Endocrine System

Hormones

Hormones are molecules that function as chemical signals. Endocrine cells usually aggregate as endocrine glands, where they typically arrange themselves as cords of cells. A notable exception is the thyroid gland, in which the cells are organized as microspheres called follicles. In addition to the glands, there are many isolated endocrine cells in the body, such as the endocrine cells of the digestive tract, the cells of the placenta, the cells of the heart that produce the atrial natriuretic factor, and the juxtaglomerular cells of the kidney. Most hormones act at a distance from the site of their secretion. Therefore, the endocrine cells are always very close to blood capillaries, which receive the secreted hormones and distribute them throughout the organism.

Endocrine glands are also target organs providing a way for the body to control hormone secretion through a mechanism of feedback and to keep blood hormonal levels within strict limits.

The endocrine system, however, does not act alone in the control of body functions. It interacts closely with the nervous system (mainly through the connection between the adenohypophysis and the central nervous system) and the immune system. Endocrine disfunctions may affect the immune response and vice versa.

Hypophysis (pituitary gland)

The **hypophysis** (Gr. *hypo,* under, + *physis,* growth), or **pituitary gland,** weighs about 0.5 g, and its normal dimensions in humans are about 10 x 13 x 6 mm. It lies in a cavity of the sphenoid bone—**the sella turcica**—an important radiological landmark. During embryogenesis, the hypophysis develops partly from oral ectoderm and partly from nerve tissue. The neural component arises as an evagination from the floor of the diencephalon and grows caudally as a stalk without detaching itself from the brain. The oral component arises as an outpocketing of ectoderm from the roof of the primitive mouth of the embryo and grows cranially, forming a structure called **Rathke's pouch.** Later, a constriction at the base of this pouch separates it from the oral cavity. At the same time, its anterior wall thickens, reducing the lumen of Rathke's pouch to a small fissure.

Because of its dual origin, the hypophysis actually consists of two glands—the **neurohypophysis** and the **adenohypophysis**—that are united anatomically but that have different functions. The **neurohypophysis,** the part of the hypophysis that develops from nerve tissue, consists of a large portion, the **pars nervosa,** and the smaller **infundibulum,** or **neural stalk**. The neural stalk is composed of the stem and median eminence. The part of the hypophysis that arises from oral ectoderm is known as the **adenohypophysis** and is subdivided into three portions: a large **pars distalis,** or **anterior lobe;** a cranial part, the **pars tuberalis,** which surrounds the neural stalk; and the **pars intermedia**.

The Hypothalamo-Hypophyseal System

Because of its embryological origin, the hypophysis is connected to the hypothalamus, with which it has important anatomic and functional relationships.

In the hypothalamo-hypophyseal system there are three known sites of production of hormones that liberate three groups of hormones:

1. The first group consists of peptides produced by aggregates (nuclei) of secretory neurons in the hypothalamus: the supraoptic and the paraventricular nuclei. The hormones are transported along the axons of these neurons and accumulate in the ends of these axons, which are situated in the neurohypophysis. These hormones are released by exocytosis, enter capillaries of the neurohypophysis, and are distributed by the blood.
2. The second group of peptide hormones is produced by neurons of the dorsal medial, ventral medial, and infundibular nuclei of the hypothalamus. These hormones are carried along axons that end in the median eminence where the hormones are stored. After being released these hormones enter the blood capillaries of the median eminence and are transported to the adenohypophysis through the first stretch of the hypophyseal portal system.
3. The third group of hormones consists of proteins and glycoproteins produced by cells of the pars distalis and liberated into blood capillaries of the second stretch of the portal system. These capillaries surround the secretory cells and distribute the hormones to the general circulation.

Adenohypophysis

Pars Distalis The main components of the pars distalis are cords of epithelial cells interspersed with capillaries. The hormones produced by these cells are stored as secretory granules. The few fibroblasts that are present produce reticular fibers that support the cords of hormone-secreting cells. The pars distalis accounts for 75% of the mass of the hypophysis. Common stains allow the recognition of three cell types in the pars distalis: **chromophobes** (Gr. *chroma*, color, + *phobos*, fear) and two types of **chromophils** (Gr. *chroma* + *philein*, to love) called **basophils** and **acidophils** according to their affinity for basic and acid dyes, respectively. The subtypes of basophil and acidophil cells are named for the hormones they produce. Chromophobes do not stain intensely and, when observed with an electron microscope, show two populations of cells. One has few secretory granules and the other has none. The group with no secretory granules probably contains undifferentiated cells and follicular cells. With the exception of the gonadotropic cell, which produces two hormones, the other cells produce only a single hormone. Many dyes have been used in attempts to distinguish the five types of hormone-secreting cells, but with little success. Immunocytochemical methods and electron microscopy are currently the only reliable techniques to distinguish these cell types. The hormones produced by the hypophysis have widespread physiological activity; they regulate almost all other endocrine glands, the secretion of milk, and the metabolism of muscle, bone, and adipose tissue.

Secretory Cells of the Pars Distalis.

Cell Type	**Stain Affinity**	**HormoneProduced**	**Main Physiological Activities**
Somatotropic cell	Acidophilic	Growth hormone (GH, somatotropin)	Anabolic activity: increased protein, DNA, RNA synthesis, increased blood glucose, increased use of fat in fat cells (some of these effects via insulin-like growth factor [IGF]-1, produced mainly in the liver)
			Stimulates growth of long bones via IGF-1 produced locally acting on differentiation of chondrocytes
Mammotropic cell	Acidophilic	Prolactin (PRL)	Promotes milk secretion (depends on earlier action of estrogen, progesterone, and placental hormones)
Gonadotropic cell	Basophilic	Follicle-stimulating hormone (FSH)	Promotes ovarian follicle development and estrogen secretion in women
			Stimulates spermatogenesis in men
		Luteinizing hormone (LH)	Promotes ovarian follicle maturation and progesterone secretion in women
			Leydig cell stimulation and androgen secretion in men
Thyrotropic cell	Basophilic	Thyrotropin (TSH)	Stimulates thyroid hormone synthesis, storage, and liberation
Corticotropic cell	Basophilic	Corticotropin (ACTH)	Stimulates secretion of adrenal cortex hormones
Melanotropes?	Basophilic	-Melanocyte-stimulating hormone? (-MSH)	Darkening of skin, inhibition of appetite in the hypothalamus, other actions

Pars Tuberalis The pars tuberalis is a funnel-shaped region surrounding the infundibulum of the neurohypophysis. Most of the cells of the pars tuberalis secrete gonadotropins (follicle-stimulating hormone and luteinizing hormone) and are arranged in cords alongside the blood vessels.

Pars Intermedia The pars intermedia, which develops from the dorsal portion of Rathke's pouch, is, in humans, a rudimentary region made up of cords and follicles of weakly basophilic cells that contain small secretory granules. -Melanocyte-stimulating hormone (-MSH) is probably produced in the intermediate zone, and probably also by basophils of the pars distalis.

Neurohypophysis:

The neurohypophysis consists of the pars nervosa and the neural stalk. The pars nervosa, unlike the adenohypophysis, does not contain secretory cells. It is composed of some 100,000 unmyelinated axons of secretory neurons situated in the supraoptic and paraventricular nuclei. The secretory neurons have all the characteristics of typical neurons, including the ability to conduct an action potential, but have well-developed Nissl bodies related to the production of the neurosecretory material. The neurosecretions are transported along the axons and accumulate at their endings in the pars nervosa. Here they form structures known as **Herring bodies,** which are visible in the light microscope. The electron microscope reveals that the Herring bodies contain many neurosecretory granules that have a diameter of 100–200 nm and are surrounded by a membrane. The granules are released and their content enters the fenestrated capillaries that exist in large numbers in the pars nervosa; the hormones are then distributed to the general c circulation.

The **neurosecretory material** consists of two hormones, both cyclic peptides made up of nine amino acids. The hormones have a slightly different amino acid composition, which results in different primary actions with some overlapping functions. They are **argininevasopressin**—also called **antidiuretic hormone** (**ADH**)—and **oxytocin.** Each hormone is joined to a binding protein (**neurophysin**). The hormone-neurophysin complex is synthesized as a single protein and is transported to the neurohypophysis where it is stored. Proteolysis of this protein yields the hormone and its specific binding protein. Vasopressin and oxytocin are released into the blood because of impulses in the nerve fibers from the hypothalamus. Although there is some overlap, the fibers from supraoptic nuclei are mainly concerned with vasopressin secretion, whereas most of the fibers from the paraventricular nuclei are concerned with oxytocin secretion.

Cells of the Neurohypophysis

Although the neurohypophysis consists mainly of *axons from hypothalamic neurons*, about 25% of its volume consists of a specific type of highly branched *glial cell called a* ***pituicyte****.*

Actions of the Hormones of the Neurohypophysis

Argininevasopressin or ADH is released in response to increased tonicity of the blood, usually resulting from water loss or intake of salt, which is recognized by osmoreceptor cells present in the hypothalamus. The main effect of ADH is to increase the permeability of collecting tubules of the kidney to water. As a result, more water is resorbed instead of being eliminated in the urine. Thus, vasopressin helps to regulate the osmotic balance of the internal milieu. In large doses, vasopressin may induce the contraction of smooth muscle of small arteries and arterioles. It is doubtful, however, if the amount of endogenous vasopressin is sufficient to exert any appreciable effect on blood pressure.

Oxytocin stimulates contraction of the myoepithelial cells that surround the alveoli and ducts of the mammary glands during nursing and of the smooth muscle of the uterine wall during copulation and childbirth. The secretion of oxytocin is stimulated by nursing or by distention of the vagina or the uterine cervix. This occurs via nerve tracts that act on the hypothalamus. The neurohormonal reflex triggered by nursing is called the **milk-ejection reflex**.

Adrenal (Suprarenal) Glands

The adrenal glands are paired organs that lie near the superior poles of the kidneys, embedded in adipose tissue. They are flattened structures with a half-moon shape; in the human, they are about 4–6 cm long, 1–2 cm wide, and 4–6 mm thick. Together they weigh about 8 g, but their weight and size vary with the age and physiological condition of the individual. Examination of a fresh section of adrenal gland shows that it is formed by two concentric layers: a yellow peripheral layer, the **adrenal cortex;** and a reddish-brown central layer, the **adrenal medulla**.

The layer immediately beneath the connective tissue capsule is the ***zona glomerulosa***, in which columnar or pyramidal cells are arranged in closely packed, rounded, or arched cords surrounded by capillaries.

The next layer of cells is known as the ***zona fasciculata*** because of the arrangement of the cells in one- or two-cell thick straight cords that run at right angles to the surface of the organ and have capillaries between them . The cells of the zona fasciculata are polyhedral, with a great number of lipid droplets in their cytoplasm. As a result of the dissolution of the lipids during tissue preparation, the fasciculata cells appear vacuolated in common histological preparations. Because of their vacuolization, the cells of the fasciculata are also called **spongyocytes.**

The ***zona reticularis***, the innermost layer of the cortex, lies between the zona fasciculata and the medulla; it contains cells disposed in irregular cords that form an anastomosing network. These cells are smaller than those of the other two layers. Lipofuscin pigment granules in the cells are large and quite numerous. Irregularly shaped cells with pyknotic nuclei—suggesting cell death—are often found in this layer.

Cortical Hormones & Their Actions

Adrenal steroids originate from modifications of the molecule of cholesterol. Cholesterol is obtained by the cortical cells from the blood (mainly as low-density lipoproteins [LDL] and, secondarily, can be synthesized from acetate (in the form of acetyl coenzyme A) in the smooth endoplasmic reticulum. Cholesterol is converted to the final hormones partly in the mitochondria and partly in the smooth endoplasmic reticulum—a clear example of collaboration between two cell organelles.

The steroids secreted by the cortex can be divided into three groups, according to their main physiological action: **mineralocorticoids, glucocorticoids,** and **androgens**. The main product of the zona glomerulosa is a mineralocorticoid called **aldosterone;** the zona fasciculata and possibly the zona reticularis secrete glucocorticoids, especially **cortisol;** the zona reticularis produces **dehydroepiandrosterone,** a weak androgen.

The adrenal cortex and the adrenal medulla can be considered two organs with distinct origins, functions, and morphological characteristics that became united during embryonic development. They arise from different germ layers. The cortex arises from the coelomic epithelium, whereas the cells of the medulla derive from the neural crest, from which sympathetic ganglion cells also originate.

The general histological appearance of the adrenal gland is typical of an endocrine gland in which cells of both cortex and medulla are grouped in cords along capillaries.

The dense connective tissue capsule that covers the adrenal gland sends thin septa to the interior of the gland as trabeculae. The stroma consists mainly of a rich network of reticular fibers that supports the secretory cells.

Adrenal Cortex

The cells of the adrenal cortex, which have the typical ultrastructure of steroid-secreting cells, do not store their secretory products in granules; rather, they synthesize and secrete steroid hormones upon demand. Steroids, being low-molecular-weight lipid-soluble molecules, diffuse through the plasma membrane and do not require the specialized process of exocytosis for their release.

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The **mineralocorticoids** act mainly on the distal renal tubules as well as on the gastric mucosa, colon, and salivary and sweat glands, stimulating the reabsorption of sodium by epithelial cells.

The **glucocorticoids** affect the metabolism of carbohydrates by stimulating both the production of glucose from amino acids or fatty acids (gluconeogenesis) and the conversion of glucose into glycogen. Cortisol may decrease the uptake of glucose by cells, which together with the increased production of glucose may lead to hyperglycemia or to the maintenance of adequate levels of glucose in the blood during hunger and stress reactions. In the skin, muscle and adipose tissue, glucocorticoids not only decrease synthetic activity but also promote protein and lipid degradation. The by-products of degradation, amino acids and fatty acids, are removed from the blood and used by the hepatocytes for gluconeogenesis and protein synthesis.

Glucocorticoids also suppress the immune response by destroying circulating lymphocytes, inhibiting mitotic activity in lymphocyte-forming organs, and controlling secretion of cytokines.

The separation of steroids produced by the adrenal cortex into glucocorticoids and mineralocorticoids is, however, somewhat arbitrary, because most glucocorticoids also act on ion transport.

Dehydroepiandrosterone (DHEA) is the only sex hormone that is secreted in significant physiological quantities by the adrenal cortex. DHEA is a weak androgen that circulates in the blood as a sulfate and exerts its actions after being converted into testosterone in several tissues.

Adrenal Medulla

The adrenal medulla is composed of polyhedral cells arranged in cords or clumps and supported by a reticular fiber network. A profuse capillary supply intervenes between adjacent cords, and there are a few parasympathetic ganglion cells. The medullary cells arise from neural crest cells, as do the postganglionic neurons of sympathetic and parasympathetic ganglia. Thus, the cells of the adrenal medulla can be considered modified sympathetic postganglionic neurons that have lost their axons and dendrites during embryonic development and have become secretory cells.

Medullary cells have abundant membrane-limited electron-dense secretory granules, 150–350 nm in diameter. These granules contain one or the other of the catecholamines, **epinephrine** or **norepinephrine.** The secretory granules also contain adenosine triphosphate (ATP), proteins called **chromogranins** (which may serve as binding proteins for catecholamines), dopamine -hydroxylase (which converts dopamine to norepinephrine), and opiatelike peptides (enkephalins) .

A large body of evidence shows that epinephrine and norepinephrine are secreted by two different types of cells in the medulla. When observed with the transmission electron microscope epinephrine-secreting cells show smaller and less electron-dense granules, whose contents fill the granule. Norepinephrine-secreting cells have larger, more electron-dense granules. Their content is irregular in shape, and there is an electronlucent layer beneath the surrounding membrane. About 80% of the catecholamine output of the adrenal vein is epinephrine.

Unlike the cortex, which does not store steroids, cells of the medulla accumulate and store their hormones in granules. The adrenal medullary cells are innervated by cholinergic endings of preganglionic sympathetic neurons. Glucocorticoids produced in the cortex, which reach the medulla through capillaries that bathe cells of the cortex, constitute another mechanism of control.

Islets of Langerhans

The islets of Langerhans are multihormonal endocrine microorgans; they appear as rounded clusters of cells embedded within the exocrine pancreatic tissue.

Although most islets are 100–200 µm in diameter and contain several hundred cells, small groups of endocrine cells are also found interspersed among the pancreatic exocrine cells. There may be more than 1 million islets in the human pancreas, with a slight tendency for islets to be more abundant in the tail of the pancreas. A fine capsule of reticular fibers surrounds each islet, separating it from the adjacent pancreatic tissue.

Each islet consists of lightly stained polygonal or rounded cells, arranged in cords separated by a network of blood capillaries.

Routine stains or trichrome stains allow the recognition of acidophils (α) and basophils (β) . Using immunocytochemical methods, four types of cells—A, B, D, and F—have been recognized in the islets.. The ultrastructure of these cells resembles that of cells synthesizing polypeptides. The secretory granules of cells of the islets vary according to the species studied. In humans, the A cells have regular granules with a dense core surrounded by a clear region bounded by a membrane. The B (insulin-producing) cells have irregular granules with a core formed of irregular crystals of insulin in complex with zinc.

The relative quantities of the four cell types found in islets are not uniform; they vary considerably with the islet's location in the pancreas. Table 20–3 summarizes the types, quantities, and functions of the hormones produced by the islet cells.

Table 20-3. Cell Types in Human Islets of Langerhans.

Cell Type	Quantity	Position	Hormone Produced	Hormonal Function
A	20%	Usually in periphery	Glucagon	Acts on several tissues to make energy stored in glycogen and fat available through glycogenolysis and lipolysis; increases blood glucose content
B		Central region	Insulin	Acts on several tissues to cause entry of glucose into cells and promotes decrease of blood glucose content

	70%			
D	<5%	Variable	Somatostatin	Inhibits release of other islet cell hormones through local paracrine action
F	Rare	Variable	Pancreatic polypeptide	Control of gastric secretion? Control of secretion of the exocrine

Both the endocrine cells and the blood vessels of the islets are innervated by autonomic nerve fibers. Sympathetic and parasympathetic nerve endings have been found in close association with about 10% of the A, B, and D cells. These nerves function as part of the insulin and glucagon control system. Gap junctions presumably transfer the ionic changes associated with autonomic discharge to the other cells.

Thyroid

The thyroid gland, located in the cervical region anterior to the larynx, consists of two lobes united by an isthmus. It originates in early embryonic life from the endoderm of the initial portion of the primitive gut. Its function is to synthesize the hormones thyroxine (T_4) and triiodothyronine (T_3), which are important for growth, for cell differentiation, and for the control of oxygen consumption and the basal metabolic rate in the body. Thyroid hormones affect the metabolism of proteins, lipids, and carbohydrates. Thyroid tissue is composed of 20–30 million microscopic spheres called **thyroid follicles.** The follicles are lined by a simple epithelium and their central cavity contains a gelatinous substance called **colloid**. The thyroid is the only endocrine gland whose secretory product is stored in great quantity. This accumulation is also unusual in that it occurs in the extracellular colloid. In humans, there is sufficient hormone within the follicles to supply the organism for up to 3 months. Thyroid colloid is composed of a glycoprotein of high molecular mass (660 kDa) called **thyroglobulin.** In sections, follicular cells range from squamous to columnar and the follicles have an extremely variable diameter. The gland is covered by a loose connective tissue capsule that sends septa into the parenchyma. As these septa gradually become thinner they reach all the follicles, separating them from one another by fine, irregular connective tissue composed mainly of reticular fibers. The thyroid is an extremely vascularized organ, with an extensive blood and lymphatic capillary network surrounding the follicles. Endothelial cells of these capillaries are fenestrated, as they are in other endocrine glands. This configuration facilitates the transport of molecules between the gland cells and the blood capillaries.

The morphological appearance of thyroid follicles varies according to the region of the gland and its functional activity. In the same gland, larger follicles that are full of colloid and have a cuboidal or squamous epithelium are found alongside follicles that are lined by columnar epithelium. Despite this variation, the gland is considered hypoactive when the average composition of these follicles is squamous.

The thyroid epithelium rests on a basal lamina. Its cells exhibit the characteristics of a cell that simultaneously synthesizes, secretes, absorbs, and digests proteins (Figures 20–27 and 20–28). The basal part of these cells is rich in rough endoplasmic reticulum. The nucleus is generally round and situated in the center of the cell. The apical pole has a discrete Golgi complex and small secretory granules whose content is similar to that of the follicular colloid. Abundant lysosomes, 0.5–0.6 µm in diameter, and some large phagosomes are found in this region. The cell membrane of the apical pole has a moderate number of microvilli. Mitochondria and cisternae of rough endoplasmic reticulum are dispersed throughout the cytoplasm.

Another type of cell present in the thyroid, the **parafollicular,** or **C, cell,** is found as part of the follicular epithelium or as isolated clusters between thyroid follicles (Figures 20–26 and 20–28). Parafollicular cells are larger than thyroid follicular cells and with the light microscope appear less stained. They have a small amount of rough endoplasmic reticulum, long mitochondria, and a large Golgi complex. The most striking feature of these cells is their numerous small (100–180 nm in diameter) granules containing hormone. These cells are responsible for the synthesis and secretion of **calcitonin,** a hormone whose main effect is to lower blood calcium levels by inhibiting bone resorption. Secretion of calcitonin is triggered by an elevation in blood calcium concentration.

Control of the Thyroid

The major regulator of the anatomic and functional state of the thyroid is thyroid-stimulating hormone (TSH; thyrotropin), secreted by the anterior pituitary. TSH stimulates all stages of production and release of thyroid hormones. Thyroid hormones inhibit the synthesis of TSH maintaining an adequate quantity of T_4 and T_3 in the organism. TSH increases the height of the follicular epithelium and decreases the quantity of the colloid and the size of the follicles. The cell membrane of the basal portion of follicular cells is rich in receptors for thyrotropin. Secretion of thyrotropin is also increased by exposure to cold and decreased by heat and stressful stimuli.

Synthesis & Accumulation of Hormones by Follicular Cells

Synthesis and accumulation of hormones take place in four stages: synthesis of thyroglobulin, uptake of iodide from the blood, activation of iodide, and iodination of the tyrosine residues of thyroglobulin.

1. **Synthesis of thyroglobulin** is similar to that in other protein-exporting cells. Briefly, the secretory pathway consists of the synthesis of protein in

the rough endoplasmic reticulum, the addition of carbohydrate in the endoplasmic reticulum and the Golgi complex, and the release of thyroglobulin from formed vesicles at the apical surface of the cell into the lumen of the follicle.

2. The **uptake of circulating iodide** is accomplished in the thyroid follicular cells by a membrane transport protein. This protein, called the Na/I symporter (NIS), is located in the basolateral membrane of the follicular cells and simultaneously carries two molecules, sodium and iodide. Serum iodine plays an important role in regulating thyroid function because low iodine levels increase the amount of NIS and thus increase the uptake, compensating for the lower serum concentration.

3. Iodide is **oxidized** by thyroid peroxidase and is transported into the follicle cavity by an anion transporter called pendrin.

4. Within the colloid occurs the **iodination of tyrosine residues** of thyroglobulin, also catalyzed by thyroid peroxidase, resulting in the formation of monoiodotyrosine and diiodotyrosine. The coupling of these molecules produces the hormones T_3 and T_4, which become part of the much larger thyroglobulin molecule.

Liberation of T_3 & T_4

When stimulated by TSH, thyroid follicular cells take up colloid by endocytosis. The colloid within the endocytic vesicles is then digested by lysosomal enzymes. Hydrolysis of thyroglobulin results in T_4, T_3, diiodotyrosine, and monoiodotyrosine, which are liberated into the cytoplasm. The free T_4 and T_3 cross the basolateral cell membrane and are discharged into the capillaries. Monoiodotyrosine and diiodotyrosine are not secreted into the blood, and their iodine is removed by a deiodinase. The products of this enzymatic reaction, iodine and tyrosine, are reused by the follicular cells. T_4 is the more abundant compound, constituting 90% of the circulating thyroid hormone, although T_3 acts more rapidly and is more potent.

Parathyroid Glands

The parathyroids are four small glands—3 x 6 mm—with a total weight of about 0.4 g. They are located behind the thyroid gland, one at each end of the upper and lower poles, usually in the capsule that covers the lobes of the thyroid. Sometimes they are embedded in the thyroid gland. The parathyroid glands are derived from the pharyngeal pouches—the superior glands from the fourth pouch and the inferior glands from the third pouch. They can also be found in the mediastinum, lying beside the thymus, which originates from the same pharyngeal pouches.

Each parathyroid gland is contained within a connective tissue capsule. These capsules send septa into the gland, where they merge with the reticular fibers that support elongated cordlike clusters of secretory cells.

The endocrine cells of the parathyroid are arranged in cords. There are two types of cells: the chief, or principal, cells and the oxyphil cells.

The **chief cells** are small polygonal cells with a vesicular nucleus and a pale-staining, slightly acidophilic cytoplasm. Electron microscopy shows irregularly shaped granules (200–400 nm in diameter) in their cytoplasm. They are the secretory granules containing **parathyroid hormone,** which is a polypeptide in its active form. **Oxyphil cells** constitute a smaller population. They are larger polygonal cells, and their cytoplasm contains many acidophilic mitochondria with abundant cristae. The function of the oxyphil cells is not known.

Action of Parathyroid Hormone & Its Interrelation with Calcitonin

Parathyroid hormone binds to receptors in osteoblasts. This is a signal for these cells to produce an osteoclast-stimulating factor, which increases the number and activity of osteoclasts and thus promotes the absorption of the calcified bone matrix and the release of Ca^{2+} into the blood. The resulting increase in the concentration of Ca^{2+} in the blood suppresses the production of parathyroid hormone. Calcitonin from the thyroid gland also influences osteoclasts by inhibiting both their resorptive action on bone and the liberation of Ca^{2+}. Calcitonin thus lowers blood Ca^{2+} concentration and increases osteogenesis; its effect is opposite to that of parathyroid hormone. These hormones constitute a dual mechanism to regulate blood levels of Ca^{2+}, an important factor in homeostasis.

In addition to increasing the concentration of Ca^{2+}, parathyroid hormone reduces the concentration of phosphate in the blood. This effect is a result of the activity of parathyroid hormone on kidney tubule cells, diminishing the absorption of phosphate and causing an increase of phosphate excretion in urine. Parathyroid hormone indirectly increases the absorption of Ca^{2+} from the gastrointestinal tract by stimulating the synthesis of vitamin D, which is necessary for this absorption. The secretion of parathyroid cells is regulated by blood Ca^{2+} levels.

Pineal Gland

The pineal gland is also known as the **epiphysis cerebri,** or **pineal body.** In the adult, it is a flattened conical organ situated on the roof of the diencephalons, measuring approximately 5–8 mm in length and 3–5 mm at its greatest width and weighing about 120 mg.

The pineal gland is covered by pia mater. Connective tissue septa containing blood vessels and unmyelinated nerve fibers originate in the pia mater and penetrate the pineal tissue. Along with the capillaries, they surround the cellular cords and follicles, forming irregular lobules.

The pineal gland consists of several types of cells, principally **pinealocytes** and astrocytes. Pinealocytes have a slightly basophilic cytoplasm with large irregular or lobate nuclei and sharply defined nucleoli. When impregnated with silver salts, the pinealocytes appear to have long and tortuous branches reaching out to the vascular connective tissue septa, where they end as flattened dilatations. These cells produce **melatonin** and some ill-defined pineal peptides.

The **astrocytes** of the pineal gland are a specific type of cell characterized by elongated nuclei that stain more heavily than do those of parenchymal cells. They are observed between the cords of pinealocytes and in perivascular areas. These cells have long cytoplasmic processes that contain a large number of intermediate filaments 10 nm in diameter.