

| The Thyroid Gland

By the end of this section, you will be able to:

- Describe the location and anatomy of the thyroid gland
- Discuss the synthesis of triiodothyronine and thyroxine
- Explain the role of thyroid hormones in the regulation of basal metabolism
- Identify the hormone produced by the parafollicular cells of the thyroid

A butterfly-shaped organ, the **thyroid gland** is located anterior to the trachea, just inferior to the larynx (**Figure 17.12**). The medial region, called the isthmus, is flanked by wing-shaped left and right lobes. Each of the thyroid lobes are embedded with parathyroid glands, primarily on their posterior surfaces. The tissue of the thyroid gland is composed mostly of thyroid follicles. The follicles are made up of a central cavity filled with a sticky fluid called **colloid**. Surrounded by a wall of epithelial follicle cells, the colloid is the center of thyroid hormone production, and that production is dependent on the hormones' essential and unique component: iodine.

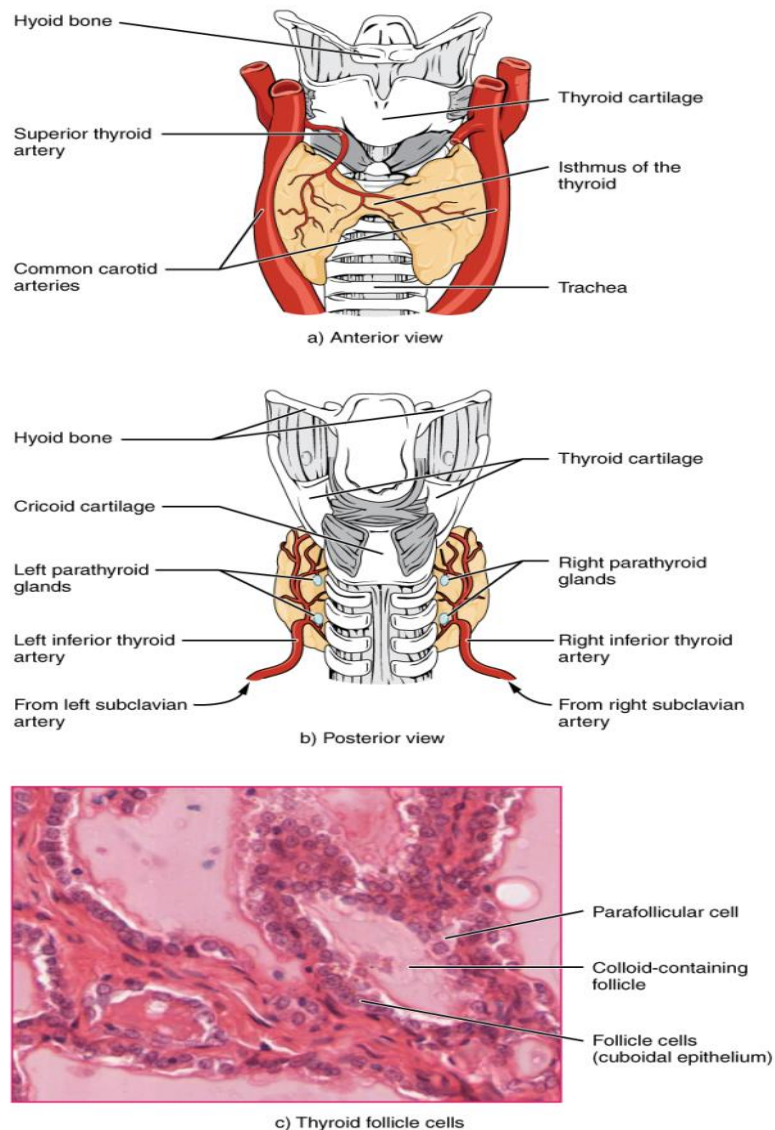


Figure 17.12 Thyroid Gland The thyroid gland is located in the neck where it wraps around the trachea. (a) Anterior view of the thyroid gland. (b) Posterior view of the thyroid gland. (c) The glandular tissue is composed primarily of thyroid follicles. The larger parafollicular cells often appear within the matrix of follicle cells. LM \times 1332.

Synthesis and Release of Thyroid Hormones

Hormones are produced in the colloid when atoms of the mineral iodine attach to a glycoprotein, called thyroglobulin, that is secreted into the colloid by the follicle cells. The following steps outline the hormones' assembly:

1. Binding of TSH to its receptors in the follicle cells of the thyroid gland causes the cells to actively transport iodide ions (I^-) across their cell membrane, from the bloodstream into the cytosol. As a result, the concentration of iodide ions "trapped" in the follicular cells is many times higher than the concentration in the bloodstream.
2. Iodide ions then move to the lumen of the follicle cells that border the colloid. There, the ions undergo oxidation (their negatively charged electrons are removed). The oxidation of two iodide ions ($2 I^-$) results in iodine (I_2), which passes through the follicle cell membrane into the colloid.
3. In the colloid, peroxidase enzymes link the iodine to the tyrosine amino acids in thyroglobulin to produce two intermediaries: a tyrosine attached to one iodine and a tyrosine attached to two iodines. When one of each of these intermediaries is linked by covalent bonds, the resulting compound is **triiodothyronine** (T_3), a thyroid hormone with three iodines. Much more commonly, two copies of the second intermediary bond, forming tetraiodothyronine, also known as **thyroxine** (T_4), a thyroid hormone with four iodines.

These hormones remain in the colloid center of the thyroid follicles until TSH stimulates endocytosis of colloid back into the follicle cells. There, lysosomal enzymes break apart the thyroglobulin colloid, releasing free T_3 and T_4 , which diffuse across the follicle cell membrane and enter the bloodstream.

In the bloodstream, less than one percent of the circulating T_3 and T_4 remains unbound. This free T_3 and T_4 can cross the lipid bilayer of cell membranes and be taken up by cells. The remaining 99 percent of circulating T_3 and T_4 is bound to specialized transport proteins called thyroxine-binding globulins (TBGs), to albumin, or to other plasma proteins. This "packaging" prevents their free diffusion into body cells. When blood levels of T_3 and T_4 begin to decline, bound T_3 and T_4 are released from these plasma proteins and readily cross the membrane of target cells. T_3 is more potent than T_4 , and many cells convert T_4 to T_3 through the removal of an iodine atom.

Regulation of TH Synthesis

The release of T_3 and T_4 from the thyroid gland is regulated by thyroid-stimulating hormone (TSH). As shown in **Figure 17.13**, low blood levels of T_3 and T_4 stimulate the release of thyrotropin-releasing hormone (TRH) from the hypothalamus, which triggers secretion of TSH from the anterior pituitary. In turn, TSH stimulates the thyroid gland to secrete T_3 and T_4 . The levels of TRH, TSH, T_3 , and T_4 are regulated by a negative feedback system in which increasing levels of T_3 and T_4 decrease the production and secretion of TSH.

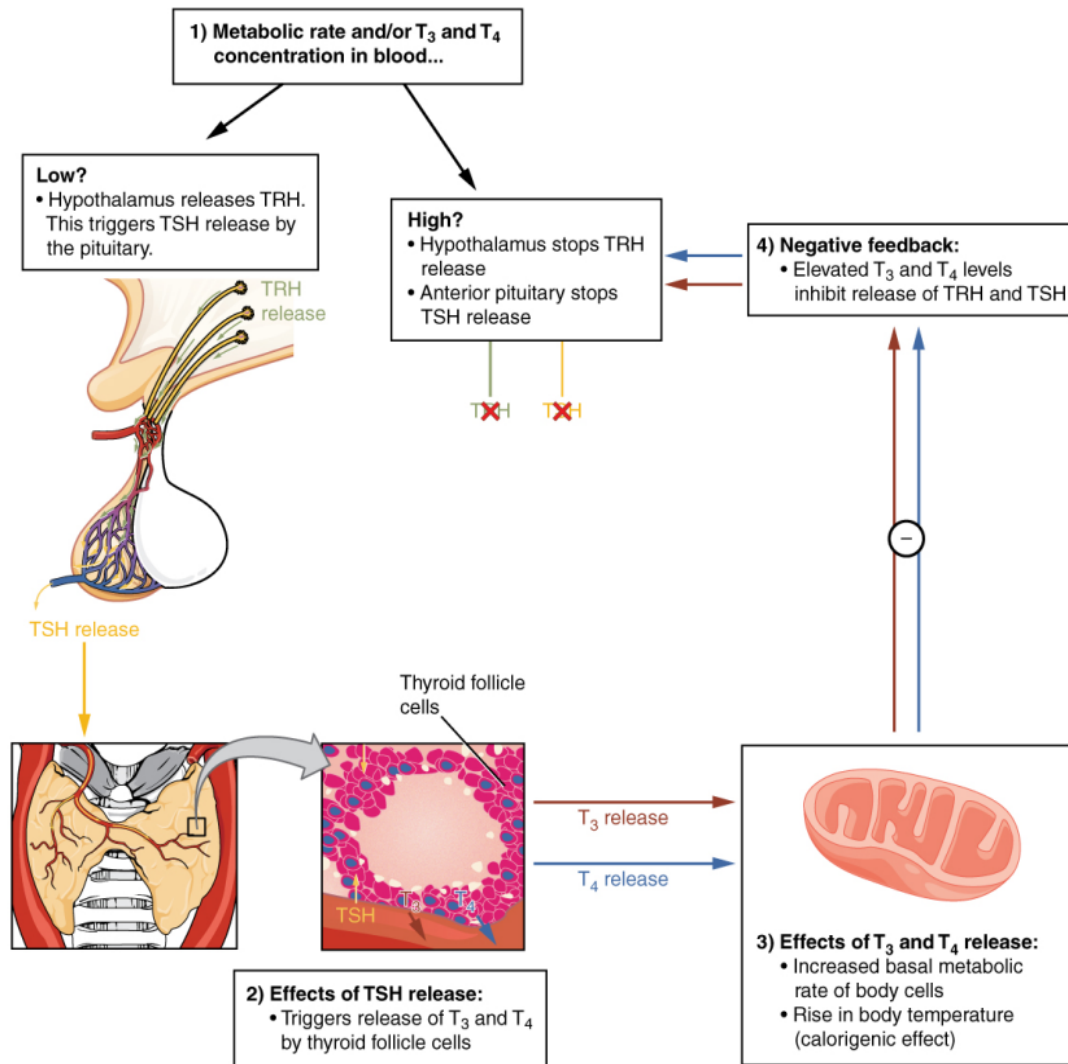


Figure 17.13 Classic Negative Feedback Loop A classic negative feedback loop controls the regulation of thyroid hormone levels.

Functions of Thyroid Hormones

The thyroid hormones, T_3 and T_4 , are often referred to as metabolic hormones because their levels influence the body's basal metabolic rate, the amount of energy used by the body at rest. When T_3 and T_4 bind to intracellular receptors located on the mitochondria, they cause an increase in nutrient breakdown and the use of oxygen to produce ATP. In addition, T_3 and T_4 initiate the transcription of genes involved in glucose oxidation. Although these mechanisms prompt cells to produce more ATP, the process is inefficient, and an abnormally increased level of heat is released as a byproduct of these reactions. This so-called calorigenic effect (calor- = "heat") raises body temperature.

Adequate levels of thyroid hormones are also required for protein synthesis and for fetal and childhood tissue development and growth. They are especially critical for normal development of the nervous system both in utero and in early childhood, and they continue to support neurological function in adults. As noted earlier, these thyroid hormones have a complex interrelationship with reproductive hormones, and deficiencies can influence libido, fertility, and other aspects of reproductive function. Finally, thyroid hormones increase the body's sensitivity to catecholamines (epinephrine and norepinephrine) from the adrenal medulla by upregulation of receptors in the blood vessels. When levels of T_3 and T_4 hormones are excessive, this effect accelerates the heart rate, strengthens the heartbeat, and increases blood pressure. Because thyroid hormones regulate metabolism, heat production, protein synthesis, and many other body functions, thyroid disorders can have severe and widespread consequences.

Calcitonin

The thyroid gland also secretes a hormone called **calcitonin** that is produced by the parafollicular cells (also called C cells) that stud the tissue between distinct follicles. Calcitonin is released in response to a rise in blood calcium levels. It appears to have a function in decreasing blood calcium concentrations by:

- Inhibiting the activity of osteoclasts, bone cells that release calcium into the circulation by degrading bone matrix
- Increasing osteoblastic activity
- Decreasing calcium absorption in the intestines
- Increasing calcium loss in the urine

However, these functions are usually not significant in maintaining calcium homeostasis, so the importance of calcitonin is not entirely understood. Pharmaceutical preparations of calcitonin are sometimes prescribed to reduce osteoclast activity in people with osteoporosis and to reduce the degradation of cartilage in people with osteoarthritis. The hormones secreted by thyroid are summarized in **Table 17.4**.

Thyroid Hormones

Associated hormones	Chemical class	Effect
Thyroxine (T ₄), triiodothyronine (T ₃)	Amine	Stimulate basal metabolic rate
Calcitonin	Peptide	Reduces blood Ca ²⁺ levels

Table 17.4

Of course, calcium is critical for many other biological processes. It is a second messenger in many signaling pathways, and is essential for muscle contraction, nerve impulse transmission, and blood clotting. Given these roles, it is not surprising that blood calcium levels are tightly regulated by the endocrine system. The organs involved in the regulation are the parathyroid glands.

| The Parathyroid Glands

By the end of this section, you will be able to:

- Describe the location and structure of the parathyroid glands
- Describe the hormonal control of blood calcium levels
- Discuss the physiological response of parathyroid dysfunction

The **parathyroid glands** are tiny, round structures usually found embedded in the posterior surface of the thyroid gland (**Figure 17.15**). A thick connective tissue capsule separates the glands from the thyroid tissue. Most people have four parathyroid glands, but occasionally there are more in tissues of the neck or chest. The function of one type of parathyroid cells, the oxyphil cells, is not clear. The primary functional cells of the parathyroid glands are the chief cells. These epithelial cells produce and secrete the **parathyroid hormone (PTH)**, the major hormone involved in the regulation of blood calcium levels.

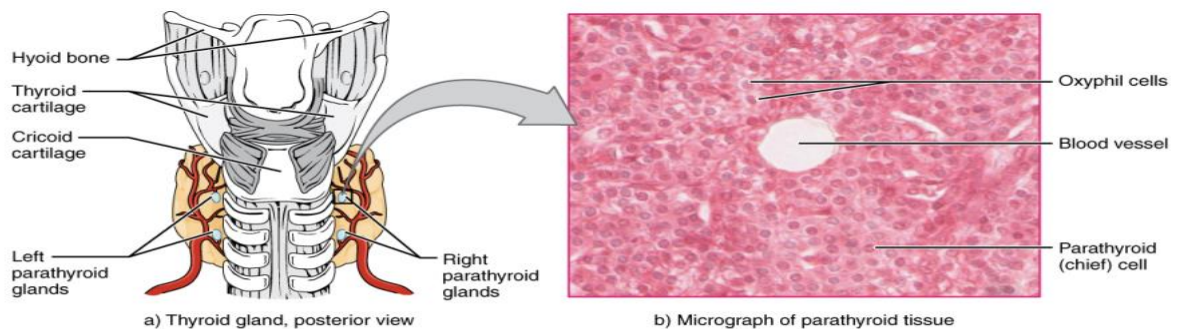


Figure 17.15 Parathyroid Glands The small parathyroid glands are embedded in the posterior surface of the thyroid gland. LM \times 760.

Lecture 8

The parathyroid glands produce and secrete PTH, a peptide hormone, in response to low blood calcium levels (**Figure 17.16**). PTH secretion causes the release of calcium from the bones by stimulating osteoclasts, which secrete enzymes that degrade bone and release calcium into the interstitial fluid. PTH also inhibits osteoblasts, the cells involved in bone deposition, thereby sparing blood calcium. PTH causes increased reabsorption of calcium (and magnesium) in the kidney tubules from the urine filtrate. In addition, PTH initiates the production of the steroid hormone calcitriol (also known as 1,25-dihydroxyvitamin D), which is the active form of vitamin D₃, in the kidneys. Calcitriol then stimulates increased absorption of dietary calcium by the intestines. A negative feedback loop regulates the levels of PTH, with rising blood calcium levels inhibiting further release of PTH.

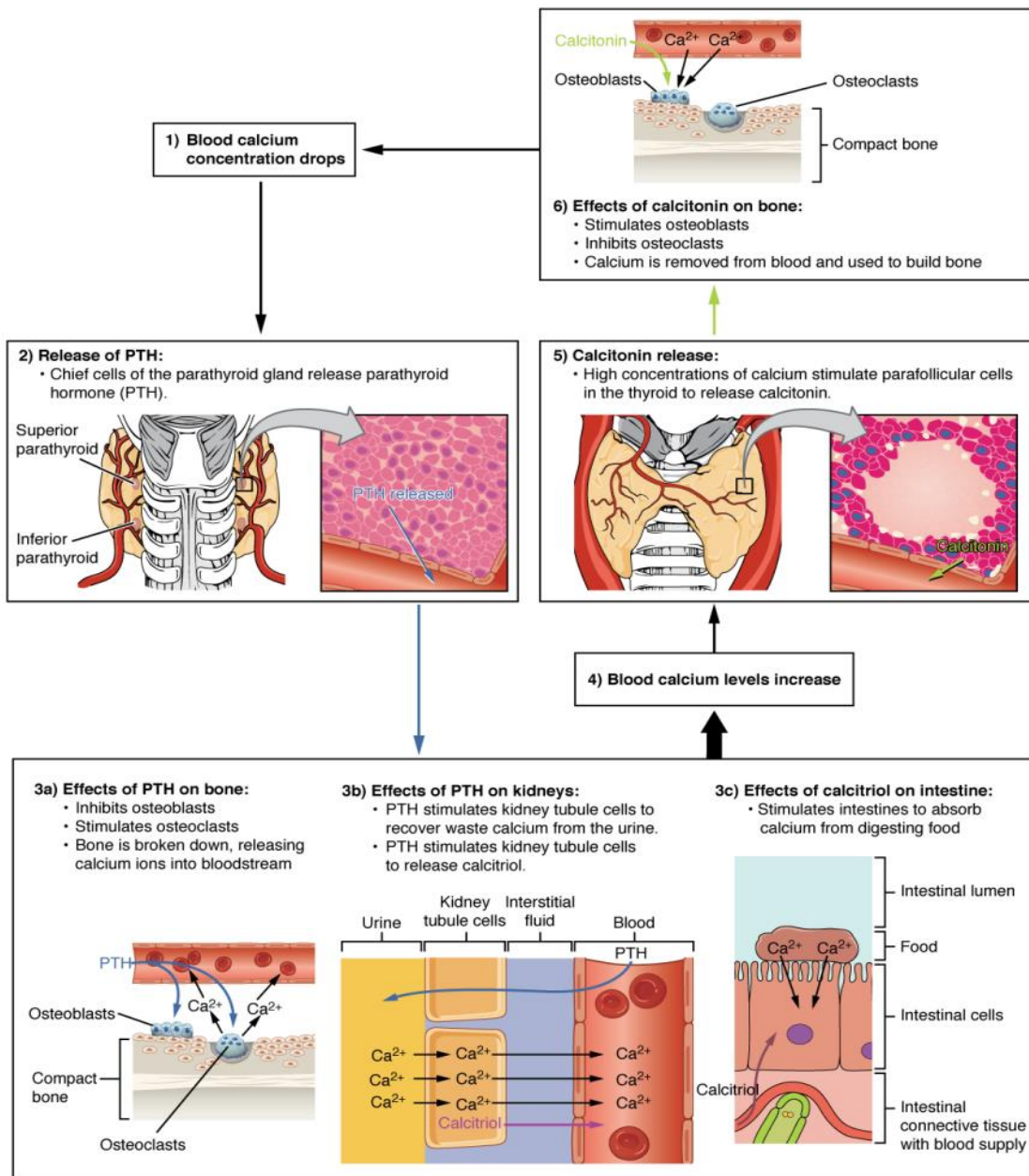


Figure 17.16 Parathyroid Hormone in Maintaining Blood Calcium Homeostasis Parathyroid hormone increases blood calcium levels when they drop too low. Conversely, calcitonin, which is released from the thyroid gland, decreases blood calcium levels when they become too high. These two mechanisms constantly maintain blood calcium concentration at homeostasis.

Lecture 8

Abnormally high activity of the parathyroid gland can cause **hyperparathyroidism**, a disorder caused by an overproduction of PTH that results in excessive calcium reabsorption from bone. Hyperparathyroidism can significantly decrease bone density, leading to spontaneous fractures or deformities. As blood calcium levels rise, cell membrane permeability to sodium is decreased, and the responsiveness of the nervous system is reduced. At the same time, calcium deposits may collect in the body's tissues and organs, impairing their functioning.

In contrast, abnormally low blood calcium levels may be caused by parathyroid hormone deficiency, called **hypoparathyroidism**, which may develop following injury or surgery involving the thyroid gland. Low blood calcium increases membrane permeability to sodium, resulting in muscle twitching, cramping, spasms, or convulsions. Severe deficits can paralyze muscles, including those involved in breathing, and can be fatal.

When blood calcium levels are high, calcitonin is produced and secreted by the parafollicular cells of the thyroid gland. As discussed earlier, calcitonin inhibits the activity of osteoclasts, reduces the absorption of dietary calcium in the intestine, and signals the kidneys to reabsorb less calcium, resulting in larger amounts of calcium excreted in the urine.

| The Adrenal Glands

By the end of this section, you will be able to:

- Describe the location and structure of the adrenal glands
- Identify the hormones produced by the adrenal cortex and adrenal medulla, and summarize their target cells and effects

The **adrenal glands** are wedges of glandular and neuroendocrine tissue adhering to the top of the kidneys by a fibrous capsule (**Figure 17.17**). The adrenal glands have a rich blood supply and experience one of the highest rates of blood flow in the body. They are served by several arteries branching off the aorta, including the suprarenal and renal arteries. Blood flows to each adrenal gland at the adrenal cortex and then drains into the adrenal medulla. Adrenal hormones are released into the circulation via the left and right suprarenal veins.

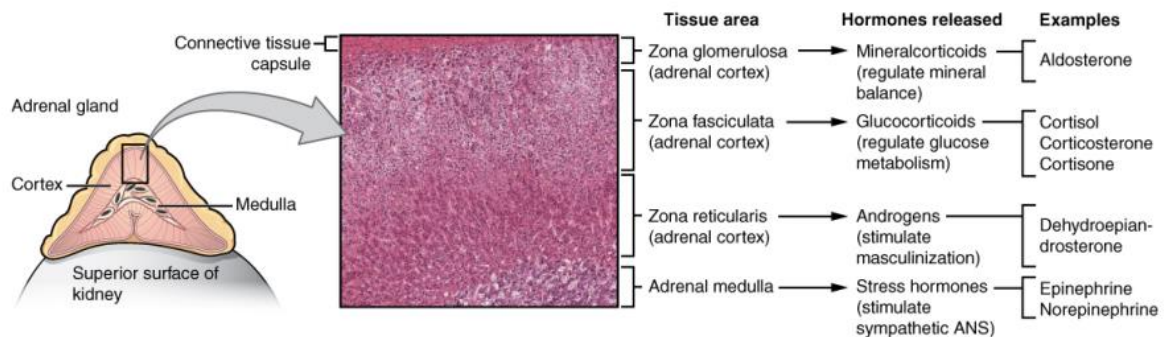


Figure 17.17 Adrenal Glands Both adrenal glands sit atop the kidneys and are composed of an outer cortex and an inner medulla, all surrounded by a connective tissue capsule. The cortex can be subdivided into additional zones, all of which produce different types of hormones. LM × 204.

The adrenal gland consists of an outer cortex of glandular tissue and an inner medulla of nervous tissue. The cortex itself is divided into three zones: the **zona glomerulosa**, the **zona fasciculata**, and the **zona reticularis**. Each region secretes its own set of hormones.

The **adrenal cortex**, as a component of the hypothalamic-pituitary-adrenal (HPA) axis, secretes steroid hormones important for the regulation of the long-term stress response, blood pressure and blood volume, nutrient uptake and storage, fluid and electrolyte balance, and inflammation. The HPA axis involves the stimulation of hormone release of adrenocorticotropic hormone (ACTH) from the pituitary by the hypothalamus. ACTH then stimulates the adrenal cortex to produce the hormone cortisol. This pathway will be discussed in more detail below.

Lecture 8

The **adrenal medulla** is neuroendocrine tissue composed of postganglionic sympathetic nervous system (SNS) neurons. It is really an extension of the autonomic nervous system, which regulates homeostasis in the body. The sympathomedullary (SAM) pathway involves the stimulation of the medulla by impulses from the hypothalamus via neurons from the thoracic spinal cord. The medulla is stimulated to secrete the amine hormones epinephrine and norepinephrine.

One of the major functions of the adrenal gland is to respond to stress. Stress can be either physical or psychological or both. Physical stresses include exposing the body to injury, walking outside in cold and wet conditions without a coat on, or malnutrition. Psychological stresses include the perception of a physical threat, a fight with a loved one, or just a bad day at school.

The body responds in different ways to short-term stress and long-term stress following a pattern known as the **general adaptation syndrome (GAS)**. Stage one of GAS is called the **alarm reaction**. This is short-term stress, the fight-or-flight response, mediated by the hormones epinephrine and norepinephrine from the adrenal medulla via the SAM pathway. Their function is to prepare the body for extreme physical exertion. Once this stress is relieved, the body quickly returns to normal. The section on the adrenal medulla covers this response in more detail.

If the stress is not soon relieved, the body adapts to the stress in the second stage called the **stage of resistance**. If a person is starving for example, the body may send signals to the gastrointestinal tract to maximize the absorption of nutrients from food.

If the stress continues for a longer term however, the body responds with symptoms quite different than the fight-or-flight response. During the **stage of exhaustion**, individuals may begin to suffer depression, the suppression of their immune response, severe fatigue, or even a fatal heart attack. These symptoms are mediated by the hormones of the adrenal cortex, especially cortisol, released as a result of signals from the HPA axis.

Adrenal hormones also have several non-stress-related functions, including the increase of blood sodium and glucose levels, which will be described in detail below.

Adrenal Cortex

The adrenal cortex consists of multiple layers of lipid-storing cells that occur in three structurally distinct regions. Each of these regions produces different hormones.

Hormones of the Zona Glomerulosa

The most superficial region of the adrenal cortex is the zona glomerulosa, which produces a group of hormones collectively referred to as **mineralocorticoids** because of their effect on body minerals, especially sodium and potassium. These hormones are essential for fluid and electrolyte balance.

Aldosterone is the major mineralocorticoid. It is important in the regulation of the concentration of sodium and potassium ions in urine, sweat, and saliva. For example, it is released in response to elevated blood K^+ , low blood Na^+ , low blood pressure, or low blood volume. In response, aldosterone increases the excretion of K^+ and the retention of Na^+ , which in turn increases blood volume and blood pressure. Its secretion is prompted when CRH from the hypothalamus triggers ACTH release from the anterior pituitary.

Aldosterone is also a key component of the renin-angiotensin-aldosterone system (RAAS) in which specialized cells of the kidneys secrete the enzyme renin in response to low blood volume or low blood pressure. Renin then catalyzes the conversion of the blood protein angiotensinogen, produced by the liver, to the hormone angiotensin I. Angiotensin I is converted in the lungs to angiotensin II by **angiotensin-converting enzyme (ACE)**. Angiotensin II has three major functions:

1. Initiating vasoconstriction of the arterioles, decreasing blood flow
2. Stimulating kidney tubules to reabsorb $NaCl$ and water, increasing blood volume
3. Signaling the adrenal cortex to secrete aldosterone, the effects of which further contribute to fluid retention, restoring blood pressure and blood volume

For individuals with hypertension, or high blood pressure, drugs are available that block the production of angiotensin II. These drugs, known as ACE inhibitors, block the ACE enzyme from converting angiotensin I to angiotensin II, thus mitigating the latter's ability to increase blood pressure.

Hormones of the Zona Fasciculata

The intermediate region of the adrenal cortex is the zona fasciculata, named as such because the cells form small fascicles (bundles) separated by tiny blood vessels. The cells of the zona fasciculata produce hormones called **glucocorticoids** because of their role in glucose metabolism. The most important of these is **cortisol**, some of which the liver converts to cortisone. A glucocorticoid produced in much smaller amounts is corticosterone. In response to long-term stressors, the hypothalamus secretes CRH, which in turn triggers the release of ACTH by the anterior pituitary. ACTH triggers the release of the glucocorticoids. Their overall effect is to inhibit tissue building while stimulating the breakdown of stored nutrients to maintain adequate fuel supplies. In conditions of long-term stress, for example, cortisol promotes the catabolism of glycogen to glucose, the catabolism of stored triglycerides into fatty acids and glycerol, and the catabolism of muscle proteins into amino acids. These raw materials can then be used to synthesize additional glucose and ketones for use as body fuels. The hippocampus, which is part of the temporal lobe of the cerebral cortex and important in memory formation, is highly sensitive to stress levels because of its many glucocorticoid receptors.

You are probably familiar with prescription and over-the-counter medications containing glucocorticoids, such as cortisone injections into inflamed joints, prednisone tablets and steroid-based inhalers used to manage severe asthma, and hydrocortisone creams applied to relieve itchy skin rashes. These drugs reflect another role of cortisol—the downregulation of the immune system, which inhibits the inflammatory response.

Hormones of the Zona Reticularis

The deepest region of the adrenal cortex is the zona reticularis, which produces small amounts of a class of steroid sex hormones called androgens. During puberty and most of adulthood, androgens are produced in the gonads. The androgens produced in the zona reticularis supplement the gonadal androgens. They are produced in response to ACTH from the anterior pituitary and are converted in the tissues to testosterone or estrogens. In adult women, they may contribute to the sex drive, but their function in adult men is not well understood. In post-menopausal women, as the functions of the ovaries decline, the main source of estrogens becomes the androgens produced by the zona reticularis.

Adrenal Medulla

As noted earlier, the adrenal cortex releases glucocorticoids in response to long-term stress such as severe illness. In contrast, the adrenal medulla releases its hormones in response to acute, short-term stress mediated by the sympathetic nervous system (SNS).

The medullary tissue is composed of unique postganglionic SNS neurons called **chromaffin** cells, which are large and irregularly shaped, and produce the neurotransmitters **epinephrine** (also called adrenaline) and **norepinephrine** (or noradrenaline). Epinephrine is produced in greater quantities—approximately a 4 to 1 ratio with norepinephrine—and is the more powerful hormone. Because the chromaffin cells release epinephrine and norepinephrine into the systemic circulation, where they travel widely and exert effects on distant cells, they are considered hormones. Derived from the amino acid tyrosine, they are chemically classified as catecholamines.

The secretion of medullary epinephrine and norepinephrine is controlled by a neural pathway that originates from the hypothalamus in response to danger or stress (the SAM pathway). Both epinephrine and norepinephrine signal the liver and skeletal muscle cells to convert glycogen into glucose, resulting in increased blood glucose levels. These hormones increase the heart rate, pulse, and blood pressure to prepare the body to fight the perceived threat or flee from it. In addition, the pathway dilates the airways, raising blood oxygen levels. It also prompts vasodilation, further increasing the oxygenation of important organs such as the lungs, brain, heart, and skeletal muscle. At the same time, it triggers vasoconstriction to blood vessels serving less essential organs such as the gastrointestinal tract, kidneys, and skin, and downregulates some components of the immune system. Other effects include a dry mouth, loss of appetite, pupil dilation, and a loss of peripheral vision. The major hormones of the adrenal glands are summarized in **Table 17.5**.

Hormones of the Adrenal Glands

Adrenal gland	Associated hormones	Chemical class	Effect
Adrenal cortex	Aldosterone	Steroid	Increases blood Na ⁺ levels
Adrenal cortex	Cortisol, corticosterone, cortisone	Steroid	Increase blood glucose levels
Adrenal medulla	Epinephrine, norepinephrine	Amine	Stimulate fight-or-flight response

Table 17.5

Disorders Involving the Adrenal Glands

Several disorders are caused by the dysregulation of the hormones produced by the adrenal glands. For example, Cushing's disease is a disorder characterized by high blood glucose levels and the accumulation of lipid deposits on the face and neck. It is caused by hypersecretion of cortisol. The most common source of Cushing's disease is a pituitary tumor that secretes

cortisol or ACTH in abnormally high amounts. Other common signs of Cushing's disease include the development of a moon-shaped face, a buffalo hump on the back of the neck, rapid weight gain, and hair loss. Chronically elevated glucose levels are also associated with an elevated risk of developing type 2 diabetes. In addition to hyperglycemia, chronically elevated glucocorticoids compromise immunity, resistance to infection, and memory, and can result in rapid weight gain and hair loss.

In contrast, the hyposecretion of corticosteroids can result in Addison's disease, a rare disorder that causes low blood glucose levels and low blood sodium levels. The signs and symptoms of Addison's disease are vague and are typical of other disorders as well, making diagnosis difficult. They may include general weakness, abdominal pain, weight loss, nausea, vomiting, sweating, and cravings for salty food.

| The Pineal Gland

By the end of this section, you will be able to:

- Describe the location and structure of the pineal gland
- Discuss the function of melatonin

Recall that the hypothalamus, part of the diencephalon of the brain, sits inferior and somewhat anterior to the thalamus. Inferior but somewhat posterior to the thalamus is the **pineal gland**, a tiny endocrine gland whose functions are not entirely clear. The **pinealocyte** cells that make up the pineal gland are known to produce and secrete the amine hormone **melatonin**, which is derived from serotonin.

The secretion of melatonin varies according to the level of light received from the environment. When photons of light stimulate the retinas of the eyes, a nerve impulse is sent to a region of the hypothalamus called the suprachiasmatic nucleus (SCN), which is important in regulating biological rhythms. From the SCN, the nerve signal is carried to the spinal cord and eventually to the pineal gland, where the production of melatonin is inhibited. As a result, blood levels of melatonin fall, promoting wakefulness. In contrast, as light levels decline—such as during the evening—melatonin production increases, boosting blood levels and causing drowsiness.

The secretion of melatonin may influence the body's circadian rhythms, the dark-light fluctuations that affect not only sleepiness and wakefulness, but also appetite and body temperature. Interestingly, children have higher melatonin levels than adults, which may prevent the release of gonadotropins from the anterior pituitary, thereby inhibiting the onset of puberty. Finally, an antioxidant role of melatonin is the subject of current research.

Jet lag occurs when a person travels across several time zones and feels sleepy during the day or wakeful at night. Traveling across multiple time zones significantly disturbs the light-dark cycle regulated by melatonin. It can take up to several days for melatonin synthesis to adjust to the light-dark patterns in the new environment, resulting in jet lag. Some air travelers take melatonin supplements to induce sleep.

| Gonadal and Placental Hormones

By the end of this section, you will be able to:

- Identify the most important hormones produced by the testes and ovaries
- Name the hormones produced by the placenta and state their functions

Lecture 8

This section briefly discusses the hormonal role of the gonads—the male testes and female ovaries—which produce the sex cells (sperm and ova) and secrete the gonadal hormones. The roles of the gonadotropins released from the anterior pituitary (FSH and LH) were discussed earlier.

The primary hormone produced by the male testes is **testosterone**, a steroid hormone important in the development of the male reproductive system, the maturation of sperm cells, and the development of male secondary sex characteristics such as a deepened voice, body hair, and increased muscle mass. Interestingly, testosterone is also produced in the female ovaries, but at a much reduced level. In addition, the testes produce the peptide hormone **inhibin**, which inhibits the secretion of FSH from the anterior pituitary gland. FSH stimulates spermatogenesis.

The primary hormones produced by the ovaries are **estrogens**, which include estradiol, estriol, and estrone. Estrogens play an important role in a larger number of physiological processes, including the development of the female reproductive system, regulation of the menstrual cycle, the development of female secondary sex characteristics such as increased adipose tissue and the development of breast tissue, and the maintenance of pregnancy. Another significant ovarian hormone is **progesterone**, which contributes to regulation of the menstrual cycle and is important in preparing the body for pregnancy as well as maintaining pregnancy. In addition, the granulosa cells of the ovarian follicles produce inhibin, which—as in males—inhibits the secretion of FSH. During the initial stages of pregnancy, an organ called the placenta develops within the uterus. The placenta supplies oxygen and nutrients to the fetus, excretes waste products, and produces and secretes estrogens and progesterone. The placenta produces human chorionic gonadotropin (hCG) as well. The hCG hormone promotes progesterone synthesis and reduces the mother's immune function to protect the fetus from immune rejection. It also secretes human placental lactogen (hPL), which plays a role in preparing the breasts for lactation, and relaxin, which is thought to help soften and widen the pubic symphysis in preparation for childbirth. The hormones controlling reproduction are summarized in **Table 17.6**.

Reproductive Hormones

Gonad	Associated hormones	Chemical class	Effect
Testes	Testosterone	Steroid	Stimulates development of male secondary sex characteristics and sperm production
Testes	Inhibin	Protein	Inhibits FSH release from pituitary
Ovaries	Estrogens and progesterone	Steroid	Stimulate development of female secondary sex characteristics and prepare the body for childbirth
Placenta	Human chorionic gonadotropin	Protein	Promotes progesterone synthesis during pregnancy and inhibits immune response against fetus

Table 17.6

| The Endocrine Pancreas

By the end of this section, you will be able to:

- Describe the location and structure of the pancreas, and the morphology and function of the pancreatic islets
- Compare and contrast the functions of insulin and glucagon

The **pancreas** is a long, slender organ, most of which is located posterior to the bottom half of the stomach (**Figure 17.18**). Although it is primarily an exocrine gland, secreting a variety of digestive enzymes, the pancreas has an endocrine function. Its **pancreatic islets**—clusters of cells formerly known as the islets of Langerhans—secrete the hormones glucagon, insulin, somatostatin, and pancreatic polypeptide (PP).

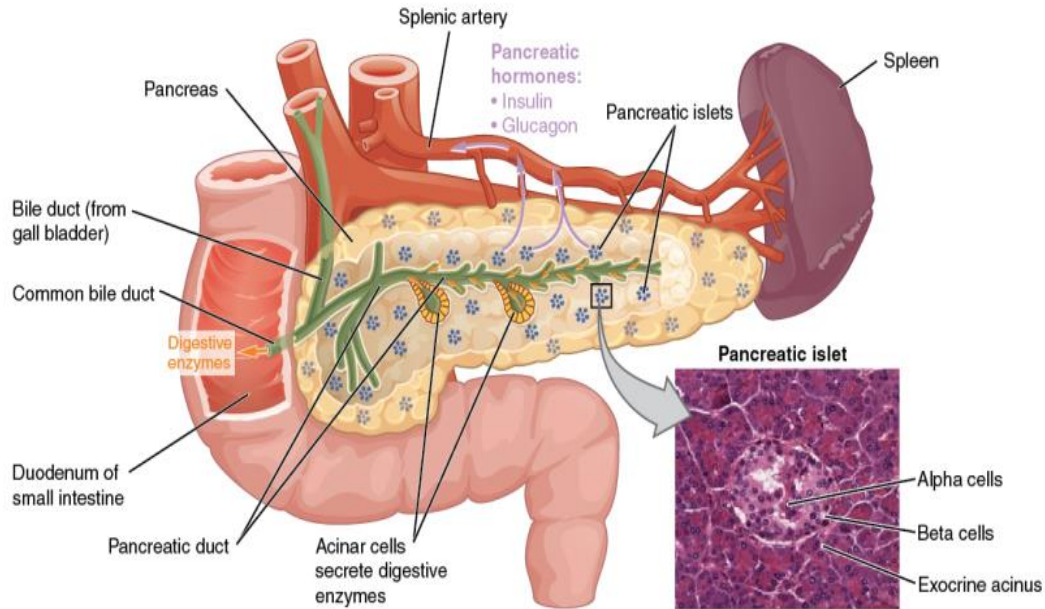


Figure 17.18 Pancreas The pancreatic exocrine function involves the acinar cells secreting digestive enzymes that are transported into the small intestine by the pancreatic duct. Its endocrine function involves the secretion of insulin (produced by beta cells) and glucagon (produced by alpha cells) within the pancreatic islets. These two hormones regulate the rate of glucose metabolism in the body. The micrograph reveals pancreatic islets. LM \times 760.

Cells and Secretions of the Pancreatic Islets

The pancreatic islets each contain four varieties of cells:

- The **alpha cell** produces the hormone glucagon and makes up approximately 20 percent of each islet. Glucagon plays an important role in blood glucose regulation; low blood glucose levels stimulate its release.
- The **beta cell** produces the hormone insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.
- The **delta cell** accounts for four percent of the islet cells and secretes the peptide hormone somatostatin. Recall that somatostatin is also released by the hypothalamus (as GHIH), and the stomach and intestines also secrete it. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.
- The **PP cell** accounts for about one percent of islet cells and secretes the pancreatic polypeptide hormone. It is thought to play a role in appetite, as well as in the regulation of pancreatic exocrine and endocrine secretions. Pancreatic polypeptide released following a meal may reduce further food consumption; however, it is also released in response to fasting.

Regulation of Blood Glucose Levels by Insulin and Glucagon

Glucose is required for cellular respiration and is the preferred fuel for all body cells. The body derives glucose from the breakdown of the carbohydrate-containing foods and drinks we consume. Glucose not immediately taken up by cells for fuel can be stored by the liver and muscles as glycogen, or converted to triglycerides and stored in the adipose tissue. Hormones regulate both the storage and the utilization of glucose as required. Receptors located in the pancreas sense blood glucose levels, and subsequently the pancreatic cells secrete glucagon or insulin to maintain normal levels.

Glucagon

Receptors in the pancreas can sense the decline in blood glucose levels, such as during periods of fasting or during prolonged labor or exercise (Figure 17.19). In response, the alpha cells of the pancreas secrete the hormone **glucagon**, which has several effects:

- It stimulates the liver to convert its stores of glycogen back into glucose. This response is known as glycogenolysis. The glucose is then released into the circulation for use by body cells.
- It stimulates the liver to take up amino acids from the blood and convert them into glucose. This response is known as gluconeogenesis.
- It stimulates lipolysis, the breakdown of stored triglycerides into free fatty acids and glycerol. Some of the free glycerol released into the bloodstream travels to the liver, which converts it into glucose. This is also a form of gluconeogenesis.

Taken together, these actions increase blood glucose levels. The activity of glucagon is regulated through a negative feedback mechanism; rising blood glucose levels inhibit further glucagon production and secretion.

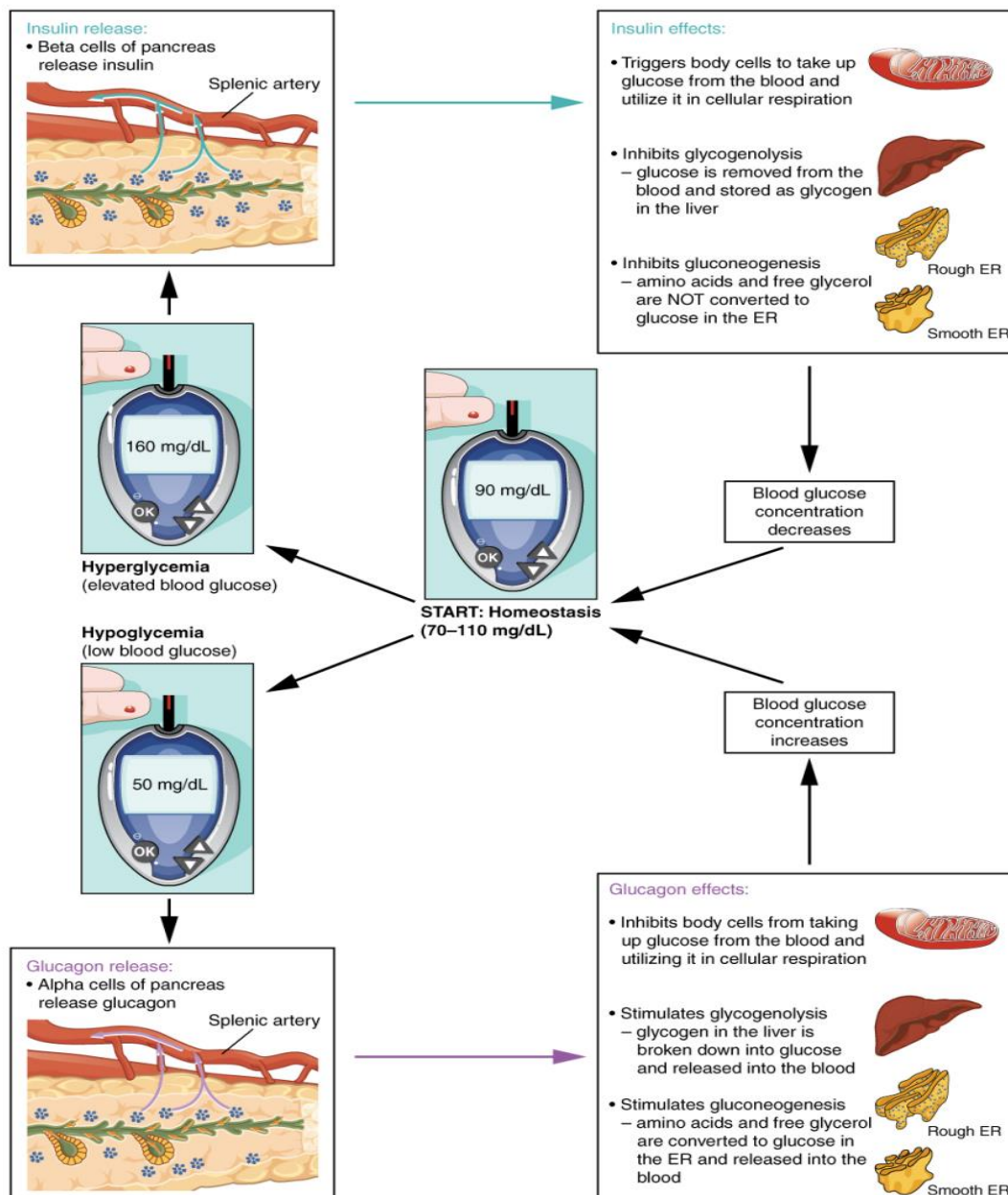


Figure 17.19 Homeostatic Regulation of Blood Glucose Levels Blood glucose concentration is tightly maintained between 70 mg/dL and 110 mg/dL. If blood glucose concentration rises above this range, insulin is released, which stimulates body cells to remove glucose from the blood. If blood glucose concentration drops below this range, glucagon is released, which stimulates body cells to release glucose into the blood.

Insulin

The primary function of **insulin** is to facilitate the uptake of glucose into body cells. Red blood cells, as well as cells of the brain, liver, kidneys, and the lining of the small intestine, do not have insulin receptors on their cell membranes and do not require insulin for glucose uptake. Although all other body cells do require insulin if they are to take glucose from the bloodstream, skeletal muscle cells and adipose cells are the primary targets of insulin.

The presence of food in the intestine triggers the release of gastrointestinal tract hormones such as glucose-dependent insulintropic peptide (previously known as gastric inhibitory peptide). This is in turn the initial trigger for insulin production and secretion by the beta cells of the pancreas. Once nutrient absorption occurs, the resulting surge in blood glucose levels further stimulates insulin secretion.

Precisely how insulin facilitates glucose uptake is not entirely clear. However, insulin appears to activate a tyrosine kinase receptor, triggering the phosphorylation of many substrates within the cell. These multiple biochemical reactions converge to support the movement of intracellular vesicles containing facilitative glucose transporters to the cell membrane. In the absence of insulin, these transport proteins are normally recycled slowly between the cell membrane and cell interior. Insulin triggers the rapid movement of a pool of glucose transporter vesicles to the cell membrane, where they fuse and expose the glucose transporters to the extracellular fluid. The transporters then move glucose by facilitated diffusion into the cell interior.

Insulin also reduces blood glucose levels by stimulating glycolysis, the metabolism of glucose for generation of ATP. Moreover, it stimulates the liver to convert excess glucose into glycogen for storage, and it inhibits enzymes involved in glycogenolysis and gluconeogenesis. Finally, insulin promotes triglyceride and protein synthesis. The secretion of insulin is regulated through a negative feedback mechanism. As blood glucose levels decrease, further insulin release is inhibited. The pancreatic hormones are summarized in **Table 17.7**.

Hormones of the Pancreas

Associated hormones	Chemical class	Effect
Insulin (beta cells)	Protein	Reduces blood glucose levels
Glucagon (alpha cells)	Protein	Increases blood glucose levels
Somatostatin (delta cells)	Protein	Inhibits insulin and glucagon release
Pancreatic polypeptide (PP cells)	Protein	Role in appetite

Table 17.7

| Organs with Secondary Endocrine Functions

By the end of this section, you will be able to:

- Identify the organs with a secondary endocrine function, the hormone they produce, and its effects

In your study of anatomy and physiology, you have already encountered a few of the many organs of the body that have secondary endocrine functions. Here, you will learn about the hormone-producing activities of the heart, gastrointestinal tract, kidneys, skeleton, adipose tissue, skin, and thymus.

Heart

When the body experiences an increase in blood volume or pressure, the cells of the heart's atrial wall stretch. In response, specialized cells in the wall of the atria produce and secrete the peptide hormone **atrial natriuretic peptide (ANP)**. ANP signals the kidneys to reduce sodium reabsorption, thereby decreasing the amount of water reabsorbed from the urine filtrate and reducing blood volume. Other actions of ANP include the inhibition of renin secretion and the initiation of the renin-angiotensin-aldosterone system (RAAS) and vasodilation. Therefore, ANP aids in decreasing blood pressure, blood volume, and blood sodium levels.

Gastrointestinal Tract

The endocrine cells of the GI tract are located in the mucosa of the stomach and small intestine. Some of these hormones are secreted in response to eating a meal and aid in digestion. An example of a hormone secreted by the stomach cells is gastrin, a peptide hormone secreted in response to stomach distention that stimulates the release of hydrochloric acid. Secretin is a peptide hormone secreted by the small intestine as acidic chyme (partially digested food and fluid) moves from the stomach. It stimulates the release of bicarbonate from the pancreas, which buffers the acidic chyme, and inhibits the further secretion of hydrochloric acid by the stomach. Cholecystokinin (CCK) is another peptide hormone released from the small intestine. It promotes the secretion of pancreatic enzymes and the release of bile from the gallbladder, both of which facilitate digestion. Other hormones produced by the intestinal cells aid in glucose metabolism, such as by stimulating the pancreatic beta cells to secrete insulin, reducing glucagon secretion from the alpha cells, or enhancing cellular sensitivity to insulin.

Kidneys

The kidneys participate in several complex endocrine pathways and produce certain hormones. A decline in blood flow to the kidneys stimulates them to release the enzyme renin, triggering the renin-angiotensin-aldosterone (RAAS) system, and stimulating the reabsorption of sodium and water. The reabsorption increases blood flow and blood pressure. The kidneys also play a role in regulating blood calcium levels through the production of calcitriol from vitamin D₃, which is released in response to the secretion of parathyroid hormone (PTH). In addition, the kidneys produce the hormone **erythropoietin (EPO)** in response to low oxygen levels. EPO stimulates the production of red blood cells (erythrocytes) in the bone marrow, thereby increasing oxygen delivery to tissues. You may have heard of EPO as a performance-enhancing drug (in a synthetic form).

Skeleton

Although bone has long been recognized as a target for hormones, only recently have researchers recognized that the skeleton itself produces at least two hormones. Fibroblast growth factor 23 (FGF23) is produced by bone cells in response

to increased blood levels of vitamin D₃ or phosphate. It triggers the kidneys to inhibit the formation of calcitriol from vitamin D₃ and to increase phosphorus excretion. Osteocalcin, produced by osteoblasts, stimulates the pancreatic beta cells to increase insulin production. It also acts on peripheral tissues to increase their sensitivity to insulin and their utilization of glucose.

Adipose Tissue

Adipose tissue produces and secretes several hormones involved in lipid metabolism and storage. One important example is **leptin**, a protein manufactured by adipose cells that circulates in amounts directly proportional to levels of body fat. Leptin is released in response to food consumption and acts by binding to brain neurons involved in energy intake and expenditure. Binding of leptin produces a feeling of satiety after a meal, thereby reducing appetite. It also appears that the binding of leptin to brain receptors triggers the sympathetic nervous system to regulate bone metabolism, increasing deposition of cortical bone. Adiponectin—another hormone synthesized by adipose cells—appears to reduce cellular insulin resistance and to protect blood vessels from inflammation and atherosclerosis. Its levels are lower in people who are obese, and rise following weight loss.

Skin

The skin functions as an endocrine organ in the production of the inactive form of vitamin D₃, cholecalciferol. When cholesterol present in the epidermis is exposed to ultraviolet radiation, it is converted to cholecalciferol, which then enters the blood. In the liver, cholecalciferol is converted to an intermediate that travels to the kidneys and is further converted to calcitriol, the active form of vitamin D₃. Vitamin D is important in a variety of physiological processes, including intestinal calcium absorption and immune system function. In some studies, low levels of vitamin D have been associated with increased risks of cancer, severe asthma, and multiple sclerosis. Vitamin D deficiency in children causes rickets, and in adults, osteomalacia—both of which are characterized by bone deterioration.

Thymus

The **thymus** is an organ of the immune system that is larger and more active during infancy and early childhood, and begins to atrophy as we age. Its endocrine function is the production of a group of hormones called **thymosins** that contribute to the development and differentiation of T lymphocytes, which are immune cells. Although the role of thymosins is not yet well understood, it is clear that they contribute to the immune response. Thymosins have been found in tissues other than the thymus and have a wide variety of functions, so the thymosins cannot be strictly categorized as thymic hormones.

Liver

The liver is responsible for secreting at least four important hormones or hormone precursors: insulin-like growth factor (somatomedin), angiotensinogen, thrombopoetin, and hepcidin. Insulin-like growth factor-1 is the immediate stimulus for growth in the body, especially of the bones. Angiotensinogen is the precursor to angiotensin, mentioned earlier, which increases blood pressure. Thrombopoetin stimulates the production of the blood's platelets. Hepcidins block the release of iron from cells in the body, helping to regulate iron homeostasis in our body fluids. The major hormones of these other organs are summarized in [Table 17.8](#).

Organs with Secondary Endocrine Functions and Their Major Hormones

Organ	Major hormones	Effects
Heart	Atrial natriuretic peptide (ANP)	Reduces blood volume, blood pressure, and Na ⁺ concentration
Gastrointestinal tract	Gastrin, secretin, and cholecystokinin	Aid digestion of food and buffering of stomach acids
Gastrointestinal tract	Glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide 1 (GLP-1)	Stimulate beta cells of the pancreas to release insulin
Kidneys	Renin	Stimulates release of aldosterone
Kidneys	Calcitriol	Aids in the absorption of Ca ²⁺
Kidneys	Erythropoietin	Triggers the formation of red blood cells in the bone marrow

Table 17.8

Organs with Secondary Endocrine Functions and Their Major Hormones

Organ	Major hormones	Effects
Skeleton	FGF23	Inhibits production of calcitriol and increases phosphate excretion
Skeleton	Osteocalcin	Increases insulin production
Adipose tissue	Leptin	Promotes satiety signals in the brain
Adipose tissue	Adiponectin	Reduces insulin resistance
Skin	Cholecalciferol	Modified to form vitamin D
Thymus (and other organs)	Thymosins	Among other things, aids in the development of T lymphocytes of the immune system
Liver	Insulin-like growth factor-1	Stimulates bodily growth
Liver	Angiotensinogen	Raises blood pressure
Liver	Thrombopoetin	Causes increase in platelets
Liver	Hepcidin	Blocks release of iron into body fluids

Table 17.8

| Development and Aging of the Endocrine System

By the end of this section, you will be able to:

- Describe the embryonic origins of the endocrine system
- Discuss the effects of aging on the endocrine system

The endocrine system arises from all three embryonic germ layers. The endocrine glands that produce the steroid hormones, such as the gonads and adrenal cortex, arise from the mesoderm. In contrast, endocrine glands that arise from the endoderm and ectoderm produce the amine, peptide, and protein hormones. The pituitary gland arises from two distinct areas of the ectoderm: the anterior pituitary gland arises from the oral ectoderm, whereas the posterior pituitary gland arises from the neural ectoderm at the base of the hypothalamus. The pineal gland also arises from the ectoderm. The two structures of the adrenal glands arise from two different germ layers: the adrenal cortex from the mesoderm and the adrenal medulla from ectoderm neural cells. The endoderm gives rise to the thyroid and parathyroid glands, as well as the pancreas and the thymus.

As the body ages, changes occur that affect the endocrine system, sometimes altering the production, secretion, and catabolism of hormones. For example, the structure of the anterior pituitary gland changes as vascularization decreases and the connective tissue content increases with increasing age. This restructuring affects the gland's hormone production. For example, the amount of human growth hormone that is produced declines with age, resulting in the reduced muscle mass commonly observed in the elderly.

The adrenal glands also undergo changes as the body ages; as fibrous tissue increases, the production of cortisol and aldosterone decreases. Interestingly, the production and secretion of epinephrine and norepinephrine remain normal throughout the aging process.

A well-known example of the aging process affecting an endocrine gland is menopause and the decline of ovarian function. With increasing age, the ovaries decrease in both size and weight and become progressively less sensitive to gonadotropins. This gradually causes a decrease in estrogen and progesterone levels, leading to menopause and the inability to reproduce. Low levels of estrogens and progesterone are also associated with some disease states, such as osteoporosis, atherosclerosis, and hyperlipidemia, or abnormal blood lipid levels.

Testosterone levels also decline with age, a condition called andropause (or viropause); however, this decline is much less dramatic than the decline of estrogens in women, and much more gradual, rarely affecting sperm production until very old age. Although this means that males maintain their ability to father children for decades longer than females, the quantity, quality, and motility of their sperm is often reduced.

As the body ages, the thyroid gland produces less of the thyroid hormones, causing a gradual decrease in the basal metabolic rate. The lower metabolic rate reduces the production of body heat and increases levels of body fat. Parathyroid hormones, on the other hand, increase with age. This may be because of reduced dietary calcium levels, causing a compensatory increase in parathyroid hormone. However, increased parathyroid hormone levels combined with decreased

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levels of calcitonin (and estrogens in women) can lead to osteoporosis as PTH stimulates demineralization of bones to increase blood calcium levels. Notice that osteoporosis is common in both elderly males and females.

Increasing age also affects glucose metabolism, as blood glucose levels spike more rapidly and take longer to return to normal in the elderly. In addition, increasing glucose intolerance may occur because of a gradual decline in cellular insulin sensitivity. Almost 27 percent of Americans aged 65 and older have diabetes.

KEY TERMS

- acromegaly** disorder in adults caused when abnormally high levels of GH trigger growth of bones in the face, hands, and feet
- adenylyl cyclase** membrane-bound enzyme that converts ATP to cyclic AMP, creating cAMP, as a result of G-protein activation
- adrenal cortex** outer region of the adrenal glands consisting of multiple layers of epithelial cells and capillary networks that produces mineralocorticoids and glucocorticoids
- adrenal glands** endocrine glands located at the top of each kidney that are important for the regulation of the stress response, blood pressure and blood volume, water homeostasis, and electrolyte levels
- adrenal medulla** inner layer of the adrenal glands that plays an important role in the stress response by producing epinephrine and norepinephrine
- adrenocorticotrophic hormone (ACTH)** anterior pituitary hormone that stimulates the adrenal cortex to secrete corticosteroid hormones (also called corticotropin)
- alarm reaction** the short-term stress, or the fight-or-flight response, of stage one of the general adaptation syndrome mediated by the hormones epinephrine and norepinephrine
- aldosterone** hormone produced and secreted by the adrenal cortex that stimulates sodium and fluid retention and increases blood volume and blood pressure
- alpha cell** pancreatic islet cell type that produces the hormone glucagon
- angiotensin-converting enzyme** the enzyme that converts angiotensin I to angiotensin II
- antidiuretic hormone (ADH)** hypothalamic hormone that is stored by the posterior pituitary and that signals the kidneys to reabsorb water
- atrial natriuretic peptide (ANP)** peptide hormone produced by the walls of the atria in response to high blood pressure, blood volume, or blood sodium that reduces the reabsorption of sodium and water in the kidneys and promotes vasodilation
- autocrine** chemical signal that elicits a response in the same cell that secreted it
- beta cell** pancreatic islet cell type that produces the hormone insulin
- calcitonin** peptide hormone produced and secreted by the parafollicular cells (C cells) of the thyroid gland that functions to decrease blood calcium levels
- chromaffin** neuroendocrine cells of the adrenal medulla
- colloid** viscous fluid in the central cavity of thyroid follicles, containing the glycoprotein thyroglobulin
- cortisol** glucocorticoid important in gluconeogenesis, the catabolism of glycogen, and downregulation of the immune system
- cyclic adenosine monophosphate (cAMP)** second messenger that, in response to adenylyl cyclase activation, triggers a phosphorylation cascade
- delta cell** minor cell type in the pancreas that secretes the hormone somatostatin
- diabetes mellitus** condition caused by destruction or dysfunction of the beta cells of the pancreas or cellular resistance to insulin that results in abnormally high blood glucose levels
- diacylglycerol (DAG)** molecule that, like cAMP, activates protein kinases, thereby initiating a phosphorylation cascade
- downregulation** decrease in the number of hormone receptors, typically in response to chronically excessive levels of a hormone

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endocrine gland tissue or organ that secretes hormones into the blood and lymph without ducts such that they may be transported to organs distant from the site of secretion

endocrine system cells, tissues, and organs that secrete hormones as a primary or secondary function and play an integral role in normal bodily processes

epinephrine primary and most potent catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called adrenaline

erythropoietin (EPO) protein hormone secreted in response to low oxygen levels that triggers the bone marrow to produce red blood cells

estrogens class of predominantly female sex hormones important for the development and growth of the female reproductive tract, secondary sex characteristics, the female reproductive cycle, and the maintenance of pregnancy

exocrine system cells, tissues, and organs that secrete substances directly to target tissues via glandular ducts

first messenger hormone that binds to a cell membrane hormone receptor and triggers activation of a second messenger system

follicle-stimulating hormone (FSH) anterior pituitary hormone that stimulates the production and maturation of sex cells

G protein protein associated with a cell membrane hormone receptor that initiates the next step in a second messenger system upon activation by hormone–receptor binding

general adaptation syndrome (GAS) the human body's three-stage response pattern to short- and long-term stress

gigantism disorder in children caused when abnormally high levels of GH prompt excessive growth

glucagon pancreatic hormone that stimulates the catabolism of glycogen to glucose, thereby increasing blood glucose levels

glucocorticoids hormones produced by the zona fasciculata of the adrenal cortex that influence glucose metabolism

goiter enlargement of the thyroid gland either as a result of iodine deficiency or hyperthyroidism

gonadotropins hormones that regulate the function of the gonads

growth hormone (GH) anterior pituitary hormone that promotes tissue building and influences nutrient metabolism (also called somatotropin)

hormone receptor protein within a cell or on the cell membrane that binds a hormone, initiating the target cell response

hormone secretion of an endocrine organ that travels via the bloodstream or lymphatics to induce a response in target cells or tissues in another part of the body

hyperglycemia abnormally high blood glucose levels

hyperparathyroidism disorder caused by overproduction of PTH that results in abnormally elevated blood calcium

hyperthyroidism clinically abnormal, elevated level of thyroid hormone in the blood; characterized by an increased metabolic rate, excess body heat, sweating, diarrhea, weight loss, and increased heart rate

hypoparathyroidism disorder caused by underproduction of PTH that results in abnormally low blood calcium

hypophyseal portal system network of blood vessels that enables hypothalamic hormones to travel into the anterior lobe of the pituitary without entering the systemic circulation

hypothalamus region of the diencephalon inferior to the thalamus that functions in neural and endocrine signaling

hypothyroidism clinically abnormal, low level of thyroid hormone in the blood; characterized by low metabolic rate, weight gain, cold extremities, constipation, and reduced mental activity

infundibulum stalk containing vasculature and neural tissue that connects the pituitary gland to the hypothalamus (also called the pituitary stalk)

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inhibin hormone secreted by the male and female gonads that inhibits FSH production by the anterior pituitary

inositol triphosphate (IP₃) molecule that initiates the release of calcium ions from intracellular stores

insulin-like growth factors (IGF) protein that enhances cellular proliferation, inhibits apoptosis, and stimulates the cellular uptake of amino acids for protein synthesis

insulin pancreatic hormone that enhances the cellular uptake and utilization of glucose, thereby decreasing blood glucose levels

leptin protein hormone secreted by adipose tissues in response to food consumption that promotes satiety

luteinizing hormone (LH) anterior pituitary hormone that triggers ovulation and the production of ovarian hormones in females, and the production of testosterone in males

melatonin amino acid–derived hormone that is secreted in response to low light and causes drowsiness

mineralocorticoids hormones produced by the zona glomerulosa cells of the adrenal cortex that influence fluid and electrolyte balance

neonatal hypothyroidism condition characterized by cognitive deficits, short stature, and other signs and symptoms in people born to women who were iodine-deficient during pregnancy

norepinephrine secondary catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called noradrenaline

osmoreceptor hypothalamic sensory receptor that is stimulated by changes in solute concentration (osmotic pressure) in the blood

oxytocin hypothalamic hormone stored in the posterior pituitary gland and important in stimulating uterine contractions in labor, milk ejection during breastfeeding, and feelings of attachment (also produced in males)

PP cell minor cell type in the pancreas that secretes the hormone pancreatic polypeptide

pancreas organ with both exocrine and endocrine functions located posterior to the stomach that is important for digestion and the regulation of blood glucose

pancreatic islets specialized clusters of pancreatic cells that have endocrine functions; also called islets of Langerhans

paracrine chemical signal that elicits a response in neighboring cells; also called paracrine factor

parathyroid glands small, round glands embedded in the posterior thyroid gland that produce parathyroid hormone (PTH)

parathyroid hormone (PTH) peptide hormone produced and secreted by the parathyroid glands in response to low blood calcium levels

phosphodiesterase (PDE) cytosolic enzyme that deactivates and degrades cAMP

phosphorylation cascade signaling event in which multiple protein kinases phosphorylate the next protein substrate by transferring a phosphate group from ATP to the protein

pineal gland endocrine gland that secretes melatonin, which is important in regulating the sleep-wake cycle

pinealocyte cell of the pineal gland that produces and secretes the hormone melatonin

pituitary dwarfism disorder in children caused when abnormally low levels of GH result in growth retardation

pituitary gland bean-sized organ suspended from the hypothalamus that produces, stores, and secretes hormones in response to hypothalamic stimulation (also called hypophysis)

progesterone predominantly female sex hormone important in regulating the female reproductive cycle and the maintenance of pregnancy

prolactin (PRL) anterior pituitary hormone that promotes development of the mammary glands and the production of breast milk

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protein kinase enzyme that initiates a phosphorylation cascade upon activation

second messenger molecule that initiates a signaling cascade in response to hormone binding on a cell membrane receptor and activation of a G protein

stage of exhaustion stage three of the general adaptation syndrome; the body's long-term response to stress mediated by the hormones of the adrenal cortex

stage of resistance stage two of the general adaptation syndrome; the body's continued response to stress after stage one diminishes

testosterone steroid hormone secreted by the male testes and important in the maturation of sperm cells, growth and development of the male reproductive system, and the development of male secondary sex characteristics

thymosins hormones produced and secreted by the thymus that play an important role in the development and differentiation of T cells

thymus organ that is involved in the development and maturation of T-cells and is particularly active during infancy and childhood

thyroid gland large endocrine gland responsible for the synthesis of thyroid hormones

thyroid-stimulating hormone (TSH) anterior pituitary hormone that triggers secretion of thyroid hormones by the thyroid gland (also called thyrotropin)

thyroxine (also, tetraiodothyronine, T₄) amino acid-derived thyroid hormone that is more abundant but less potent than T₃ and often converted to T₃ by target cells

triiodothyronine (also, T₃) amino acid-derived thyroid hormone that is less abundant but more potent than T₄

upregulation increase in the number of hormone receptors, typically in response to chronically reduced levels of a hormone

zona fasciculata intermediate region of the adrenal cortex that produce hormones called glucocorticoids

zona glomerulosa most superficial region of the adrenal cortex, which produces the hormones collectively referred to as mineralocorticoids

zona reticularis deepest region of the adrenal cortex, which produces the steroid sex hormones called androgens