Clinical Case Study

A 38-year-old woman visited her family doctor because she had been experiencing chronic fatigue and weakness, especially in her legs. Upon greeting the patient, the doctor noted that although she was mildly obese, her face seemed unusually round. During questioning, he learned that at her recent 20-year high school reunion, nobody recognized her because her face had changed so much. He also learned that she suffered a chronic unrelenting headache. Physical examination yielded, in addition to the facial findings, an unusual fat distribution that included a hump on the upper back and marked truncal obesity. Additional findings included hypertension and blindness in the lateral visual fields of both eyes (bitemporal hemianopsia). Laboratory findings were remarkable for elevated blood glucose and other evidence that glucocorticoid levels were high.

Can a correlation be drawn between the patient’s visual findings and the rest of her clinical picture? Explain. In which endocrine organ does the primary disease process reside? Does that same organ produce the hormones that directly cause the patient’s signs and symptoms? Explain. Do you suppose that a tumor elsewhere in the endocrine system could produce similar findings?

Hints: Study figure 14.8 and note the position of the endocrine glands with respect to the optic nerve and optic chiasma. Also, review the actions of hormones in table 14.4.
INTRODUCTION TO THE ENDOCRINE SYSTEM

Hormones are regulatory chemicals secreted by the endocrine glands into the blood, which transports them to their target cells. Feedback mechanisms in the target cells control the secretion (production) of the hormones.

Objective 1  Distinguish between endocrine and exocrine glands.

Objective 2  Compare and contrast the nervous and endocrine systems as to how they regulate body functions and maintain homeostasis.

Objective 3  Define mixed gland and identify the endocrine glands that are mixed.

Objective 4  Describe the action of a hormone on its target cell and explain how negative feedback regulates hormonal secretion.

Objective 5  Differentiate between the three principal kinds of hormones.

The numerous glands of the body can be classified as either of two types based on structure and function: exocrine or endocrine. Exocrine glands, such as sweat, salivary, and mucous glands, produce secretions that are transported through ducts to their respective destinations. Each of the exocrine glands functions within a particular system of the body. The endocrine glands constitute a system of their own, the endocrine system. In contrast to exocrine glands, endocrine glands are ductless; they secrete specific chemicals called hormones directly into the blood or surrounding interstitial fluid (fig. 14.1). The blood then transports these hormones to specific sites called target cells, where they perform precise functions.

The endocrine system functions closely with the nervous system in regulating and integrating body processes and maintaining homeostasis. The nervous system regulates body activities through the action of electrochemical impulses that are transmitted by means of neurons, resulting in rapid, but usually brief, responses. By contrast, the glands of the endocrine system secrete chemical regulators that travel through the bloodstream or interstitial fluid to their intended sites; their action is relatively slow, but their effects are prolonged. Neurological responses are measured in milliseconds, but hormonal action requires seconds or days to elicit a response. Some hormones may have an effect that lasts for minutes; for others, the effect may last for weeks or months.

The nervous and endocrine systems are closely coordinated in autonomically controlling the functions of the body. Three endocrine glands are located within the cranial cavity, where certain structures of the brain routinely stimulate or inhibit the release of hormones. Likewise, certain hormones may stimulate or inhibit the activities of the nervous system. The functions of the two body control systems are compared in table 14.1.

exocrine: Gk. exo, outside; krinein, to separate
endocrine: Gk. endon, within; krinein, to separate
hormone: Gk. hormon, to set in motion

TABLE 14.1  Comparison of the Endocrine and Nervous Systems

<table>
<thead>
<tr>
<th>Endocrine System</th>
<th>Nervous System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretes hormones that are transported to target cells via the blood or by surrounding interstitial fluid</td>
<td>Transmits neurochemical impulses via nerve fibers</td>
</tr>
<tr>
<td>Causes changes in the metabolic activities in specific cells</td>
<td>Causes muscles to contract or glands to secrete</td>
</tr>
<tr>
<td>Action is relatively slow (seconds or even days)</td>
<td>Action is very rapid (milliseconds)</td>
</tr>
<tr>
<td>Effects are relatively prolonged</td>
<td>Effects are relatively brief</td>
</tr>
</tbody>
</table>
Glands of the Endocrine System

The endocrine glands are distributed throughout the body (fig. 14.2). The pituitary gland, the hypothalamus, and the pineal gland are associated with the brain within the cranial cavity. The thyroid gland and parathyroid glands are located in the neck. The adrenal glands and pancreas are located within the abdominal region. The gonads (ovaries) of the female are located within the pelvic cavity, whereas the gonads (testes) of the male are located in the scrotum. The pancreas and gonads are frequently classified as mixed glands because they have exocrine as well as endocrine functions.

The endocrine system is unique in that its glands are widely scattered throughout the body, with no anatomical continuity. By contrast, the organs of the other body systems are physically linked together in some fashion.

In addition to the glands just mentioned, several others may be considered part of the endocrine system because they have endocrine functions. These include the thymus, located in the lower median neck region; the stomach; the kidneys; the mucosal cells of the duodenum; and the placenta, associated with the fetus. The principal endocrine glands of the body, their hormones, and the effects of these hormones are listed in table 14.2.

Hormones and Their Actions

Hormones are specific organic substances that act as the chemical messengers of the endocrine system. The three basic kinds of hormones (proteins, steroids, and amines) are derived either from amino acids or cholesterol (fig. 14.3).
### TABLE 14.2 The Principal Endocrine Glands

<table>
<thead>
<tr>
<th>Endocrine Gland</th>
<th>Major Hormones</th>
<th>Primary Target Organs</th>
<th>Primary Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal cortex</td>
<td>Glucocorticoids, Aldosterone</td>
<td>Liver and muscles</td>
<td>Glucocorticoids influence glucose metabolism; aldosterone promotes Na⁺ retention, K⁺ excretion</td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Epinephrine</td>
<td>Heart, bronchioles, and blood vessels</td>
<td>Causes adrenergic stimulation</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Releasing and inhibiting hormones</td>
<td>Anterior pituitary</td>
<td>Regulate secretion of anterior pituitary hormones</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Secretin and cholecystokinin</td>
<td>Stomach, liver, and pancreas</td>
<td>Inhibit gastric motility and stimulate bile and pancreatic juice secretion</td>
</tr>
<tr>
<td>Pancreatic islets</td>
<td>Insulin, Glucagon</td>
<td>Many organs</td>
<td>Insulin promotes cellular uptake of glucose and formation of glycogen and fat; glucagon stimulates hydrolysis of glycogen and fat</td>
</tr>
<tr>
<td>Ovaries</td>
<td>Estradiol-17β and progesterone</td>
<td>Female reproductive tract and mammary glands</td>
<td>Maintain structure of reproductive tract and promote secondary sex characteristics</td>
</tr>
<tr>
<td>Parathyroid glands</td>
<td>Parathyroid hormone</td>
<td>Bone, intestine, and kidneys</td>
<td>Increases Ca²⁺ concentration in blood</td>
</tr>
<tr>
<td>Pineal gland</td>
<td>Melatonin</td>
<td>Hypothalamus and anterior pituitary</td>
<td>Affects secretion of gonadotrophic hormones</td>
</tr>
<tr>
<td>Pituitary, anterior</td>
<td>Trophic hormones</td>
<td>Endocrine glands and other organs</td>
<td>Stimulate growth and development of target organs; stimulate secretion of other hormones</td>
</tr>
<tr>
<td>Pituitary, posterior</td>
<td>Antidiuretic hormone, Oxytocin</td>
<td>Kidneys and blood vessels</td>
<td>Antidiuretic hormone promotes water retention and vasoconstriction; oxytocin stimulates contraction of uterus and mammary secretory units</td>
</tr>
<tr>
<td>Stomach</td>
<td>Gastrin</td>
<td>Stomach</td>
<td>Stimulates acid secretion</td>
</tr>
<tr>
<td>Testes</td>
<td>Testosterone</td>
<td>Prostate, seminal vesicles, and other organs</td>
<td>Stimulates secondary sexual development</td>
</tr>
<tr>
<td>Thymus</td>
<td>Thymosin</td>
<td>Lymph nodes</td>
<td>Stimulates white blood cell production</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Thyroxine (T₄), triiodothyronine, and T₃; calcitonin</td>
<td>Blood and most organs</td>
<td>Thyroxine and triiodothyronine promote growth and development and stimulate basal rate of cell respiration (basal metabolic rate or BMR); calcitonin regulates Ca²⁺ levels within blood by inhibiting bone decalcification</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Erythropoietin</td>
<td>Bone marrow</td>
<td>Stimulates red blood cell production</td>
</tr>
</tbody>
</table>

**FIGURE 14.3** Chemical structures exemplifying the three basic kinds of hormones: (a) a protein, (each circle represents an amino acid), (b) a steroid, and (c) an amine.
Proteins are composed of amino acids bound together in peptide chains (fig. 14.3a). Most of the hormones of the body are proteins, including calcitonin from the thyroid gland and hormones secreted by the pituitary gland, the pancreas, and the parathyroid glands. Protein hormones cannot be administered orally because the peptide bonds would be split during the hydrolytic reaction of digestion; thus, they must be injected intravenously, intramuscularly, or subcutaneously.

A steroid is a lipid synthesized from cholesterol. Steroids exist as complex rings of carbon and hydrogen atoms (fig. 14.3b). The types of atoms attached to the rings determine the specific kind of steroid. There are more than 20 steroid hormones in the body, including such common ones as cortisol, cortisone, estrogen, progesterone, and testosterone. The sex hormones produced by the gonads and the hormones produced by the adrenal cortex are all steroids. Steroids can be taken orally or intravenously to regulate body activity if glandular dysfunction prevents the natural production of normal amounts.

Amines are produced from amino acids but do not contain peptide bonds. Amine molecules contain atoms of carbon, hydrogen, and nitrogen and always have an associated amine group (—NH₂) (fig. 14.3c). Thyroxine produced in the thyroid gland, epinephrine (adrenaline) and norepinephrine produced in the adrenal gland, and melatonin produced in the pineal gland are examples of amines.

Thyroxine is usually administered orally, whereas epinephrine is administered intravenously to produce a fast response. Epinephrine can also be administered as an inhalant when it is necessary to enlarge the air-conducting passageways within the lungs.

A summary of the basic types of hormones is presented in table 14.3.

The usual action of hormones is to speed up or slow down metabolism in the target cells. Hormones are extremely specific as to which cells they affect and the cellular changes they elicit. The ability of a hormone to affect a particular cell depends on the presence of receptor molecules in the cell or specific receptor sites on its cell membrane.

**TABLE 14.3 Classes of Hormones**

<table>
<thead>
<tr>
<th>Type of Hormone</th>
<th>Composition/Structure</th>
<th>Examples</th>
<th>Method of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>Amino acids bonded by peptide chains</td>
<td>Pituitary hormones, pancreatic hormones, parathyroid hormones, and calcitonin from thyroid gland</td>
<td>Intravenously, intramuscularly, or subcutaneously</td>
</tr>
<tr>
<td>Steroid</td>
<td>Lipid with a cholesterol-type nucleus</td>
<td>Sex hormones and hormones from adrenal cortex</td>
<td>Orally, intravenously, or intramuscularly</td>
</tr>
<tr>
<td>Amine</td>
<td>Amino acids with no peptide bonds; molecule contains —NH₂ group</td>
<td>Thyroxine from thyroid gland, adrenaline from adrenal gland, and melatonin from pineal gland</td>
<td>Orally, subcutaneously, intravenously, or as an inhalant</td>
</tr>
</tbody>
</table>

**FIGURE 14.4** The mechanism of the action of a steroid hormone (H) on the target cells. A steroid hormone passes through the cell membrane and unites with a receptor protein in the cytoplasm. The steroid-protein complex then enters the cell nucleus and activates the synthesis of messenger RNA (mRNA). The messenger RNA then disperses into the cytoplasm where it activates the synthesis of proteins by means of ribosomes.
Steroid hormones are soluble in lipids and can readily pass through a cell membrane. Once inside a cell, the steroid combines with a protein to form a steroid-protein complex (fig. 14.4). This complex is necessary for the synthesis of specific kinds of messenger RNA molecules.

Protein and amine hormones are insoluble in lipids and therefore must attach to specific receptor sites on the cell membrane. These hormones do not enter the cell, but their attachment increases the activity of an enzyme in the cell membrane called adenylate cyclase (a-den’i-t si’klās). In the presence of adenylate cyclase, ATP molecules in the cell are converted to cyclic AMP (adenosine monophosphate), which in turn disperses throughout the cell to cause changes in cellular processes (fig. 14.5). These changes may include increasing protein synthesis, altering membrane permeability, or activating certain cellular enzymes.

Control of Hormone Secretion

The rate of secretion of a particular hormone and the rate of usage by the target cells are closely balanced. The stability of hormone levels is maintained by a negative feedback system and autonomic neural impulses.

Negative feedback (fig. 14.6) is a homeostatic mechanism that maintains the status quo of supply and demand between hormone normal levels and the needs of the target cells. An endocrine gland will continue to secrete hormones that affect target cells until messages come back from the cells reporting that sufficient amounts of these hormones are present. These messages are generally in the form of hormones secreted by the target cells. This chemical feedback information signals the endocrine gland to inhibit secretion (fig. 14.6). The primary endocrine gland will resume secretions when the blood levels of inhibiting chemicals become low again.

Neural impulses through the autonomic nervous system cause certain endocrine glands, such as the adrenal medulla, to secrete hormones. One specialized kind of neural impulse involves the hypothalamus and the pituitary gland (fig. 14.7). In this system, chemical secretions from neurosecretory cells in the hypothalamus called releasing factors influence specific target cells in the pituitary gland. Stimulation of the pituitary by a releasing factor causes the secretion of specific hormones. The
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V. Integration and Coordination
14. Endocrine System
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Knowing knowledge continues to secrete the releasing factor until a given level of hormones is present in the body fluids and is detected by the hypothalamus through a negative feedback mechanism.

Knowledge Check

1. What are some of the ways in which endocrine and exocrine glands differ structurally?
2. How are the nervous and endocrine systems functionally related?
3. List the body organs that are exclusively endocrine in function. Also list the organs that serve other body functions, in addition to secreting hormones.
4. Using diagrams, describe the mechanism of steroid hormone action and the mechanism of protein hormone action within cells.
5. List the three kinds of hormones, give examples of each, and describe their chemical compositions.

PITUITARY GLAND

The neurohypophysis of the pituitary gland releases hormones that are produced by the hypothalamus, whereas the adenohypophysis of the pituitary gland secretes its own hormones in response to regulation from hypothalamic hormones. The secretions of the pituitary gland are thus controlled by the hypothalamus, as well as by negative feedback influences from the target glands.

Objective 6 List the hormones secreted by the adenohypophysis and neurohypophysis.

Objective 7 Describe, in a general way, the actions of anterior pituitary hormones.

Objective 8 Explain how the secretions of anterior and posterior pituitary hormones are controlled by the hypothalamus.

Objective 9 Explain how the secretion of anterior pituitary hormones is regulated by negative feedback.

Description of the Pituitary Gland

The pituitary (pit-too’ter-e) gland, or cerebral hypophysis (hi-po’f-t-sis) is located on the inferior aspect of the brain in the region of the diencephalon and is attached to the brain by a structure called the pituitary stalk (fig. 14.8). The pituitary is a rounded, pea-shaped gland measuring about 1.3 cm (0.5 in.) in diameter. It is covered by the dura mater and is supported by the sella turcica of the sphenoid bone. The cerebral arterial circle surrounds the highly vascular pituitary gland, providing it with a rich blood supply (see figs. 16.23 and 16.24).

The pituitary gland is structurally and functionally divided into an anterior lobe, or adenohypophysis (ad”n-o-hi-po’f-t-sis), and a posterior lobe called the neurohypophysis (noor”o-hi-po’f-t-sis). The adenohypophysis consists of two parts in adults: (1) the pars distalis (anterior pituitary) is the bulbar portion, and (2) the pars tuberalis is the thin extension in contact with the infundibulum (fig. 14.8). A pars intermedia, a strip of tissue between the anterior and posterior lobes, exists in the fetus. During fetal development, its cells mingle with those of the anterior lobe, and in adults they no longer constitute a separate structure. The histology of the adenohypophysis is shown in figure 14.9.

The neurohypophysis is the neural part of the pituitary gland. It consists of the bulbar lobus nervosa (posterior pituitary), which is in contact with the adenohypophysis, and the funnel-shaped infundibulum, a stalk of tissue that connects the pitu-
FIGURE 14.8 The pituitary gland. (a) Attached by the pituitary stalk to the hypothalamus, the pituitary gland lies in the sella turcica of the sphenoid bone. (b) A diagram of the pituitary gland showing the various portions.
CHAPTER 14

Pituitary Hormones

The pituitary gland releases nine important hormones. The first seven in the following list are secreted by the anterior pituitary. The seventh is secreted by certain cells that are remnants of the pars intermedia. The last two are produced in the hypothalamus. As with all body cells by assisting in the breakdown of fats. The secretion of TSH, however, is partly regulated by the hypothalamus through the secretion of thyrotropin-releasing hormone (TRH). External factors may influence the release of TSH as well. Exposure to cold, certain illnesses, and emotional stress may trigger an increased output of TSH.

2. Thyroid-stimulating hormone (TSH). TSH, frequently called thyrotropin, regulates the hormonal activity of the thyroid gland. The secretion of TSH, however, is partly regulated by the hypothalamus through the secretion of thyrotropin-releasing hormone (TRH). External factors may influence the release of TSH as well. Exposure to cold, certain illnesses, and emotional stress may trigger an increased output of TSH.

3. Adrenocorticotropic hormone (ACTH). ACTH promotes normal functioning of the adrenal cortex. It also acts on all body cells by assisting in the breakdown of fats. The release of ACTH is controlled by a corticotropin-releasing hormone (CRH) produced in the hypothalamus. As with TSH, stress further influences the release of ACTH.

4. Follicle-stimulating hormone (FSH). In males, FSH stimulates the testes to produce sperm. In females, FSH regulates the monthly development of the follicle and egg. It also stimulates the secretion of the female sex hormone estrogen.

5. Luteinizing hormone (LH). LH works with FSH, and together they are referred to as gonadotrophins, which means their target cells are located within the gonads or reproductive organs. In females, LH works with FSH in bringing about ovulation. It also stimulates the formation of the corpus luteum and the production of another female sex hormone, progesterone (see chapter 21). In males, the luteinizing hormone is called interstitial cell-stimulating hormone (ICSH) and stimulates the interstitial cells of the testes to develop and secrete the male sex hormone testosterone (see chapter 20). The mechanism that controls the production and release of gonadotrophic hormones is not well understood. It is known, however, that following puberty (see chapters 20 and 21) the hypothalamus releases a hormone called gonadotrophin-releasing hormone (GnRH) that regulates the secretion of both LH and FSH.
6. **Prolactin.** Prolactin is secreted in both males and females, but it functions primarily in females after parturition. Prolactin assists other hormones in initiating and sustaining milk production by the mammary glands. The hypothalamus plays an important role in the release of this hormone through the production of prolactin-inhibiting hormone (PIH), now known to be dopamine. When PIH is secreted, the secretion of prolactin is inhibited; when PIH is not secreted, prolactin is released.

7. **Melanocyte-stimulating hormone (MSH).** The exact action of MSH in humans is unknown, but it can cause darkening of the skin by stimulating the dispersion of melanin granules within melanocytes. Secretion of MSH is stimulated by corticotropin-releasing hormone and inhibited by dopamine, both of which come from the hypothalamus.

8. **Oxytocin.** Oxytocin is produced by specialized cells in the hypothalamus. It then travels through axons in the infundibulum to the lobus nervosa, where it is stored and released in response to neural impulses from the hypothalamus. Oxytocin influences physiological activity in the female reproductive system. It is released near the end of gestation and causes uterine contractions during labor. It also stimulates contraction of the mammary gland alveoli and ducts, producing the milk-ejection reflex during lactation (see chapter 21). In males, a rise in oxytocin at the time of ejaculation has been measured, but the physiological significance of this hormone in males has yet to be demonstrated.

9. **Antidiuretic hormone (ADH).** ADH is similar to oxytocin in its site of production and release. Like oxytocin, it is a polypeptide. The major function of ADH is to inhibit the formation of urine in the kidneys, or more specifically, to reduce the amount of water excreted from the kidneys. This hormone is also called vasopressin because it causes vasoconstriction at high concentrations.

Diabetes insipidus results from a marked decrease in ADH output caused by trauma or disease to the hypothalamus or neurohypophysis. The symptoms of this disease are polyuria (voiding excessive dilute urine), concentrated body fluids with dehydration, and a particularly heightened sensation of thirst.

Oxytocin and antidiuretic hormone are released by the posterior pituitary (pars nervosa of the neurohypophysis). These two hormones, however, are actually produced in neuron cell bodies of the supraoptic nuclei and paraventricular nuclei of the hypothalamus. These nuclei within the hypothalamus are thus endocrine glands; the hormones they produce are transported along axons of the hypothalamo-hypophyseal (hi-pof’i˘-se’al) tract (fig. 14.10) to the posterior pituitary, which stores and later releases them. The posterior pituitary is thus more of a storage organ than a true gland.

The secretion of oxytocin and ADH from the posterior pituitary is controlled by neuroendocrine reflexes. In nursing mothers, for example, the stimulus of sucking acts via sensory nerve impulses to the hypothalamus to stimulate the reflex secretion of oxytocin. The secretion of ADH is stimulated by osmoeceptor neurons in the hypothalamus in response to a rise in blood osmotic pressure; its secretion is inhibited by sensory impulses from stretch receptors in the left atrium of the heart in response to a rise in blood volume.

At one time, the anterior pituitary was called the “master gland” because it secretes hormones that regulate other endocrine glands (see table 14.4 and fig. 14.11). Adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and the gonadotrophic hormones (FSH and LH) stimulate the adrenal cortex, thyroid, and gonads, respectively, to secrete their hormones. The anterior pituitary hormones also have a trophic effect on their target glands in that the health of these glands depends on adequate stimulation by anterior pituitary hormones. The anterior pituitary, however, is not really the master gland, because secretion of its hormones is in turn controlled by hormones secreted by the hypothalamus.
Releasing and inhibiting hormones from the hypothalamus travel through the hypothalamo-hypophyseal portal system to control the secretion of hormones from the anterior pituitary. Neurons in the hypothalamus secrete hormones into the region of the median eminence, where they enter a network of primary capillaries (fig. 14.12). Venous drainage through the pituitary stalk transports the hypothalamic hormones to a network of secondary capillaries within the anterior pituitary. This system is considered a portal system because there are two sets of capillaries in a series (fig. 14.12). (This is analogous to the hepatic portal system that delivers venous blood from the pancreas, spleen, and GI tract to the liver, as described in chapter 16.)

6. List the hormones secreted by the anterior pituitary and explain how the hypothalamus controls the secretion of each hormone.
7. Which hormone secreted by the anterior pituitary does not affect some other endocrine gland?
8. List the hormones released by the posterior pituitary. State the origin of these hormones and the mechanisms by which their secretions are regulated.
9. Which hormone secreted by the pituitary gland affects only females?
FIGURE 14.11 The hormones secreted by the anterior pituitary and the target organs for those hormones.
THYROID AND PARATHYROID GLANDS

The thyroid gland secretes thyroxine and triiodothyronine, which function in the regulation of energy metabolism. These hormones are critically important for proper growth and development. The thyroid also secretes calcitonin, which may antagonize the action of parathyroid hormone in the regulation of calcium and phosphate balance.

Objective 10  Describe the location and structure of the thyroid gland and list the actions of the thyroid hormones.

Objective 11  Describe the location and structure of the parathyroid glands and list the actions of parathyroid hormone.

Description of the Thyroid Gland

The thyroid gland is located in the neck, just below the larynx (fig. 14.13). Its two lobes, each about 5 cm (2 in.) long, are positioned on either lateral side of the trachea and connected anteriorly by a bridge of tissue called the isthmus. The thyroid is the largest of the endocrine glands, weighing between 20 and 25 g. It receives an abundant blood supply (80–120 ml/min) through the paired superior thyroid branches of the external carotid arteries and the paired inferior thyroid branches of the subclavian arteries. The venous return is through the paired superior and middle

thyroid: Gk. thyros, oblong shield
isthmus: L. isthmus, narrow portion
thyroid veins that pass into the internal jugular veins and through the inferior thyroid veins that empty into the brachiocephalic veins.

On a microscopic level, the thyroid gland consists of numerous spherical hollow sacs called thyroid follicles (fig. 14.14). These follicles are lined with a simple cuboidal epithelium composed of follicular cells. The follicular cells synthesize the two principal thyroid hormones (see table 14.5). The interior of the follicles contains colloid (kol’oid), a protein-rich fluid. Between the follicles are epithelial cells called parafollicular cells that produce a hormone called calcitonin (kal”sit-to’nin), or thyrocalcitonin.

The thyroid is innervated by postganglionic neurons from the superior and middle cervical sympathetic ganglia and preganglionic neurons from ganglia derived from the second through the seventh thoracic segment of the spinal cord.

![Thyroid gland diagram](image)

**FIGURE 14.13** The thyroid gland. (a) Its relationship to the larynx and trachea and (b) a normal scan of the thyroid gland 24 hours after the intake of radioactive iodine.

![Histology of thyroid gland](image)

**FIGURE 14.14** The histology of the thyroid gland showing numerous thyroid follicles. Each follicle consists of follicular cells surrounding the fluid known as colloid.

### TABLE 14.5 Hormones of the Thyroid Gland

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Action</th>
<th>Source of Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroxine (T₄)</td>
<td>Increases rate of protein synthesis and rate of energy release from carbohydrates; regulates rate of growth; stimulates maturity of nervous system</td>
<td>Hypothalamus and release of TSH from adenohypophysis of pituitary gland</td>
</tr>
<tr>
<td>Triiodothyronine (T₃)</td>
<td>Same as above, but more potent than T₄</td>
<td>Same as above</td>
</tr>
<tr>
<td>Calcitonin (thyrocalcitonin)</td>
<td>Lowers blood calcium by inhibiting the release of Ca²⁺ from bone tissue</td>
<td>Ca²⁺ levels in blood</td>
</tr>
</tbody>
</table>

**colloid:** Gk. kolla, glue
Functions of the Thyroid Gland

The thyroid gland produces two major hormones, **thyroxine** (thi-rok’sin) \((T_4)\) and **triiodothyronine** (tri’i-o˘-dō-thi’ro-nēn) \((T_3)\), and the minor hormone **calcitonin** (thyrocalcitonin). The release of thyroxine and triiodothyronine is controlled by the hypothalamus and by the TSH secreted from the adenohypophysis of the pituitary gland. Thyroxine and triiodothyronine are stored in the thyroid follicles and released as needed to control the metabolic rate of the body. More specifically, they act to increase the rate of protein synthesis and the rate of energy release from carbohydrates. They also regulate the growth rate in young people and are associated with sexual maturity and early maturation of the nervous system.

Iodine is the most common component of thyroxine and triiodothyronine, and a continual intake of iodine is essential for normal thyroid function. Seafood contains adequate amounts of iodine, and commercial salt generally has iodine as an additive. Absorbed iodine is transported through the blood to the thyroid gland, where an active transport mechanism called an iodine pump moves the iodides into the follicle cells. Here, they combine with amino acids in the synthesis of thyroid hormones.

Most of the thyroxine in blood is attached to carrier proteins. Only the very small percentage of thyroxine that is free in blood plasma can enter the target cells. In the target cells, it is converted to triiodothyronine and attached to nuclear receptor proteins. Through the activation of genes, thyroid hormones stimulate protein synthesis, promote maturation of the nervous system, and increase the rate of energy utilization by the body.

Thyroid-stimulating hormone (TSH) from the anterior pituitary stimulates the thyroid to secrete thyroxine and exerts a trophic effect on the thyroid gland. This trophic effect shows up dramatically in people who develop an iodine-deficiency (endemic) goiter. In the absence of sufficient dietary iodine, the thyroid cannot produce adequate amounts of \(T_4\) and \(T_3\). The resulting lack of negative feedback inhibition causes abnormally high levels of TSH secretion, which in turn stimulate the abnormal growth of the thyroid (a goiter). These events are summarized in figure 14.15.

Calcitonin is a polypeptide hormone produced by the parafollicular cells. It works in concert with parathyroid hormone (discussed in the following section) to regulate calcium levels in the blood. Calcitonin inhibits the breakdown of bone tissue and stimulates the excretion of calcium by the kidneys. Both actions result in the lowering of blood calcium levels.

Parathyroid Glands

The small, flattened **parathyroid glands** are embedded in the posterior surfaces of the lateral lobes of the thyroid gland (fig. 14.16). There are usually four parathyroid glands: a **superior**
and an inferior pair. Each parathyroid gland is a small yellow-
brown body 3–8 mm (0.1–0.3 in.) long, 2–5 mm (0.07–0.2 in.)
wide, and about 1.5 mm (0.05 in.) deep.

On a microscopic level, the parathyroid glands are com-
posed of two types of epithelial cells (fig. 14.17). The cells that
synthesize parathyroid hormone are called principal cells and are
scattered among oxyphil (ok’sé-fil) cells. Oxyphil cells support
the principal cells and are believed to produce reserve quantities
of parathyroid hormone.

The blood supply and drainage of the parathyroid glands
is similar to that of the thyroid gland. The innervation of the
parathyroids, however, is a bit different. The parathyroids re-
ceive neurons from the pharyngeal branches of the vagus
nerves in addition to neurons arising from the cervical sympa-
thetic ganglia.

The parathyroid glands secrete one hormone called
parathyroid hormone (PTH). This hormone promotes a rise in
blood calcium levels by acting on the bones, kidneys, and small
intestine (fig. 14.18); thus, it opposes the effects of calcitonin,
released by the thyroid gland.

Knowledge Check

10. Describe the location and structure of the thyroid gland
    and list the effects of thyroid hormones.
11. What are some possible metabolic consequences of an
    overactive thyroid gland?
12. Why is a continual supply of iodine important for body
    metabolism?
13. Describe the location and structure of the parathyroid
    glands and identify the target organs of parathyroid
    hormone.

PANCREAS

The pancreatic islets in the pancreas secrete two hormones, in-
sulin and glucagon, which are critically involved in the regulation
of blood sugar levels in the body.

Objective 12  Describe the structure of the endocrine
portion of the pancreas and the origin of insulin and
glucagon.

Objective 13  Describe the actions of insulin and glucagon.

Description of the Pancreas

The pancreas (pan’kre-us) is both an endocrine and an exocrine
gland. The gross structure of this gland and its exocrine functions
in digestion are described in chapter 18. The endocrine portion
of the pancreas consists of scattered clusters of cells called
pancreatic islets (islets of Langerhans [i’lets of lang’er-hanz]). These

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pancreas: Gk. pan, all; kreas, flesh
islets of Langerhans: from Paul Langerhans, German anatomist, 1847–88
endocrine structures are most common in the body and tail of the pancreas (fig. 14.19) and mainly consist of two types of secretory cells called alpha cells and beta cells (fig. 14.20).

Endocrine Function of the Pancreas

The endocrine function of the pancreas is to produce and secrete the hormones glucagon (gloo'ca˘-gon) and insulin. The alpha cells of the pancreatic islets secrete glucagon and the beta cells secrete insulin.

Glucagon stimulates the liver to convert glycogen into glucose, which causes the blood glucose level to rise. Apparently, the alpha cells themselves regulate the glucagon output by monitoring the blood glucose level through a feedback mechanism. If for some reason alpha cells secrete glucagon continuously, high blood sugar, or hyperglycemia (hi''per-gli-se'me-a˘), may result.

Insulin has a physiological function opposite to that of glucagon: it decreases the level of blood sugar. Insulin promotes the movement of glucose through cell membranes, especially in muscle and adipose cells. As the glucose enters the

---

*insulin: L. insula, island*
cells, the sugar level of the blood decreases. Other functions of insulin include stimulating muscle and liver cells to convert glucose to glycogen, helping amino acids to enter cells, and assisting in the synthesis of proteins and fats. Failure of beta cells to produce insulin causes the common hereditary disease diabetes mellitus (me˘-li’tus).

The action of the hormones from the pancreatic islets is summarized in table 14.6.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Action</th>
<th>Source of Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucagon</td>
<td>Stimulates the liver to convert glycogen to glucose, causing the blood glucose level to rise</td>
<td>Blood glucose level through negative feedback in pancreas</td>
</tr>
<tr>
<td>Insulin</td>
<td>Promotes movement of glucose through cell membranes; stimulates the liver to convert glucose to glycogen; promotes the transport of amino acids to cells; assists in synthesis of proteins and fats</td>
<td>Blood glucose level through negative feedback in pancreas</td>
</tr>
</tbody>
</table>

### Knowledge Check

14. Describe the specific sites of glucagon and insulin production.
15. What is the function of glucagon? Of insulin?
16. What disease is caused by the insufficient production of insulin?

### Description of the Adrenal Glands

The adrenal (a˘-dre’nal) glands (suprarenal glands) are paired organs that cap the superior borders of the kidneys (fig. 14.21). The adrenal glands, along with the kidneys, are retroperitoneal and are embedded against the muscles of the back in a protective pad of fat.

Each of the pyramid-shaped adrenal glands is about 50 mm (2 in.) long, 30 mm (1.1 in.) wide, and 10 mm (0.4 in.) deep. Each consists of an outer adrenal cortex and inner adrenal medulla (figs. 14.21 and 14.22) that function as separate glands.

The adrenal cortex makes up the bulk of the gland and is histologically subdivided into three zones: an outer zona glomerulosa (glo-mer’yo-lo’sa˘), an intermediate zona fasciculata (fak-sik’yo-lo’ta˘) and an inner zona reticularis. The adrenal medulla is composed of tightly packed clusters of chromaffin (kro-maf’in) cells, which are arranged around blood vessels. Each cluster of chromaffin cells receives direct autonomic innervation.

Like other endocrine glands, the adrenal glands are highly vascular. Three separate suprarenal arteries supply blood to each adrenal gland. One arises from the inferior phrenic artery, another from the aorta, and a third is a branch of the renal artery. The venous drainage passes through a suprarenal vein into the inferior vena cava for the right adrenal gland and through the suprarenal vein into the left renal vein for the left adrenal gland.

The adrenal glands are innervated by preganglionic neurons of the splanchic nerves and by fibers of the celiac and associated sympathetic plexuses.

### Functions of the Adrenal Glands

Over 30 hormones have been identified as being produced by the adrenal cortex. These hormones are called corticosteroids (kor’ti˘-ko-ster’oidz) or corticoids, for short. The adrenal corticoids are grouped into three functional categories: mineralocorticoids, glucocorticoids, and gonadocorticoids.

The mineralocorticoids are produced by the zona glomerulosa of the adrenal cortex and regulate the concentrations of extracellular electrolytes. Of the three hormones secreted by this layer, aldosterone (al-dos’ter-ön) is the most important. Aldosterone affects the kidneys, causing them to reabsorb sodium and increase potassium excretion. At the same time, it promotes water reabsorption and reduces urine output.

The glucocorticoids are produced primarily by the zona fasciculata of the adrenal gland and influence the metabolism of carbohydrates, proteins, and fats. The glucocorticoids also promote vasoconstriction, act as antiinflammatory compounds, and help the body resist stress. The most abundant and physiologically important glucocorticoid is cortisol (kor’tı˘-sol) (hydrocortisone).

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adrenal: L. ad, to; renes, kidney
Cortisol and related anti-inflammatory compounds are commonly used to treat patients suffering from arthritis and various allergies. They are also frequently used to treat traumatized joints and to suppress the immune rejection of transplanted tissues. Unfortunately, cortisol inhibits the regeneration of connective tissues, and therefore should be used sparingly and only when necessary.

Gonadocorticoids are the sex hormones that are secreted by the zona reticularis of the adrenal cortex. The majority of these hormones are adrenal androgens, but small quantities of adrenal estrogens and progesterones are produced as well. It is thought that these hormones supplement the sex hormones produced in the gonads. There is also evidence that androgen concentrations in both males and females play a role in determining the sex drive.

A summary of the hormones secreted from the adrenal cortex is presented in table 14.7.

The chromaffin cells of the adrenal medulla produce two closely related hormones: epinephrine and norepinephrine. Both of these hormones are classified as amines—more specifically, as catecholamines (kat′e-kol′ə-mēz)—because they contain amine
groups (see fig. 14.3). The effects of these hormones are similar to those caused by stimulation of the sympathetic division of the ANS, except that the hormonal effects are about 10 times longer lasting. The hormones from the adrenal medulla increase cardiac output and heart rate, dilate coronary blood vessels, increase mental alertness, increase the respiratory rate, and elevate metabolic rate. The effects of epinephrine and norepinephrine are compared in table 14.8.

The adrenal medulla is innervated by sympathetic neurons. The impulses are initiated from the hypothalamus via the spinal cord in response to stress. Stress therefore activates the adrenal medulla, as well as the adrenal cortex. Activation of the adrenal medulla prepares the body for greater physical performance—the fight-or-flight response (fig. 14.23).

Excessive stimulation of the adrenal medulla can result in depletion of the body’s energy reserves, and high levels of corticosteroid secretion from the adrenal cortex can significantly impair the immune system. It is reasonable to expect, therefore, that prolonged stress can result in increased susceptibility to disease. Indeed, many studies show that prolonged stress results in an increased incidence of cancer and other diseases.

Knowledge Check

17. Describe the location and appearance of the adrenal gland. Diagram and label the layers of the adrenal gland that can be seen in a sagittal section as, for example, in a histological slide.
18. List the hormones of the adrenal medulla and describe their effects.
19. List the categories of corticosteroids and identify the zones of the adrenal cortex that secrete these hormones.
GONADS AND OTHER ENDOCRINE GLANDS

The gonads produce sex hormones that control the development and function of the male and female reproductive systems. Additionally, many other organs secrete hormones that help regulate digestion, metabolism, growth, and immunity.

Objective 16  Discuss the endocrine functions of the gonads.
Objective 17  Describe the structure and location of the pineal and thymus glands and their endocrine functions.

Gonads

The gonads are the male and female primary sex organs. The male gonads are called testes and the female gonads are called ovaries. The gonads are mixed glands in that they produce both sex hormones and sex cells, or gametes (see chapters 20 and 21).

Testes

The interstitial cells of the testes produce and secrete the male sex hormone testosterone. Testosterone controls the development and function of the male secondary sex organs—the penis, accessory glands, and ducts. It also promotes the male secondary sex characteristics (see chapter 20) and somewhat determines the sex drive.

Ovaries

The endocrine function of the ovaries is the production of the female sex hormones, estrogens and progesterone. Estrogens are
produced in the ovarian (graafian) follicles and corpus luteum of the ovaries. They are also produced in the placenta, adrenal cortex, and even in the testes of the male. Estrogens are responsible for (1) development and function of the secondary sex organs, (2) menstrual changes of the uterus, (3) development of the female secondary sex characteristics (see chapter 21), and (4) regulation of the sex drive.

Progesterone is produced by the corpus luteum and is primarily associated with pregnancy in preparing the uterus for implantation and preventing abortion of the fetus.

Most cultures of the world practice birth control, or contraception, in one form or another. It has a long history, dating back to the ancient Egyptians who used various substances to inhibit sperm survival and motility. In the age of hormonal biochemistry, birth-control techniques have become increasingly sophisticated. The female, rather than the male, has been the target of hormonal birth-control techniques for the following reasons: (1) ovulation is cyclic; (2) the genetic structure of each ovum is established by the time of the female’s birth, whereas sperm production is a continuous process, and therefore more vulnerable to genetic damage; (3) the female system has more potential sites for hormonal interference than does the male system; and (4) the female is usually more conscientious about practicing birth control because she has far more invested in pregnancy than does the male.

Pineal Gland

The small, cone-shaped pineal (pin’e-al) gland (pineal body) (see fig. 14.2), is located in the roof of the third ventricle, near the corpora quadrigemina, where it is encapsulated by the meninges covering the brain. In a child, the pineal gland weighs about 0.2 g and is 5–8 mm (0.2–0.3 in.) long and 9 mm (0.4 in.) wide. It begins to regress in size at about the age of 7, and in the adult it appears as a thickened strand of fibrous tissue. Histologically, the pineal gland consists of specialized parenchymal and neuroglial cells. Although it lacks direct nervous connection to the rest of the brain, the pineal gland is highly innervated by the sympathetic division of the ANS from the superior cervical ganglion.

The function of the pineal gland in some vertebrates is well known but is not well understood in humans. Secretion of its principal hormone, melatonin, follows a circadian (daily) rhythm tied to daily and seasonal changes in light. Melatonin is thought to affect the hypothalamus by stimulating the secretion of certain releasing factors (fig 14.24). These factors in turn...
affect the secretion of gonadotrophin and the ACTH from the adenohypophysis of the pituitary gland. Excessive melatonin secretion in humans is associated with a delay in the onset of puberty; however the role of melatonin in sexual maturation is still highly controversial.

**Thymus**

The thymus (*thi’mus*) is a bilobed organ positioned in the upper mediastinum, in front of the aorta and behind the manubrium of the sternum (fig. 14.25). Although the size of the thymus varies considerably from person to person, it is relatively large in newborns and children and then sharply regresses in size after puberty. Besides decreasing in size, the thymus of adults becomes infiltrated with strands of fibrous and fatty connective tissue.

The principal function of the thymus is associated with the lymphatic system (see chapter 16) in maintaining body immunity through the maturation and discharge of a specialized group of lymphocytes called T cells (*thymus-dependent cells*). The thymus also secretes a hormone called thymosin, which is believed to stimulate the T cells after they leave the thymus.

thymus: Gk. *thymos*, a warty excrescence

**TABLE 14.9**  **Effects of Gastrointestinal Hormones**

<table>
<thead>
<tr>
<th>Endocrine Organ</th>
<th>Hormone</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>Gastrin</td>
<td>Stimulates parietal cells to secrete HCl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stimulates chief cells to secrete pepsinogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintains structure of gastric mucosa</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Secretin</td>
<td>Stimulates water and bicarbonate secretion in pancreatic juice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potentiates actions of cholecystokinin on pancreas</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Cholecystokinin (CCK)</td>
<td>Stimulates contraction of the gallbladder</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stimulates secretion of pancreatic juice enzymes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potentiates action of secretin on pancreas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintains structure of exocrine pancreas (acini)</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Gastric inhibitory peptide (GIP)</td>
<td>Inhibits gastric emptying</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhibits gastric acid secretion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stimulates secretion of insulin from pancreatic islets</td>
</tr>
</tbody>
</table>
EXPLANATION

The endocrine system is the only anatomical body system whose organs are not structurally connected. Because these organs are isolated from each other and are distributed throughout the body, each endocrine organ has a separate and independent development. All three embryonic germ layers (endoderm, mesoderm, and ectoderm) contribute to the development of the endocrine system.

The following sections describe, in turn, the development of the pituitary, thyroid, pancreas, and adrenal glands. The development of the testes and ovaries is discussed in chapters 20 and 21, respectively.

Pituitary Gland

Although the pituitary gland is a single organ, it is actually composed of two distinct types of tissues that have different embryonic origins. These two types of tissues release different hormones and are under different control systems. The anterior portion of the hypophysis, called the adenohypophysis, develops from ectoderm that lines the primitive oral cavity. The posterior portion, called the neurohypophysis, develops from neuroectoderm of the developing brain (exhibit I).

The adenohypophysis begins to develop during the fourth week as a diverticulum, a pouchlike extension, called the...
hypophyseal (Rathke’s) pouch. It arises from the roof of the primitive oral cavity and grows toward the brain. At the same time, another diverticulum called the infundibulum forms from the diencephalon on the inferior aspect of the brain. As the two diverticula come in contact, the hypophyseal pouch loses its connection with the oral cavity, and the primordial tissue of the adenohypophysis is formed. The fully developed adenohypophysis includes the pars distalis and the pars intermedia. Cells of the pars intermedia become mingled with those of the pars distalis, so that the pars intermedia no longer constitutes a separate structure in the adult.

The neurohypophysis develops as the infundibulum extends internally from the diencephalon to come in contact with the developing adenohypophysis. The fully formed neurohypophysis consists of the infundibulum and the lobus nervosa. Specialized nerve fibers that connect the hypothalamus with the lobus nervosa develop within the infundibulum.

Notice that the neurohypophysis is essentially an extension of the brain; indeed, the entire pituitary gland, like the brain, is surrounded by the meninges. The adenohypophysis, by contrast, is derived from nonneural tissue (the same embryonic tissue that will form the epithelium over the roof of the mouth). These different embryologies have important consequences with regard to the functions of the two parts of the pituitary gland.

**Thyroid Gland**

The thyroid gland is derived from endoderm and begins its development during the fourth week as a thickening in the floor of the primitive pharynx. The thickening soon evaginates (outpouches) downward as the thyroid diverticulum (exhibit II). A narrow thyroglossal duct connects the descending primordial thyroid tissue to the pharynx. As the descent continues, the tongue starts to develop, and the opening into the thyroglossal duct, called the foramen cecum (se’kam) pierces through the base of the tongue. By the seventh week, the thyroid gland occupies a position immediately inferior to the larynx, surrounding the front and lateral sides of the trachea. At this time, the thyroglossal duct disappears and the foramen cecum regresses in size to a vestigial pit that persists throughout life.

**Pancreas**

The pancreas begins development during the fifth week, as dorsal and ventral pancreatic buds of endoderm arise from the caudal portion of the foregut. These primordial pancreatic tissues continue to grow independently until the ventral bud is carried dorsally and fuses with the dorsal bud as the duodenum rotates to the right. The fusion of the two portions of the pancreas occurs during the seventh week.

The pancreas develops from and maintains connections with the small intestine (via the pancreatic duct). The exocrine products of the pancreas, contained in pancreatic juice, are channeled through the pancreatic duct to the small intestine. The endocrine parts of the pancreas—the pancreatic islets—however, secrete their products (insulin and glucagon) into the blood. The precise origin of the endocrine cells of the pancreas remains uncertain. It is believed that some of the endocrine cells develop as buds from pancreatic ductules and that others arise from neuroectodermal cells that migrate to the pancreas to form these endocrine cells and the autonomic innervation of the pancreas.

**Adrenal Glands**

The adrenal glands begin development during the fifth week from two different germ layers. Each adrenal gland has an outer part, or adrenal cortex, which develops from mesoderm, and an inner part, or adrenal medulla, which develops from neuroectoderm. The mesodermal ridge that forms the adrenal cortex is in the same region from which the gonads develop.

The neuroectodermal cells that form the adrenal medulla are derived from the neural crest of the neural tube. The developing adrenal medulla is gradually encapsulated by the adrenal cortex, a process that continues into the fetal stage. The formation of the adrenal gland is not completed until the end of the third year of age.

Notice that the adrenal gland, like the pituitary, has a dual origin; part is neural and part is not. Like the pituitary, the adrenal cortex and adrenal medulla are in fact two different endocrine tissues. Although they are located in the same organ, they secrete different hormones and are regulated by different control systems.

**Stomach and Small Intestine**

Certain cells of the mucosal linings of the stomach and small intestine secrete hormones that promote digestive activities (see chapter 18). The effects of these hormones, summarized in table 14.9, coordinate the activities of different regions of the GI tract and the secretions of pancreatic juice and bile in conjunction with regulation by the autonomic nervous system.

**Placenta**

The placenta (plà-sen’tà) is the organ responsible for nutrient and waste exchange between the fetus and the mother (see chapter 22). The placenta is also an endocrine gland; it secretes...
large amounts of estrogens and progesterone, as well as a number of polypeptide and protein hormones that are similar to some hormones secreted by the anterior pituitary. These latter hormones include human chorionic gonadotrophin (hCG), which is similar to LH, and somatomammotrophin, which is similar in action to growth hormone and prolactin. Detection of hCG in urine is an indication of pregnancy and is the basis of home pregnancy tests.

Knowledge Check

20. Where is testosterone produced? What are its functions?
21. What are the functions of estrogens and progesterone? Where are they produced?
22. Describe the location of the pineal gland and the action of melatonin.
23. Describe the location and function of the thymus.
Diagnosis of Endocrine Disorders

Certain endocrine disorders affect the patient’s physical appearance and behavior; therefore, observation is very important in diagnosis. The patient’s clinical history is also important in evaluating the rate of progress and stage of development of an endocrine disorder.

The confirmation of endocrine disorders requires laboratory tests, particularly of blood and urine samples. These samples are important because hormones are distributed via the blood, and urine is produced from the metabolic wastes filtered from the blood. A radioimmunoassay (RIA) is a laboratory test to determine the concentration of hormones in blood and urine. Other blood tests include the protein-bound iodine (PBI) test to determine the level of iodine in the blood, and hence thyroid problems; measurement of blood cholesterol content for thyroid problems; measurement of sodium-potassium ratios to detect Addison’s disease; and blood sugar tests, including testing glucose tolerance in a fasting patient to examine for diabetes mellitus.

A urinalysis can be important in the diagnosis of several endocrine disorders. A high level of glucose in a fasting patient indicates diabetes mellitus. A patient who has diabetes insipidus will produce a large volume (5–10 L per day) of dilute urine of low specific gravity. Certain diseases of the adrenal glands can also be detected by examining for changes in urine samples collected over a 24-hour period.

Basal metabolism rate (BMR) and thyroid scans (see fig. 14.13b) are tests for thyroid disorders. A visual-field examination may be important in detecting a tumor of the pituitary gland. Radiographs and electrocardiograms also may be helpful in diagnosing endocrine disorders.

Disorders of the Pituitary Gland

The pituitary is a remarkable gland. It simultaneously carries out several functions, yet more than 90% of the gland must be destroyed before pituitary function becomes severely impaired.

Panhypopituitarism

A reduction in the activity of the pituitary gland is called hypopituitarism (hi'po-pi-tu're-alm) It can result from intracranial hemorrhage, a blood clot, prolonged steroid treatments, or a tumor. Total pituitary impairment, termed panhypopituitarism, brings about a progressive and general loss of hormonal activity. For example, the gonads stop functioning and the person suffers from amenorrhea (lack of menstruation) or aspermatism (no sperm production) and loss of pubic and axillary hair. The thyroid and adrenals also eventually stop functioning. People with this condition and those who have had their pituitary surgically removed—a procedure called hypophysectomy (hi-pof''ı-sék'to-mê)—receive thyroxine, cortisone, growth hormone, and gonadal hormones throughout life to maintain normal body function.

Abnormal Growth Hormone Secretion

Inadequate growth hormone secretion during childhood causes pituitary dwarfism (fig. 14.26a). Hypersecretion of growth hormone in an adult produces a rare condition called pituitary cachexia (kak''ke-se''-á) (Simmonds’ disease). One of the symptoms of this disease is premature aging caused by tissue atrophy. By contrast, oversecretion of growth hormone during childhood causes gigantism (fig. 14.26b), an abnormal increase in the length of long bones. Excessive growth hormone secretion in an adult does not cause further growth in bone length because the epiphyseal plates have already ossified. Hypersecretion of growth hormone in an adult causes acromegaly (ak''ro-még''á-le) (fig. 14.26c), in which the person’s appearance gradually changes as a result of thickening of bones and growth of soft tissues, particularly in the face, hands, and feet.

Simmonds’ disease: from Morris Simmonds, German physician, 1855–1925
acromegaly: Gk. akron, extremity; megal, large
Inadequate ADH Secretion

A dysfunction of the neurohypophysis results in a deficiency in ADH secretion, causing a condition called diabetes insipidus. Symptoms of this disease include polyuria (excessive urination), polydipsia (consumption of large amounts of water), and severe ionic imbalances. Diabetes insipidus is treated by injections of ADH.

Disorders of the Thyroid and Parathyroid Glands

Hypothyroidism

The infantile form of hypothyroidism is known as cretinism (kre-tı˘-nizm). An affected child usually appears normal at birth because thyroxine is received from the mother through the placenta. The clinical symptoms of cretinism are stunted growth, thickened facial features, abnormal bone development, mental retardation, low body temperature, and general lethargy. If cretinism is diagnosed early, it can be successfully treated by administering thyroxine.

Myxedema

Hypothyroidism in an adult causes myxedema (mik''-së-de''-mä). This disorder affects body fluids, causing edema and increasing blood volume, hence increasing blood pressure. A person with myxedema has a low metabolic rate, lethargy, sensitivity to cold, and a tendency to gain weight. This condition is treated with thyroxine or triiodothyronine, both of which are taken orally.

Endemic Goiter

A goiter is an abnormal growth of the thyroid gland. When this is a result of inadequate dietary intake of iodine, the condition is called endemic goiter (fig. 14.27). In this case, growth of the thyroid is due to excessive TSH secretion, which results from low levels of thyroxine secretion. Endemic goiter is thus associated with hypothyroidism.

Graves' Disease

Graves' disease, also called toxic goiter, involves growth of the thyroid associated with hypersecretion of thyroxine. This condition is more common in women than men. Graves' disease may be associated with perinuclear antibodies, which are directed against the TSH receptor.

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myxedema: Gk. myxa, mucus; roidema, swelling
Graves' disease: from Robert James Graves, Irish physician, 1796–1853
hyperthyroidism is produced by antibodies that act like TSH and stimulate the thyroid; it is an autoimmune disease. As a consequence of high levels of thyroxine secretion, the metabolic rate and heart rate increase, there is loss of weight, and the autonomic nervous system induces excessive sweating. In about half of the cases, exophthalmos (ex’of-thal’mos) or bulging of the eyes, also develops (fig. 14.28) because of edema in the tissues of the eye sockets and swelling of the extrinsic eye muscles.

Disorders of the Parathyroid Glands

Surgical removal of the parathyroid glands sometimes unintentionally occurs when the thyroid is removed because of a tumor or the presence of Graves’ disease. The resulting fall in parathyroid hormone (PTH) causes a decrease in plasma calcium levels, which can lead to severe muscle tetany. Hyperparathyroidism is usually caused by a tumor that secretes excessive amounts of PTH. This stimulates demineralization of bone, which makes the bones soft and raises the blood levels of calcium and phosphate. As a result of these changes, the bones are subject to deformity and fracture, and stones composed of calcium phosphate are likely to develop in the urinary tract.

exophthalmos: Gk. ex, out; ophthal’mos, eyeball

CHAPTER 14

FIGURE 14.27 An endemic goiter is caused by insufficient iodine in the diet.

FIGURE 14.28 Hyperthyroidism is characterized by an increased metabolic rate, weight loss, muscular weakness, and nervousness. Protrusion of the eyeballs (exophthalmos) may also occur.

Disorders of the Pancreatic Islets

Diabetes Mellitus

Diabetes mellitus is characterized by fasting hyperglycemia and the presence of glucose in the urine. There are two forms of this disease. Type I, or insulin-dependent diabetes mellitus, is caused by destruction of the beta cells and the resulting lack of insulin secretion. Type II, or non-insulin-dependent diabetes mellitus (which is the more common form), is caused by decreased tissue sensitivity to the effects of insulin, so that increasing large amounts of insulin are required to produce a normal effect. Type II diabetes is often controllable by diet and exercise. Both types of diabetes mellitus are also associated with abnormally high levels of glucagon secretion.

Treatment of advanced diabetes mellitus requires administering the necessary amounts of insulin to maintain a balanced carbohydrate metabolism. If excessive amounts of insulin are given, the person will experience extreme nervousness and tremors, perhaps followed by convulsion and loss of consciousness. This condition, commonly called insulin shock, can be treated by administering glucose intravenously.

Reactive Hypoglycemia

People who have a genetic predisposition for type II diabetes mellitus often first develop reactive hypoglycemia. In this condition, the rise in blood glucose that follows the ingestion of carbohydrates stimulates an excessive secretion of insulin, which in turn causes the blood glucose levels to fall below the normal range. This can result in weakness, changes in personality, and mental disorientation.
Disorders of the Adrenal Glands

**Tumors of the Adrenal Medulla**

Tumors of the chromaffin cells of the adrenal medulla are referred to as pheochromocytomas (fe-o-kro”mo-si-to’maz). These tumors cause hypersecretion of epinephrine and norepinephrine whose effects are similar to those of continuous sympathetic nervous stimulation. The symptoms of this condition are hypertension, elevated metabolism, hyperglycemia and sugar in the urine, nervousness, digestive problems, and sweating. It does not take long for the body to become totally fatigued under these conditions, making the patient susceptible to other diseases.

**Addison’s Disease**

This disease is caused by an inadequate secretion of both glucocorticoids and mineralocorticoids, which results in hypoglycemia, sodium and potassium imbalance, dehydration, hypotension, rapid weight loss, and generalized weakness. A person with this condition who is not treated with corticosteroids will die within a few days because of severe electrolyte imbalance and dehydration. Another symptom of this disease is darkening of the skin. This is caused by high secretion of ACTH and possibly MSH (because MSH is derived from the same parent molecule as ACTH), which is a result of lack of negative feedback inhibition of the pituitary by corticosteroids.

**Cushing’s Syndrome**

Hypersecretion of corticosteroids results in Cushing’s syndrome. This condition is generally caused by a tumor of the adrenal cortex or by oversecretion of ACTH from the adenohypophysis. Cushing’s syndrome is characterized by changes in carbohydrate and protein metabolism, hyperglycemia, hypertension, and muscular weakness. Metabolic problems give the body a puffy appearance and can cause structural changes characterized as “buffalo hump” and “moon face.” Similar effects are also seen when people with chronic inflammatory diseases receive prolonged treatment with corticosteroids, which are given to reduce inflammation and inhibit the immune response.

**Adrenogenital Syndrome**

Usually associated with Cushing’s syndrome, this condition is caused by hypersecretion of adrenal sex hormones, particularly the androgens. Adrenogenital syndrome in young children causes premature puberty and enlarged genitals, especially the penis in males and the clitoris in females. An increase in body hair and a deeper voice are other characteristics. This condition in a mature woman can cause growth of a beard.

As with most other endocrine disorders, problems of the adrenal cortex are treated either through surgery (if there is a tumor causing hypersecretion) or by the administration of the necessary levels of appropriate hormones (in the case of tissue dysfunction with hyposecretion).

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**Clinical Case Study Answer**

The visual findings are probably the result of a pituitary tumor (adenoma) eroding and pushing upward on the optic chiasma. The optic chiasma contains nerve tracts that emanate from the medial portions of each retina and receive light from the lateral (temporal) visual fields. The pituitary tumor is secreting either increased or unregulated amounts of ACTH (adrenocorticotropic hormone), which in turn are causing overproduction of adrenocortical hormones. These include glucocorticoids, mineralocorticoids, and various androgens, which in combination are producing the patient’s constellation of findings.

This specific condition, hypersecretion of adrenocortical hormones secondary to an ACTH-producing pituitary adenoma, is known as Cushing’s disease. It is usually treated by transsphenoidal excision of the tumor. When conditions are not right for surgery, radiation or drugs may be used. Elevated levels of adrenocortical hormones can result from endocrine tumors other than pituitary. An example would be an adrenal tumor, either cancerous or benign, that was producing adrenocortical hormones. The physical effects of this condition and all others that involve high levels of adrenocortical hormones are known collectively as Cushing’s syndrome, which is not to be confused with Cushing’s disease. The latter term is specifically reserved for hyperadrenalism caused by a pituitary adenoma.
A 43-year-old man presents to an acute care clinic following motor vehicle accident. He is visibly shaken, and your initial assessment rules out life- or limb-threatening injuries. On secondary assessment you notice coarse facial features including a prominent jaw, very large hands and feet, and a husky voice. Upon examination of the cranial nerves, you're sure he has a definite loss of lateral peripheral vision in both eyes. This leads you to inquire about the details of the motor vehicle accident, to which he says he didn’t see the other car. You then ask to see the photo on his driver's license. The photo is only 9 years old, but the pictured facial features are quite normal. With further questioning you learn that his shoe size, glove size, and ring size have been increasing in recent years.

You tell him you think the accident did not hurt him, but you would like to refer him to an optometrist for formal visual field testing. You suspect that, in the end, this patient will need to see a neurosurgeon.

**QUESTIONS**

1. What lab test are you most interested in?
2. What radiological exam will you need before sending the patient to see the neurosurgeon?
3. On the basis of the adjacent MR image, how can you explain the vision loss?

**Chapter Summary**

**Introduction to the Endocrine System** *(pp. 455–460)*

1. Hormones are regulatory molecules released into the blood by endocrine glands. The action of a hormone on target cells is dependent on its concentration and the specific receptor sites on cell membranes.
2. Hormones are classified chemically as steroids, proteins, and amines.
3. Negative feedback occurs when information concerning an imbalance in hormone concentration is fed back to an organ that acts to correct the imbalance.

**Pituitary Gland** *(pp. 460–465)*

1. The pituitary gland (hypophysis) is divided into an anterior adenohypophysis and a posterior neurohypophysis.
   - (a) In adults the adenohypophysis consists of a glandular pars distalis and a thin proximal extension called the pars tuberalis. A pars intermedia is present in the fetus but does not constitute a separate structure in the adult.
   - (b) The neurohypophysis consists of the lobus nervosa and the infundibulum.
2. The anterior pituitary produces and secretes growth hormone, thyroid-stimulating hormone, adrenocorticotropic hormone, follicle-stimulating hormone, luteinizing hormone, prolactin, and melanocyte-stimulating hormone.
3. The posterior pituitary releases oxytocin and antidiuretic hormone.
4. Secretions of the anterior pituitary are controlled by hypothalamic hormones and regulated by the feedback of hormones from the target cells. Release of hormones from the posterior pituitary are controlled by the hypothalamo-hypophyseal nerve tract.

**Thyroid and Parathyroid Glands** *(pp. 466–469)*

1. The bilobed thyroid gland is located in the neck, just below the larynx. Four small parathyroid glands are embedded in its posterior surface.
2. Thyroid follicles secrete thyroxine and triiodothyronine, which increase the rate of protein synthesis and the rate of energy release from carbohydrates. They also regulate the rate of growth and the rate of maturation of the nervous system.
3. Parafollicular cells of the thyroid secrete the hormone calcitonin, which lowers blood calcium by inhibiting the release of calcium from bone tissue and stimulating the excretion of calcium by the kidneys.
4. Parathyroid hormone causes an increase in blood calcium and a decrease in blood phosphate levels. It acts on the large intestine, kidneys, and bones.

**Pancreas** *(pp. 469–471)*

1. The pancreas is a mixed endocrine and exocrine gland, located in the abdominal cavity.
2. The pancreatic islets contain beta cells that secrete insulin and alpha cells that secrete glucagon.
   - (a) Insulin lowers blood glucose and stimulates the production of glycogen, fat, and protein.
   - (b) Glucagon raises blood glucose by stimulating the breakdown of liver glycogen.

**Adrenal Glands** *(pp. 471–474)*

1. Each adrenal gland consists of an adrenal cortex and an adrenal medulla and is positioned along the superior border of a kidney.
2. Hormones of the adrenal cortex include mineralocorticoids, which regulate sodium reabsorption and potassium excretion; glucocorticoids, which influence metabolism by promoting vasoconstriction and resistance to stress; and gonadocorticoids, which supplement gonadal hormones.
3. Epinephrine and norepinephrine, secreted from the adrenal medulla, produce effects similar to those of the sympathetic division of the ANS.
Gonads and Other Endocrine Glands
(pp. 474–479)

1. Testes are the male gonads that produce the male sex hormone testosterone within the interstitial cells.
2. Ovaries are the female gonads that produce estrogens within the ovarian follicles and corpus luteum.

Review Activities

Objective Questions

March the gland to its embryonic origin.
1. adenohypophysis (a) endoderm of pharynx
2. neurohypophysis (b) diverticulum from brain
3. adrenal medulla (c) endoderm of foregut
4. pancreas (d) neural crest ectoderm
5. thyroid gland (e) hypophysial pouch

6. The sella turcica that supports the pituitary gland is located in which bone?
   (a) the ethmoid bone
   (b) the frontal bone
   (c) the sphenoid bone
   (d) the occipital bone

7. The hormone primarily responsible for setting the basal metabolic rate and for promoting the maturation of the brain is
   (a) cortisol. (c) TSH. (d) ACTH. (e) thyroxine.

8. Which of the following statements about the adrenal medulla is true?
   (a) It develops from mesoderm.
   (b) It secretes some androgens.
   (c) Its secretion prepares the body for the fight-or-flight response.
   (d) The zona fasciculata is stimulated by ACTH.
   (e) All of the above are true.

9. Which of the following statements about the hormone insulin is true?
   (a) It is secreted by alpha cells in the pancreatic islets.
   (b) It is secreted in response to a rise in blood glucose.
   (c) It stimulates the production of glycogen and fat.
   (d) Both a and b are true.
   (e) Both b and c are true.

Essay Questions

1. Explain how the nervous and endocrine systems differ in maintaining body homeostasis.
2. List the glands of the endocrine system and describe their general locations.
3. Give examples of steroids, proteins, and amines and describe the various ways in which they are administered.
4. Define negative feedback. Why is this a reliable mechanism for controlling hormonal secretion?
5. Which endocrine glands, or portions of endocrine glands, develop through the process of germ layer invagination? Which develop as an outgrowth or pouch?
6. Why is the pituitary frequently considered two separate glands?
7. List the hormones secreted by the adenohypophysis and describe the general functions of each.
8. Describe the location and gross structure of the neurohypophysis. What hormones are released from this portion of the pituitary gland and how is their release regulated?
9. List the hormones secreted by the thyroid gland and discuss the general function of each.

Essay Questions

1. The anterior pituitary has often been characterized as the “master gland.” In what sense might this description be correct? In what sense is it misleading?
2. A 38-year-old woman experienced a milky discharge through the nipples of her breasts that occurred periodically over a 6-month period. She was not pregnant and her youngest child was 7 years old. Her physician referred to this as galactorrhea—the medical term for a whitish or greenish discharge from one or both breasts—and scheduled her for a blood test to determine possible hormonal dysfunction that might be linked to a benign growth on the pituitary gland. How could a tumor of the pituitary result in this woman’s symptoms?
3. Brenda, your roommate, has been having an awful time lately. She can’t even muster enough energy to go out on a date. She’s been putting on weight, she’s always cold, and every time she pops in the “Buns of Steel” workout video, she...
complains of weakness. When she finally goes to her doctor, he finds her to have a slow pulse and low blood pressure. Further tests indicate thyroid hormone deficiency—a condition termed hypothyroidism. This endocrine disorder is very common and occurs 8 times more often in females than males. Why would Brenda’s symptoms be typical of this disorder? What type of treatment will the doctor prescribe?”

4. You decide it’s time that your college basketball team make it to the final four. You figure your pal Bubba has the competitive spirit needed to step in as the new star center—if only he weren’t 5 ft 8 in. Confronting the problem head-on, you start slipping growth hormone into Bubba’s morning orange juice—a clever strategy, you think.

After a time, however, you begin to realize that Bubba isn’t growing any taller. In fact, he hasn’t grown an inch. Instead, his jaw and forehead seem disproportionately large, and his hands and feet are swollen. To make matters worse, he has developed a horrendous body odor.

Explain why giving growth hormones to an adult does not change the person’s height. Explain the physical changes that can occur when an adult is administered growth hormones.

5. Suppose a person with a normal thyroid gland took thyroid pills. Would he or she lose weight? Why or why not? What endocrine changes would be produced by those pills? If, after a few months, the person stopped taking the pills, what would happen to his or her body weight? Explain.