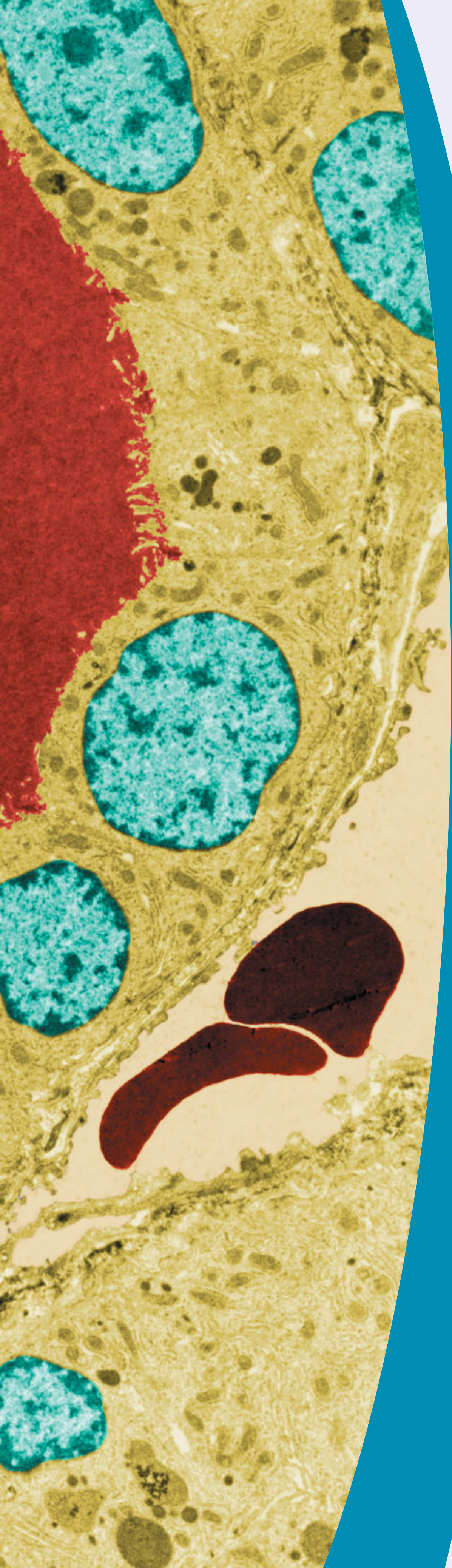


The Endocrine System 17

Portions of thyroid follicles surrounding a fenestrated capillary containing RBC (colored TEM).

The **endocrine system** is a series of ductless glands that secrete messenger molecules called **hormones** into the circulation. The circulating hormones travel to distant body cells and signal characteristic physiological responses in those cells. Through its hormonal signals, the endocrine system controls and integrates the functions of other organ systems in the body. In its general integrative role, the endocrine system resembles the nervous system, with which it closely interacts. However, because hormones travel more slowly than nerve impulses, the endocrine system tends to regulate slow processes, such as growth and metabolism, rather than processes that demand rapid responses, such as the contraction of skeletal muscle. Some major processes controlled by the endocrine system are growth of the body and of the reproductive organs, the mobilization of body defenses against stress, maintenance of proper blood chemistry, and control of the rate of oxygen use by the body's cells. The scientific study of hormones and the endocrine glands is called **endocrinology.**

OVERVIEW

- List the major endocrine organs, and describe their locations.
- Describe how hormones are classified chemically.
- Describe the basic interaction between hormones and their target cells. Describe three mechanisms that control hormone secretion.

Endocrine Organs

Compared to most other organs of the body, the endocrine organs **(Figure 17.1)** are small and unimpressive. Indeed, to collect 1 kg (2.2 pounds) of hormone-producing tissue, you would need to collect all of the endocrine glands from *nine* adults! In addition, unlike the organs of most other systems, which are anatomically continuous, the endocrine organs are widely scattered throughout the body.

The endocrine cells of the body are partly contained within "pure" endocrine organs and partly within organs of other body systems. The purely endocrine organs are the *pituitary gland* at the base of the brain; the *pineal gland* in the roof of the diencephalon; the *thyroid* and *parathyroid glands* in the neck; and the *adrenal glands* on the kidneys (each adrenal gland is actually two glands, an *adrenal cortex* and an *adrenal medulla*). Organs that belong to other body systems but also contain a large proportion of endocrine cells include the *pancreas,* the *thymus,* the *gonads,* and the *hypothalamus* of the brain. Because the hypothalamus produces hormones in addition to performing its nervous functions, it is considered a *neuroendocrine* organ. Numerous other organs, for example the heart, digestive tract, kidneys, and skin, also contain scattered or small pockets of cells that secrete hormones.

Most endocrine cells—like most gland cells in the body—are of *epithelial* origin. However, the endocrine system is so diverse that it also includes hormone-secreting neurons, muscle cells, and fibroblast-like cells.

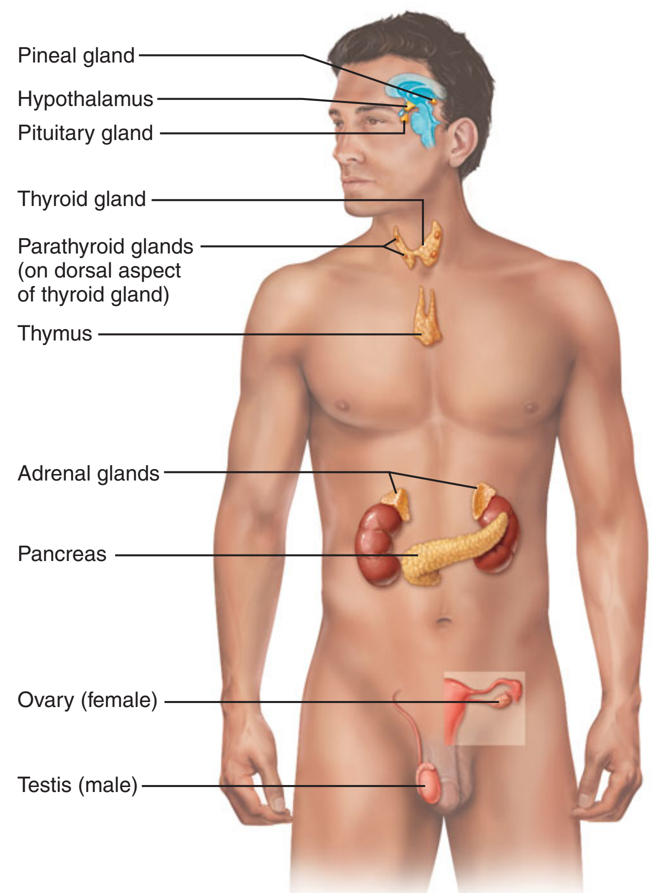


FIGURE 17.1 Location of the major endocrine organs. Endocrine cells also occur in the heart, alimentary canal, kidney, skin, placenta, and elsewhere.

Endocrine glands are richly supplied with blood and lymphatic vessels. Typically, endocrine cells are arranged in small clusters, cords, or branching networks, an arrangement that maximizes their contact with large numbers of capillaries. After endocrine cells release their hormones into the surrounding extracellular space, the hormones immediately enter the adjacent capillaries.

Hormones

Classes of Hormones

The body produces many different kinds of hormones, all with distinct chemical structures. Most hormones, however, belong to one of two broad molecular categories: amino acid–based molecules and steroid molecules. **Amino acid–based hormones** include modified amino acids (or *amines*), peptides (short chains of amino acids), and proteins (long chains of amino acids). **Steroids,** by contrast, are lipid molecules derived from cholesterol.

Basic Hormone Action

All major hormones circulate throughout the entire body, leave the bloodstream at the capillaries, and encounter virtually all tissues. Nevertheless, a given hormone influences

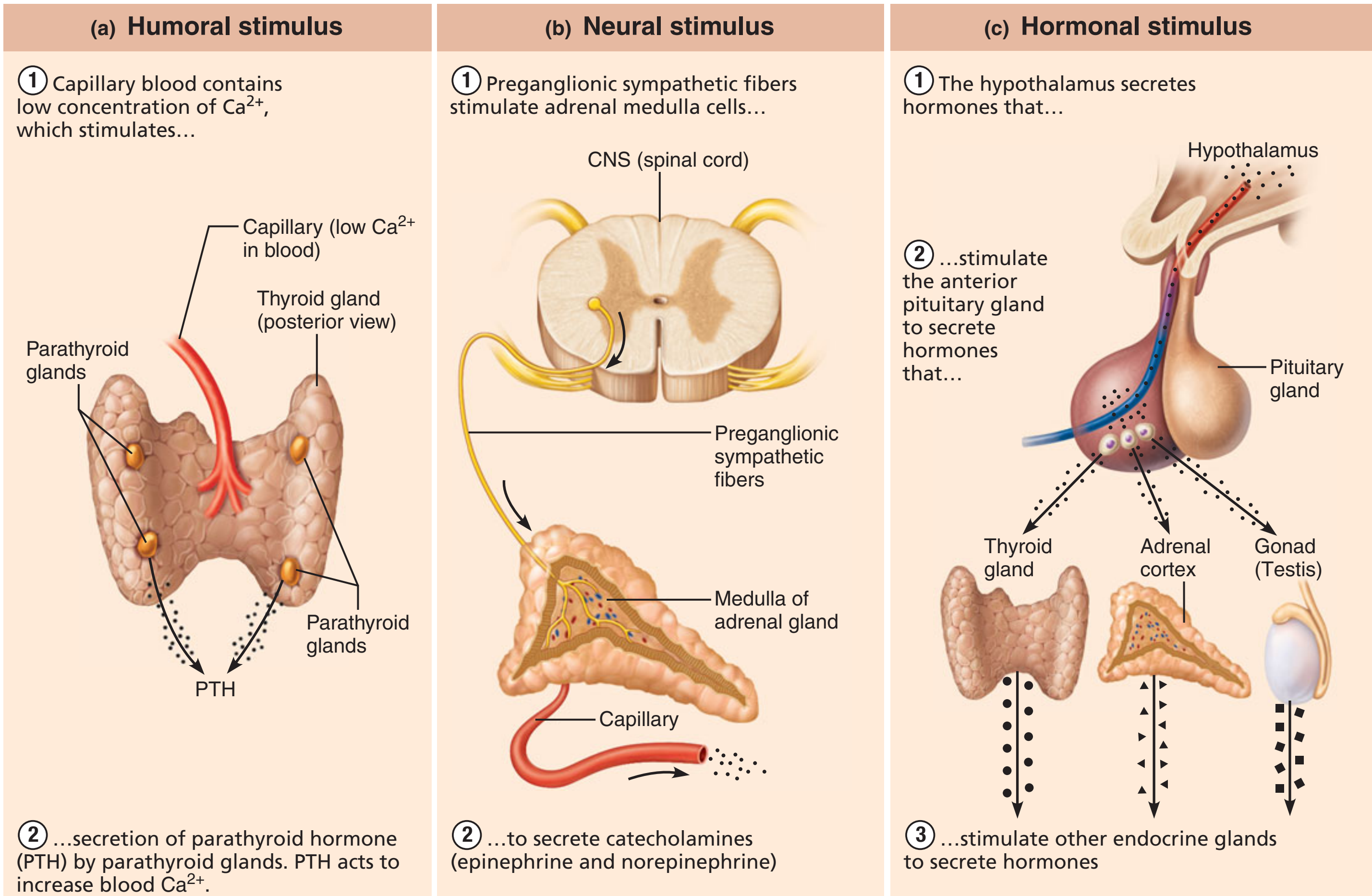


FIGURE 17.2 Three types of endocrine gland stimuli.

only specific tissue cells, called its **target cells.** The ability of a target cell to respond to a hormone depends on the presence of specific receptor molecules on the target cell to which that particular hormone can bind. Once binding has occurred, the target cell reacts in a preprogrammed way.

Each kind of hormone produces its own characteristic effects within the body. These effects result from the preprogrammed responses of the target cells, not from any information contained in the hormone molecule itself. In fact, hormones with similar molecular structures often have very dissimilar functions, and the same hormone can have different effects on different target cells. Hormones are just molecular triggers—they do not carry any coded information.

Control of Hormone Secretion

The various endocrine cells of the body are stimulated to make and secrete their hormones by three major types of stimuli **(Figure 17.2)**: *humoral, neural,* and *hormonal* stimuli.

Endocrine glands that secrete their hormones in direct response to changing levels of ions or nutrients in the blood are said to be controlled by **humoral stimuli** (*humoral* = relating to the blood and other body fluids). This is the simplest endocrine control mechanism. For example, the cells of the parathyroid gland (Figure 17.2a) directly monitor the concentration of calcium ions (Ca^{2+}) in the blood and then respond to any decline in this concentration by secreting a hormone that acts to increase blood calcium levels.

The secretion of a few endocrine glands is controlled by **neural stimuli** (Figure 17.2b). For example, sympathetic nerve fibers stimulate cells in the adrenal medulla to release epinephrine and norepinephrine during fight-or-flight situations.

Finally, many endocrine glands secrete their hormones in response to **hormonal stimuli** received from other endocrine glands; that is, certain hormones have the sole purpose of promoting the secretion of other hormones (Figure 17.2c). For example, the hypothalamus of the brain secretes some hormones that stimulate the anterior part of the pituitary gland to secrete its hormones, which in turn stimulate hormonal secretion by other endocrine glands: the thyroid, the adrenal cortex, and the gonads. As you will see, the hypothalamus controls many functions of the endocrine system, through hormonal and other mechanisms.

No matter how it is stimulated, hormone secretion is always controlled by *feedback loops.* In a negative feedback loop, more hormone is secreted if its blood concentration declines below a minimum set point; then hormone production is halted if the maximum set point is exceeded. This ensures that hormone concentrations stay within a narrow, “desirable” range in the blood. Secretion of certain hormones is regulated by a positive feedback loop: As blood concentrations of the hormone increase, the response of the effector organ stimulates further secretion. The hormone that controls the progression of labor in childbirth, oxytocin, operates via positive feedback—oxytocin stimulates the uterus to contract, and contraction of the uterus stimulates further secretion of oxytocin.

check your understanding

1. How do hormones reach their target cells?
2. What are the three types of stimuli that regulate secretion from endocrine cells?

For answers, see Appendix B.

THE MAJOR ENDOCRINE ORGANS

The major endocrine organs are the pituitary gland, thyroid gland, parathyroid glands, adrenal (suprarenal) glands, pineal gland, pancreas, thymus, and gonads.

The Pituitary Gland

- Name the basic divisions of the pituitary gland.
- List the cell types in the anterior lobe, the hormones secreted by each cell, and the basic functions of each hormone.
- Explain how the hypothalamus controls secretion of anterior lobe hormones. Define releasing hormones, and trace their path through the pituitary gland.
- Describe the structure of the posterior lobe and the functions of the hormones it releases.

The **pituitary gland,** or **hypophysis** (hi-pof′ĭ-sis; "undergrowth [from the brain]"), is an important endocrine organ that secretes at least nine major hormones. It sits just inferior to the brain in the hypophyseal fossa, a depression in the sella turcica of the sphenoid bone **(Figure 17.3)**. The pituitary gland closely resembles a golf club: The gland itself forms the head of the club, and the stalk of the pituitary, called the **infundibulum** ("funnel"), forms the shaft of the club. The infundibulum connects superiorly to a part of the hypothalamus called the tuber cinereum, which lies between the optic chiasma anteriorly and the mammillary bodies posteriorly.

The pituitary gland has two basic divisions, an **anterior lobe** or **adenohypophysis** (ad″ĕ-no-hi-pof′ĭ-sis; "glandular hypophysis"), composed of glandular tissue, and a **posterior lobe** or **neurohypophysis** (nu″ro-hi-pof′ĭ-sis; "neural hypophysis"), composed of neural tissue and a part of the brain. The anterior lobe has three subdivisions (Figure 17.3c). The largest is the anteriormost **pars distalis.** Just posterior to this lies the **pars intermedia,** and just superior to it lies the **pars tuberalis,** which wraps around the infundibulum like a tube. The posterior lobe has two subdivisions, the **pars nervosa,** inferiorly, and the **infundibular.**

Arterial blood reaches the hypophysis through two branches of the internal carotid artery, one of the large arteries that supplies blood to the brain. The **superior hypophyseal artery** supplies the entire adenohypophysis and the infundibulum (see Figure 17.4a), whereas the **inferior hypophyseal artery** supplies the pars nervosa (see Figure 17.4b). The veins from the extensive capillary beds in the pituitary gland drain into the cavernous sinus and other nearby dural sinuses described on p. 602.

The Anterior Lobe

This description of the anterior lobe concentrates on its largest division, the *pars distalis,* which contains five different types of endocrine cells that make and secrete at least seven different hormones (**Table 17.1** on p. 520). Four of the hormones secreted by the anterior lobe—thyroid-stimulating hormone, adrenocorticotropic hormone, follicle-stimulating hormone, and luteinizing hormone—regulate the secretion of hormones by other endocrine glands. These hormones are called **tropic hormones** (tro′pik; "changing"). The remaining three adenohypophysis hormones—growth hormone, prolactin, and melanocyte-stimulating hormone—act directly on nonendocrine target tissues.

Growth Hormone (GH) **Growth hormone (GH),** also called **somatotropic hormone** (so″mah-to-tro′pik; "body changing"), is produced in the somatotropic cells, the most abundant cell type in the anterior lobe. This hormone stimulates growth of the entire body by stimulating body cells to increase their production of proteins and by stimulating growth of the epiphyseal plates of the skeleton. It stimulates these actions directly, and also indirectly by signaling the liver to secrete *insulin-like growth factor-1,* which acts together with GH. The current and potential uses of GH are explored in A Closer Look on p. 530.

Thyroid-Stimulating Hormone (TSH) **Thyroid-stimulating hormone (TSH)** is produced by thyrotropic cells. TSH signals the thyroid gland to secrete its own hormone, thyroid hormone, and thus ultimately controls metabolic rate.

Adrenocorticotropic Hormone (ACTH) **Adrenocorticotropic** (ad-re″no-kor″tĭ-ko-trō′pik; "adrenal cortex changing") **hormone (ACTH)** and the next hormone described are split from a common parent molecule produced by corticotropic cells in the anterior lobe. ACTH stimulates the adrenal cortex (as its name implies) to secrete hormones that help the body cope with stress.

Melanocyte-Stimulating Hormone (MSH) **Melanocyte-stimulating hormone (MSH)** is also formed from the precursor molecule produced by corticotropic cells. In more primitive vertebrates, amphibians and reptiles, MSH stimulates melanocytes to produce more melanin, the pigment responsible for skin coloration. In humans, MSH functions in the CNS in appetite suppression; its actions outside the CNS are not known.

Gonadotropins **Follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)** are produced by gonadotropic cells in the anterior lobe and together are referred to as **gonadotropins** (go-nad″o-trō′pinz). These hormones act on

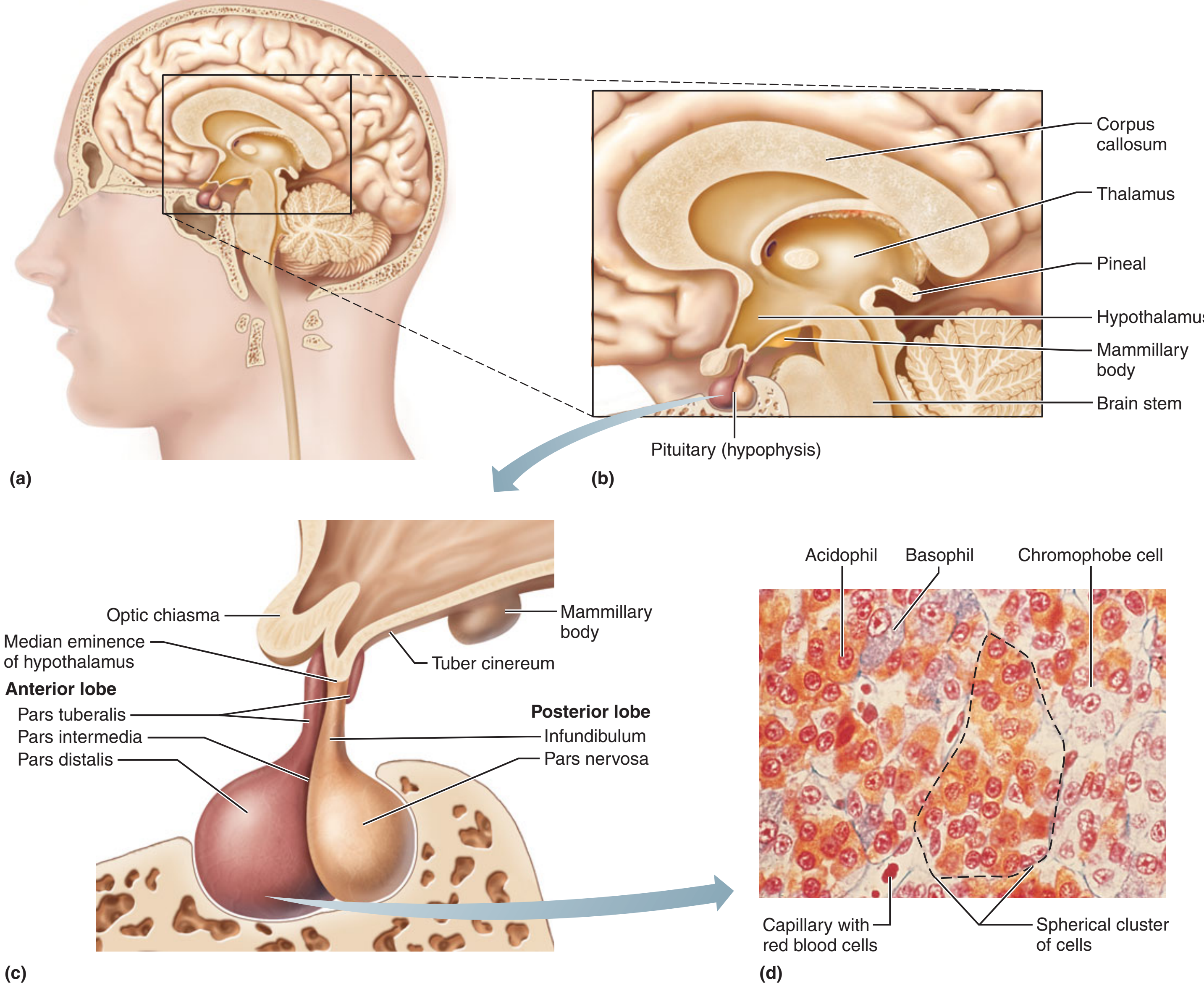


FIGURE 17.3 The pituitary gland (hypophysis). (a) Orientation diagram showing the brain cut in half midsagittally. **(b)** Enlargement of the diencephalon, showing the location of the pituitary gland. **(c)** Basic regions of the pituitary gland. Note that the anterior aspect is to the left. **(d)** Histology of the pars distalis of the anterior lobe (330×).

the gonads, stimulating maturation of the sex cells and inducing the secretion of sex hormones. In females, FSH and LH stimulate the maturation of the egg-containing ovarian follicles and the secretion of androgens, estrogens, and progesterone from cells in the ovary. Furthermore, a large amount of LH is secreted in the middle of the menstrual cycle to induce ovulation. In males, LH signals the secretion of androgens (primarily testosterone) by interstitial cells in the testes, and FSH stimulates the maturation of sperm cells and the production of androgen-binding protein by cells in the sperm-forming tubules. (See Chapter 25 for a full discussion of these actions.)

Prolactin (PRL) **Prolactin (PRL)** (pro-lak′tin) is produced by prolactin cells in the anterior lobe. PRL targets the milk-producing glands in the breast, the lactiferous glands, and stimulates the manufacture of milk.

The endocrine cells of the pars distalis are clustered into spheres and branching cords separated by capillaries. When tissue of the pars distalis is stained with typical histological dyes and viewed by light microscopy, its five cell types can be classified in three categories (Figure 17.3d): (1) **acidophils,** which stain with acidic stains and include the somatotropic and prolactin cells; (2) **basophils,** which stain with basic stains and include the thyrotropic, corticotropic, and gonadotropic cells; and (3) **chromophobes** ("color avoiders"), which stain poorly. Chromophobes are either immature cells or cells whose supply of hormone has been depleted.

TABLE 17.1 Pituitary Hormones: Summary of Target Organs and Effects

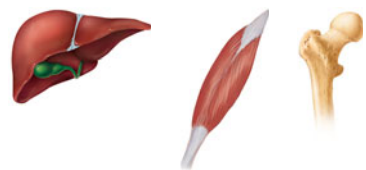
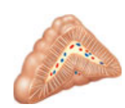
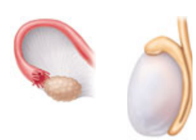
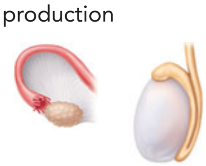
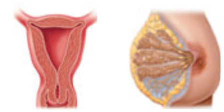
Hormone (Cell Type)	Target Organ and Effects	Effects of Hyposecretion ↓ and Hypersecretion ↑
 **ANTERIOR LOBE HORMONES**		
Growth hormone (GH) (somatotroph)	 Liver, muscle, bone, cartilage, and other tissues: stimulates protein synthesis and somatic growth; mobilizes fats; increases blood glucose	↓ Pituitary dwarfism in children ↑ Gigantism in children; acromegaly in adults
Thyroid-stimulating hormone (TSH) (thyrotroph)	 Thyroid gland: stimulates thyroid gland to release thyroid hormones	↓ Cretinism in children; myxedema in adults ↑ Hyperthyroidism; effects similar to those of Graves' disease, in which antibodies mimic TSH
Adrenocorticotropic hormone (ACTH) (corticotroph)	 Adrenal cortex: promotes release of glucocorticoids and androgens (mineralocorticoids to a lesser extent)	↓ Rare ↑ Cushing's disease
Follicle-stimulating hormone (FSH) (gonadotroph)	 Ovaries and testes: in females, stimulates ovarian follicle maturation and estrogen production; in males, stimulates sperm production	↓ Failure of sexual maturation ↑ No important effects
Luteinizing hormone (LH) (gonadotroph)	 Ovaries and testes: in females, triggers ovulation and stimulates ovarian production of estrogen and progesterone; in males, promotes testosterone production	As for FSH
Prolactin (PRL) (prolactin cells)	 Breast secretory tissue: promotes lactation	↓ Poor milk production in nursing women ↑ Inappropriate milk production (galactorrhea); cessation of menses in females; impotence in males

TABLE 17.1 *continued*

Hormone (Cell Type)	Target Organ and Effects	Effects of Hyposecretion ↓ and Hypersecretion ↑
 **POSTERIOR LOBE HORMONES (MADE BY HYPOTHALAMIC NEURONS AND STORED IN POSTERIOR LOBE)**		
Oxytocin (from neurons in paraventricular nucleus hypothalamus)	 Uterus: stimulates uterine contractions; initiates labor; breast: initiates milk ejecton	Unknown
Antidiuretic hormone (ADH) or **vasopressin** (from neurons in supraoptic nucleus of hypothalamus)	 Kidneys: stimulates kidney tubule cells to resorb water	↓ Diabetes insipidus ↑ Syndrome of inappropriate ADH secretion (SIADH)

The pars distalis is by far the most important division of the anterior lobe; the other divisions—the *pars intermedia* and *pars tuberalis*—are not as well understood. The pars intermedia contains corticotropic cells that secrete more MSH than ACTH. The pars tuberalis contains gonadotropic cells, thyrotropic cells, and unique, *pars tuberalis–specific endocrine cells* that have receptors for melatonin, a hormone that is secreted by the pineal gland and regulates daily (circadian) rhythms according to light/dark cycles (photoperiod). Therefore, the pars tuberalis may be where sexual functions and metabolic rate are brought under the influence of circadian rhythms and photoperiod. The function of the pineal gland and the role of melatonin are discussed on p. 393.

Hypothalamic Control of Hormone Secretion from the Anterior Lobe

The secretion of hormones by the anterior lobe is controlled by the hypothalamus of the brain. The hypothalamus exerts its control by secreting peptide hormones called **releasing hormones (releasing factors),** which then prompt the cells in the anterior lobe to release their hormones. The hypothalamus also secretes **inhibiting hormones,** which *turn off* the secretion of hormones by the anterior lobe when necessary. There are distinct releasing and inhibiting hormones for almost every anterior lobe hormone.

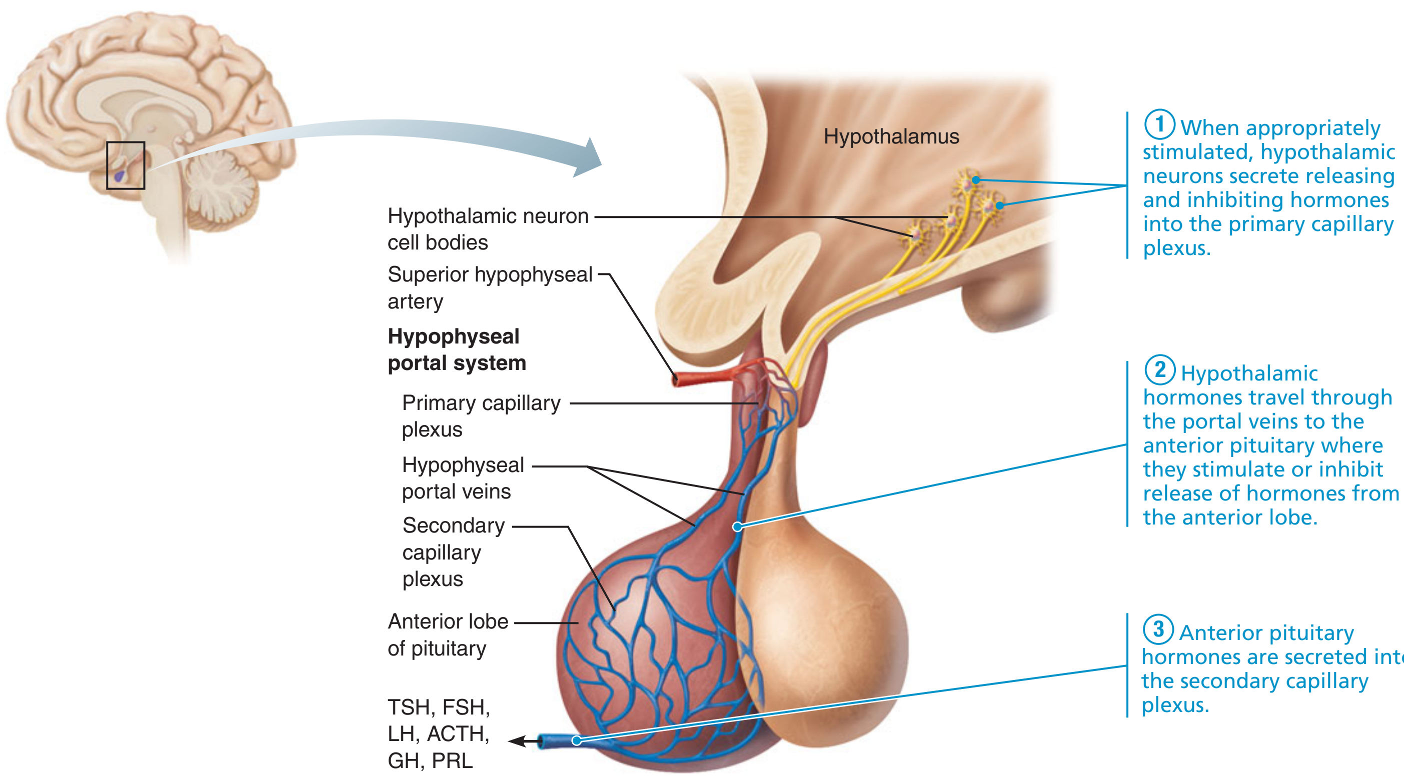
Releasing hormones from the hypothalamus signal the secretion of anterior lobe hormones **(Figure 17.4a)**. Releasing hormones made in hypothalamic neurons are secreted like neurotransmitters from the axon terminals of these neurons (Figure 17.4a, 1). (Note that in this case neurons are serving as endocrine cells.) The secreted releasing hormones enter a **primary capillary plexus** in the median eminence of the hypothalamus and then travel inferiorly in **hypophyseal portal veins** to a **secondary capillary plexus** in the anterior lobe. The releasing hormones leave the bloodstream and attach to the anterior lobe cells and stimulate these cells to secrete hormones (GH, LH, TSH, PRL, and so on) (Figure 17.4a, 2). The hormones secreted from the anterior lobe cells enter the secondary plexus. From there the newly secreted anterior lobe hormones proceed into the general circulation and travel to their target organs throughout the body (Figure 17.4a, 3).

Inhibiting hormones secreted by the hypothalamus follow the same route but function to inhibit hormone secretion by the cells of the anterior lobe.

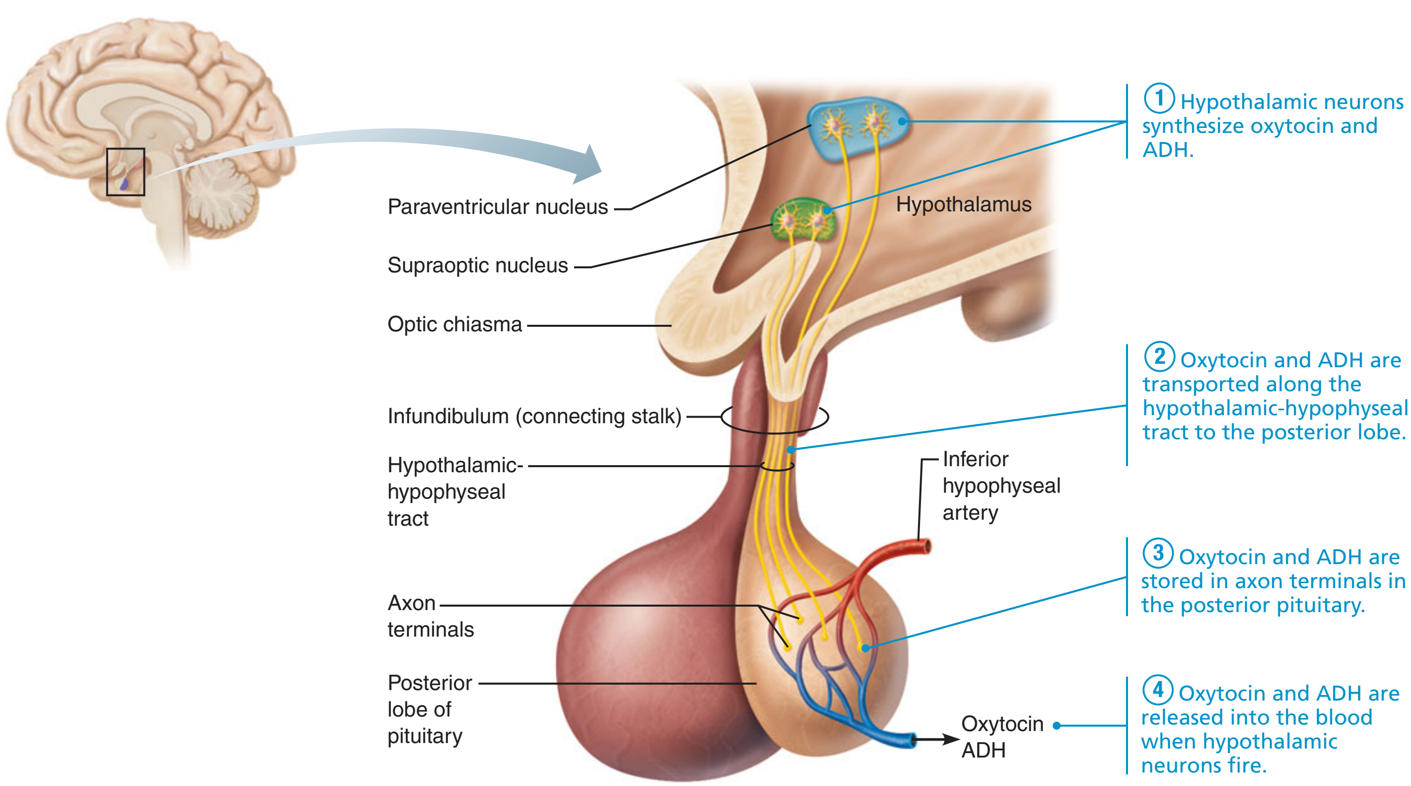
The primary and secondary capillary plexuses in the pituitary gland, plus the intervening hypophyseal portal veins, constitute the **hypophyseal portal system,** shown in Figure 17.4a.

A *portal system* refers to a system of blood vessels in which blood is collected from one capillary bed and travels in veins to a second capillary bed. In the first capillary bed, blood picks up molecules (in this case, releasing or inhibiting hormones) that are then carried to the tissues supplied by the second capillary bed (in this case, the anterior pituitary).

In summary, the hypothalamus controls the secretion of hormones by the anterior lobe, which in turn controls the secretion of hormones by the thyroid gland, the adrenal cortex, and the gonads. In this way, the brain controls these important endocrine glands, as illustrated in Figure 17.2c.



(a) Relationship between the anterior pituitary and the hypothalamus



(b) Relationship between the posterior pituitary and the hypothalamus

FIGURE 17.4 **Relationships of the pituitary gland and hypothalamus.**

The Posterior Lobe

The posterior lobe, which secretes two hormones, is structurally a part of the brain (Figure 17.4b). It consists of nervous tissue that contains unmyelinated axons and neuroglial cells. Its axons make up the **hypothalamic-hypophyseal tract,** which arises from neuron cell bodies in the supraoptic and paraventricular nuclei in the hypothalamus and ends in axon terminals in the pars nervosa. The posterior lobe hormones are made in the neuron cell bodies, transported along the axons, and stored in dilated axon terminals called *neurosecretory bodies (Herring bodies)* (Figure 17.4b 1 through 3). When the neurons fire, they release the stored hormones into a capillary bed in the pars nervosa for distribution throughout the body (Figure 17.4b 4). Therefore, the posterior lobe does not make hormones but only stores and releases hormones produced in the hypothalamus. The posterior lobe releases two peptide hormones: *antidiuretic hormone* (an″tĭ-di″u-ret′ik; "inhibiting urination") and *oxytocin* (ok″sĭ-to′sin; "childbirth hormone"). See Table 17.1, p. 521.

Made in the neurons of the supraoptic nucleus, **antidiuretic hormone (ADH),** also called *vasopressin,* targets the kidneys. They respond by resorbing more water and returning it to the bloodstream. The details of this process are described with the urinary system, Chapter 24. In this way, ADH helps the body retain as much fluid as possible when thirst (dehydration) or fluid loss (severe bleeding) occurs. Also, when fluid loss lowers blood pressure, ADH signals the peripheral arterioles to constrict, thus raising blood pressure to normal (*vasopressin* = vessel constrictor).

Oxytocin, produced in the paraventricular nucleus, induces contraction of the smooth musculature of reproductive organs in both males and females. Most important, it signals the smooth muscle in the wall of the uterus to contract, expelling the infant during childbirth; it also induces contraction of muscle-like cells (myoepithelial cells) around the secretory alveoli in the breast to eject milk during breast-feeding. Finally, in monogamous mammals both oxytocin and ADH cause a desire to cuddle, groom, and bond with a mate. Their roles in human socialization are under investigation.

THERAPEUTIC USES OF OXYTOCIN When a pregnancy has lasted well beyond the estimated due date, a physician may deem it necessary to induce labor. The most effective way of inducing labor is to inject the mother with natural or synthetic oxytocin, which initiates uterine contractions. Oxytocin also functions to stop the bleeding following delivery (by causing constriction of the ruptured blood vessels at the site of placental detachment) and to stimulate the ejection of milk by the mammary glands. This dual function of oxytocin on both uterine and mammary tissue is the cause of the intense and painful uterine contractions that can occur during breast-feeding in the early postpartum weeks.

check your understanding

3. How do tropic hormones secreted by the pituitary differ in action from the other pituitary hormones?
4. Where are the hormones produced that are secreted by the posterior lobe of the pituitary? Where are the hormones produced that are secreted by the anterior lobe?
5. Name the target organ(s) for each pituitary hormone listed: (a) oxytocin, (b) ACTH, (c) FSH, (d) ADH.

For answers, see Appendix B.

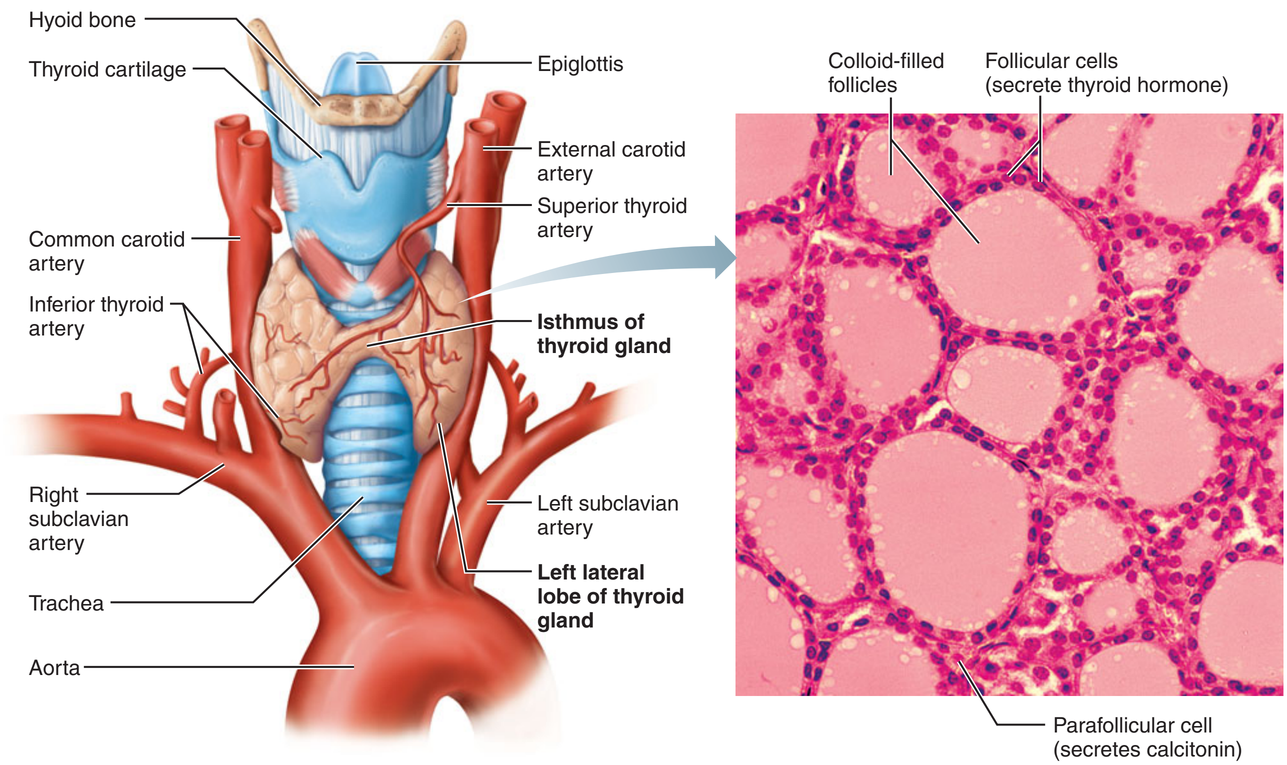
The Thyroid Gland

- Describe the anatomy of the thyroid gland.
- Define and describe the effects of thyroid hormone (TH) and calcitonin, and explain how TH is secreted.

The butterfly-shaped **thyroid gland** is located in the anterior neck, on the trachea just inferior to the larynx. It has two lateral **lobes** (the butterfly's "wings") connected by a median bridge called the **isthmus** **(Figure 17.5a)**. You may be able to feel the isthmus of the thyroid gland as a spongy cushion over the second to fourth tracheal ring. Then, try to palpate the two soft lateral lobes of your thyroid gland along the sides of the trachea. The thyroid gland is the largest purely endocrine gland in the body and has a prodigious blood supply from the superior and inferior thyroid arteries.

Internally, the thyroid gland is composed of hollow, approximately spherical **follicles** separated by an areolar connective tissue rich in capillaries (Figure 17.5b). The walls of each follicle are formed by a layer of cuboidal or squamous epithelial cells called **follicular cells,** and the central lumen is filled with a jellylike substance called **colloid** (kol′oid; "gluelike") consisting of **thyroglobulin** (thi″ro-glob′u-lin), a protein from which thyroid hormone is ultimately derived. Lying within the follicular epithelium are **parafollicular (C) cells,** which appear to project into the surrounding connective tissue.

The thyroid produces two hormones: thyroid hormone and calcitonin. The follicle cells of the thyroid gland secrete **thyroid hormone (TH),** a name that actually applies to two similar molecules called thyroxine (thi-rok′sin) or T_4, and triiodothyronine (tri″i-o″do-thi′ro-nēn) or T_3. Each of these hormone molecules is constructed from a pair of amino acids and contains the element iodine, which is essential to the function of the hormone. Thyroid hormone affects many target cells throughout the body. Its main function is increasing the basal metabolic rate (the rate at which the body uses oxygen to transform nutrients into energy). Individuals who secrete an excess of TH have a high activity level, are fidgety, and continually feel warm, whereas those who do not produce enough TH are sluggish and feel cold. These and other disorders of the endocrine glands are covered in more detail on pp. 531–532.



(a) Gross anatomy of the thyroid gland, anterior view

(b) Photomicrograph of thyroid gland follicles (160×)

FIGURE 17.5 The thyroid gland. (See *A Brief Atlas of the Human Body,* Second Edition, Plate 54.)

TH is made and secreted by the thyroid follicle cells. The follicular cells continuously synthesize the precursor protein thyroglobulin and secrete it into the center of the follicle for iodination and storage. The thyroid gland is the only endocrine gland that stores its hormone extracellularly and in large quantities—it stores enough TH to last several months. To initiate secretion of the stored TH into the blood, the *pituitary gland* releases thyroid-stimulating hormone (TSH), which signals the follicular cells to reclaim the thyroglobulin by endocytosis. Next, TH is cleaved off the thyroglobulin molecules by lysosomal enzymes in the cytoplasm of the follicular cell. TH then diffuses out of the follicular cells into the capillaries around the follicle.

The parafollicular cells of the thyroid secrete the protein hormone **calcitonin** (kal″sĭ-to′nin) when blood calcium levels are high. Calcitonin lowers blood levels of Ca^{2+} by slowing the calcium-releasing activity of osteoclasts in bone and increasing calcium secretion by the kidney. Calcitonin has no demonstrable function in adults; it seems to act mostly during childhood, when the skeleton grows quickly and osteoclast activity must be slowed to allow bone deposition and bone growth.

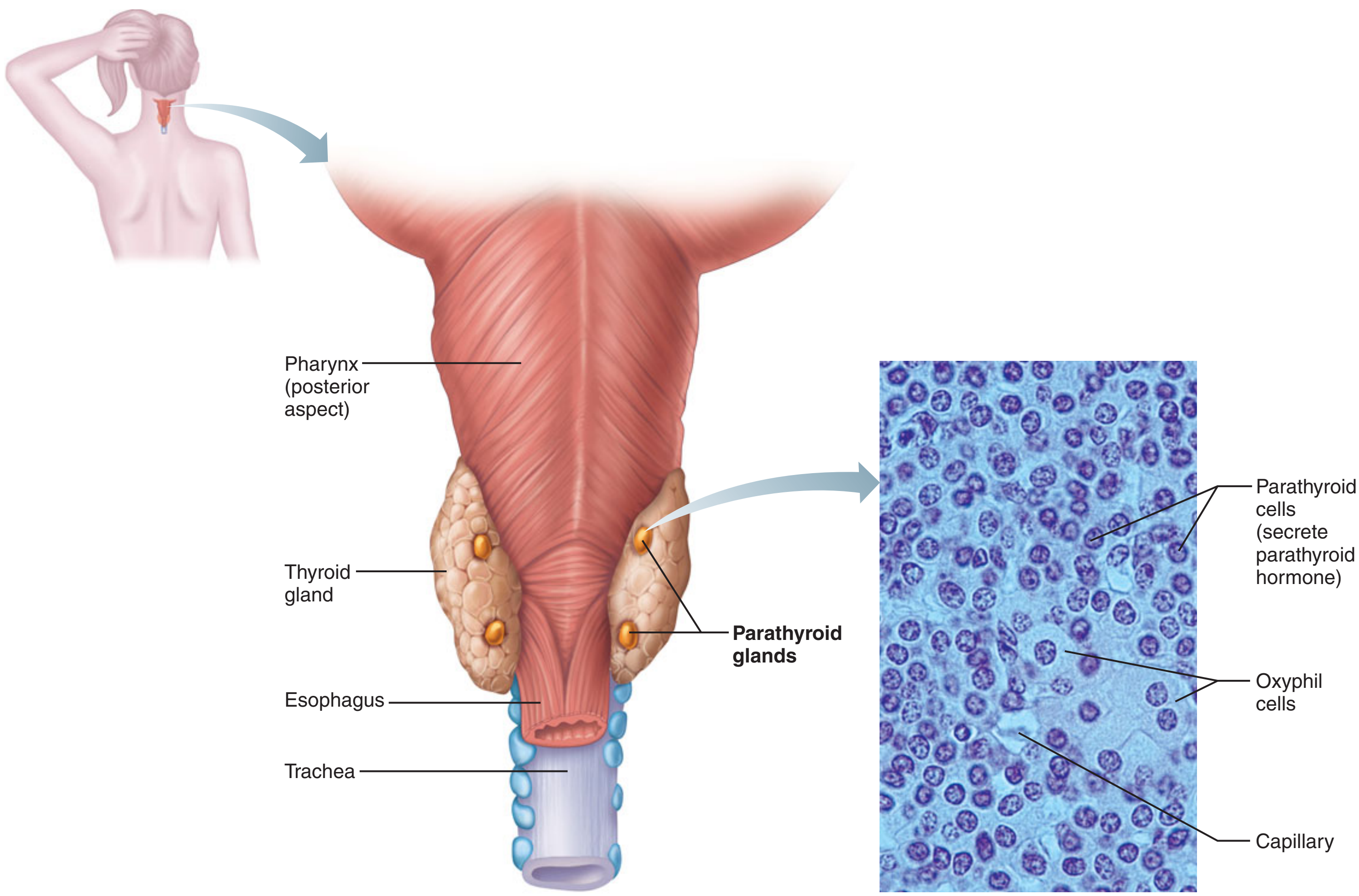
The Parathyroid Glands

➤ Describe the anatomy of the parathyroid gland and the function of parathyroid hormone.

The small, yellow-brown **parathyroid glands** lie on the posterior surface of the thyroid gland **(Figure 17.6a)**. Even though they may be embedded in the substance of the thyroid, the parathyroids always remain distinct organs surrounded by their own connective tissue capsules. Most people have two pairs of parathyroid glands, but the precise number varies among individuals. As many as eight glands have been reported, and some may be located in other regions of the neck or even in the thorax.

Histologically, the parathyroid gland contains thick, branching cords composed of two types of endocrine cells (Figure 17.6b): Small, abundant **parathyroid cells** (chief cells) and rare, larger **oxyphil cells** (ok′sĭ-fil; "acid-loving" = "stains with acidic dyes"). The function of oxyphil cells is unknown. The parathyroid cells produce a small protein hormone called **parathyroid hormone** (**PTH,** or **parathormone**), which increases the blood concentration of Ca^{2+} whenever it falls below some threshold value. PTH raises blood calcium by (1) stimulating osteoclasts to release more Ca^{2+} from bone, (2) decreasing the excretion of Ca^{2+} by the kidney, and (3) activating vitamin D, which stimulates the uptake of Ca^{2+} by the intestine.

PTH is essential to life because low Ca^{2+} levels lead to lethal neuromuscular disorders. Before PTH was discovered, it was observed that some patients recovered uneventfully after partial (or even total) removal of the thyroid gland, but others exhibited uncontrolled muscle spasms and severe pain and soon died. The lethal neuromuscular disorders resulted when surgeons unwittingly removed the parathyroid glands along with the thyroid.



(a) Location of parathyroid glands, posterior view

(b) Photomicrograph of parathyroid gland tissue (360×)

FIGURE 17.6 The parathyroid glands. The parathyroid glands may be more inconspicuous than illustrated in (a).

Note that parathyroid hormone and calcitonin have *opposite,* or antagonistic, effects: PTH raises blood calcium, whereas calcitonin lowers it.

check your understanding

6. Would a patient with hypothyroidism (low thyroid hormone) have concerns about blood calcium regulation? Explain why or why not.

For the answer, see Appendix B.

The Adrenal (Suprarenal) Glands

➤ Name the two divisions of the adrenal gland and compare and contrast them in terms of their structure and the hormones they secrete.

The paired **adrenal (suprarenal) glands** are pyramidal or crescent-shaped organs perched on the superior surface of the kidneys **(Figure 17.7)**. Each adrenal gland is supplied by up to 60 small *suprarenal arteries,* which form three groups: the superior suprarenal arteries from the inferior phrenic artery, the middle suprarenal arteries from the aorta, and the inferior suprarenal arteries from the renal artery. The left *suprarenal vein* drains into the renal vein, whereas the *right suprarenal vein* drains into the inferior vena cava (diagrammed on p. 606). The nerve supply consists almost exclusively of sympathetic fibers to the adrenal medulla (discussed on p. 473).

Each adrenal gland is two endocrine glands in one (Figure 17.7a). The internal *adrenal medulla* is more like a cluster of neurons than a gland. It is derived from the neural crest and it acts as part of the sympathetic nervous system. The external *adrenal cortex,* surrounding the medulla and forming the bulk of the gland, is derived from somatic mesoderm. The cortex and medulla secrete hormones of entirely different chemical types, but all adrenal hormones help people cope with extreme situations associated with danger, terror, or stress.

The Adrenal Medulla

The centrally located **adrenal medulla** is discussed in Chapter 15 (p. 473) as a part of the autonomic nervous system, so it is covered only briefly here. Its spherical **chromaffin**

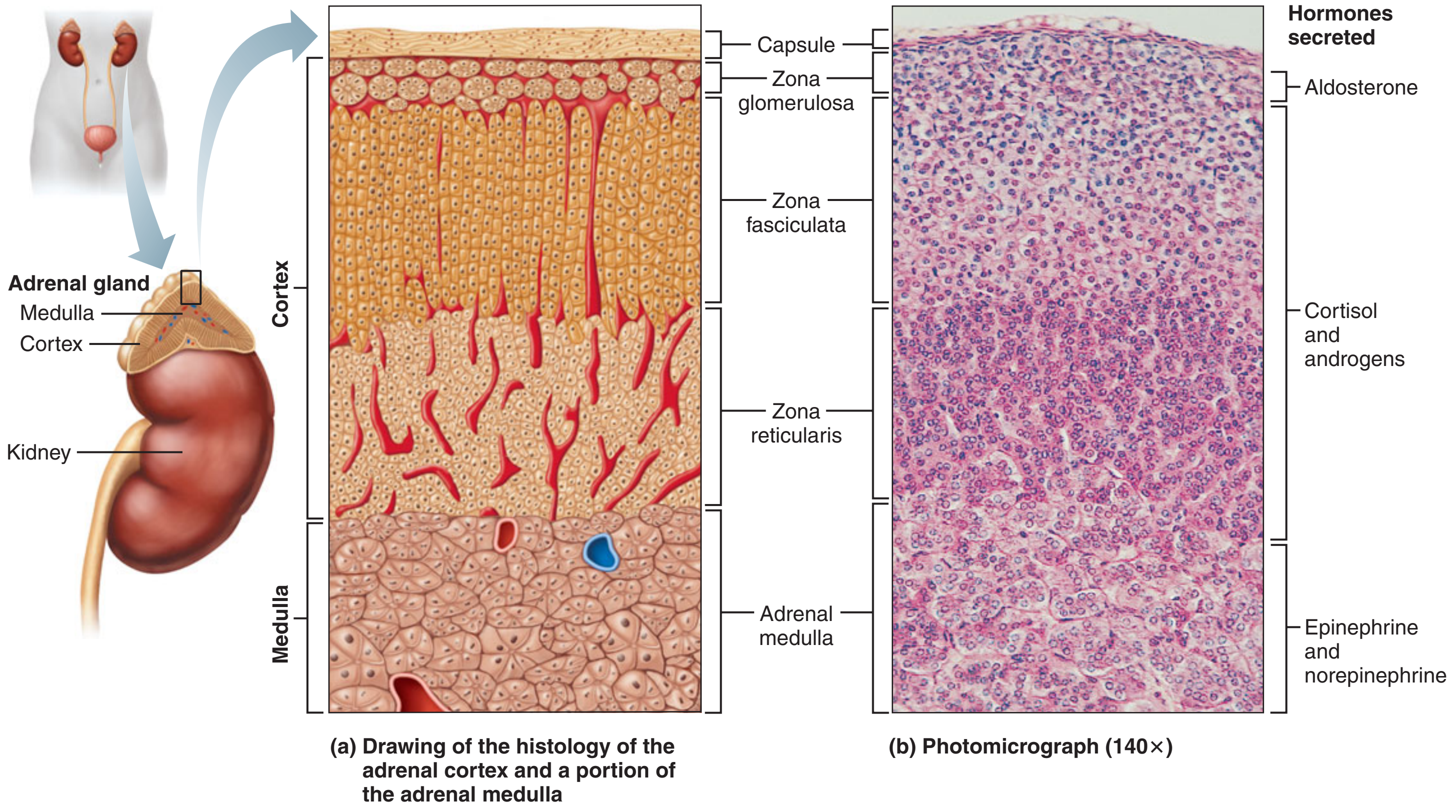


FIGURE 17.7 The adrenal gland, gross and microscopic structure. (See *A Brief Atlas of the Human Body*, Second Edition, Plate 55.)

(kro-maf′in) **cells** are modified ganglionic sympathetic neurons that secrete the amine hormones epinephrine and norepinephrine into the blood to enhance the fight-or-flight response. These hormones are stored in secretory vesicles within the cell that can be stained with salts containing chromium metal. (Indeed, *chromaffin* literally means "with an affinity for chromium.") Within the adrenal medulla, the chromaffin cells are arranged in spherical clusters (Figure 17.7b) with some branching cords.

The Adrenal Cortex

The thick **adrenal cortex** secretes a variety of hormones, all of which are lipid-based *steroid hormones*. Microscopically, this cortex exhibits three distinct layers, or zones (Figure 17.7). From external to internal, these are as follows:

1. **Zona glomerulosa** (glo-mer-u-lōs′ah), which contains cells arranged in spherical clusters (*glomerulus* = ball of yarn)
2. **Zona fasciculata** (fah-sik″u-lah′tah), whose cells are arranged in parallel cords (*fascicle* = bundle of parallel sticks) and contain an abundance of lipid droplets
3. **Zona reticularis** (rĕ-tik′u-lar″is), whose cells are arranged in a branching network (*reticulum* = network) and stain intensely with the pink dye eosin

The hormones secreted by the adrenal cortex are **corticosteroids** (kor″tĭ-ko-ste′roids), which, along with the sex hormones, are the body's major steroid hormones. Adrenal corticosteroids are of two main classes: *mineralocorticoids* (min″er-al-o-kor′tĭ-koids) and *glucocorticoids* (gloo″ko-kor′tĭ-koids).

The main **mineralocorticoid,** called **aldosterone** (al-dos′ter-ōn), is secreted by the zona glomerulosa in response to a decline in either blood volume or blood pressure, as occurs in severe hemorrhage. Aldosterone is the terminal hormone secreted by a complex cascade of hormonal secretions that is initiated in the kidneys in response to low blood volume or low blood pressure (the renin-angiotensin mechanism). To compensate for either decline, aldosterone prompts the ducts in the kidney to resorb more sodium into the blood; water passively follows, thus increasing blood volume.

Glucocorticoids, of which **cortisol** is the main type, are secreted by the zona fasciculata and zona reticularis to help the body deal with stressful situations such as fasting, anxiety, trauma, crowding, and infection. In essence, glucocorticoids keep blood glucose levels high enough to support the brain's activities while forcing most other body cells to switch to fats and amino acids as energy sources. Glucocorticoids also redirect circulating lymphocytes to lymphoid and peripheral tissues, where most pathogens are. When present in large quantities, however, glucocorticoids depress the inflammatory response and inhibit the immune system. Indeed, glucocorticoids are administered as anti-inflammatory drugs to treat rheumatoid arthritis, severe allergies, tendinitis, joint injuries, and other inflammatory disorders.

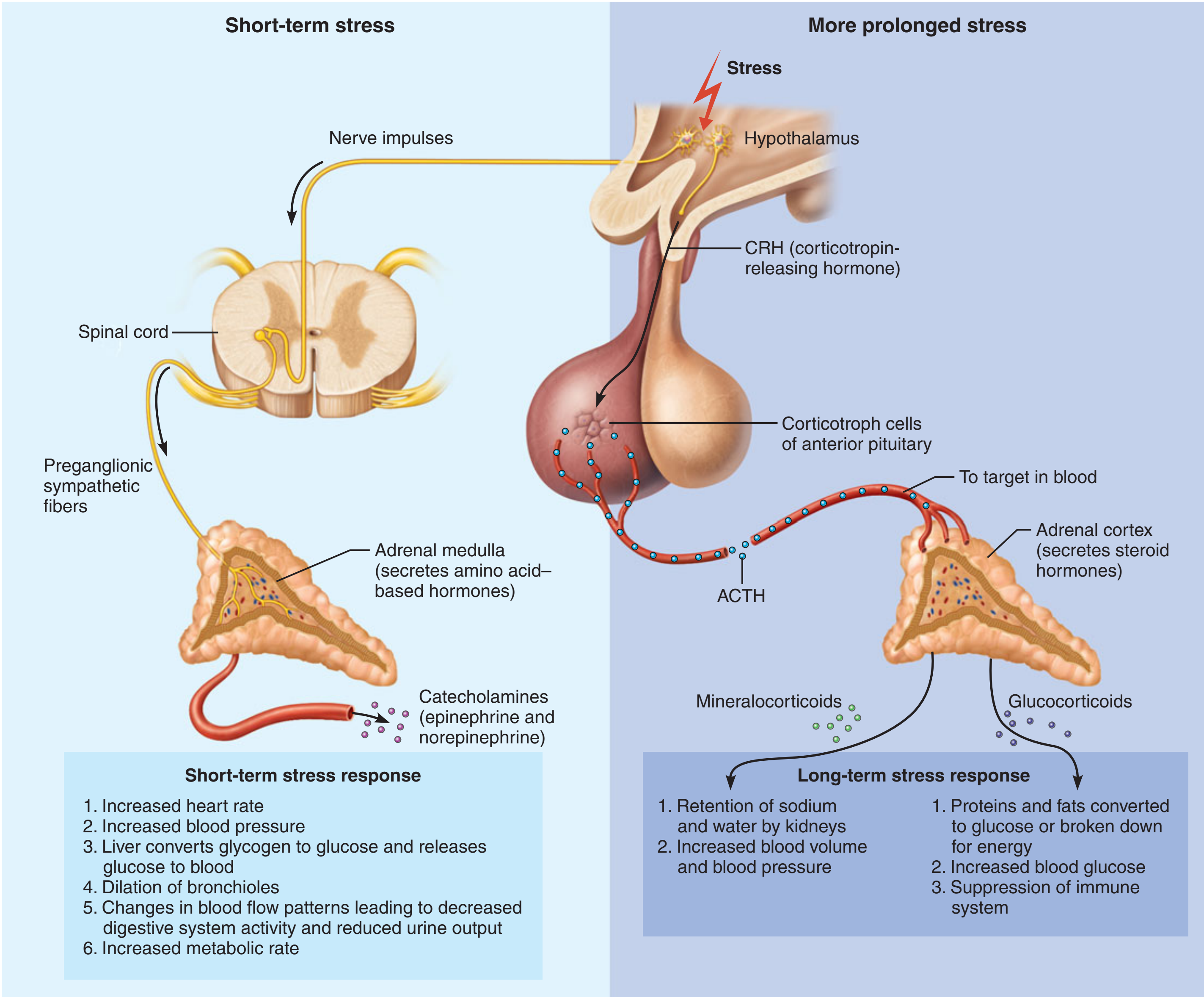


FIGURE 17.8 **Stress and the adrenal gland.**

In response to prolonged stress, the hypothalamus releases corticotropin-releasing hormone (CRH) **(Figure 17.8)**. This hormone reaches the adenohypophysis and stimulates the secretion of adrenocorticotropic hormone (ACTH). ACTH travels to the adrenal cortex, where it signals glucocorticoid and mineralocorticoid secretion. In addition to this hormonal pathway, the sympathetic nervous system can also stimulate glucocorticoid secretion. Figure 17.8 summarizes the response of the adrenal gland to both short-term and prolonged stress.

The zona reticularis also secretes large quantities of an androgen hormone called dehydroepiandrosterone (DHEA), the function of which remains unclear. After its secretion (via the stress-CRH-ACTH pathway) and its release from the adrenal cortex, DHEA is converted to testosterone and estrogens in the peripheral tissues. Proposed beneficial effects of DHEA include counteracting stress, boosting immunity, and improving mood. DHEA has also been suggested as an antiaging molecule. Levels of DHEA are high during young adulthood and decline with age. Despite the hype, clinical uses for this hormone have not been substantiated by scientific research.

check your understanding

7. What specific region of the adrenal gland produces aldosterone?
8. Why is the adrenal medulla referred to as a modified sympathetic ganglion?
9. What hormone directly stimulates the secretion of the glucocorticoids from the adrenal cortex, and where is this hormone produced?

For answers, see Appendix B.

The Pineal Gland

➤ Describe the endocrine functions of the pineal gland, pancreas, thymus, and gonads.

The **pineal gland** (pineal body) is a small, pinecone-shaped structure at the end of a short stalk on the roof of the diencephalon (see Figures 17.1 and 17.3b). Its endocrine cells, called *pinealocytes,* are arranged in both spherical clusters and branching cords. Pinealocytes are star-shaped cells with long, branching cell processes. Within the adult pineal gland, dense particles of calcium lie between the cell clusters, forming the "pineal sand." The pineal gland is easy to locate in X-ray images of the brain because the dense calcium minerals in the pineal sand are radiopaque (X rays cannot penetrate them). Thus it stands out in a radiograph and is used as a landmark for identifying other brain structures.

Via a remarkably indirect route, the brain signals the pinealocytes to secrete the hormone **melatonin,** which helps regulate circadian rhythms. During the darkness of night, the "clock" that controls daily rhythms and melatonin secretion—the suprachiasmatic nucleus of the hypothalamus (shown on p. 392)—responds to a lack of visual input from the retina by sending signals to the preganglionic sympathetic neurons in the upper thoracic spinal cord. The signals then go to ganglionic neurons in the superior cervical ganglion, whose axons run on the internal carotid artery to stimulate the pineal gland to secrete melatonin.

The Pancreas

Located in the posterior wall of the abdominal cavity, the tadpole-shaped **pancreas** contains both exocrine and endocrine cells. The exocrine *acinar cells,* forming most of the gland, secrete digestive enzymes into the small intestine during digestion of food.

The endocrine cells of the pancreas are contained in spherical bodies called **pancreatic islets** or **islets of Langerhans** (Figure 17.9), about a million of which are scattered among the exocrine acini. In each islet, the endocrine cells are arranged in twisted, branching cords separated by capillaries. The main cell types in the islets are alpha and beta cells. **Alpha (α) cells (A cells)** secrete **glucagon** (gloo′kah-gon), a protein hormone that signals *liver* cells to release glucose from their glycogen stores, thus raising blood sugar levels whenever they fall too low. **Beta (β) cells (B cells)** secrete **insulin** ("hormone from the islets"), a protein hormone that signals most cells of the body to take up glucose from the blood and promotes the storage of glucose as glycogen in the liver, thus lowering excessive blood sugar levels (after the digestion of a sugary snack, for example). Most alpha cells lie at the periphery of the pancreatic islets, whereas the more abundant beta cells occupy the central part.

The pancreatic islets also contain two rare cell types (not illustrated): **Delta (D) cells** secrete **somatostatin** (so″mah-to-stat′in), a peptide hormone that inhibits the secretion of glucagon and insulin by the nearby alpha and beta cells; **F (PP) cells** secrete **pancreatic polypeptide,** a hormone that may inhibit the exocrine activity of the pancreas.

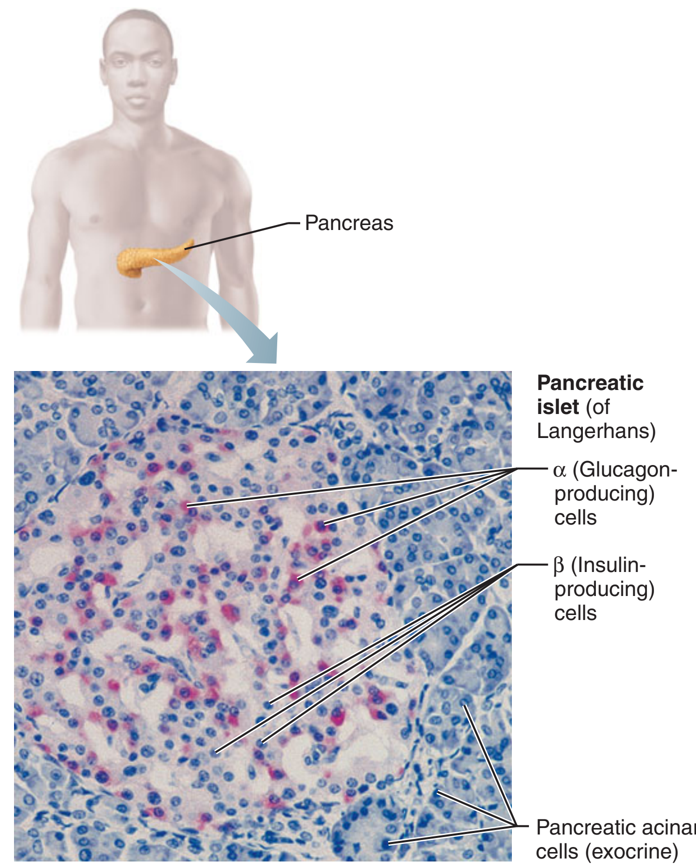


FIGURE 17.9 Photomicrograph of a pancreatic islet. A pancreatic islet is surrounded by the acinar cells (exocrine portion, stained blue-gray). Beta cells of the islets produce insulin (stained light purple), and the alpha cells produce glucagon (stained bright pink). (See *A Brief Atlas of the Human Body,* Second Edition, Plate 46.)

The Thymus

Located in the lower neck and anterior thorax is the lobulated **thymus** (see Figure 17.1). The thymus is an important immune organ, the site at which the white blood cells called T lymphocytes arise from precursor cells. This transformation seems to be stimulated by **thymic hormones,** which are secreted by the structural cells of the thymus, the epithelial reticular cells. Thymic hormones are a family of peptide molecules, including thymopoietin (thi″mo-poi′e-tin) and thymosin (thi′mo-sin). The thymus is described in detail with the lymphatic system in Chapter 21 on p. 627.

The Gonads

The gonads—**testes** and **ovaries**—are the main source of the steroid sex hormones. In the testes, **interstitial cells** between the sperm-forming tubules secrete **androgens** (primarily **testosterone**), which maintain the reproductive organs and the secondary sex characteristics of males and help promote the formation of sperm. In the ovaries, androgens are secreted and directly converted into *estrogens* by ovarian follicle cells. The follicle cells also produce *progesterone*. Following ovulation, estrogens and progesterone continue to be secreted by the remnant of the ovarian follicle, the *corpus luteum*. **Estrogens** maintain the reproductive organs and secondary sex characteristics of females, whereas **progesterone** signals the uterus to prepare for pregnancy. Full details are presented with the reproductive system, Chapter 25, pp. 734, 750, and 749.

OTHER ENDOCRINE STRUCTURES

- Name a hormone produced by the heart, and define diffuse neuroendocrine system (DNES).
- Briefly explain the endocrine functions of the placenta, kidney, and skin.

Other endocrine cells occur within various organs of the body, including the following:

1. **The heart.** The atria of the heart contain some specialized cardiac muscle cells that secrete **atrial natriuretic peptide (ANP)** (na″tre-u-ret′ik; "producing salty urine"), a hormone that decreases excess blood volume, high blood pressure, and high blood sodium concentration, primarily by stimulating the kidney to increase its secretion of salt and its production of salty urine.
2. **The gastrointestinal tract and its derivatives.** *Enteroendocrine cells* are hormone-secreting cells scattered within the epithelial lining of the digestive tract. Related endocrine cells occur within organs that derive from the embryonic gut, such as the respiratory tubes, pancreas, prostate, and thyroid gland. Collectively, all these scattered epithelial cells make up the **diffuse neuroendocrine system (DNES).** To give some concrete examples from this chapter, the parafollicular cells in the thyroid belong to this system, as do the cells of the pancreatic islets. Over 35 kinds of DNES cells secrete amine and peptide hormones that perform such functions as regulating digestion, controlling aspects of blood chemistry, and adjusting local blood flow. Many of these hormones are chemically identical to neurotransmitter molecules, and some of them signal nearby target cells without first entering the bloodstream. These are neuron-like characteristics, explaining why the DNES epithelial cells are called neuroendocrine cells.
3. **The placenta.** Besides sustaining the fetus during pregnancy, the placenta secretes several steroid and protein hormones—including estrogens, progesterone, corticotropin-releasing hormone, and human chorionic gonadotropin (see pp. 759–760)—that influence the course of pregnancy. *Human chorionic gonadotropin (hCG)* is the hormone that is tested for in pregnancy tests. It is produced as the fertilized egg implants into the uterus. A positive test indicates the presence of this hormone, thus a positive test for pregnancy.
4. **The kidneys.** Various cells in the kidneys produce hormones. The specialized muscle cells of the juxtaglomerular apparatus, the granular cells (see p. 717), secrete the protein hormone *renin,* which indirectly signals the adrenal cortex to secrete aldosterone. Other kidney cells—either in the interstitial connective tissue between the kidney tubules or in the endothelial cells of the peritubular capillaries—secrete *erythropoietin* (e-rith″ro-poi′e-tin), which signals the bone marrow to increase the production of red blood cells.
5. **The skin.** When exposed to ultraviolet radiation, keratinocytes in the epidermis convert a modified cholesterol molecule into a precursor of *vitamin D*. Vitamin D is a steroid hormone that is essential for calcium metabolism (see p. 109). The precursor molecules then enter the bloodstream through the dermal capillaries, undergo chemical modification in the liver, and become fully activated vitamin D in the proximal tubules of the kidney. Vitamin D signals the intestine to absorb Ca^{2+} from the diet. Without this vitamin, the bones weaken from insufficient calcium content (see discussion of rickets on p. 141).

check your understanding

10. Where are the endocrine cells of the pancreas located?
11. What structure, other than the ovaries, produces estrogens and progesterone?

For answers, see Appendix B.

DISORDERS OF THE ENDOCRINE SYSTEM

- Describe the effects of excessive and inadequate hormonal secretion by the pituitary, thyroid, and adrenal glands; define diabetes mellitus.

Most disorders of endocrine glands involve either a hypersecretion (oversecretion) or a hyposecretion (undersecretion) of a given hormone. Hypersecretion often results from a tumor in an endocrine gland, in which the rapidly proliferating tumor cells secrete hormone at an uncontrolled rate. Hyposecretion, by contrast, typically results from damage to the endocrine gland by infection, autoimmune attack, or physical trauma.

Pituitary Disorders

Some disorders of the adenohypophysis affect the secretion of growth hormone (GH). A tumor that causes hypersecretion of GH in children causes **gigantism,** in which the child grows exceptionally fast and becomes extremely tall, often reaching 2.4 meters (8 feet). If excessive amounts of GH are secreted after the bones' epiphyseal plates have closed, the result is **acromegaly** (ak-ro-meg′ah-le; "enlargement of the extremities"), characterized by enlargement of bony areas that still have active growth areas and are still responsive to GH—the hands, feet, and face.

Hyposecretion of GH in children produces **pituitary dwarfs,** who have bodies of normal proportions but rarely reach 1.2 meters (4 feet) in height. As discussed in **A Closer Look** on p. 530, many children with this condition can reach nearly normal stature if given GH injections.

a closer look

Potential Uses for Growth Hormone

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

GH is administered legally to children who do not produce it naturally or who have chronic kidney failure, to allow these children to grow to near-normal height. Unfortunately, some physicians have also prescribed GH for children who do produce it but who are shorter than their parents wish they were.

In a controversial move, the FDA recently approved GH for long-term treatment of children who are extremely short for no known reason. The FDA defines short stature as more than 2.25 standard deviations below the mean height for one's age and gender, that is, the shortest 1.2% of the population. For 10-year-old boys and girls, for example, this means a height shorter than 1.25 meters (4 feet 1 inch). (In adult men and women, this corresponds to heights of less than 1.6 meters [5 feet 3 inches] and 1.5 meters [4 feet 11 inches], respectively.) Many physicians question the FDA ruling because it allows medical intervention for a nonmedical problem. Furthermore, GH treatment is expensive—$10,000 to $40,000 per year depending on dosage, age, weight, and height—and the results are not necessarily dramatic: In one study, children who took GH for over 4 years ended up only 3.81 cm (1.5 inches) taller than children who took a placebo.

Should short children be "treated" with growth hormone?

Researchers have also discovered many nongrowth effects of GH, mainly by administering it to adults with a growth-hormone deficiency. GH decreases body fat and increases lean body mass, bone density, and muscle mass. It also increases performance of the muscle of the heart, decreases blood cholesterol, boosts the immune system, and perhaps improves psychological outlook. Such effects have led to abuse of GH by bodybuilders and athletes, which is one reason this substance remains restricted.

GH may also reverse some effects of aging. Many people naturally stop producing it after age 60, and this may explain why their ratio of lean-to-fat mass declines and their skin thins. Administration of GH to elderly patients can reverse these declines, which has led to media fanfare that GH is a "youth potion."

In one study, men and women (ages 65 to 88) who took GH for six months showed a significant increase in lean body mass and a decrease in fat tissue. However, although their muscle mass increased, their strength did not, and researchers speculate that the hormone caused their lean tissue to gain water, making cells bigger without improving their function. Men in the study showed improvements in aerobic capacity, but the women did not.

Offsetting these gains are the hormone's substantial side effects, which include fluid retention, carpal tunnel syndrome, joint and muscle pain, high blood sugar, and gynecomastia (breast enlargement in males). Hypertension, heart enlargement, diabetes, and colon cancer may result from high doses of the hormone, and edema and headaches occur with even small amounts. A careful study of very sick patients in intensive care units (where GH is routinely given to restore nitrogen balance) found that large doses are actually associated with *increased* mortality. Doctors caution that GH should not be administered to the very old or the critically ill. As for antiaging claims, at this point its disadvantages far outweigh its benefits.

GH may help AIDS patients, however. Because of improved antibiotics, fewer AIDS patients are dying from opportunistic infections, leaving more to die from "wasting" weight loss. It has been shown that injections of GH can actually reverse wasting during AIDS, leading to weight gain—a gain of lean muscle. In 1996, the FDA approved GH to treat such wasting.

GH is not a wonder drug, even in cases where it is beneficial. Clearly, intensive research into its potential benefits will keep this hormone in the public eye for years to come.

In **diabetes insipidus** (di″ah-be′tēz in-sĭ′pĭ-dus; "passing of dilute [urine]"), the pars nervosa of the posterior pituitary does not make or secrete sufficient antidiuretic hormone (or, more rarely, the kidney does not respond to this hormone). Because individuals with this condition produce large volumes of dilute urine, they compensate by drinking large quantities of water. Diabetes insipidus can be caused by either a blow to the head that damages the posterior pituitary, a tumor that compresses the pars nervosa, or kidney damage.

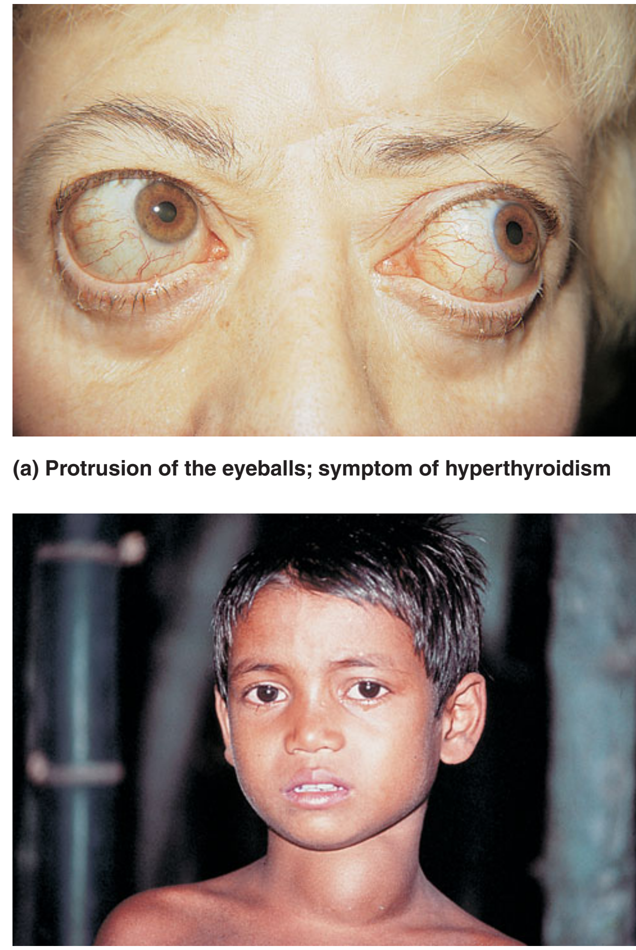
A Disorder of the Pancreas: Diabetes Mellitus

Diabetes mellitus, which affects about 7% of Americans and has a strong hereditary component, is caused either by insufficient secretion of insulin or resistance of body cells to the effects of insulin. As a result, glucose cannot enter most cells, so blood sugar remains high and glucose appears in an abundant urine. Because glucose is unavailable as fuel, the body's cells metabolize fats, whose acidic breakdown products, ketones, accumulate in the blood. Left untreated, the increased urination depletes the body of water and electrolytes, and the ketone acidosis depresses almost all physiological functions and leads to coma.

Of the two types of diabetes mellitus, the more serious is **type 1 diabetes** (formerly called **insulin-dependent diabetes**), which develops suddenly, usually before age 15. Because an autoimmune response destroys the insulin-secreting beta cells in the pancreas, insulin must be administered to type 1 diabetics several times daily to control blood glucose levels. After 20–30 years with the disease, most type 1 diabetics develop health-threatening complications: The high level of lipids in their blood predisposes them to atherosclerosis (hardening of the arteries discussed on p. 610), and the excessive sugar in their body fluids disrupts capillary functions (see *microangiopathy of diabetes* on p. 611). Research on type 1 diabetes has demonstrated that regular exercise and careful management of diet and blood sugar level can delay the onset of complications.

Type 2 (non-insulin-dependent) diabetes develops more slowly (usually appearing after age 40), and accounts for over 90% of all cases of diabetes. Most type 2 diabetics produce some insulin, but their cells have a reduced sensitivity to the effects of insulin. More easily managed than type 1, type 2 diabetes can usually be controlled by dietary modification (such as losing weight and avoiding high-calorie, sugar-rich foods) and regular exercise. If such measures fail, the condition is treated with insulin injections or oral medications that raise blood insulin levels or lower blood glucose levels.

Type 2 diabetes is increasing at an alarming rate in the United States. The increased incidence of this disease is associated with decreased activity levels and increased rates of obesity. Regular exercise has been found not only to help control type 2 diabetes but also to decrease the likelihood of its development. One component of this link between exercise and blood sugar regulation is a hormone produced by osteoblasts, the bone-producing cells. Osteoblast activity increases in response to weight-bearing exercise. *Osteocalcin*, a hormone secreted by osteoblasts, stimulates pancreatic secretion of insulin and stimulates fat cells to secrete a hormone that increases the insulin sensitivity of cells. Thus, increased activity of osteoblasts also functions to control blood sugar levels.



(a) Protrusion of the eyeballs; symptom of hyperthyroidism

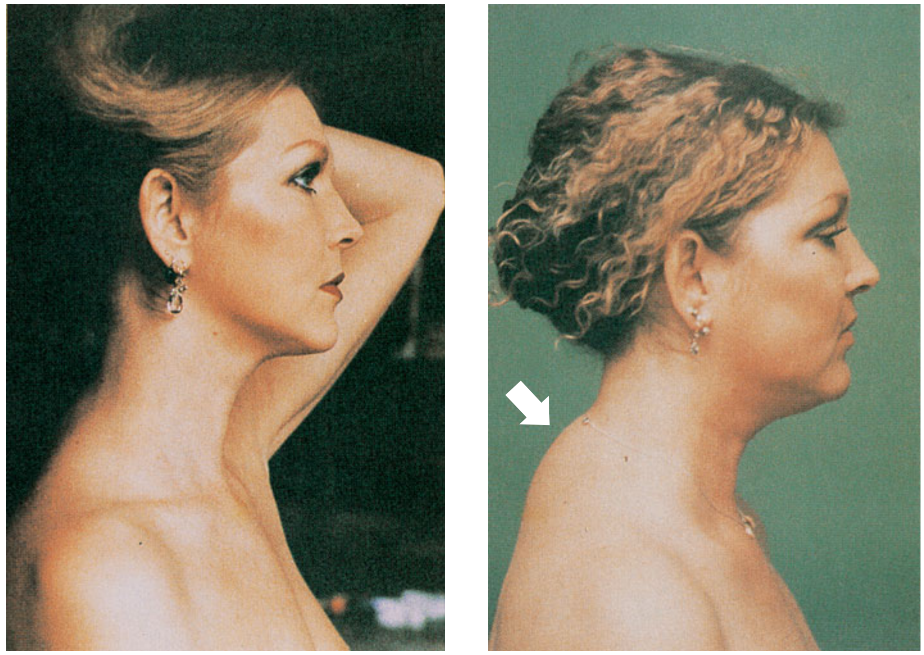
(b) An enlarged thyroid (goiter); due to insufficient iodine

FIGURE 17.10 Thyroid disorders.

Disorders of the Thyroid Gland

The most common form of hyperthyroidism is **Graves' disease,** apparently an autoimmune disease in which the immune system makes abnormal antibodies that mimic TSH and stimulate the oversecretion of TH by follicular cells of the thyroid. Typical signs and symptoms of Graves' disease include elevated metabolic rate, rapid heart rate, sweating, nervousness, and weight loss despite normal food intake. Additionally, the eyeballs may protrude, perhaps because of edema in the orbital tissue behind the eyes or because the abnormal antibodies affect the extrinsic eye muscles **(Figure 17.10a)**. Graves' disease develops most often in middle-aged women and affects 1 of every 20 women overall.

Insufficient secretion of TH produces different effects at different stages of life. In adults, such hyposecretion of TH results in **adult hypothyroidism** or **myxedema** (mik″se-de′mah; "mucous swelling"), typically an autoimmune disease in which



(a) Patient before onset

(b) Same patient with Cushing's syndrome. The white arrow shows the characteristic "buffalo hump" of fat on the upper back.

FIGURE 17.11 The effects of excess glucocorticoid.

antibodies attack and destroy thyroid tissue. Signs and symptoms of this condition, which occurs in 7% of women and 3% of men, include a low metabolic rate, weight gain, lethargy, constant chilliness, puffy eyes, edema, and mental sluggishness (but not retardation).

Hypothyroidism can also result from an insufficient amount of iodine in the diet. In such cases, the thyroid gland enlarges, producing in the anterior neck a large, visible lump called an **endemic goiter** (Figure 17.10b). Because the cells of the thyroid follicles produce colloid but cannot iodinate it or make functional hormones, the pituitary gland secretes increasing amounts of TSH in a futile attempt to stimulate the thyroid to produce TH. This action causes the follicles to accumulate ever more colloid, and the thyroid gland swells. The commercial marketing of iodized salts has significantly reduced the incidence of goiters in regions that have iodine-poor soils or lack access to iodine-rich shellfish.

In children, hypothyroidism leads to **cretinism** (cre′tĭ-nizm), a condition characterized by a short, disproportionate body, a thick tongue and neck, and mental retardation.

Disorders of the Adrenal Cortex

Hypersecretion of glucocorticoid hormones leads to **Cushing's disease (Cushing's syndrome),** caused either by an ACTH-secreting pituitary tumor or (rarely) by a tumor of the adrenal cortex. This condition is characterized by high levels of glucose in the blood, loss of protein from muscles, and lethargy. The so-called "cushingoid signs" include a swollen face and the redistribution of fat to the posterior neck, causing a "buffalo hump" **(Figure 17.11)**, as well as depression of the immune and inflammatory responses. Mild cases can result from large doses of glucocorticoids prescribed as drugs to suppress inflammation.

Addison's disease, the major hyposecretory disorder of the adrenal cortex, usually involves deficiencies of both glucocorticoids and mineralocorticoids. Blood levels of glucose and sodium drop, and severe dehydration and low blood pressure are common. Other symptoms include fatigue, loss of appetite, and abdominal pain.

check your understanding

12. Addison's, Graves', and Cushing's (sounds like a law firm): Name the endocrine gland affected by each disorder, whether hypersecretion or hyposecretion is the cause, and the typical symptoms of each.

For answers, see Appendix B.

THE ENDOCRINE SYSTEM THROUGHOUT LIFE

➤ Describe the development of the major endocrine glands.

➤ Describe the effect of aging on some endocrine organs.

The diverse and widely distributed endocrine organs arise from all three germ layers.

The *thyroid gland* forms from a thickening of endoderm on the floor of the pharynx **(Figure 17.12a)** that first appears on the posterior part of the future tongue and then migrates

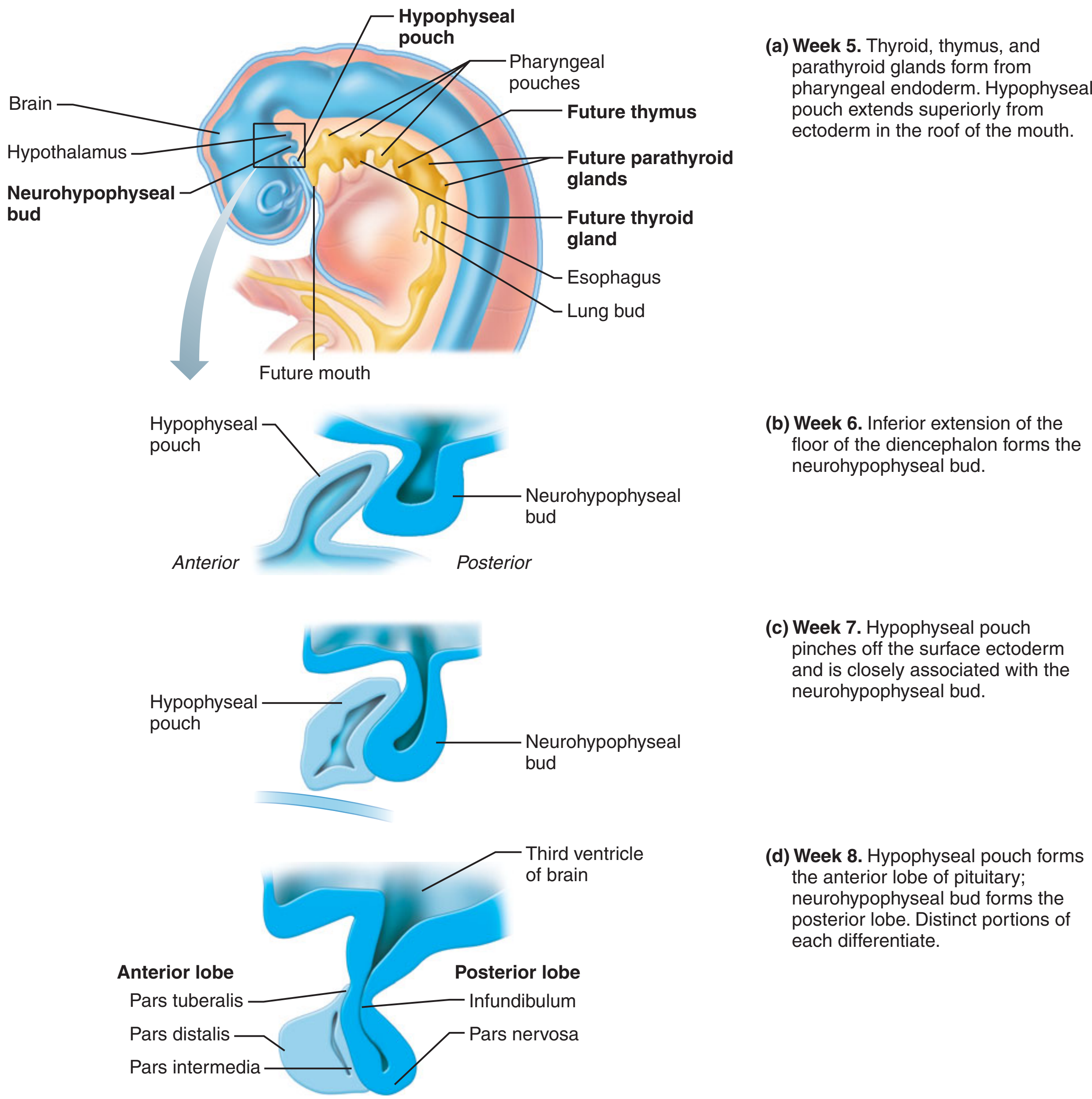


FIGURE 17.12 Embryonic development of some major endocrine organs.

caudally into the neck. Both the *parathyroid glands* and the *thymus* arise from the endoderm lining the pharyngeal pouches and then migrate to their final positions in the neck and thorax. The parafollicular cells arise in the wall of the last pharyngeal pouch and then migrate caudally, into the thyroid gland. The *pineal gland* arises from ectodermally derived ependymal cells that line the roof of the embryonic diencephalon. (Remember ependymal cells are the glial cells that line the hollow neural tube.)

The *pituitary gland* has a dual origin (Figure 17.12b and c). The anterior lobe arises from the roof of the mouth as a pouch of ectoderm—the **hypophyseal pouch,** or *Rathke's pouch.* This pouch contacts the future posterior lobe, which grows inferiorly from the floor of the brain as the **neurohypophyseal bud.**

The adrenal gland also has a dual embryonic origin (see Figure 15.13, p. 478). Whereas its medulla originates from the neural crest cells of nearby sympathetic trunk ganglia, the cortex develops from somatic mesoderm lining the coelom on the dorsal abdominal wall.

Barring hypersecretory and hyposecretory disorders of the endocrine glands, most endocrine organs operate smoothly throughout life until old age. Then, a number of changes become evident. In the anterior pituitary, the amounts of connective tissue and aging pigment (lipofuscin) increase, vascularization decreases, and the number of hormone-secreting cells declines. These changes may or may not affect hormone production: For example, blood levels of TSH decline slightly with normal aging, ACTH remains constant, and gonadotropins actually *increase* with age.

The adrenal cortex also shows structural changes with age, but normal rates of glucocorticoid secretion appear to persist as long as an individual is healthy. No age-related changes in the release of the amine hormones epinephrine and norepinephrine by the adrenal medulla have been found.

The synthesis and release of thyroid hormones diminish somewhat with normal aging. Typically, the thyroid follicles are loaded with colloid in the elderly, and fibrosis of the gland occurs. Autoimmune diseases of the thyroid become common, affecting about 5% of older women.

The parathyroid glands change little with age, but a tendency for the concentration of PTH in the blood to increase compensates for a lowered intake of calcium and vitamin D as the quality of the diet declines. Furthermore, the decline in estrogen secretion after menopause may sensitize women to the bone-demineralizing effects of PTH.

Only growth hormone (GH) from the anterior pituitary, dehydroepiandrosterone (DHEA) from the adrenal cortex, and the sex hormones (estrogens and testosterone) show marked drops in secretion with age. The deterioration of the musculoskeletal, cardiovascular, immune, and other organs that accompany these hormonal declines is discussed elsewhere in this book (see pp. 257, 612, and 631). So closely do the effects of withdrawing these hormones parallel the symptoms of aging that all three have been commercialized as "antiaging drugs" in recent years.

RELATED CLINICAL TERMS

HYPERCALCEMIA Elevated concentrations of calcium ions in the blood caused by either primary hyperparathyroidism or malignancies. In primary hyperparathyroidism, a parathyroid gland spontaneously (usually as a result of a tumor) secretes large amounts of calcium-raising parathyroid hormone. Many different kinds of malignancies also raise blood calcium levels by secreting chemicals that either stimulate osteoclasts to dissolve bone or stimulate calcium resorption in the kidney.

HYPOPHYSECTOMY Surgical removal of the pituitary gland.

PANCREATIC TRANSPLANTATION A procedure performed on people with type 1 diabetes whose lives are threatened by gradually failing kidneys as *microangiopathy of diabetes* (p. 611) destroys the kidney capillaries. The transplanted pancreas secretes insulin and halts the diabetes, and a healthy kidney may be transplanted at the same time to take over for the recipient's failing kidneys. The donated pancreas is placed in the pelvis and sutured to the bladder so that the digestive enzymes it produces can drain into the bladder and be flushed from the body in the urine, instead of irritating the pelvic peritoneum and causing peritonitis. The recipient must take immunosuppressive drugs for life. The success rate for pancreatic transplantation is about 70%. Techniques to transplant only the pancreatic islets have been developed. Islets from a deceased donor are injected into the recipient's liver. Transplanted islets become vascularized and start secreting insulin. Although still experimental, this treatment has met with a moderate degree of success. It also requires that the recipient take immunosuppressive drugs for life.

PHEOCHROMOCYTOMA (fe″o-kro″mo-si″to′mah; "dusky color tumor") Tumor of the chromaffin cells of the adrenal medulla; results in excessive secretion of the hormones epinephrine and norepinephrine, which produces the symptoms of prolonged sympathetic response (especially hypertension).

PROLACTINOMA (*oma* = tumor) The most common type of pituitary gland tumor, characterized by a hypersecretion of prolactin, excessive secretion of milk, and menstrual disturbances in women. In men, it causes milk production, a loss of libido, and impotence.

PSYCHOSOCIAL DWARFISM Dwarfism (and failure to thrive) resulting from childhood stress and emotional disorders that suppress the hypothalamic release of growth hormone–releasing hormone and thus anterior pituitary secretion of GH.

THYROID CANCER The most common malignancy of the endocrine glands, affecting about 1% of all people, typically between the ages of 25 and 65; characterized by firm, fixed nodules in the thyroid. Incidence is increasing, especially among individuals who had external irradiation of the head and neck when young. Treatment of this highly curable cancer involves removing some or all of the thyroid, then administering a radioactive form of iodine, which is actively taken up by the remaining thyroid follicular cells (normal and cancerous). The sequestered radioactive iodine then kills the cancer cells with a minimum of harm to nonthyroidal tissues.

THYROID STORM (THYROID CRISIS) A sudden and dangerous increase in the effects of thyroid hormone resulting from excessive amounts of TH in the circulation; metabolic rate is greatly increased, as indicated by fever, rapid heart rate, high blood pressure, nervousness, and tremors. Precipitating factors include stressful situations, excessive intake of TH supplements, and trauma to the thyroid gland.

CHAPTER SUMMARY

You can use the following media study tool for additional help when you review specific key topics in Chapter 17.

PAL = ***Practice Anatomy Lab***™

1. Endocrine organs are ductless glands that release hormones into the blood or lymph.
2. Hormones are messenger molecules that travel in the circulatory vessels and signal physiological changes in target cells.
3. Hormonally regulated processes include reproduction, growth, mobilization of body defenses against stress, maintenance of the proper chemistry of the blood and body fluids, and regulation of cellular metabolism.

Overview (pp. 516–518)

Endocrine Organs (p. 516)

4. The endocrine organs are small and widely separated from one another within the body. The pure endocrine organs are the pituitary,

thyroid, parathyroid, adrenal, and pineal glands. Other organs that contain endocrine cells are the gonads, pancreas, kidney, alimentary canal, heart, thymus, and skin. The hypothalamus of the brain is a neuroendocrine organ.

5. Endocrine organs are richly vascularized.

6. Although most endocrine cells are modified epithelial cells, others are neurons, muscle cells, or fibroblast-like cells.

Hormones (pp. 516–518)

7. Most hormones are either amino acid derivatives (amines, peptides, proteins) or steroids (lipid-based molecules derived from cholesterol).

8. Hormones produce their effects by leaving the capillaries and binding to specific receptor molecules in or on their target cells. Such binding triggers a preprogrammed response in the target cell.

9. Endocrine organs are stimulated to release their hormones by humoral, neural, or hormonal stimuli. Hormonal secretion is controlled by feedback loops.

10. The hypothalamus of the brain regulates many functions of the endocrine system through the hormones it secretes.

The Major Endocrine Organs (pp. 518–529)

The Pituitary Gland (pp. 518–523)

11. The golf club–shaped pituitary gland is suspended from the diencephalon of the brain by its stalk (infundibulum) and lies in the hypophyseal fossa of the sella turcica of the sphenoid bone. It consists of an anterior lobe (adenohypophysis) and a posterior lobe (neurohypophysis).

12. The anterior lobe has three parts: pars distalis, pars intermedia, and pars tuberalis. The posterior lobe has two parts: pars nervosa and infundibulum.

13. The pituitary gland receives its rich blood supply from the superior and inferior hypophyseal arteries.

14. The largest part of the anterior lobe is the pars distalis. Its five cell types secrete seven protein hormones. Four of the hormones secreted are tropic hormones (TSH, ACTH, FSH, LH) that influence the secretion of other endocrine glands; three others directly influence nonendocrine target tissues.

15. The hormones secreted by the anterior lobe and their functions are as follows. Growth hormone (GH), secreted by somatotropic cells, stimulates growth of the body and skeleton, Thyroid-stimulating hormone (TSH), produced by thyrotropic cells, stimulates secretion of the thyroid gland. Adrenocorticotropic hormone (ACTH), which stimulates the secretion of hormones from the adrenal cortex, and melanocyte-stimulating hormone (MSH), whose function is uncertain, are secreted by corticotropic cells. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH), produced by gonadotropic cells, signal the maturation of sex cells and the secretion of sex hormones. Prolactin, secreted by prolactin cells, stimulates milk production in breast tissue.

16. The hypothalamus of the brain controls the secretion of hormones from the anterior lobe. First, certain hypothalamic neurons make releasing hormones and inhibiting hormones, which they secrete into a primary capillary plexus in the median eminence. These hormones then travel through hypophyseal portal veins to a secondary capillary plexus in the pars distalis. They leave this plexus to signal the anterior lobe cells to secrete their hormones, which then enter the secondary capillary plexus and travel to their target cells throughout the body.

17. The posterior lobe which consists of nervous tissue, contains the hypothalamic-hypophyseal axon tract. The cell bodies of the neurons that form this tract are located in the paraventricular and supraoptic nuclei of the hypothalamus. These neurons synthesize oxytocin and ADH (vasopressin), respectively, and store them in their axon terminals in the pars nervosa. Here, the stored hormones are released into capillaries when the neurons fire.

18. The posterior lobe hormones have the following functions: ADH increases resorption of water from the urine and raises blood pressure, and oxytocin induces labor and ejection of milk from the breasts. Both these hormones are involved with social bonding.

The Thyroid Gland (pp. 523–524)

19. The thyroid gland, which lies on the superior trachea, consists of spherical follicles covered by epithelial follicle cells and separated by a capillary-rich connective tissue. The follicles are filled with a colloid of thyroglobulin, a storage protein containing thyroid hormone.

20. Thyroid hormone (TH), which contains iodine and increases basal metabolic rate, is made continuously by follicular cells and stored within the follicles until TSH from the pituitary gland signals the follicular cells to reclaim the TH and secrete it into the extrafollicular capillaries.

21. Parafollicular cells protrude from the thyroid follicles and secrete the hormone calcitonin, which can lower blood calcium concentrations in children.

The Parathyroid Glands (pp. 524–525)

22. Several pairs of parathyroid glands lie on the dorsal aspect of the thyroid gland. Their parathyroid cells are arranged in thick, branching cords and secrete parathyroid hormone, which raises low blood calcium levels.

The Adrenal (Suprarenal) Glands (pp. 525–527)

23. The paired adrenal glands lie on the superior surface of each kidney. Each adrenal gland has two distinct parts, an outer cortex and an inner medulla.

24. The adrenal medulla consists of spherical clusters (and some branching cords) of chromaffin cells. Upon sympathetic stimulation, these cells secrete epinephrine and norepinephrine into the blood—the surge of adrenaline that is experienced during fight-or-flight situations.

25. The adrenal cortex has three layers: outer zona glomerulosa, middle zona fasciculata, and inner zona reticularis; the name of each zone describes its histological structure.

26. The steroid hormones secreted by the adrenal cortex (corticosteroids) include mineralocorticoids (mostly from the zona glomerulosa), glucocorticoids (mostly from the zona fasciculata and reticularis), and the androgen DHEA (from the zona reticularis). Mineralocorticoids (mainly aldosterone) conserve water and sodium by increasing resorption of these substances by the kidney. Glucocorticoids (mainly cortisol) help the body cope with stress by stabilizing blood glucose levels; in large quantities they also inhibit inflammation and the immune system. The functions of DHEA are unclear.

The Pineal Gland (p. 528)

27. The pineal gland, on the roof of the diencephalon, contains pinealocytes, which cluster into spherical clumps and cords separated by dense particles of calcium called pineal sand.

28. Pinealocytes secrete the hormone melatonin, which helps regulate circadian rhythms. This secretion is signaled by the suprachiasmatic nucleus of the hypothalamus through a sympathetic pathway.

The Pancreas (p. 528)

29. The endocrine structures in the pancreas are the spherical pancreatic islets. These islets consist of alpha (α), beta (β), delta (Δ) and F (PP) cells arranged in twisting cords.

30. Alpha cells secrete glucagon, which raises blood sugar levels, whereas beta cells secrete insulin, which lowers blood sugar levels.

The Thymus (p. 528)

31. The thymus, an important organ of the immune system, secretes thymic hormones that are essential for the production of T lymphocytes.

The Gonads (pp. 528–529)

32. Various cells in the ovaries and testes secrete steroid sex hormones, estrogens and androgens.

Other Endocrine Structures (p. 529)

33. Some muscle cells in the atria of the heart secrete atrial natriuretic peptide (ANP), which stimulates loss of body fluids and salts through the production of a sodium-rich urine.

34. Endocrine cells are scattered within the epithelium of the digestive tube and other gut-derived organs (respiratory tubes and so on). These epithelial cells, which have some neuronlike properties, make up the diffuse neuroendocrine system (DNES). There are many classes of DNES cells, some of which secrete hormones that regulate digestion.

35. The placenta secretes hormones of pregnancy, the kidney secretes renin and erythropoietin, and the skin produces vitamin D.

PAL **Human Cadaver/Endocrine System**

Disorders of the Endocrine System (pp. 529–532)

36. Most disorders of endocrine glands involve either hypersecretion or hyposecretion of a hormone. *Hyper*secretion of GH leads to gigantism, of TH leads to Graves' disease, and of ACTH or glucocorticoids leads to Cushing's disease. *Hypo*secretion of GH leads to pituitary dwarfism, of TH leads to adult hypothyroidism or cretinism, of glucocorticoids and mineralocorticoids leads to Addison's disease, and of insulin leads to type 1 diabetes mellitus.

The Endocrine System Throughout Life (pp. 532–534)

37. The endocrine glands have diverse developmental origins from all three germ layers. The anterior pituitary arises from ectoderm on the roof of the mouth, and the posterior pituitary arises from the floor of the brain. The endocrine organs in the neck (thyroid, parathyroids, thymus) derive from the endoderm of the pharynx. The pineal gland forms from the ectodermally derived ependyma of the roof of the brain, the adrenal medulla develops from sympathetic trunk ganglia, and the adrenal cortex arises from the mesoderm of the dorsal abdominal wall.

38. The efficiency of some endocrine organs gradually declines as the body ages. The hormones whose secretions decline most are GH, DHEA, estrogens, and testosterone.

REVIEW QUESTIONS

Multiple Choice/Matching Questions

For answers, see Appendix B.

1. The major stimulus for the release of estrogens is (a) hormonal, (b) humoral, (c) nervous.

2. Choose the correct hormone from the key for each description.

____ **(1)** stimulates cell division in the epiphyseal plates of growing bones

____ **(2)** involved in water balance; causes the kidneys to conserve water

____ **(3)** stimulates milk production

____ **(4)** stimulates milk ejection

____ **(5)** tropic hormone that stimulates the gonads to secrete sex hormones

____ **(6)** increases basal metabolic rate

____ **(7)** tropic hormone that stimulates the thyroid gland to secrete thyroid hormone

____ **(8)** adjusts blood sugar levels and helps the body cope with stress

____ **(9)** is secreted by the pineal gland

____ **(10)** increases blood calcium levels

____ **(11)** is secreted by the posterior lobe of the pituitary (two possible choices)

____ **(12)** the only steroid hormone in the list

Key:

(a) melatonin

(b) antidiuretic hormone (ADH)

(c) growth hormone (GH)

(d) luteinizing hormone (LH)

(e) thyroid hormone (TH)

(f) thyroid-stimulating hormone (TSH)

(g) prolactin (PRL)

(h) oxytocin

(i) cortisol

(j) parathyroid hormone (PTH)

3. The pars distalis of the anterior pituitary does not secrete (a) antidiuretic hormone, (b) growth hormone, (c) gonadotropins, (d) thyroid-stimulating hormone.

4. Endocrine cells secrete either protein hormones or steroid hormones. For each endocrine cell described, indicate whether it produces (a) a protein hormone or (b) a steroid hormone.

____ **(1)** any endocrine cell in the pars distalis

____ **(2)** interstitial cell in the testis

____ **(3)** parathyroid cells in the parathyroid gland

____ **(4)** zona fasciculata cell

____ **(5)** follicle cell in the ovary that secretes sex hormones

____ **(6)** parafollicular cells in the thyroid gland

5. From the key, choose the best description of histological structure for each of the following glands. More than one answer may be correct.

Key: **(a)** spherical clusters of cells **(d)** follicles
(b) parallel cords of cells **(e)** nervous tissue
(c) branching cords of cells

_____ **(1)** pars nervosa of pituitary gland
_____ **(2)** zona glomerulosa of adrenal gland
_____ **(3)** pars distalis of pituitary gland
_____ **(4)** thyroid gland
_____ **(5)** zona fasciculata of adrenal gland

6. The divisions of the posterior pituitary are the (a) anterior lobe and posterior lobe; (b) pars emphasis, metropolis, and hypothesis; (c) pars distalis, tuberalis, and intermedia; (d) pars nervosa and infundibulum; (e) pars glomerulosa, fasciculata, and reticularis.

7. Which of the following cells secrete releasing hormones? (a) neurons, (b) chromaffin cells, (c) cells in the anterior lobe of the pituitary, (d) parafollicular cells.

8. Chromaffin cells occur in the (a) parathyroid gland, (b) pars distalis, (c) pituitary gland, (d) adrenal gland, (e) pineal gland.

9. The anterior lobe of the pituitary gland is the same as the (a) neurohypophysis, (b) pars nervosa, (c) adenohypophysis, (d) hypothalamus.

10. Many endocrine glands produce multiple hormones. Indicate the two hormones from column B that are secreted by each endocrine gland listed in column A.

Column A	Column B
_____, _____ **(1)** thyroid gland	**(a)** glucagon
_____, _____ **(2)** pancreas	**(b)** calcitonin
_____, _____ **(3)** adrenal gland	**(c)** cortisol
_____, _____ **(4)** posterior lobe of the pituitary	**(d)** oxytocin
_____, _____ **(5)** ovaries	**(e)** progesterone
	(f) norepinephrine
	(g) insulin
	(h) antidiuretic hormone
	(i) estrogen
	(j) thyroid hormone

11. Indicate with a check mark which of the organs listed below have some endocrine function.

_____ (a) kidney, _____ (b) mammary glands, _____ (c) pancreas, _____ (d) stomach, _____ (e) heart, _____ (f) urinary bladder, _____ (g) respiratory tubes, _____ (h) skin, _____ (i) salivary glands, _____ (j) thymus.

Short Answer Essay Questions

12. (a) Describe where in the body each of the following endocrine glands is located: anterior and posterior lobe of the pituitary, pineal, thyroid, parathyroids, and adrenals. (b) List the hormones secreted by each of these glands.

13. The anterior lobe of the pituitary secretes so many hormones that it is often called the master endocrine organ, but it too has a "master." What structure controls the release of anterior pituitary hormones?

14. When Joshua explained to his classmate Jennifer that the thyroid gland contains parathyroid cells in its follicles and that the parathyroid cells secrete parathyroid hormone and calcitonin, Jennifer told him he was all mixed up again. Correct Josh's mistakes.

15. (a) Define hormone. (b) Name a hormone secreted by a muscle cell and a hormone secreted by a neuron.

16. On a realistic drawing of the endocrine glands in the body, such as a photocopy of Figure 17.1, indicate the gland associated with (a) cretinism, (b) diabetes mellitus, (c) acromegaly, (d) secreting thyroid-stimulating hormone, (e) secreting a hormone that regulates the nightly activities of our circadian rhythms, (f) secreting estrogens, (g) secreting DHEA.

17. On a realistic drawing of the endocrine glands in the body, trace the following hormones from their glands of origin all the way to their target organs: (a) vitamin D, (b) glucagon, (c) erythropoietin, (d) oxytocin.

18. On a realistic drawing of the endocrine glands in the body, mark and label the endocrine organs that develop from the (a) roof of the embryonic mouth, (b) floor of the diencephalon, (c) endoderm on the posterior part of the future tongue, (d) endoderm of the pharyngeal pouches (two answers here), (e) neural crest of early sympathetic trunk ganglia.

19. Compare and contrast the functions of both sets of capillaries in the hypophyseal portal system.

20. List the hormones secreted by each of the three zonas of the adrenal cortex.

CRITICAL REASONING & CLINICAL APPLICATION QUESTIONS

1. The brain senses when a person is in a stressful situation, and the hypothalamus responds by secreting a releasing hormone called corticotropin-releasing hormone, which, through a sequence of events, helps the body to deal with the stressful situation. Outline this entire sequence, starting with corticotropin-releasing hormone and ending with the release of cortisol. (As you do this, be sure to trace the hormones through the hypophyseal portal system and out of the pituitary gland.)
2. Jeremy, a 5-year-old boy, has been growing by leaps and bounds such that his height is 70% above normal for his age group. A CT scan reveals a pituitary tumor. (a) What hormone is being secreted in excess? (b) What condition will Jeremy exhibit if corrective measures are not taken?
3. An accident victim who had not been wearing a seat belt received trauma to his forehead when he was thrown against the windshield. The physicians in the emergency room worried that his brain stem may have been driven inferiorly through the foramen magnum. To help assess this, they quickly took a standard X-ray film of his head and searched for the position of the pineal gland. How could anyone expect to find this tiny, boneless gland in a radiograph?
4. Mrs. Giardino had an abnormally high concentration of calcium in her blood, and her physicians were certain she had a tumor of the parathyroid gland. However, when surgery was performed on her neck, the surgeon could not find the parathyroid glands at all. Where should the surgeon look next to find the tumorous parathyroid gland?
5. Explain how endocrine disorders produced the physical characteristics described: (a) obesity in a man with hypothyroidism, (b) small stature and gigantism in people with pituitary disorders, (c) facial hair on a woman with an adrenal tumor, and (d) protrusion of the eyes in a person with Graves' disease.
6. For what therapeutic purposes would pharmaceutical companies seek to design drugs that either mimic atrial natriuretic peptide (ANP) or slow the rate at which ANP is broken down in the body?