td>
<td>Brain: suppresses appetite and increases energy expenditure.</td>
</tr>
<tr>
<td>Resistin</td>
<td>Peptide</td>
<td>Adipose tissue</td>
<td>Unknown</td>
<td>Fat, muscle, liver: antagonizes insulin’s action on liver cells.</td>
</tr>
</tbody>
</table>
HOMEOSTATIC RELATIONSHIPS BETWEEN THE ENDOCRINE SYSTEM AND OTHER BODY SYSTEMS

Nervous System
- Many hormones (growth hormone, thyroxine, sex hormones) influence normal maturation and function of the nervous system
- Hypothalamus controls anterior pituitary function

Respiratory System
- Epinephrine influences ventilation (dilates bronchioles)
- Respiratory system provides oxygen; disposes of carbon dioxide; converting enzyme in lungs converts angiotensin I to angiotensin II

Cardiovascular System
- Several hormones influence blood volume, blood pressure, and heart contractility; erythropoietin stimulates red blood cell production
- Blood is the main transport medium of hormones; heart produces atrial natriuretic peptide

Reproductive System
- Hypothalamic, anterior pituitary, and gonadal hormones direct reproductive system development and function; oxytocin and prolactin involved in birth and breastfeeding
- Gonadal hormones feed back to influence endocrine system function

Integumentary System
- Androgens activate sebaceous glands; estrogen increases skin hydration
- Skin produces a precursor of vitamin D (cholecalciferol or provitamin D)

Muscular System
- Growth hormone is essential for normal muscular development; other hormones (thyroxine and catecholamines) influence muscle metabolism
- Muscular system mechanically protects some endocrine glands; muscular activity promotes catecholamine release

Lymph System
- Aldosterone and ADH influence renal function; erythropoietin released by kidneys promotes red blood cell formation
- Kidneys activate vitamin D (considered a hormone)
“derail” the stress defense equilibrium and alter general body metabolism. Additionally, exposure to many pesticides, industrial chemicals, dioxin, and other soil and water pollutants diminishes endocrine function, which may explain the higher cancer rates among older adults in certain areas of the country. Older people are often mildly hypothyroid, and all older people have some decline in insulin production, and type 2 diabetes is most common in this age group.

SUMMARY
Media study tools that provide additional review of key topics of Chapter 9 are referenced below.

- IP = InterActive Physiology
- WEB = The A&P Place

The Endocrine System and Hormone Function—An Overview (pp. 310–313)

1. The endocrine system is a major controlling system of the body. Through hormones, it stimulates such long-term processes as growth and development, metabolism, reproduction, and body defense.

2. Endocrine organs are small and widely separated in the body. Some are part of mixed glands (both endocrine and exocrine in function). Others are purely hormone producing.

3. Nearly all hormones are amino acid-based or steroids.

4. Endocrine organs are activated to release their hormones into the blood by hormonal, humoral, or neural stimuli. Negative feedback is important in regulating hormone levels in the blood.

5. Bloodborne hormones alter the metabolic activities of their target organs. The ability of a target organ to respond to a hormone depends on the presence of receptors in or on its cells to which the hormone binds or attaches.

6. Amino acid-based hormones act through second messengers. Steroid hormones directly influence the target cell's DNA.

WEB Exercise: Chapter 9, Hormones and Their Target Cells.

The Major Endocrine Organs (pp. 313–332)

1. Pituitary gland

   a. The pituitary gland hangs from the hypothalamus of the brain by a stalk and is enclosed by bone. It consists of a glandular (anterior) portion and a neural (posterior) portion.

   b. Except for growth hormone and prolactin, hormones of the anterior pituitary are all tropic hormones.

      (1) Growth hormone (GH): An anabolic and protein-conserving hormone that promotes total body growth. Its most important effect is on skeletal muscles and bones. Untreated hyposecretion during childhood results in pituitary dwarfism; hypersecretion produces gigantism (in childhood) and acromegaly (in adulthood).

      (2) Prolactin (PRL): Stimulates production of breast milk.

      (3) Adrenocorticotropic hormone (ACTH): Stimulates the adrenal cortex to release its hormones.

      (4) Thyroid-stimulating hormone (TSH): Stimulates the thyroid gland to release thyroid hormone.

      (5) Gonadotropic hormones

         a. Follicle-stimulating hormone (FSH): Beginning at puberty, stimulates follicle development and estrogen production by the female ovaries; promotes sperm production in the male.

         b. Luteinizing hormone (LH): Beginning at puberty, stimulates ovulation, causes the ruptured ovarian follicle to produce progesterone; stimulates the male's testes to produce testosterone.
c. Releasing and inhibiting hormones made by the hypothalamus regulate release of hormones made by the anterior pituitary. The hypothalamus also makes two hormones that are transported to the posterior pituitary for storage and later release.

**Endocrine System; Topic: Hypothalamic-Pituitary Axis, pp. 1–3.**

**d. The posterior pituitary stores and releases hypothalamic hormones on command.**


2. Antidiuretic hormone (ADH): Causes kidney tubule cells to reabsorb and conserve body water and increases blood pressure by constricting blood vessels. Hyposecretion leads to diabetes insipidus.

**WEB Exercise: Chapter 9, Endocrine Case Study.**

2. Thyroid gland

a. The thyroid gland is located in the anterior throat.

b. Thyroid hormone (thyroxine [T₄] and triiodothyronine [T₃]) is released from the thyroid follicles when blood levels of TSH rise. Thyroid hormone is the body’s metabolic hormone. It increases the rate at which cells oxidize glucose and is necessary for normal growth and development. Lack of iodine leads to goiter. Hyposecretion of thyroxine results in cretinism in children and myxedema in adults. Hypersecretion results from Graves' disease or other forms of hyperthyroidism.

**WEB Exercise: Chapter 9, At the Clinic: Endocrine System.**

**3. Parathyroid glands**

a. The parathyroid glands are four small glands located on the posterior aspect of the thyroid gland.

b. Low blood levels of calcium stimulate the parathyroid glands to release parathyroid hormone (PTH). It causes bone calcium to be liberated into the blood. Hyposecretion of PTH results in tetany; hypersecretion leads to extreme bone wasting and fractures.

**WEB Exercise: Chapter 9, Ionic Calcium Levels in the Blood.**

4. Adrenal glands

a. The adrenal glands are paired glands perched on the kidneys. Each gland has two functional endocrine portions, the cortex and the medulla.

b. Adrenal cortex hormones include:

1. Mineralocorticoids, primarily aldosterone, regulate sodium ion (Na⁺) and potassium ion (K⁺) reabsorption by the kidneys. Their release is stimulated primarily by low Na⁺ and/or high K⁺ levels in blood.

2. Glucocorticoids enable the body to resist long-term stress by increasing blood glucose levels and depressing the inflammatory response.

3. Sex hormones (mainly androgens) are produced in small amounts throughout life.

c. Generalized hypoactivity of the adrenal cortex results in Addison’s disease. Hypersecretion can result in hyperaldosteronism, Cushing’s disease, and/or masculinization.

d. The adrenal medulla produces catecholamines (epinephrine and norepinephrine) in response to sympathetic nervous system stimulation. Its catecholamines enhance and prolong the effects of the “fight-or-flight” (sympathetic nervous system) response to short-term stress. Hypersecretion leads to symptoms typical of sympathetic nervous system overactivity.

**WEB Endocrine System; Topic: Hormone Imbalances, pp. 4–5.**

5. Pancreatic islets

a. Located in the abdomen close to the stomach, the pancreas is both an exocrine and endocrine gland. The endocrine portion (islets) releases insulin and glucagon to blood.

b. Insulin is released when blood levels of glucose are high. It increases the rate of glucose uptake and metabolism by body cells. Hyposecretion of insulin results in diabetes mellitus, which severely disturbs body metabolism. Cardinal signs are polyuria, polydipsia, and polyphagia.

c. Glucagon, released when blood levels of glucose are low, stimulates the liver to release glucose to blood, thus increasing blood glucose levels.

**WEB Endocrine System; Topic: Hormone Imbalances, p. 2.**
WEB Exercise: Chapter 9, Regulation of Blood Sugar Levels by Insulin and Glycogen.

6. The pineal gland, located posterior to the third ventricle of the brain, releases melatonin, which affects sleep as well as biological rhythms and reproductive behavior in other animals.

7. The thymus gland, located in the upper thorax, functions during youth but atrophies in old age. Its hormone, thymosin, promotes maturation of T lymphocytes, important in body defense.

8. Gonads
   a. The ovaries of the female release:
      (1) Estrogens: Release of estrogens by ovarian follicles begins at puberty under the influence of FSH. Estrogens stimulate maturation of the female reproductive organs and female secondary sex characteristics. With progesterone, they cause the menstrual cycle.
      (2) Progesterone: Progesterone is released from the ovary in response to high blood levels of LH. It works with estrogens in establishing the menstrual cycle.
   b. The testes of the male begin to produce testosterone at puberty in response to LH stimulation. Testosterone promotes maturation of the male reproductive organs, male secondary sex characteristics, and production of sperm by the testes.
   c. Hyposecretion of gonadal hormones results in sterility in both females and males.

Other Hormone-Producing Tissues and Organs (p. 332)

1. The placenta is a temporary organ formed in the uterus of pregnant women. Its primary endocrine role is to produce estrogen and progesterone, which maintain pregnancy and ready breasts for lactation.

2. Several organs that are generally nonendocrine in overall function, such as the stomach, small intestine, kidneys, and heart, have cells that secrete hormones.

3. Certain cancer cells secrete hormones.

Developmental Aspects of the Endocrine System (pp. 332, 335)

1. In the absence of disease, efficiency of the endocrine system remains high until old age.

2. Decreasing function of female ovaries at menopause leads to such symptoms as osteoporosis, increased chance of heart disease, and possible mood changes.

3. Efficiency of all endocrine glands gradually decreases with aging, which leads to a generalized increase in incidence of diabetes mellitus, immune system depression, lower metabolic rate, and, in some areas, cancer rates.

REVIEW QUESTIONS

Multiple Choice

More than one choice may apply.

1. The major endocrine organs of the body
   a. tend to be very large organs.
   b. are closely connected with each other.
   c. all contribute to the same function (digestion).
   d. tend to lie near the midline of the body.

2. Which is generally true of hormones?
   a. Exocrine glands produce them.
   b. They travel throughout the body in the blood.
   c. They affect only nonendocrine-producing organs.
   d. All steroid hormones produce very similar physiological effects in the body.

3. Which of the following hormones is (are) secreted by neurons?
   a. Oxytocin
   b. Insulin
   c. ADH
   d. Cortisol

4. ANP, the hormone secreted by the heart, has exactly the opposite function to this hormone secreted by the outermost zone of the adrenal cortex.
   a. Epinephrine
   b. Cortisol
   c. Aldosterone
   d. Testosterone

5. Hormones that act directly or indirectly to elevate blood glucose include which of the following?
   a. GH
   b. Cortisol
   c. insulin
   d. ACTH

6. Hypertension may result from hypersecretion of
   a. thyroxine.
   b. cortisol.
   c. aldosterone.
   d. ADH.

7. Hormones that regulate mineral (salt) levels include
   a. calcitonin.
   b. aldosterone.
   c. atrial natriuretic peptide.
   d. glucagon.

8. Which of the following is given as a drug to reduce inflammation?
   a. Epinephrine
   b. Cortisol
   c. Aldosterone
   d. ADH
9. The element needed for thyroid gland function is
   a. potassium.  c. calcium.
   b. iodine.  d. manganese.

**Short Answer Essay**

10. Explain how the nervous and endocrine systems differ in (a) the rate of their control, (b) the way in which they communicate with body cells, and (c) the types of body processes they control.

11. Which endocrine organs are actually mixed (endocrine and exocrine) glands? Which are purely endocrine?

12. Describe the chemical nature of hormones.

13. Provide one example for each way endocrine glands are stimulated to release their hormones.

14. Define negative feedback, and explain how it regulates blood levels of the various hormones.

15. Explain why not all organs are target organs for all hormones.

16. Describe the body location of each of the following endocrine organs: anterior pituitary, pineal gland, thymus, pancreas, ovaries, testes. Then, for each organ, name its hormones and their effect(s) on body processes. Finally, for each hormone, list the important results of its hypersecretion or hyposecretion.

17. Name two endocrine-producing glands (or regions) that are important in the stress response, and explain why they are important.

18. The anterior pituitary is often referred to as the master endocrine gland, but it too has a “master.” What controls the release of hormones by the anterior pituitary?

19. What is the most common cause of hypersecretion by endocrine organs?

20. Name three hormone antagonists of insulin and one of PTH.

21. Two hormones are closely involved in the regulation of the fluid and electrolyte balance of the body. Name them, and explain their effects on their common target organ.

22. What causes a simple goiter?

23. In general, the endocrine system becomes less efficient as we age. List some examples of problems that elderly individuals have as a result of decreasing hormone production.

**CRITICAL THINKING AND CLINICAL APPLICATION QUESTIONS**

24. A woman with excessive body hair and a deep voice shows the outward symptoms of which hormonal dysfunction?

25. The parents of 14-year-old Megan are concerned about her height because she is only 4 feet tall and they are both close to 6 feet tall. After tests by their doctor, certain hormones are prescribed for the girl. What is the probable diagnosis? What hormones are prescribed, and why might the girl expect to reach normal height?

26. Paula, a 28-year-old, has been in the first stage of labor for 15 hours. Her uterine contractions are weak, and her labor is not progressing normally. Paula and her doctor desire a vaginal delivery, so the physician orders that Pitocin (a synthetic oxytocin) be infused. What is the effect of this hormone?

27. Mr. Holt brings his wife to the clinic, concerned about her nervousness, heart palpitations, and excessive sweating. Tests show hyperglycemia and hypertension. What hormones are probably being hypersecreted? What is the cause? What physical factors allow you to rule out thyroid problems?

28. What are the possible harmful effects of using anabolic steroids to increase muscle mass and strength?

29. Bertha Wise, age 40, comes to the clinic, troubled by swelling in her face and unusual fat deposition on her back and abdomen. She reports that she bruises easily. Blood tests show elevated glucose levels. What is your diagnosis, and what glands might be causing the problem?

30. Maryanne, a street person, is pregnant. She has had no prenatal care, and her diet consists of what she is able to salvage from trash cans. What could you surmise about the PTH levels in her blood?

31. Richard Neis had symptoms of excessive secretion of PTH (high blood calcium levels), and his physicians were certain he had a parathyroid gland tumor. Yet when surgery was performed on his neck, the surgeon could not find the parathyroid glands at all. Where should the surgeon look next to find the tumorous parathyroid gland?