Endocrine Organs and the Endocrine System

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The endocrine system is an important and complex topic of the preclinical studies. The control of bodily functions through the messengers (hormones) of the endocrine system is the subject of anatomy, physiology, and biochemistry; an accurate understanding of the hormones and their functions is essential for the clinical routine as well. The endocrine organs, in the stricter sense, include the pituitary, thyroid, parathyroid, adrenal, and pineal gland. They are easy to identify by their characteristic structure in the histological examination, but there are several things that should be considered. This article summarizes the most important facts about the endocrine organs.

The Endocrine System (Hormone System)

The **endocrine system** consists of those organs of the body that are producing hormones. Many different bodily functions are coordinated and regulated by hormones, i.e. metabolic regulation, water and electrolyte balance, maturation and growth processes as well as reproduction.

Serving as messengers, hormones reach their target cells via the blood.

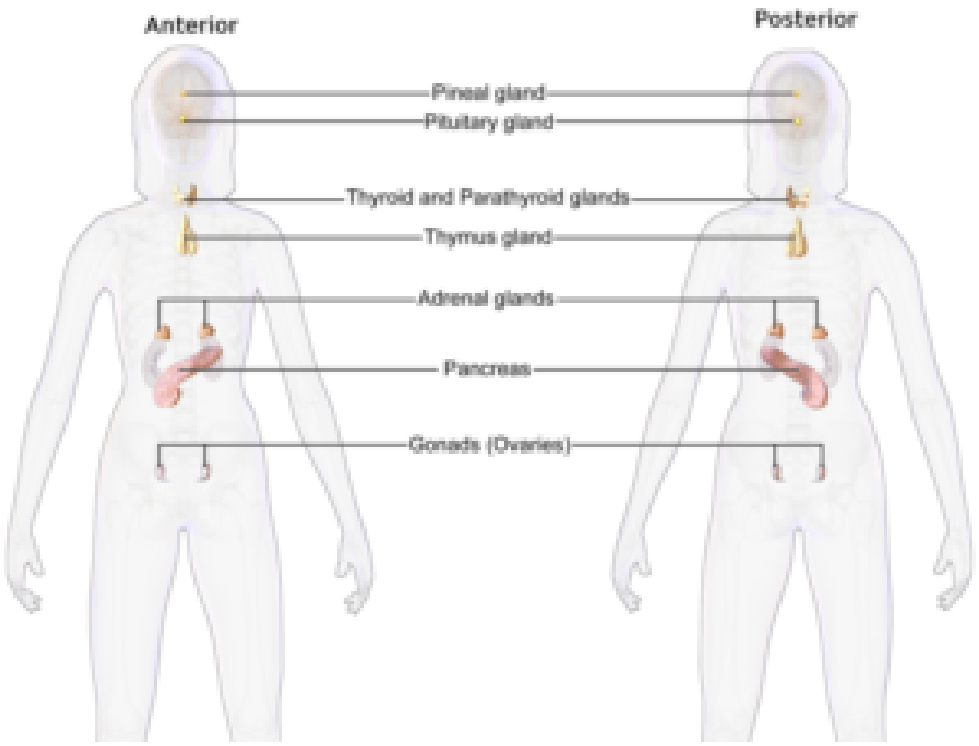


Image: “Endocrine System Female” by Bruce Blaus, License: CC BY 3.0

Endocrine Organs

Endocrine glands are glands that produce hormones and deliver them to the bloodstream. Contrary to the exocrine glands, endocrine glands do not possess excretory ducts. They deliver their product directly into the bloodstream or they act in an autocrine or paracrine manner. For this reason, the endocrine tissue is usually provided with many **capillaries**.

The endocrine glands, in the stricter sense, include **pituitary, thyroid, parathyroid, adrenal gland, and pineal glands.**

In addition, there are organs with endocrine cell groups, like the ovary, testes, and the gastrointestinal tract – the latter containing even more endocrine cells than the **adenohypophysis**. The **pancreas,** with its islet cells, the thymus, heart, and kidneys produce hormones as well. As these organs also perform other essential tasks, they are not primarily regarded as endocrine glands.

Special Features of Endocrine Cells

Peptide hormones (such as insulin) are usually produced as prohormones and stored in **granules** in the cell. Cells producing peptide hormones feature a rough endoplasmic reticulum (ER) and a prominent Golgi apparatus. In the **cytoplasm,** there are small secretory granules whose content is released via **exocytosis**.

Steroid hormones are lipophilic molecules whose structure is derived from cholesterol. Examples of steroid hormones are **testosterone** and **estrogen.** They are not stored, but leave the cell by diffusion.
Cells producing steroid hormones are characterized by a smooth ER, tubular mitochondria, and lipid inclusions. Secretory granules, however, are not found in these

cells since steroid hormones diffuse into the blood immediately after their synthesis.

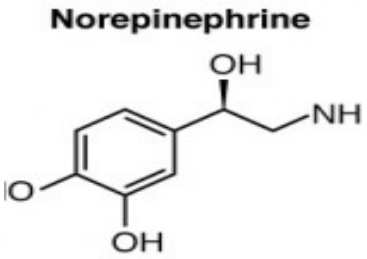
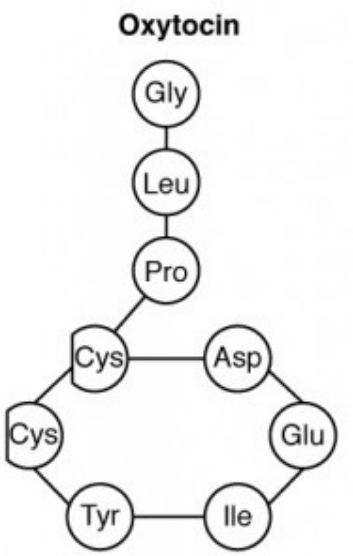
Forms of hormone secretion

Endocrine signaling occurs if an endocrine organ, such as the thyroid, secretes its hormone into the blood. The hormone is spread throughout the body via the bloodstream and thus reaches its target cells. Nerve cells may form hormones as well. If these are secreted into the blood, the process is called **neuroendocrine secretion.**

In **paracrine secretion,** however, hormones diffuse through the connective tissue to their vicinal target cells. These hormones are also called mediators or tissue hormones. They include, among others, the **cytokines, histamines, nitric oxide (NO), serotonin,** and **bradykinin.**

Autocrine secretion means that the hormone produced by the cell reacts to the same cell. The cell thus affects itself. This process is especially important in the differentiation of cells in embryonic development.

Autocrine and paracrine signaling play a role in inflammation processes and immune reactions, among others. The boundaries between the mechanisms are not completely defined. Hormones like insulin may act in an endocrine as well as paracrine and autocrine manner.

Hormone class	Components	Examples
Amine hormones	Amino acids with modified groups	
Peptide hormones	Short chains of linked amino acids	

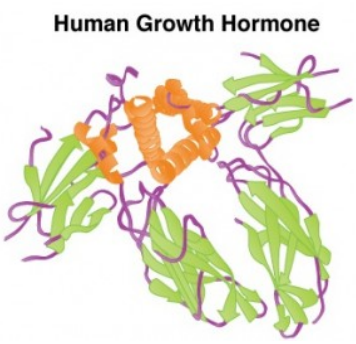
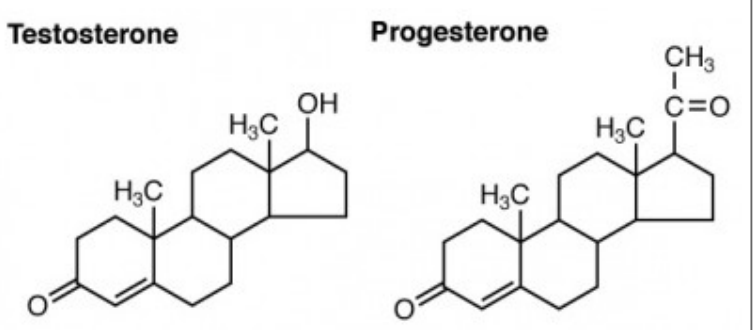
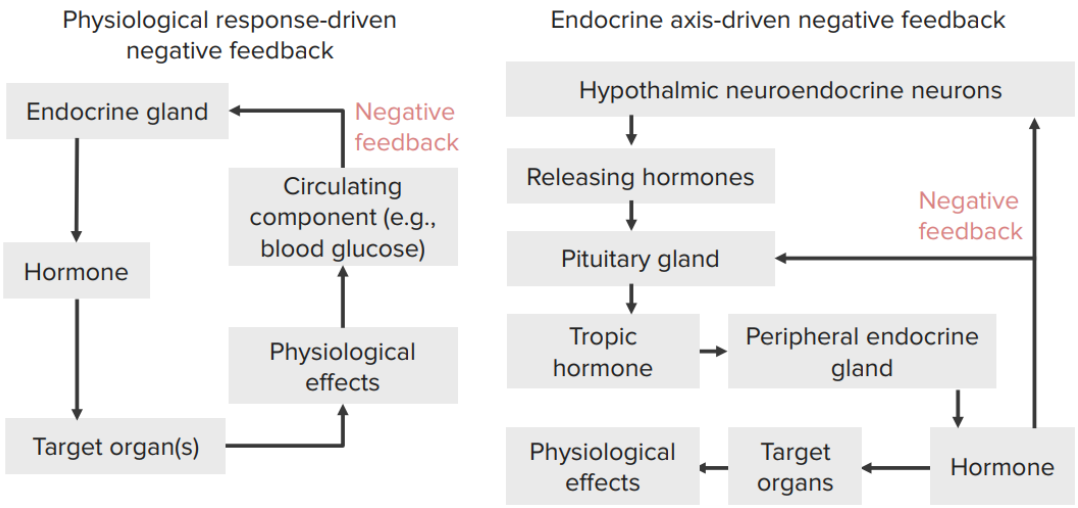
Protein hormones	Long chains of linked amino acids	
Steroid hormones	Derived from lipophilic cholesterol	

Table: “Types of Hormones” by Phil Schatz, License: CC BY 4.0

Types of feedback loops



Hypothalamus and the Pituitary Gland

The hypothalamus is part of the **diencephalon** (interbrain) and serves as a super-ordinated structure of the hormone system and the autonomic nervous system. Certain hypothalamic nuclei (nerve cells) form control hormones, which regulate the hormone production of the **adenohypophysis**.

In addition, the large **perikarya** of the hypothalamic nuclei ***Ncl. supraopticus*** and ***Ncl. paraventrikularis*** produces both effector hormones anti-diuretic hormone (ADH) and oxytocin. These are bound to carrier proteins and transported into the **neurohypophysis** along the axons.

The **neurohypophysis** (posterior lobe of the pituitary) consists of neural tissue. Here, no hormone production takes place. Instead, the axons of the hypothalamic nuclei, which

produce oxytocin and ADH, end here. This is where the hormones are released into the bloodstream, which is why this area is called a neurohemal region.

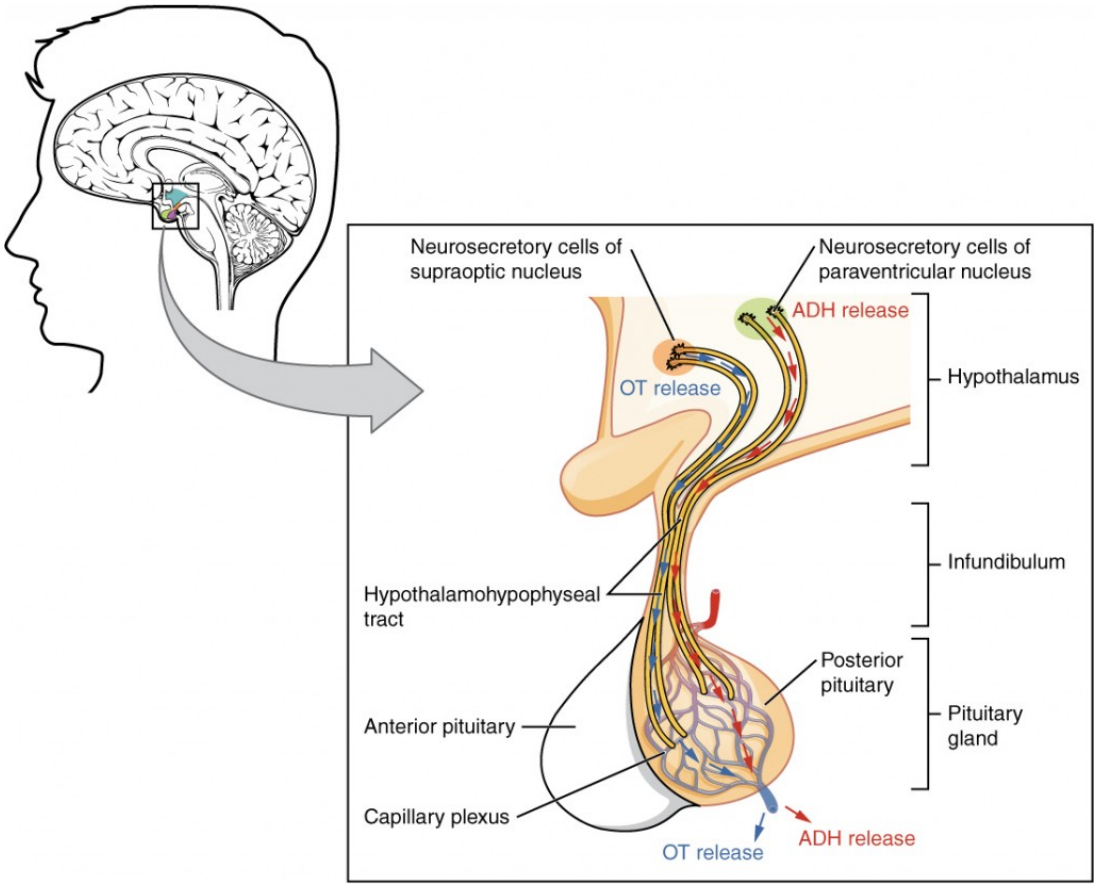


Image: "The Posterior Pituitary Complex" by Phil Schatz, License: CC BY 4.0

ADH and oxytocin are **nonapeptides.** ADH (vasopressin) ensures reduced water excretion in the kidney. If there is an ADH-deficiency, i.e. through traumatic destruction of the **pituitary stalk**, the condition of **diabetes insipidus** will occur. Here, large amounts of hypoosmolar urine are excreted.

Cells of other hypothalamic nuclei produce the **releasing and inhibiting hormones** (liberins and statins). These are transported axonally in the **eminentia mediana** (pituitary stalk) and secreted into the bloodstream there. The hormones reach their target cells in the **adenohypophysis** through portal vessels. They affect them either in an activating or inhibiting manner.

Structure of the pituitary gland

The pituitary gland (Latin ***glandula pituitaria***) is about the size of a hazelnut and weights 0.5–1.5 g. It is located at the base of the brain, directly below the hypothalamus in the sella turcica of the sphenoid bone. It is enclosed between the inner and outer layer of the dura mater.

In the histological sectional image, it is easy to see that the **pituitary consists of 2 parts:** the adenohypophysis (anterior lobe of the pituitary) and neurohypophysis (posterior lobe of the pituitary).

Neurohypophysis and portal system

The neurohypophysis is connected to the hypothalamus through the **infundibulum**, the pituitary stalk. The neurohypophysis is a protuberance of the midbrain and therefore consists of nerve tissue. This is the endpoint of the axons of the neurosecretory neurons of the ***Ncl. supraopticus*** and ***Ncl. paraventricularis***. Their hormones, oxytocin, and ADH, are stored in granules and released into the blood via exocytosis when needed.

There is no hormone production in the **neurohypophysis** itself. Instead, the neuroendocrine hormones reach the posterior pituitary via axonal transport. They are secreted into the blood here, in the so-called neurohemal region. Thus, the neurohypophysis is a part of the **circumventricular organs** (circumscribed areas where the blood-brain barrier is lifted).

Moreover, particular glia cells with visible cell nuclei (pituicytes) and capillaries with endothelium, can be found in the neurohypophysis.

The **pituitary portal system** is located in the area of the **infundibulum** as well. Here, vessels of the **eminentia media** (also a neurohemal region) transport the releasing and inhibitory hormones, which are produced in the hypothalamus, to their target cells in the adenohypophysis.

Regions and cells of the adenohypophysis

The **adenohypophysis** (anterior lobe of the pituitary) is constructed of epithelial cells and has a rich blood supply. It can be divided into 3 regions: the pars distalis, located in the front; the pars intermedia, with its transition into the posterior pituitary; and the pars tuberalis located next to the pituitary stalk. There are 3 different types of cells: **acidophilic cells** (colored red in the H & E stain), producing prolactin and growth hormones, and **basophilic cells** (colored blue in the H & E stain), secreting melanocyte-stimulating hormone (MSH), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Furthermore, there are rare **chromophobe cells** that are unstained and presumably consist of exhausted endocrine cells as well as stem cells and stellate cells. The groups of cells producing hormones are surrounded by a capillary network.

Function and Morphology of the Thyroid

Image: “Hypophysis” by Držiak, License: CC BY-SA 3.0

The thyroid (***gl. thyroidea***) is an important endocrine organ. It influences the metabolism of nearly all body cells with its hormones **thyroxine (T_4)** and **triiodothyronine (T_3)** and plays an important role in the development of the nervous system.

Microscopically, the thyroid consists of thyroid follicles. These are lined with a single layer of epithelium, the **follicular epithelium.** The height of the follicle epithelium varies depending on its functional state. If many hormones are currently produced, the number of epithelial cells is higher.

In the follicular lumen, there is a homogeneous mass, the **colloid,** colored pink in the H &

E stain. The colloid contains **thyroglobulin,** the storage form of the **thyroid hormones** T_3 and T_4. Here, the hormones may be stored outside the cell for up to 2 weeks.

In fibrous septa, located between the follicles, there are blood capillaries and lymphatic vessels. The thyroid is surrounded by a connective tissue capsule on the outside.

The iodine-containing thyroid hormones

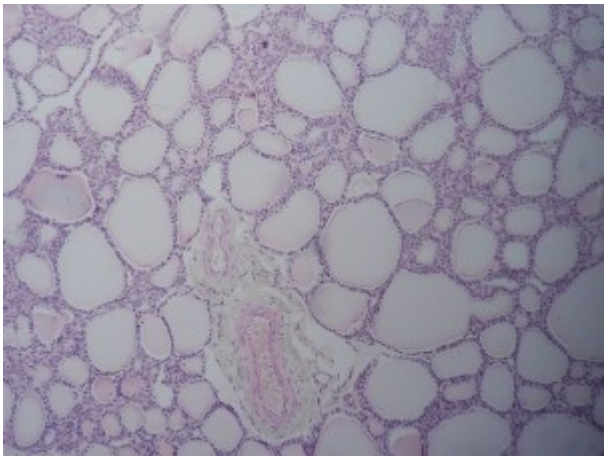


Image: “Thyroid, 400X; Hematoxilina-eosina” by Andrea Mazza, License: CC BY 3.0

The protein **thyroglobulin** is formed by follicular epithelium cells, which transport it to the colloid. Here, it is iodinated to its tyrosine residues. The required iodine is taken with food. In Germany, the demand is 200 µg/day.

T_4 and T_3 are released through the return transport and hydrolysis of thyroglobulin. They consist of 2 iodinated **tyrosine residues,** whereby T_4 consists of 4 and T_3 of 3 iodine atoms. They eventually diffuse into the bloodstream from the cytoplasm of the follicular epithelial cell.

The functions of the follicular epithelium are regulated through TSH**,** which is produced by the adenohypophysis.

C cells and calcitonin

Isolated between the epithelial cells are the C cells, which do not have any contact with the follicles. They are hardly visible in the H & E stain and are therefore detected by immuno-histochemical methods, for instance. C cells are cells of the neural crest. They migrate to the thyroid through the **ultimobranchial body** during the embryonic period. The ultimobranchial body regresses in humans before birth.

The C cells produce the peptide hormone **calcitonin, the antagonist of the parathyroid hormone** of the parathyroid. Calcitonin reduces the calcium level in the blood and promotes the incorporation of calcium into the bones. This effect was previously used therapeutically for the treatment of osteoporosis.

Struma

An enlargement of the thyroid is called **goiter.** This enlargement may be an expression of various thyroid diseases. **Hypothyroidism** (underactive thyroid) may be caused by lack of iodine in the nutrition. **Hashimoto’s disease**, an autoimmune disease, leads

to **hypothyroidism** as well.

Euthyroid goiter occurs during normal hormone production. A goiter may also appear during **hyperthyroidism** (overactive thyroid). This is especially observed in the case of **Graves' disease.** Here, autoantibodies to TSH receptors of the follicular epithelial cells are formed.

Parathyroid Gland (Epithelium)

The parathyroid gland, also referred to as epithelium, can be found in 4 places in humans: 1 pair each on the upper and lower thyroid pole. The parathyroid glands (***gl. parathyroideae*)** are about the size of a grain of wheat and are characterized by their simple histological structure. They produce **parathyroid hormones** that control calcium metabolism via vitamin D and calcitonin.

Densely packed, small epithelial cells, which are arranged in balls, are found in the H & E stain. With increasing age, **univacuolar fat cells** are more frequently found between the epithelial cells. The parathyroid gland is well vascularized, which means that a lot of capillaries can be found. Sometimes, small miniature follicles filled with colloid can also be seen.

The epithelial cells of the parathyroid gland

The **endocrine glandular cells** of the parathyroid gland are chief cells. There are bright chief cells that are rich in glycogen and are at rest, meaning, they are currently producing little hormone. The dark chief cells, on the other hand, are regarded as the hormonally active cells since they contain more cell organelles. Finally, there is a special form of chief cells, the so-called **oxyphil (acidophilic) cells**. They are large and rich in mitochondria and have a reddish cytoplasm. They represent less than 3% of the epithelial cells.

Parathyroid hormone – the hormone of the parathyroid gland

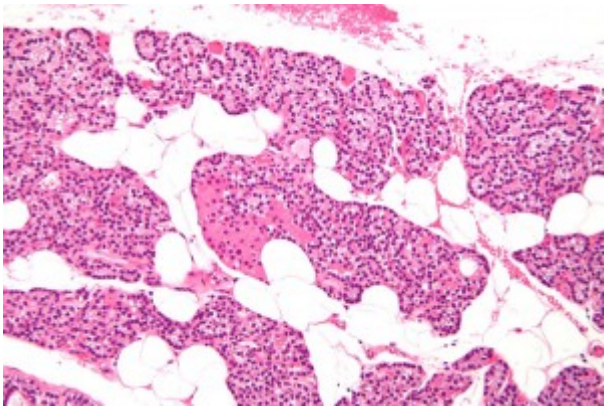


Image: "Intermediate magnification micrograph of the parathyroid gland" by Nephron, License: CC BY 3.0

The epithelial cells form the **parathyroid hormone.** The parathyroid hormone is an important hormone in calcium and phosphate metabolism. It prevents the decrease of the blood calcium level and indirectly activates the osteoclasts, which transfer calcium out of the bone.

Please note: The parathyroid hormone provides calcium in the blood.

Adrenal Glands

The paired adrenal glands (***gl. suprarenalis***) are located to the right and left side on the upper renal pole, like a cap. They are supplied by 3 arteries and a vein each. On the outside, they are covered by a capsule.

Structure of the adrenal gland

The adrenal glands consist of 2 parts that are different with regard to their evolution, the **adrenal medulla,** and the **adrenal cortex.** The cortex represents about 80% of the organ and produces, glucocorticoids like the 'stress hormone' cortisol. The smaller medulla produces epinephrine and noradrenaline. A histological feature in the adrenal medulla are the so-called **jugular veins.**

Structure of the adrenal cortex

The adrenal cortex (**cortex)** is divided into 3 zones that merge continuously into each other. The 3 zones, from the outside in, are:

- **Zona glomerulosa**: epithelial cells form balls or arcades; here mineralocorticoids (**aldosterone**) are produced.
- **Zona fasciculata**: a wider area, and polygonal cells with a bright nucleus and lipid droplets; produces glucocorticoids (**cortisol**) under the control of pituitary ACTH.
- **Zona reticularis**: branched cell cords with acidophilic cytoplasm; formation of **androgens** takes place here. These are then converted into testosterone and estrogen in the ovary and testes.

The adrenal medulla

The adrenal medulla (**medulla**) produces epinephrine and (to a lesser extent) noradrenaline. These substances belong to the class of **catecholamines.** Because of their dyeability, they are also referred to as **chromaffin cells** (Other chromaffin cells are, e.g, the serotonin-containing cells in the gastrointestinal tract).

The cells of the adrenal medulla

The medullary cells are modified sympathetic neurons, which do not have an extension. They are, in turn, innervated by the **preganglionic cholinergic sympathetic neurons**. The cells of the adrenal medulla can, therefore, be regarded as an **endocrine sympathetic ganglion** as well. It is also called **paraganglion suprarenale.**

The venous plexuses are located between the medullary cells. The larger veins have smooth musculature and are called jugular veins. The ***vena suprarenalis***, the central vein, is located inside the medulla. Epinephrine and noradrenaline get into the bloodstream through it.

Eight-five percent of the medullary cells produce epinephrine; 15% produce noradrenaline. Tumors producing catecholamines are called pheochromocytoma. The tumor originates from the cells of the adrenal medulla in 90% of the cases.

Epiphysis

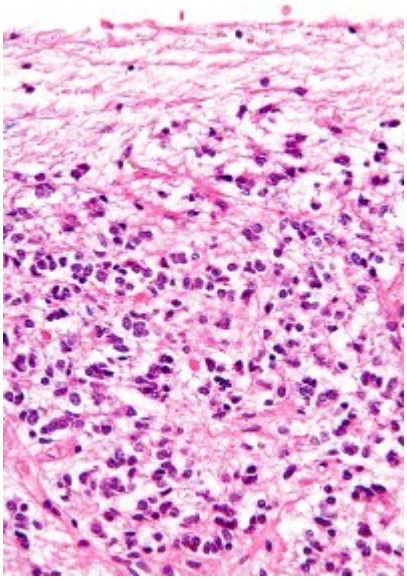


Image: “Very high magnification micrograph of a normal pineal gland” by Nephron, License: CC BY 3.0

The epiphysis also referred to as pineal gland or **corpus pineale** holds a special status among the endocrine organs. It actually is no gland at all, but rather a **light-receptive neuroendocrine organ** controlling the circadian rhythm as a part of the midbrain. Pineal cells, the **pinealocytes**, produce the hormone melatonin. The pinealocytes are surrounded by **interstitial glial cells.**

Melatonin is formed from serotonin, its secretion increases in the darkness and is slowed down in the daylight. Melatonin is also used for the treatment of insomnia and as an anti-jetlag pill in tablet form. It also serves as an antioxidant, protecting against oxygen radicals.

Learning Table: Endocrine Glands and Their Main Hormones

Endocrine gland	Appropriate hormones	Chemical name	Effect
Pituitary (anterior)	Growth hormone	Protein	Promotes the growth of body tissues
	Prolactin	Peptide	Promotes milk production
	Thyrotropin (TSH)	Glycoprotein	Stimulates thyroid hormone secretion
	ACTH	Peptide	Stimulates the release of hormones by the adrenal cortex
	FSH	Glycoprotein	Stimulates the gamete production
	LH	Glycoprotein	Stimulates the androgen production through gonads
Pituitary (posterior)	ADH	Peptide	Stimulates water absorption of the kidneys
	Oxytocin	Peptide	Stimulates uterine contractions during childbirth
Thyroid	Thyroxin (T_4); triiodothyronine (T_3)	Amine	Stimulates basal metabolic rate
	Calcitonin	Peptide	Reduces Ca^{2+}– blood level
Parathyroid glands	Parathyroid hormone	Peptide	Increases Ca^{2+}– blood level
Adrenal glands (cortex)	Aldosterone	Steroid	Increases Na^{+}– blood level
	Cortisol, corticosterone, and cortisone	Steroid	Increase blood sugar level
Adrenal glands (medulla)	Epinephrine, noradrenaline	Amine	Stimulates *fight or flight* reaction
Pineal gland	Melatonin	Amine	Controls sleep cycles
Pancreas	Insulin	Protein	Reduces blood sugar level
	Glucagon	Protein	Increases blood sugar level
Testes	Testosterone	Steroid	Stimulates the development of the secondary male sexual characteristics and sperm production
Ovaries	Estrogen and progesterone	Steroid	Stimulates the development of the secondary female sexual characteristics and prepare the body for childbirth

Table: “Endocrine Glands and Their Major Hormones” by Phil Schatz, License: CC BY 4.0

Review Questions

The answers are below the references.

1. Hormones T_3 and T_4 …

A. …are cholesterol derivatives
B. …reduce the basal metabolic rate
C. …are formed in the C cells of the thyroid gland
D. …are stored outside the cells
E. …are secreted directly into the blood

2. The pheochromocytoma

A. ….is a tumor of the adrenal cortex
B. ….forms oxytocin and ADH
C. …originates from the adrenal medulla in 90% of the cases
D. ….always causes hypertension
E. ….causes a strong facial flush in the patient

3. Which association is correct?

A. Zona glomerulosa of the adrenal medulla – glucocorticoids
B. Zona fasciculata – aldosterone
C. Zona reticularis – testosterone
D. C cells of the thyroid – parathyroid hormone
E. Epiphysis – melatonin

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Correct answers: 1D, 2C, 3E

Notes