The Endocrine System

CHAPTER 10

John F. Kennedy, the youngest man to be elected president, appeared healthy, vigorous, and active throughout his entire political career. Photos of the president showed a handsome, tanned sailor at the family estate in Massachusetts; others showed the Kennedy family playing football. However, throughout Kennedy's entire political life, he and his staff took great pains to hide his many ailments—in particular, the fact that Kennedy suffered from Addison's disease. This rare illness is caused by a deficiency of adrenal cortex hormones, and you can read about it on pages 219–220. (Ironically, one symptom of Addison's disease is skin that looks like JFK's signature suntan.) Although he was hospitalized many times, Kennedy repeatedly denied having the disease or any other serious health problems. Yet, medical records tell a different story—the president was in almost constant pain, in part because his vertebrae had been destroyed by the medication for Addison's disease. At autopsy, his adrenal glands were shrunken and nonfunctional. Still, there is no evidence that Kennedy's illness affected his performance as president, and he left a legacy that includes the space program and the Peace Corps.

Learning Outcomes

After you have studied this chapter, you should be able to:

10.1 Endocrine Glands (p. 208)

1. Define a hormone, and state the function of hormones.
2. Discuss the difference in mode of action between peptide and steroid hormones.
3. Name the major endocrine glands, and identify their locations.
4. Discuss the control of glandular secretion by humoral, hormonal, and nervous mechanisms, and give an example of how negative feedback functions in these control mechanisms.

10.2 Hypothalamus and Pituitary Gland (p. 212)

5. Explain the anatomical and functional relationships between the hypothalamus and the pituitary gland.
6. Name and discuss two hormones produced by the hypothalamus that are secreted by the posterior pituitary.
7. Name the hormones produced by the anterior pituitary, and describe their function. Indicate which of these hormones control other endocrine glands.

10.3 Thyroid and Parathyroid Glands (p. 215)

8. Discuss the anatomy of the thyroid gland, and the chemical structure and physiological function of its hormones. Describe the effects of thyroid abnormalities.
9. Discuss the function of parathyroid hormone, and describe the effects of parathyroid hormone abnormalities.

10.4 Adrenal Glands (p. 217)

10. Describe the anatomy of the adrenal glands.
11. Discuss the function of the adrenal medulla and its relationship to the nervous system.
12. Name three categories of hormones produced by the adrenal cortex, give an example of each category, and discuss their actions. Describe the effects of adrenal cortex malfunction.

10.5 Pancreas (p. 221)

13. Describe the anatomy of the pancreas.
14. Name three hormones produced by the pancreas, and discuss their functions.
15. Discuss the two types of diabetes mellitus, and contrast hypoglycemia with hyperglycemia.

10.6 Additional Endocrine Glands (p. 224)

16. Name the most important male and female sex hormones. Discuss their functions.
17. State the location and function of the pineal gland and the thymus gland.
18. Discuss atrial natriuretic hormone, leptin, ghreline, growth factors, and prostaglandins as hormones not produced by endocrine glands.

10.7 The Importance of Chemical Signals (p. 225)

19. Give examples to show that chemical signals can act between organs, cells, and individuals.

10.8 Effects of Aging (p. 227)

20. Discuss the anatomical and physiological changes that occur in the endocrine system as we age.

10.9 Homeostasis (p. 227)

21. Discuss how the endocrine system works with other systems of the body to maintain homeostasis.

Visual Focus

The Hypothalamus and the Pituitary (p. 213)

I.C.E.—In Case of Emergency

Insulin Shock and Diabetic Ketoacidosis (p. 222)

What's New

Options for Type I Diabetics: The Artificial Pancreas System and the Biocapsule (p. 223)

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Human Systems Work Together

Endocrine System (p. 228)

10.1 Endocrine Glands

1. Define a hormone, and state the function of hormones.
2. Discuss the difference in mode of action between peptide and steroid hormones.
3. Name the major endocrine glands, and identify their locations.
4. Discuss the control of glandular secretion by humoral, hormonal, and nervous mechanisms, and give an example of how negative feedback functions in these control mechanisms.

The endocrine system consists of glands and tissues that secrete hormones. This chapter will give many examples of the close association between the endocrine and nervous systems. Like the nervous system, the endocrine system is intimately involved in homeostasis.

Hormones are chemical signals that affect the behavior of other glands or tissues. Hormones influence the metabolism of cells, the growth and development of body parts, and homeostasis. **Endocrine glands** are ductless; they secrete their hormones directly into tissue fluid. From there, the hormones diffuse into the bloodstream for distribution throughout the body. Endocrine glands can be contrasted with exocrine glands, which have ducts and secrete their products into these ducts. For example, the salivary glands send saliva into the mouth by way of the salivary ducts.

Each type of hormone has a unique composition. Even so, hormones can be categorized as either **peptide hormones** (which include proteins, glycoproteins, and modified amino acids) or **steroid hormones.** All steroid hormones are lipids that have the same four-carbon ring complex, but each has different side chains. The majority of hormones are peptides.

Figure 10.1 depicts the locations of the major endocrine glands in the body, and Table 10.1 lists the hormones they release. It's important for you to remember that other organs produce hormones, too. These additional hormones and their actions will be described in detail in later chapters. Further, hormones aren't the only type of chemical signal. Neurotransmitters (which you learned about in Chapter 9) are one example of signaling molecules that allow direct communication from cell to cell, and you'll learn about others here as well.

How Hormones Function

Along with fundamental differences in structure, peptide and steroid hormones also function differently. Most peptide hormones bind to a receptor protein in the plasma membrane and activate a "second messenger" system (Fig. 10.2). The "second messenger" causes the cellular changes for which the hormone is credited. As an analogy, suppose you're the person in charge of a crew assigned to redecorate a room. As such, you stand outside the room and direct the workers inside the room. The workers clean, paint, apply wallpaper, etc. Like the "boss" in this analogy, the peptide hormone stays outside the cell and directs activities within. The peptide hormone, or "first messenger," activates a "second messenger"—the crew workers inside the cell. Common second messengers found in many body cells include **cyclic AMP** (made from ATP, and abbreviated cAMP) and calcium. The second messenger sets in motion an enzyme cascade, so called because each enzyme in turn activates several others, and so on. These intracellular enzymes cause the changes in the cell that are associated with the hormone. Because of the second messenger system, the binding of a single peptide hormone can result in as much as a thousandfold response. The cellular response can be a change in cellular behavior or the formation of an end product that leaves the cell. For example, by activating a second messenger, insulin causes the facilitated diffusion of glucose into body cells, while thyroid-stimulating hormone causes thyroxine release from the thyroid gland.

Because steroid hormones are lipids, they diffuse across the plasma membrane and other cellular membranes (Fig. 10.3). Inside the cell, steroid hormones such as estrogen and progesterone bind to receptor proteins. The hormone-receptor complex then binds to DNA, activating particular genes. Activation leads to production of a cellular enzyme in varying quantities. Again, it is largely intracellular enzymes that cause the cellular changes for which the hormone receives credit. For example, estrogen directs cellular enzymes that cause the growth of axillary and pubic hair in an adolescent female.

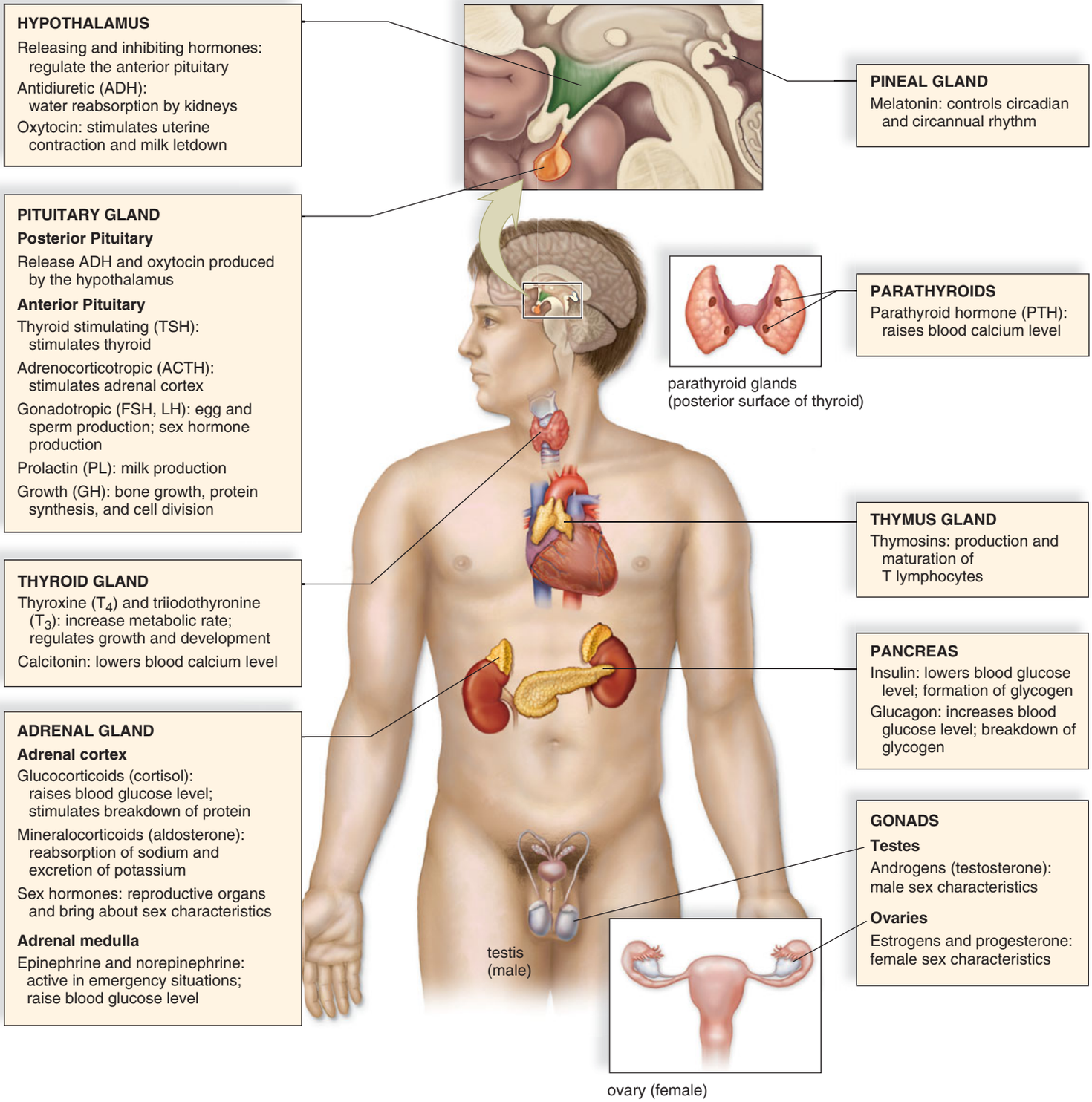
When protein hormones such as insulin are used for medical purposes, they must be administered by injection. If these hormones were taken orally, they would be acted on by digestive enzymes. Once digested, insulin cannot carry out its functions. Steroid hormones, such as those in birth control pills, can be taken orally because they're water-insoluble lipids and poorly digested. Steroids can pass through the digestive tract largely undigested, and then diffuse through the plasma membrane into the cell.

Hormone Control

The release of hormones is usually controlled by one or more of three mechanisms: (1) the concentration of dissolved molecules or ions in the blood, referred to as *humoral* control; (2) by the actions of other hormones; and/or (3) by the nervous system.

It's important for ions or molecules in the body to be kept within a normal range to maintain homeostasis. Thus, humoral control determines the secretion of many body hormones. For example, when the blood glucose level rises following a meal, the pancreas secretes insulin. Insulin causes the liver to store glucose and the cells to take up glucose, and blood glucose is lowered back to normal. Once the blood glucose concentration is corrected, the pancreas stops producing insulin. In much the same way, a low level of calcium ions in the blood stimulates the secretion of parathyroid hormone (PTH) from the parathyroid gland. When blood calcium rises to a normal level, secretion of PTH stops. These examples of humoral control illustrate regulation by negative feedback.

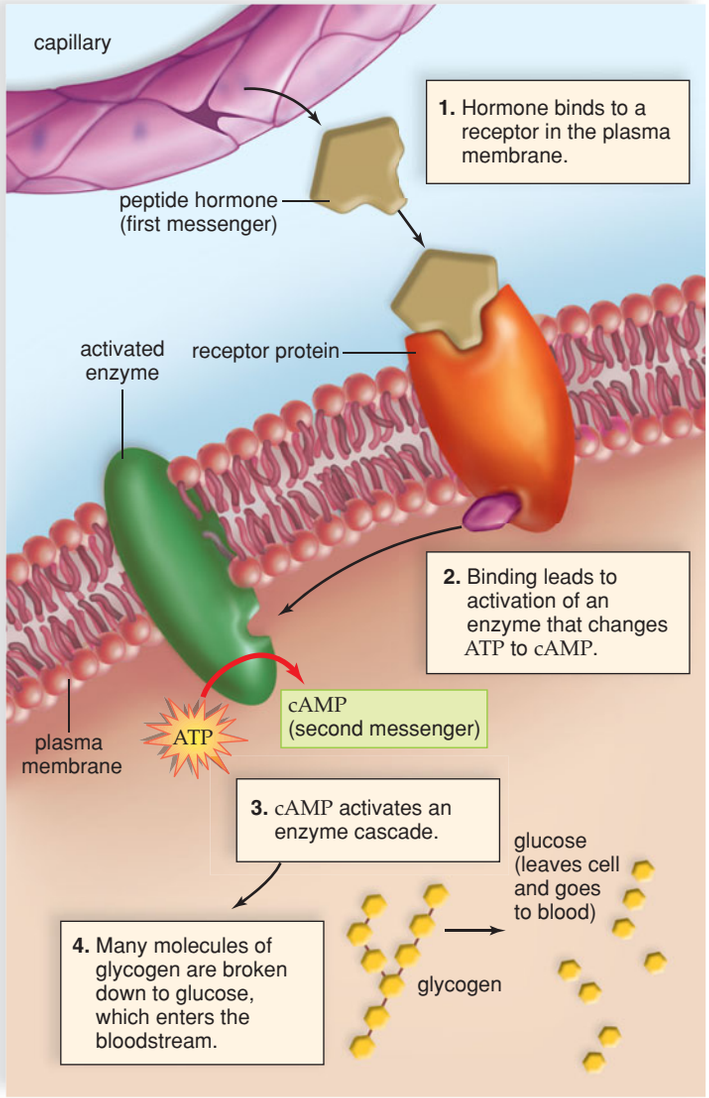
Hormone release can also be controlled by specific stimulating or inhibiting hormones. Thyroid-stimulating hormone (TSH) from the pituitary gland (also called **thyrotropin**) does exactly what its name implies—it stimulates the thyroid gland to produce thyroid hormone. By contrast, the release of insulin is inhibited by the production of glucagon by the pancreas. Insulin lowers the blood glucose level, whereas glucagon raises it. In subsequent sections of this



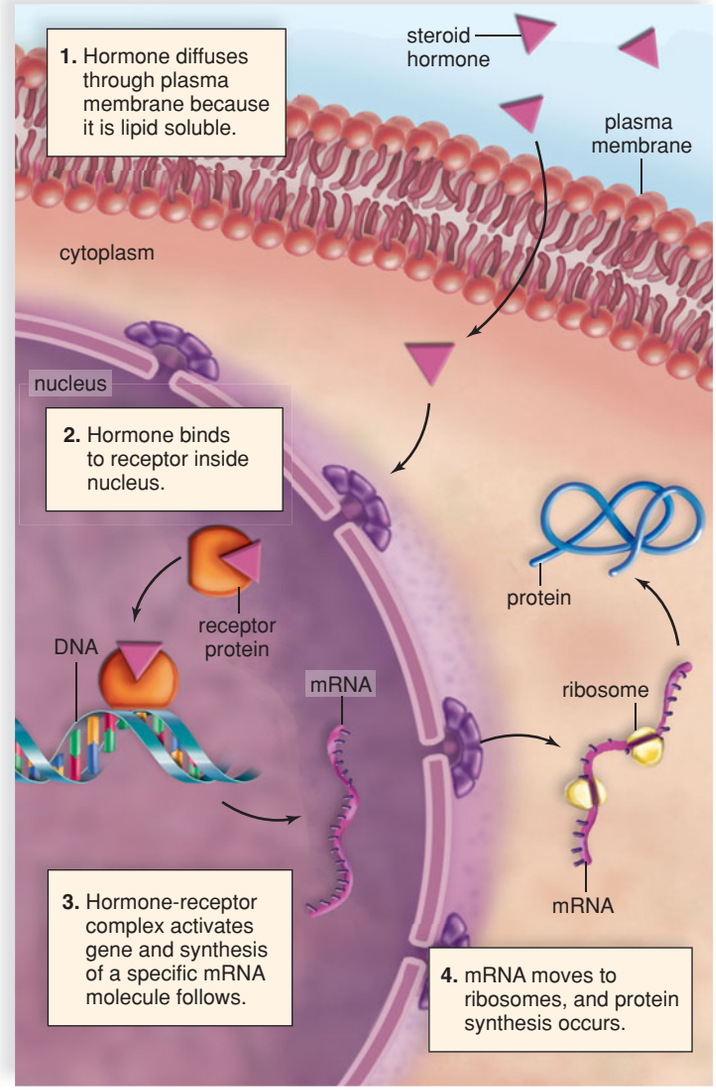
AP|R Figure 10.1 Anatomical location of major endocrine glands in the body. The hypothalamus, pituitary, and pineal glands are in the brain, the thyroid and parathyroids are in the neck, and the adrenal glands and pancreas are in the abdominal cavity. The gonads include the ovaries in females, located in the pelvic cavity, and the testes in males, located outside this cavity in the scrotum. The thymus gland lies within the thoracic cavity.

TABLE 10.1 Principal Endocrine Glands and Hormones

Endocrine Gland	Hormone Released	Chemical Class	Target Tissues/Organs	Chief Function(s) of Hormone
Hypothalamus	Hypothalamic-releasing and inhibiting hormones	Peptide	Anterior pituitary	Regulate anterior pituitary hormones
Produced by hypothalamus, released from posterior pituitary	Antidiuretic (ADH)	Peptide	Kidneys	Stimulates water reabsorption by kidneys and blood vessel constriction
	Oxytocin	Peptide	Uterus, mammary glands	Stimulates uterine muscle contraction, release of milk by mammary glands
Anterior pituitary	Thyroid-stimulating (TSH)	Glycoprotein	Thyroid	Stimulates thyroid gland
	Adrenocorticotropic (ACTH)	Peptide	Adrenal cortex	Stimulates adrenal cortex
	Gonadotropic Follicle-stimulating (FSH) Luteinizing (LH)	Glycoprotein	Gonads	Egg and sperm production; sex hormone production
	Prolactin (PRL)	Protein	Mammary glands	Milk production
	Growth (GH)	Protein	Soft tissues, bones	Cell division, protein synthesis, and bone growth
	Melanocyte-stimulating (MSH)	Peptide	Melanocytes in skin	Unknown function in humans; regulates skin color in lower vertebrates
Thyroid	Thyroxine (T_4) and triiodothyronine (T_3)	Iodinated amino acid	All tissues	Increases metabolic rate; regulates growth and development
	Calcitonin	Peptide	Bones, kidneys, intestine	Lowers blood calcium level
Parathyroids	Parathyroid (PTH)	Peptide	Bones, kidneys, intestine	Raises blood calcium level
Adrenal gland				
Adrenal cortex	Glucocorticoids (cortisol)	Steroid	All tissues	Raise blood glucose level; stimulate breakdown of protein
	Mineralocorticoids (aldosterone)	Steroid	Kidneys	Reabsorb sodium and excrete potassium
	Sex hormones	Steroid	Gonads, skin, muscles, bones	Stimulate reproductive organs and bring about sex characteristics
Adrenal medulla	Epinephrine and norepinephrine	Modified amino acid	Cardiac and other muscles	Released in emergency situations; raise blood glucose level
Pancreas	Insulin	Protein	Liver, muscles, adipose tissue	Lowers blood glucose level; promotes formation of glycogen
	Glucagon	Protein	Liver, muscles, adipose tissue	Raises blood glucose level
	Somatostatin	Protein	Pancreatic alpha + beta cells	Inhibits insulin and glucagon, prevents wide fluctuations in blood glucose
Gonads				
Testes	Androgens (testosterone)	Steroid	Gonads, skin, muscles, bones	Stimulate male sex characteristics
Ovaries	Estrogens and progesterone	Steroid	Gonads, skin, muscles, bones	Stimulate female sex characteristics
Thymus	Thymosins	Peptide	T lymphocytes	Stimulate production and maturation of T lymphocytes
Pineal gland	Melatonin	Modified amino acid	Brain	Controls circadian and circannual rhythms; possibly involved in maturation of sexual organs



AP|R **Figure 10.2 Action of a peptide hormone.** The binding of a peptide hormone leads to cAMP and then to activation of an enzyme cascade. In this example, the hormone causes glycogen to be broken down to glucose.



AP|R **Figure 10.3 Action of a steroid hormone.** A steroid hormone results in a hormone-receptor complex that activates DNA and protein synthesis.

chapter, you'll learn about other instances in which pairs of hormones work opposite to one another, and thereby bring about the regulation of a substance in the blood.

The nervous system is an important controller of the endocrine system. Upon receiving sensory information from the body, the brain can make appropriate adjustments to hormone secretion to ensure homeostasis. For example, while you eat a meal, sensory information is relayed to the brain. In turn, the brain signals parasympathetic motor neurons to cause the release of insulin from the pancreas. (Recall that the parasympathetic neurons control "rest and digest" functions.) Insulin will allow body cells to take up glucose from digested food.

It's important to stress that many hormones are influenced by more than one control mechanism. In the previous examples, you can see that insulin release is influenced by all three controllers: humoral, hormonal, and neural control. For the majority of hormones, control is regulated by negative feedback. As you know from Chapter 1, in a negative feedback system, a stimulus causes a body response. The body response, in turn, corrects the initial stimulus. The result is that the activity of the hormone is maintained within normal limits and homeostasis is ensured. However, in a few instances, positive feedback controls the release of a hormone—for example, release of oxytocin during labor and delivery (discussed on page 212).

Content CHECK-UP!

1. Antidiuretic hormone (ADH), a peptide hormone, works by:
   a. binding to a receptor outside the cell and activating a second messenger.
   b. diffusing into the cell, binding to a receptor inside the cell, and activating a second messenger.
   c. diffusing into the cell, binding to a receptor inside the cell, and activating genes in DNA.
2. Testosterone, a steroid hormone, works by:
   a. binding to a receptor outside the cell and activating a second messenger.
   b. diffusing into the cell, binding to a receptor inside the cell, and activating a second messenger.
   c. diffusing into the cell, binding to a receptor inside the cell, and activating genes in DNA.
3. Antidiuretic hormone stimulates the kidneys to reabsorb water and return it to the blood plasma. ADH release is controlled by a negative feedback system. Which action causes ADH to be released?
   a. drinking a big bottle of water
   b. finishing a marathon race and becoming dehydrated

Answers in Appendix B.

10.2 Hypothalamus and Pituitary Gland

5. Explain the anatomical and functional relationships between the hypothalamus and the pituitary gland.
6. Name and discuss two hormones produced by the hypothalamus that are secreted by the posterior pituitary.
7. Name the hormones produced by the anterior pituitary, and describe their function. Indicate which of these hormones control other endocrine glands.

The **hypothalamus** regulates the internal environment. For example, through the autonomic nervous system, the hypothalamus helps control heartbeat, body temperature, and water balance (by creating thirst). The hypothalamus also controls the glandular secretions of the **pituitary gland (hypophysis).** The pituitary, a small gland about 1 cm in diameter, is connected to the hypothalamus by a stalklike structure. The pituitary has two portions: the **posterior pituitary (neurohypophysis)** and the **anterior pituitary (adenohypophysis).**

Posterior Pituitary

Neurons in the hypothalamus called neurosecretory cells produce the hormones antidiuretic hormone (ADH) and oxytocin (Fig. 10.4, *left*). These hormones pass through axons into the posterior pituitary (neurohypophysis) where they are stored in axon endings. Thus, the hypothalamic hormones antidiuretic hormone and oxytocin are produced in the hypothalamus, but are released into the bloodstream from the posterior pituitary.

Antidiuretic Hormone and Oxytocin

Certain neurons in the hypothalamus are sensitive to the water-salt balance of the blood. When these cells determine that the blood is too concentrated, **antidiuretic hormone** (**ADH,** also called *vasopressin*) is released from the posterior pituitary. In your body, blood becomes concentrated if you have just finished exercising heavily and body water has been lost as sweat. Upon reaching the kidneys, ADH causes more water to be reabsorbed into kidney capillaries. As the blood becomes diluted once again, ADH is no longer released. This is an example of control by negative feedback because the effect of the hormone (to dilute blood) acts to shut down the release of the hormone. An additional effect of ADH is to raise blood pressure, by vasoconstriction of blood vessels throughout the body (hence, the hormone's additional name of vasopressin). This mechanism also illustrates negative feedback: Blood pressure falls because body water is lost as sweat (stimulus); vasopressin is released (response); blood vessels constrict and blood pressure rises to normal (stimulus corrected). Negative feedback maintains stable conditions and homeostasis.

Inability to produce ADH causes **diabetes insipidus** (watery urine), in which a person produces copious amounts of urine with a resultant loss of ions from the blood. The condition can be corrected by the administration of ADH.

It's interesting to note that alcohol suppresses ADH production and release. When ADH is absent, the kidneys don't reabsorb as much water. The person drinking alcohol urinates more often and may become dehydrated as a result. The symptoms of the drinker's "hangover"—headache, nausea, dizziness—are largely due to dehydration.

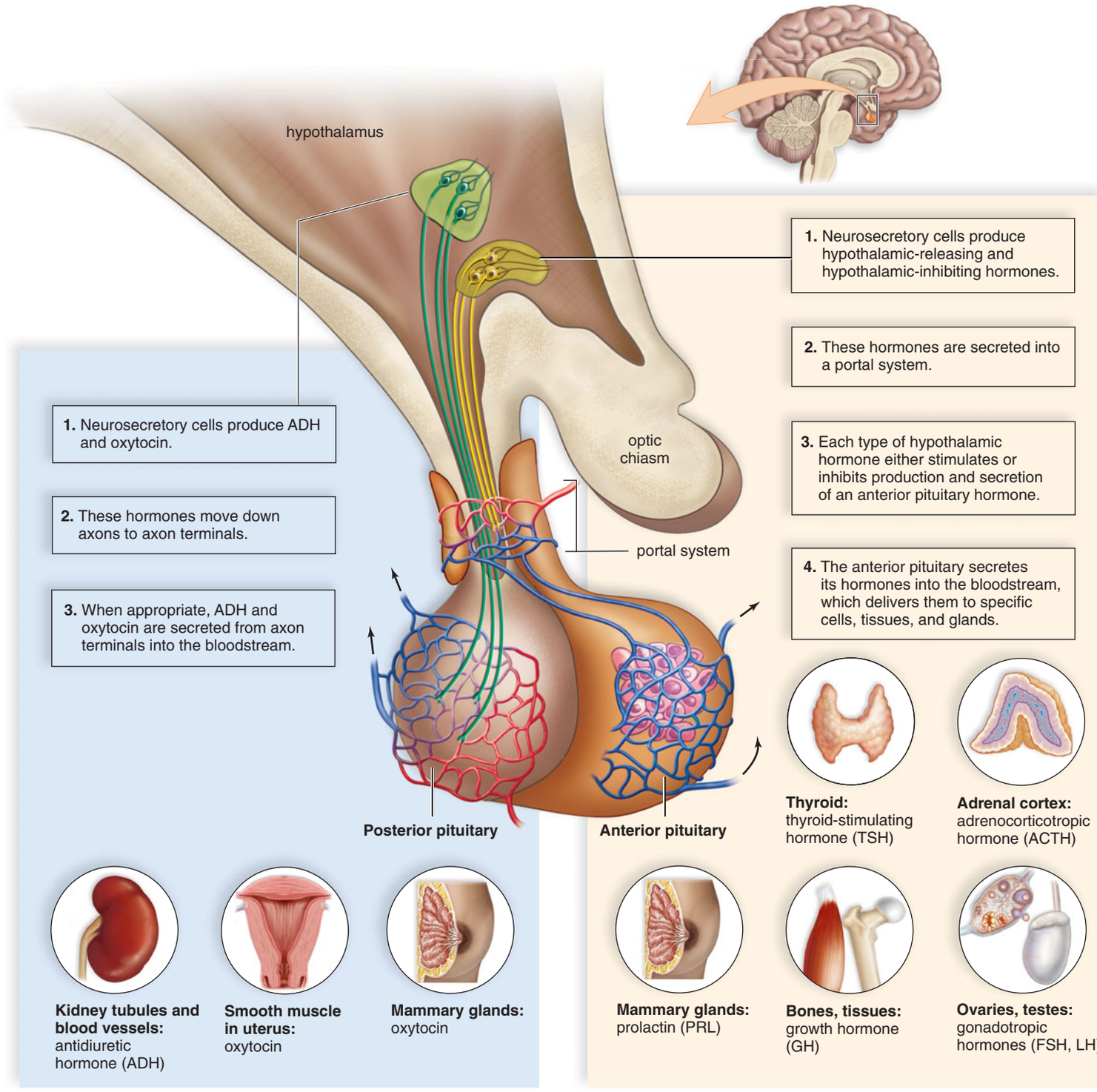
Oxytocin, the other hormone made in the hypothalamus, causes uterine contraction during childbirth and milk letdown when a baby is nursing. The more the uterus contracts during labor, the more nerve impulses reach the hypothalamus, causing oxytocin to be released. Similarly, the more a baby suckles, the more oxytocin is released. In both instances, the release of oxytocin from the posterior pituitary is controlled by **positive feedback**—that is, the stimulus continues to bring about an effect that continues to increase in intensity. Positive feedback is not the best way to maintain stable conditions and homeostasis. However, it works during childbirth and nursing because external mechanisms interrupt the process. In childbirth, the delivery of the baby and afterbirth (the placenta and membranes surrounding the baby) eventually stops oxytocin secretion. When a baby with a full tummy stops nursing, that, too, halts oxytocin secretion. For a nursing mother, the letdown response to oxytocin becomes automatic over time. Thus, it is referred to as a *neuroendocrine reflex*. When the baby begins to suckle, the pressure and touch sensations signal the hypothalamus, oxytocin is released, and the stream of breast milk begins. Similarly, hearing a baby cry—even someone else's baby—will cause a nursing mother's breast milk to flow.

Anterior Pituitary

A portal system lies between the hypothalamus and the anterior pituitary (Fig. 10.4, *center*). In this example, the term **portal system** is used to describe the following unique pattern of circulation:

capillaries → vein → capillaries → vein

The hypothalamus controls the anterior pituitary by producing **hypothalamic-releasing hormones** and **hypothalamic-inhibiting hormones.** For example, there is a thyrotropin-releasing hormone

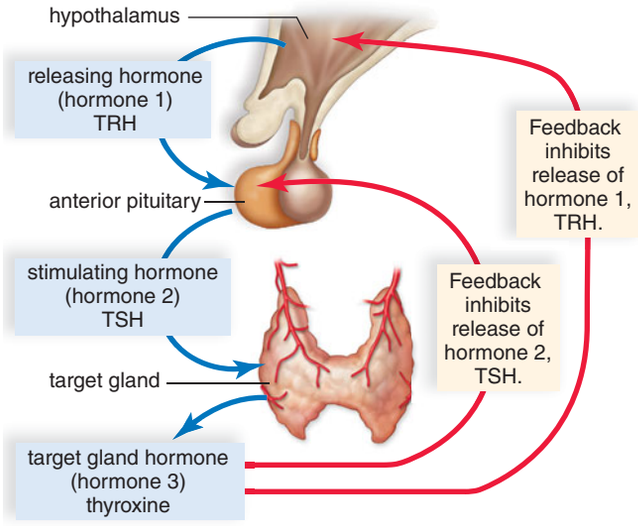


AP|R **Figure 10.4 The hypothalamus and the pituitary.** *Left:* The hypothalamus produces two hormones, ADH and oxytocin, which are stored and secreted by the posterior pituitary. *Right:* The hypothalamus controls the secretions of the anterior pituitary, and the anterior pituitary controls the secretions of the thyroid, adrenal cortex, and gonads, which are also endocrine glands. It also secretes growth hormone and prolactin.

(TRH) and a prolactin-inhibiting hormone (PIH). TRH stimulates the anterior pituitary to secrete thyroid-stimulating hormone, and PIH inhibits the pituitary from secreting prolactin.

Hormones That Affect Other Glands

Four of the hormones produced by the anterior pituitary have an effect on other glands: **Thyroid-stimulating hormone (TSH,** or **thyrotropin)** stimulates the thyroid to produce the thyroid hormones; **adrenocorticotropic hormone (ACTH,** or **corticotropin)** stimulates the adrenal cortex to produce its hormones; and **gonadotropic hormones** (**follicle-stimulating hormone—FSH** and **luteinizing hormone—LH**) stimulate the gonads—the testes in males and the ovaries in females—to produce gametes and sex hormones. The hypothalamus, the anterior pituitary, and other glands controlled by the anterior pituitary are all involved in self-regulating negative feedback mechanisms that maintain stable conditions. In each instance, the blood level of the last hormone in the sequence exerts negative feedback control over the secretion of the first two hormones:



Effects of Other Hormones

Other hormones produced by the anterior pituitary do not affect other endocrine glands. **Prolactin (PRL)** is produced beginning at about the fifth month of pregnancy, and is produced in quantity after childbirth. It causes the mammary glands in the breasts to develop and produce milk. It also plays a role in carbohydrate and fat metabolism.

Growth hormone (GH), or somatotropic hormone, stimulates protein synthesis within cartilage, bone, and muscle. It stimulates the rate at which amino acids enter cells and protein synthesis occurs. It also promotes fat metabolism as opposed to glucose metabolism.

Begin Thinking Clinically

An adenoma, which is one type of pituitary gland tumor, can affect the production of one or more pituitary hormones. What would be the effect of a prolactin adenoma in a man?

Answer and discussion in Appendix B.

Effects of Growth Hormone

The amount of GH produced by the anterior pituitary affects the height of the individual. The quantity of GH produced is greatest during childhood and adolescence, when most body growth is occurring. If too little GH is produced during childhood, the individual has **pituitary dwarfism,** characterized by perfect proportions but small stature. If too much GH is secreted, a person can become a giant (Fig. 10.5). Giants usually have poor health, primarily because GH has a secondary effect on the blood sugar level, promoting an illness called diabetes mellitus (see pages 221–222).

On occasion, GH is overproduced in the adult and a condition called **acromegaly** results. Because long bone growth is no longer possible in adults, the feet, hands, and face (particularly the chin, nose, and eyebrow ridges) can respond, and these portions of the body become overly large (Fig. 10.6).

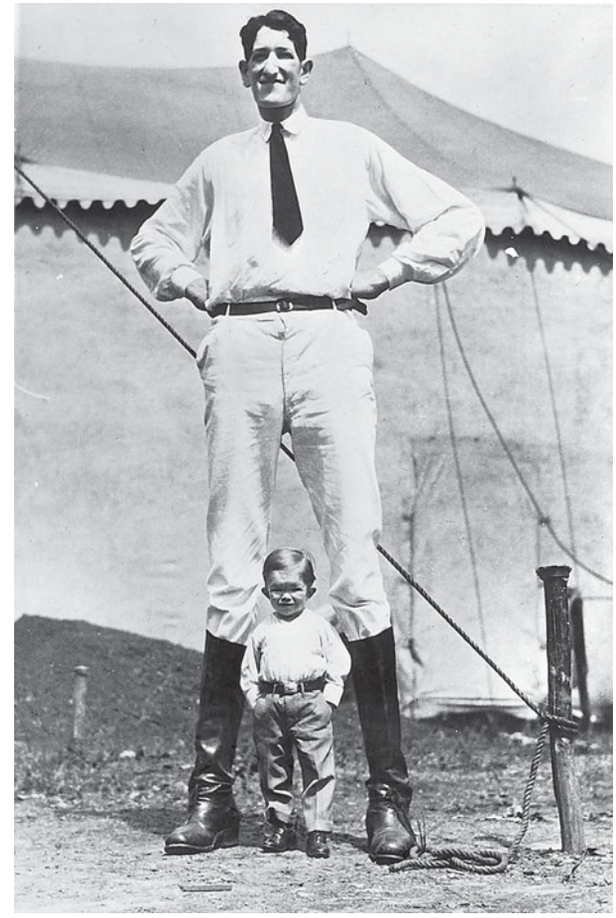


Figure 10.5 Effect of growth hormone. The amount of growth hormone produced by the anterior pituitary during childhood affects the height of an individual. Too much growth hormone can lead to giantism, while an insufficient amount results in limited stature and even pituitary dwarfism.

Figure 10.6 **Acromegaly.** Acromegaly is caused by overproduction of GH in the adult. It is characterized by enlargement of the bones in the face, the fingers, and the toes as a person ages.

Content **CHECK-UP!**

4. Name three anterior pituitary hormones that cause the release of another hormone(s).
5. Oxytocin release from the hypothalamus during labor and delivery is a mechanism that works by:
   a. positive feedback. b. negative feedback.
6. Which of the following is an effect of growth hormone?
   a. It promotes fat metabolism.
   b. It stimulates protein synthesis in bone and cartilage.
   c. It causes a person to grow taller.
   d. All of the above

Answers in Appendix B.

10.3 Thyroid and Parathyroid Glands

8. Discuss the anatomy of the thyroid gland, and the chemical structure and physiological function of its hormones. Describe the effects of thyroid abnormalities.
9. Discuss the function of parathyroid hormone, and describe the effects of parathyroid hormone abnormalities.

The **thyroid gland** is a large gland located in the neck, where it is attached to the trachea just below the larynx (see Fig. 10.1). The parathyroid glands are embedded in the posterior surface of the thyroid gland.

Thyroid Gland

The thyroid gland is composed of a large number of follicles, each a small spherical structure made of thyroid cells filled with **triiodothyronine** (T_3), which contains three iodine atoms, and **thyroxine** (T_4), which contains four iodine atoms. These are the two forms of thyroid hormone; T_3 is thought to have the greatest effect on the body.

Effects of Thyroid Hormones

To produce triiodothyronine and thyroxine, the thyroid gland actively acquires iodine. The concentration of iodine in the thyroid gland can increase to as much as 25 times that of the blood. If iodine is lacking in the diet, the thyroid gland is unable to produce the thyroid hormones. In response to constant stimulation by the anterior pituitary, the thyroid enlarges, resulting in a **simple, or endemic, goiter** (Fig. 10.7). Some years ago, it was discovered that

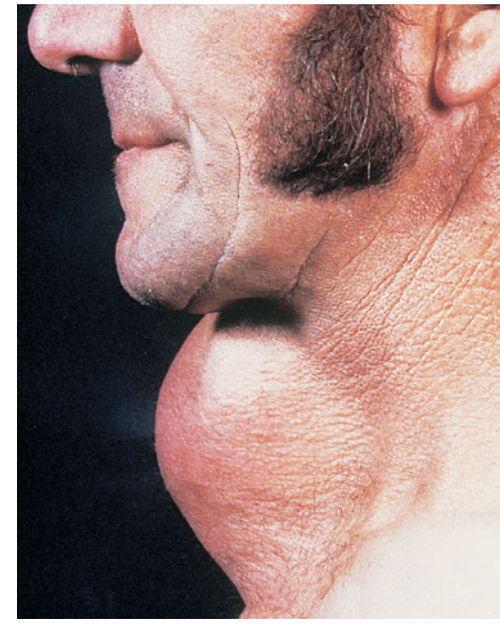


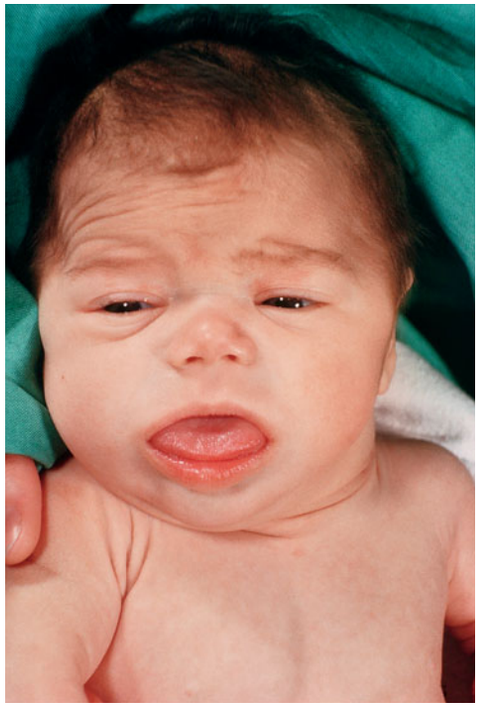
Figure 10.7 **Simple goiter.** An enlarged thyroid gland is often caused by a lack of iodine in the diet. Without iodine, the thyroid is unable to produce its hormones, and continued anterior pituitary stimulation causes the gland to enlarge.

the use of iodized salt allows the thyroid to produce the thyroid hormones, and therefore helps prevent simple goiter.

Thyroid hormones increase the metabolic rate. They do not have a single target organ; instead, they stimulate all cells of the body to metabolize at a faster rate. More glucose is broken down, and more energy is utilized.

If the thyroid fails to develop properly, a condition called **congenital hypothyroidism** results (Fig. 10.8). Individuals with this condition are short and stocky and have had extreme hypothyroidism (undersecretion of thyroid hormone) since infancy or childhood. Thyroid hormone therapy can initiate growth, but unless treatment is begun within the first two months of life, severe developmental delay results. The occurrence of hypothyroidism in adults produces the condition known as **myxedema,** which is characterized by lethargy, weight gain, loss of hair, slower pulse rate, lowered body temperature, and thickness and puffiness of the skin. The administration of adequate doses of thyroid hormones restores normal function and appearance.

In the case of hyperthyroidism (oversecretion of thyroid hormone), as seen in **Graves' disease,** the thyroid gland is overactive, and a goiter forms. This type of goiter is called **exophthalmic goiter.** The eyes protrude because of edema in eye socket tissues and swelling of the muscles that move the eyes. The patient usually becomes hyperactive, nervous, and irritable, and suffers from insomnia. Removal or destruction of a portion of the thyroid by means of radioactive iodine is generally effective in curing the condition. Hyperthyroidism can also be caused by a thyroid tumor, which is usually detected as a lump during physical examination. Again, the treatment is surgery in combination with administration of radioactive iodine. The prognosis for most patients is excellent.



AP|R **Figure 10.8 Congenital hypothyroidism.** Individuals who have hypothyroidism since infancy or childhood do not grow and develop as others do. Unless medical treatment is begun, the body is short and stocky. Developmental delay is also likely.

Calcitonin

Calcium (Ca^{2+}) plays a significant role in both nervous conduction and muscle contraction. It is also necessary for coagulation (clotting) of blood. The blood calcium level is regulated in part by **calcitonin,** a hormone secreted by the thyroid gland when the blood calcium level rises (Fig. 10.9). The primary effect of calcitonin is to bring about the deposit of calcium in the bones. It does this by temporarily reducing the activity and number of osteoclasts. Recall from Chapter 6 that these cells break down bone. When the blood calcium lowers to normal, the release of calcitonin by the thyroid is inhibited, but a low calcium level stimulates the release of parathyroid hormone (PTH) by the parathyroid glands. Calcitonin is an important hormone in children, whose skeleton is undergoing rapid growth. By contrast, calcitonin is of minor importance in adults because parathyroid hormone is the major controller of calcium homeostasis. However, calcitonin can be used therapeutically in adults to reduce the effects of osteoporosis (see the Medical Focus on page 102).

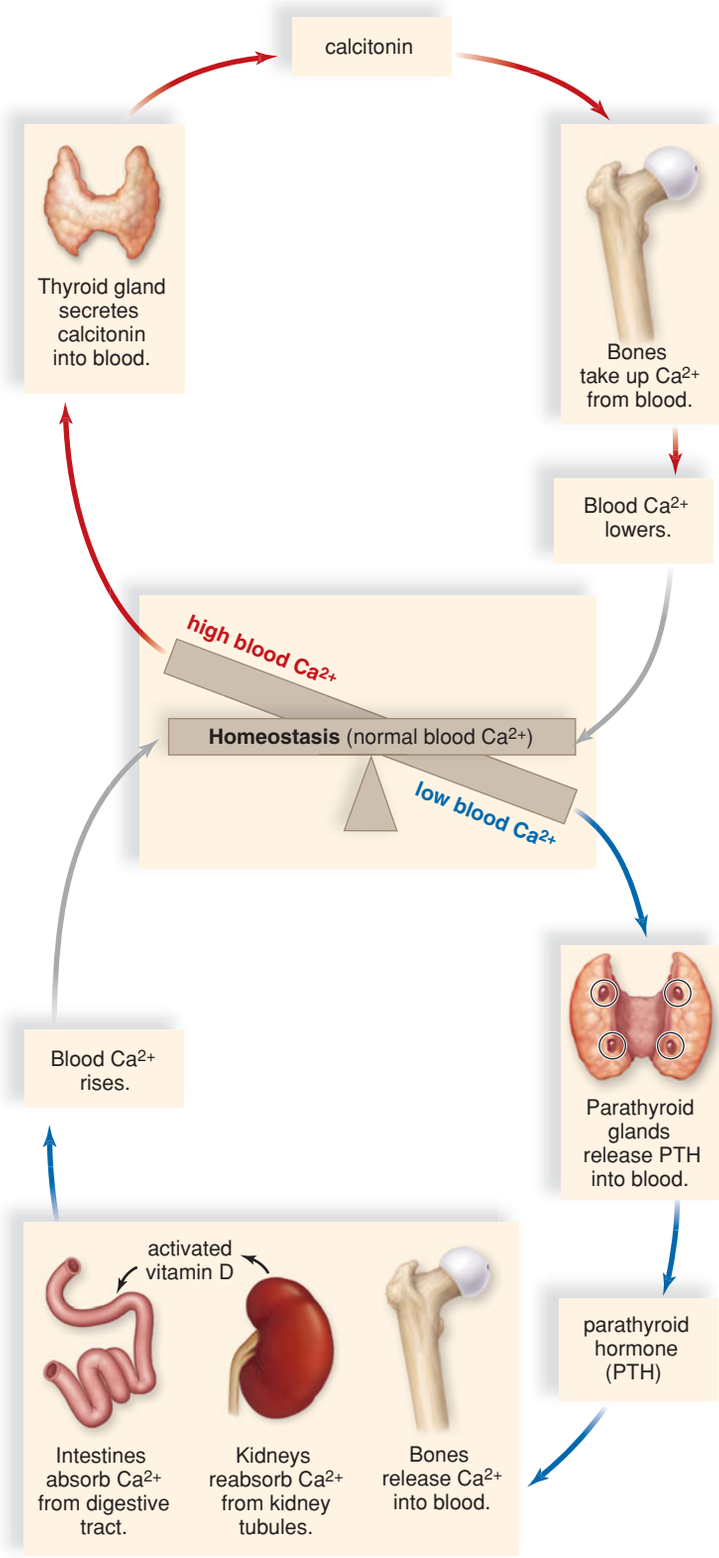
Parathyroid Glands

Parathyroid hormone (PTH), the hormone produced by the **parathyroid glands,** causes the blood phosphate (HPO_4^{2-}) level to decrease and the ionic blood calcium (Ca^{2+}) level to increase. The antagonistic actions of calcitonin, from the thyroid gland, and parathyroid hormone, from the parathyroid glands, maintain the blood calcium level within normal limits.

Note in Figure 10.9 that after a low blood calcium level stimulates the release of PTH, the hormone promotes release of calcium from the bones. (It does this by promoting the activity of osteoclasts.) PTH promotes the reabsorption of calcium by the kidneys, where it also activates a form of vitamin D called **calcitriol**. Calcitriol, in turn, stimulates the absorption of calcium from the intestine. These effects bring the blood calcium level back to the normal range so that the parathyroid glands no longer secrete PTH.

Many years ago, the four parathyroid glands were sometimes mistakenly removed during thyroid surgery because of their size and location in the thyroid. When insufficient parathyroid hormone production leads to a dramatic drop in the blood calcium level, hypocalcemia results. **Hypocalcemia** can result in seizures, abnormal heart rhythms, and hypocalcemic tetany. In **tetany,** the body shakes from continuous muscle contraction. This effect is brought about by increased excitability of the nerves, which initiate nerve impulses spontaneously and without rest. In severe cases, hypocalcemic tetany is fatal because of muscular spasms of the airways and heart failure.

Excessive parathyroid hormone secretion can result from a tumor involving parathyroid tissue, or from a genetic disorder. In this case, **hypercalcemia** results. Excessive blood calcium in hypercalcemia can cause muscle weakness, abnormal heart rhythms, renal failure, and coma. Extreme hypercalcemia causes heart failure and death.



AP|R **Figure 10.9 Regulation of blood calcium level.** *Top:* When the blood calcium (Ca^{2+}) level is high, the thyroid gland secretes calcitonin. Calcitonin promotes the uptake of Ca^{2+} by the bones, and therefore the blood Ca^{2+} level returns to normal. *Bottom:* When the blood Ca^{2+} level is low, the parathyroid glands release parathyroid hormone (PTH). PTH causes the bones to release Ca^{2+}. It also causes the kidneys to reabsorb Ca^{2+} and activate vitamin D; thereafter, the intestines absorb Ca^{2+}. Therefore, the blood Ca^{2+} level returns to normal.

Content CHECK-UP!

7. Which of the following conditions is caused by excessive thyroid hormone?
- a. Graves' disease
- b. cretinism (congenital hypothyroidism)
- c. simple goiter
- d. myxedema

8. Which mineral is necessary to manufacture thyroid hormones?
- a. sodium
- b. iron
- c. calcium
- d. iodine

9. The target organs for parathyroid hormone are:
- a. kidney, liver, stomach.
- b. kidney, bone, liver.
- c. kidney, bone, small intestine.
- d. bone, liver, small intestine.

Answers in Appendix B.

10.4 Adrenal Glands

10. Describe the anatomy of the adrenal glands.
11. Discuss the function of the adrenal medulla and its relationship to the nervous system.
12. Name three categories of hormones produced by the adrenal cortex, give an example of each category, and discuss their actions. Describe the effects of adrenal cortex malfunction.

The **adrenal glands** sit atop the kidneys (see Fig. 10.1). Each adrenal gland consists of an inner portion called the **adrenal medulla** and an outer portion called the **adrenal cortex.** These portions, like the anterior pituitary and the posterior pituitary, have no physiological connection with one another. The adrenal medulla is under nervous control, and the adrenal cortex is under the control of ACTH (also called **corticotropin**), an anterior pituitary hormone. Stress of all types, including emotional and physical trauma, prompts the hypothalamus to stimulate the adrenal glands (Fig. 10.10).

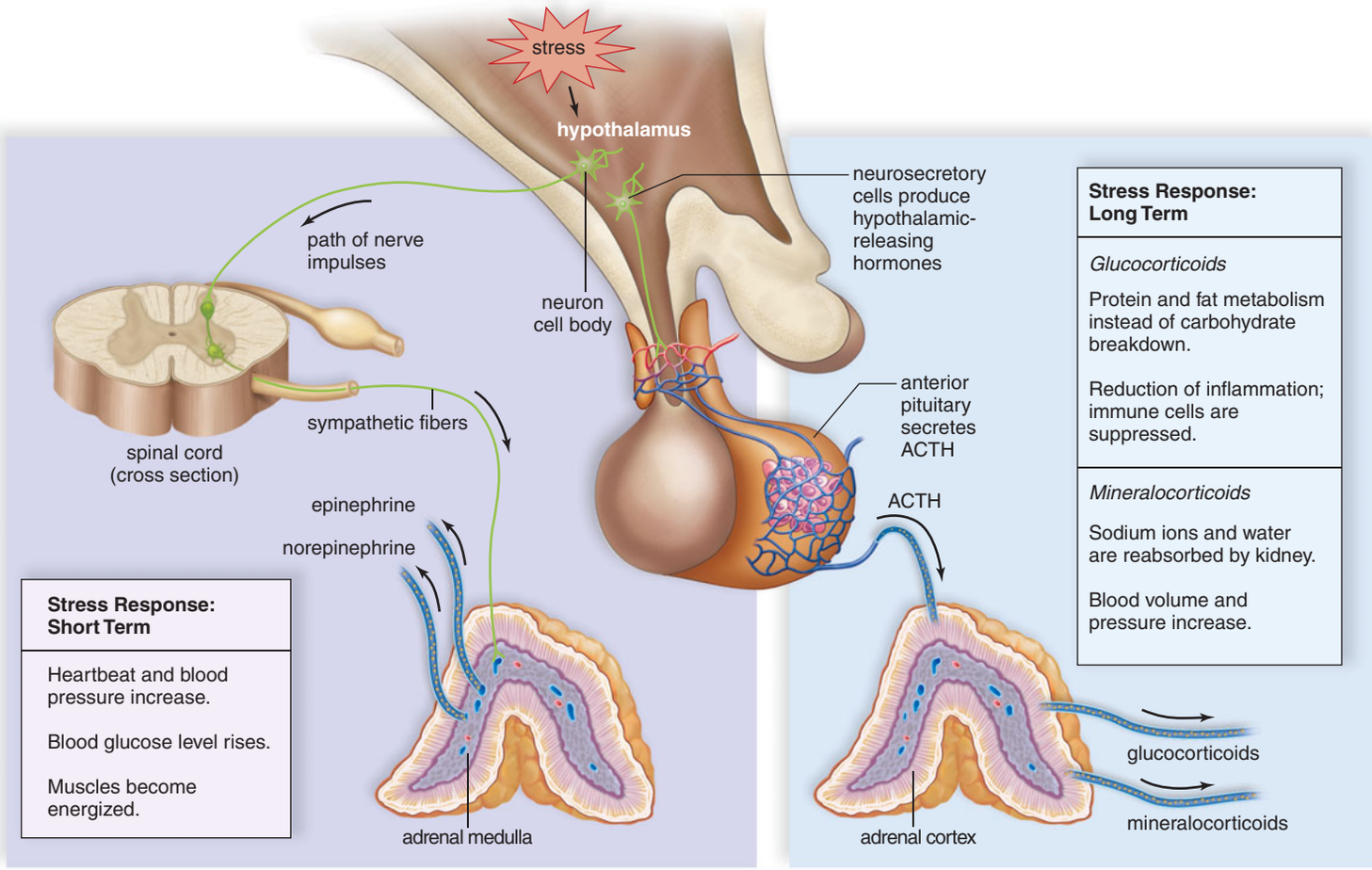
Adrenal Medulla

The hypothalamus initiates nerve impulses that travel by way of the brain stem, spinal cord, and sympathetic nerve fibers to the adrenal medulla, which then secretes its hormones.

Epinephrine (adrenaline) and **norepinephrine** (noradrenaline) produced by the adrenal medulla rapidly bring about all the body changes that occur when an individual reacts to an emergency situation. The release of epinephrine and norepinephrine achieves the same results as sympathetic stimulation—the "fight-or-flight" responses: increased heart rate, rapid respiration, dilation of the pupils, etc. Thus, these hormones assist sympathetic nerves in providing a short-term response to stress.

Adrenal Cortex

There are three layers in the adrenal cortex, and each produces a different set of steroid hormones. The hormones produced by the adrenal cortex provide a long-term response to stress (Fig. 10.10). The two major types of hormones produced by the adrenal cortex are the mineralocorticoids and the glucocorticoids. The **mineralocorticoids** regulate salt and water balance, leading



AP|R **Figure 10.10 Adrenal glands.** Both the adrenal medulla and the adrenal cortex are under the control of the hypothalamus when they help us respond to stress. *Left:* The adrenal medulla provides a rapid, but short-term stress response. *Right:* The adrenal cortex provides a slower, but long-term stress response.

to increases in blood volume and blood pressure. The **glucocorticoids** regulate carbohydrate, protein, and fat metabolism, leading to an increase in blood glucose level. Cortisone, the medication often administered for inflammation of joints, is a glucocorticoid.

The adrenal cortex also secretes small amounts of both male and female sex hormones—regardless of one's gender. Both male and female sex hormones promote skeletal growth in adolescents. The male hormones from the adrenal gland stimulate the growth of axillary and pubic hair at puberty. In addition, male hormones help to sustain the sex drive, or *libido,* in both men and women.

Glucocorticoids

Cortisol is a biologically significant glucocorticoid produced by the adrenal cortex. Cortisol raises the blood glucose level in at least two ways: (1) It promotes the breakdown of muscle proteins to amino acids, which are taken up by the liver from the bloodstream. The liver then converts these excess amino acids to glucose, which enters the blood. (2) Cortisol promotes the metabolism of fatty acids rather than carbohydrates, and this spares glucose for the brain.

Glucocorticoid Therapy

Cortisol and other forms of glucocorticoids suppress the body's normal reaction to disease—the inflammatory reaction (see Fig. 13.3) and the immune process. Cortisone is the glucocorticoid that is used as a medication. Because it reduces inflammation, cortisone reduces swelling and pain in joint disorders such as tendonitis and osteoarthritis. Clinicians also treat autoimmune disorders, such as rheumatoid arthritis, organ transplant rejection, allergies, and severe asthma by suppressing the immune response with cortisone therapy. However, cortisone should be used for the minimum time possible because long-term administration for therapeutic purposes causes some degree of Cushing's syndrome (see pages 219–220). Further, impaired immunity resulting from cortisone use predisposes the individual to infection and increased cancer risk. In addition, sudden withdrawal from cortisone therapy causes symptoms of diminished secretory activity by the adrenal cortex. This occurs because cortisone medication suppresses the release of adrenocorticotropic hormone (ACTH) by the anterior pituitary, leading to a decrease in natural glucocorticoid production by the adrenal cortex. Therefore, withdrawal of cortisone following long-term use must be tapered. During an alternate-day schedule, the dosage is gradually reduced and then finally discontinued as the patient's adrenal cortex resumes activity.

Mineralocorticoids

Aldosterone is the most important of the mineralocorticoids. Aldosterone primarily targets the kidney, where it promotes renal absorption of sodium (Na^+) and water, and renal excretion of potassium (K^+).

As one might expect, secretion of mineralocorticoids from the adrenal cortex is influenced by ACTH (adrenocorticotropic hormone or corticotropin) from the pituitary gland. However, the pituitary hormone is not the primary controller for aldosterone secretion. When the blood sodium level and therefore the blood pressure are low, the kidneys secrete **renin** (Fig. 10.11). Renin is an enzyme that converts the plasma protein angiotensinogen to angiotensin I. Angiotensin I is fully activated to angiotensin II by a converting enzyme found in lung capillaries. Angiotensin II stimulates the adrenal cortex to release aldosterone. The effect of this system, called the renin-angiotensin-aldosterone system, is to raise blood pressure in two ways: Angiotensin II constricts arterioles, and aldosterone causes the kidneys to reabsorb sodium. When the blood sodium level rises, water is reabsorbed, in part because the hypothalamus secretes ADH (see page 212). Reabsorption means that water enters kidney capillaries and thus returns to the blood. Then blood pressure increases to normal.

As you might have already guessed, there is an antagonistic hormone to aldosterone. When the atria of the heart are stretched due to increased blood volume, cardiac cells release a hormone called **atrial natriuretic hormone** (**ANH**, or **atriopeptide**), which inhibits the secretion of aldosterone from the adrenal cortex. The effect of ANH is the excretion of sodium in the urine—that is, *natriuresis*. When sodium is excreted, so is water, and therefore blood pressure lowers to normal.

Malfunction of the Adrenal Cortex

Malfunction of the adrenal cortex can lead to a **syndrome,** a set of symptoms that occur together. The syndromes commonly associated with the adrenal cortex are Addison's disease and Cushing's syndrome.

Addison's Disease and Cushing's Syndrome

When the level of adrenal cortex hormones is low due to hyposecretion, a person develops **Addison's disease.** The presence of excessive but ineffective ACTH causes a bronzing of the skin because ACTH can lead to a buildup of melanin (see Fig. 10.12 and the Chapter Introduction). Without cortisol, glucose cannot be replenished when a stressful situation arises. Even a mild infection can lead to death. The lack of aldosterone results in a loss of sodium and water, the development of low blood pressure, and possibly severe dehydration. Left untreated, Addison's disease can be fatal.

When the level of adrenal cortex hormones is high due to hypersecretion, a person develops **Cushing's syndrome** (Fig. 10.13). The excess cortisol results in a tendency toward diabetes mellitus as muscle protein is metabolized and subcutaneous fat is deposited in the midsection. The trunk is obese, while the arms and legs remain a normal size. An excess of aldosterone and reabsorption of sodium and water by the kidneys leads to a basic blood pH and hypertension. The face is moon-shaped due to edema. Masculinization may occur in women because of excess adrenal male sex hormones.

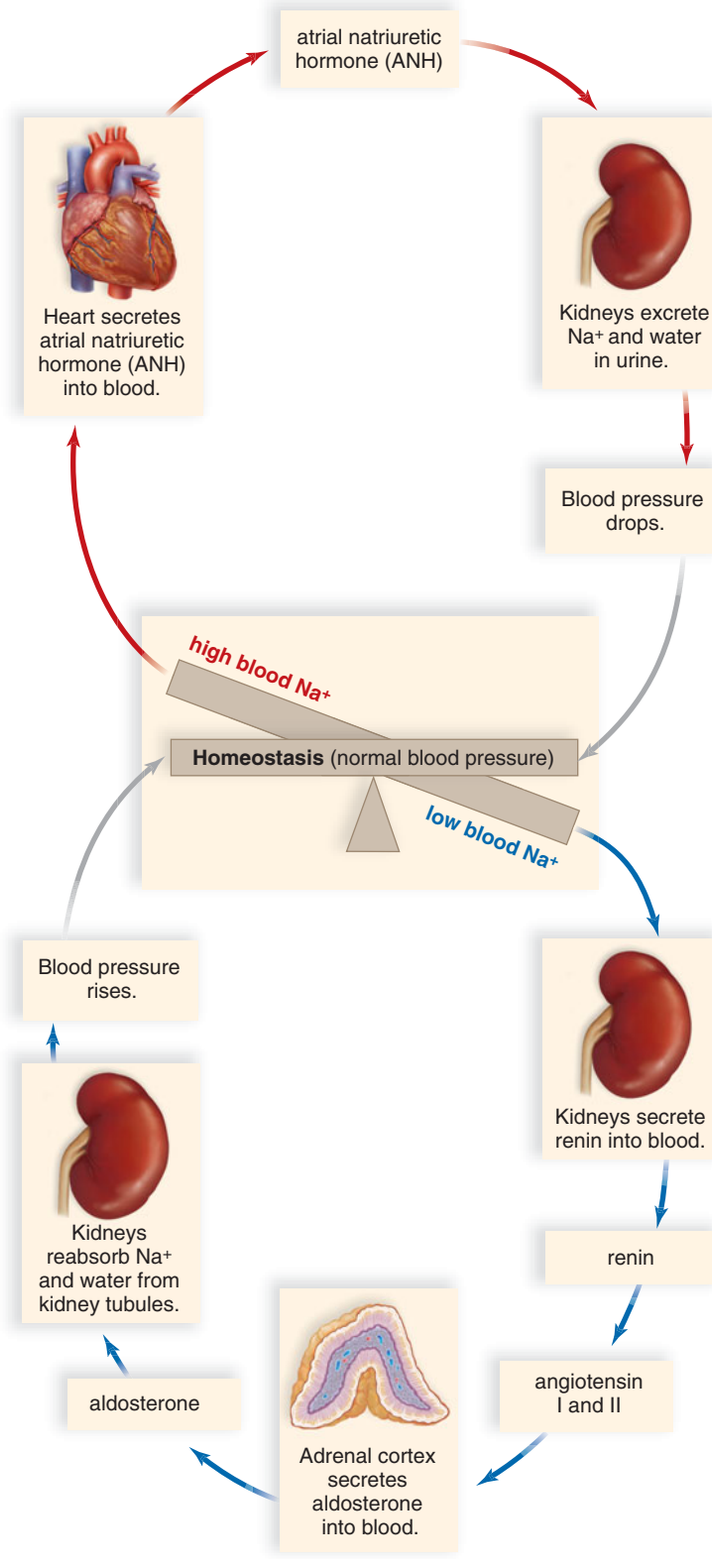
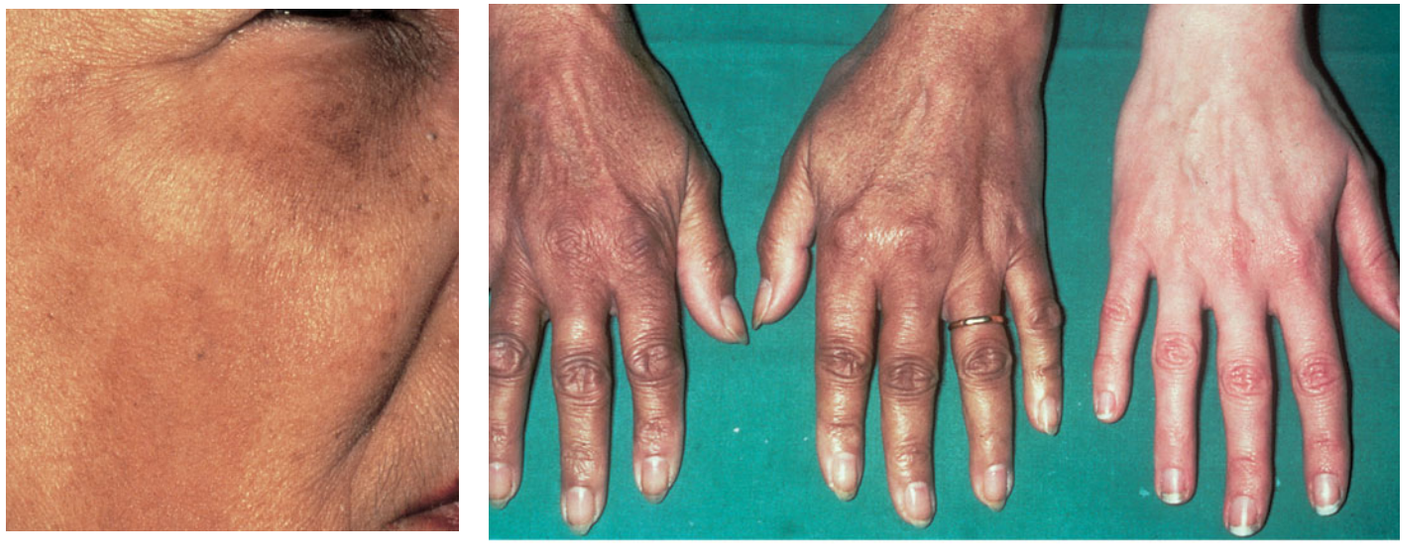
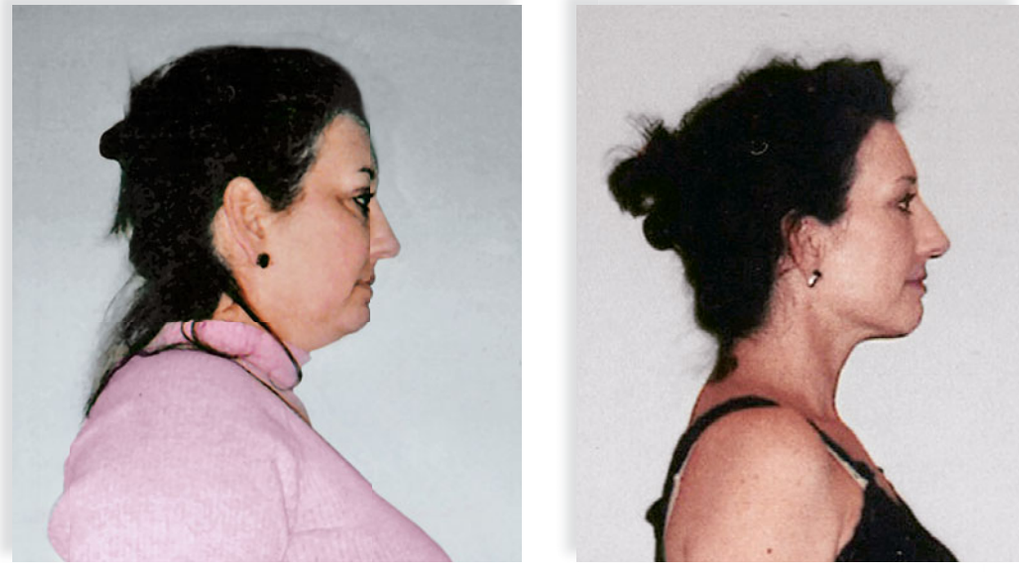


Figure 10.11 Regulation of blood pressure and volume. *Bottom:* When the blood sodium (Na^+) level is low, low blood pressure causes the kidneys to secrete renin. Renin leads to the secretion of aldosterone from the adrenal cortex. Aldosterone causes the kidneys to reabsorb Na^+, and water follows, so that blood volume and pressure return to normal. *Top:* When the blood Na^+ is high, a high blood volume causes the heart to secrete atrial natriuretic hormone (ANH). ANH causes the kidneys to excrete Na^+, and water follows. The blood volume and pressure return to normal.



a. b.

Figure 10.12 **Addison's disease.** Addison's disease is characterized by a peculiar bronzing of the skin, particularly noticeable in these light-skinned individuals. Note the color of **(a)** the face and **(b)** the hands compared to the hand of an individual without the disease.



a. b.

Figure 10.13 **Cushing's syndrome.** Cushing's syndrome results from hypersecretion of adrenal cortex hormones. **a.** Patient at the time of surgery to remove a pituitary tumor. The tumor secreted excess ACTH, which caused excess adrenal cortex secretion and Cushing's syndrome. **b.** Patient one year after surgery.

Content CHECK-UP!

10. From the following list of hormones of the adrenal cortex and their corresponding effects, choose the pair, or pairs, that are correct.

a. male hormones → stimulate sex drive
b. aldosterone → increases sodium concentration in the blood
c. female hormones → promote long bone growth in adolescents
d. Pairs b and c are correct.
e. All are correct.

11. Which hormone opposes the effect of aldosterone in the body?

a. renin
b. angiotensin I
c. atrial natriuretic hormone
d. cortisol

12. Aldosterone returns blood pressure to normal by causing the kidneys to reabsorb water and sodium. Because it works by a negative feedback mechanism, which of the following actions could cause aldosterone to be released?

a. giving a unit of blood
b. drinking a big bottle of a sports drink
c. running a marathon and becoming dehydrated
d. Both a and c are correct.

Answers in Appendix B.

10.5 Pancreas

13. Describe the anatomy of the pancreas.
14. Name three hormones produced by the pancreas, and discuss their functions.
15. Discuss the two types of diabetes mellitus, and contrast hypoglycemia with hyperglycemia.

The **pancreas** is a long organ that lies transversely in the abdomen between the kidneys and near the duodenum of the small intestine. It is composed of two types of tissue. Exocrine tissue produces and secretes digestive juices that go by way of ducts to the small intestine. Pancreatic endocrine tissue includes three types of hormone-producing cells, found in clusters called the **pancreatic islets** (islets of Langerhans). Pancreatic alpha cells produce **glucagon,** beta cells produce **insulin,** and delta cells produce **somatostatin.** All three hormones are released directly into the blood.

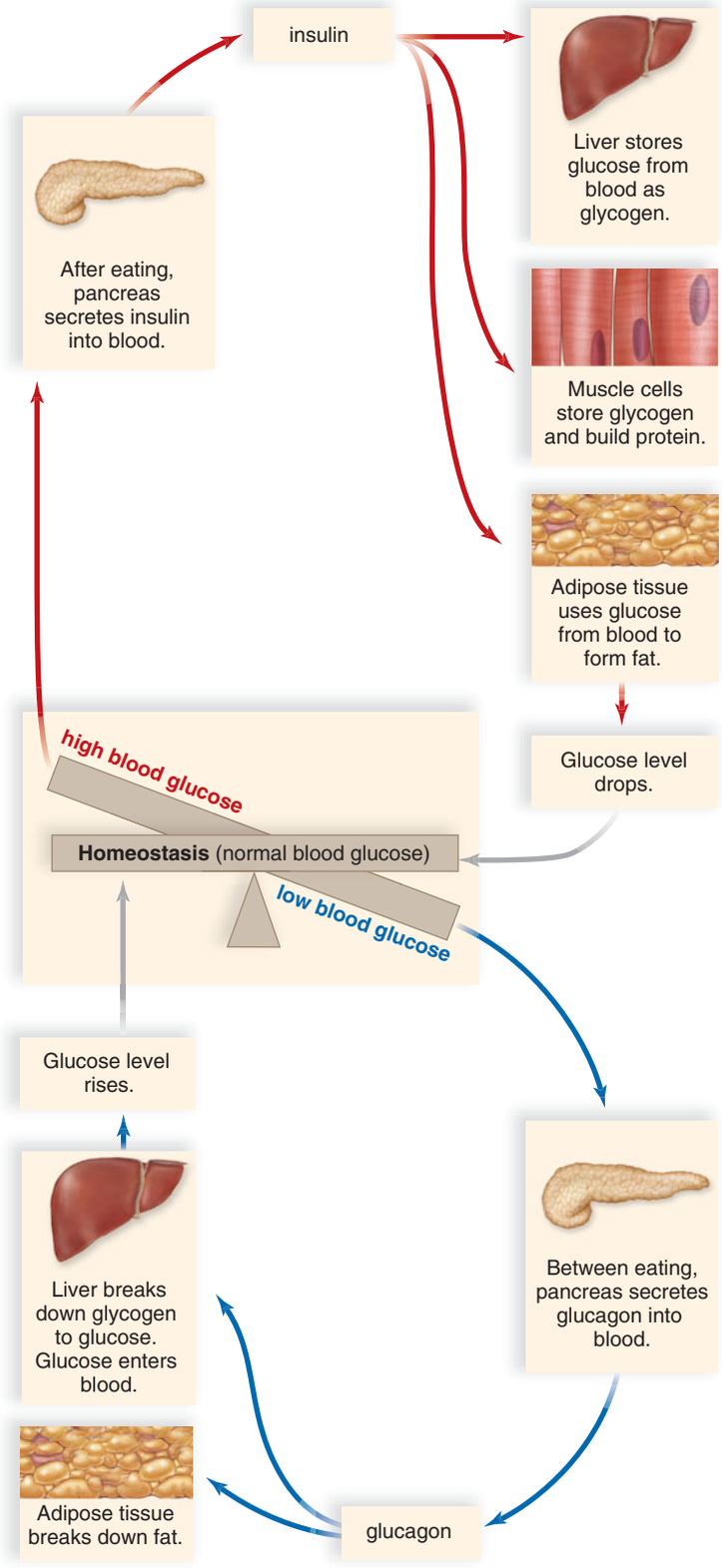
The two antagonistic hormones, insulin and glucagon, both produced by the pancreas, help maintain the normal level of glucose in the blood. Insulin is secreted when the blood glucose level is high, which usually occurs just after eating. Insulin stimulates the uptake of glucose by most body cells. Insulin is not necessary for the transport of glucose into brain or red blood cells, but muscle cells and adipose tissue cells require insulin for glucose transport. In liver and muscle cells, insulin stimulates enzymes that promote the storage of glucose as glycogen. In muscle cells, the glucose supplies energy for muscle contraction, and in fat cells, glucose enters the metabolic pool and thereby supplies glycerol for the formation of fat. In these ways, insulin lowers the blood glucose level.

Glucagon is secreted from the pancreas, usually between meals, when the blood glucose level is low. The major target tissues of glucagon are the liver and adipose tissue. Glucagon stimulates the liver to break down glycogen to glucose and to use fat and protein in preference to glucose as energy sources. Adipose tissue cells break down fat to glycerol and fatty acids. The liver takes these up and uses them as substrates for glucose formation. In these ways, glucagon raises the blood glucose level (Fig. 10.14).

Somatostatin prevents the release of the other two hormones. In this way, it prevents wide swings in blood sugar that might occur between meals.

Diabetes Mellitus

Diabetes mellitus is a fairly common hormonal disease in which insulin-sensitive body cells are unable to take up and/or metabolize glucose. Therefore, the blood glucose level is elevated—a condition called **hyperglycemia.** Because body cells cannot access glucose, starvation occurs at the cell level. The person becomes extremely hungry—a condition called **polyphagia.** As the blood glucose level rises, glucose will be lost in the urine (**glycosuria**). Glucose in the urine causes excessive water loss through urination (**polyuria**). The loss of water in this way causes the diabetic to be extremely thirsty (**polydipsia**). Glucose is not being metabolized, so the body turns to the breakdown of protein and fat for energy. Fat metabolism leads to the buildup of ketones in the blood, and excretion of ketones in the urine (**ketonuria**). Because ketones are acidic, their buildup in the blood causes **acidosis** (acid blood), which can lead to coma and death.



AP|R **Figure 10.14 Regulation of blood glucose level.** *Top:* When the blood glucose level is high, the pancreas secretes insulin. Insulin promotes the storage of glucose as glycogen in the liver and muscles and the use of glucose to form fat in adipose tissue. Therefore, insulin lowers the blood glucose level. *Bottom:* When the blood glucose level is low, the pancreas secretes glucagon. Glucagon acts opposite to insulin; therefore, glucagon raises the blood glucose level to normal.

I.C.E. — IN CASE OF EMERGENCY

Insulin Shock and Diabetic Ketoacidosis

If you're someone with *diabetes mellitus,* the disorder involving the hormone insulin, you already know the importance of maintaining a stable blood glucose level to ensure your long-term health. If your roommate, friend, or loved one is a diabetic, you need to be informed, too, because a diabetic's possible problems don't always take a long time to develop. Insulin shock and diabetic ketoacidosis (DKA) can develop very rapidly, and both can be fatal or result in permanent brain damage. It's important for diabetics and their friends and family to recognize the symptoms of insulin shock and DKA, and know how to use a glucometer to measure blood glucose and how to give an injection.

Insulin shock (also called an *insulin reaction*) results when blood glucose falls to critically low levels—a condition called **hypoglycemia.** It often results when the diabetic patient accidentally injects too much insulin, or takes her insulin but misses a meal. The patient is likely to feel anxious, sweat profusely, and complain of a headache. She may become hyperactive, confused, and even psychotic as the condition worsens. Eventually, she'll lose consciousness and lapse into a so-called **diabetic coma.**

It's critical for first responders to try to raise the patient's blood glucose as quickly as possible. If she is conscious and alert, she can quickly drink milk, juice, or soda, or eat something sweet. She may be able to self-inject with glucagon, the hormone that raises blood glucose. If the blood glucose isn't too low, the insulin shock can be corrected at home. However, one should never attempt to give food or drinks to someone who is semiconscious or unconscious—she could easily choke. Instead, the inside of her cheeks can be smeared with glucose gel, honey, syrup, or frosting, which will melt and be swallowed. If the patient doesn't quickly become alert enough to eat or drink, she must be transported to an emergency room. There, an injection of glucagon or an intravenous solution will quickly raise the blood glucose level.

Diabetic ketoacidosis is caused by blood glucose that is too high. It commonly results when the diabetic eats a meal, but forgets to inject insulin. Infection, injury, or extreme stress can also lead to DKA. The symptoms of DKA are increased thirst, frequent urination, nausea, and vomiting. The patient breathes rapidly, and his breath smells like fruit-flavored gum. His pulse is very fast, but his blood pressure is low. Without an identifying bracelet or tag, he could easily be mistaken as someone who's had too much to drink: sluggish, lethargic, and increasingly sleepy. If untreated, he'll eventually fall into a diabetic coma. Fortunately, under a physician's direction, a trained paramedic can start an intravenous solution to help dilute the patient's blood. As he is being transported to the emergency room, EMS personnel can then measure the glucose and ketones in his blood to provide a complete history, in preparation for more complete treatment in the hospital.

We now know that diabetes mellitus exists in two forms. In type I, often called **insulin-dependent diabetes mellitus (IDDM),** the pancreas does not produce insulin. This condition is believed to be brought on, at least in part, by exposure to an environmental agent. This agent—very likely a virus—causes an extreme immune response, and immune cells destroy the pancreatic islets. As a result, the individual must have daily insulin injections. Daily injections control the diabetic symptoms, but diabetics can still experience life-threatening problems, as described in the I.C.E. box, Insulin Shock and Diabetic Ketoacidosis.

Of the 25.8 million people who now have diabetes in the United States, most have type II, often called **noninsulin-dependent diabetes (NIDDM).** This type of diabetes mellitus usually occurs in people of any age who tend to be obese. Researchers theorize that perhaps adipose tissue produces a substance that interferes with the transport of glucose into cells. The amount of insulin in the blood of these patients is normal or elevated, but the insulin receptors on the cells do not respond to it. It is possible to prevent, or at least control, type II diabetes by adhering to a low-fat, low-sugar diet, maintaining a healthy weight, and exercising regularly. If these attempts fail, oral drugs are available to stimulate the pancreas to secrete more insulin. Other oral medications enhance the metabolism of glucose in the liver and muscle cells. It is projected that as many as 7 million Americans may have type II diabetes without being aware of it. Yet another 79 million Americans have **prediabetes,** a condition in which blood glucose is chronically elevated. Prediabetes will often lead to full-blown diabetes. It's important to note that the effects of untreated type II diabetes are as serious as those of type I diabetes. In addition, without stringent control, the NIDDM diabetic will ultimately require insulin injections, thus becoming insulin-dependent.

Long-term complications of both types of diabetes are blindness, kidney disease, and circulatory disorders, including atherosclerosis, heart disease, stroke, and reduced circulation. The latter can lead to gangrene in the arms and legs. Pregnancy carries an increased risk of diabetic coma, and the child of a diabetic is somewhat more likely to be stillborn or to die shortly after birth. However, these complications of diabetes are not expected to appear if the mother's blood glucose level is carefully regulated and kept within normal limits during the pregnancy.

What's New

Options for Type I Diabetics: *The Artificial Pancreas System and the Biocapsule*

"I can remember getting sick with the flu when I was 11. I missed two or three days of school, and I just never got my strength back. I ate and drank constantly because I was thirsty and hungry all the time. I was always in the bathroom, and I started wetting the bed—can you imagine, at age 11? I fell asleep in school, and the teacher could barely get me to wake up. That's when my doctor diagnosed my diabetes for the first time."

The patient, age 25, is a typical type I insulin-dependent diabetic. Her symptoms are typical of this form of diabetes mellitus (IDDM) (see pages 221-222). As you know, in insulin-dependent diabetes, the body's own immune cells destroy pancreatic beta cells. To treat their illness, type I diabetic patients inject insulin three or more times daily or use an insulin pump device continuously. Patients constantly use blood tests to check their blood glucose levels. Further, diabetics must also monitor their diet, activity, and stress levels. Regular exercise is also a must.

However, ongoing research into diabetes therapy continues and holds promise of treatment that will be much safer and more effective. Currently, scientists are developing an artificial pancreas system (APS) which will combine two exisiting technologies. The first is the insulin pump, a cell-phone-sized device which constantly injects insulin into the patient's body through fine tubing which the patient positions under the abdominal skin. The second device is a continuous glucose monitor (CGM), which can constantly sample glucose levels in subcutaneous tissue fluid and give real-time information about the patient's status. Unfortunately, current CGMs can track glucose, but cannot determine the correct insulin dose. The diabetic herself must still do that, and it can be tricky--meal size, stress, exercise, illness, and multiple other factors can cause dramatic swings in blood glucose.

Using computer models similar to those developed for speech recognition, engineers are investigating ways to effectively "marry" the two technologies, so that as the CGM detects blood glucose changes, the insulin pump responds appropriately, metering the injected insulin so that blood glucose is constantly maintained in the normal range. When the APS is perfected, researchers hope it will respond much as a real pancreas does: delivering just the right amount of insulin at just the right moment, day in and day out.

Whole pancreatic transplant can be a permanent cure for diabetes, but there is a shortage of donor organs. Further, the transplant is major surgery, and recipients must have lifelong anti-rejection medications, which have severe side effects (recurring infections, increased cancer risk, kidney damage, etc.). Pancreatic islet cell transplantation shows great promise as a permanent cure for type I diabetes, and it is a relatively simple procedure. Cadaver beta cells are directly injected into the liver, where they form colonies and produce insulin. Though anti-rejection drugs are needed, new research has refined the combination to produce fewer side effects. Currently, both animal and living human donor cells continue to be investigated as potential sources for the large quantities of islet cells used for transplant (Fig. 10A).

A technique called *microencapsulation* shields donor cells from being rejected by enclosing them in tiny membrane capsules. A new biocapsule, consisting of minute carbon tubes called nanotubes, is under development at the National Aeronautic and Space Administration (NASA) Biosciences labs. The porous biocapsule is about the size of a pencil tip; once filled with beta cells, it could be placed directly into the patient's body, where the cells would be shielded from the immune system and could safely produce insulin. If these studies are successful, patients won't need anti-rejection medication or insulin injections.

In the meantime, researchers are actively exploring insulin delivery options that are less painful, and potentially more effective and reliable than injections. Several forms of insulin pills are now in clinical trials, being tested on volunteers. Currently, diabetics can't swallow their insulin because harsh stomach acid destroys the protein, digesting it before it can be absorbed. A newly developed gel that can be used in pill form successfully shields the insulin as it passes through the stomach. The gel then attaches to the wall of the intestine, allowing insulin to be successfully taken into the bloodstream. Researchers are optimistic that insulin pills might soon be available for use.

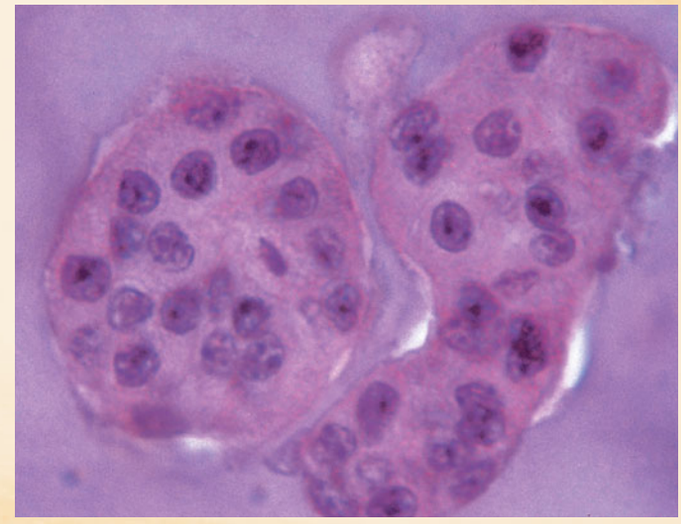


Figure 10 A Encapsulated insulin-producing pancreatic islet cells from pigs can be transplanted into patients without the need for immune system–suppressing drugs.

Content CHECK-UP!

13. Insulin-sensitive cells in the human body include:

a. muscle cells.
b. adipose tissue cells.
c. brain and nerve cells.
d. a and b.
e. All of the above.

14. Which of the following is an effect of glucagon?

a. causes the liver to break down stored glycogen
b. causes adipose tissue to store fat
c. lowers blood glucose level
d. stimulates the liver to store glucose as glycogen

15. Glucagon release is controlled by a negative feedback system. Which action causes glucagon to be released?

a. skipping breakfast and going to morning classes with an empty stomach
b. eating a big holiday meal
c. running a marathon race for several hours without pausing for food
d. a and c
e. b and c

Answers in Appendix B.

10.6 Additional Endocrine Glands

16. Name the most important male and female sex hormones. Discuss their functions.
17. State the location and function of the pineal gland and the thymus gland.
18. Discuss atrial natriuretic hormone, leptin, ghrelin, growth factors, and prostaglandins as hormones not produced by endocrine glands.

The body has a number of other endocrine glands, including the **gonads** (testes in males and the ovaries in females). Other lesser-known glands, such as the thymus gland and the pineal gland, also produce hormones. Many other organs have their own roles as endocrine glands, and researchers continue to discover additional hormones and/or growth factors, suggesting that numerous other tissues and organs are functionally endocrine glands as well. Even individual body cells produce local messenger chemicals termed prostaglandins.

Testes and Ovaries

The **testes** (sing., testis) are located in the scrotum, and the **ovaries** are located in the pelvic cavity. The testes produce **androgens** (e.g., **testosterone**), which are the male sex hormones, and the ovaries produce **estrogens** and **progesterone,** the female sex hormones. The hypothalamus and the pituitary gland control the hormonal secretions of these organs in the manner previously described on pages 213–214.

Androgens

Puberty is the time of life when sexual maturation occurs. Greatly increased testosterone secretion during puberty stimulates the growth of the penis and the testes. Testosterone also brings about and maintains the male secondary sex characteristics that develop during puberty, including the growth of a beard, axillary (underarm) hair, and pubic hair. It prompts the larynx and the vocal cords to enlarge, causing the voice to change. It is partially responsible for the muscular strength of males. This is why some athletes take supplemental amounts of **anabolic steroids,** which are either testosterone or related chemicals. The contraindications of taking anabolic steroids are discussed in the Medical Focus on pages 226–227. Testosterone also stimulates oil and sweat glands in the skin; therefore, it is largely responsible for acne and body odor. Another side effect of testosterone is baldness. Genes for baldness are probably inherited by both sexes, but baldness is seen more often in males because of the presence of testosterone (see Chapter 5 Introduction).

Estrogen and Progesterone

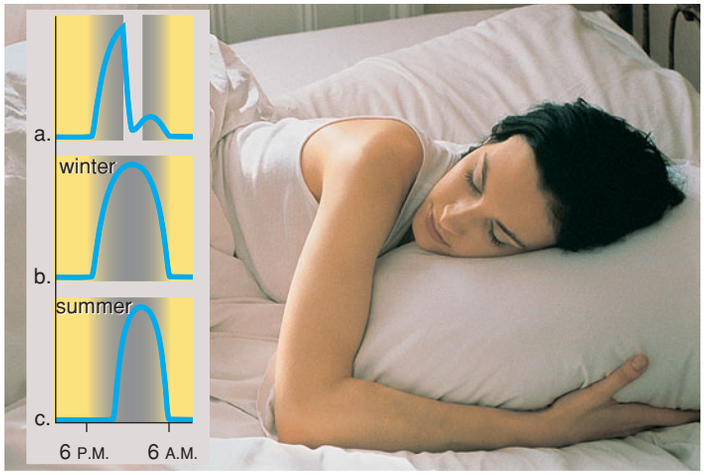
The female sex hormones, estrogens and progesterone, have many effects on the body. In particular, estrogens secreted during puberty stimulate the growth of the uterus and the vagina. Estrogen is necessary for ovum maturation and is largely responsible for the secondary sex characteristics in females, including female body hair and fat distribution. In general, females have a more rounded appearance than males because of a greater accumulation of fat beneath the skin. Also, the pelvic girdle is wider in females than in males, resulting in a larger pelvic cavity. Both estrogen and progesterone are required for breast development and for regulation of the uterine cycle, which includes monthly menstrual periods (discharge of blood and mucosal tissues from the uterus).

Thymus Gland

The lobular **thymus gland,** which lies just beneath the sternum (see Fig. 10.1), reaches its largest size and is most active during childhood. It then shrinks in size throughout one's adult life. **Lymphocytes** are white blood cells that originate in the bone marrow and are responsible for specific defenses against a particular invader. When lymphocytes complete development in the thymus, they are transformed into **thymus-derived lymphocytes,** or **T lymphocytes.** The lobules of the thymus are lined by epithelial cells that secrete hormones called **thymosins.** These hormones aid in the differentiation of lymphocytes packed inside the lobules. Although the hormones secreted by the thymus ordinarily work only in the thymus, researchers hope that these hormones could be injected into AIDS or cancer patients where they would enhance T-lymphocyte function.

Pineal Gland

The **pineal gland,** which is located in the brain, produces the hormone **melatonin,** primarily at night. Melatonin is involved in our daily sleep-wake cycle; normally we grow sleepy at night when melatonin levels increase and awaken once daylight returns and melatonin levels are low (Fig. 10.15). Daily 24-hour cycles such as this are called **circadian rhythms.** Circadian rhythms are controlled by an internal timing mechanism called a biological clock.



AP|R **Figure 10.15 Melatonin production.** Melatonin production is greatest at night when we are sleeping. Light suppresses melatonin production **(a)** so its duration is longer in the winter **(b)** than in the summer **(c).**

Based on animal research, it appears that melatonin also regulates sexual development. It has also been noted that children whose pineal gland has been destroyed due to a brain tumor experience early puberty.

Hormones from Other Tissues

We have already mentioned that the heart produces atrial natriuretic hormone (see page 219). The kidney also influences cardiovascular system function by producing the hormone erythropoietin (EPO), which stimulates red blood cell production by the bone marrow. This hormone and its effects are detailed in Chapter 11. Further, you'll see in Chapter 15 that organs and tissues of the digestive system produce an entire set of so-called *enteric* hormones as well.

Leptin and Ghrelin

Leptin is a protein hormone produced by adipose tissue. Leptin acts on the hypothalamus, where it signals satiety—that the individual has had enough to eat. Strange to say, the blood of obese individuals may be rich in leptin. It is possible that the leptin they produce is ineffective because of a genetic mutation, or else their hypothalamic cells lack a suitable number of receptors for leptin. **Ghrelin** is an antagonist to leptin that is produced by the stomach. Where leptin signals fullness, ghrelin signals hunger.

Growth Factors

A number of different types of organs and cells produce peptide **growth factors,** which stimulate cell division and mitosis. Some, such as lymphokines, are released into the blood; others diffuse to nearby cells. Growth factors of particular interest are the following:

Granulocyte and macrophage colony-stimulating factor (GM-CSF) is secreted by many different tissues. GM-CSF causes bone marrow stem cells to form either granulocyte or macrophage cells (both are forms of white blood cells, or leukocytes), depending on whether the concentration is low or high.

Platelet-derived growth factor is released from platelets and from many other cell types. It helps in wound healing and causes an increase in the number of fibroblasts, smooth muscle cells, and certain cells of the nervous system.

Epidermal growth factor and *nerve growth factor* stimulate the cells indicated by their names, as well as many others. These growth factors are also important in wound healing.

Tumor angiogenesis factor stimulates the formation of capillary networks and is released by tumor cells. One treatment for cancer is to prevent the activity of this growth factor.

Prostaglandins

Prostaglandins are potent chemical signals produced within cells from arachidonate, a fatty acid. Prostaglandins are not distributed in the blood; instead, they act locally, quite close to where they were produced. In the uterus, prostaglandins cause muscles to contract and may be involved in the pain and discomfort of menstruation. Also, prostaglandins mediate the effects of *pyrogens,* chemicals that are believed to reset the temperature regulatory center in the brain. For example, aspirin reduces body temperature and controls pain because of its effect on prostaglandins.

Certain prostaglandins reduce gastric secretion and have been used to treat ulcers; others lower blood pressure and have been used to treat hypertension; and still others inhibit platelet aggregation and have been used to prevent thrombosis (the formation of stationary clots in blood vessels). However, different prostaglandins have contrary effects, and it has been very difficult to successfully standardize their use.

Content CHECK-UP!

16. From the following list of endocrine glands and their hormones, choose the pair that is correct:

a. ovaries → androgens
b. thymus → insulin
c. kidney → aldosterone
d. adipose tissue → leptin

17. Which of the following is a local tissue messenger that stimulates nearby cells?

a. leptin
b. prostaglandin
c. melatonin
d. thymosin

18. Describe three functions of the female sex hormones.

Answers in Appendix B.

10.7 The Importance of Chemical Signals

19. Give examples to show that chemical signals can act between organs, cells, and individuals.

Chemical signals are molecules that affect the behavior of those cells that have receptor proteins to receive them. For example, a hormone that binds to a receptor protein affects the metabolism of

MEDICAL FOCUS

Side Effects of Anabolic Steroids

They're called "performance-enhancing steroids," and their use is alleged to be widespread in athletics, both amateur and professional. Whether the sport is baseball, football, professional cycling, or track and field events, no activity seems to be safe from drug abuse. Even the Olympic games have been affected: Steroid abuse admitted by Marion Jones has forever changed Olympic history. Jones was the first female athlete to win five medals for track and field events during the 2000 Sydney Olympics. In 2008, she was stripped of all medals she had earned, as well as disqualified from a fifth-place finish in the 2004 Athens games. Future Olympic record books will not include her name, and the records of her teammates in the relay events have also been tainted.

Baseball records will also likely require revisions. The exciting slugfest between Mark McGwire and Sammy Sosa in the summer of 1998 was largely credited with reviving national interest in baseball. Yet, the great home-run competition drew unwanted attention to the darker side of professional sports, when it was alleged that both McGwire and Sosa were using anabolic steroids at the time. Similar charges of drug abuse may prevent baseball great Roger Clemens from entering the Baseball Hall of Fame, despite his record for the number of Cy Young awards he holds. Likewise, because controversy continues to surround baseball legend Barry Bonds, this talented athlete may never achieve Hall of Fame status. Although he scored a record 715 home runs and won more Most Valuable Player awards than anyone in history, Bonds remains accused of steroid abuse. Jose Canseco of the Oakland Athletics and Jason Giambi of the New York Yankees have both admitted using performance-enhancing drugs.

Most athletes and officials continue to deny that anabolic steroids are widely used in professional sports. However, many people from both inside and outside the industry maintain that such abuse has been going on for many years, and that it continues despite the negative publicity. Congress continues to investigate the controversy, yet the finger-pointing and accusations increase. Of tremendous concern to lawmakers, educators, and parents is the increased use of steroids by teens wishing to bulk up quickly, perhaps seeking to be just like the sports figures they admire.

Anabolic steroids are synthetic forms of the male sex hormone testosterone. Taking doses 10 to 100 times the amount prescribed by doctors for various illnesses promotes larger muscles when the person also exercises. Trainers may have been the first to acquire anabolic steroids for weight lifters, bodybuilders, and other athletes, such as professional baseball players. However, being a steroid user can have serious detrimental effects. Men often experience decreased sperm counts and decreased sexual desire due to atrophy of the testicles. Some develop an enlarged prostate gland or grow breasts. On the other hand, women can develop male sexual characteristics. They grow hair on their chests and faces, and lose hair from their heads; many experience abnormal enlargement of the clitoris. Some cease ovulating or menstruating, sometimes permanently.

Some researchers predict that two or three months of high-dosage use of anabolic steroids as a teen can cause death by age 30 or 40. Steroids have even been linked to heart disease in both sexes and have been implicated in the deaths of young athletes from liver cancer and one type of kidney tumor. Steroids can cause the body to retain fluid, which results in increased blood pressure. Users then try to get rid of "steroid

the cell. Cells, organs, and even individuals communicate with one another by using chemical signals.

We are most familiar with chemical signals that are produced by organs some distance from one another in the body. For example, hormones produced by the anterior pituitary influence the function of numerous organs throughout the body. Insulin, produced by the pancreas, is transported in blood to muscle, adipose, and other insulin-sensitive cells. The nervous system at times utilizes chemical signals that are produced by an organ distant from the one being affected, as when the hypothalamus produces releasing hormones. As you know, these releasing hormones then travel in a portal system to the anterior pituitary gland.

Many chemical signals act locally—that is, from cell to cell. Prostaglandins are *local hormones,* and certain neurotransmitter substances released by one neuron affect a neuron nearby. Growth factors, which fall into this category, are very important regulators of cell division. Some growth factors are being used as medicines to promote the production of blood cells in AIDS and cancer patients.

Cancer cells produce their own sets of growth factors, and discovering them all remains a challenge for cancer research scientists. When a tumor develops, cell division occurs even when no detectable stimulatory growth factor has been received. Further, cancerous tumors are known to produce a growth factor called tumor angiogenesis factor, which promotes the formation of capillary networks to service its cells. Currently, several forms of cancer treatment involve shutting down the activity of cancer growth factors, and more of these treatments will likely be discovered in the future (see the "What's New" article entitled "Targeting the Traitor Inside" on page 77 for more about this type of therapy).

Chemical Signals Between Individuals

Chemical signals that act between individuals are called *pheromones* (see the Introduction, Chapter 17). Pheromones are well exemplified in other animals, but they may also be effective between people. Humans produce airborne chemicals from a variety of areas, including the scalp, oral cavity, armpits, genital areas, and feet. For example, the armpit secretions of one woman could possibly affect the menstrual cycle of another woman. Women who live in the same household often have menstrual cycles during the same times of the month. Further, when women with irregular cycles are exposed to extracts of male armpit secretions, their cycle length tends to become more normal.

bloat" by taking large doses of diuretics. A young California weight lifter had a fatal heart attack after using steroids, and the postmortem showed a lack of **electrolytes,** salts that help regulate the heart. Finally, steroid abuse has psychological effects, including depression, hostility, aggression, and eating disorders. Unfortunately, these drugs make a person feel invincible. One abuser even had his friend videotape him as he drove his car at 40 miles an hour into a tree!

The many harmful effects of anabolic steroids are given in Figure 10B. The Federal Food and Drug Administration now bans most steroids, and steroid use has also been banned by the National Collegiate Athletic Association (NCAA), the National Football League (NFL), and the International Olympic Committee (IOC).

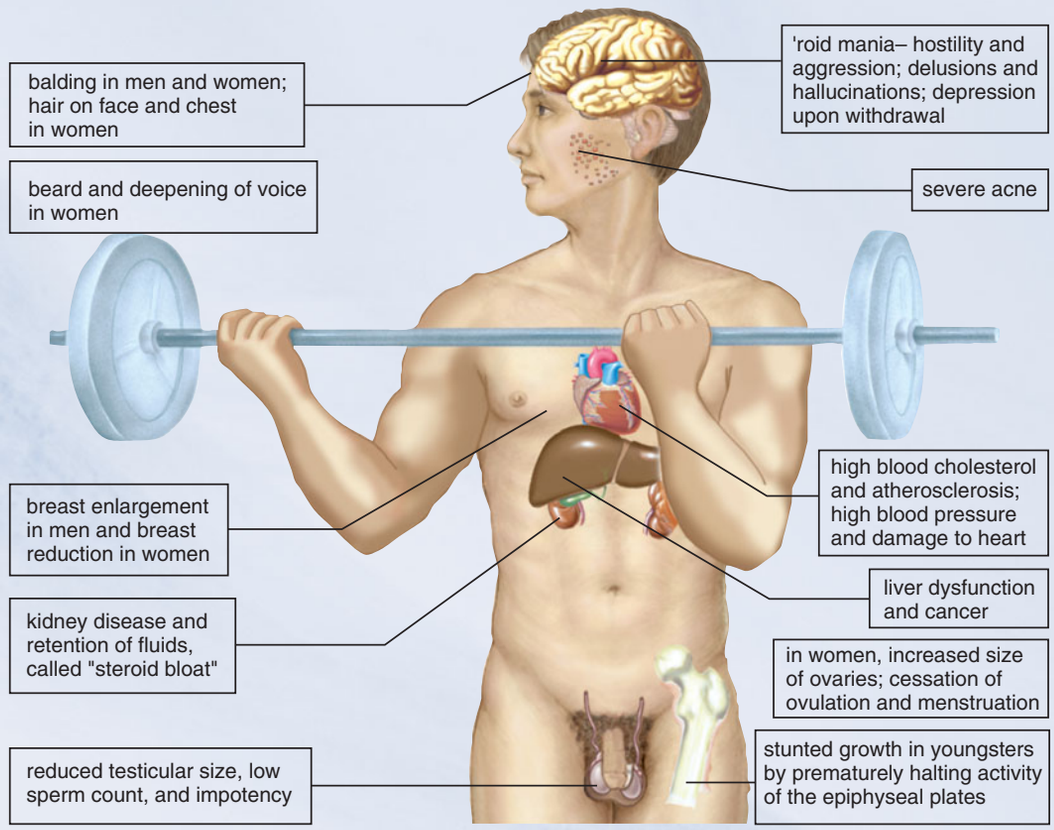


Figure 10 B **The effects of anabolic steroid use.**

10.8 Effects of Aging

20. Discuss the anatomical and physiological changes that occur in the endocrine system as we age.

Thyroid disorders and diabetes are the most significant endocrine problems affecting health and function as we age. Both hypothyroidism and hyperthyroidism are seen in the elderly. Graves' disease is an autoimmune disease that targets the thyroid, resulting in symptoms of cardiovascular disease, increased body temperature, and fatigue. In addition, a patient may experience weight loss of as much as 20 pounds, depression, and mental confusion. Hypothyroidism (myxedema) may fail to be diagnosed because the symptoms of hair loss, skin changes, and mental deterioration are attributed simply to the process of aging.

Both the thymus gland and the pineal gland decrease in size as a person ages. Thymic atrophy is thought to contribute to declining immune response observed with age, as described in Chapter 13.

The true incidence of IDDM diabetes among the elderly is unknown. Its symptoms can be confused with those of other medical conditions that are present. As in all adults, NIDDM diabetes is associated with being overweight and often can be controlled by proper diet.

The effect of age on the sex organs is discussed in Chapter 17.

10.9 Homeostasis

21. Discuss how the endocrine system works with other systems of the body to maintain homeostasis.

The endocrine system and the nervous system work together to regulate the organs of the body and thereby maintain homeostasis. It is clear from reviewing the Human Systems Work Together illustration on page 228 that the endocrine system particularly influences the digestive, cardiovascular, and urinary systems in a way that maintains homeostasis.

The endocrine system helps regulate digestion. The digestive system adds nutrients to the blood, and hormones produced by the digestive system influence the gallbladder and pancreas to send their secretions to the digestive tract. Another hormone, gastrin, promotes the digestion of protein by the stomach. Through its influence on the digestive process, the endocrine system promotes

Human Systems Work Together

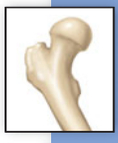
ENDOCRINE SYSTEM

Integumentary System

Androgens activate sebaceous glands and help regulate hair growth.

Skin provides sensory input that results in the activation of certain endocrine glands.

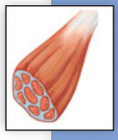
Skeletal System



Growth hormone regulates bone development; parathyroid hormone and calcitonin regulate Ca^{2+} content.

Bones provide protection for glands; store Ca^{2+} used as second messenger.

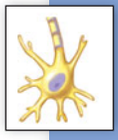
Muscular System



Growth harmone and androgens promote growth of skeletal muscle; epinephrine stimulates heart and constricts blood vessels.

Muscles help protect glands.

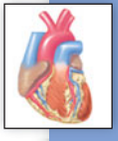
Nervous System



Hormones affect development of brain.

Hypothalamus, pituitary, and pineal gland are part of endocrine system; nerves innervate glands of secretion.

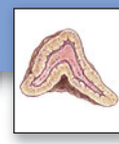
Cardiovascular System

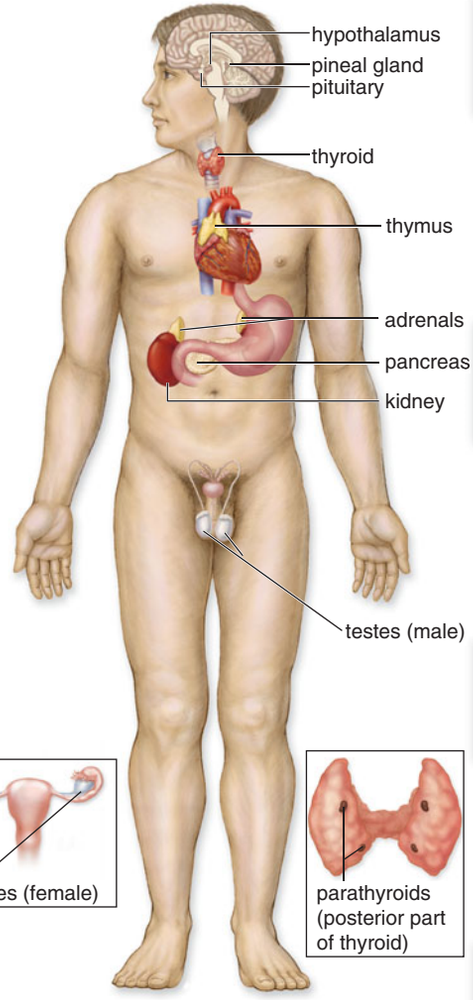


Epinephrine increases blood pressure; ADH, aldosterone, and atrial natriuretic hormone help regulate blood volume; growth factors control blood cell formation.

Blood vessels transport hormones from glands; blood services glands; heart produces atrial natriuretic hormones.

How the Endocrine System works with other body systems.





ovaries (female)

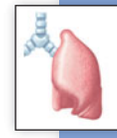
parathyroids (posterior part of thyroid)

Lymphatic System/Immunity

Thymus is necessary for maturity of T lymphocytes.

Lymphatic vessels pick up excess tissue fluid; immune system protects against infections.

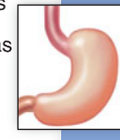
Respiratory System



Epinephrine promotes ventilation by dilating bronchioles; growth factors control production of red blood cells that carry oxygen.

Gas exchange in lungs provides oxygen and rids body of carbon dioxide.

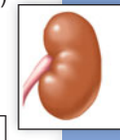
Digestive System



Hormones help control secretion of digestive glands and accessory organs; insulin and glucagon regulate glucose storage in liver.

Stomach and small intestine produce hormones.

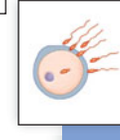
Urinary System



ADH, aldosterone, and atrial natriuretic hormone regulate reabsorption of water and Na^+ by kidneys.

Kidneys keep blood values within normal limits so that transport of hormones continues.

Reproductive System



Hypothalamic, pituitary, and sex hormones control sex characteristics and regulate reproductive processes.

Gonads produce sex hormones.

the presence of nutrients in the blood. Leptin (from adipose tissue) and ghrelin (from the stomach) regulate satiety (the feeling of fullness) and hunger.

The endocrine system helps regulate fuel metabolism. Controlling the level of glucose in the blood is the function of insulin and glucagon. Just after eating, insulin encourages the uptake of glucose by cells and the storage of glucose as glycogen in the liver and muscles. In between meals, glucagon stimulates the liver to break down glycogen to glucose so that the blood glucose level stays constant. Somatostatin helps to prevent wide swings in blood glucose between meals by inhibiting both insulin and glucagon secretion. Adrenaline (epinephrine) from the adrenal medulla also stimulates the liver to release glucose. Glucagon (from the pancreas) and cortisol (from the adrenal cortex) promote the breakdown of protein to amino acids, which can be converted to glucose by the liver. They also promote the metabolism of fatty acids to conserve glucose, a process called **glucose sparing.** Finally, the thyroid hormones thyroxine and triiodothyronine set the body's metabolic rate, and thus are the hormones that ultimately regulate fuel metabolism.

The endocrine system helps regulate blood pressure and volume. ADH produced by the hypothalamus (but secreted by the posterior pituitary) promotes reabsorption of water by the kidneys, especially when we have not been drinking water that day. Aldosterone produced by the adrenal cortex causes the kidneys to reabsorb sodium, and when the level of sodium rises, water is automatically reabsorbed so that blood volume and pressure rise together. Regulation by the endocrine system often involves antagonistic hormones; in this case, ANH (atriopeptide) produced by the heart causes sodium and water excretion.

The endocrine system helps regulate calcium balance. The concentration of calcium (Ca^{2+}) in the blood is critical because this ion is important to nervous conduction, muscle contraction, and the action of hormones. As you know from studying Chapter 6, the bones serve as a reservoir for calcium. When the blood calcium concentration lowers, parathyroid hormone (PTH) promotes the breakdown of bone and the reabsorption of calcium by the kidneys. PTH also stimulates absorption of calcium by the intestines by activating Vitamin D. Opposing the action of parathyroid hormone, calcitonin secreted by the thyroid brings about the deposit of calcium in the bones (although this function of calcitonin is more important in growing children than in adults).

The endocrine system helps regulate response to the external environment. In "fight-or-flight" situations, the nervous system stimulates the adrenal medulla to release epinephrine (adrenaline) and norepinephrine, which have a powerful effect on various organs. This, too, is important to homeostasis because it allows us to behave in a way that keeps us alive. Any damage due to stress is then repaired by the action of other hormones, including cortisol. Glucocorticoid (e.g., cortisone) therapy is useful for its antiinflammatory and immunosuppressive effects.

SELECTED NEW TERMS

Basic Key Terms

adenohypophysis (ad′ĕn-ō-hī-pŏ′fī-sĭs), p. 212
adrenal cortex (ŭh-drē′nŭl kŏr′tĕks), p. 217
adrenal gland (ŭh-drē′nŭl glănd), p. 217
adrenal medulla (ŭh-drē′nŭl mĕ dūl′ŭh), p. 217
adrenocorticotropic hormone (ŭh-drē′nō-kŏr″tī-kō trōp′ĭk hŏr′mōn), p. 214
aldosterone (ăl″dŏs′tĕr-ōn), p. 219
anabolic steroid (ăn″ŭh-bŏl′ĭk stĕ′rōyd), p. 224
androgen (ăn′drō-jĕn), p. 224
anterior pituitary (ăn-tēr′ē-ŏr pĭ-tū′ĭ-tār″ē), p. 212
antidiuretic hormone (ăn″tī-dī″yū-rĕt′ĭk hŏr′mōn), p. 212
atrial natriuretic hormone (ā′trē-ŭhl nā″trē-yū-rĕt′ĭk hŏr′mōn), p. 219
atriopeptide (ā-trē-yō-pĕp-tīd), p. 219
calcitonin (kăl″sĭ-tō′nĭn), p. 216
calcitriol (kăl″sĭ-trī′ăwl), p. 216
circadian rhythm (sĕr″kā′dē-ăn rĭ′thm), p. 224
corticotropin (kŏr′tĭ-kō-trōh-pĭn), p. 214, 217
cortisol (kŏr′tĭ-sŏl), p. 218
cyclic AMP (sĭk′lĭk AMP), p. 208
endocrine gland (ĕn′dō-krĭn glănd), p. 208
epinephrine (ĕp″ĭ-nĕf′rĭn), p. 217
estrogen (ĕs′trō-jĕn), p. 224
follicle-stimulating hormone (fól′ĭk-kl stĭm″yoō-lā′tĭng hŏr′mōn), p. 214
ghrelin (grĕl′ŭhn), p. 225
glucagon (glū′kŭh-gŏn), p. 221
glucocorticoid (glū′kō-kŏr′tĭ-kōyd), p. 218
gonad (gō′năd), p. 224
gonadotropic hormone (gō″năd-ō-trōp′ĭk hŏr′mōn), p. 214
growth factor (grōth făk′tŏr), p. 225
growth hormone (grōth hŏr′mōn), p. 214
hormone (hŏr′mōn), p. 208
hypothalamic-inhibiting hormone (hī″pō-thĕ-lăm′ĭk-ĭn-hĭb′ĭt-ĭng hŏr′mōn), p. 212
hypothalamic-releasing hormone (hī″pō-thĕ-lăm′ĭk-rē-lēs′ĭng hŏr′mōn), p. 212
hypothalamus (hī′pō-thăl′ă-mŭs), p. 212
insulin (in′sŭh-lĭn), p. 221
leptin (lĕp′tĭn), p. 225
luteinizing hormone (lū′tŭh-nī″zĭng hŏr′mōn) p. 214
melatonin (mĕl″ŭh-tō′nĭn), p. 224
mineralocorticoids (mĭn″ĕr-ăl-ō-kŏr′tĭ-kōyds), p. 217
neurohypophysis (nū′rō-hī-pŏf′ĭ-sĭs), p. 212
norepinephrine (nŏr′ĕp-ĭ-nĕf′rĭn), p. 217
ovary (ō′văr-ē), p. 224
oxytocin (ŏk″sī-tō′sĭn), p. 212
pancreas (păn′krē-ŭs), p. 221
pancreatic islets (of Langerhans) (păn″krē-ăt′ĭk ī′lĕts ŏv lăhng′ĕr-hănz), p. 221
parathyroid gland (pār″ŭh-thī′rōyd glănd), p. 216
parathyroid hormone (pār″ŭh-thī′rōyd hŏr′mōn), p. 216
peptide hormone (pĕp′tid hŏr′mōn), p. 208
pineal gland (pīn′ē-ul glănd), p. 224
pituitary gland (pĭ-tū′ĭ-tār″ē glănd), p. 212
portal system (pŏr′tŭl sĭs′tĕm), p. 212
posterior pituitary (pōs-tēr′ē-ŏr pĭ-tū′ĭ-tār″ē), p. 212
progesterone (prō-jĕs′tĕr-ōn), p. 224
prolactin (prō-lăk′tĭn), p. 214
prostaglandins (prŏs″tŭh-glăn′dĭnz), p. 224
renin (rē′nĭn), p. 219
somatostatin (sō′măt-ō-stăt′ĭn), p. 221
steroid hormone (stēr′ōyd hŏr′mōn), p. 208
testes (tĕs′tēz), p. 224
testosterone (tĕs-tŏs′tĕ-rōn), p. 224
thymosin (thī′mō-sĭn), p. 224
thymus gland (thī′mŭs glănd), p. 224
thyroid gland (thī′rōyd glănd), p. 215
thyroid-stimulating hormone (thī′rōyd stim′yū-lāt-ĭng hŏr′mōn), p. 214

thyrotropin (thī′rō-trō′pĭn), p. 214
thyroxine (thī-rŏk′sĭn), p. 215
triiodothyronine (trī′ī-ō-dō-thī′rō-nēn), p. 215

Clinical Key Terms

acidosis (ăs′ĭ-dō′sĭs), p. 221
acromegaly (ăk″rō-mĕg′ŭh-lē), p. 214
Addison's disease (ă′dĭ-sŏns dĭ-zēz′), p. 219
congenital hypothyroidism (kŏn-gĕn′ĭ-tŭl hī″pō-thī′rōy-dĭzm), p. 216
Cushing's syndrome (kŭsh′ĭngs sĭn′drōm), p. 219
diabetes insipidus (dī″ŭh-bē′tēz ĭn-sĭp′ĭ-dus), p. 212
diabetic coma (dī″ŭh-bĕ-tĭk kō′-mŭh), p. 222
diabetic ketoacidosis (dī″ŭh-bĕ-tĭk kē′tō′ăs-ĭ-dō′sŭs), p. 222
exophthalmic goiter (ĕk″sŏf-thăl′mĭk gōy′tĕr), p. 216
glycosuria (glī″kō-sūr′ē-ŭh), p. 221
Graves'disease (grāvz dĭ-zēz′), p. 216
hypercalcemia (hī″pĕr-kăl-sē′mē-ŭh), p. 216
hyperglycemia (hī″pĕr-glī-sē′mē-ŭh), p. 222
hypocalcemia (hī″pō-kăl-sē′mē-ŭh), p. 216
hypoglycemia (hī″pō-glī-sē′mē-ŭh), p. 222
insulin-dependent diabetes mellitus (ĭn′sŭl-ĭn-dē-pĕn′dĕnt dī″ŭh-bē′tēz mĕ-lī′tŭs), p. 222
insulin shock (ĭn′sŭl-ĭn shŏk), p. 222
ketonuria (kē″tō-nū′rē-ŭh), p. 221
myxedema (mĭk″sĕ-dē′mŭh), p. 216
noninsulin-dependent diabetes (nŏn′ĭn′sŭl-ĭn-dē-pĕn′dĕnt dī″ŭh-bē′tēz), p. 222
pituitary dwarfism (pĭ-tū′ĭ-tăr″e dwărf′ĭzm), p. 214
polydipsia (pŏl″ē-dĭp′sē-ŭh), p. 221
polyphagia (pŏl″ē-fā-jē-ŭh), p. 221
polyuria (pŏl″ē-yū′rē-ŭh), p. 221
prediabetes (prē′dī-ŭh-bē″tēz), p. 222
simple (endemic) goiter (sĭm′pl ĕn-dĕm′ĭk gōy′tĕr), p. 215
syndrome (sĭn′drōm), p. 219
tetany (tĕt′ŭh-nē), p. 216

SUMMARY

10.1 Endocrine Glands

A. Endocrine glands secrete hormones into the bloodstream, and from there they are distributed to target organs or tissues.

B. Hormones are either peptides or steroids. Reception of a peptide hormone at the plasma membrane activates an enzyme cascade inside the cell. Steroid hormones combine with a receptor in the cell, and the complex attaches to and activates DNA. Protein synthesis follows. The major endocrine glands and hormones are listed in Table 10.1. Neural mechanisms, hormonal mechanisms, and/or negative feedback control the effects of hormones.

10.2 Hypothalamus and Pituitary Gland

A. Neurosecretory cells in the hypothalamus produce antidiuretic hormone (ADH) and oxytocin, which are stored in axon endings in the posterior pituitary until they are released.

B. The hypothalamus produces hypothalamic-releasing and hypothalamic-inhibiting hormones, which pass to the anterior pituitary by way of a portal system. The anterior pituitary produces at least six types of hormones, and some of these stimulate other hormonal glands to secrete hormones.

10.3 Thyroid and Parathyroid Glands

The thyroid gland requires iodine to produce triiodothyronine (T_3) and thyroxine (T_4), which increase the metabolic rate. If iodine is available in limited quantities, a simple goiter develops; if the thyroid is overactive, an exophthalmic goiter develops. The thyroid gland also produces calcitonin, which helps lower the blood calcium level. The parathyroid glands secrete parathyroid hormone, which raises the blood calcium and decreases the blood phosphate levels. Parathyroid hormone is the primary hormone responsible for calcium regulation.

10.4 Adrenal Glands

The adrenal glands respond to stress: Immediately, the adrenal medulla secretes epinephrine and norepinephrine, which bring about responses we associate with emergency situations. On a long-term basis, the adrenal cortex produces the glucocorticoids (e.g., cortisol) and the mineralocorticoids (e.g., aldosterone). Cortisol stimulates hydrolysis of proteins to amino acids that are converted to glucose; in this way, it raises the blood glucose level. Aldosterone causes the kidneys to reabsorb sodium ions (Na^+) and to excrete potassium ions (K^+). Addison's disease develops when the adrenal cortex is underactive, and Cushing's syndrome develops when the adrenal cortex is overactive.

10.5 Pancreas

The pancreatic islets secrete insulin, which lowers the blood glucose level, and glucagon, which has the opposite effect. The most common illness caused by hormonal imbalance is diabetes mellitus, which is due to the failure of the pancreas to produce insulin and/or the failure of the cells to take it up.

10.6 Additional Endocrine Glands

A. The gonads produce the sex hormones. The thymus secretes thymosins, which stimulate T-lymphocyte production and maturation. The pineal gland produces melatonin, which is involved in circadian rhythms and may affect development of the reproductive organs.

B. Tissues also produce hormones. Adipose tissue produces leptin and the stomach produces ghrelin. Both act on the hypothalamus, and various tissues produce growth factors. Prostaglandins are produced and act locally.

10.7 The Importance of Chemical Signals

In the human body, some chemical signals, such as traditional endocrine hormones and secretions of neurosecretory cells, act at a distance. Others, such as prostaglandins, growth factors, and neurotransmitters, act locally. Whether humans have pheromones is under study.

10.8 Effects of Aging

Two concerns often seen in the elderly are thyroid malfunctioning and diabetes mellitus. The thymus gland atrophies, shrinking in size. As a result, the immune response is diminished in the elderly.

10.9 Homeostasis

Hormones particularly help maintain homeostasis in several ways: Hormones help maintain the level of nutrients (e.g., amino acids and glucose in blood); help maintain blood volume and pressure by regulating the sodium content of the blood; help maintain the blood calcium level; help regulate fuel metabolism; and help regulate our response to the external environment.

STUDY QUESTIONS

1. Explain how peptide hormones and steroid hormones affect the metabolism of the cell. (p. 208)
2. Contrast hormonal and neural signals, and show that there is an overlap between the mode of operation of the nervous system and that of the endocrine system. (pp. 208, 211)
3. Explain the relationship of the hypothalamus to the posterior pituitary gland and to the anterior pituitary gland. List the hormones secreted by the posterior and anterior pituitary glands. (pp. 209–210, 212–214.)
4. Give an example of the negative feedback relationship among the hypothalamus, the anterior pituitary, and other endocrine glands. (pp. 212–214)
5. Discuss the effect of growth hormone on the body and the result of having too much or too little growth hormone when a young person is growing. What is the result if the anterior pituitary produces growth hormone in an adult? (pp. 214–215)
6. What types of goiters are associated with a malfunctioning thyroid? Explain each type. (pp. 215–216)
7. How do the thyroid and the parathyroid work together to control the blood calcium level? (pp. 216–217)
8. How do the adrenal glands respond to stress? What hormones are secreted by the adrenal medulla, and what effects do these hormones have? (pp. 217–219)
9. Name the most significant glucocorticoid and mineralocorticoid, and discuss their functions. Explain the symptoms of Addison's disease and Cushing's syndrome. (pp. 217–220)
10. Draw a diagram to explain how insulin and glucagon maintain the blood glucose level. Use your diagram to explain the major symptoms of type I diabetes mellitus. (pp. 221–222)
11. Name the additional endocrine glands discussed in this chapter, and discuss the functions of the hormones they secrete. (pp. 224–225)
12. What are leptin, ghrelin, growth factors, and prostaglandins? How do these substances act? (p. 225)
13. Discuss five ways the endocrine system helps maintain homeostasis. (pp. 227–229)

LEARNING OUTCOME QUESTIONS

Fill in the blanks.

1. Generally, hormone production is self-regulated by a _____ mechanism.
2. The hypothalamus _____ the hormones _____ and _____, released by the posterior pituitary.
3. The _____ secreted by the hypothalamus control the anterior pituitary.
4. Growth hormone is produced by the _____ pituitary.
5. Simple goiter occurs when the thyroid is producing (too much or too little) _____ because it has (too much or too little) _____.
6. Parathyroid hormone increases the level of _____ in the blood.
7. Adrenocorticotropic hormone (ACTH), produced by the anterior pituitary, stimulates the _____ of the adrenal glands.
8. An overproductive adrenal cortex results in the condition called _____.
9. Type I diabetes mellitus is due to a malfunctioning _____, but type II diabetes is due to malfunctioning _____.
10. Prostaglandins are not carried in the _____ as are hormones secreted by the endocrine glands.
11. Whereas _____ hormones are lipid soluble and bind to receptor proteins within the cytoplasm of target cells, _____ hormones bind to membrane-bound receptors, thereby activating second messengers.
12. Whereas the adrenal _____ is under the control of the autonomic nervous system, the adrenal _____ secretes its hormones in response to _____ from the anterior pituitary gland.

MEDICAL TERMINOLOGY EXERCISE

Consult Appendix A for help in pronouncing and analyzing the meaning of the terms that follow.

1. antidiuretic (ăn″tī-dī″yū-rĕt′ĭk)
2. hypophysectomy (hī-pŏf″ĭ-sĕk′tō-mē)
3. gonadotropic (gō″năd-ō-trōp′ĭk)
4. hypokalemia (hī″pō-kăl″ē′mē-ŭh)
5. lactogenic (lăk″tō-jĕn′ĭk)
6. adrenopathy (ăd″rĕn-ŏp′ŭh-thē)
7. adenomalacia (ăd″ĕ-nō-mŭh-lā′shē-ŭh)
8. parathyroidectomy (pār″ŭh-thī″rōy-dĕk′tō-mē)
9. polydipsia (pŏl″ē-dĭp′sē-ŭh)
10. dyspituitarism (dĭs-pĭ-tu′ĭ-tĕr′ĭzm)
11. thyroiditis (thī-rōy-dī′tĭs)
12. glucosuria (glū-cō-sū′rē-ŭh)
13. microsomia (mī′krō-sō′mē-ŭh)

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