10-3 The bilobed pituitary gland is an endocrine organ that releases nine peptide hormones

The pituitary gland, or hypophysis (hi-PÖF-i-sis), secretes nine different hormones. All are peptides or small proteins that bind to membrane receptors, and all use cAMP as a second messenger. The pituitary gland is a small, oval gland nestled within the sella turcica, a depression in the sphenoid bone of the skull (Figure 10-5). It hangs beneath the hypothalamus, connected by a slender stalk, the infundibulum (in-fun-DIB-ulhum; funnel). The pituitary gland has a complex structure, including distinct anterior and posterior regions.

THE ANTERIOR PITUITARY GLAND

The anterior pituitary gland contains endocrine cells surrounded by an extensive capillary network. This capillary network, which provides entry into the circulatory system for the hormones secreted by endocrine cells of the anterior pituitary, is part of the hypophyseal portal system.

The Hypophyseal Portal System

As previously noted, regulatory hormones produced by the hypothalamus control the activities of the anterior pituitary.

These hormones, released by hypothalamic neurons near the attachment of the infundibulum, enter a network of highly permeable capillaries. Before leaving the hypothalamic capillary network unites to form a series of slightly larger vessels that descend to the anterior pituitary before forming a second capillary network (Figure 10-6).

The circulatory arrangement illustrated in Figure 10-6, in which blood flows from one capillary bed to another, is very unusual. Typically, blood flows from the heart through increasingly smaller arteries to a capillary network and then returns to the heart through increasingly larger veins. Blood vessels that link two capillary networks—including the vessels between the hypothalamus and the anterior pituitary—are called portal vessels; in this case, they have the structure of veins, their entire complex is termed a portal system.

Portal systems ensure that all of the blood entering the portal vessels reaches certain target cells before returning to the general circulation. Portal systems are named after their destinations, so this particular network is called the hypothalamic (hi-po-FL-se-aI) portal system.

Hypothalamic Control of the Anterior Pituitary

An endocrine cell in the anterior pituitary may be controlled by releasing hormones (RH), inhibiting hormones (IH), or some combination of the two. The regulatory hormones released at the hypothalamus are transported directly to the anterior pituitary by the hypophyseal portal system.

FIGURE 10-5 The Location and Anatomy of the Pituitary Gland.
The rate of regulatory hormone secretion by the hypothalamus is regulated through negative feedback mechanisms. The basic regulatory patterns are diagrammed in Figure 10-7; these will be referenced in the following description of pituitary hormones. Many of these regulatory hormones are called tropic hormones (trapos, a turning) because they "turn on" other endocrine glands or support the functions of other organs.

Hormones of the Anterior Pituitary

The anterior pituitary gland produces seven hormones. The first four described in the following list regulate the production of hormones by other endocrine glands.

1. Thyroid-stimulating hormone (TSH), or thyrotropin, targets the thyroid gland and triggers the release of thyroid hormones. TSH is released in response to thyrotropin-releasing hormone (TRH) from the hypothalamus. As circulating concentrations of thyroid hormones rise, the rates of TRH and TSH production decline (Figure 10-7a).

2. Adrenocorticotropic hormone (ACTH) stimulates the release of steroid hormones by the suprarenal cortex, the outer portion of the suprarenal glands. ACTH specifically targets cells producing hormones called glucocorticoids (gloo-kō-KOR-ti-koydz), which affect glucose metabolism. ACTH release occurs under the stimulation of corticotropin-releasing hormone (CRH) from the hypothalamus. A rise in glucocorticoid levels causes a decline in the production of ACTH and CRH. This type of negative feedback control is comparable to that for TSH (Figure 10-7a).

A group of hormones called gonadotropins (gō-nad-ō-TRÖ-pinz) regulates the activities of the male and female sex organs, or gonads. The production of gonadotropins is stimulated by gonadotropin-releasing hormone (GnRH) from the hypothalamus. An abnormally low production of gonadotropins produces hypogonadism. Children with this condition will not undergo sexual maturation, and adults with hypogonadism cannot produce functional sperm or ova. The anterior pituitary produces two gonadotropins: follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

3. Follicle-stimulating hormone (FSH) promotes follicle (and egg) development in females, and it stimulates the secretion of estrogens—steroid hormones produced by ovarian cells. In males, FSH production supports sperm production in the testes. A peptide hormone called inhibin, released by the cells of the testes and ovaries, inhibits the release of FSH and GnRH through a negative feedback control mechanism comparable to that for TSH (Figure 10-7a).

4. Luteinizing (LOO-tē-in-zing) hormone (LH) induces ovulation, the production of reproductive cells in females. It also promotes the secretion by the ovaries of estrogens and progesterins (such as progesterone), which prepare the body for possible pregnancy. In males, LH is sometimes called interstitial cell-stimulating hormone (ICSH) because it stimulates the interstitial cells of the testes to produce sex hormones. These sex hormones are called androgens (AN-drō-jenz; andros, man); the most important is testosterone. GnRH production is inhibited
FIGURE 10-7 Negative Feedback Control of Endocrine Secretion. (a) In the typical pattern of regulation (in which multiple endocrine organs are active), the hypothalamus produces a releasing hormone (RH) to stimulate hormone production by other glands, only to occur via negative feedback. (b) Shown here are two variations on the theme outlined in part (a). For the regulation of prolactin (PRL) production by the anterior pituitary in the hypothalamus produces both a releasing factor (RH) and an inhibiting hormone (PIH): when one is stimulated, the other is inhibited. In the regulation of growth hormone (GH) production by the anterior pituitary (at right), whenever GH–RH release is inhibited, GH–IH release is stimulated.

6. Growth hormone (GH), also called human growth hormone (hGH) or somatotropin (soma, body), stimulates cell growth and replication by accelerating the rate of protein synthesis. Although virtually every tissue responds to some degree, skeletal muscle cells and chondrocytes (cartilage cells) are particularly sensitive to growth hormone.

The stimulation of growth by GH involves two mechanisms. The indirect, primary mechanism is best understood. Liver cells respond to the presence of growth hormone by synthesizing and releasing somatomedins, or insulin-like growth factors (IGFs), which are peptide hormones that bind to receptor sites on a variety of cell membranes. Somatomedins increase the rates at which amino acids are taken up and incorporated into new proteins. These effects develop almost immediately after GH release occurs, and they are particularly important after a meal, when blood glucose and amino acid concentrations are high.
The direct actions of GH usually do not appear until after blood glucose and amino acid concentrations have returned to normal levels. In epithelia and connective tissues, GH stimulates stem cell divisions and the differentiation of daughter cells. GH also has metabolic effects in adipose tissue and in the liver. In adipose tissue, it stimulates the breakdown of stored fats and the release of fatty acids into the blood. In turn, many tissues stop breaking down glucose and start breaking down fatty acids to generate ATP. This process is termed a glucose-sparing effect. In the liver, GH stimulates the breakdown of glycogen reserves and the release of glucose into the circulation. Thus, GH plays a role in mobilizing energy reserves.

The production of GH is regulated by growth hormone-releasing hormone (GH–RH) and growth hormone-inhibiting hormone (GH–IH) from the hypothalamus. Somatomedins stimulate GH–IH and inhibit GH–RH. This regulatory mechanism is summarized in Figure 10–7b.

7. Melanocyte-stimulating hormone (MSH) stimulates the melanocytes in the skin to increase their production of melanin. MSH is important in the control of skin and hair pigmentation in fishes, amphibians, reptiles, and many mammals other than primates. The MSH-producing cells of the pituitary gland in adult humans are virtually nonfunctional, and the circulating blood usually does not contain MSH. However, the human pituitary secretes MSH (1) during fetal development, (2) in very young children, (3) in pregnant women, and (4) in some diseases. The functions of MSH under these circumstances are not known. The administration of a synthetic form of MSH causes darkening of the skin, so MSH has been suggested as a means of obtaining a “sunless tan.”

THE POSTERIOR PITUITARY GLAND

The posterior pituitary gland contains axons from two different groups of neurons located within the hypothalamus. One group manufactures antidiuretic hormone (ADH) and the other oxytocin. These products are transported within axons along the infundibulum to the posterior pituitary, as indicated in Figure 10–6.

Antidiuretic hormone (ADH) is released when the body is low on water. Stimuli for its release include a rise in the concentration of electrolytes in the blood (an increased osmotic pressure), or a fall in blood volume or pressure. The primary function of ADH is to decrease the amount of water lost in the urine. With losses minimized, any water absorbed from the digestive tract will be retained, reducing the concentration of electrolytes. ADH also causes vasoconstriction, a constriction of peripheral blood vessels that helps increase blood pressure. ADH release is inhibited by alcohol, which explains the increased fluid excretion that follows the consumption of alcoholic beverages.

In women, oxytocin (οὐκτόκος, swift birth), or OXT, stimulates smooth muscle contractions in the wall of the uterus during labor and delivery and in special contractile cells associated with the mammary glands. Until the final stages of pregnancy, the uterine muscles are insensitive to oxytocin, but they become more sensitive as the time of delivery approaches. The stimulation of uterine muscles by oxytocin helps maintain and complete normal labor and childbirth (discussed in Chapter 20). After delivery, oxytocin also stimulates the contraction of special cells surrounding the secretory cells and ducts of the mammary glands. In the “milk let-down” reflex, oxytocin secreted in response to suckling triggers the release of milk from the breasts.

Although oxytocin’s functions in sexual activity remain uncertain, circulating oxytocin levels are known to rise during sexual arousal and peak at orgasm in both sexes. In men, oxytocin stimulates smooth muscle contractions in the walls of the sperm duct and prostate gland. These actions may be important in emission, the ejection of prostatic secretions, sperm, and the secretions of other glands into the male reproductive tract before ejaculation. In women, oxytocin released during intercourse

**Clinical Note**

**Diabetes Insipidus**

Diabetes (diabetes, to pass through) occurs in several forms, all characterized by excessive urine production (polyuria). Although diabetes can be caused by physical damage to the kidneys, most forms are the result of endocrine abnormalities. The two most important forms are diabetes mellitus and diabetes insipidus. Diabetes mellitus is described on p. 366.

**Diabetes insipidus** (insipidus, tasteless) develops when the posterior pituitary no longer releases adequate amounts of ADH or the kidneys fail to respond to ADH.

Water conservation at the kidneys is impaired, and excessive amounts of water are lost in the urine. As a result, the individual is constantly thirsty—a condition known as polydipsia (dipsa, thirst)—but the body does not retain the fluids consumed. Mild cases may not require treatment, so long as fluid and electrolyte intake keeps pace with urinary losses. In severe cases, fluid losses can reach 10 liters per day, and a fatal dehydration will occur unless treatment is provided.
FIGURE 10-8 Pituitary Hormones and Their Targets.

may stimulate smooth muscle contractions in the uterus and vagina that promote the transport of sperm toward the uterine tubes.

The hypothalamus produces regulatory factors that adjust the activities of the anterior pituitary gland, which produces seven hormones. Most of these hormones control other endocrine organs, including the thyroid gland, suprarenal gland, and gonads. It also produces growth hormone, which stimulates cell growth and protein synthesis. The posterior pituitary gland releases two hormones produced in the hypothalamus: ADH restricts water loss and promotes thirst, and oxytocin stimulates smooth muscle contractions in the mammary glands and uterus (in females) and in the prostate gland (in males).

Figure 10-8 and Table 10-1 (p. 357) summarize important information concerning the hormones produced by the pituitary gland.

CHECKPOINT

7. If a person were dehydrated, how would the amount of ADH released by the posterior pituitary change?
8. A blood sample contains elevated levels of somatotropin. Which pituitary hormone would you also expect to be elevated?
9. What effect would elevated circulating levels of cortisol, a hormone from the suprarenal cortex, have on the pituitary secretion of ACTH?

See the blue Answers tab at the back of the book.