25. In order to focus on objects that are close to the viewer,
    a. the suspensory ligaments must be pulled tight.
    b. the lens needs to become more rounded.
    c. the ciliary muscle will be relaxed.
    d. the image must focus on the area of the optic nerve.

26. Which abnormality of the eye is incorrectly matched with its cause?
    a. astigmatism—either the lens or cornea is not even
    b. farsightedness—eyeball is shorter than usual
    c. nearsightedness—image focuses behind the retina
    d. color blindness—genetic disorder in which certain types of cones may be missing

27. Which of these associations is incorrectly matched?
    a. semicircular canals—inner ear
    b. utricle and saccule—outer ear
    c. auditory canal—outer ear
    d. cochlea—inner ear
    e. ossicles—middle ear

28. Which of the following wouldn't you mention if you were tracing the path of sound vibrations?
    a. auditory canal
    b. tympanic membrane
    c. ossicles
    d. semicircular canals
    e. cochlea

29. The middle ear is separated from the inner ear by
    a. the oval window.
    b. the tympanic membrane.
    c. the round window.
    d. Both a and c are correct.

30. Which one of these correctly describes the location of the spiral organ?
    a. between the tympanic membrane and the oval window in the inner ear
    b. in the utricle and saccule within the vestibule
    c. between the tectorial membrane and the basilar membrane in the cochlear canal
    d. between the nasal cavities and the throat
    e. between the outer and inner ear within the semicircular canals

31. Which of the following could result in hearing loss?
    a. symphony orchestra
    b. earphone use
    c. consistent use of loud equipment such as a jackhammer
    d. use of firearms
    e. All of these are correct.

32. Which of the following structures would allow you to know that you were upside down, even if you were in total darkness?
    a. utricle and saccule
    b. cochlea
    c. semicircular canals
    d. tectorial membrane

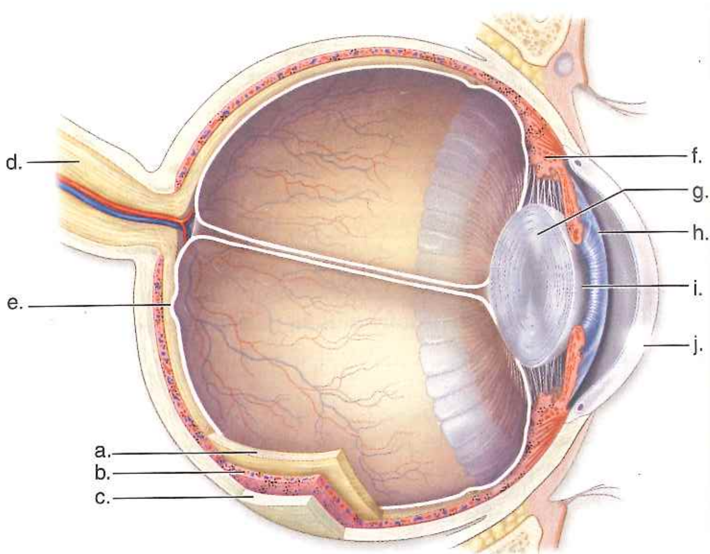
33. Which of these is an incorrect difference between olfactory receptors and equilibrium receptors?

	Olfactory Receptors	Equilibrium Receptors
a.	located in nasal cavities	located in the inner ear
b.	chemoreceptors	mechanoreceptors
c.	respond to molecules in the air	respond to movements of the body
d.	communicate with brain via a tract	communicate with brain via vestibular nerve

    e. All of these contrasts are correct.

34. Both olfactory receptors and sound receptors
    a. are chemoreceptors.
    b. are a part of the brain.
    c. are mechanoreceptors.
    d. initiate nerve impulses.
    e. All of these are correct.

35. Label this diagram of a human eye.



Thinking Critically About the Concepts

Ian, from the opening story, and his friends' trip to the amusement park focused primarily on the role of sensory receptors in gathering information about external surroundings. Keep in mind the hugely important role of the interoreceptors in homeostasis. When Olivia (from the opening story in Chapter 9) held her breath during her temper tantrum, her blood pH dropped (became more acidic) when blood CO_2 increased. Chemoreceptors in her blood vessels then signaled her brain about the change in pH. Olivia eventually had to exhale when her blood pH fell out of the acceptable range for pH. Any unacceptable changes in homeostatic conditions is reported to the brain by some kind of interoreceptor.

1. What kind of receptors would have recognized the changes in blood pressure stimulated by Ashley's (opening story from Chapter 1) sympathetic nervous system response to the scary movie?
2. Besides the blood pH mentioned above, what other homeostasis conditions will be monitored by chemoreceptors?
3. Ian and his friends were exposed to a great deal of environmental stimuli during their day at the amusement park.
   a. What different kinds of receptors were responsible for their ability to sense the wide variety of stimuli?
   b. What different parts of the brain would have interpreted the information about the variety of environmental stimuli at the amusement park?
4. Amusement-park workers are likely to be exposed to continuous, loud noises. What would you predict the long-term effect on their hearing to be? Why?

CHAPTER 15

Endocrine System

At 4' 11", Adam Casey was the shortest boy in eighth grade at his school. The growth spurt most boys his age experience never happened to him. Classmates, who towered over him, called him "shrimp" and teased him about being a midget or dwarf. His younger brother was already 2 in. taller than Adam. Adam's parents worried about how their son would be treated if he failed to reach what is considered to be a respectable height for a man.

The Caseys decided to investigate how growth hormone (GH) treatment might help Adam gain some additional inches. They made an appointment to see Dr. Drake, an endocrinologist, who could advise them of their options. Dr. Drake told them that Adam might be a candidate for GH therapy if the epiphyseal plates of his long bones had not yet fused. Blood work to assess Adam's GH levels would help determine the course of action as well.

X-rays of Adam's long bones showed unfused epiphyseal plates, and his blood work results indicated lower than normal levels of GH. Dr. Drake seemed to think GH injections could help Adam gain a significant number of inches. Some of Dr. Drake's other patients had grown 5–7 in. following two years of injections. Dr. Drake cautioned them that the injections might cause headaches and nausea and that long-term risks were unknown. The injections would be very expensive ($30,000 per year), and health insurance may or may not cover the cost. The Caseys decided to proceed with the injections in the hopes that any increase in height would improve Adam's self-esteem and potential success as an adult.

CHAPTER CONCEPTS

15.1 Endocrine Glands
Endocrine glands produce hormones that are secreted into the bloodstream and distributed to target cells where they alter cellular metabolism.

15.2 Hypothalamus and Pituitary Gland
The hypothalamus controls the secretions of the pituitary gland, which, in turn, controls the secretion of certain other glands. Growth hormone produced by the anterior pituitary determines our height.

15.3 Thyroid and Parathyroid Glands
Some hormones secreted by the thyroid gland stimulate cellular metabolism, and another helps control Ca^{2+} blood levels, as does parathyroid hormone.

15.4 Adrenal Glands
The adrenal glands respond to both long-term and short-term stress.

15.5 Pancreas
The pancreas secretes insulin and glucagon, which together keep the blood glucose level fairly constant.

15.6 Other Endocrine Glands
Other endocrine glands include the testes and ovaries, which are discussed in Chapter 16, the thymus gland, which was discussed in Chapter 7, and the pineal gland.

15.7 Homeostasis
The nervous and endocrine systems work together to control and regulate the other systems.

15.1 Endocrine Glands

The nervous system and the endocrine system work together to regulate the activities of the other systems. Both systems use chemical signals when they respond to changes that might threaten homeostasis, but they have different means of delivering these signals (Fig. 15.1). As discussed, the nervous system is composed of neurons. In this system, sensory receptors (specialized dendrites) detect changes in the internal and external environment. The CNS integrates the information and responds by stimulating muscles and glands. Communication depends on nerve impulses, conducted in axons, and neurotransmitters, which cross synapses. Axon conduction occurs rapidly and so does diffusion of a neurotransmitter across the short distance of a synapse. In other words, the nervous system is organized to respond rapidly to stimuli. This is particularly useful if the stimulus is an external event that endangers our safety—we can move quickly to avoid being hurt.

The endocrine system functions differently. The endocrine system is largely composed of glands (Fig. 15.2). These glands secrete **hormones,** which are carried by the bloodstream to target cells throughout the body. In the opening story, Adam was short for a boy because his blood didn't contain enough growth hormone produced by the anterior pituitary. Growth hormone stimulates the growth of long bones, and in this way affects the height of an individual. It takes time to deliver hormones, and it takes time for cells to respond, but the effect is longer lasting. In other words, the endocrine system is organized for a slow but prolonged response.

Endocrine glands can be contrasted with exocrine glands. Exocrine glands have ducts and secrete their products into these ducts, which take them to the lumens of other organs or outside the body. For example, the salivary glands send saliva into the mouth by way of the salivary ducts. **Endocrine glands,** as stated, secrete their products into the bloodstream, which delivers them throughout the body. It must be stressed that only certain cells, called target cells, can respond to certain hormones. If a cell can respond to a hormone, the hormone and receptor proteins bind together as a key fits a lock.

It is of interest to note that both the nervous system and the endocrine system make use of negative feedback mechanisms. If the blood pressure falls, sensory receptors signal a control center in the brain. This center sends out nerve impulses to the arterial walls so that they constrict, and blood pressure rises. Now the sensory receptors are no longer stimulated, and the feedback mechanism is inactivated. Similarly, a rise in blood glucose level causes the pancreas to release insulin, which, in turn, promotes glucose uptake by the liver, muscles, and other cells of the body (Fig. 15.1). When the blood glucose level falls, the pancreas no longer secretes insulin.

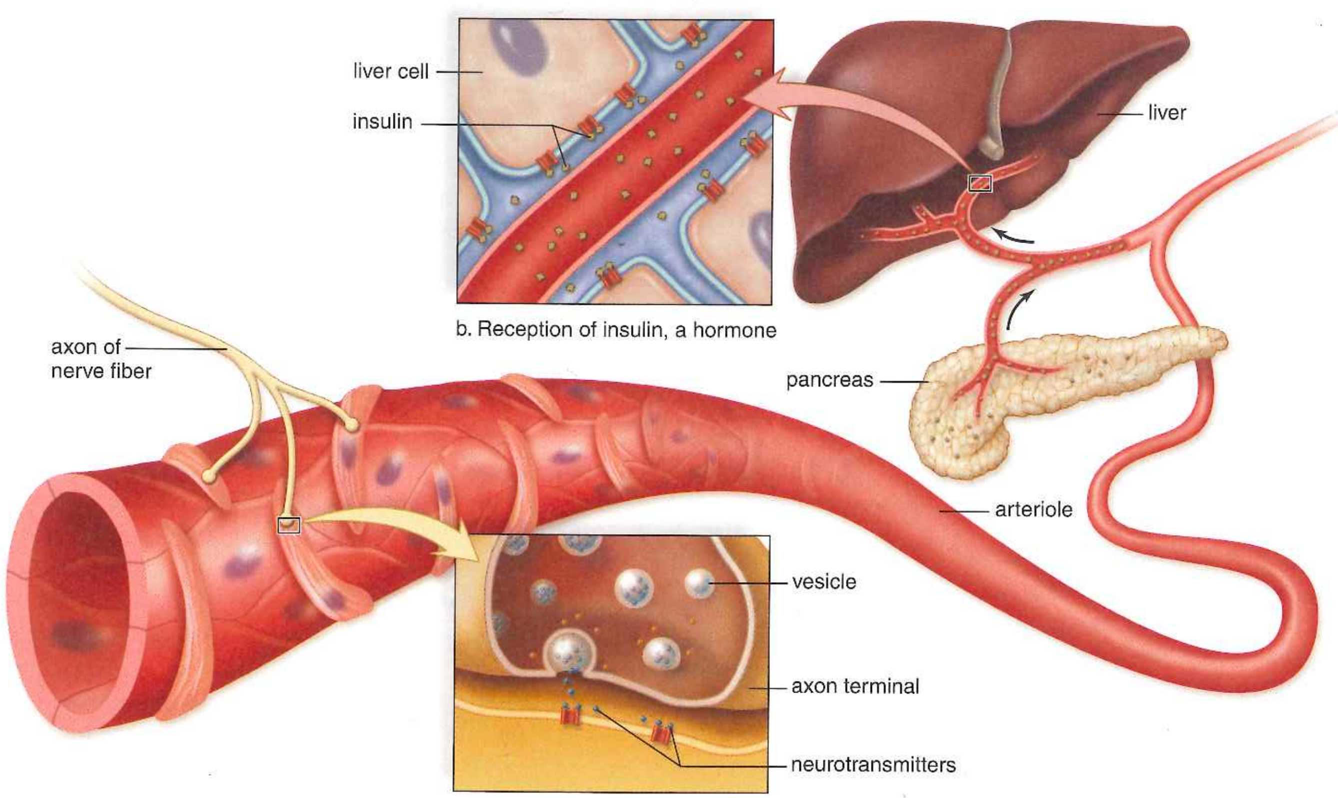


Figure 15.1 Modes of action of the nervous and endocrine systems.
a. Nerve impulses passing along an axon cause the release of a neurotransmitter. The neurotransmitter, a chemical signal, causes the wall of an arteriole to constrict. b. The hormone insulin, a chemical signal, travels in the cardiovascular system from the pancreas to the liver, where it causes liver cells to store glucose as glycogen.

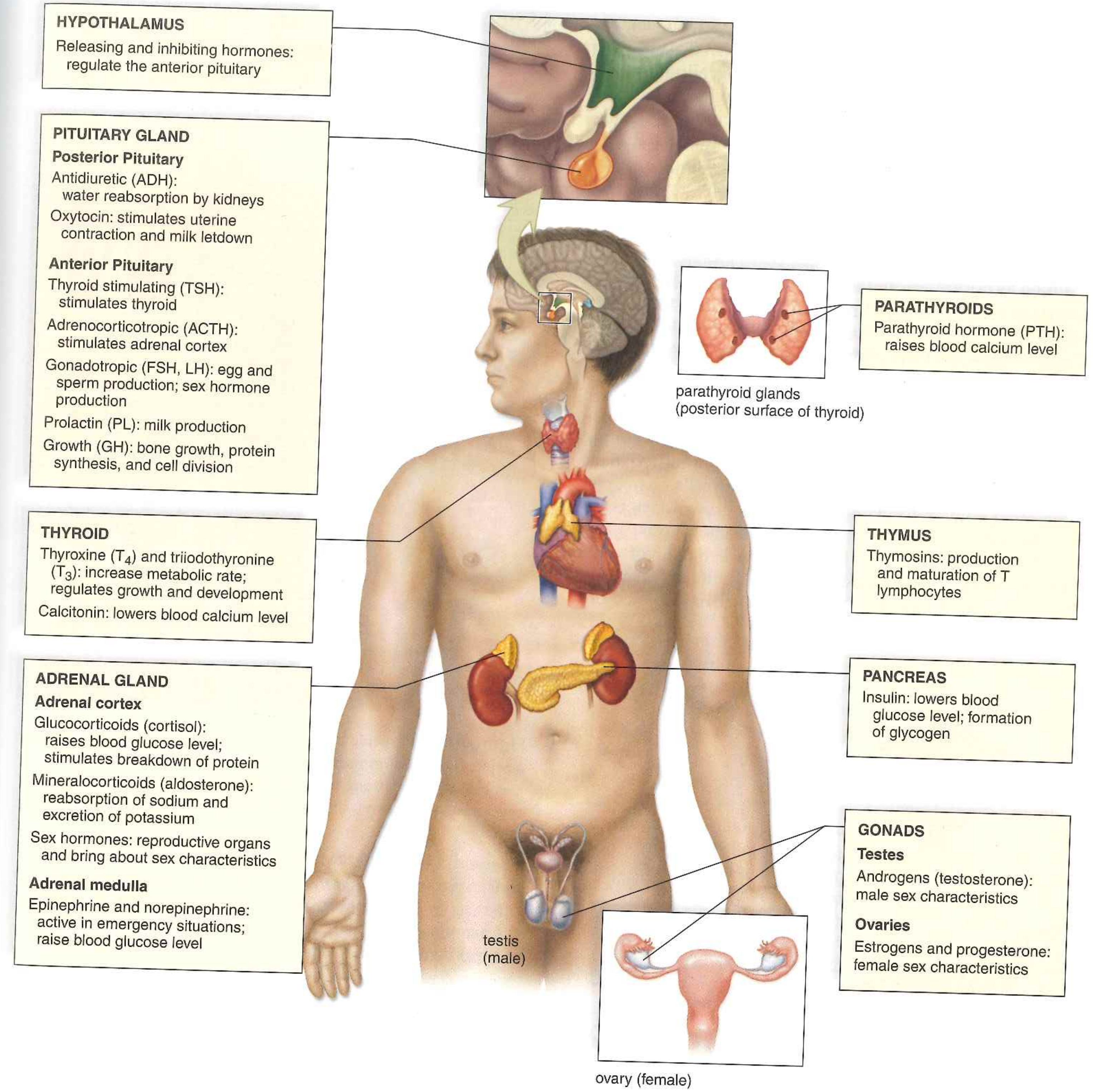


Figure 15.2 Major glands of the human endocrine system.
Major glands and the hormones they produce are depicted. Also, the endocrine system includes other organs such as the kidneys, gastrointestinal tract, and the heart, which also produce hormones but not as a primary function of these organs.

Hormones Are Chemical Signals

Like other **chemical signals,** hormones are a means of communication between cells, between body parts, and even between individuals. They typically affect the metabolism of cells that have receptors to receive them (Fig. 15.3). In a condition called androgen insensitivity, an individual has X and Y sex chromosomes, and the testes, which remain in the abdominal cavity, produce the sex hormone testosterone. However, the body cells lack receptors that are able to combine with testosterone, and the individual appears to be a normal female.

Like testosterone, most hormones act at a distance between body parts. They travel in the bloodstream from the gland that produced them to their target cells. Also counted as hormones are the secretions produced by neurosecretory cells in the hypothalamus, a part of the brain. They travel in the capillary network that runs between the hypothalamus and the pituitary gland. Some of these secretions stimulate the pituitary to secrete its hormones, and others prevent it from doing so.

Not all hormones act between body parts. As we shall see, prostaglandins are a good example of a *local hormone.* After prostaglandins are produced, they are not carried in the bloodstream; instead, they affect neighboring cells, sometimes promoting pain and inflammation. Also, growth factors are local hormones that promote cell division and mitosis.

Chemical signals that influence the behavior of other individuals are called **pheromones.** Pheromones have been released by other animals and a researcher has isolated one released by men that reduces premenstrual nervousness and tension in women. Women who live in the same household often have menstrual cycles in synchrony, perhaps because the armpit secretions of a woman who is menstruating affects the menstrual cycle of other women in the household.

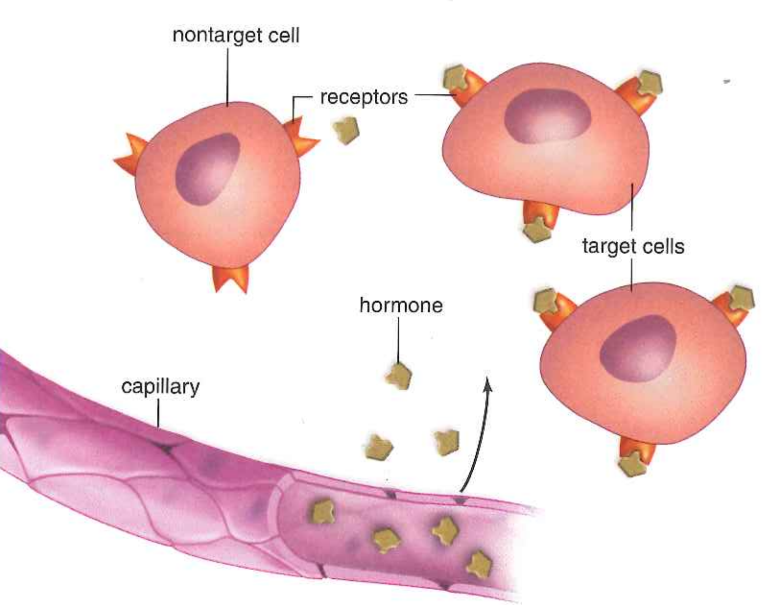


Figure 15.3 Target cell concept.
Most hormones are distributed by the bloodstream to target cells. Target cells have receptors for the hormone, and the hormone combines with the receptor as a key fits a lock.

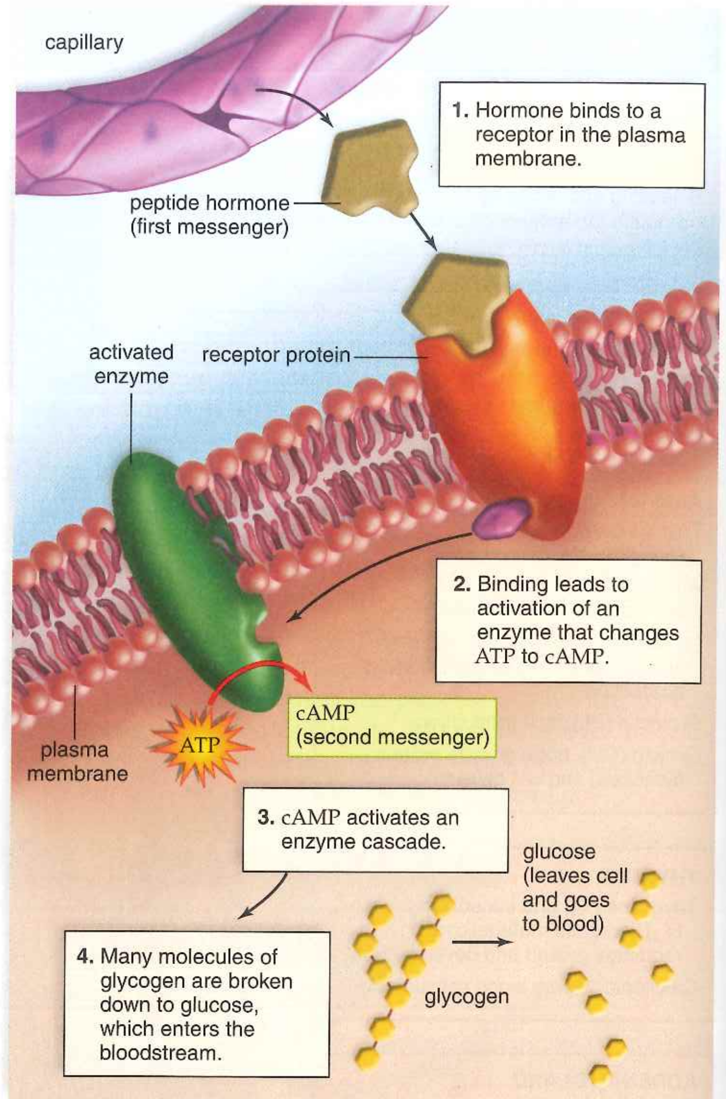


Figure 15.4 Peptide hormone.
A peptide hormone (first messenger) binds to a receptor in the plasma membrane. Thereafter, cyclic AMP (second messenger) forms and activates an enzyme cascade.

The Action of Hormones

Hormones have a wide range of effects on cells. Some of these effects induce a target cell to increase its uptake of particular substances, such as glucose, or ions, such as calcium. Some bring about an alteration of the target cell's structure in some way. Some simply influence cell metabolism. Growth hormone is a peptide hormone that influences cell metabolism leading to a change in the structure of bone. This hormone, mentioned in the opening story, is a **peptide hormone.** The term peptide hormone is used to include hormones that are peptides, proteins, glycoproteins, and modified amino acids. Growth hormone is a protein produced and secreted by the anterior pituitary. **Steroid hormones** have the same complex of four carbon rings because they are all derived from cholesterol (see Fig. 2.17).

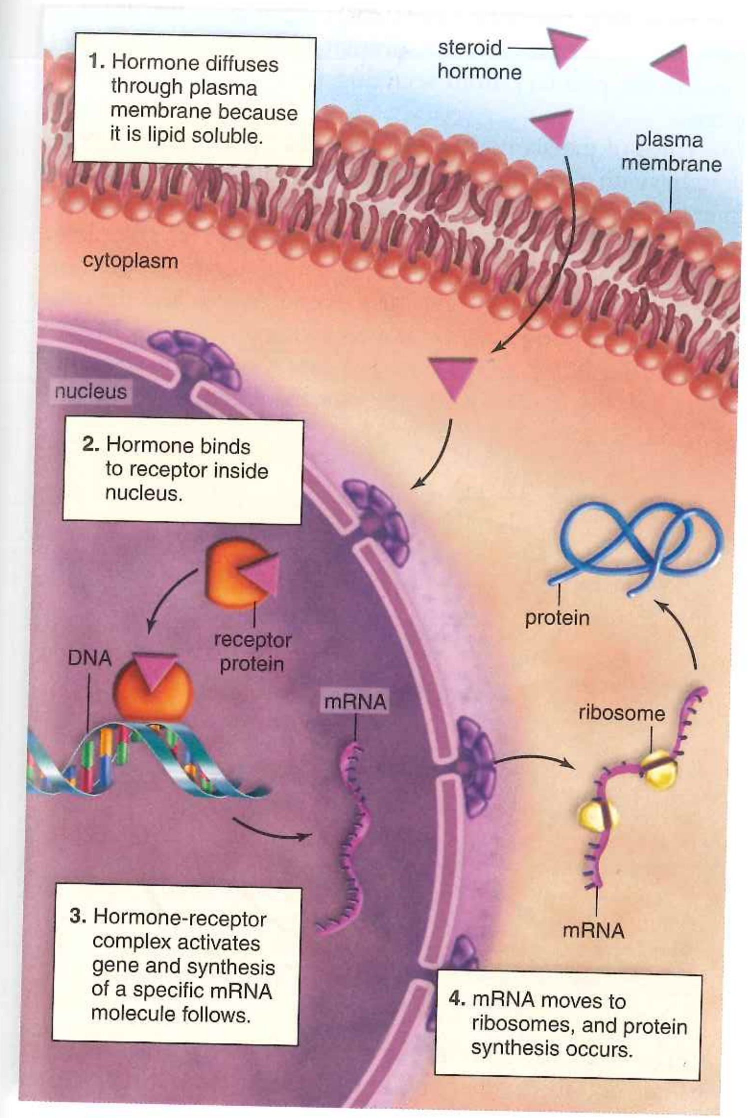


Figure 15.5 Steroid hormone.
A steroid hormone passes directly through the target cell's plasma membrane before binding to a receptor in the nucleus or cytoplasm. The hormone-receptor complex binds to DNA, and gene expression follows.

The Action of Peptide Hormones Most hormonal glands secrete peptide hormones. The actions of peptide hormones can vary, and we will concentrate on what happens in muscle cells after the hormone epinephrine binds to a receptor in the plasma membrane (Fig. 15.4). In muscle cells, the reception of epinephrine leads to the breakdown of glycogen to glucose, which provides energy for ATP production. The immediate result of binding is the formation of **cyclic adenosine monophosphate (cAMP).** Cyclic AMP contains one phosphate group attached to adenosine at two locations. Therefore, the molecule is cyclic. Cyclic AMP activates a protein kinase enzyme in the cell, and this enzyme, in turn, activates another enzyme, and so forth. The series of enzymatic reactions that follows cAMP formation is called an enzyme cascade. Because each enzyme can be used over and over again at every step of the cascade, more enzymes are involved. Finally, many molecules of glycogen are broken down to glucose, which enters the bloodstream.

Typical of a peptide hormone, epinephrine never enters the cell. Therefore, the hormone is called the **first messenger,** while cAMP, which sets the metabolic machinery in motion, is called the **second messenger.** To explain this terminology, let's imagine that the adrenal medulla, which produces epinephrine, is like the home office that sends out a courier (i.e., the hormone epinephrine is the first messenger) to a factory (the cell). The courier doesn't have a pass to enter the factory, so when he arrives at the factory, he tells a foreman through the screen door that the home office wants the factory to produce a particular product. The foreman (i.e., cAMP, the second messenger) walks over and flips a switch that starts the machinery (the enzymatic pathway), and a product is made.

The Action of Steroid Hormones Only the adrenal cortex, the ovaries, and the testes produce steroid hormones. Thyroid hormones act similarly to steroid hormones, even though they have a different structure. Steroid hormones do not bind to plasma membrane receptors, and instead they are able to enter the cell because they are lipids (Fig. 15.5). Once inside, a steroid hormone binds to a receptor, usually in the nucleus but sometimes in the cytoplasm. Inside the nucleus, the hormone-receptor complex binds with DNA and activates certain genes. Messenger RNA (mRNA) moves to the ribosomes in the cytoplasm and protein (e.g. enzyme) synthesis follows. To continue our analogy, a steroid hormone is like a courier that has a pass to enter the factory (the cell). Once inside, it makes contact with the plant manager (DNA) who sees to it that the factory (cell) is ready to produce a product.

Steroids act more slowly than peptides because it takes more time to synthesize new proteins than to activate enzymes already present in cells. Their action lasts longer, however.

Check Your Progress 15.1

1. How can the nervous system be contrasted with the endocrine system?
2. What is a hormone?
3. How do hormones affect the metabolism of cells?

15.2 Hypothalamus and Pituitary Gland

The **hypothalamus** regulates the internal environment through the autonomic system. For example, it helps control heartbeat, body temperature, and water balance. The hypothalamus also controls the glandular secretions of the **pituitary gland.** 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 and the anterior pituitary.

Posterior Pituitary

Neurons in the hypothalamus called neurosecretory cells produce the hormones **antidiuretic hormone (ADH)** and oxytocin (Fig. 15.6, *left*). These hormones pass through axons into the **posterior pituitary** where they are stored in axon endings. 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, ADH is released from the posterior pituitary. Upon reaching the kidneys, ADH causes more water to be reabsorbed into kidney capillaries. As the blood becomes dilute, 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. Negative feedback maintains stable conditions and homeostasis.

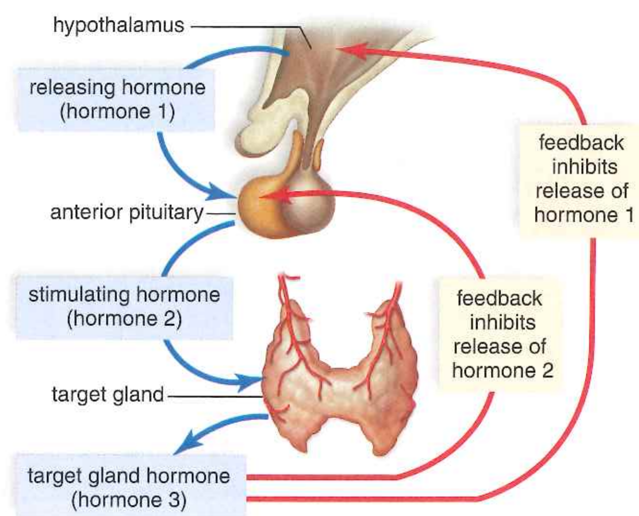
Inability to produce ADH causes diabetes insipidus (watery urine), in which a person produces copious amounts of urine with a resultant loss of ions from the blood. The condition can be corrected by the administration of ADH.

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. The sound of a baby crying may also stimulate the release of oxytocin. 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 ever increases in intensity. Positive feedback terminates due to some external event as when a baby is full and stops suckling. Positive feedback is not a way to maintain stable conditions and homeostasis.

Anterior Pituitary

A portal system, consisting of two capillary systems connected by a vein, lies between the hypothalamus and the **anterior pituitary** (Fig. 15.6, *right*). The hypothalamus controls the anterior pituitary by producing **hypothalamic-releasing** and **hypothalamic-inhibiting hormones** which pass from the hypothalamus to the anterior pituitary by way of the portal system. To take an example, there is a thyroid-releasing hormone (TRH) and a thyroid-inhibiting hormone (TIH). TRH stimulates the anterior pituitary to secrete thyroid-stimulating hormone, and TIH inhibits the pituitary from secreting thyroid-stimulating hormone.

Three of the six hormones produced by the anterior pituitary have an effect on other glands: **Thyroid-stimulating hormone (TSH)** stimulates the thyroid to produce the thyroid hormones; **adrenocorticotropic hormone (ACTH)** stimulates the adrenal cortex to produce cortisol; and **gonadotropic hormones** stimulate the gonads—the testes in males and the ovaries in females—to produce gametes and sex hormones. 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:



The other three hormones produced by the anterior pituitary do not affect other endocrine glands. **Prolactin (PRL)** is produced in quantity only 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.

Melanocyte-stimulating hormone (MSH) causes skin-color changes in many fishes, amphibians, and reptiles having melanophores, special skin cells that produce color variations. The concentration of this hormone in humans is very low.

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

In the 1980s, growth hormone became a biotechnology product, and it was possible to treat short children and those diagnosed as pituitary dwarfs. A growth hormone blood test can be done in order to tell if a child is able to produce the normal amount of growth hormone. If not, like Adam in the opening story, growth hormone can be injected as a medication.

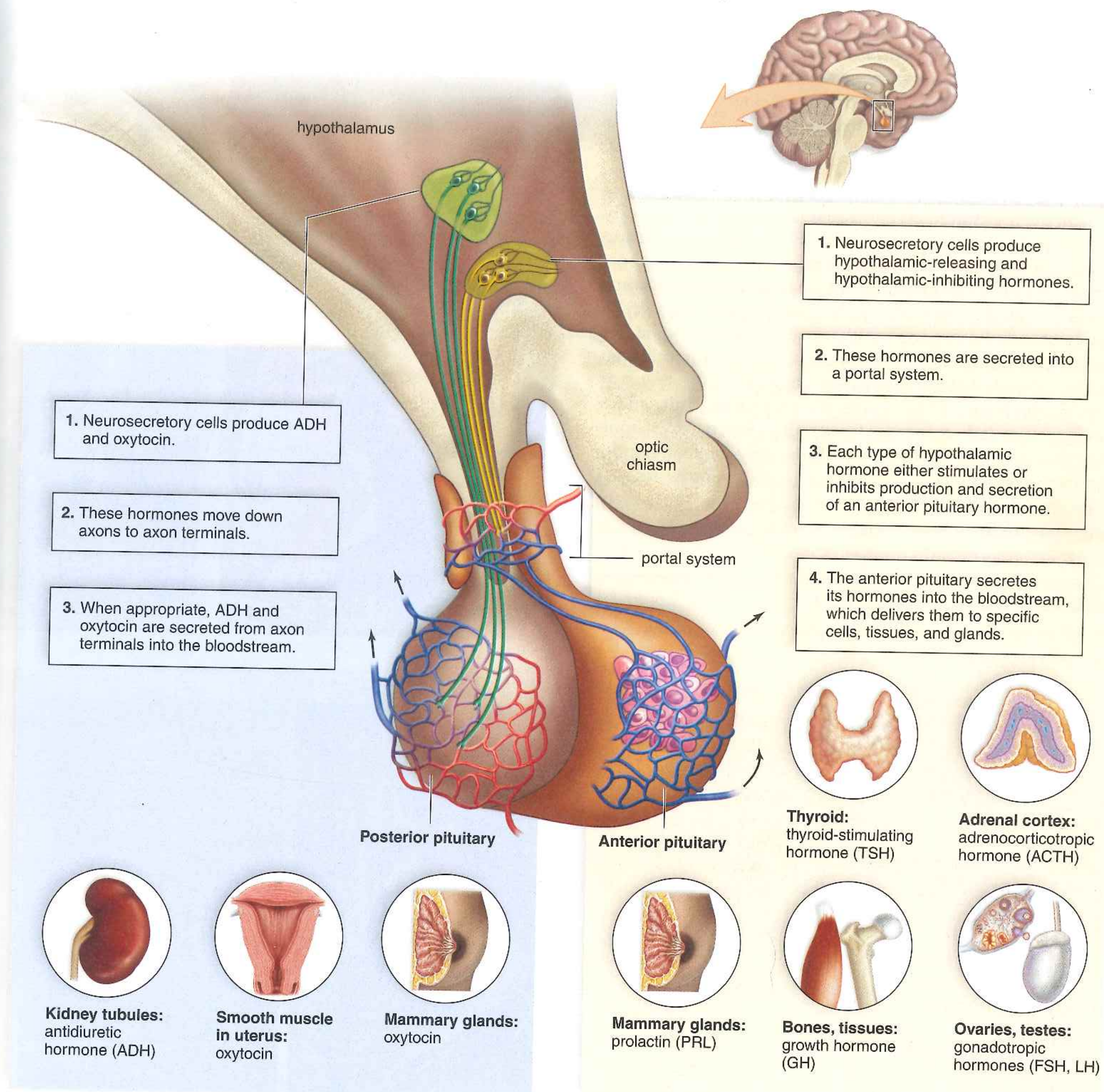


Figure 15.6 Hypothalamus and the pituitary.
Left: The hypothalamus produces two hormones, ADH and oxytocin, which are stored and secreted by the posterior pituitary. *Right:* The hypothalamus controls the secretions of the anterior pituitary, and the anterior pituitary controls the secretions of the thyroid, adrenal cortex, and gonads, which are also endocrine glands.

Figure 15.7
Effect of growth hormone.
a. The amount of growth hormone produced by the anterior pituitary during childhood affects the height of an individual. Plentiful growth hormone produces very tall basketball players. **b.** Too much growth hormone can lead to gigantism, while an insufficient amount results in limited stature and even pituitary dwarfism.

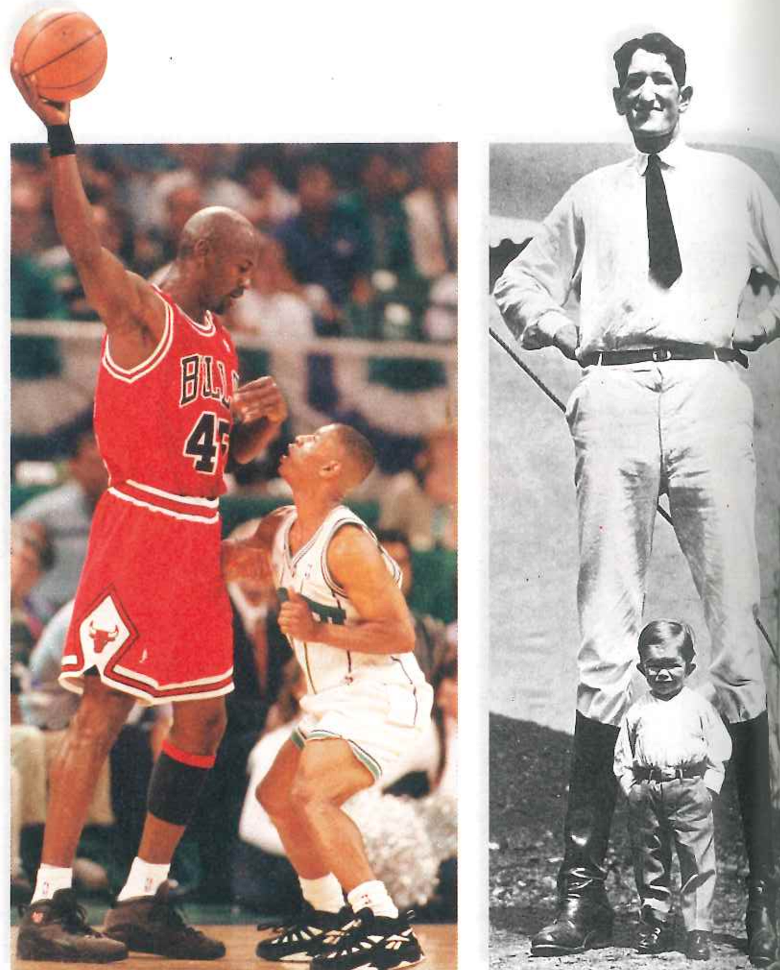
Effects of Growth Hormone

GH is produced by the anterior pituitary. The quantity 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. 15.7). 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 309–10).

On occasion, GH is overproduced in the adult, and a condition called **acromegaly** results. Since long bone growth is no longer possible in adults, only the feet, hands, and face (particularly the chin, nose, and eyebrow ridges) can respond, and these portions of the body become overly large (Fig. 15.8).

Check Your Progress 15.2

1. What role does the hypothalamus play in the endocrine system?
2. What hormones are produced by the anterior pituitary?



a. b.

Age 9 Age 16 Age 33 Age 52

Figure 15.8 **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.

15.3 Thyroid and Parathyroid Glands

The **thyroid gland** is a large gland located in the neck, where it is attached to the trachea just below the larynx (see Fig. 15.2). 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.

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 goiter** (Fig. 15.9*a*). Some years ago, it was discovered that 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 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. 15.9*b*). 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, mental retardation 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), the thyroid gland is overactive, and a goiter forms. This type of goiter is called **exophthalmic goiter** (Fig. 15.9*c*). 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 sometimes 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.

a. Simple goiter b. Congenital hypothyroidism c. Exophthalmic goiter

Figure 15.9 **Abnormalities of the thyroid.**
a. 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. **b.** Individuals who develop hypothyroidism during infancy or childhood do not grow and develop as others do. Unless medical treatment is begun, the body is short and stocky; mental retardation is also likely. **c.** In exophthalmic goiter, a goiter is due to an overactive thyroid, and the eyes protrude because of edema in eye socket tissue.

Calcitonin

Calcium (Ca^{2+}) plays a significant role in both nervous conduction and muscle contraction. It is also necessary for blood clotting. The blood Ca^{2+} level is regulated in part by **calcitonin,** a hormone secreted by the thyroid gland when the blood Ca^{2+} level rises (Fig. 15.10). The primary effect of calcitonin is to bring about the deposit of Ca^{2+} in the bones. It also temporarily reduces the activity and number of osteoclasts. When the blood Ca^{2+} level lowers to normal, the release of calcitonin by the thyroid is inhibited, but a low level stimulates the release of **parathyroid hormone (PTH)** by the parathyroid glands.

Parathyroid Glands

Many years ago, the four parathyroid glands were sometimes mistakenly removed during thyroid surgery because of their size and location. PTH, the hormone produced by the **parathyroid glands,** causes the blood Ca^{2+} level to increase.

A low blood Ca^{2+} level stimulates the release of PTH. PTH promotes the activity of osteoclasts and the release of calcium from the bones. PTH also promotes the reabsorption of calcium by the kidneys, where it activates vitamin D. Activated vitamin D is a hormone sometimes called calcitriol, which stimulates the absorption of Ca^{2+} from the intestine. These effects bring the blood Ca^{2+} level back to the normal range so that the parathyroid glands no longer secrete PTH.

When insufficient PTH production leads to a dramatic drop in the blood calcium level, tetany results. 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.

Healing a Fracture

Remember Katie, who suffered a burst vertebra in the opening story for Chapter 11? In order for her injury to heal, osteoclasts will have to destroy old bone, and osteoblasts will have to lay down new bone. Many factors influence the growth of forming new bone, including parathyroid hormone, calcitonin, and vitamin D. Working together, the calcium needed to fuse her vertebrae would be made readily available as new blood capillaries penetrated the area.

Check Your Progress 15.3

1. a. What hormones are produced by the thyroid gland? b. How do thyroid hormones affect the metabolic rate?
2. a. What hormone is produced by the parathyroid gland? b. What is the function of this hormone? c. What hormone is secreted by the thyroid gland when the blood Ca^{2+} levels are high?

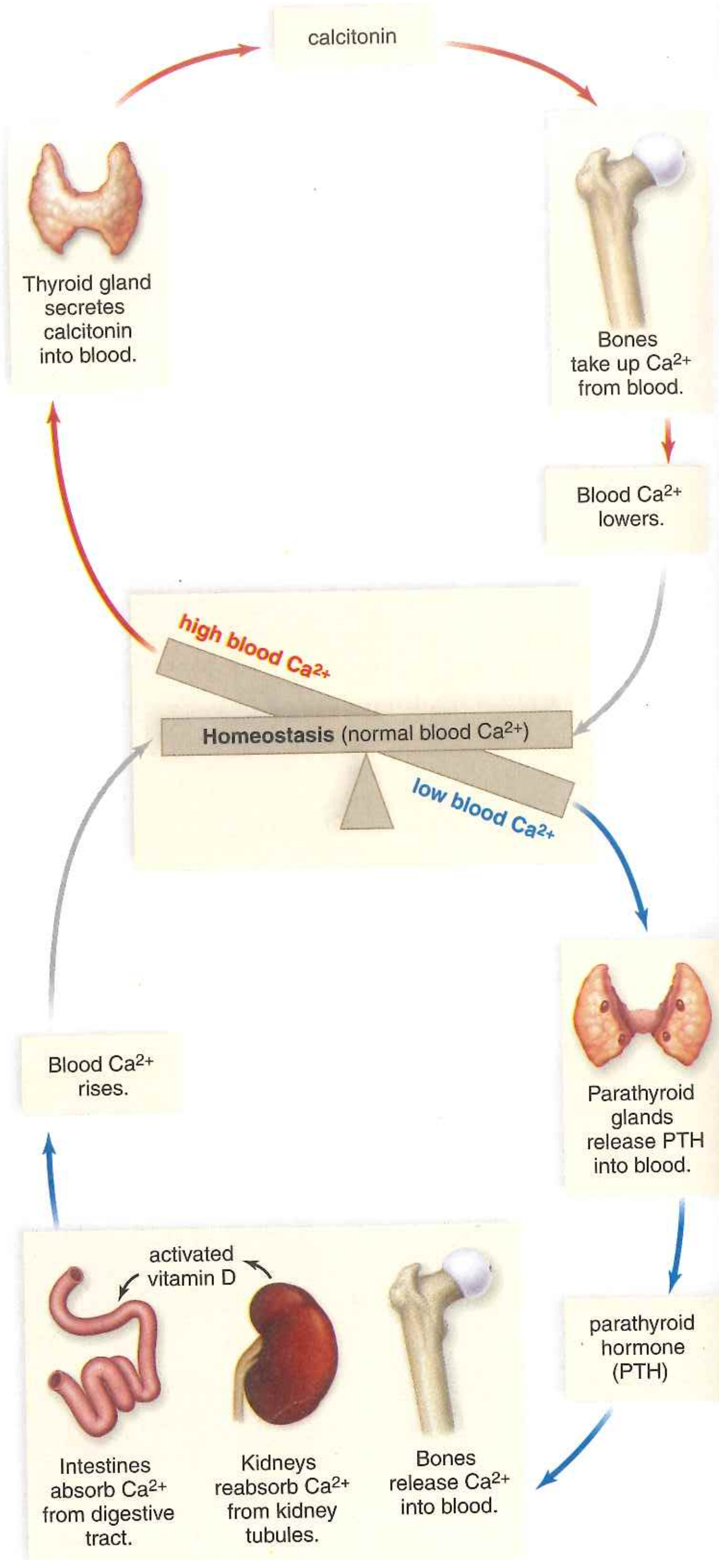


Figure 15.10 Regulation of blood calcium level.
Top: When the blood calcium (Ca^{2+}) level is high, the thyroid gland secretes calcitonin. Calcitonin promotes the uptake of Ca^{2+} by the bones, and therefore, the blood Ca^{2+} level returns to normal. *Bottom:* When the blood Ca^{2+} level is low, 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.

15.4 Adrenal Glands

The **adrenal glands** sit atop the kidneys (see Fig. 15.2). 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 and the posterior pituitary, are two functionally distinct endocrine glands. The adrenal medulla is under nervous control, and portions of the adrenal cortex are under the control of ACTH, an anterior pituitary hormone. Stress of all types, including emotional and physical trauma, prompts the hypothalamus to stimulate a portion of the adrenal glands (Fig. 15.11).

Adrenal Medulla

The hypothalamus initiates nerve impulses that travel by way of the brain stem, spinal cord, and preganglionic sympathetic nerve fibers to the adrenal medulla, which then secretes its hormones. The cells of the adrenal medulla are thought to be modified postganglionic neurons.

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 in a fight-or-flight manner. The effect of these hormones provide a short-term response to stress.

Adrenal Cortex

In contrast, the hormones produced by the adrenal cortex provide a long-term response to stress (Fig. 15.11). 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 to increases in blood volume and blood pressure. The **glucocorticoids,** whose secretion is controlled by ACTH, regulate carbohydrate, protein, and fat metabolism, leading to an increase in blood glucose level. Glucocorticoids also suppress the body's inflammatory response. Cortisone, the medication often administered for inflammation of joints, is a glucocorticoid.

The adrenal cortex also secretes a small amount of male sex hormones and a small amount of female sex hormones in both sexes. That is, in both males and females, both male and female sex hormones are produced by the adrenal cortex.

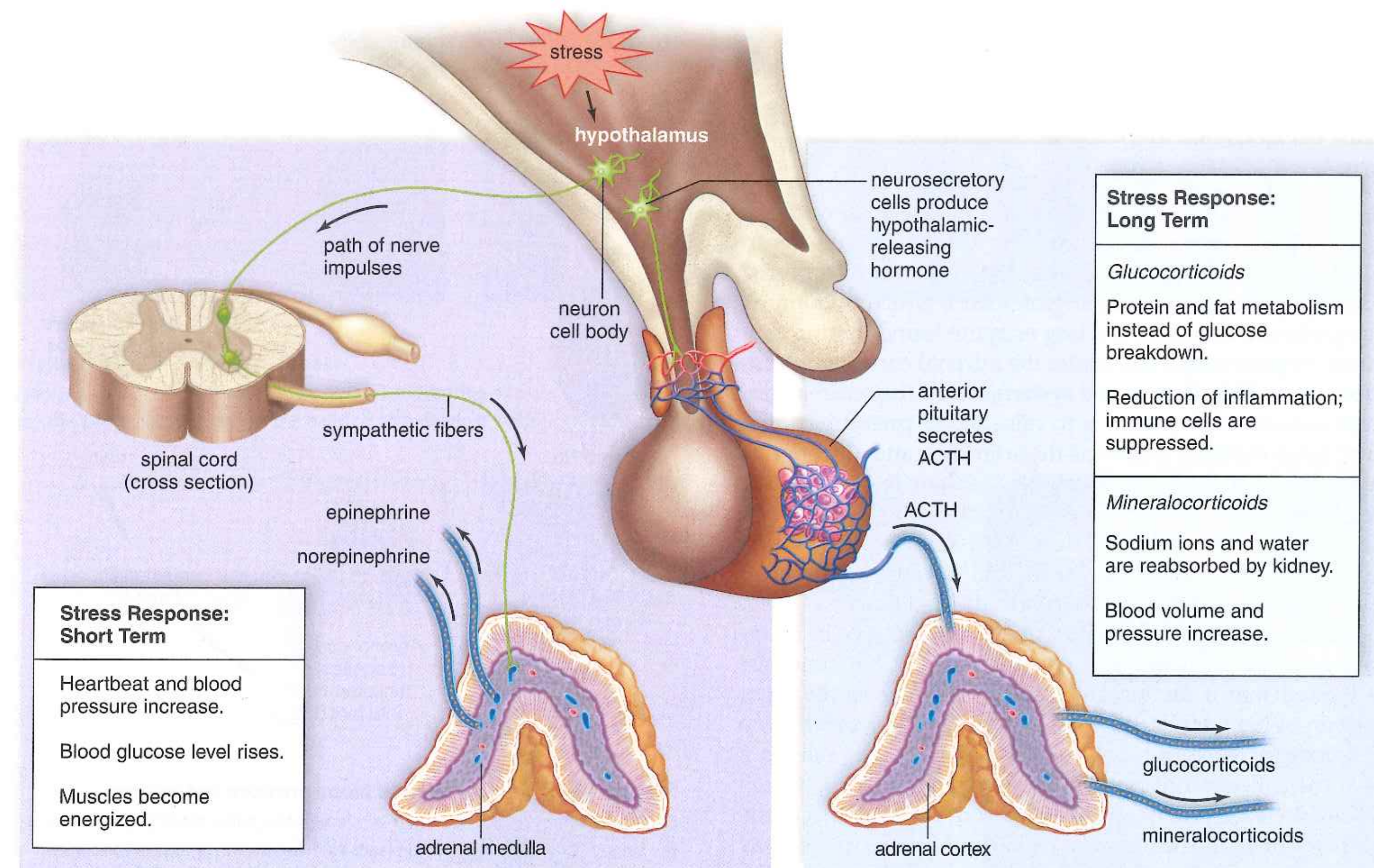


Figure 15.11 Adrenal glands.
Both the adrenal cortex and the adrenal medulla are under the control of the hypothalamus when they help us respond to stress. *Left:* Nervous stimulation causes the adrenal medulla to provide a rapid, but short-term, stress response. *Right:* The adrenal cortex provides a slower, but long-term, stress response. ACTH causes the adrenal cortex to release glucocorticoids. Independently, the adrenal cortex releases mineralocorticoids.

Glucocorticoids

ACTH stimulates those portions of the adrenal cortex which secrete the glucocorticoids. **Cortisol** and also cortisone are biologically significant glucocorticoids. Glucocorticoids raise the blood glucose level in at least two ways: (1) They promote the breakdown of muscle proteins to amino acids, which are taken up by the liver from the bloodstream. The liver then breaks down these excess amino acids to glucose, which enters the blood. (2) They promote the metabolism of fatty acids rather than carbohydrates, and this spares glucose.

The glucocorticoids also counteract the inflammatory response that leads to the pain and swelling of joints in arthritis and bursitis. The administration of cortisone aids these conditions because it reduces inflammation. Very high levels of glucocorticoids in the blood can suppress the body's defense system, including the inflammatory response that occurs at infection sites. Cortisone and other glucocorticoids can relieve swelling and pain from inflammation, but by suppressing pain and immunity, they can also make a person highly susceptible to injury and infection.

Mineralocorticoids

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

The secretion of mineralocorticoids is not controlled by the anterior pituitary. When the blood Na^+ level and, therefore, the blood pressure are low, the kidneys secrete **renin** (Fig. 15.12). Renin is an enzyme that converts the plasma protein angiotensinogen to angiotensin I, which is changed 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 the arterioles, and aldosterone causes the kidneys to reabsorb Na^+. When the blood Na^+ level rises, water is reabsorbed, in part, because the hypothalamus secretes ADH (see page 300). Reabsorption means that water enters kidney capillaries and thus the blood. Then blood pressure increases to normal.

Recall that we studied the role of the kidneys in maintaining blood pressure on pages 197–98. At that time, we mentioned that if the blood pressure rises due to the reabsorption of Na^+, the atria of the heart are apt to stretch. Due to a great increase in blood volume, cardiac cells release a chemical called **atrial natriuretic hormone (ANH),** which inhibits the secretion of aldosterone from the adrenal cortex. In other words, the heart is among various organs in the body that releases a hormone, but obviously not as its major function. (Therefore, the heart is not included as an endocrine gland in Figure 15.2.) The effect of this ANH is to cause the excretion of Na^+—that is, *natriuresis.* When Na^+ is excreted, so is water, and therefore, blood pressure lowers to normal.

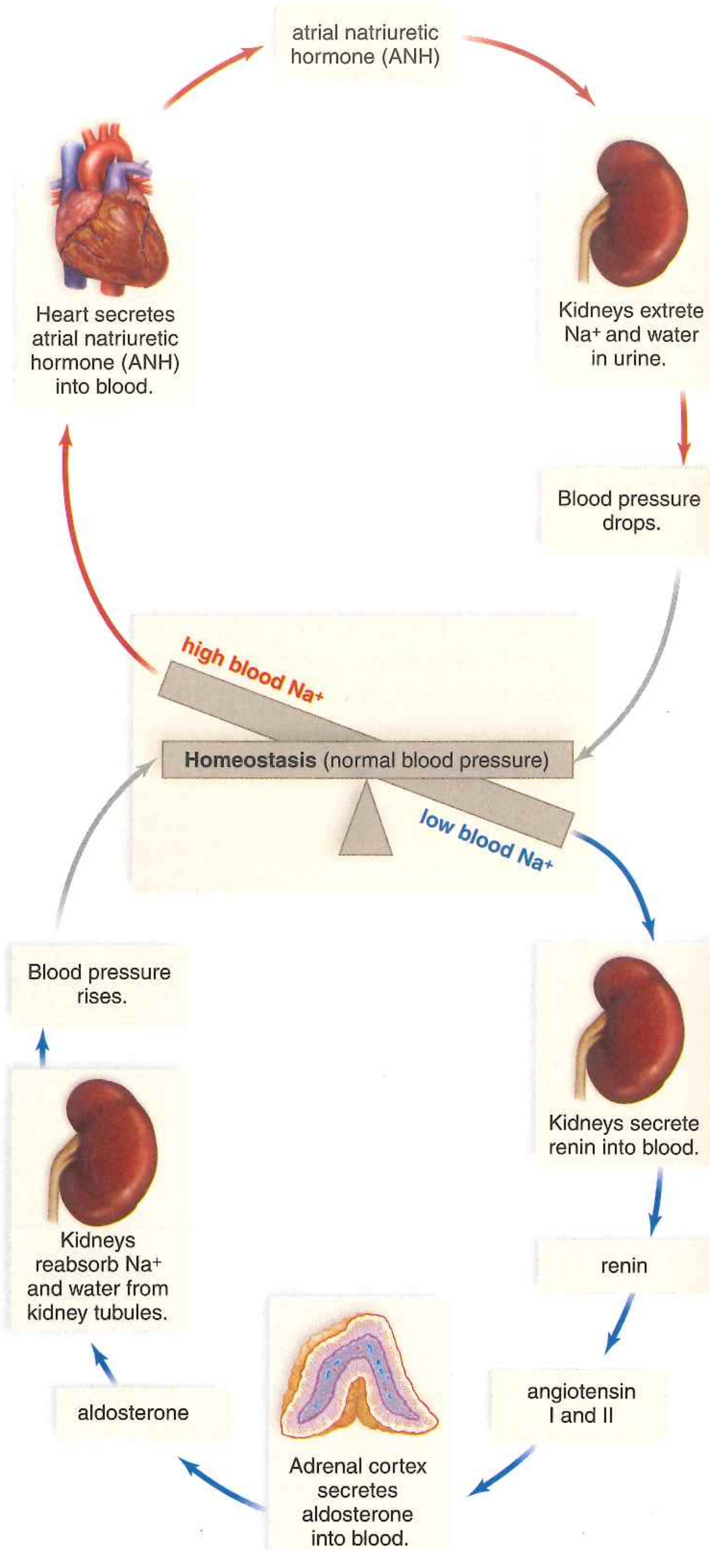


Figure 15.12 Regulation of blood pressure and volume.
Bottom: When the blood sodium (Na^+) level is low, a low blood pressure causes the kidneys to secrete renin. Renin leads to the secretion of aldosterone from the adrenal cortex. Aldosterone causes the kidneys to reabsorb Na^+, and water follows, so that blood volume and pressure return to normal. *Top:* When a high blood Na^+ level accompanies a high blood volume, the heart secretes atrial natriuretic hormone (ANH). ANH causes the kidneys to excrete Na^+, and water follows. The blood volume and pressure return to normal.

Malfunction of the Adrenal Cortex

When the blood level of glucocorticoids is low due to hyposecretion, a person develops **Addison disease.** The presence of excessive but ineffective ACTH causes a bronzing of the skin because ACTH, like MSH, can lead to a buildup of melanin (Fig. 15.13). Without the glucocorticoids, glucose cannot be replenished when a stressful situation arises. Even a mild infection can lead to death. In some cases, hyposecretion of aldosterone results in a loss of sodium and water, the development of low blood pressure, and possibly severe dehydration. Left untreated, Addison disease can be fatal.

When the level of glucocorticoids is high due to hypersecretion, a person develops **Cushing syndrome.** The excess glucocorticoids result in a tendency toward diabetes mellitus, as muscle protein is metabolized and subcutaneous fat is deposited in the midsection. The result is a swollen "moon" face and an obese trunk, with arms and legs of normal size. Children will show obesity and poor growth in height (Fig. 15.14). Depending on the cause and duration of the Cushing syndrome, some people may have more dramatic changes, including masculinization with increased blood pressure and weight gain.

Check Your Progress 15.4

1. What are the two major hormones produced by the adrenal cortex, and what do they regulate?

a. b.

Figure 15.13 Addison disease.
Addison 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 with the hand of an individual without the disease.

Figure 15.14 Cushing syndrome.
Cushing syndrome results from hypersecretion of adrenal cortex hormones. *Left:* Patient first diagnosed with Cushing syndrome. *Right:* Four months later, after therapy.

15.5 Pancreas

The **pancreas** is a fish-shaped organ that stretches across the abdomen behind the stomach 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. Endocrine tissue, called the **pancreatic islets** (islets of Langerhans), produces and secretes the hormones **insulin** and **glucagon** directly into the blood (Fig. 15.15).

The pancreas is not under pituitary control. Insulin is secreted when the blood glucose level is high, which usually occurs just after eating. Insulin stimulates the uptake of glucose by cells, especially liver cells, muscle cells, and adipose tissue cells. In liver and muscle cells, glucose is then stored 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 various ways, insulin lowers the blood glucose level (Fig. 15.16, *top*)

Glucagon is secreted from the pancreas, usually between eating, 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. 15.16, *bottom*).

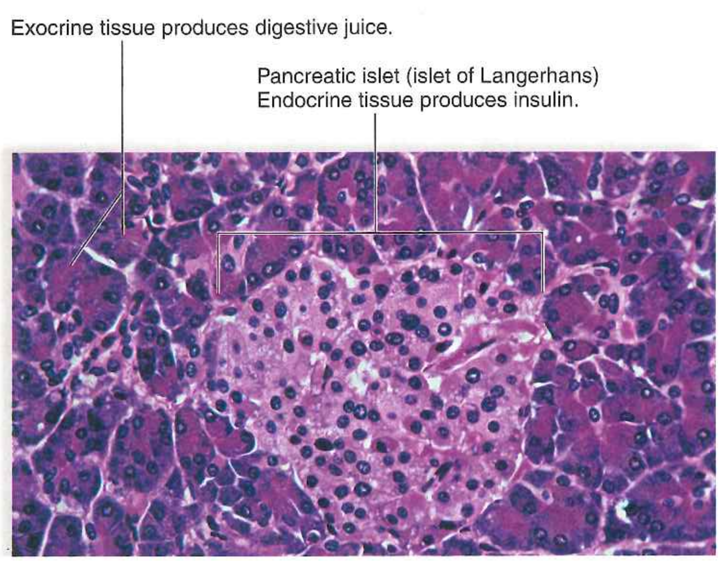


Figure 15.15 Pancreas. This light micrograph shows that the pancreas has two types of cells. The exocrine tissue produces a digestive juice and the endocrine tissue produces the hormone insulin.

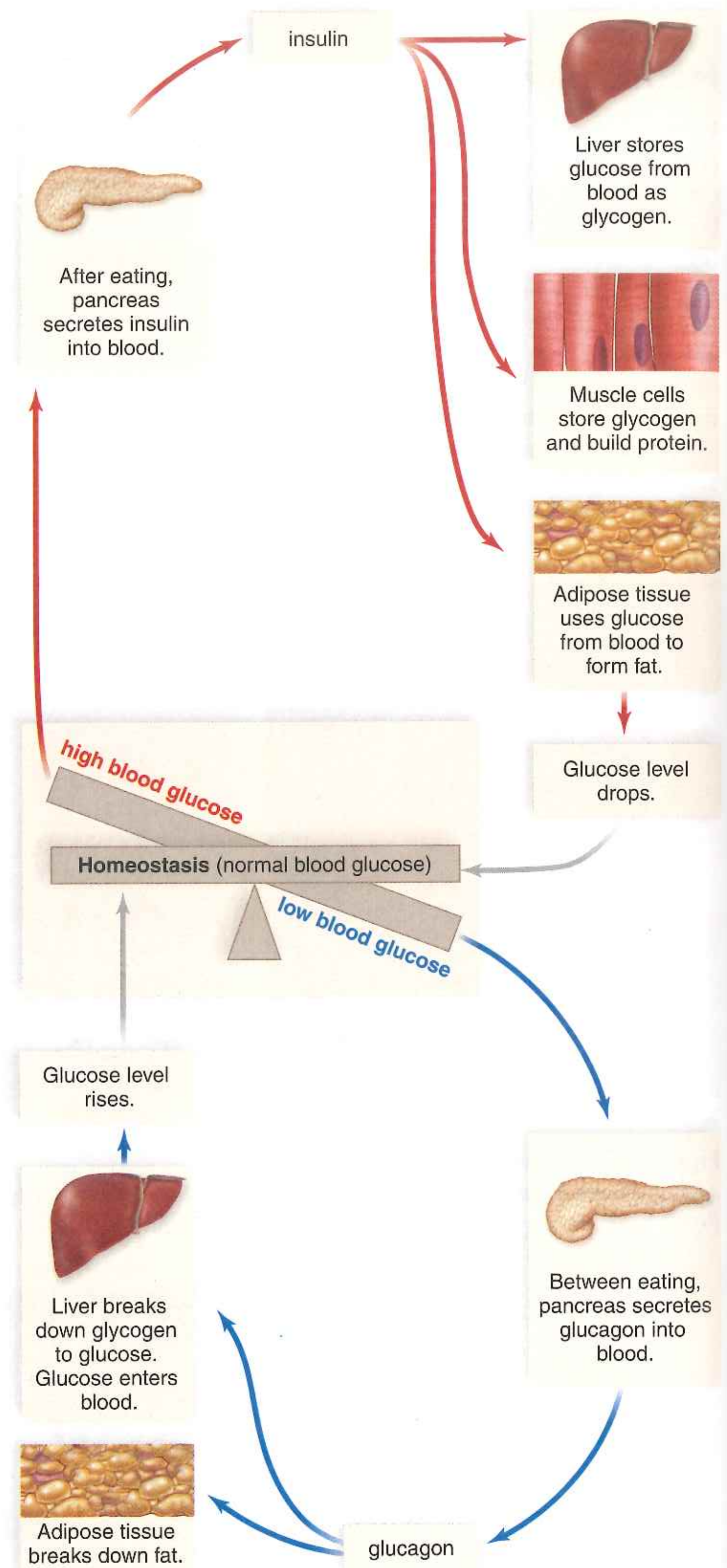


Figure 15.16 Regulation of blood glucose level. *Top:* When the blood glucose level is high, the pancreas secretes insulin. Insulin promotes the storage of glucose as glycogen and the synthesis of proteins and fats. Therefore, insulin lowers the blood glucose level. *Bottom:* When the blood glucose level is low, the pancreas secretes glucagon. Glucagon acts opposite to insulin; therefore, glucagon raises the blood glucose level to normal.

Health Focus

Do You Have Diabetes?

The world is experiencing a diabetes epidemic—more and more people are being diagnosed with the condition. In the United States, 18 million people now have either diabetes mellitus type 1 or diabetes type 2. The number of those with diabetes type 2, in particular, is expected to rise at an alarming rate. By 2025, the incidence of diabetes type 2 is expected to double over what it is now.

Diagnosing Diabetes

People with diabetes have to check their blood sugar level, usually before meals and at bedtime. Today, automatic lancets prick the finger and computerized devices can record readings automatically (Fig. 15A). In people without diabetes, the device records a blood sugar level between 70 and 110 mg/dL (milligrams per deciliter which is .10 liters). In diabetics, the blood sugar level is more than 140 mg/dL. What's wrong? In the nondiabetic, the hormone insulin secreted by the pancreas causes tissue cells (particularly fat, muscle, and liver cells) to take up glucose so that the blood sugar level remains within the normal range. In diabetes type 1, the pancreas fails to secrete insulin—the cells that make insulin have died off! In diabetes type 2, the pancreas usually fails to secrete enough insulin, but the real problem is that the cells are resistant to insulin. Receptors in the plasma membrane don't bind insulin properly, and then the plasma membrane doesn't have enough carrier proteins to transport the glucose into the cell.

Most people don't have a means to check their blood glucose level, so how do they become aware that they have diabetes? These symptoms can help you decide if a physician should check you out:

- Frequent urination, especially at night
- Unusual hunger and/or thirst
- Unexplained change of weight
- Blurred vision
- Sores that do not heal
- Excessive fatigue

A physician has a number of other ways to diagnose diabetes. One of the most common is to test for sugar in the urine. When the blood sugar level is high, the kidneys excrete sugar, and a lab test can detect its presence in the urine. Excessive thirst accompanies untreated diabetes because the kidneys use large amounts of water to flush the excess glucose out of the body. Hunger and exhaustion occur because the cells are starving for glucose in the midst of plenty. Without glucose, some cells cannot produce ATP, the energy currency of cells.

What Causes Diabetes

Diabetes type 1 runs in families, and researchers have identified about 20 genes that can increase your risk of diabetes. Diabetes type 1 usually occurs after a viral infection. The immune system gears up to fight the infection by killing off cells that are harboring the virus. When the infection is over, the immune system keeps on killing cells—this time the pancreatic cells that produce insulin. Diabetes type 1 is clearly a self-inflicted disease, but in another way, so is diabetes type 2. Diabetes type 2 used to be thought of as an adult-onset disorder. Now more and more children have it. The risk factors for getting diabetes type 2 are excessive food intake leading to obesity, especially fat located in the abdominal region, and physical inactivity.

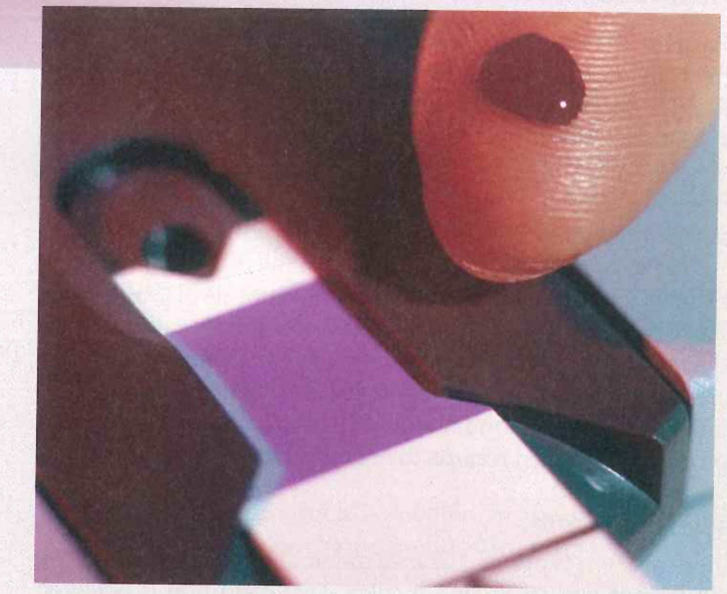


Figure 15A Testing the blood sugar level. Diabetics have to test their blood sugar level during the day and just before retiring to make sure their treatment is keeping it within the normal range.

Treatment for Diabetes

Those with diabetes type 1 must have insulin injections, but those with diabetes type 2 usually receive metformin, a medication that makes cells more likely to respond to the presence of insulin.

A healthy diet and exercise are emphasized as an important part of their regimen. Even limited weight loss can often lead to better blood glucose regulation. Foods rich in complex carbohydrates, including dietary fiber and fruit, are preferred over easily digested foods such as many junk foods (for example, potato chips). Building up the muscles and using them regularly by, say, walking, riding a bike, or dancing uses up glucose and improves insulin efficiency. All diabetics must work closely with a physician to tailor the correct regimen of medications, diet, and exercise for them.

Diabetes is associated with the possibility of blindness, cardiovascular diseases, and kidney disease. Nerve deterioration can lead to an inability to feel pain, particularly in the hands and feet. If so, treatment of an infection may be delayed to the point that limb amputation is required. Diabetes is definitely a disorder to avoid if at all possible. The very best course of action is to adopt a healthy lifestyle—the younger the better—in order to keep this condition at bay. This is the way you can help your body maintain homeostasis, the relative constancy of the internal environment; in this case, a normal blood glucose level.

Diabetes Mellitus

Diabetes mellitus is a fairly common hormonal disease in which liver cells, and indeed most body cells, are unable to take up glucose as they should. Therefore, cellular famine exists in the midst of plenty, and the person becomes extremely hungry. As the blood glucose level rises, glucose, along with water, is excreted in the urine. Urination is frequent, and the loss of water causes the diabetic to be extremely thirsty.

The glucose tolerance test assists in the diagnosis of diabetes mellitus. After the patient is given 100 grams of glucose, the blood glucose concentration is measured at intervals. In a diabetic, the blood glucose level rises greatly and remains elevated for several hours (Fig. 15.17). In the meantime, glucose appears in the urine. In a nondiabetic, the blood glucose level rises somewhat and then returns to normal after about two hours.

Types of Diabetes

There are two types of diabetes mellitus. In *diabetes type 1*, the pancreas is not producing insulin. This condition is believed to be brought on by exposure to an environmental agent, most likely a virus, whose presence causes cytotoxic T cells to destroy the pancreatic islets. The body turns to the metabolism of fat, which leads to the buildup of ketones in the blood and, in turn, to acidosis (acid blood), which can lead to coma and death. As a result, the individual must have daily insulin injections. These injections control the diabetic symptoms but can still cause inconveniences because the blood sugar level may swing between hypoglycemia (low blood glucose level) and hyperglycemia (high blood glucose level). Without testing the blood glucose level, it is difficult to be certain which of these is present because the symptoms are similar. The symptoms include perspiration, pale skin, shallow breathing, and anxiety. Whenever these symptoms appear, immediate attention is required to bring the blood glucose level to its proper level. If the problem is hypoglycemia, the cure is a cube of sugar, and if hyperglycemia, the cure is insulin.

Some diabetics have learned to use an insulin pump to better regulate their blood sugar level. The pump is worn outside the body, usually attached to a belt or waistband. Insulin is pumped from a reservoir through a tube inserted under the skin of the abdominal wall. It is also possible to transplant a working pancreas into patients with diabetes type 1. To do away with the necessity of taking immunosuppressive drugs after the transplant, fetal pancreatic islet cells have been injected into patients. Another experimental procedure is to place pancreatic islet cells in a capsule that allows insulin to get out but prevents antibodies and T lymphocytes from getting in. This artificial organ is implanted in the abdominal cavity.

Of the 16 million people who now have diabetes in the United States, most have *diabetes type 2*. Often, the patient is obese. Usually, after insulin binds to a plasma membrane receptor, the number of protein carriers for glucose increases, and more glucose than usual enters the cell. In the case of diabetes type 2, glucose binds to the receptor, but the number of carriers does not increase. Therefore, the cell is said to be insulin resistant.

It is possible to prevent or at least control diabetes type 2 by adhering to a low-fat, low-sugar diet and exercising regularly. If this fails, oral drugs that stimulate the pancreas to secrete more insulin and enhance the metabolism of glucose in the liver and muscle cells are available. It is projected as many as seven million Americans may have diabetes type 2 without being aware of it. Yet, the effects of untreated diabetes type 2 are as serious as those of diabetes type 1.

Long-term complications of both types of diabetes are blindness, kidney disease, and cardiovascular 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. These complications of diabetes are not expected to appear if the mother's blood glucose level is carefully regulated and kept within normal limits.

Check Your Progress 15.5

1. What hormones are produced by the pancreas and how does each affect blood glucose?
2. What is diabetes mellitus?

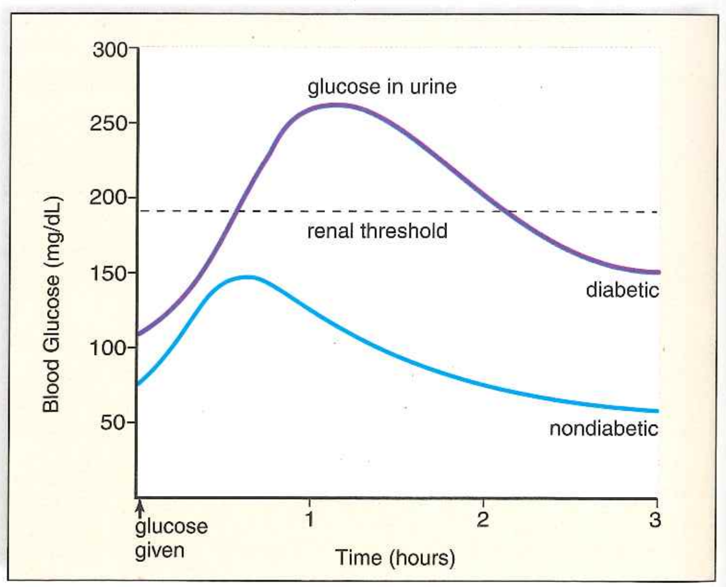


Figure 15.17 Glucose tolerance test.
Following the administration of 100 grams of glucose, the blood glucose level rises dramatically in the diabetic, and glucose appears in the urine. Also, the blood glucose level at 2 hours is equal to more than 200 mg/dL.

15.6 Other Endocrine Glands

The **gonads** are the testes in males and the ovaries in females. The gonads are endocrine glands. Other lesser known glands and some tissues also produce hormones.

Testes and Ovaries

The activity of the testes and ovaries are controlled by the hypothalamus and pituitary. The **testes** 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. These hormones feedback to control the hypothalamus secretion of GnRH (gonadotropic releasing hormone) and the pituitary gland secretion of FSH and LH, the gonadotropic hormones (Fig. 15.18). The activities of FSH and LH are discussed in Chapter 16.

Under the influence of the gonadotropic hormones, the testes begin to release increased amounts of testosterone at the time of puberty, and testosterone 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 lower. 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. Although females, like males, do inherit genes for baldness, baldness is seen more often in males because of the presence of testosterone. Testosterone is partially responsible for the muscular strength of males, and this is why some athletes take supplemental amounts of **anabolic steroids,** which are either testosterone or related chemicals. The Bioethical Focus on page 241 discusses the detrimental effect anabolic steroids can have on the body.

The female sex hormones, estrogens (often referred to in the singular) and progesterone, have many effects on the body. In particular, estrogen secreted at the time of puberty stimulates the growth of the uterus and the vagina. Estrogen is necessary for egg 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 menstruation (discharge of blood and mucosal tissues from the uterus).

Thymus Gland

The lobular **thymus gland** lies just beneath the sternum (see Fig. 15.2). This organ reaches its largest size and is most active during childhood. With aging, the organ gets smaller and becomes fatty. Lymphocytes that originate in the bone marrow and then pass through the thymus are transformed into 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 in the thymus, there is 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 (see Fig. 15.2), produces the hormone **melatonin,** primarily at night. Melatonin is involved in our daily sleep-wake cycle; nor-

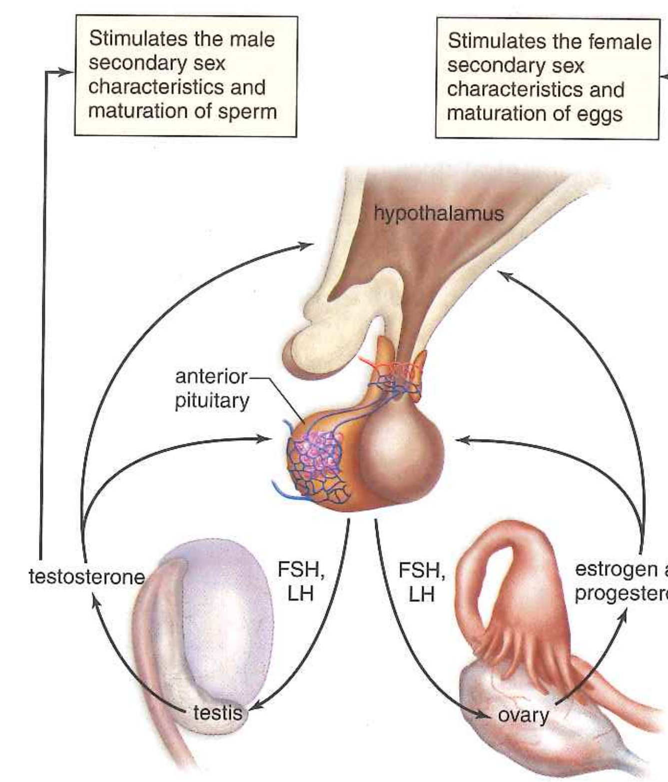


Figure 15.18 Regulation of the gonadotropic and sex hormones.
The testes and ovaries secrete the sex hormones. The testes secrete testosterone, and the ovaries secrete estrogens and progesterone. In each sex, secretion of GnRH from the hypothalamus and secretion of FSH and LH from the pituitary are controlled by their respective hormones.

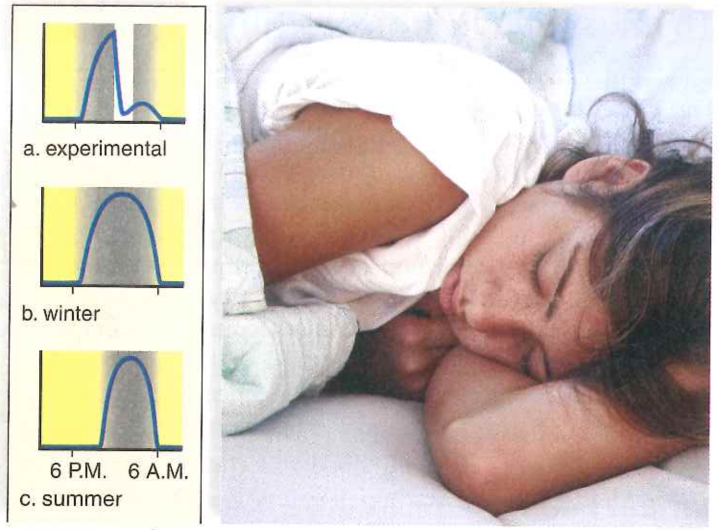


Figure 15.19 Melatonin production.
Melatonin production is greatest at night when we are sleeping. Light suppresses melatonin production (a), so it is secreted for a longer time in the winter (b) than in the summer (c).

mally we grow sleepy at night when melatonin levels increase and awaken once daylight returns and melatonin levels are low (Fig. 15.19). Daily 24-hour cycles such as this are called **circadian rhythms,** and these rhythms are controlled by a biological clock located in the hypothalamus.

Animal research suggests that melatonin also regulates sexual development. In keeping with these findings, it has been noted that children whose pineal gland has been destroyed due to a brain tumor experience early puberty.

Hormones from Other Organs/Tissues

Some organs that are not usually considered endocrine glands do indeed secrete hormones (Table 15.1). We have already mentioned that the kidneys secrete renin and that the heart produces atrial natriuretic hormone (see page 306). And you will recall that the stomach and the small intestine produce peptide hormones that regulate digestive secretions. A number of other types of tissues produce hormones.

Table 15.1 Hormones from Other Organs/Tissues

	Hormone	Function
Kidney	Renin	Leads to aldosterone and higher blood pressure
	Erythropoietin	Stimulates red bone marrow to produce red blood cells
Heart	Atrial natriuretic hormone	Lowers blood pressure
GI tract	Secretin, gastrin, cholecystokinin	Control secretion of some GI enzymes and bile
Fat cells	Leptin	Helps regulate appetite
Tissue cells	Prostaglandins	Various functions

Erythropoietin

In response to a low oxygen blood level, the kidneys secrete erythropoietin, which stimulates red blood cell formation in the red bone marrow. A number of different types of organs and cells also produce peptide growth factors, which stimulate cell division and mitosis. Growth factors can be considered hormones because they act on cell types with specific receptors to receive them. Some are released into the blood; others diffuse to nearby cells.

Leptin

Leptin is a protein hormone produced by adipose tissue. Leptin acts on the hypothalamus, where it signals satiety—that is, 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.

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; therefore, they are implicated in the pain and discomfort of menstruation in some women. Also, prostaglandins mediate the effects of pyrogens, chemicals that are believed to reset the temperature regulatory center in the brain. Aspirin reduces body temperature and controls pain because of its effect on prostaglandins.

Certain prostaglandins reduce gastric secretion and have been used to treat gastric reflux; others lower blood pressure and have been used to treat hypertension; and yet others inhibit platelet aggregation and have been used to prevent thrombosis. However, different prostaglandins have contrary effects, and it has been very difficult to successfully standardize their use. Therefore, prostaglandin therapy is still considered experimental.

Check Your Progress 15.6

1. a. What other organs are considered major endocrine glands?
   b. Which of these are under the control of the anterior pituitary?
2. A number of other organs/tissues secrete hormones. Give some specific examples.
3. a. What is a local hormone? b. Give an example.

Bioethical Focus

Hormone Replacement Therapy

Menopause is the time in a woman's life when menstruation comes to an end. During menopause, which may begin as early as 35 years of age, the ovaries gradually produce lower levels of the sex hormones. Doctors may recommend using hormone replacement therapy (HRT) to counter some of the problems often associated with menopause (hot flashes, night sweats, sleeplessness, mood swings, and vaginal dryness) or to prevent some long-term conditions that are more common in postmenopausal women, such as osteoporosis. HRT used to be quite common. Data from a 1997 national survey showed that 45% of U.S. women born between 1897 and 1950 used menopausal hormones for at least one month, and 20% continued use for five or more years.

In recent years, a number of long-term studies have attempted to assess the risks and benefits of HRT. The best data comes from the Women's Health Initiative (WHI), a large, randomized clinical trial of over 16,000 healthy women, ages 50 through 79, in which half of the participants took hormones and the other half took a placebo pill (which does not contain any drug). The trial, sponsored by the National Institutes of Health (NIH), was halted early when, in July 2002, investigators reported that the overall risks of HRT outweighed the benefits. What were the results of this study with regard to quality of life, cancer and cardiovascular disease risk, and osteoporosis?

Quality of Life On the basis of the WHI study and others, HRT has no significant effects on the general health, vitality, mental health, depressive symptoms, or sexual satisfaction of women. Although hormone use was associated with a small benefit in terms of sleep disturbance, physical functioning, and bodily pain after one year of use, the effect was too small to be considered clinically significant. However, the risk of developing dementia (including Alzheimer disease) was double in women age 65 and older.

Cancer HRT significantly increased the risk of developing breast cancer in women ages 50 to 64. Current hormone users were also more likely to die from breast cancer than women who did not use them. Within about five years of stopping use, the increased risk largely disappeared. Although not as definite as breast cancer, the possibility exists that HRT also increases a woman's risk of endometrial cancer (cancer of the lining of the uterus) and ovarian cancer.

As a benefit, women on HRT have fewer cases of colorectal cancer compared with women taking a placebo.

Cardiovascular Disease HRT may increase the risk of heart disease among generally healthy postmenopausal women. The greatest increased risk occurred in the first year. Women on HRT have double the combined rate of blood clots in the lungs and legs. Studies have consistently reported increased risks of blood clots in the lungs (pulmonary embolisms) and deep veins in the legs with hormone use. The WHI study also indicated that the risk of a stroke increases when women use HRT.

Osteoporosis Osteoporosis is the loss of bone mass and density, which causes bones to become fragile and increases the chance of bone fractures. As a benefit, estrogen alone and estrogen combined with progestin have been shown to protect against osteoporosis. Results from the WHI showed that estrogen plus progestin can prevent fractures of the hip, vertebrae, and other bones.

Conclusion The WHI found that use of this estrogen plus progestin pill increases the risk of breast cancer, heart disease, stroke, and blood clots. The study also found that there were fewer cases of hip fractures and colon cancer among women using estrogen plus progestin than in those taking a placebo. Therefore, women are now advised to discuss the pros and cons of HRT with their physician and decide for themselves if they wish to use it (Fig. 15B). In other words, the patient has to be aware of the risks and accept the responsibility for taking replacement hormones.

Decide Your Opinion

1. Should physicians wait to recommend medications until they are certain about their benefits? Or, are they duty-bound to make recommendations based on incomplete information if there is a possibility of improving the health of millions of people?
2. Should patients accept the responsibility of deciding for themselves if they should take a medicine, or should physicians assume this responsibility?
3. HRT must be prescribed by a physician. Should women who suffered health consequences after undergoing HRT be encouraged to sue the physicians who wrote prescriptions that allowed them to use the therapy?

Figure 15B Thinking it through.
Menopausal women are now advised to consult their physicians and then to decide for themselves if they wish to be on hormone replacement therapy.

15.7 Homeostasis

The nervous and endocrine systems exert control over the other systems and thereby maintain homeostasis (Fig. 15.20).

Responding to External Changes

The nervous system is particularly able to respond to changes in the external environment. Some responses are automatic as you can testify by trying this: Take a piece of clear plastic and hold it just in front of your face. Get someone to gently toss a soft object, such as a wadded-up piece of paper, at the plastic. Can you prevent yourself from blinking? This reflex protects your eyes.

The eyes and other organs that have sensory receptors provide us with valuable information about the external environment. The central nervous system, which is on the receiving end of millions of bits of information, integrates information, compares it with previously stored memories, and "decides" on the proper course of action. Suppose you have spent the morning skiing; your muscles ache, your stomach churns, and your toes are cold. The brain will send out the motor impulses that will soon have you recovering from your exertions. The nervous system often responds to changes in the external environment through body movement. It gives us the ability to stay in as moderate an environment as possible—one that is not too hot or cold, for example. Otherwise, we test the ability of the nervous system to maintain homeostasis despite extreme conditions.

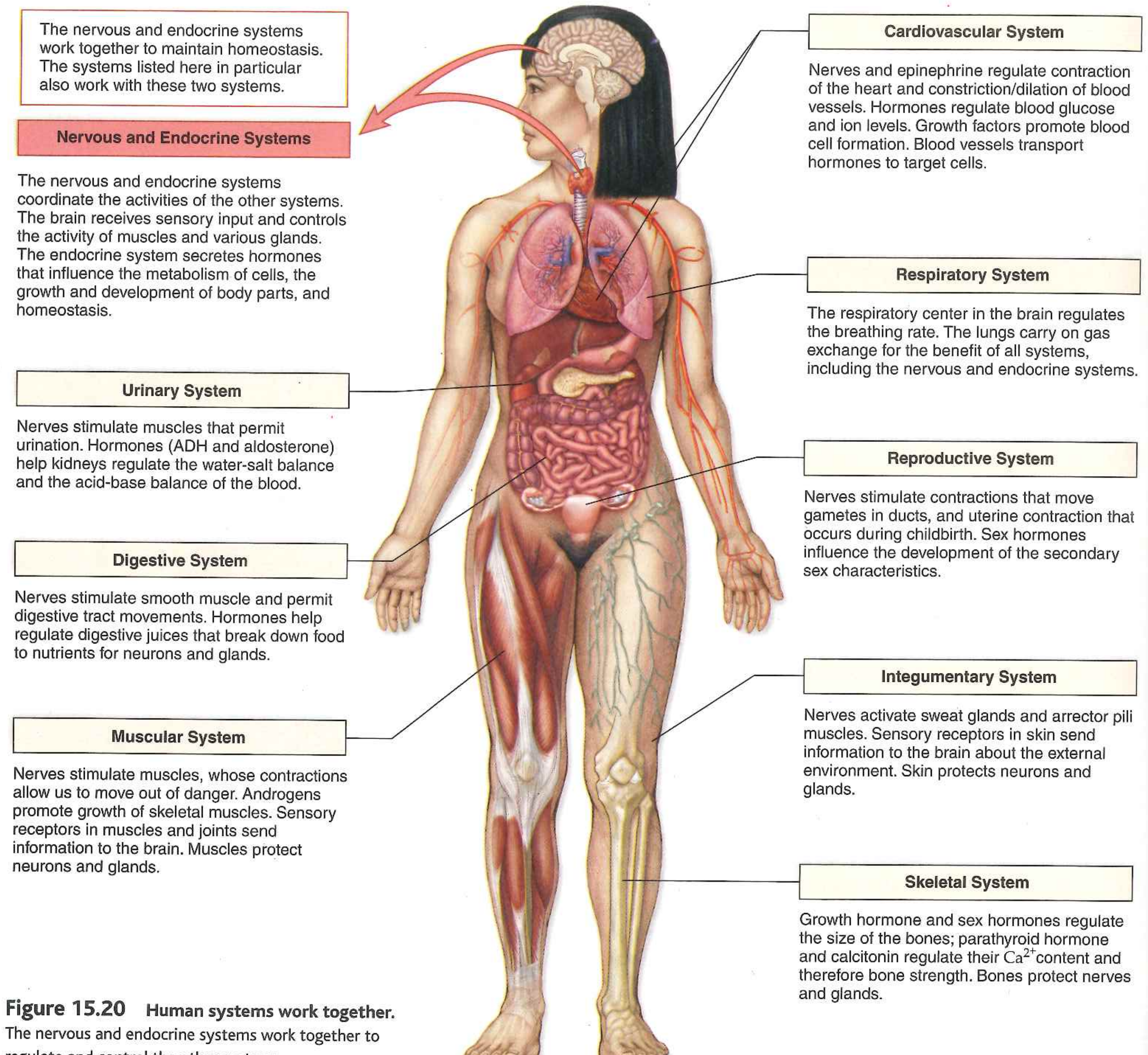


Figure 15.20 **Human systems work together.** The nervous and endocrine systems work together to regulate and control the other systems.

Responding to Internal Changes

The governance of internal organs usually requires that the nervous and endocrine systems work together, usually below the level of consciousness. Subconscious control often depends on reflex actions that involve the hypothalamus and the medulla oblongata. Let's take blood pressure as an example. You've just run three miles to raise money for hunger relief and decide to sit down under a tree to rest a bit. When you stand up to push off again, you feel faint, but it quickly passes because the medulla oblongata responds to input from the baroreceptors in the aortic arch and carotid arteries and immediately acts through the sympathetic system to increase heart rate and constrict the blood vessels so that your blood pressure rises. Sweating may have upset the water-salt balance of your blood. If so, the hormone aldosterone from the adrenal cortex will act on the kidney tubules to conserve Na^+, and water reabsorption will follow. The hypothalamus can also help by sending antidiuretic hormone (ADH) to the posterior pituitary gland, which releases it into the blood. ADH actively promotes water reabsorption by the kidney tubules.

Recall from Chapter 13 that certain drugs, such as alcohol, can affect ADH secretion. When you consume alcohol, it is quickly absorbed across the stomach lining into the bloodstream, where it travels to the hypothalamus and inhibits ADH secretion. When ADH levels fall, the kidney tubules absorb less water. The result is increased production of dilute urine. Excessive water loss, or dehydration, is a disturbance of homeostasis. This is why drinking alcohol when you are exercising, or simply perspiring heavily on a hot day, is not a good idea. Instead of keeping you hydrated, an alcoholic beverage, such as beer, will have just the opposite effect.

Controlling the Reproductive System

Few systems intrigue us more than the reproductive system, which couldn't function without nervous and endocrine control (Fig. 15.21). The hypothalamus controls the anterior pituitary, which, in turn, controls the release of hormones from the testes and the ovaries and the production of their gametes. The nervous system directly controls the muscular contractions of the ducts, which propel the sperm, and the oviducts, which move a developing embryo to the uterus, where development continues. Without the positive feedback cycle involving oxytocin, produced by the hypothalamus and released by the posterior pituitary, birth might not occur.

Figure 15.21 **Control of reproduction.** Successful reproduction requires the participation of both the nervous and endocrine systems.

The Neuroendocrine System

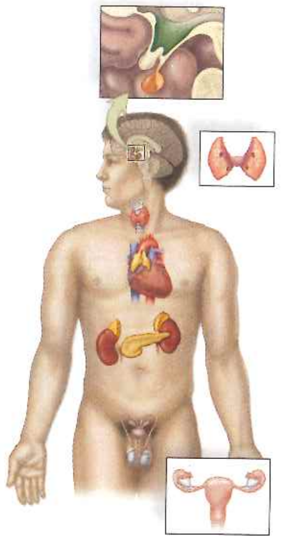
The nervous and endocrine systems work so closely together, they form what is sometimes called the neuroendocrine system. As we have seen, the hypothalamus certainly bridges the regulatory activities of both the nervous and endocrine systems. In addition to producing the hormones released by the posterior pituitary, the hypothalamus produces hormones that control the anterior pituitary. And the hypothalamus acts directly through the nerves of the autonomic system to control other organs. The hypothalamus truly belongs to both the nervous and endocrine systems. Indeed, it is often and appropriately referred to as a neuroendocrine organ.

Check Your Progress 15.7

1. If sweating has caused you to lose Na^+ and water, how will your body restore its salt-water balance?
2. Give examples to show that the hypothalamus belongs to both the nervous system and the endocrine system.

Summarizing the Concepts

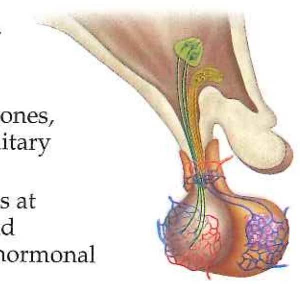
15.1 Endocrine Glands



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

- Hormones are a type of chemical signal that usually act at a distance between body parts.
- 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, and the complex attaches to and activates DNA. Protein synthesis follows.

15.2 Hypothalamus and Pituitary Gland



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

- 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.

15.3 Thyroid and Parathyroid Glands

The thyroid gland requires iodine to produce triiodothyronine and thyroxine, 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 produces calcitonin, which helps lower the blood calcium level.
- The parathyroid glands secrete parathyroid hormone, which raises the blood calcium level.

15.4 Adrenal Glands

The adrenal glands respond to stress:

- **Adrenal Medulla** The adrenal medulla immediately secretes epinephrine and norepinephrine. Heartbeat and blood pressure increase; blood glucose level rises; muscles become energized.
- **Adrenal Cortex** The adrenal cortex produces the glucocorticoids (e.g., cortisol) and the mineralocorticoids (e.g., aldosterone). The glucocorticoids regulate carbohydrate, protein, and fat metabolism and also suppress the inflammatory response. Mineralocorticoids regulate salt and water balance, leading to increases in blood volume and blood pressure.

15.5 Pancreas

The pancreatic islets secrete the hormones insulin and glucagon.

- Insulin lowers the blood glucose level.
- Glucagon raises the blood glucose level.
- Diabetes mellitus is due to the failure of the pancreas to produce insulin or the failure of the cells to take it up.

15.6 Other Endocrine Glands

Other endocrine glands produce hormones.

- The testes and ovaries produce the sex hormones. Male sex hormones are the androgens (e.g., testosterone); female sex hormones are the estrogens and progesterone.
- The thymus gland secretes thymosins, which stimulate T-lymphocyte production and maturation.
- The pineal gland produces melatonin, which may be involved in circadian rhythms and the development of the reproductive organs.

Tissues also produce hormones.

- Kidneys produce erythropoietin.
- Adipose tissue produces leptin, which acts on the hypothalamus.
- Prostaglandins are produced within cells and act locally.

15.7 Homeostasis

The nervous and endocrine systems exert control over the other systems and thereby maintain homeostasis.

- The nervous system is able to respond to the external environment after receiving data from the sensory receptors. Sensory receptors are present in such organs as the eyes and ears.
- The nervous and endocrine systems work together to govern the subconscious control of internal organs. This control often depends on reflex actions involving the hypothalamus and medulla oblongata.
- The nervous and endocrine systems work so closely together that they form what is sometimes called the neuroendocrine system.

Understanding Key Terms

acromegaly 302
Addison disease 307
adrenal cortex 305
adrenal gland 305
adrenal medulla 305
adrenocorticotropic hormone (ACTH) 300
aldosterone 306
anabolic steroid 311
androgen 311
anterior pituitary 300
antidiuretic hormone (ADH) 300
atrial natriuretic hormone (ANH) 306
calcitonin 304
chemical signal 298
circadian rhythm 312
congenital hypothyroidism 303
cortisol 306
Cushing syndrome 307
cyclic adenosine monophosphate (cAMP) 299
diabetes mellitus 310
endocrine gland 296
epinephrine 305
estrogen 311
exophthalmic goiter 303
first messenger 299
glucagon 308
glucocorticoid 305
gonad 311
gonadotropic hormone 300
growth hormone (GH) 300
hormone 296
hypothalamic-inhibiting hormone 300
hypothalamic-releasing hormone 300
hypothalamus 300

insulin 308
leptin 312
melanocyte-stimulating hormone (MSH) 300
melatonin 311
mineralocorticoid 305
myxedema 303
norepinephrine 305
ovary 311
oxytocin 300
pancreas 308
pancreatic islets 308
parathyroid gland 304
parathyroid hormone (PTH) 304
peptide hormone 299
pheromone 298
pineal gland 311
pituitary dwarfism 302
pituitary gland 300
positive feedback 300
posterior pituitary 300
progesterone 311
prolactin (PRL) 300
prostaglandin 312
renin 306
second messenger 299
simple goiter 303
steroid hormone 299
testes 311
testosterone 311
tetany 304
thymosin 311
thymus gland 311
thyroid gland 303
thyroid-stimulating hormone (TSH) 300
thyroxine (T_4) 303

Match the key terms to these definitions.

a. ________ Organ that is in the neck and secretes several important hormones, including thyroxine and calcitonin.

b. ________ Condition characterized by high blood glucose level and the appearance of glucose in the urine.

c. ________ Hormone secreted by the anterior pituitary that stimulates portions of the adrenal cortex.

d. ________ Type of hormone that causes the activation of an enzyme cascade in cells.

e. ________ Hormone released by the posterior pituitary that causes contraction of the uterus and milk letdown.

Testing Your Knowledge of the Concepts

1. Compare and contrast the nervous and endocrine systems. (page 296)
2. How does the action of a peptide hormone differ from that of a steroid hormone? (pages 298–99)
3. Explain the relationship between the hypothalamus and the posterior pituitary gland and to the anterior pituitary gland. List the hormones secreted by the anterior pituitary and the posterior pituitary glands and their actions. (pages 300–301)
4. Give an example of the negative feedback relationship among the hypothalamus, the anterior pituitary, and other endocrine glands. (page 300)
5. Discuss the action of growth hormone on the body. What occurs if there is too much or too little GH during the growing years? What occurs if there if too much GH in an adult? (pages 300, 302–3)
6. What types of goiters and other conditions are associated with a malfunctioning thyroid gland? Explain each type. (page 303)
7. Explain how the thyroid and parathyroid glands work together to maintain blood calcium homeostasis. (pages 303–4)
8. What type of tissue is the adrenal medulla made of? What are its hormones and their actions? (page 305)
9. What hormones are secreted by the adrenal cortex, and what are their actions? (pages 305–6)
10. What are the causes and symptoms of Addison disease and Cushing syndrome? (page 307)
11. Explain how insulin and glucagon maintain blood glucose homeostasis. What are the two types of diabetes mellitus, and what are the major symptoms? (pages 308–10)
12. Name the other endocrine glands and tissues mentioned in the chapter, and discuss the actions of the hormones they secrete. (pages 311–12)
13. How does the neuroendocrine system work with other systems to maintain homeostasis? (pages 314–15)
14. Hormones are never
    a. steroids.
    b. amino acids.
    c. glycoproteins.
    d. fats (triglycerides).
15. Which type of glands are ductless?
    a. exocrine
    b. endocrine
    c. Both a and b are correct.
    d. Neither a nor b is correct.
16. Which hormones can cross cell membranes?
    a. peptide hormones
    b. steroid hormones
    c. Both a and b are correct.
    d. Neither a nor b is correct.
17. The anterior pituitary controls the secretion(s) of
    a. both the adrenal medulla and the adrenal cortex.
    b. both thyroid and adrenal cortex.
    c. both ovaries and testes.
    d. Both b and c are correct.
18. Growth hormone is produced by the
    a. posterior adrenal gland.
    b. posterior pituitary.
    c. anterior pituitary.
    d kidneys.
    e. None of these is correct.
19. ________ is released through positive feedback and causes ________.
    a. Insulin, stomach contractions
    b. Oxytocin, stomach contractions
    c. Oxytocin, uterine contractions
    d. None of these is correct.
20. PTH causes the blood levels of calcium to ________, and calcitonin causes it to ________.
    a. increase, increase
    b. increase, decrease
    c. decrease, increase
    d. decrease, decrease
21. Bodily response to stress includes
    a. water reabsorption by the kidneys.
    b. blood pressure increase.
    c. increase in blood glucose levels.
    d. heart rate increase.
    e. All of these are correct.
22. Anabolic steroid use can cause
    a. liver damage.
    b. severe acne.
    c. balding.
    d. reduced testicular size.
    e. All of these are correct.