## HISTOLOGY 2024-2025

## Endocrine Glands Part II/II

### PARATHYROID GLANDS

These are four small ovoid masses—each 3 × 6 mm—with a total weight of about 0.4 g. They are located on theback of the thyroid gland, usually embedded in the larger gland's capsule. Each parathyroid gland is contained within a thin capsule from which septa extend into the gland. A sparse reticular stroma supports dense elongated clusters of secretory cells.

The endocrine cells of the parathyroid glands, called **principal (chief) cells**, are small polygonal cells with round nuclei and pale-staining, slightly acidophilic cytoplasm. Irregularly shaped cytoplasmic granules contain the polypeptide parathyroid hormone (PTH), an important regulator of blood calcium levels, PTH has three major targets:

- Osteoblasts respond to PTH by producing an osteoclast-stimulating factor, which increases the number andactivity of osteoclasts. The resulting resorption of the calcified bone matrix and release of $Ca^{2+}$ increase the concentration of circulating $Ca^{2+}$, which suppresses PTH production.
- In the distal convoluted tubules of the renal cortex, PTH stimulates $Ca^{2+}$ reabsorption (and inhibits phosphate reabsorption in the proximal tubules).
- PTH also indirectly increases the $Ca^{2+}$ absorption in the small intestine by stimulating vitamin D activation.

With increasing age, many secretory cells are replaced with adipocytes, which may constitute more than 50% of the gland in older people.

Much smaller populations of **oxyphil cells**, often clustered, are sometimes also present in parathyroid glands, more commonly in older individuals. These are much larger than the principal cells and are characterized by very acidophilic cytoplasm filled with abnormally shaped mitochondria.

### ADRENAL GLANDS

The adrenal (or suprarenal) glands are paired organs lying near the superior poles of the kidneys, embedded inthe pararenal adipose tissue and fascia. They are flattened structures with a half-moon shape, about 4-6-cm long, 1-2-cm wide, and 4-6-mm thick in adults. 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. The cortex arises from mesoderm and the medulla from the neural crest.

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

**Blood supply**

The adrenal gland lacks a hilum, 3 adrenal arteries penetrate the capsule independently and branch immediatelyto form subcapsular arterial plexus. From this plexus 2 groups of arterioles arise; arterioles for the adrenal cortexand others for the medulla bypassing the cortex. Cortical capillaries irrigate endocrine cells of the cortex and then drain into the microvasculature of the medulla. The adrenal medulla has two a dual blood supply: arterialblood from the medullary arterioles and venous blood capillaries of the cortex. Venous drainage from the glandsoccurs via the suprarenal veins.

*The conversion of norepinephrine to epinephrine by chromaffin cells is dependent on phenylethanolamine N-methyltransferase (PNMT), an enzyme needs to be activated by cortisol transported by the cortical capillaries to medullary venous sinuses*

**Adrenal cortex**

Cells of the adrenal cortex have characteristic features of steroid-secreting cells: acidophilic cytoplasm rich in lipid droplets, with central nuclei. Ultrastructurally their cytoplasm shows an exceptionally profuse smooth ER (SER) of interconnected tubules, which contain the enzymes for cholesterol synthesis and conversion of the steroid prohormone pregnenolone into specific active steroid hormones. The mitochondria are often spherical,with tubular rather than shelflike cristae. These mitochondria not only synthesize ATP but also contain the enzymes for converting cholesterol to pregnenolone and for some steps in steroid synthesis. The function of steroid-producing cells involves close collaboration between SER and mitochondria.

The adrenal cortex has three concentric zones in which the cords of epithelial steroid-producing cells are arranged somewhat differently and which synthesize different classes of steroid hormones (summarized in below table 2):

| table 2 | Zona Glomerulosa | Zona Fasciculata | Zona Reticularis |
|---|---|---|---|
| **% of the cortex** | 15% | 65-80% | 10% |
| **Shape of cells** | Columnar or pyramidal | Large polyhedral cells, with lipid droplets and appear vacuolated (**spongiocytes**) | Smaller cells, few lipid droplets & more lipofuscin pigment |
| **Arrangement of cells** | Rounded or arched cords | Long cords, one or two cells thick | Network or irregular cords |
| **Hormones produced** | Mineralocorticoids; **aldosterone** | Glucocorticoids; **cortisol** | Adrenal (weak) androgens **DHEA** > testosterone |
| **ACTH control** | Weak stimulation by ACTH | Yes, with feedback regulation | Yes, with feedback regulation |
| **Other control** | Angiotensin II (from RAAS) & high K level | N/A | N/A |
| **Action of hormone** | Increase Na reabsorption & K & H excretion | Gluconeogenesis in many cells and glycogen synthesis in the liver, muscle proteolysis & fat mobilization, suppress immune system. | development of the male sex organs in childhood normal onset of female body hair following puberty |

*Addison's disease or adrenal cortical insufficiency is a disorder, usually autoimmune in origin, which causes degeneration in any layer of adrenal cortex, with concomitant loss of glucocorticoids, mineralocorticoids, or androgen production. At the same time there will be no negative feedback from cortical hormones resulting in elevated ACTH and MSH levels from the anterior pituitary consequently, results in skin darkening from the effect of high MSH.*

*Aldosterone-secreting tumors (of zona glomerulosa cells) causing a group of symptoms called Conn's syndrome.*

*Adrenal cortical adenoma that secretes cortisol resulting in Cushing syndrome.*

## Adrenal medulla

It can be considered a modified sympathetic ganglion, lacking axons and dendrites and its ganglionic cells have specialized as secretory cells. The medulla is composed of large pale-staining polyhedral cells called **chromaffin cells** arranged in cords or clumps and supported by reticular fiber stroma intervened by profuse supply of fenestrated capillaries. Unlike cells of the adrenal cortex, chromaffin cells contain many electron-dense granules for the storage and secretion of catecholamines (epinephrine and norepinephrine). The granules of epinephrine-secreting cells are less electron-dense and generally smaller than those of norepinephrine-secreting cells. Both catecholamines, together with Ca2+ and ATP, are bound in granular storage complexes with proteins called **chromogranins** (catecholamine-binding protein). About 80% of the catecholamines secreted from the adrenal is epinephrine during fight-or-flight response. Adrenal medulla also contains scattered sympathetic ganglion cells.

Medullary chromaffin cells are innervated by preganglionic sympathetic neurons, which trigger epinephrine andnorepinephrine release during stress and intense emotional reactions. Epinephrine increases heart rate, dilatesbronchioles, dilates pupils and dilates arteries of cardiac and skeletal muscle. Norepinephrine constricts vessels of the digestive system and skin, increasing blood flow to the heart, muscles, and brain. Both hormones stimulate glycogen breakdown, elevating blood glucose levels.

*In the adrenal medulla, benign pheochromocytomas periodically secrete high levels of catecholamines that cause episodes of palpitation, chest pains, sweating, anxiety and swings in blood pressure between hypertension and hypotension.*

## PINEAL GLAND

Also known as hypophysis cerebri, is a small pine cone-shaped gland, about 5-8 mm by 3-5 mm in the posterior wall of third ventricle attached to the brain by a stalk. It develops from neuroectoderm. The pineal gland is covered by connective tissue derived from pia mater, from which septa divide the parenchyma of the gland intolobules.

The main cells in the gland parenchyma are secretory cells called **pinealocytes**, they have lightly basophilic stained cytoplasm and irregular euchromatic nucleus. Pinealocytes appear to have long cytoplasmic processes

extending to vascular connective tissue septa ending in dilatation near capillaries. **Interstitial glial cells** (modified astrocytes) can also be seen between cords of pinealocytes and around capillaries with elongated nuclei and more heavily stained than those of pinealocytes. The secretory cells of the pineal gland secret melatonin.

A characteristic feature of the pineal gland is the presence of variously sized concretions of calcium and magnesium salts called **corpora arenacea**, or brain sand. They gradually increase in number and size with age, with no apparent effect on the gland's function.

Melatonin release from pinealocytes is promoted by darkness and inhibited by daylight. The resulting diurnal fluctuation in blood melatonin levels induces rhythmic changes in the activity of the hypothalamus, pituitary gland, and other endocrine tissues that characterize the circadian (24 hours, day/night) rhythm of physiological functions and behaviors. the cycle of light and darkness is detected within the retinas and transmitted to the pineal via the retinohypothalamic tract, the suprachiasmatic nucleus, and the tracts of sympathetic fibers entering the pineal.

## PANCREATIC ISLETS (OF LANGERHANS)

These are compact spherical or ovoid masses of endocrine cells embedded within the acinar exocrine tissue of the pancreas. Each of these islets contains several hundred cells, but some have only a few cells. The pancreas has more than 1 million islets, mostly in the gland's narrow tail region, but they only constitute 1%-2% of the organ's total volume.

A very thin reticular capsule surrounds each islet, separating it from the adjacent acinar tissue. Pancreatic islets have the same embryonic origin as the pancreatic acinar tissue. The cells of islets are polygonal or rounded, smaller & more lightly stained than the surrounding acinar cells arranged in cords that are separated by fenestrated capillaries.

The major islet cells are most easily identified and studied by immunohistochemistry:

- α or A cells secrete primarily glucagon and are usually located peripherally.
- β or B cells produce insulin (L. insula, island), are the most numerous, and are located centrally.
- δ or D cells, secreting somatostatin, are scattered and much less abundant.
- PP cells, produce pancreatic polypeptide, these cells are more common in the islets located within the headof pancreas.

***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 |

Pancreatic islets also normally contain a few enterochromaffin cells, like those of the digestive tract, which are also scattered in the pancreatic acini and ducts and which secrete other hormones affecting the digestive system. Sympathetic and parasympathetic nerve endings are closely associated with about 10% of α, β, and δ cells and can also function as part of the control system for insulin and glucagon secretion. Sympathetic fibers increase glucagon release and inhibit insulin release; parasympathetic fibers increase secretion of both glucagon and insulin.

*Diabetes mellitus DM is characterized by loss of the insulin effect and a subsequent failure of cells to take up glucose, leading to elevated blood sugar. Type 1 DM (insulin-dependent DM) is caused by loss of the β cells from autoimmune destruction and is treated by regular injections of insulin. Type 2 DM (insulin-non-dependent DM), β cells are present but fail to produce adequate levels of insulin in response to hyperglycemia and the peripheral target cells "resist" or no longer respond to the hormone. Type 2 diabetes commonly occurs with obesity, and poorly understood, multifactorial genetic com ponents are also important in this disease's onset.*