Lecture No . 3

Pituitary Hormones and Their Control by the Hypothalamus

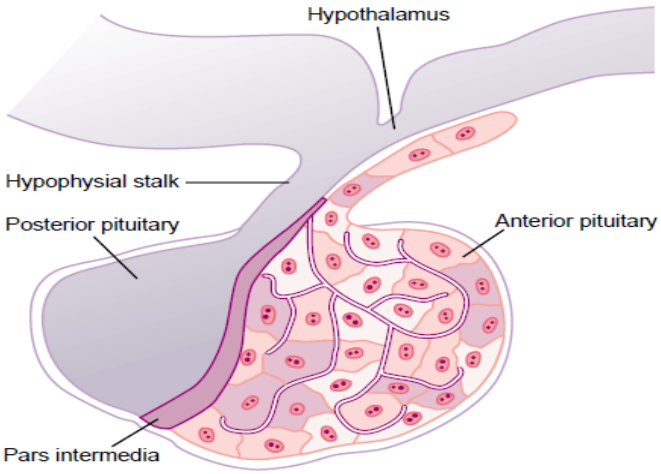

Figure 75–1
Pituitary gland.

Pituitary Gland: Two Distinct Parts–The Anterior and Posterior Lobes.

The *pituitary gland* also called the *hypophysis*, is a small gland - about 1 centimeter in diameter and 0.5 to 1 gram in weight - that lies in the *sella turcica*, a bony cavity at the base of the brain, and is connected to the hypothalamus by the *pituitary* (or *hypophysial)* stalk. Physiologically, the pituitary gland is divisible into two distinct portions: the *anterior pituitary*, also known as the *adenohypophysis*, and the *posterior pituitary*, also known as the *neurohypophysis*. Between these is a small, relatively avascular zone called the *pars intermedia*, which is almost absent in the human being but is much larger and much more functional in some lower animals.

Embryologically, the two portions of the pituitary originate from different Sources - the anterior pituitary from *Rathke's pouch,* which is an embryonic invagination of the pharyngeal epithelium, and the posterior pituitary from a neural tissue outgrowth from the hypothalamus.The origin of the anterior pituitary from the pharyngeal epithelium explains the epithelioid nature of its cells,and the origin of the posterior pituitary from neural tissue explains the presenceof large numbers of glial-type cells in this gland.

The hormones of the anterior pituitary play major roles in the control of metabolic functions throughout the body.

• *Growth hormone* promotes growth of the entire body by affecting protein formation, cell multiplication, and cell differentiation.
• *Adrenocorticotropin (corticotropin)* controls the secretion of some of the adrenocortical hormones, which affect the metabolism of glucose, proteins, and fats.
• *Thyroid-stimulating hormone (thyrotropin)* controls the rate of secretion of thyroxine and triiodothyronine by the thyroid gland, and these hormones control the rates of most intracellular chemical reactions in the body.
• *Prolactin* promotes mammary gland development and milk production.
• Two separate gonadotropic hormones, *follicle-stimulating hormone* and *luteinizing hormone,* control growth of the ovaries and testes, as well as their hormonal and reproductive activities.

The two hormones secreted by the posterior pituitary play other roles.
• *Antidiuretic hormone* (also called *vasopressin*) controls the rate of water excretion into the urine, thus helping to control the concentration of water in the body fluids.
• *Oxytocin* helps express milk from the glands of the breast to the nipples during suckling and possibly helps in the delivery of the baby at the end of gestation .

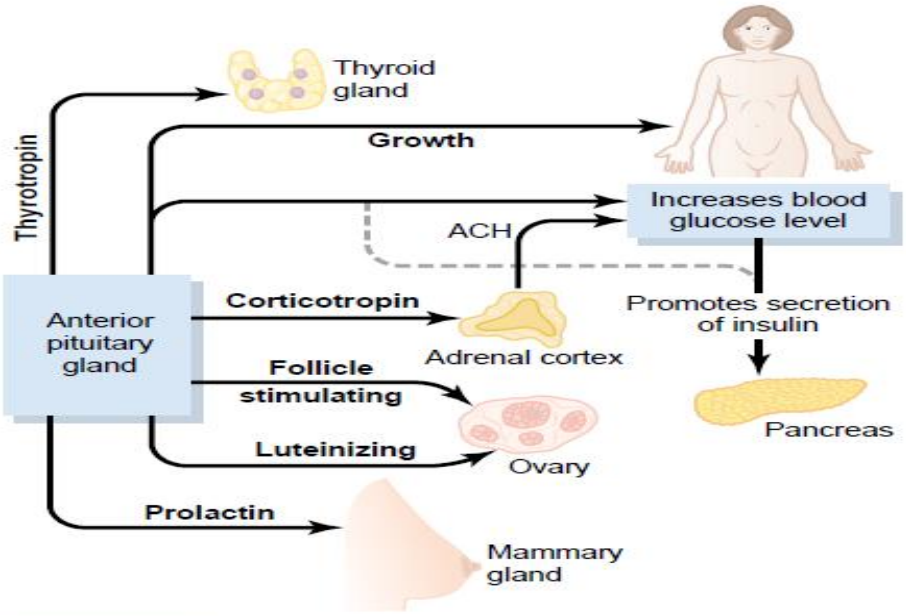

Figure 75–2

Metabolic functions of the anterior pituitary hormones. ACH, adrenal corticosteroid hormones.

Anterior Pituitary Gland Contains Several Different Cell Types That Synthesize and Secrete Hormones.

Usually, there is one cell type for each major hormone formed in the anterior pituitary gland. With special stains attached to, high-affinity antibodies that bind with the distinctive hormones, at least five cell types can be differentiated. These five cell types are:

1. *Somatotropes*—human growth hormone (hGH)
2. *Corticotropes*—adrenocorticotropin (ACTH)
3. *Thyrotropes*—thyroid-stimulating hormone (TSH)
4. *Gonadotropes*—gonadotropic hormones, which include both luteinizing hormone (LH) and folliclestimulating hormone (FSH)
5. *Lactotropes*—prolactin (PRL)

About 30 to 40 per cent of the anterior pituitary cells are somatotropes that secrete growth hormone, and about 20 per cent are corticotropes that secrete ACTH. Each of the other cell types accounts for only 3 to 5 percent of the total; nevertheless, they secrete powerful hormones for controlling thyroid function, sexual functions, and milk secretion by the breasts. Somatotropes stain strongly with acid dyes and aretherefore called *acidophils.* Thus, pituitary tumors that secrete large quantities of human growth hormone are called *acidophilic tumors.*

Posterior Pituitary Hormones Are Synthesized by Cell Bodies in the Hypothalamus.

The bodies of the cells that secrete the *posterior* pituitary hormones are not located in the pituitary gland itself but are large neurons, called *magnocellular neurons,* located in the *supraoptic* and *paraventricular nuclei* of the hypothalamus. The hormones are then transported in the axoplasm of the neurons' nerve fibers passing from the hypothalamus to the posterior pituitary gland.

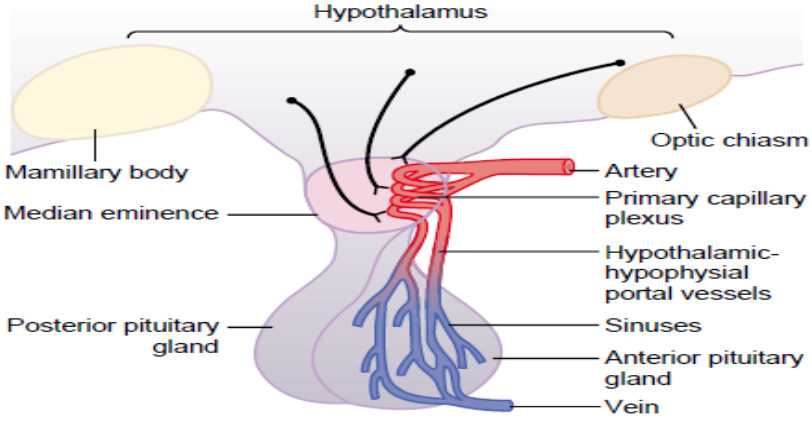

Figure 75–4

Hypothalamic-hypophysial portal system.

Hypothalamus Controls Pituitary Secretion

Almost all secretion by the pituitary is controlled by either hormonal or nervous signals from the hypothalamus. Indeed, when the pituitary gland is removed from its normal position beneath the hypothalamus and transplanted to some other part of the body, itsrates of secretion of the different hormones (except for prolactin) fall to very low levels.

Secretion from the posterior pituitary is controlled by nerve signals that originate in the hypothalamus and terminate in the posterior pituitary. In contrast, secretion by the anterior pituitary is controlled by hormones called *hypothalamic releasing* and *hypothalamic inhibitory hormones* (or *factors*) secreted within the hypothalamus itself and then conducted, as shown in Figure 75–4, to the anterior pituitary through minute blood vessels called *hypothalamic-hypophysial portal vessels.* In the anterior pituitary, these releasing and inhibitory hormones act on the glandular cells to control their secretion. The hypothalamus receives signals from many sources in the nervous system. Thus, when a person is exposed to pain, a portion of the pain signal is transmitted into the hypothalamus. Likewise, when a person experiences some powerful depressing or exciting thought, a portion of the signal is transmitted into the hypothalamus. Olfactory stimuli denoting pleasant or unpleasant smells transmit strong signal components directly and through the amygdaloid nuclei into the hypothalamus. Even the concentrations of nutrients, electrolytes, water, and various hormones in the blood excite or inhibit various portions of the hypothalamus. Thus, the hypothalamus is a collecting center for information concerning the internal well-being of the body, and much of this information is used to control secretions of the many globally important pituitary hormones.

Physiological Functions of Growth Hormone

All the major anterior pituitary hormones, except for growth hormone, exert their principal effects by stimulating target glands, including thyroid gland, adrenal cortex, ovaries, testicles, and mammary glands. The functions of each of these pituitary hormones are so intimately concerned with the functions of the respective target glands that, except for growth hormone, Growth hormone, incontrast to other hormones, does not function through a target gland but exerts its effects directly on all or almost all tissues of the body.

Growth Hormone Has Several Metabolic Effects

Aside from its general effect in causing growth, growth hormone has multiple specific metabolic effectsincluding (1) increased rate of protein

synthesis in most cells of the body; (2) increased mobilization of fatty acids from adipose tissue, increased free fatty acids in the blood, and increased use of fatty acids for energy; and (3) decreased rate of glucose utilization throughout the body. Thus, in effect, growth hormone enhances body protein, uses up fat stores, and conserves carbohydrates.

Growth Hormone Stimulates Cartilage and Bone Growth

Although growth hormone stimulates increased deposition of protein and increased growth in almostall tissues of the body, its most obvious effect is toincrease growth of the skeletal frame.This results from multiple effects of growth hormone on bone, including (1) increased deposition of protein by the chondrocytic and osteogenic cells that cause bone growth, (2) increased rate of reproduction of these cells, and (3) a specific effect of converting chondrocytes into osteogenic cells, thus causing deposition of new bone.

There are two principal mechanisms of bone growth. First, in response to growth hormone stimulation, the long bones grow in length at the epiphyseal cartilages, where the epiphyses at the ends of the bone are separated from the shaft. This growth first causes deposition of new cartilage, followed by its conversion into new bone, thus elongating the shaft and pushing the epiphyses farther and farther apart. At the same time, the epiphyseal cartilage itself is progressively used up, so that by late adolescence, no additional epiphyseal cartilage remains to provide for further long bone growth. At this time, bony fusion occurs between the shaft and the epiphysis at each end, so that no further lengthening of the long bone can occur. Second, *osteoblasts* in the bone periosteum and insome bone cavities deposit new bone on the surfaces of older bone. Simultaneously, *osteoclasts* in the bone remove old bone. When the rate of deposition is greater than that of resorption, the thickness of the bone increases. *Growth hormone strongly stimulates osteoblasts.* Therefore, the bones can continue to become thicker throughout life under the influence of growth hormone; this is especially true for the membranous bones. For instance, the jaw bones can be stimulated to grow even after adolescence,causing forward protrusion of the chin andlower teeth. Likewise, the bones of the skull can growin thickness and give rise to bony protrusions over the eyes.

***Abnormalities of Growth Hormone Secretion Panhypopituitarism*.**

This term means decreased secretion of all the anterior pituitary hormones. The decrease in secretion may be congenital (present from birth), or it may occur suddenly or slowly at any time during life, most often resulting from a pituitary tumor that destroys the pituitary gland.

Dwarfism. Most instances of dwarfism result from generalized deficiency of anterior pituitary secretion (panhypopituitarism) during childhood. In general, all the physical parts of the body develop in appropriate proportion to one another, but the rate of development is greatly decreased. A child who has reached the age of 10 years may have the bodily development of a child aged 4 to 5 years, and the same person at age 20 years may have the bodily development of a child aged 7 to 10 years. A person with panhypopituitary dwarfism does not pass through puberty and never secretes sufficient quantities of gonadotropic hormones to develop adult sexual functions. In one third of such dwarfs, however, only growth hormone is deficient; these persons do mature sexually and occasionally reproduce. In one type of dwarfism (the African pygmy and the Lévi-Lorain dwarf), the rate of growth hormone secretion is normal or high, but there is a hereditary inability to form somatomedin C, which is a key step for the promotion of growth by growth hormone.

Gigantism. Occasionally, the acidophilic, growth hormone–producing cells of the anterior pituitary gland become excessively active, and sometimes even acidophilic tumors occur in the gland. As a result, large quantities of growth hormone are produced. All body tissues grow rapidly, including the bones. If the condition occurs before adolescence, before the epiphyses of the long bones have become fused with the shafts, height increases so that the person becomes a giant— up to 8 feet tall. The giant ordinarily has *hyperglycemia*, and the beta cells of the islets of Langerhans in the pancreas are prone to degenerate because they become overactive owing to the hyperglycemia. Consequently, in about 10 per cent of giants, full-blown *diabetes mellitus* eventually develops. In most giants, panhypopituitarism eventually develops if they remain untreated, because the gigantism is usually caused by a tumor of the pituitary gland that grows until the gland itself is destroyed. This eventual general deficiency of pituitary hormones usually causes death in early adulthood. However, once gigantism is diagnosed, further effects can often be blocked by microsurgical removal of the tumor or by irradiation of the pituitary gland.

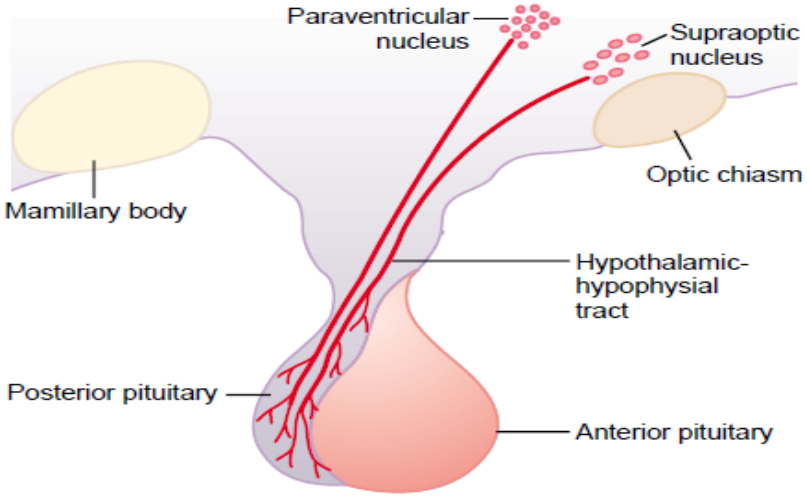

Figure 75–9

Hypothalamic control of the posterior pituitary.

Posterior Pituitary Gland and Its Relation to theHypothalamus

The *posterior pituitary gland*, also called the *neurohypophysis*, is composed mainly of glial-like cells called *pituicytes.*The pituicytes do not secrete hormones; they act simply as a supporting structure for large numbers of *terminal nerve fibers* and *terminal nerve endings* from nerve tracts that originate in the *supraoptic* and *paraventricular nuclei* of the hypothalamus, as shown in Figure 75–9. These tracts pass to the neurohypophysis through the *pituitary stalk* (hypophysial stalk).The nerve endings are bulbous knobs that contain many secretory granules.These endings lie on the surfaces of capillaries, where they secrete two posterior pituitary hormones: (1) *antidiuretic hormone* (ADH), also called *vasopressin*, and (2) *oxytocin.*

Physiological Functions of ADH

The injection of extremely minute quantities of ADH—as small as 2 nanograms—can cause decreased excretion of water by the kidneys (antidiuresis). Briefly, in the absence of ADH, the collecting tubules and ducts become almost impermeable to water, which prevents significant reabsorption of water and therefore allows extreme loss of water into the urine, also causing extreme dilution of the urine. Conversely, in the presence of ADH, the permeability of the collecting ducts and tubules to water increases greatly and allows most of the water to be reabsorbed as the tubular fluid passes through these ducts, thereby conserving water in the body and producing very concentrated urine. The precise mechanism by which ADH acts on the collecting ducts to increase their permeability is only partially known. Without ADH, the luminal membranes of the

tubular epithelial cells of the collecting ducts are almost impermeable to water. However, immediately inside the cell membrane are a large number of special vesicles that have highly waterpermeable pores called *aquaporins.* When ADH acts on the cell, it first combines with membrane receptors that activate adenylyl cyclase and cause the formation of cAMP inside the tubular cell cytoplasm.This causes phosphorylation of elements in the special vesicles, which then causes the vesicles to insert into the apical cell membranes, thus providing many areas of high water permeability. All this occurs within 5 to 10 minutes. Then, in the absence of ADH, the entire process reverses in another 5 to 10 minutes. Thus, this process temporarily provides many new pores that allow free diffusion of water from the tubular fluid through the tubular epithelial cells and into the renal interstitial fluid.Water is then absorbed from the collecting tubules and ducts by osmosis.

Oxytocic Hormone

Oxytocin Causes Contraction of the Pregnant Uterus.

The hormone *oxytocin,* in accordance with its name, powerfully stimulates contraction of the pregnant uterus, especially toward the end of gestation. Therefore, many obstetricians believe that this hormone is at least partially responsible for causing birth of the baby.This is supported by the following facts: (1) In a hypophysectomized animal, the duration of labor is prolongedindicating a possible effect of oxytocin during delivery. (2) The amount of oxytocin in the plasma increases during labor, especially during the last stage. (3) Stimulation of the cervix in a pregnant animal elicits nervous signals that pass to the hypothalamus and cause increased secretion of oxytocin.

Oxytocin Aids in Milk Ejection by the Breasts

Oxytocin also plays an especially important role in lactation—a role that is far better understood than its role in delivery. In lactation, oxytocin causes milk to be expressed from the alveoli into the ducts of the breast so that the baby can obtain it by suckling. This mechanism works as follows:The suckling stimulus on the nipple of the breast causes signals to be transmitted through sensory nerves to the oxytocin neurons in the paraventricular and supraoptic nuclei in the hypothalamus, which causes release of oxytocin by the posterior pituitary gland. The oxytocin is then carried by the blood to the breasts, where it causes contraction of *myoepithelial cells* that lie outside of and form a latticework surrounding the alveoli of the mammary glands. In less than a minute after the beginning of suckling, milk begins to flow.