chapter 14

Endocrine System

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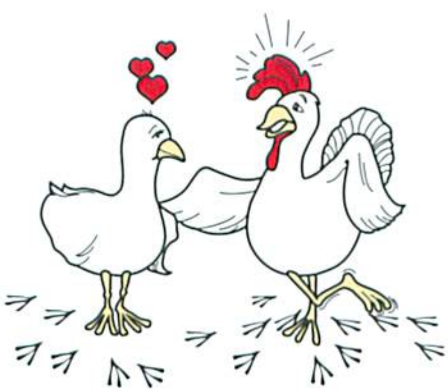
Key Terms

adenohypophysis (p. 263)
adrenal glands (p. 271)
catecholamines (p. 271)
endocrine glands (p. 259)
hormone (p. 259)
neurohypophysis (p. 266)
pancreas (p. 274)
parathyroid glands (p. 269)
pineal gland (p. 277)
steroids (p. 261)
thymus gland (p. 277)
thyroid gland (p. 267)

Objectives

1. List the functions of the endocrine system.
2. Discuss the role and function of hormones in the body, including:
   - Define *hormone*.
   - Explain the process by which hormones bind to the receptor sites of specific tissues (targets).
   - Explain the three mechanisms that control the secretion of hormones.
3. Discuss the pituitary gland, including:
   - Describe the relationship of the hypothalamus to the pituitary gland.
   - Describe the location, regulation, and hormones of the pituitary gland.
4. Identify the other major endocrine glands and their hormones, and explain the effects of hyposecretion and hypersecretion.

While performing his mating ritual, Rooster is dancing out the meaning of the word *hormone*, the main focus of the endocrine system. It is a Greek term meaning "to arouse or to set into motion." Rooster's testosterone has truly set him in motion. It has him prancing and dancing his mating ritual and has both him and Hen aroused.



The nervous system and the endocrine system are the two chief communicating and coordinating systems in the body. They regulate almost all organ systems. Although the nervous and endocrine systems work together closely, they have several differences. The nervous system communicates through electrical signals called *nerve impulses*. Nerve impulses communicate information rapidly and generally achieve short-term effects. The endocrine system, in contrast, communicates through chemical signals called *hormones*. The endocrine system responds more slowly and generally exerts longer-lasting effects.

ENDOCRINE GLANDS

The endocrine system is composed of endocrine glands that are widely distributed throughout the body (Figure 14-1). **Endocrine glands** secrete the chemical substances called *hormones*. Endocrine glands are ductless glands—that is, they secrete the hormones directly into the blood and not into ducts. For example, the pancreas secretes the hormone insulin into the blood, which then delivers the insulin to cells throughout the body. Many hormones are also secreted by organs, such as the stomach, kidney, and heart: these hormones will be described in later chapters.

HORMONES

A **hormone** is a chemical messenger that influences or controls the activities of other tissues or organs. In general, the endocrine system and its hormones help regulate metabolic processes involving carbohydrates, proteins, and fats. Hormones also play an important role in growth and reproduction and help regulate water and electrolyte balance. When you become hungry, thirsty, hot, or cold, your body's response includes the secretion of hormones. Finally, hormones help your body meet the demands of infection, trauma, and stress. The study of the endocrine system is called *endocrinology*.

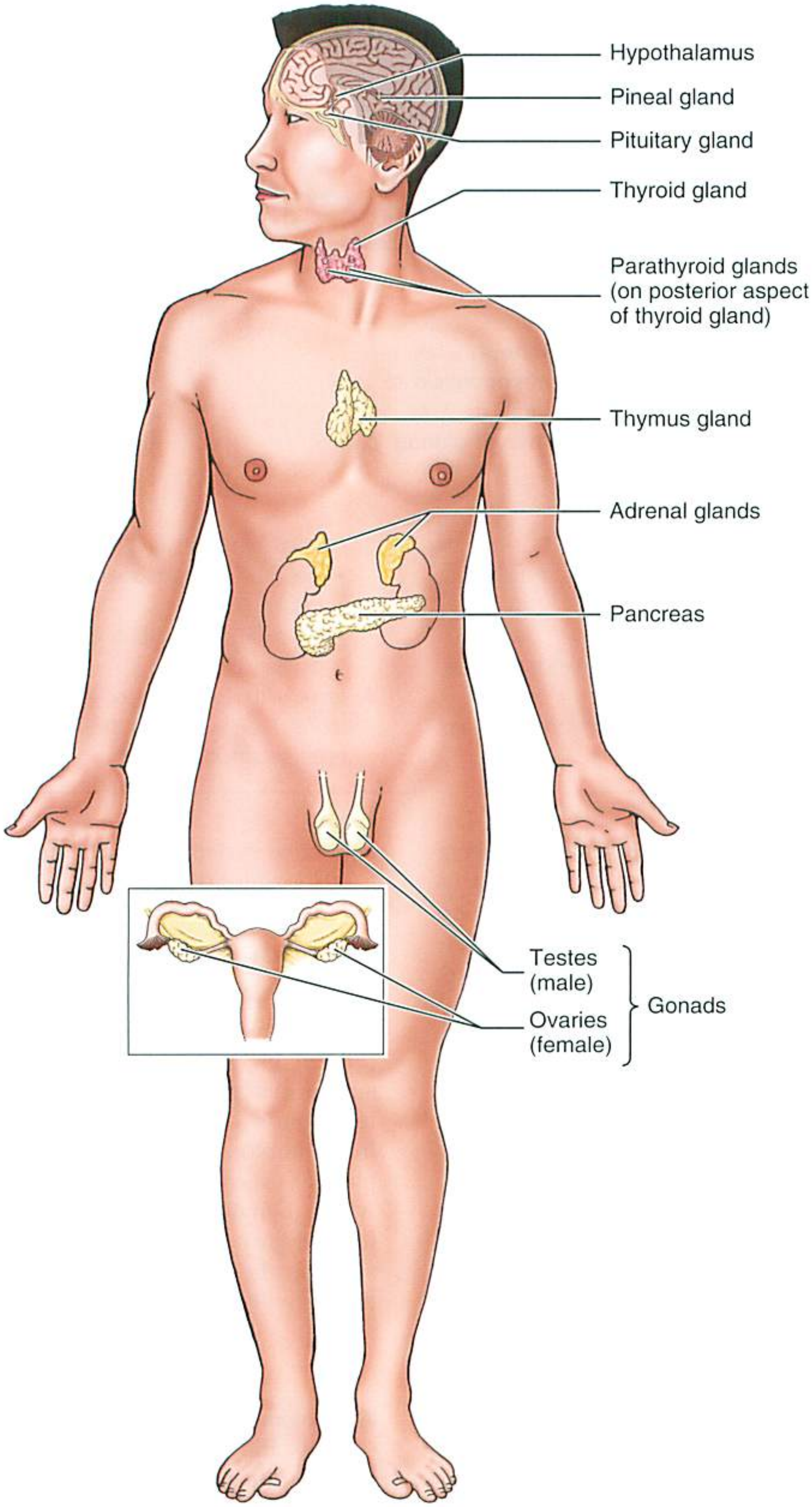


FIGURE 14-1 Major endocrine glands of the body.

CLASSIFICATION OF HORMONES

Chemically, hormones are classified as either proteins (and protein-related substances) or **steroids**. With the exception of secretions from the adrenal cortex and the sex glands, all hormones are protein or protein related. The adrenal cortex and the sex glands secrete steroids.

TARGETS

Each hormone binds to a specific tissue, called its *target tissue* or *organ* (Figure 14-2, *A*). The target tissue may be located close to or at a distance from the endocrine gland. Some hormones, such as thyroid hormone and insulin, have many target tissues and therefore exert more widespread, or generalized, effects. Other hormones, such as parathyroid hormone (PTH), have fewer target tissues and therefore exert fewer effects.

HORMONE RECEPTORS

Hormones bind to the receptor sites of the cells of their target tissues. The two types of receptors are those located on the outer surface of the cell membrane (membrane receptors) and those located within the cell (intracellular receptors).

How do hormones recognize their target tissues? The hormone and its receptor can be compared to a lock and key. The key must fit the lock. The same is true for the hormone and receptor; a part of the hormone (key) "fits into" its receptor (lock) on the target. Unless the match is perfect, the hormone cannot lock into and stimulate the receptor. For example, the hormone insulin circulates throughout the body in the blood and is therefore delivered to every cell in the body. Insulin, however, can only stimulate the cells that have insulin receptors. Insulin does not affect cells that lack insulin receptors. The lock-and-key theory guarantees that a particular hormone affects only certain cells. The hormone-receptor relationship ensures specificity, meaning that there is a specific hormone for each receptor.

Protein hormones generally bind to receptor sites located on the cell membrane (see Figure 14-2, *B*). The interaction of the hormone with its receptor stimulates the production of a second messenger such as cyclic adenosine monophosphate (cAMP). The cAMP, in turn, helps activate the enzymes in the cell. For

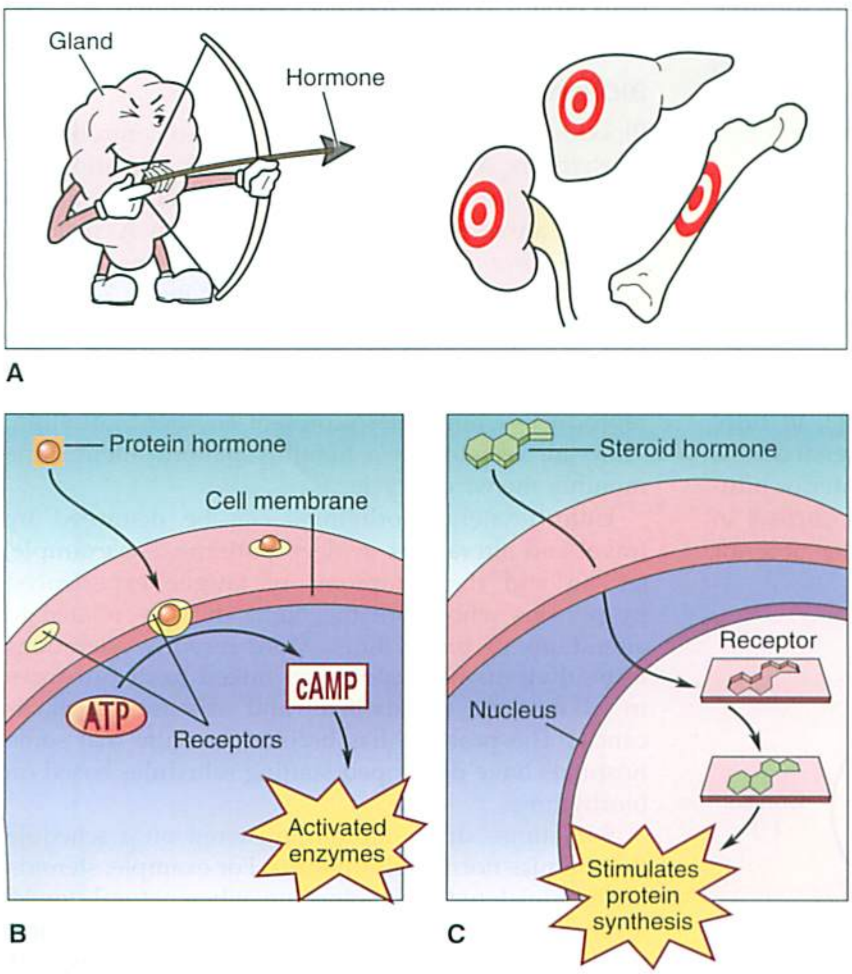


FIGURE 14-2 What hormones do. **A,** Hormones: aim at target tissues or target organs. **B,** Protein hormones and membrane receptors. **C,** Steroid hormones and intracellular receptors.

example, when epinephrine stimulates its receptors on the heart, cAMP is formed and then stimulates the heart itself.

The second type of receptor is located intracellularly (see Figure 14-2, C). Steroid hormones, which are lipid soluble, pass through the plasma membrane of the target cell and bind to receptors in the nucleus. The steroid-receptor complex then stimulates protein synthesis. The newly synthesized protein alters cellular function.

? Re-Think

1. What is a target organ?
2. How does a hormone recognize its target cell?

CONTROL OF HORMONE SECRETION

Three mechanisms control the secretion of hormones: feedback control loops, biorhythms, and control by the central nervous system (CNS).

NEGATIVE FEEDBACK LOOP, OR "ENOUGH IS ENOUGH"

Normal endocrine function depends on the normal plasma levels of hormones. Life-threatening complications develop when the glands hypersecrete or hyposecrete hormones. For example, if too much or too little steroid is secreted by the adrenal cortex, the person develops signs and symptoms that are potentially life threatening. So how does the adrenal cortex, a steroid-secreting gland, know when it has secreted enough steroid?

The pattern of adrenocorticotropic hormone (ACTH) and cortisol secretion is one example of a negative feedback loop (Figure 14-3). ACTH, secreted by the anterior pituitary gland, stimulates its target organ (adrenal cortex) to secrete cortisol. As blood levels of cortisol increase, the cortisol in the blood chemically "tells" the anterior pituitary gland to slow further secretion of ACTH. The diminished ACTH, in turn, decreases the secretion of cortisol by the adrenal cortex.

What information was fed back to the anterior pituitary gland? It was the increasing level of cortisol in the blood. What was the response of the anterior pituitary gland? The gland decreased its secretion of ACTH. Because the cortisol diminished the secretion of the anterior pituitary gland, the response is referred to as *negative feedback control*. Why doesn't the adrenal cortex completely stop its secretion of cortisol? Over time, the plasma level of cortisol declines as the hormone is degraded and eliminated from the body; the negative inhibition by cortisol is relieved and ACTH is again secreted. (ACTH regulation is described more completely later in the chapter.)

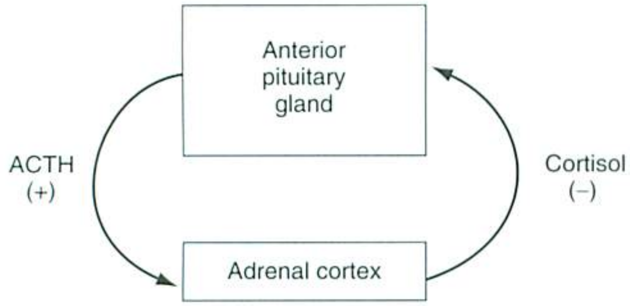


FIGURE 14-3 Negative feedback loop.

POSITIVE FEEDBACK LOOP, OR "GIVE ME MORE"

Unlike the inhibition of a negative feedback loop, a positive feedback loop causes an enhanced response, a self-amplification cycle in which a change is the stimulus for an even greater change in the same direction—the "give me more" effect. For example, during early labor, the head of the baby stretches the cervix, the neck of the uterus. The stretch causes nerve impulses to travel from the cervix to the brain, which in turn causes the secretion of a hormone called *oxytocin*. The oxytocin is carried by the blood to the uterus, where it stimulates the contraction of the uterus. In response to uterine contraction, the cervix is stretched further by the baby's head, causing the release of additional oxytocin. This positive feedback cycle continues until the baby is born. Positive feedback loops are often designed to produce a rapid response.

BIORHYTHMS

Blood levels of most hormones are also controlled by biorhythms. A biorhythm is a rhythmic alteration in a hormone's rate of secretion. Some hormones, such as cortisol, are secreted in a circadian rhythm. A circadian rhythm (*circa-* means "around"; *-dian* means "day") is a 24-hour rhythm; its pattern repeats every 24 hours. Because of its circadian rhythm, cortisol secretion is highest in the morning hours (peak at 8 AM) and lowest in the evening hours (lowest at midnight). The female reproductive hormones represent another biorhythm. They are secreted in a monthly pattern—hence, the monthly menstrual cycle.

Unfortunately, biorhythms can be disturbed by travel and alterations in sleep patterns. For example, jet lag and the symptoms of fatigue experienced by persons who work the night shift are related to alterations of biorhythms. More recently alterations in biorhythms have also been linked to disturbances in cholesterol metabolism and diseases such as cancer. The problem has become so acute that some hospitals have developed staffing schedules based on biorhythms.

Sometimes drugs are administered on a schedule that mimics normal biorhythms. For example, steroids are administered in the morning, when natural steroid levels are highest. Coordinating with the natural rhythms increases the effectiveness of the drug and causes fewer side effects. The effect of biorhythms on drug effects is so important that a branch of pharmacology addresses this issue: chronopharmacology.

CONTROL BY THE CENTRAL NERVOUS SYSTEM

The CNS helps control the secretion of hormones in two ways: activation of the hypothalamus and stimulation of the sympathetic nervous system. Think about this. The CNS exerts a powerful influence over the endocrine system. Because the CNS is also the center for our emotional life, it is not surprising that our emotions, in turn, affect the endocrine system.

For example, when we are stressed out, the CNS causes several of the endocrine glands to secrete stress hormones, thereby alerting every cell in the body to the threat. Many women have experienced the effect of stress on the menstrual cycle. Stress can cause the menstrual period to occur early or late; it may even cause the cycle to skip a month. These effects illustrate the power of emotions on our body. In fact, the functions of the nervous system and the endocrine system are so closely related that the word *psychoneuroendocrinology* is used.

? Re-Think

Referring to Figure 14-3, explain the concept of negative feedback control.

2+2 Sum It Up!

The endocrine system is composed of endocrine glands widely distributed throughout the body. The endocrine glands secrete hormones. Hormones stimulate target tissues by binding to cell receptors. The receptors are located either on the cell membrane or within the cell. Three control mechanisms regulate the secretion of hormones: negative and positive feedback loops, biorhythms, and CNS activity.

PITUITARY GLAND

PITUITARY GLAND AND HYPOTHALAMUS

The pituitary gland, also called the *hypophysis* (hye-POF-is-sis), is a pea-sized gland located in a depression of the sphenoid bone. It is attached to the undersurface of the hypothalamus by a short stalk called the *infundibulum*. The pituitary contains two main parts: the anterior pituitary gland and posterior pituitary gland. A tiny third lobe exists only in the fetus. The major hormones and their target glands are shown in Figure 14-4, *A*.

The secretion of the anterior pituitary gland is controlled by the hypothalamus. Although it is part of the brain, the hypothalamus secretes several hormones and is therefore considered to be an endocrine gland. These hormones are called *releasing hormones* and *release-inhibiting hormones*. They either stimulate or inhibit the secretion of anterior pituitary hormones. For example, prolactin-releasing hormone, secreted by the hypothalamus, stimulates the pituitary gland to secrete prolactin. Prolactin-inhibiting hormone (PIH), secreted by the hypothalamus, inhibits the secretion of prolactin by the anterior pituitary gland.

How do the hypothalamic hormones reach the anterior pituitary gland? The hypothalamus secretes its hormones into a network of capillaries (tiny blood vessels) that connect the hypothalamus with the anterior pituitary gland (see Figure 14-4, *B*). These connecting capillaries are called the *hypothalamic-hypophyseal portal system*. Thus, hormones secreted by the hypothalamus flow through the portal capillaries to the anterior pituitary.

Do You Know...

Why the Pituitary Gland Is "Uppity" but Not Snotty?

The pituitary gland is also known as the *master gland*, and a pretty important gland it is! When first discovered, however, the pituitary gland was relegated to the lowly role of mucus secretion (*pituita* is the Greek word for "mucus"). The gland was credited with secreting mucus as a cooling agent. After cooling the body, mucus was then eliminated through the nose. Obviously, this is not true. Mucus is secreted by the mucous membrane that lines the nasal passages and does not act as a coolant. Mucus merely does the nasal housework—it traps the dust and gets blown out of your nose. The pituitary gland, on the other hand, has more important things to do. It secretes many hormones and controls much of the endocrine function of the body. Unfortunately, this master gland is stuck with the name *pituitary* (mucus-making). Its other name, hypophysis, isn't much more flattering; it means "undergrowth" (referring to its location under the brain). Mucus and undergrowth—humbling for a master gland!

ANTERIOR PITUITARY GLAND

The anterior pituitary gland is composed of glandular epithelial tissue and is also called the **adenohypophysis** (ad-eh-no-hye-POF-i-sis). The anterior pituitary gland secretes six major hormones (Table 14-1; Figure 14-4, *A*). These hormones control other glands and affect many organ systems. In fact, the anterior pituitary affects so many other glands that it is often called the *master gland*.

The hormones of the anterior pituitary include thyroid-stimulating hormone (TSH), ACTH, growth hormone (GH), the gonadotropins, and prolactin (PRL).

Remember!

PRO	Prolactin
ATHletes	ACTH
Go**t**	Gonadotropins (FSH, LH)
To	TSH
GROW	Growth hormone

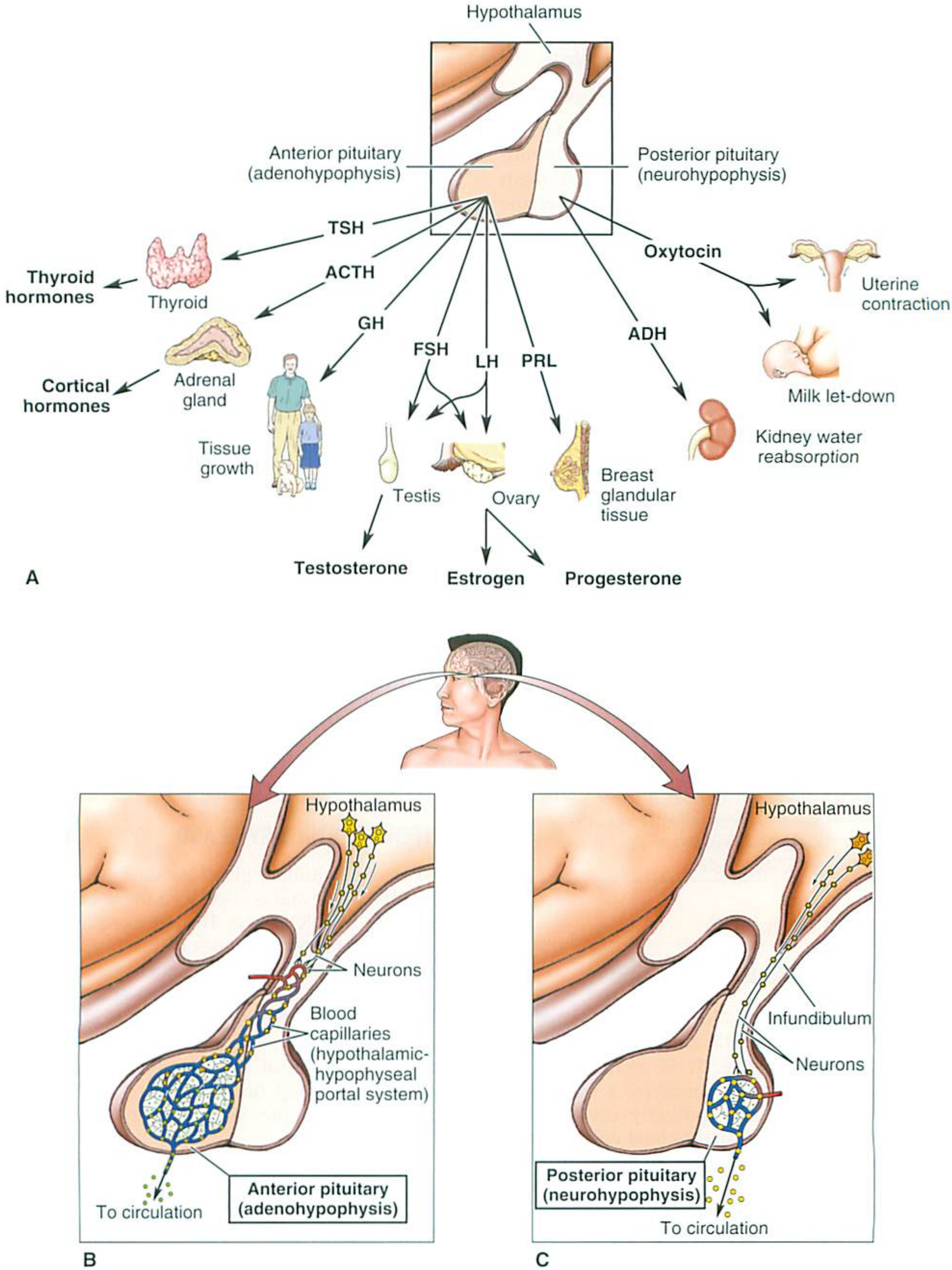


FIGURE 14-4 Pituitary gland. **A,** Hormones and target organs of the anterior and posterior pituitary glands. **B,** Relationship of the hypothalamus to the anterior pituitary gland. **C,** Relationship of the hypothalamus to the posterior pituitary gland.

Table 14-1 Hormones and Their Functions

HORMONE	FUNCTION
Anterior Pituitary Gland	
Growth hormone (GH)	Stimulates the growth of bone, cartilage, and skeletal muscle; stimulates the synthesis of glucose during periods of fasting
Prolactin	Stimulates the breast to develop and produce milk
Thyroid-stimulating hormone (TSH)	Stimulates the thyroid gland to produce thyroid hormones (T_3 and T_4)
Adrenocorticotropic hormone (ACTH)	Stimulates the adrenal cortex to secrete steroids, especially cortisol
Gonadotropic hormones	
Follicle-stimulating hormone (FSH)	Stimulates the development of ova and sperm
Luteinizing hormone (LH)	Causes ovulation in women; stimulates secretion of progesterone in women and testosterone in men
Posterior Pituitary Gland	
Antidiuretic hormone (ADH)	Stimulates water reabsorption by the kidneys; also constricts blood vessels
Oxytocin	Contracts uterine muscle during labor; releases milk from the mammary glands (during breast-feeding)
Hormones of the Thyroid and Parathyroid Glands	
Thyroid hormones (T_3, T_4)	Triiodothyronine (T_3) and tetraiodothyronine (T_4, or thyroxine) secreted by the thyroid gland; control metabolic rate and regulate growth and development
Calcitonin	Secreted by the thyroid gland; decreases plasma levels of calcium
Parathyroid hormone (PTH)	Secreted by the parathyroid glands; increases plasma calcium
Hormones of the Adrenal Gland	
Catecholamines Epinephrine Norepinephrine	Stimulate the "fight-or-flight" response
Steroids	
Cortisol	Glucocorticoid that helps regulate glucose, fat, and protein metabolism; is part of the stress response
Aldosterone	Mineralocorticoid that causes the kidneys to reabsorb sodium and water and excrete potassium; helps regulate fluid and electrolyte balance
Sex hormones	The androgens (especially testosterone) help develop the secondary sex characteristics in the female and male
Hormones of the Pancreas	
Insulin	Secreted by beta cells of the islets of Langerhans; helps regulate the metabolism of carbohydrates, proteins, and fats; lowers blood glucose levels
Glucagon	Secreted by the alpha cells of the islets of Langerhans; raises blood glucose levels
Other Hormones	
Estrogens and progesterone	Secreted by the ovaries; stimulate the development of the ova (eggs) and development of secondary sex characteristics in the female
Testosterone	Secreted primarily by the testes; chief male androgen; stimulates development of sperm and secondary sex characteristics in the male
Thymosins	Stimulates maturation of the T lymphocytes
Melatonin	Secreted by the pineal gland; helps set the biorhythms

GROWTH HORMONE

Growth hormone (GH) is also called *somatotropin* or *somatotropic hormone*. Its primary effects are on the growth of bones, cartilage, and skeletal muscles, thereby determining a person's size and height. GH also exerts powerful metabolic effects. It causes amino acids to be built into proteins and fats to be broken down and used for energy. It also stimulates the conversion of protein to glucose (gluconeogenesis), especially during periods of fasting between meals. GH thus causes blood glucose levels to rise. GH also affects electrolyte balance: it stimulates the kidneys to reabsorb sodium (Na^+), potassium (K^+), and chloride (Cl^-) and the digestive tract to absorb dietary calcium. These electrolytes then become available to growing tissue. In addition to the direct effects of GH on tissue growth, it also stimulates growth indirectly. GH stimulates the liver to produce growth stimulants called *insulin-like growth factors* (or somatomedins). GH is secreted during periods of exercise, sleep, and hypoglycemia. Like your mother said, "Plenty of rest and exercise makes you grow big and strong." (And you thought she didn't know her physiology!)

As its name implies, GH exerts a profound effect on growth. A person who hypersecretes GH as a child develops gigantism and will grow very tall, often achieving a height of 8 or 9 feet. If hypersecretion of GH occurs in an adult after the epiphyseal discs of the long bones have sealed, only the bones of the jaw (called "lantern jaw"), eyebrow ridges, nose, hands, and feet enlarge. This condition is called *acromegaly*. GH deficiency in childhood causes the opposite effect, a pituitary dwarfism. With this condition, body proportions are normal, but the person's height is very short.

PROLACTIN

Prolactin (PRL) is also called *lactogenic hormone*. As its name suggests (*pro-* means "for"; *-lact-* means "milk"), PRL promotes milk production in women. PRL stimulates the growth of the mammary glands and the production of milk after childbirth. As long as the lactating mother continues to breast-feed, PRL levels remain high and milk is produced. (PRL is discussed in more detail in Chapter 27.) The role of PRL in males is not fully understood but is known to increase the secretion of testosterone.

TROPIC HORMONES

The remaining hormones of the anterior pituitary gland are tropic hormones, which are aimed at and control other glands. The names of tropic hormones usually end in *-tropin*, or *-tropic*, as in thyrotropin or adrenocorticotropic hormone. The tropic hormones include the following:

- *Thyrotropin, or thyroid-stimulating hormone (TSH).* The target gland for TSH is the thyroid gland. TSH stimulates the thyroid gland to secrete two thyroid hormones.
- *Adrenocorticotropic hormone (ACTH).* The target gland for ACTH is the adrenal cortex. ACTH stimulates the adrenal cortex to secrete steroids.
- *Gonadotropic hormones.* The target glands for the gonadotropic hormones are the gonads, or sex glands (ovaries and testes). The two gonadotropins are follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH stimulates the development of ova (eggs) in the female and sperm in the male. LH causes ovulation in the female and causes the secretion of sex hormones in both the male and the female. LH in the male is also called *interstitial cell–stimulating hormone* (ICSH) because it stimulates the interstitial cells in the testes to synthesize and secrete testosterone. (These hormones are described further in Chapter 26.)

POSTERIOR PITUITARY GLAND

The posterior pituitary gland is an extension of the hypothalamus (see Figure 14-4, C). The posterior pituitary is composed of nervous tissue and is therefore called the **neurohypophysis** (noo-roh-hye-POF-i-sis). The two hormones of the posterior pituitary gland are produced in the hypothalamus and transported to the gland, where they are stored until needed. The two hormones are antidiuretic hormone (ADH) and oxytocin. The secretion of the posterior pituitary gland is controlled by neuroendocrine reflexes. In other words, the hormones are released in response to signals from the nervous system.

ANTIDIURETIC HORMONE

Antidiuretic hormone (ADH) is released from the posterior pituitary gland in an attempt to conserve water. The primary target organ for ADH is the kidney. ADH causes the kidney to reabsorb water from the urine and return it to the blood. By so doing, the amount of urine that the kidney excretes decreases—hence, the term *antidiuretic hormone* (*anti-* means "against"; *diuresis* means "urine flow").

What is the signal for the release of ADH? ADH is released in response to a concentrated blood (increased osmolarity) and decreased blood volume; both occur in dehydration. Other triggers for the release of ADH are stress, trauma, and drugs such as morphine. Alcohol, in contrast, inhibits ADH secretion—hence, the excessive urination that accompanies beer drinking!

In the absence of ADH, a profound diuresis occurs, and the person may excrete up to 25 L/day of dilute urine. This ADH deficiency disease is called *diabetes insipidus* and should not be confused with the more common *diabetes mellitus*, which is an insulin deficiency. (The effect of ADH on the kidneys is described in Chapter 24.)

ADH also causes the blood vessels to constrict, thereby elevating blood pressure. Because of this blood pressure–elevating effect, ADH is also called *vasopressin* (vay-so-PREHS-in). (A vasopressor agent is one that elevates blood pressure.)

OXYTOCIN

The second posterior pituitary hormone is oxytocin. The target organs of oxytocin (ahk-see-TOH-sin) in the female are the uterus and the mammary glands (breasts). Oxytocin stimulates the muscles of the uterus to contract and plays a role in labor and the delivery of a baby. The word *oxytocin* literally means "swift birth," and an oxytocic drug is one that causes uterine contractions and hastens delivery. You have probably heard of the use of IV "pit" (or Pitocin, the trade name for oxytocin) to initiate labor.

Oxytocin also plays a role in breast-feeding. When the baby suckles at the breast, oxytocin is released and stimulates contraction of the smooth muscles around the mammary ducts within the breasts, thereby releasing breast milk. The release of milk in response to suckling is called the *milk let-down reflex* (discussed further in Chapter 27). The role of oxytocin in the male is not fully understood; it is thought to help move the semen along the male reproductive tract. Oxytocin has recently been dubbed the bonding or relationship hormone; it seems that a high blood level of oxytocin generates feelings of goodwill and an urge to be cooperative, protective, and friendly. It makes sense that breast-feeding (and the release of oxytocin) facilitates bonding between Mom and Baby.

A TINY THIRD LOBE... A FETAL STRUCTURE

MELANOCYTE-STIMULATING HORMONE

Like the adult, the fetal pituitary gland is divided into two main parts: the anterior and posterior pituitary. The fetal pituitary gland, however, has a tiny third lobe (pars intermedia) that secretes melanocyte-stimulating hormone (MSH). MSH influences pigmentation of the skin. What eventually happens to the tiny third lobe? The cells are incorporated into the tissue of the anterior pituitary gland; hence, the adult pituitary has no tiny third lobe. These cells do not secrete MSH; instead, they produce a polypeptide called *pro-opiomelanocortin* (POMC). POMC is not secreted as a hormone; rather, it is degraded in the pituitary gland to ACTH and endorphins. Adrenal cortical insufficiency also causes a hypersecretion of ACTH derived from the POMC, causing the person to appear bronzed.

? Re-Think

1. Why is the pituitary gland sometimes called the *master gland*? Why do some call the hypothalamus the *master gland*?
2. What "happens" in the hypothalamic-hypophyseal portal system?
3. List the six hormones secreted by the anterior pituitary gland and two hormones secreted by the posterior pituitary gland.

2+2 Sum It Up!

The pituitary gland is called the *master gland* because it controls many other endocrine glands. The anterior pituitary gland (adenohypophysis) is controlled by hypothalamic hormones, called *releasing hormones* and *release-inhibiting hormones*. These hormones are secreted by the hypothalamus into the hypothalamic-hypophyseal portal system. The anterior pituitary gland secretes six major hormones, most of which are tropic hormones. The posterior pituitary gland is an extension of the hypothalamus and is called the *neurohypophysis*. The posterior pituitary gland secretes two hormones.

THYROID GLAND

The **thyroid gland** is located in the anterior neck; it is situated on the front and sides of the trachea (Figure 14-5, *A*) and is easily palpated (i.e., you can feel thyroid nodules or enlargement). The thyroid gland is butterfly shaped and has two lobes connected by a band of tissue called the *isthmus* (ISS-muss). The thyroid gland contains two types of cells: the follicular cells, located within the thyroid follicle, and the parafollicular cells, located between the follicles. Each type of cell secretes a particular hormone (see Table 14-1).

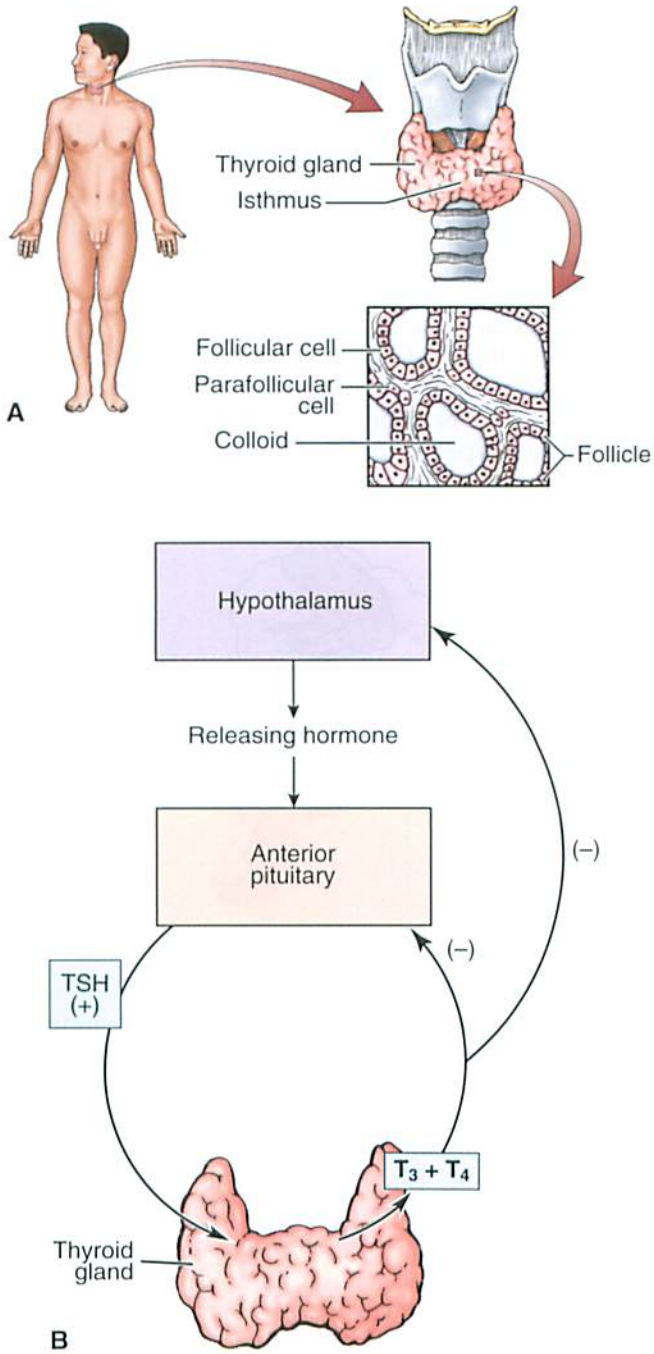


FIGURE 14-5 Thyroid gland. **A,** Location; the thyroid follicle. **B,** Control of the secretion of T_3 and T_4.

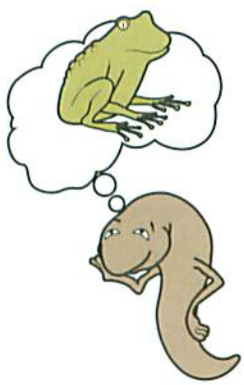
THYROID FOLLICLE

The thyroid gland is composed of many secretory units called *follicles*. The cavity in each follicle is filled with a clear, viscous substance called *colloid*. Follicular cells secrete two thyroid hormones: triiodothyronine (try-eye-oh-doh-THY-roh-neen) (T_3) and tetraiodothyronine (tet-rah-eye-oh-doh-THY-roh-neen) (T_4, or thyroxine). The term *thyroid hormones* refers to T_3 and T_4 collectively.

WHAT THYROID HORMONES (T_3 AND T_4) DO

The thyroid hormones T_3 and T_4 have similar functions, although T_3 is more potent. Thyroid hormones regulate all phases of metabolism and are necessary for the proper functioning of all other hormones. Thyroid hormones are necessary for the normal maturation of the nervous system and for normal growth and development. In addition to its many actions, thyroid hormones stimulate the secretion of GH by the anterior pituitary gland. If you were a tadpole, you would require adequate thyroid hormones before you could develop into a frog.

Perhaps the best way to describe the effects of thyroid hormones is to observe the signs and symptoms of thyroid hormone deficiency (hypothyroidism) and excess (hyperthyroidism).



HYPOTHYROIDISM

Hypothyroidism in an adult results in a condition called *myxedema*. Myxedema (mik-seh-DEE-mah) is a slowed-down metabolic state characterized by a slow heart rate, sluggish peristalsis resulting in constipation, a low body temperature, low energy, loss of hair, and weight gain. The skin becomes thick and puffy because of the accumulation of a thick fluid under the skin—hence, the name *myxedema* (*myx* means "mucus").

If an infant is born with no thyroid gland, a condition called *cretinism* develops. An infant with cretinism fails to develop both physically and mentally. The child will be short and stocky, with abnormal skeletal development and severe signs of developmental delay. Early diagnosis and prompt treatment with thyroid hormone can prevent further developmental delay.

HYPERTHYROIDISM

An excess of thyroid hormones produces hyperthyroidism, a speeded-up metabolic state. A common type of hyperthyroidism is Graves' disease. It is characterized by an increase in heart rate, increase in peristalsis resulting in diarrhea, elevation in body temperature (heat intolerance), hyperactivity, weight loss, and wide emotional swings. The hyperthyroid person exhibits an increased sensitivity to the effects of catecholamines (epinephrine) and is at risk for the development of fast rhythm disorders of the heart. Graves' disease is also characterized by bulging eyes, a condition known as *exophthalmia* (ek-soff-THAL-mee-ah). In exophthalmia, the eyes are thought to bulge because the fat pads behind the eyeballs enlarge, pushing the eyeballs forward in the eye socket. Severe exophthalmia may make it difficult for the patient to close his or her eyelids over the cornea of the eye; the exposed cornea may then dry out, ulcerate, and scar, leading to a loss of vision.

REGULATION OF SECRETION

The regulation of thyroid gland activity is illustrated in Figure 14-5, *B*. The hypothalamus secretes a releasing hormone, which stimulates the anterior pituitary to secrete TSH. TSH stimulates the thyroid gland to secrete T_3 and T_4. When the plasma levels of the thyroid hormones increase sufficiently, negative feedback inhibition prevents further secretion of TSH.

Do You Know...

Why an Overactive Thyroid Gland Is Hot Stuff?

An overactive thyroid gland secretes excess thyroid hormones. Thyroid hormones increase the utilization of oxygen by most cells of the body. As oxygen is used, excess heat is made by the working or metabolizing cells and body temperature rises. The heat-producing effect of the thyroid hormones is called its *calorigenic effect* and is responsible for the higher body temperature of someone who is hyperthyroid. Hot stuff, that thyroid disease!

THE NEED FOR IODINE

SYNTHESIS OF THYROID HORMONE

The synthesis of T_3 and T_4 requires iodine. The iodine in the body comes from dietary sources. Most of the iodine in the blood is actively pumped into the follicular cells of the thyroid gland, where it is used in the synthesis of the thyroid hormones. Tetraiodothyronine, or thyroxine, contains four (tetra-) iodine atoms and therefore is called T_4. Triiodothyronine (tri-) contains three iodine atoms and is called T_3.

IODINE DEFICIENCY

Why does an iodine-deficient diet cause the thyroid gland to enlarge? In an iodine-deficient state, the amount of T_3 and T_4 production decreases because iodine is necessary for the synthesis of the thyroid hormones. With insufficient iodine, thyroid hormones cannot be made in quantities great enough to shut off the secretion of TSH through negative feedback control. Persistent stimulation of the thyroid gland by TSH causes the thyroid gland to enlarge; an enlarged thyroid gland is called a *goiter* (GOYH-ter).

Do You Know...

What a Goiter Is Doing on the Ceiling of the Sistine Chapel?

Like many artists of the Renaissance period, Michelangelo had a fascination with goiters (from the Latin *guttur*, meaning "throat"). One of his paintings, called the "Separation of Light from Darkness," shows the Creator with a very obvious nodular goiter. It is no accident that the artist equates the appearance of the goiter with the first day of creation. Why? Michelangelo was very familiar with goiters, having grown up in the iodine-poor region of Italy (before the days of iodized salt). Michelangelo was obsessed with anatomy, having spent many hours dissecting corpses and sketching innards. He shared the view of his contemporaries that goiters were a sign of beauty and privilege, so of course he gifted God a huge goiter. Other artists not only painted gnarly goiters, but they also illustrated rather hefty body types, thereby connecting the goiter with the weight gain of hypothyroidism.

Some medical historians offer a different "take" on Michelangelo's divine goiter. It has been suggested by some that Michelangelo himself had a goiter and actually painted God in his own goitrous image. This view is certainly consistent with Michelangelo's lofty opinion of himself. It has also been suggested that the "self-portrait" theory represents his petulant response to the demand of Pope Julius that he paint the ceiling, a task that Michelangelo did not enjoy.

Clinical assessment of thyroid function makes use of the iodine-pumping activity of the gland. For example, if a patient drinks radioactive iodine (^{131}I), the thyroid gland pumps the radioactive iodine from the blood into the gland. The rate of iodine uptake by the thyroid gland can be determined by a gamma ray scanner placed over the thyroid gland. Increased iodine uptake is observed in hyperthyroid and iodine-deficient patients, whereas a decrease in iodine uptake is noted with hypothyroid patients. Larger therapeutic doses of ^{131}I can be used to destroy thyroid tissue in the hyperthyroid state.

? Re-Think

1. Why does a hypothyroid person have an elevated plasma TSH level?
2. Why does an iodine-deficient diet cause goiter formation?
3. What is the calorigenic effect of thyroid hormones?

CALCITONIN

The parafollicular cells of the thyroid gland secrete a hormone called *calcitonin*. Although calcitonin is a thyroid hormone, its effects are very different from those of T_3 and T_4. Calcitonin helps regulate blood levels of calcium. Calcitonin is secreted in response to elevated blood levels of calcium. It decreases blood calcium primarily by stimulating osteoblastic (bone-making) activity in the bones, thereby moving calcium from the blood into the bone. Calcitonin also increases the excretion of calcium in the urine. In general, calcitonin acts as an antagonist to parathyroid hormone.

PARATHYROID GLANDS

Four tiny parathyroid glands lie along the posterior surface of the thyroid gland (Figure 14-6). The **parathyroid glands** secrete PTH. The stimulus for the release of PTH is a low blood level of calcium. PTH has three target organs: bone, digestive tract (intestine), and kidneys. The overall effect of PTH is to increase blood calcium levels, which it does in four ways:

1. PTH increases the release of calcium from bone tissue, called *resorption*. (Do not confuse the word *resorption* with *reabsorption*.) It does so by stimulating osteoclastic (bone breakdown) activity. In response, calcium moves from the bone to the blood.
2. PTH stimulates the kidneys to reabsorb calcium from the urine. At the same time, PTH causes the kidneys to excrete phosphate. The excretion of phosphate by the kidneys is called its *phosphaturic* (foss-foh-TOOR-ik) *effect*. The urinary excretion of phosphate is important because of the inverse relationship of phosphate and calcium in the blood. The inverse relationship means that as phosphate levels decrease, calcium levels increase; when phosphate levels increase, calcium levels decrease. Thus, to raise blood calcium levels, it is necessary to lower blood phosphate levels.
3. Working with vitamin D, PTH increases the absorption of dietary calcium by the digestive tract (intestine). Thus, a vitamin D deficiency can decrease the dietary absorption of calcium. Remember, from Chapter 7, that a daily but brief exposure to sunlight increases the production of vitamin D by the skin.
4. Blood calcium levels control the secretion of both calcitonin and PTH through negative feedback control. High blood calcium levels stimulate secretion of calcitonin, whereas low blood calcium levels inhibit secretion of calcitonin and stimulate secretion of PTH.

BLOOD CALCIUM REGULATION: IMBALANCES

HYPOCALCEMIA

What is the hand in Figure 14-7 doing? The hand and wrist muscles are contracted and cannot relax, thereby

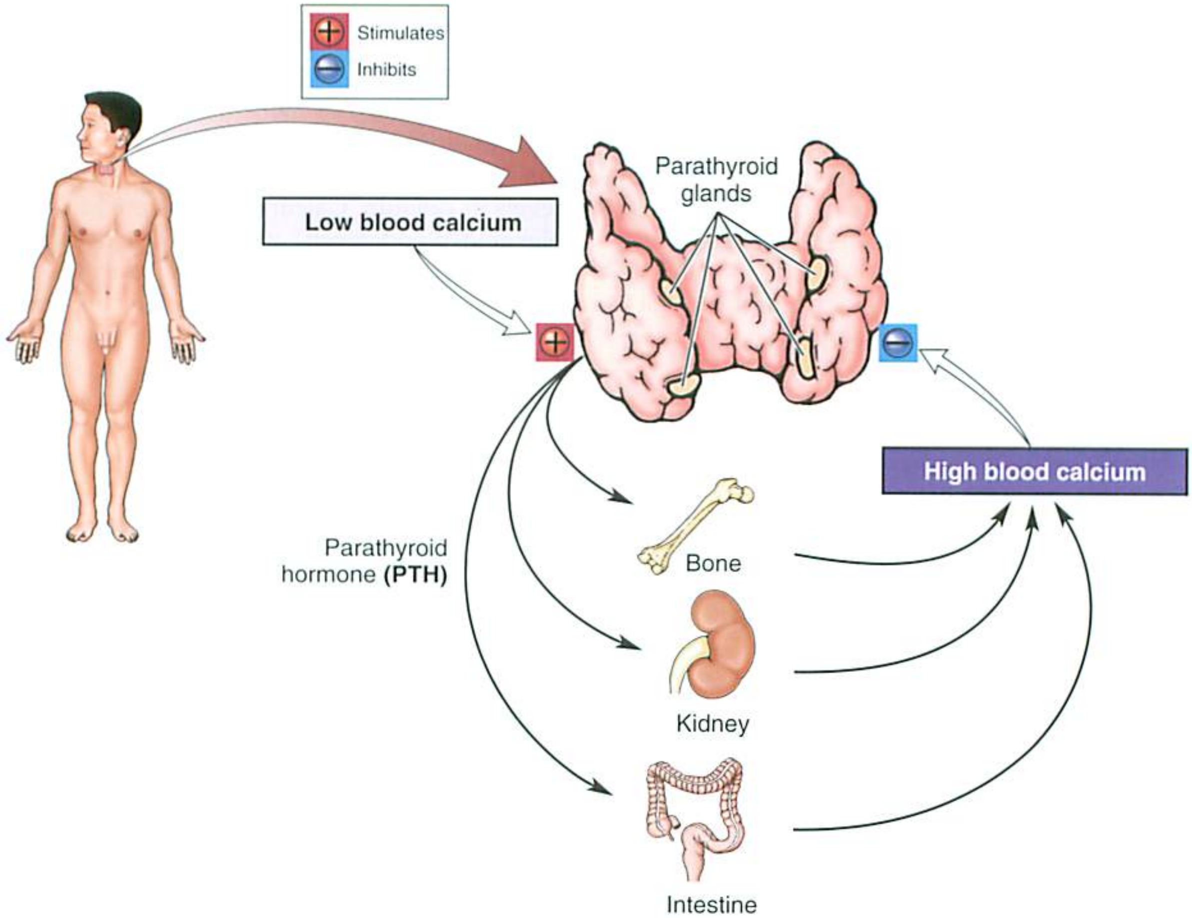


FIGURE 14-6 Parathyroid glands. Parathyroid hormone (PTH) and three target organs.

producing a carpal spasm. What causes the carpal spasm? Calcium normally stabilizes nerve and muscle membranes. With insufficient PTH, blood calcium declines, causing hypocalcemia. Consequently, the nerve and muscle membranes become unstable and continuously fire electrical signals, causing the muscles to remain contracted. Sustained skeletal muscle contraction is referred to as *tetany* (TET-ah-nee). Hypocalcemic tetany not only contorts the wrist; more seriously, it causes sustained contractions of the muscles of the larynx (laryngospasm) and the breathing muscles.

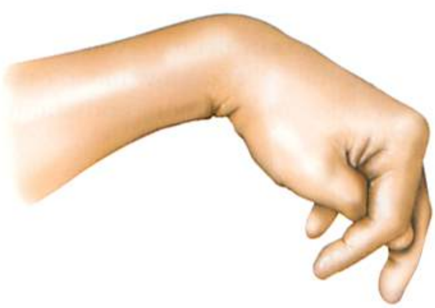


FIGURE 14-7 Carpal spasm.

Inability of these muscles to relax causes asphyxiation and death. Hypocalcemia is life threatening!

HYPERCALCEMIA

The clinical effects of hypercalcemia are best summarized as "Bones, Stones, Moans, and Groans." The patient develops hyperparathyroidism in response to a tumor in the parathyroid gland. The PTH stimulates osteoclastic activity in the bones, thereby moving calcium from the bones to the blood and causing hypercalcemia. Bone pain results from persistent osteoclastic activity (bones and groans). Hypercalcemia causes excess calcium to be filtered into the urine, causing hypercalciuria (hye-per-kal-see-YOOR-ee-ah); the excess calcium in the urine precipitates out as kidney stones (bones, stones, and groans). Hypercalcemia also depresses the nervous, cardiac, and gastrointestinal systems causing a variety of symptoms, including depression (moans), fatigue, bradycardia, anorexia, and constipation. The Groan Zone, indeed!

? Re-Think

1. List the target organs of PTH.
2. Why does a deficiency of PTH cause hypocalcemia?

Do You Know...

Why Mr. Graves's Face Is a-Twitching?

Mr. Graves just had a thyroidectomy. As part of his postsurgical care, his nurse periodically tapped the area over the facial nerve. "He is twitching," observed his nurse and immediately reported this observation as a positive Chvostek's sign. Hyperirritability of the facial nerve occurs when the blood levels of calcium decrease. Sometimes the parathyroid glands, which are embedded in the thyroid gland, are mistakenly removed or injured during thyroid surgery. If the parathyroid glands are removed, blood calcium levels decrease because there is no PTH. The nerves become so irritable that they fire continuously, causing continuous muscle contraction (tetany). Unless treated with intravenous calcium, the person may develop a fatal hypocalcemic tetany.

2+2 Sum It Up!

The thyroid gland and parathyroid glands are located in the anterior neck region. The thyroid gland secretes two iodine-containing hormones: T_3 and T_4. These hormones regulate the body's metabolic rate. Excess secretion of T_3 and T_4, called *hyperthyroidism*, increases the body's metabolic rate. Hypothyroidism causes a hypometabolic state. The thyroid gland also secretes calcitonin, which decreases blood levels of calcium. The parathyroid glands secrete PTH, which increases blood calcium levels through its effect on three target organs: bone, kidneys, and digestive tract.

ADRENAL GLANDS

The two small glands located above the kidneys are called **adrenal glands** (*ad* means "near"; *renal* means "kidney"; Figure 14-8, *A*). An adrenal gland consists of two regions: an inner medulla and an outer cortex. The medulla and the cortex secrete different hormones (see Table 14-1).

ADRENAL MEDULLA

The adrenal medulla is the inner region of the adrenal gland and is considered an extension of the sympathetic nervous system. Remember from Chapter 12 that the sympathetic nervous system is called the "fight-or-flight" system. Chromaffin cells in the adrenal medulla secrete two hormones: epinephrine (85%) and norepinephrine (15%).

Epinephrine (adrenaline) and norepinephrine, classified as **catecholamines** (kat-eh-KOHL-ah-meens), are secreted in emergency or stress situations. You may have heard the expression, "I can feel the adrenaline flowing." It is another way of saying, "I'm ready to meet the challenge." The catecholamines, like the sympathetic nervous system, help the body respond to stress by causing the following effects:

- Elevating blood pressure
- Increasing heart rate
- Converting glycogen to glucose in the liver, thereby making more glucose available to the cells
- Increasing metabolic rate of most cells, thereby providing more energy
- Causing bronchodilation (opening up of the breathing passages) to increase the flow of air into the lungs
- Changing blood flow patterns, causing dilation of the blood vessels to the heart and muscles and constriction of the blood vessels to the digestive tract

Some medullary cells extend into the inner cortical layer. When stress activates the sympathetic "fight-or-flight" response, the medullary cells stimulate the cortex to secrete steroids (also stress hormones).

Occasionally, a person develops a tumor of the adrenal medulla and displays signs and symptoms that resemble sympathetic nervous system excess. The tumor is called a *pheochromocytoma* (FEE-oh-kroh-moh-cye-TOH-mah); it causes life-threatening high blood pressure. Immediate treatment is directed at lowering the blood pressure. Long-term treatment involves surgical removal of the tumor.

ADRENAL CORTEX

The adrenal cortex, the outer region of the adrenal gland (see Figure 14-8, *A*), secretes hormones called *steroids*. Steroids are lipid-soluble hormones made from cholesterol. The adrenal cortex secretes three steroids: glucocorticoids, mineralocorticoids, and sex hormones. Adrenal cortical hormones are essential for life. If the adrenal cortex is removed or its function is lost, death will occur unless steroids are administered. An easy way to remember the functions of the adrenal cortical steroids is that they regulate sugar, salt, and sex.

Remember!

Glucocorticoids	Sugar
Mineralocorticoids	Salt
Sex hormones	Sex

GLUCOCORTICOIDS

As their name implies, the glucocorticoids affect carbohydrates. They convert amino acids into glucose (gluconeogenesis) and help maintain blood glucose levels between meals. This action ensures a steady supply of glucose for the brain and other cells. Glucocorticoids also affect protein and fat metabolism, burning both substances as fuel to increase energy production.

The chief glucocorticoid is cortisol. Cortisol is a hormone that is secreted in greater amounts during times of stress. Stress refers to physiological stress such as disease, physical injury, hemorrhage, infection, pregnancy, extreme temperature, and emotional stress, such as anger and worry. In fact, it is thought that the abdominal fat associated with heart disease is deposited in response to stress-induced chronic secretion of cortisol. Yet another reason to relax! Cortisol also has

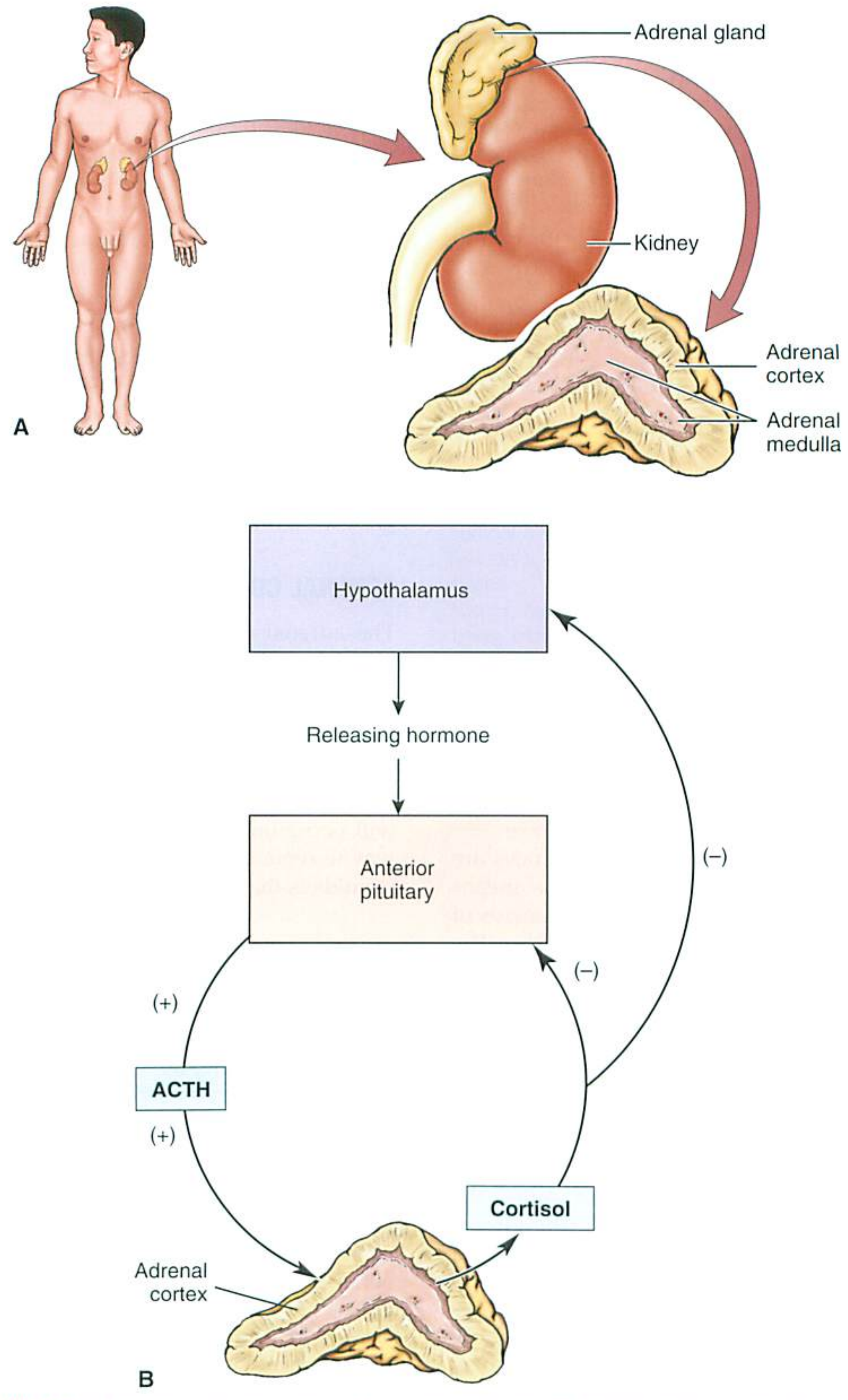


FIGURE 14-8 **A,** Adrenal glands: adrenal medulla and adrenal cortex. **B,** Control of the secretion of cortisol.

an anti-inflammatory effect. In other words, it prevents injured tissues from responding with the classic signs of inflammation: redness, heat, swelling, and pain. For this reason, cortisol is used as a drug to prevent inflammation in the treatment of arthritis and severe allergic responses.

Control of Cortisol Secretion

The secretion of cortisol involves the hypothalamus, anterior pituitary gland, and adrenal gland (see Figure 14-8, *B*). The hypothalamus secretes a releasing hormone, which then stimulates the anterior pituitary gland to secrete ACTH. ACTH, in turn, stimulates the adrenal cortex to secrete cortisol. Through negative feedback control, the cortisol inhibits the further secretion of ACTH and additional cortisol.

MINERALOCORTICOIDS

The chief mineralocorticoid is aldosterone (al-DOS-ter-own). Aldosterone plays an important role in the regulation of blood volume, blood pressure, and the concentration of electrolytes, especially Na^+ and K^+. Aldosterone is often called the salt-retaining (NaCl) hormone. The primary target organ of aldosterone is the kidney. Aldosterone reabsorbs sodium and water from the urine and eliminates potassium in the urine. The role and regulation of aldosterone are described in Chapter 24.

SEX HORMONES

The sex hormones—secreted in small amounts—include the female hormones, primarily estrogens, and male hormones, called *androgens* (primarily testosterone). The sex hormones of the ovaries usually mask the effects of the adrenal sex hormones. In females, the masculinizing effects of the adrenal androgens, such as increased body hair, may become evident after menopause, when levels of estrogen and progesterone from the ovaries decrease.

What's with the cat? His name is Steroid **CAT.** Steroid **CAT** secretes **C**ortisol, **A**ldosterone, and **T**estosterone.

STEROID	**C**	**A**	**T**
	O	**L**	**E**
	R	**D**	**S**
	T	**O**	**T**
	I	**S**	**O**
	S	**T**	**S**
	O	**E**	**T**
	L	**R**	**E**
		O	**R**
		N	**O**
		E	**N**
			E

HYPOSECRETION AND HYPERSECRETION

Hyposecretion

In some persons, the adrenal cortex fails to secrete adequate amounts of steroids. This condition is called *chronic adrenal cortical insufficiency*, or *Addison's disease*. It is characterized by generalized weakness, muscle atrophy, a bronzing of the skin, hyperkalemia (elevated K^+ in the blood), and severe loss of fluids and electrolytes, especially Na^+. Left untreated, adrenal insufficiency becomes acute and progresses to low blood volume, shock, and death. Adrenal insufficiency is life threatening and must be treated with steroids and replacement of fluids and electrolytes.

Hypersecretion

More commonly, some persons have an excess of adrenal cortical hormones. This condition may be caused by a hypersecretion of either ACTH by the anterior pituitary gland or cortisol by the adrenal cortex. Most often, however, elevated levels of cortisol are caused by the administration of steroids as drugs such as prednisone. Elevated blood levels of steroids cause a condition called *Cushing's syndrome*. It is characterized by truncal obesity, a rounded facial appearance (moon face), excess fat deposition between the shoulders (buffalo hump), masculinizing effects (virilization), facial hair (hirsutism), thin skin that bruises easily, bone loss, and muscle weakness. Salt and water retention cause blood volume and blood pressure to increase. Prolonged use of steroids causes many harmful effects, particularly in young athletes who take steroids to improve their athletic performance.

The Case of the Lazy Gland (Acute Adrenal Cortical Insufficiency)

The effects of steroid drugs on adrenal cortical function provide a dramatic example of negative feedback control. Consider this situation. A patient is given prednisone (cortisol-like) as a drug for the treatment of arthritis. As blood cortisol levels rise, the secretion of ACTH by the anterior pituitary gland is inhibited by negative feedback. In the absence of ACTH, the adrenal gland becomes "lazy" and stops its production of cortisol. As long as the person continues to take the prednisone, blood cortisol levels remain high. If, however, the person suddenly discontinues the drug, the lazy adrenal gland no longer produces cortisol, and the person eventually develops acute adrenal insufficiency and will die unless treated. (Remember: Steroids are essential for life.) Because of lazy adrenal function, steroid drugs are never discontinued abruptly; dosage is tapered off over an extended period. This gradual reduction in drug dose gives the lazy gland time to recover and regain its ability to respond to ACTH.

? Re-Think

1. List the three groups of steroids secreted by the adrenal cortex.
2. Explain the following: A person has been taking prednisone for 1 year. She suddenly stops taking the drug and develops a life-threatening acute adrenal insufficiency.

2+2 Sum It Up!

The adrenal glands are composed of the medulla and the cortex; both secrete stress hormones. The adrenal medulla is an extension of the sympathetic nervous system ("fight or flight") and secretes two catecholamines called *epinephrine* (adrenaline) and *norepinephrine*. The adrenal cortex secretes three steroids: the glucocorticoids (cortisol), the mineralocorticoids (aldosterone), and the sex hormones. The adrenal cortex is controlled by a hypothalamic-releasing hormone and ACTH from the anterior pituitary gland. The functions of the adrenal cortex are concerned with the regulation of sugar, salt, and sex.

PANCREAS

The **pancreas** (PAN-kree-ass) is a long slender organ that lies transversely across the upper abdomen, extending from the curve of the duodenum to the spleen (see Figure 14-1). The pancreas functions as both an exocrine gland and an endocrine gland. (Its exocrine function is concerned with the digestion of food and is discussed in Chapter 23.)

The pancreas secretes at least five hormones; we are concerned primarily with two hormones: insulin and glucagon. Consult Ms. PIG in Figure 14-9; she will help

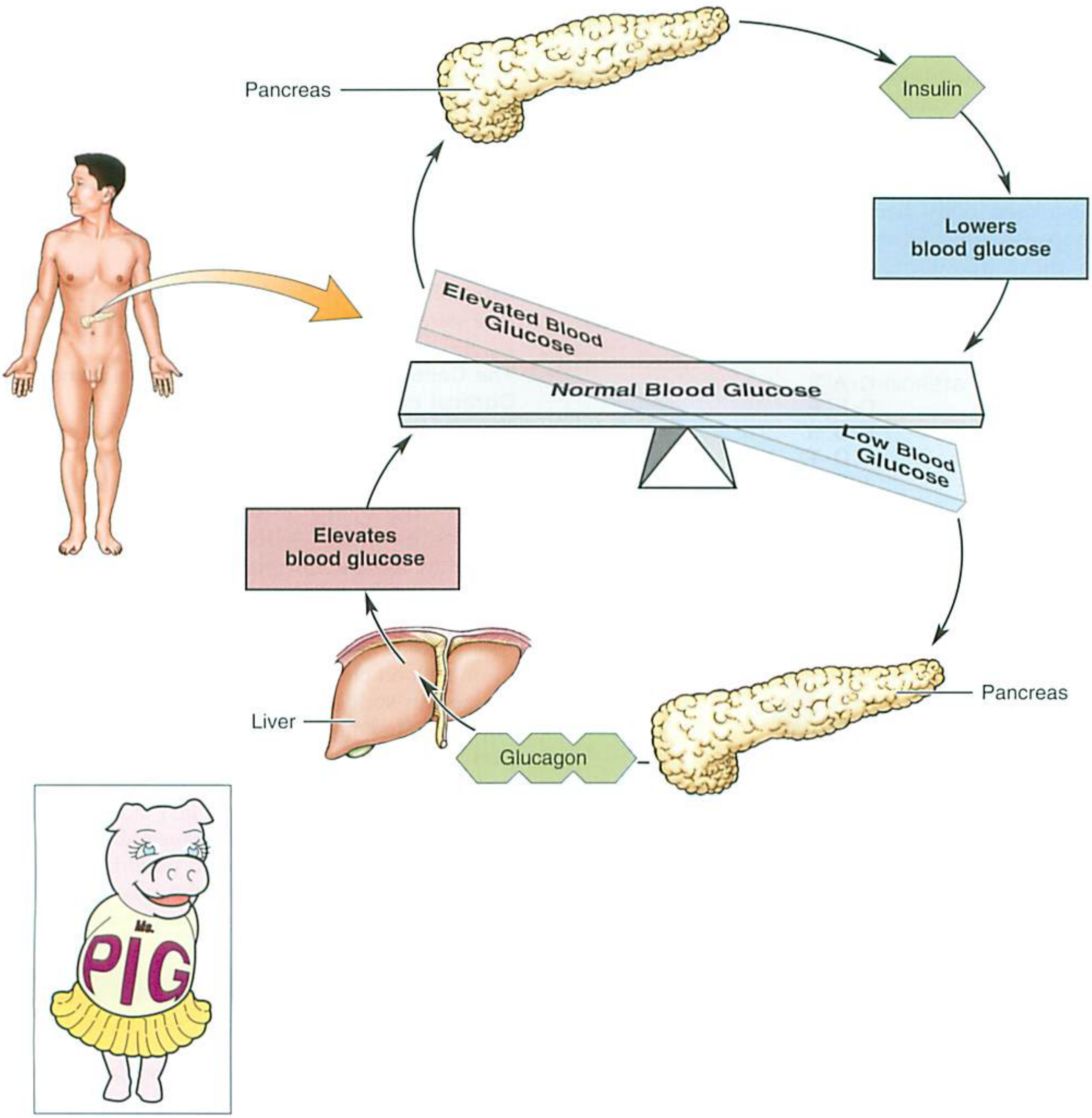


FIGURE 14-9 Pancreatic regulation of blood glucose: insulin and glucagon.

remind you that the *p*ancreas secretes *i*nsulin and *g*lucagon (Pancreas, Insulin, Glucagon). The hormone-secreting cells of the pancreas are called the *islets of Langerhans*. The islets of Langerhans have several types of cells: the alpha cells, which secrete glucagon, and the beta cells, which secrete insulin. Both insulin and glucagon help regulate blood glucose levels.

INSULIN

SECRETION AND EFFECTS

Figure 14-9 illustrates the relationship of the blood glucose level to the pancreatic hormones. Insulin is released in response to increased blood levels of glucose, such as what occurs after a meal. The secretion of insulin decreases as blood levels of glucose decrease. Insulin has many target tissues and therefore exerts widespread effects:

- Insulin helps transport glucose into most cells. Without insulin, glucose remains outside the cells, thereby depriving the cell of its fuel. (The liver and brain require glucose for their metabolic needs but do not require insulin for the transport of glucose across the cell membrane.)
- Insulin helps control carbohydrate, protein, and fat metabolism in the cell. Insulin stimulates the breakdown of glucose (glycolysis) for energy and stimulates the liver and skeletal muscles to store excess glucose as glycogen (glycogenesis). Insulin also increases the transport of amino acids into cells and then stimulates the synthesis of protein from the amino acids. Finally, insulin promotes the making of fats from fatty acids.

Do You Know...

Why Some Diabetic Persons Require an Injection of Insulin Whereas Others Can Take a Pill?

Some diabetic persons require insulin injections, and others control their diabetes with a pill. The difference is that the pancreas of a person with severe diabetes produces no insulin, so this person must receive insulin injections. Such people have insulin-dependent diabetes. In contrast, the pancreas of a person with another form of diabetes may still be able to produce some insulin. This person may not require insulin injections and may benefit from oral medication. Some diabetic pills work by stimulating the person's pancreas to produce more insulin. Others work by preventing the hepatic (liver) synthesis of glucose. A person with diabetes who does not require insulin injections is considered to have non–insulin-dependent diabetes.

INSULIN AND BLOOD GLUCOSE

Insulin decreases blood glucose levels for two reasons. First, insulin increases the transport of glucose from the blood into the cells. Second, insulin stimulates the cells to burn glucose as fuel. *Insulin is the only hormone that lowers blood glucose levels.* All other hormones increase blood glucose levels.

DIABETES MELLITUS: "A MELTING DOWN OF THE FLESH AND LIMBS INTO URINE"

Because insulin plays such an important role in the metabolism of all types of foods (carbohydrates, proteins, and fats), a deficiency of insulin causes severe metabolic disturbances. Insulin deficiency or insulin ineffectiveness is called *diabetes mellitus* (dye-ah-BEE-teez mell-EYE-tus). Before insulin therapy was discovered, diabetes mellitus was described as a "melting down of the flesh and the limbs into urine." This description attests to the devastating effects of untreated juvenile-onset diabetes mellitus. The child took one year literally to "melt away." Read on to understand the physiological effects of insulin deficiency; note specifically the three *"polys"* of diabetes mellitus: polyuria, polydipsia, and polyphagia.

Do You Know...

How One Rebounds with Somogyi?

A diabetic person takes insulin to lower his or her blood glucose level. If too much insulin is taken, the blood glucose level becomes too low (hypoglycemia). The hypoglycemia, in turn, stimulates the secretion of glucose-elevating hormones such as glucagon, cortisol, growth hormone, and epinephrine; this causes hyperglycemia. The hyperglycemia requires additional insulin to lower blood glucose levels. The additional insulin again causes hypoglycemia; thus, a vicious cycle of hypoglycemia and hyperglycemia occurs. The Somogyi effect is a rebound phenomenon in which hypoglycemia is followed by hyperglycemia as a result of a hormonal overreaction to the low blood sugar level.

- *Hyperglycemia.* Excess glucose in the blood is called *hyperglycemia.* This condition is caused by two factors. The first is the inability of glucose to enter the cells, where it can be burned for energy. Failure to move the glucose into the cells causes it to accumulate in the blood. The second is the making of additional glucose. In the absence of insulin, the body makes glucose from protein (gluconeogenesis). The excess glucose cannot be used by the cells and therefore accumulates in the blood. In essence, the diabetic body converts its protein to glucose that it cannot burn as fuel and then eliminates it in the urine. The body is "starving in the midst of plenty" (of glucose).
- *Glucosuria or glycosuria.* Glucose in the urine is called *glucosuria* or *glycosuria.* The hyperglycemia causes excess glucose to be eliminated in the urine.
- *Polyuria.* Excretion of a large volume of urine is called *polyuria.* Whenever the kidneys excrete a lot of glucose, they must also excrete a lot of water. Glucosuria therefore causes polyuria.
- *Polydipsia.* Excessive thirst is called *polydipsia.* Polyuria causes an excessive loss of body water, thereby stimulating the thirst mechanism in an attempt to replace the water lost in the urine.

- *Polyphagia.* Polyphagia refers to excessive eating. Despite plenty of glucose in the blood, the cells cannot use it; instead, the diabetic eats excessive amounts of food to fuel the cells. Despite the polyphagia, the diabetic person continues to lose weight.
- *Acidosis.* An excess of H^+ in the blood causes acidosis. Because the cells cannot burn glucose as fuel, they burn fatty acids instead. The rapid, incomplete breakdown of fatty acids produces strong acids (H^+) called *ketoacids*. This process causes a condition called *diabetic ketoacidosis*.

- *Fruity odor to the breath.* The rapid, incomplete breakdown of fatty acids causes the formation of acetone, a ketone body. Acetone smells fruity and makes the patient's breath smell like rotten apples. A fruity odor is a sign of ketoacidosis. Treatment of diabetic ketoacidosis requires the prompt administration of insulin and the correction of the fluid and electrolyte disturbances.

Do You Know...

Why You Don't Die of Hypoglycemia between Meals?

After you eat a meal, the blood level of glucose rises as food is absorbed from the digestive tract into the blood. The increased blood glucose level signals the release of insulin; the insulin then causes the blood glucose level to decrease. As blood glucose levels decrease, however, insulin secretion decreases and other hormones such as growth hormone, epinephrine, and cortisol are secreted. These other hormones antagonize the effects of insulin by increasing the blood glucose level and preventing fatal hypoglycemia. Thus, you can fast for several weeks and not become hypoglycemic. Chances are that you will not die from fasting—it will only feel as if you are dying!

INSULIN RECEPTORS AND THE DIABETIC STATE

As indicated above, diabetes mellitus can be caused by a lack of insulin. However, some diabetics with adult-onset, or type 2, diabetes mellitus have excess insulin (hyperinsulinemia) and are still hyperglycemic. What's that about? Under normal conditions, insulin binds to the insulin receptors on the cell membrane. What if:

- The insulin receptors are damaged? The damaged receptors cannot respond to the insulin and the person becomes hyperglycemic. The hyperglycemia then triggers the release of additional insulin and the person becomes hyperinsulinemic.
- There are a diminished number of receptors? The number of insulin receptors on the membrane can increase or decrease. Obesity and lack of exercise can cause the number of insulin receptors to decrease. This means that obese people can secrete plenty of insulin, but their cells cannot respond to that insulin. The good news is that weight loss and exercise increase the number of insulin receptors, thereby improving the insulin response and relieving the symptoms of diabetes.
- Excess fat (adipose) tissue secretes hormones that oppose the effects of insulin? Some cytokines antagonize insulin, causing a state of insulin resistance.

A strong link obviously exists among insulin resistance, obesity, and diabetes. A new term, *metabolic syndrome,* addresses this issue.

Do You Know...

Who is Dawn and What Is Her Phenomenon?

Dawn refers to the early morning hours, as in sunrise. Diabetics are often hyperglycemic in the early morning hours (at dawn), despite insulin therapy and the lack of food intake during the night. Why? Throughout the night, the person secretes GH. GH stimulates gluconeogenesis and increases blood glucose; this accounts for the early morning hyperglycemia. An adjustment in the timing and type of insulin therapy generally corrects the dawn phenomenon.

GLUCAGON

Glucagon, a second pancreatic hormone, is secreted by the alpha cells of the islets of Langerhans. Its primary action is to increase blood glucose levels (see Figure 14-9). Glucagon raises the blood glucose level in two ways: by stimulating the conversion of glycogen to glucose in the liver and by stimulating the conversion of proteins into glucose (gluconeogenesis). Both these processes ensure a supply of glucose for the busy cells. Because of its effect on blood glucose levels, glucagon is used clinically to treat hypoglycemia. The stimulus for the release of glucagon is a decrease in blood levels of glucose.

GLUCAGON, INFECTION, AND DIABETES

A patient with diabetes is prone to infection. Infection increases glucagon secretion as well as the secretion of all stress hormones, including epinephrine, cortisol, and growth hormone. All these hormones elevate blood glucose levels, causing hyperglycemia. Thus, diabetic people with an infection always have difficulty in controlling their blood glucose levels; they require frequent blood glucose monitoring and additional insulin.

Do You Know...

When Diabetes Is Called "Insipidus"?

"Yuck! This urine is tasteless ... it's insipid!" growled the physician as he sipped his patient's urine. What is going on here? This patient has diabetes insipidus, a condition caused by a deficiency of ADH and characterized by the excretion of a large amount of pale dilute urine.

In the "good old days," physicians actually tasted the patient's urine as a way to diagnose disease. The pale, dilute urine of ADH deficiency is tasteless, in contrast to the sweet-tasting urine of a patient with insulin deficiency, or "sugar" diabetes. The word *diabetes* refers to diuresis (increased flow of urine), whereas the words *insipidus* and *mellitus* refer to the taste of the urine; *insipidus* refers to tasteless and *mellitus* refers to honey tasting. Fortunately, and none too soon, the "Taste Bud Assay" has given way to modern lab tests.

? Re-Think

1. Explain why an insulin deficiency causes hyperglycemia, glucosuria, and polyuria.
2. Compare the effects of insulin and glucagon on blood glucose.

2+2 Sum It Up!

A number of hormones, particularly those secreted by the pancreas, regulate blood glucose levels. Insulin works in two ways to decrease blood glucose levels: (1) it increases the transport of glucose from the blood into the cells, and (2) it stimulates the cells to burn glucose as fuel. Glucagon antagonizes the effects of insulin by increasing blood glucose levels. Insulin is the only hormone that decreases blood glucose levels.

GONADS

The gonads are the sex glands and refer to the ovaries in the female and to the testes in the male. The gonads not only produce ova (eggs) and sperm, but also secrete hormones. The gonads are therefore glands. The ovaries secrete two female sex hormones: estrogen and progesterone. A female appears female (i.e., size, hair, and fat distribution) primarily because of estrogen. The testes secrete testosterone; a male appears male primarily because of testosterone. (Reproductive anatomy and physiology are discussed in Chapters 26 and 27.)

THYMUS GLAND

The **thymus gland** lies in the thoracic cavity behind the sternum. The thymus gland is much larger in a child than in an adult. The gland involutes, or shrinks, as the child enters puberty. The thymus gland secretes hormones called *thymosins,* which play a role in the immune system (described in Chapter 21).

PINEAL GLAND

The **pineal** (PIN-ee-al) **gland** is a cone-shaped gland located close to the thalamus in the brain. It has been called the body's "biological clock," controlling many of its biorhythms. The pineal gland secretes a hormone called *melatonin,* which affects the reproductive cycle by influencing the secretion of hypothalamic-releasing hormones. In general, melatonin plays an important role in sexual maturation.

Melatonin is also thought to play a role in the sleep–wake cycle. The amount of melatonin secreted is related to the amount of daylight. Melatonin secretion is lowest during daylight hours and highest at night. As melatonin levels increase, the person becomes sleepy. Melatonin is therefore said to have a tranquilizing effect. Persons who work night shifts and sleep during the day have a reversed cycle of melatonin production. The reversal of the melatonin cycle is related to the fatigue experienced by night shift workers. Elevated melatonin levels have also been implicated in a type of depression called *seasonal affective disorder* (SAD). This condition occurs primarily in parts of the world where daylight hours are short in the winter, usually in areas far north and far south.

OTHER HORMONES

ORGAN-SPECIFIC HORMONES

The glands identified in Figure 14-1 make up the endocrine system, but numerous hormone-secreting cells are scattered throughout the body. These hormones usually control the activities of a particular organ. For example, hormone-secreting cells in the digestive tract secrete cholecystokinin and gastrin, which help regulate digestion. The kidneys secrete erythropoietin, which helps regulate red blood cell production. The liver secretes a number of hormones, including insulin-like growth factor (IGF-1). IGF-1 mediates the action of growth hormone. (Organ-specific hormones are described in later chapters.)

PROSTAGLANDINS

The prostaglandins (pross-tah-GLAN-dins) are hormones derived from a fatty acid called *arachidonic* (ah-RAK-i-don-ik) *acid.* The prostaglandins are produced by many tissues and generally act locally, near their site of secretion. The prostaglandins play an important role in the regulation of smooth muscle contraction and the inflammatory response. Prostaglandins are also thought to increase the sensitivity of nerve endings to pain. Drugs such as aspirin and ibuprofen block the synthesis of prostaglandins and are therefore useful in relieving pain and inflammation.

ADIPOSE TISSUE HORMONES

Excess adipose tissue acts as a gland—a very nasty gland—that secretes hormones called *cytokines*. First, a word about fat; there is bad fat and worse fat. How so? There's the bad fat that collects around the thighs, giving the person a pear-shaped appearance. There's also a worse fat that collects around the abdominal area ("ab flab"), creating an apple shape. The apple shape is also associated with excess visceral fat (surrounding the organs).

THE TAB OF AB FLAB

The cost is high with regard to heart disease, diabetes mellitus, cancer, and joint disease. Read on!

Heart and Blood Vessels

Most believe that obesity is a risk for heart disease merely because excess weight overburdens the heart. Although this is true, excess adipose tissue, through its cytokines, affects the heart and blood vessels in other ways. For example, adipose tissue contains many narrow blood vessels; in fact, miles of additional blood vessels may be required to carry blood throughout the excess fat. The additional narrowed blood vessels increase blood pressure and strain the heart. Adipose tissue secretes several cytokines that cause the blood vessels to become even narrower. The cytokines also stimulate the immune system, causing inflammation—an important risk factor for heart disease. In fact, inflammation plays a larger role in heart attacks than the narrowing of the coronary (heart) arteries by cholesterol. The cytokines also stimulate blood clotting. Blood clots, in turn, impair blood flow to the heart and brain, thereby predisposing the obese person to heart attack and stroke.

Diabetes Mellitus

Adipose tissue secretes several cytokines that adversely affect glucose metabolism and predispose the person to type 2 diabetes mellitus. First, the cytokines oppose the action of insulin, thereby decreasing the transport of glucose into the cells. Second, the cytokines stimulate the liver to make excess glucose. Both these actions increase blood glucose levels, causing hyperglycemia, a hallmark of diabetes mellitus. In short, cytokines make the obese person resistant to insulin.

Cancer

Fat cells secrete estrogen, a hormone that has been linked to several types of cancer, especially breast cancer.

Joint Disease

The added body weight puts additional stress on joints such as the knees. The joints simply cannot support the extra weight. (So lose the potato chips, get off the couch, and exercise!) An apology to cytokines is in order. Many cytokines cause undesirable effects, as noted previously, but most cytokines exert important and beneficial physiological effects (see Chapter 21).

? Re-Think

1. What is meant by organ-specific hormones?
2. Why is adipose tissue considered a "nasty gland"?

2+2 Sum It Up!

The gonads are glands that include the ovaries in the female and the testes in the male. The ovaries secrete estrogens and progesterone; the testes secrete testosterone. Other endocrine glands include the thymus, liver, and pineal gland. The thymus gland plays an important role in the immune response. The pineal gland is thought to be the body's "biological clock," affecting reproduction and biorhythms. Other hormone-secreting cells are scattered throughout the body. Prostaglandins are chemical mediators of pain and inflammation and act locally. Excess adipose tissue functions as a nasty endocrine gland that contributes to the development of heart disease, diabetes, cancer, and joint disease.

As You Age

1. In general, age-related endocrine changes include an alteration in the secretion of hormones, circulating levels of hormones, metabolism of hormones, and biological activity of hormones.
2. Although most glands decrease their levels of secretion, normal aging does not lead to deficiency states. For example, although adrenal cortical secretion of cortisol decreases, negative feedback mechanisms maintain normal plasma levels of the hormones, thereby preserving water and electrolyte homeostasis.
3. Changes in the thyroid gland cause a decrease in the secretion of thyroid hormones, thereby decreasing the metabolic rate.
4. Decreased secretion of growth hormone causes a decrease in muscle mass and an increase in storage of fat.
5. A diminishment of circadian control of hormone secretion occurs.

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Endocrine System

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
Words			
adrenal	ad-	near	The **adrenal** glands sit atop the kidneys.
	-ren/o-	kidney	
	-al	pertaining to	
adenohypophyseal	aden/o-	gland	The **adenohypophysis** is *the anterior pituitary gland that is located under the hypothalamus.* The **neurohypophysis** (neur/o = nerve) is *the posterior pituitary gland; it is a downward extension of the hypothalamus.*
	-hypophysis-	From a Greek word meaning "to grow under"	
	-al	pertaining to	
adrenocorticotropic	adren/o-	adrenal gland	**Adrenocorticotropic hormone (ACTH)** stimulates the adrenal cortex to secrete steroids.
	-cortic/o-	cortex	
	-troph/o-	nourishment, development	
	-ic	pertaining to	
androgen	andr/o-	male	An **androgen,** such as testosterone, *stimulates the development of male or virilizing characteristics.*
	-gen	origin or production	
endocrine	endo-	within	**Endocrine** glands secrete hormones "within the body"; they are transported about the body by the blood.
	-crin/o-	to secrete	
gonadotropic	gonad/o-	gonad	**Gonadotropic** hormones (FSH and LH) target the gonads, the ovaries, and the testes.
	-troph/o-	nourishment or development	
	-ic	pertaining to	
hyperglycemia	hyper-	excessive	**Hyperglycemia** is *an increase in the amount of glucose in the blood.*
	-glyc/o-	glucose	
	-emia	condition of the blood	
Disorders			
Adrenal Gland Disorders			
adrenal cortical insufficiency and excess			Adrenal cortical deficiencies and excesses are described in the text.
pheochromocytoma	pheochromocyt/o-	catecholamine-secreting cell	**Pheochromocytoma** is *a benign tumor of the adrenal medulla that hypersecretes the catecholamines epinephrine and norepinephrine.*
	-oma	tumor	
Pituitary Gland Disorders			
somatotropic hormone imbalances	somat/o-	body	*Hypersecretion of somatotropic hormone (growth hormone [GH]).* The conditions are described in the text.
	-troph/o-	nourishment, development	
	-ic	condition of	

Continued

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Endocrine System—cont'd

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
diabetes insipidus	dia-	through	*A condition caused by a lack of ADH secretion* ***(central diabetes insipidus)*** *or by the lack of the response of the kidney to ADH* ***(nephrogenic diabetes insipidus).*** Further described in the text.
	-betes	From a Greek word *bainein*, meaning "to go or pass"	
	insipidus	Reference to the word *insipid*, meaning "tasteless"	
syndrome of inappropriate ADH (antidiuretic hormone) secretion	anti-	against	Abbreviated as **SIADH. SIADH** is caused by excess ADH secretion resulting in excess water reabsorption by the kidney, expansion of blood volume, and decreased plasma sodium.
	-diuretic	to increase the flow of urine	
Pancreatic Disorders			
diabetes mellitus	dia-	through	*A deficiency or ineffectiveness of insulin.* There are several types of diabetes mellitus (DM), which is epidemic in the United States: **Type 1 DM,** also called **juvenile-onset diabetes,** usually develops in children and must be treated with insulin. **Type 2 DM** is called **adult-onset diabetes.** The typical adult-onset diabetic is older, obese, and sedentary. **Gestational diabetes mellitus** refers to the appearance of diabetic symptoms only during pregnancy. The symptoms usually subside when the baby is delivered. Unfortunately, in the United States, type 2 diabetes is appearing in children. The development of **MODY** (**m**aturity-**o**nset **d**iabetes in **y**outh) is related to lifestyle (diet, exercise, obesity). Further described in text.
	-betes	From the Latin word *bainein*, meaning "to go or pass"	
	mellitus	honey or sweet	
Parathyroid Gland Disorders			
hyperparathyroidism	hyper-	above or excessive	*Refers to an excess secretion of parathyroid hormone (PTH) causing bone resorption and elevation of plasma calcium (hypercalcemia).* **Primary hyperparathyroidism** is caused by a hypersecretion of the parathyroid glands usually caused by a small tumor such as an adenoma. **Secondary hyperparathyroidism** occurs in response to low plasma calcium caused by vitamin D deficiency or chronic renal failure.
	-parathyroid/o-	parathyroid	
	-ism	condition of	
hypoparathyroidism	hypo-	below or deficient	*Refers to the diminished secretion of parathyroid hormone (PTH) causing low plasma levels of calcium (hypocalcemia).* Further described in the text.
	-parathyroid/o-	parathyroid	
	-ism	condition of	
Thyroid Gland Disorders			
goiter	goiter	From a Latin word meaning "struma" (throat enlargement)	*An enlargement of the thyroid gland, which may or may not be functioning normally.* A **toxic nodular goiter** contains nodules that excrete excess T_3 and T_4, thereby causing a hyperthyroid state. A **nontoxic goiter,** such as a goiter induced by an iodine-deficient diet, does not secrete excess T_3 and T_4. The person is most often euthyroid or experiences mild hypothyroidism.

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Endocrine System—cont'd

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
hyperthyroidism	hyper-	above or excessive	Also called an "overactive thyroid"; **hyperthyroidism** is due to excess synthesis of thyroid hormones (T_3, T_4) by the thyroid gland. **Graves' disease** is the most common type and is described in the text. **Thyrotoxicosis,** which presents as severe hyperthyroidism, is due to an increase in the release of stored T_3 and T_4 from the thyroid gland. **Thyroid storm,** or **thyrotoxic crisis,** is an extreme and life-threatening manifestation of **thyrotoxicosis:** clinical presentation includes extreme elevation in body temperature and cardiac stimulation (tachycardia) progressing to heart failure.
	-thyroid/o-	thyroid	
	-ism	condition of	
hypothyroidism	hypo-	below or deficient	Also called a "sluggish thyroid" and **myxedema** in the adult (described in the text). **Myxedema coma** is *an extreme and life-threatening form of hypothyroidism.* **Cretinism** is *neonatal hypothyroidism;* insufficient treatment with thyroid hormones results in severe physical and mental developmental abnormalities.
	-thyroid/o-	thyroid	
	-ism	condition of	

Get Ready for Exams!

Summary Outline

The endocrine system and the nervous system are the two major communicating and coordinating systems in the body. The endocrine system communicates through chemical signals called *hormones*.

I. Hormones

A. Classification of hormones
1. Hormones are secreted by endocrine glands directly into the blood.
2. Hormones are classified as proteins (protein-related substances) and steroids.

B. Hormone receptors
1. Hormones are aimed at receptors of target organs.
2. Receptors are located on the outer surface of the membrane or inside the cell.
3. Hormone secretion is controlled by three mechanisms: feedback control, biorhythms, and control by the central nervous system.

II. Pituitary Gland

A. Hypothalamic-hypophyseal portal system
1. The portal system is a system of capillaries that connects the hypothalamus and the anterior pituitary.
2. The portal system transports releasing hormones from the hypothalamus to the anterior pituitary gland.

B. Hormones of the anterior pituitary gland
1. Growth hormone stimulates growth and maintains blood glucose levels during periods of fasting.
2. Prolactin (lactogenic hormone) stimulates milk production by the breasts.
3. Tropic hormones stimulate other glands to secrete hormones. These include thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and the gonadotropins (FSH, LH).
4. Thyroid-stimulating hormone stimulates the thyroid gland.
5. Adrenocorticotropic hormone (ACTH) stimulates the adrenal cortex.
6. The gonadotropic hormones (FSH and LH) stimulate the gonads (ovaries and testes).

C. Hormones of the posterior pituitary gland
1. Antidiuretic hormone (ADH) stimulates the kidney to reabsorb water.
2. Oxytocin stimulates the uterine muscle to contract for labor and stimulates the breast to release milk during suckling (milk let-down reflex).

III. Other Endocrine Glands

A. Thyroid gland
1. The follicular cells synthesize triiodothyronine (T_3) and tetraiodothyronine, or thyroxine (T_4). T_3 and T_4 regulate metabolic rate.
2. The parafollicular cells secrete calcitonin. Calcitonin lowers blood calcium level.

B. Parathyroid glands
1. The parathyroid glands secrete parathyroid hormone (PTH).
2. PTH stimulates the bones, kidneys, and intestines to increase blood calcium levels.

C. Adrenal gland
1. The adrenal medulla secretes the catecholamines epinephrine and norepinephrine and causes the "fight-or-flight" response.

2. The adrenal cortex secretes the steroids: glucocorticoids, mineralocorticoids, and sex hormones.

D. Pancreas
1. The pancreas secretes insulin and glucagon.
2. Insulin lowers blood glucose levels, whereas glucagon increases blood glucose levels.

E. Gonads
1. The ovaries are stimulated by the gonadotropins and secrete estrogens and progesterone.
2. The testes are stimulated by the gonadotropins and secrete testosterone.

F. The thymus gland plays an important role in the immune response.

G. The pineal gland houses the "biological clock" and secretes melatonin.

H. Other hormones include organ-specific hormones (cholecystokinin), prostaglandins, and hormones of adipose tissue.

Review Your Knowledge

Matching: Glands

Directions: Match the following words with their descriptions below. Some words may be used more than once.

a. pancreas
b. adrenal cortex
c. anterior pituitary gland
d. adrenal medulla
e. thyroid gland
f. parathyroid glands
g. posterior pituitary gland
h. hypothalamus

1. ___ Contains the beta cells of the islets of Langerhans
2. ___ Secrete glucocorticoids, mineralocorticoids, and androgens
3. ___ Its hormonal secretion is controlled by ACTH.
4. ___ Secretes iodine-containing hormones
5. ___ Secretes releasing hormones
6. ___ Secretes ACTH, TSH, prolactin, growth hormone, and the gonadotropins
7. ___ Its hormone moves calcium from the bone to the blood.
8. ___ Secretes both insulin and glucagon
9. ___ Part of the "fight-or-flight" system; secretes catecholamines
10. ___ The neurohypophysis; secretes ADH and oxytocin

Matching: Hormones

Directions: Match the following words with their descriptions in the right column. Some words may be used more than once.

a. aldosterone
b. insulin
c. prolactin
d. growth hormone
e. parathyroid hormone
f. epinephrine
g. T_3 and T_4
h. oxytocin
i. ACTH
j. ADH

1. ___ Stimulates osteoclastic activity to increase blood calcium
2. ___ Regulates metabolic rate
3. ___ Lowers blood glucose
4. ___ Cortisol is released in response to this hormone.
5. ___ Stimulates the breast to produce milk
6. ___ Catecholamine that participates in the "fight-or-flight" response
7. ___ The neurohypophyseal hormone that controls water balance
8. ___ Prednisone (cortisol) shuts down the secretion of this adenohypophyseal hormone.
9. ___ Also called *somatotropic hormone*
10. ___ The mineralocorticoid that is called the salt-retaining hormone

Multiple Choice

1. Which of the following is true about cortisol?
   a. It is a catecholamine.
   b. It is secreted by the adrenal cortex in response to ACTH.
   c. It stimulates the secretion of ACTH.
   d. It is released by the adrenal medulla in response to sympathetic nerve stimulation.

2. Aldosterone is
   a. a mineralocorticoid secreted by the adrenal cortex.
   b. the primary regulator of blood glucose.
   c. an adenohypophyseal hormone that stimulates the adrenal cortex to secrete cortisol.
   d. a neurohypophyseal hormone that causes the kidneys to reabsorb water.

3. The pancreas
   a. secretes steroids that are concerned with sugar, salt, and sex.
   b. is controlled by a hormone secreted by the anterior pituitary gland.
   c. secretes both insulin and glucagon.
   d. secretes hormones that only lower blood glucose levels.

4. Which of the following best describes the function of insulin?
   a. Regulates blood volume
   b. Stimulates cells to make glucose (gluconeogenesis)
   c. Causes ketone body formation and acidosis
   d. Lowers blood glucose

5. As plasma levels of calcium decrease,
   a. insulin is secreted.
   b. the parathyroid glands secrete calcitonin.
   c. the kidneys excrete calcium and phosphate.
   d. PTH is secreted, thereby stimulating osteoclastic activity.

6. Hypocalcemic tetany is
   a. a consequence of a deficiency of PTH.
   b. caused by calcitonin deficiency.
   c. a consequence of osteoclastic activity.
   d. of concern because it causes osteoporosis.

7. Which of the following is true of glucagon, epinephrine, growth hormone, and cortisol? All
   a. are secreted by the anterior pituitary gland.
   b. are secreted in response to hypocalcemia.
   c. raise blood glucose.
   d. are steroids.