The Endocrine System

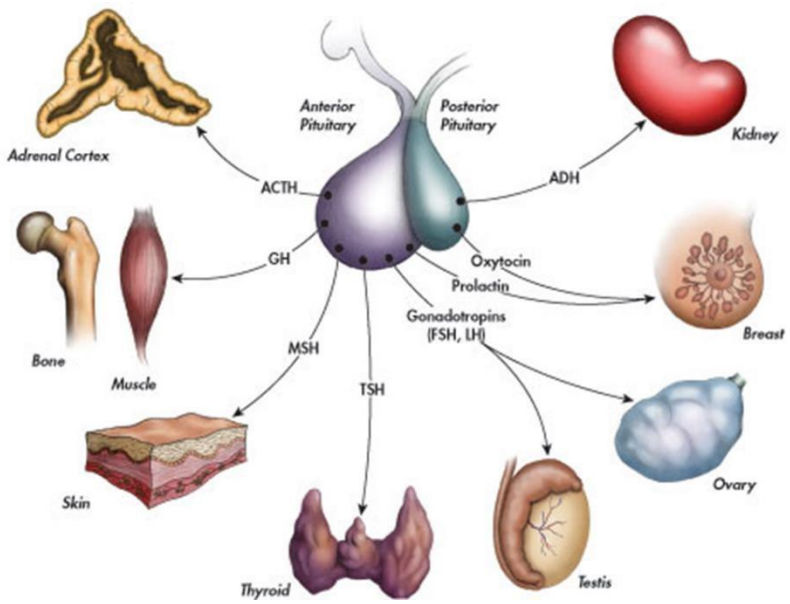
Endocrine glands **don't** have ducts. Their secretions (hormones) are secreted into the blood stream. Because of this, the hormones can act over long distances, and reach any organ in the body to co-ordinate activity. The endocrine glands include the pituitary gland, the thyroid gland, the parathyroid glands, pineal gland, the suprarenal glands (the adrenals), and islets of Langerhans.

Hormones

Hormones are molecules that function in the body as chemical signals, also called chemical transmitter, it is released in small amounts from glands, and is transported in the bloodstream to target organs or other cells. So that hormones are chemical messengers, transferring information and instructions from one set of cells to another.

Hormones regulate growth, development, mood, tissue function, metabolism, and sexual function.

Hyposecretion or hypersecretion of any hormone can be harmful to the body controlling the production of hormones can treat many hormonal disorders in the body.



They are liberated by specialized cells that are called **endocrine cells**.

Many endocrine cells, however, produce hormones that act at **a short distance**. This is called **paracrine secretion** and **juxtacrine secretion**.

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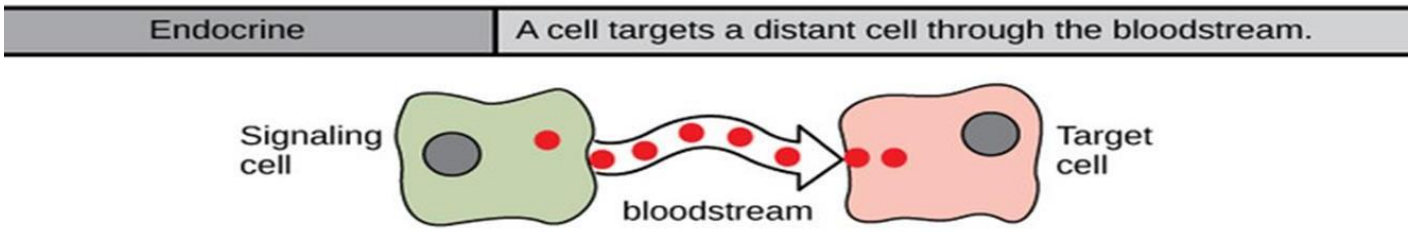
What types of signals do cells use to communicate?

Cells not only interact with their immediate microenvironment, but may also detect and respond to signals originating much further away. Signaling pathways may be classified according to the source of a signaling molecule or ligand.

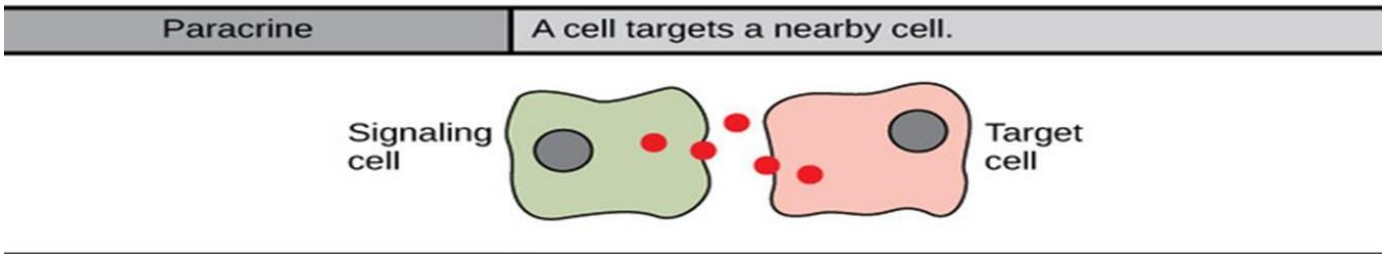
Endocrine signaling:

Endocrine signaling is an example of long-distance communication between hormone producing cells, tissues and glands and cells that express hormone receptor molecules. The hormones are usually secreted into the blood stream before being distributed throughout the body. Endocrine signals often originate from within the brain, however other glands and organs, including the thyroid gland, pancreas, liver, kidneys and reproductive organs, also produces hormones. One endocrine signal that must travel a great distance is that of follicle-stimulating hormone (FSH), which is sent from the anterior pituitary gland to the testes or ovaries where it stimulates the maturation of germ cells.



Paracrine signaling:

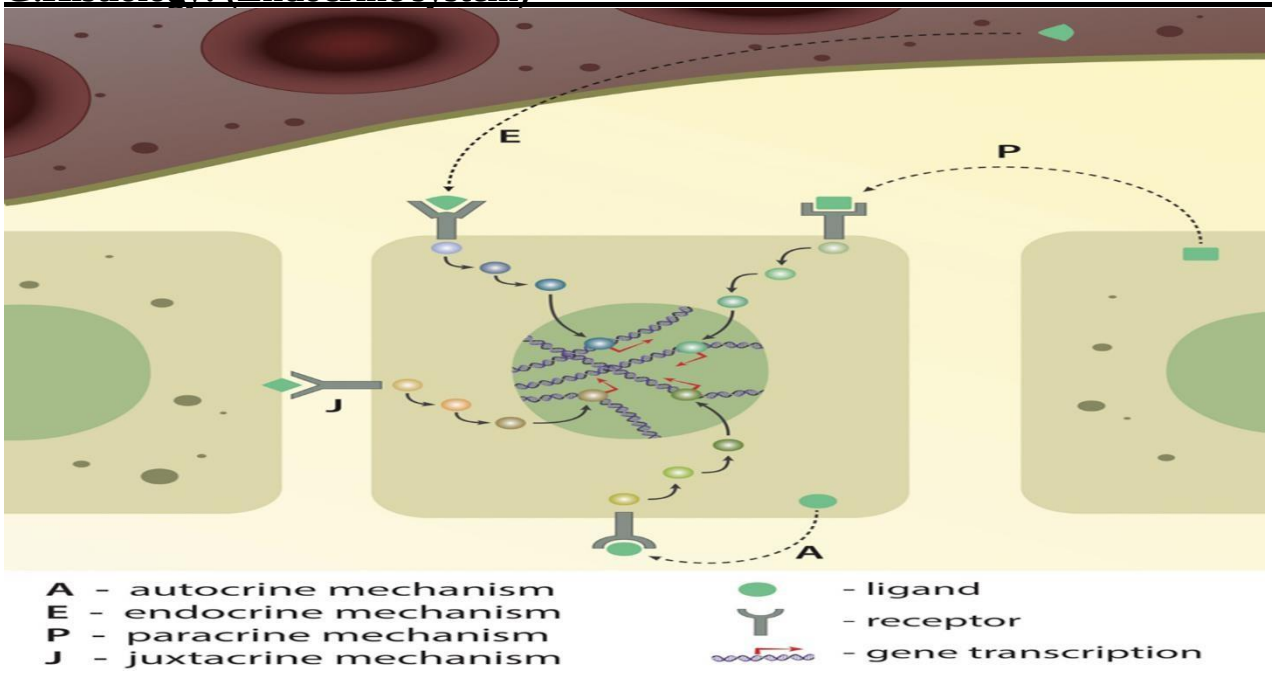
Paracrine signaling occurs between cells in close proximity to each other. A soluble signaling molecule secreted by one cell diffuses to another cell in the local neighborhood. For instance, neurotransmitters secreted by neurons diffuse a few nanometers before binding to receptors on target neurons or muscle cells. Another example is the release of chemokines by neutrophils, which attract other cells through a process known as chemotaxis.



Juxtacrine signaling:

Juxtacrine signaling occurs between neighboring cells that are in physical contact with each other. In this case, the signaling molecule is not free, but is instead bound to the membrane of the cell. It may then interact with a receptor on the membrane of an adjacent cell. An example of juxtacrine signaling is the cell-cell junctions that contain cadherin complexes also work in a similar manner

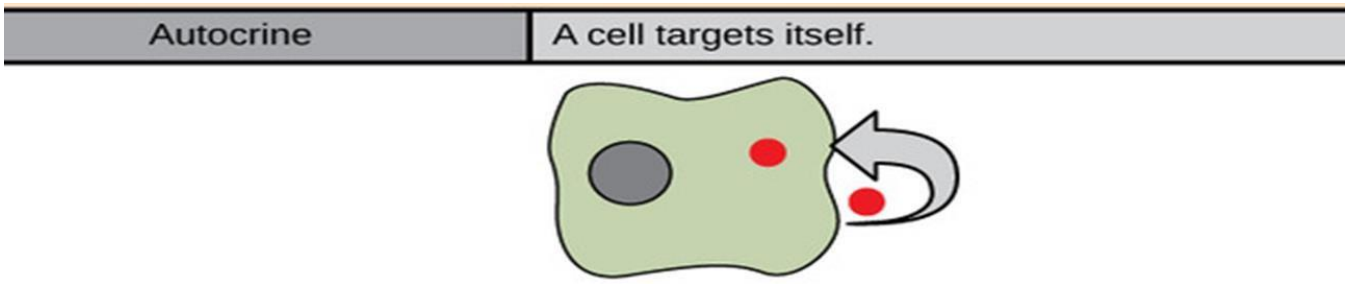
G.Histiology: (Endocrine system)



Autocrine signaling:

In autocrine signaling, the signaling molecule originates from the target cell itself. This occurs when cells express receptors to a ligand they secrete. For example, blood platelets secrete eicosanoids, which influence their own activity.

In autocrine secretion, cells may produce molecules that act on themselves or on cells of the same type. Insulin-like growth factor (IGF) produced by several cell types may act on the same cells that produced it.

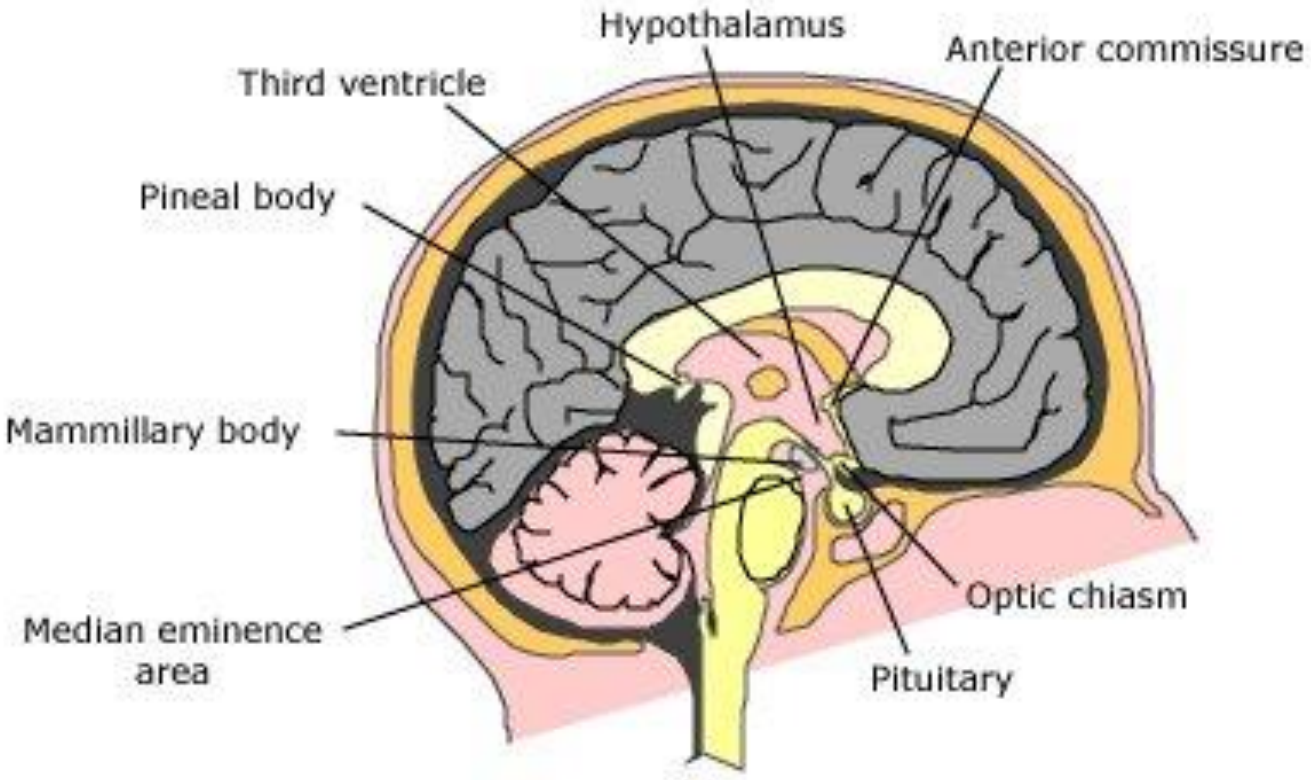


The tissues and organs on which the hormones act are called **target tissues** or **target organs**.

Endocrine glands are also target organs, the body is able to control hormone secretion through a **mechanism of feedback** and to keep blood hormonal levels within strict limits.

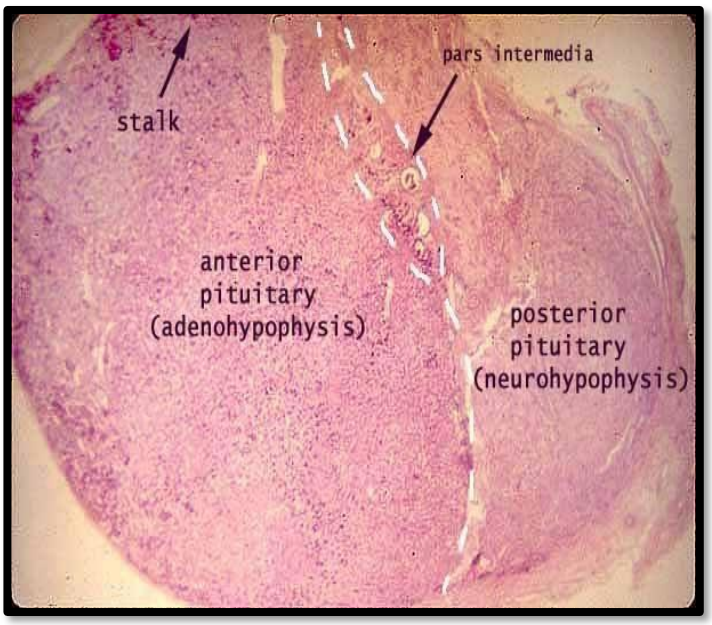
G.Histiology: (Endocrine system)

Pituitary Gland (Hypophysis)



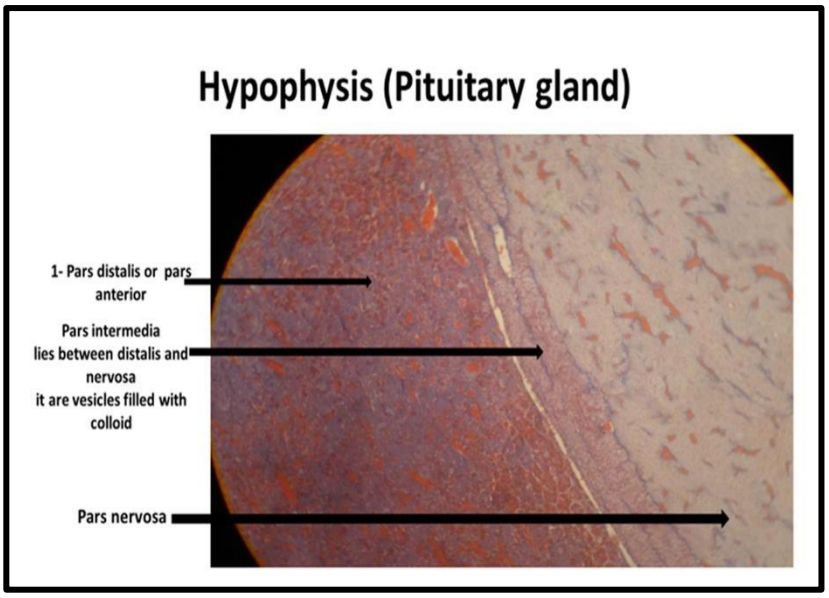
G.Histiology: (Endocrine system)

The pituitary (also known as the hypophysis) is found at the base of the brain, about 1cm in diameter, lying beneath the third ventricle in a bony cavity **(sella turcica)** in the base of the skull. The pituitary gland produces hormones that regulate **growth, metabolism, and reproduction. Composed 2 parts:**



1-The posterior part

(Neurohypophysis) of the pituitary has **its embryological origins in nervous tissue.** It is formed from a *downgrowth* of the diencephalon that forms the floor of the third ventricle.



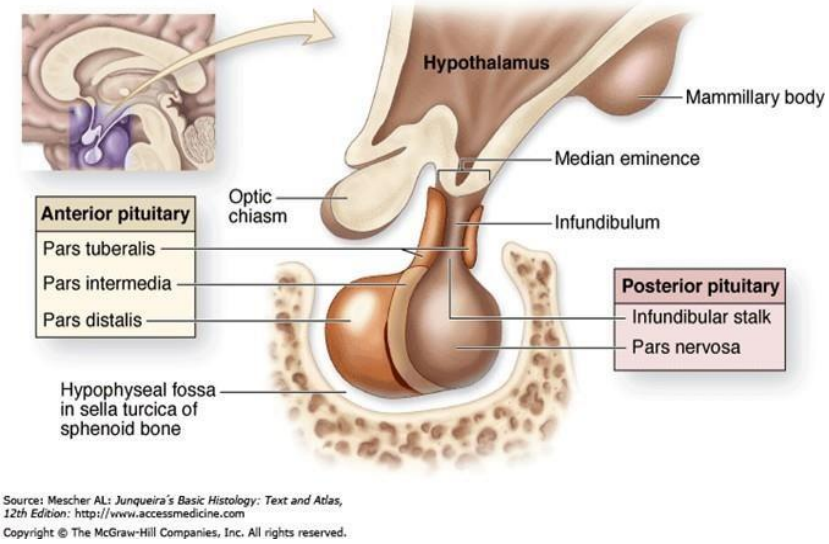
The **neurohypophysis** consists of a large portion, the **pars nervosa,** and the smaller **infundibulum or neural stalk**. The neural stalk is composed of the stem and median eminence.

2-The anterior part (Adenohypophysis) is derived from an *upgrowth* from the **oral ectoderm of the primitive oral** cavity called **Rathke's pouch.**

Along the posterior part of the anterior lobe there is a narrow region called the **pars intermedia**. The pars intermedia is poorly developed in humans.

G.Histiology: (Endocrine system)

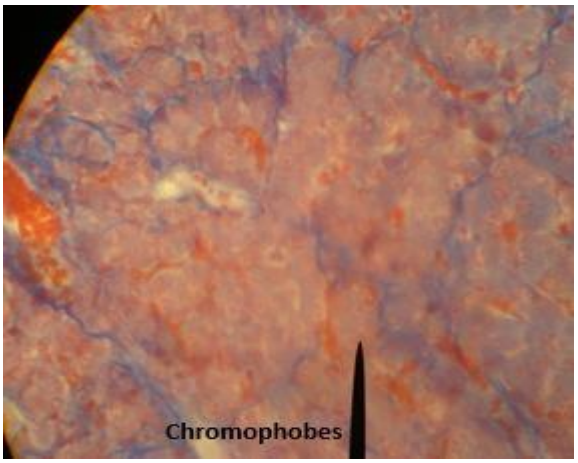
- **Adenohypophysis (Anterior part)**
- **1-Pars Distalis (Anterior lobe)**



The pars distalis of the adenohypophysis accounts for about 75% of the hypophyseal tissue.

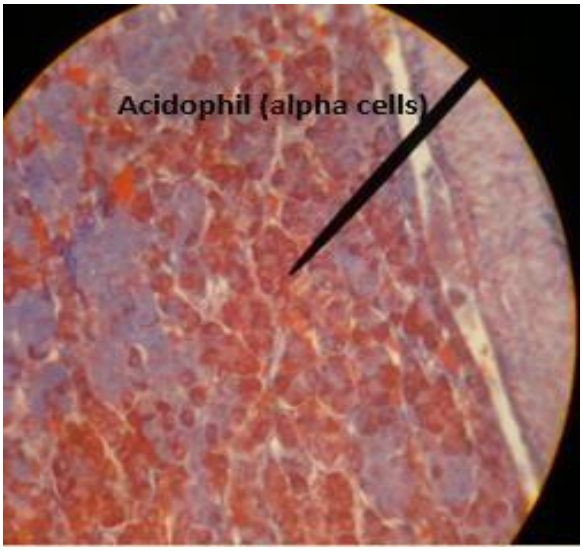
The main components of the pars distalis are **cords of epithelial cells** interspersed with capillaries.

Common stains allow the recognition of **3 cell types in the pars distalis: chromophobes** and 2 types of **chromophils** called **basophils** and **acidophils** according to their affinity for basic and acid dyes:



Chromophobe cells: Chromophobe cells are unstained or weakly stained cells.

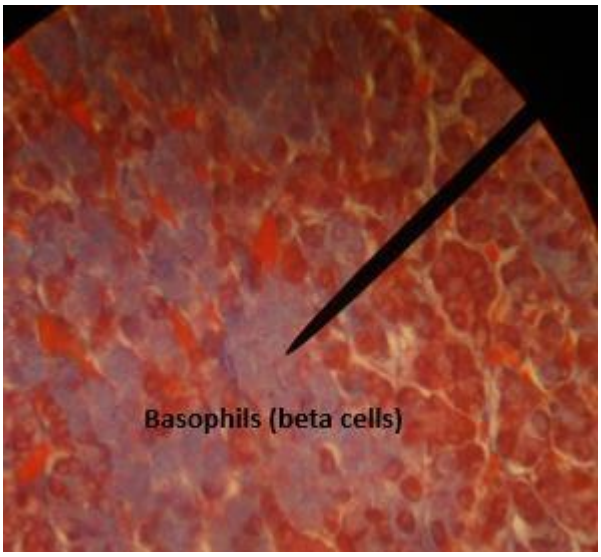
Acidophil cells (or acidophils): Acidophils are rounded cells and typically smaller than basophil cells. Acidophils account for roughly 65% of the cells in the adenohypophysis.



- The most frequent subtype of acidophils are the **somatotrophs** (which can be stained with the dye orange G). Somatotrophs produce **growth hormone** (GH or somatotropin), which e.g. stimulates liver cells to produce polypeptide growth factors which stimulate growth.

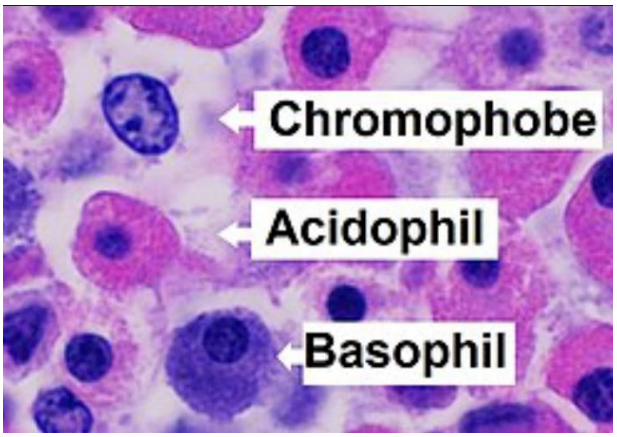
- **Mammotrophs** (or lactotrophs), the second group of acidophils secrete prolactin. Their number increases significantly in late pregnancy and the early months of lactation.

1- **Basophil cells (or basophils):** Based on their hormone products basophils are divided into three subtypes.



- **Thyrotrophs** produce thyroid stimulati ng hormone (**TSH or thyrotropin**).
- **Gonadotrophs** produce follicle stimulat ing hormone (**FSH**), which stimulates the seminiferous epithelium in males in addition to early follicular growth in females. Gonadotrophs also produce luteinizing hormone (**LH**)

- **Corticotrophs** (or adrenocorticolipotrophs) secrete adrenocorticotropic hormone (ACTH or corticotropin) and lipotropin (LPH, no known function in humans).



2- Pars Tuberalis

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

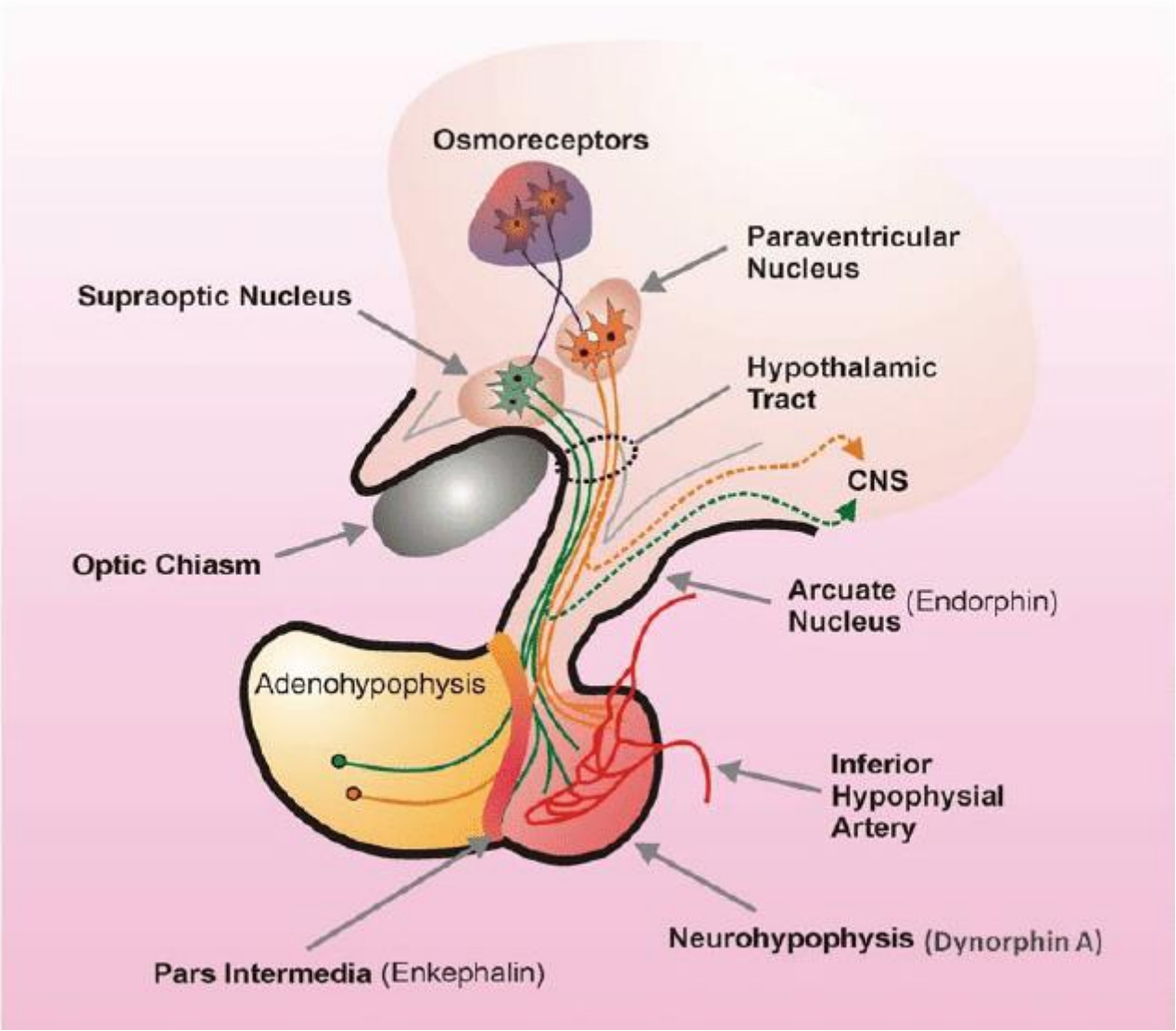
3- Pars Intermedia

The pars intermedia, which developed from the dorsal portion of **Rathke's pouch** , in humans, a rudimentary region made up of **cords** and **follicles** of weakly basophilic cells that contain small secretory granules. The function of these cells is not known.

❖ Neurohypophysis (posterior part)

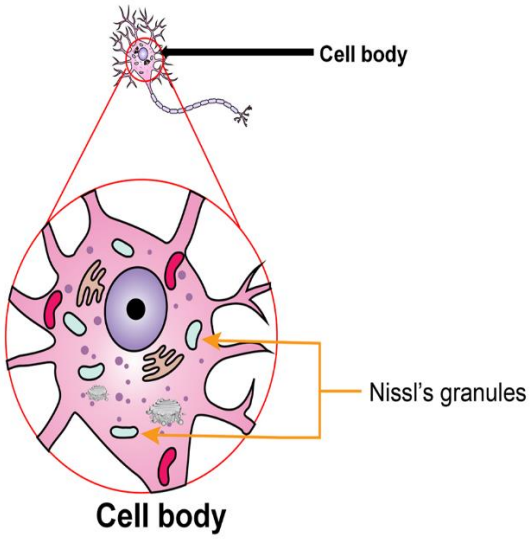
The neurohypophysis consists of

- **unmyelinated nerve** fibers derived from **neurosecretory cells** of the supraoptic and paraventricular hypothalamic nuclei
- **pituicytes**.

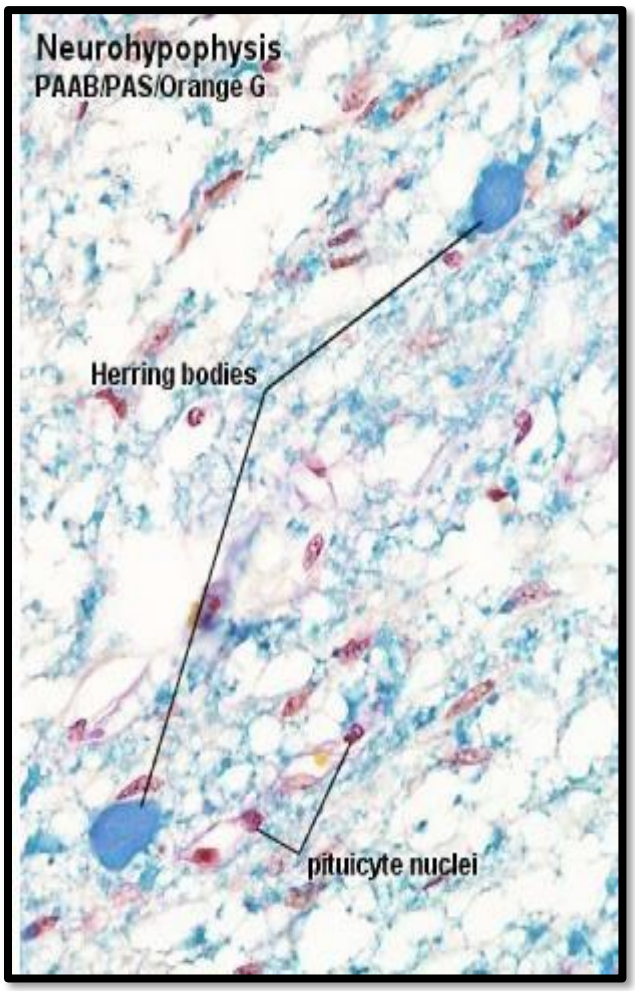


G.Histiology: (Endocrine system)

It is composed of some 100,000 unmyelinated axons. **The secretory neurons** have all the characteristics of typical neurons, including the ability to conduct an action potential, but have more 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** that are visible in the light microscope.

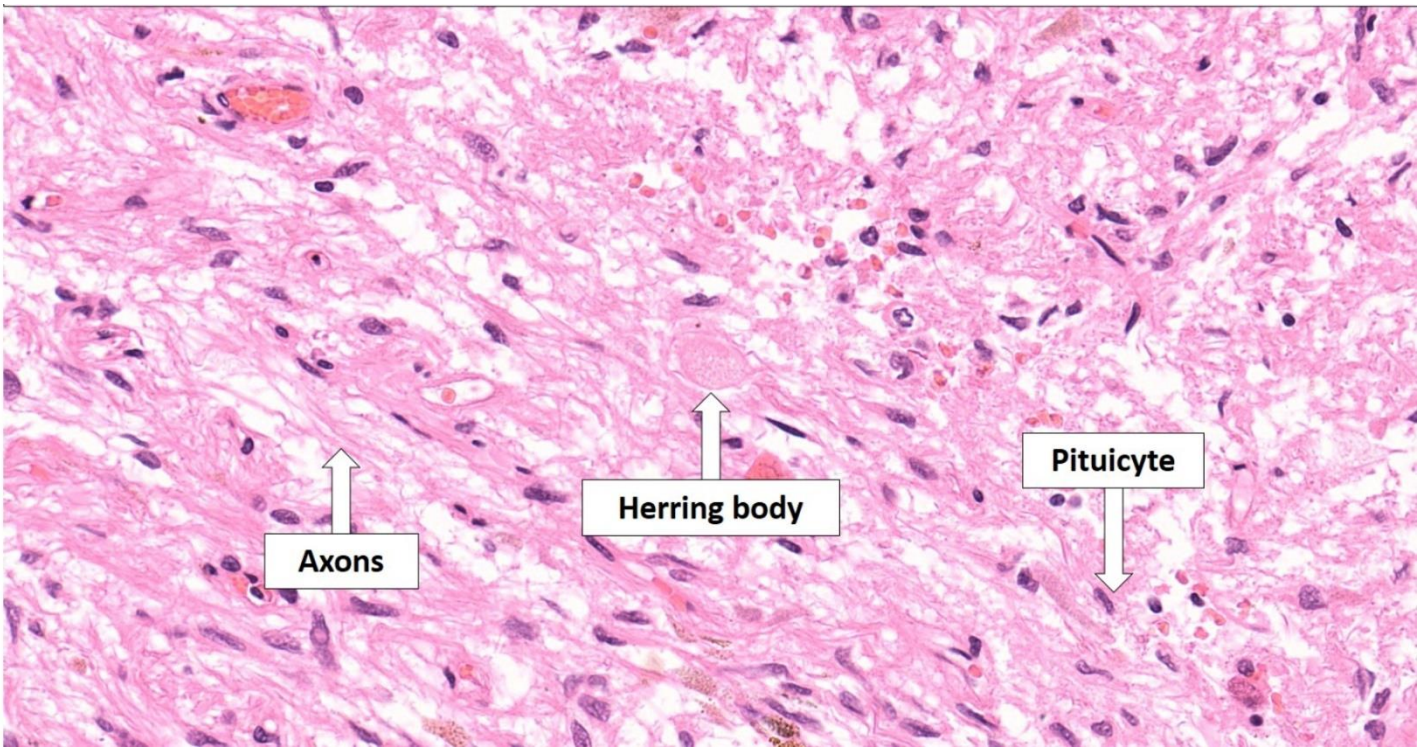


The electron microscope reveals that the Herring bodies contain **neurosecretory granules** that have a diameter of 100-200nm are surrounded by a membrane. The granules are released and enter the fenestrated capillaries that exist in large numbers in the pars nervosa; the hormones are then distributed to the general circulation.

The **neurosecretory material** consists of 2 hormones, both cyclic peptides made up of 9 amino acids. The hormones have a slightly different amino acid composition, which results in very different functions. They are **arginine vasopressin**-also called **antidiuretic hormone-and oxytocin.** Each hormone is joined to a binding protein **(neurophysin).**

Cells of the Neurohypophysis

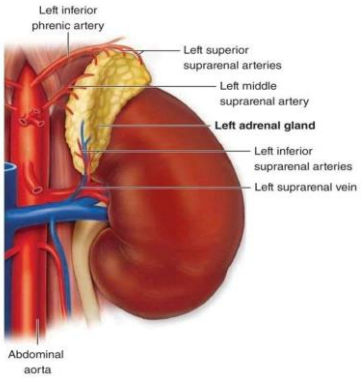
Although the neurohypophysis consists mainly of **axons** from hypothalamic neurons, about 25% of the volume of this structure consists of a specific type of highly branched glial cell called **a pituicyte**.



Adrenal glands

The adrenal (or suprarenal) glands are paired organs lying near the superior lobes of the kidneys. They are flattened structures with a half-moon shape. Together, they weigh about 8 g, but their weight and size vary with the age and physiologic condition of the individual. Adrenal glands are each covered by a dense connective tissue capsule that sends thin trabeculae into the gland's parenchyma.

The stroma consists mainly of reticular fibers supporting the secretory cells and microvasculature. Each gland has two concentric regions: a **yellowish adrenal cortex** and a **reddish-brown central adrenal medulla**.
The adrenal cortex and medulla can be considered two different organs with distinct embryonic origins, functions, and morphologic characteristics that become united during embryonic development.



Adrenal cortex

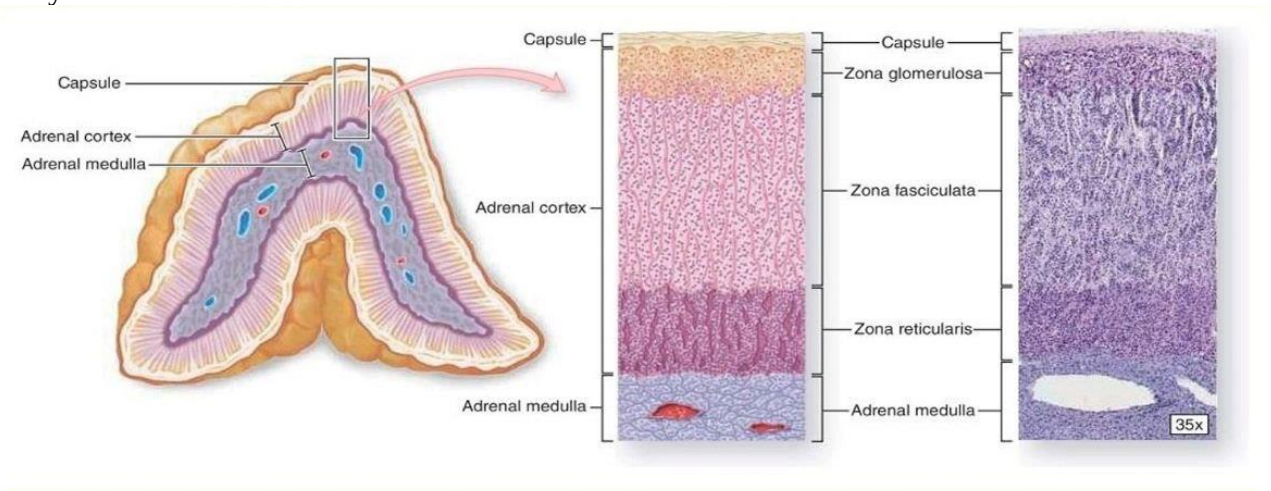
Cells of the adrenal cortex have characteristic features of steroid-secreting cells: acidophilic cytoplasm rich in lipid droplets, with central nuclei.
Steroid hormones are not stored in granules like proteins or undergo exocytosis.
As small lipid-soluble molecules, steroids diffuse freely from cells through the plasma membrane.

Zones of adrenal cortex:

- **Zona glomerulosa:** immediately inside the capsule and comprising about **15%** of the cortex, consists of closely packed, rounded or arched cords of columnar or pyramidal cells with many capillaries.
  The steroid made by these cells are called **mineralo-corticoids** because they affect uptake of Na, k, and water by cells of renal tubules. The principal product is **aldosterone**, the major regulator of salt balance. Aldosterone secretion stimulated primarily **by angiotensin II** and weakly by **ACTH.**

- **The middle zona fasciculata,** occupies **65% to 80%** of the cortex and consists of long cords of large polyhedral cells. These cells secrete **glucocorticoids**, especially **cortisol**, which affect carbohydrate metabolism. **Cortisol** also suppresses many immune functions. Secretion is controlled by **ACTH** with negative feedback proportional to the concentration of circulating glucocorticoids.

- **The innermost zona reticularis** comprises about **10%** of the cortex and consists of **smaller cells in a network of irregular cords interspersed with wide capillaries**. Cells of the reticularis also produce **cortisol** but primarily secrete the weak **androgens.** Secretion of these cells also stimulated by **ACTH.**



Adrenal Medulla

The adrenal medulla is composed of **large, pale-staining polyhedral cells** arranged in cords or clumps and supported by reticular fiber network. Medullary parenchymal cells, known as **chromaffin cells**, arise from neural crest cells.

Chromaffin cells can be considered modified sympathetic postganglionic neurons, *lacking axons and dendrites and specialized as secretory cells*. **Unlike** cells of the adrenal cortex, chromaffin, cells contain many dense granules for storage and secretion of **catecholamines**, either **epinephrine** or **norepinephrine.** About **80%** of the catecholamine secreted from the adrenal is **epinephrine.**

Epinephrine and norepinephrine are released to the blood in large quantities during intense emotional reactions, such as fright**,** and produce **vasoconstriction, increased blood pressure, changes in heart rate,** and **elevated blood glucose levels.**

PANCREATIC ISLETS

The pancreatic islets (islets of Langerhans) are compact spherical or ovoid masses of endocrine cells embedded within the acinar exocrine tissue of the pancreas. The pancreas has more than **1 million** islets.

The cells of islets are **polygonal** or **rounded**, smaller, and **more lightly stained** than surrounding acinar cells. Ultrastructural features are those of active **polypeptide**-secreting cells, with secretory granules that vary in size, morphology, and electron density from cell to cell.

The major islets cells:

(α) or **A cells:** secrete primarily **glucagon** and are usually located **peripherally.**
(β) or **B cells:** produce **insulin,** are the most numerous and are located **centrally.**
(δ) or **D cells:** secreting **somatstatin**, are **scattered** and much less abundant.

A minor forth cell type, more common in islets located within the head of the pancreas, are **PP Cells**, which secrete **pancreatic polypeptide.**

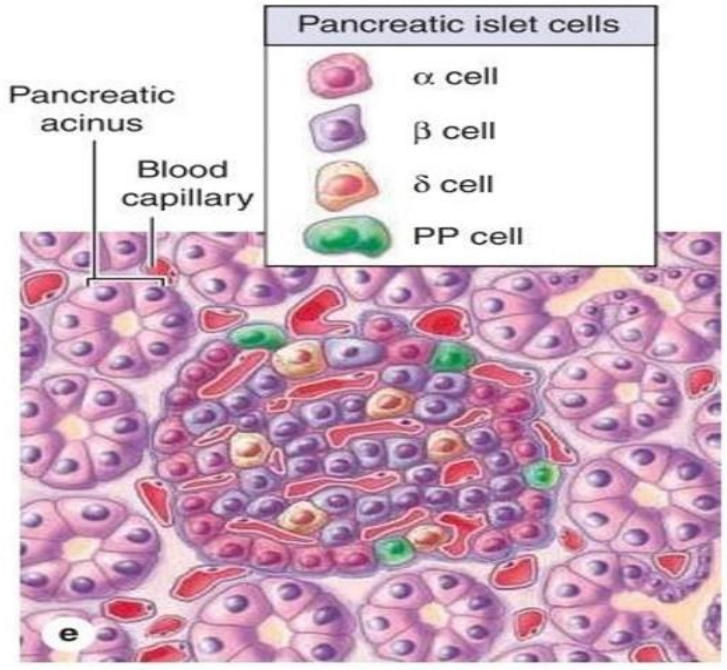


TABLE 20–4 Major cell types and hormones of pancreatic islets.

Cell Type	Quantity (%)	Hormone Produced	Hormone Structure and Size	Hormone Function
α	~20	Glucagon	Polypeptide; 3500 Da	Acts on several tissues to make energy stored in glycogen and fat available through glycogenolysis and lipolysis; increases blood glucose content
β	~70	Insulin	Dimer of α and β chains with S-S bridges; 5700-6000 Da	Acts on several tissues to cause entry of glucose into cells and promotes decrease of blood glucose content
δ or D	5-10	Somatostatin	Polypeptide; 1650 Da	Inhibits release of other islet cell hormones through local paracrine action; inhibits release of GH and TSH in anterior pituitary and HCl secretion by gastric parietal cells
PP	Rare	Pancreatic polypeptide	Polypeptide; 4200 Da	Stimulates activity of gastric chief cells; inhibits bile secretion, pancreatic enzyme and bicarbonate secretion, and intestinal motility

Thyroid gland

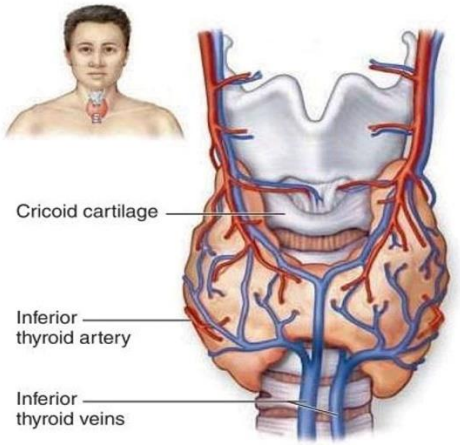
The thyroid gland located anterior and inferior to the larynx, consist of two lobes united by an isthmus. It synthesizes the ~~thyroid hormones~~ **thyroxine** (tetra-iodothyronine or T4) and tri-iodothyronine (T3), which help control the basal metabolic rate in cells throughout the body, as well as the ~~polypeptide hormone~~ **calcitonin.**
The thyroid is the **only** endocrine gland in which a large quantity of secretory product is stored. Moreover, storage is outside the cells which is also unusual.

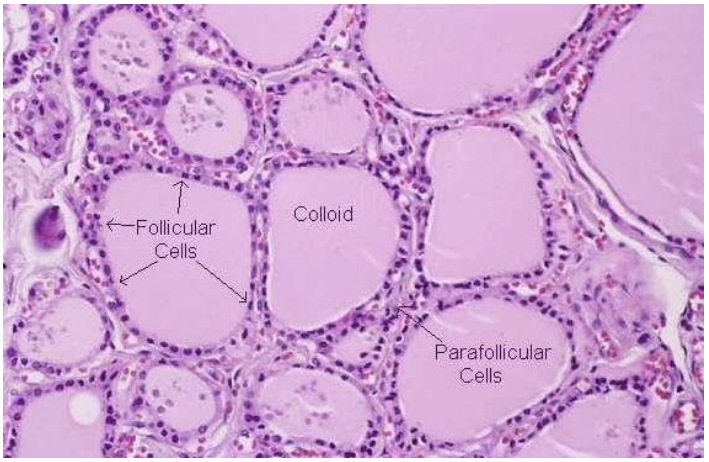
The follicular cells, or thyrocytes, range in shape from squamous to low columnar, their size and other features varying with their activity that is controlled **by thyroid-stimulating hormone (TSH)** from the **anterior pituitary.**
Active glands have more follicles of **low columnar epithelium**: glands with mostly **squamous** follicular cells are **hypoactive.**

Another endocrine cell type, the **parafollicular cell,** or **C cell,** is also found inside the basal lamina of the follicular epithelium or as isolated clusters between follicles. They are usually somewhat **larger** than follicular cells and **stain less intensely.**

Nearly all of both thyroid hormones are carried in blood tightly bound to thyroxine-binding globulin or albumin. T4 is more abundant compound, constituting **90%** of the circulating thyroid hormone.
The major regulator of thyroid gland is **TSH (thyrotropin)** from **anterior pituitary.**

FIGURE 20–18 Thyroid gland.





Parathyroid glands

The parathyroid glands are four small ovoid masses. They are located on the back of the thyroid gland, usually embedded in the larger gland's capsule.

The endocrine cells of the parathyroid gland called **principal (chief) cells.** Irregularly shaped cytoplasmic granules contain the polypeptide **parathyroid hormone (PTH),** an important regulator of **blood calcium** levels. It has three major targets:

- Producing osteoclast stimulating factor
- Reabsorption of Ca in proximal renal tubules
- Increasing absorption of Ca in small intestine

FIGURE **20–22** Parathyroid glands.

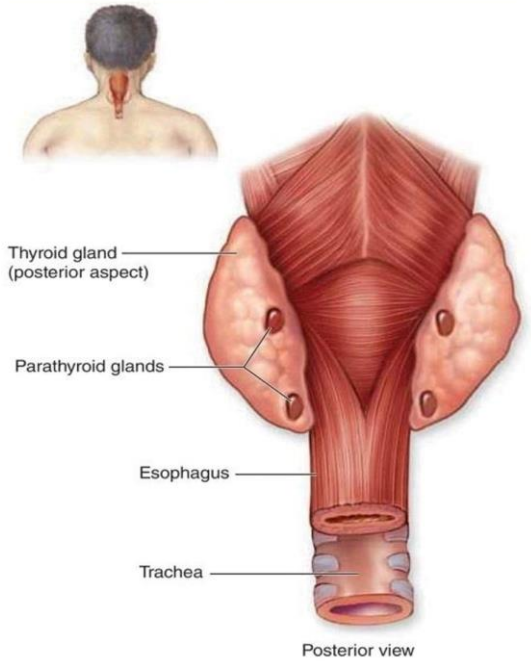
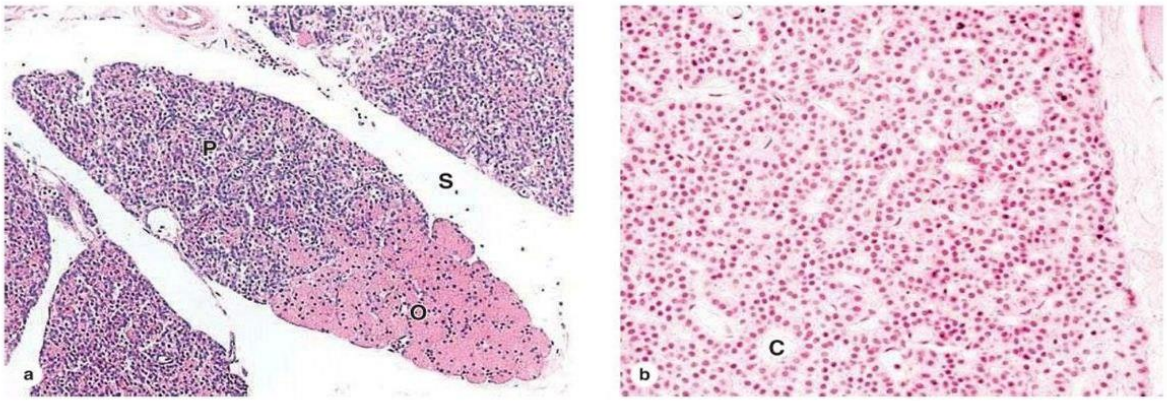


FIGURE **20–23** Parathyroid principal cells.



(a) A small lobe of parathyroid gland, surrounded by connective tissue septa (**S**), shows mainly densely packed cords of small principal cells (**P**). Older parathyroid glands show increasing numbers of much larger and acidophilic nonfunctional oxyphil cells (**O**) that may occur singly or in clumps of varying sizes. X60. H&E.

(b) Higher magnification shows that principal cells have round central nuclei and pale-staining cytoplasm. Cords of principal cells secreting PTH surround capillaries (**C**). X200. H&E.

PINEAL GLAND

The pineal gland, also known as **the epiphysis cerebri**. A small, pine cone-shaped organ.

Prominent and abundant secretory cells called **pinealocytes.** These cells produce **melatonin**, a low-molecular-weight tryptophan derivative.
Melatonin release from pinealocytes is promoted by **darkness** and inhibited by **daylight.**
The pineal gland acts as **a neuroendocrine transducer**, converting sensory input regarding light and darkness into variations in many hormonal functions.

-A characteristic feature of the pineal gland is the presence of variously sized concretions of of calcium and magnesium salts called **corpora arenacea**, or brain sand, which form as extracellular protein deposits become mineralized. Such concretions appear during childhood and gradually increase in number and size with age, with no apparent effect on the gland's function.