

Endocrine System

Endocrine glands - secrete chemical substances called hormones directly into the bloodstream for transport to target tissues.

Hormones: three basic types

1. steroid hormones: are lipid originally synthesized from cholesterol

There are more than 20 steroid hormones in the body, ie. cortisol, cortisone, estrogen, progesterone, testosterone.

Steroids are produced by the gonads (sex hormones) and by the adrenal cortex.

2. proteins: are made of amino acids linked by peptide chains.

Most of the hormones are proteins. ie. calcitonin from the thyroid gland and the hormones from the pituitary gland, pancreas, and the parathyroid glands.

Protein hormones must be injected IV, IP, or IM since oral administration results in cleavage of the peptide bonds by digestion.

3. amines: are also produced from amino acids.

: contain carbon, nitrogen, and hydrogen.

: always have an amine group (-NH₂)

examples of amines are: epinephrine and norepinephrine from the adrenal gland, thyroxin from the thyroid gland.

amines can be taken orally or IV if a faster action is desired.

Note: epinephrine may be used as an inhalant to relax the ductules of the lungs.

Function of hormones: the function of a hormone is to speed up or slow down cellular processes at the target tissue. The specific response depends on the target cell type. Hormones usually affect cells in one, or more of the following ways:

1. alter plasma membrane permeability and/or electrical state by opening or closing ion channels.
2. stimulate the synthesis of proteins or regulatory molecules within the target cell.
3. activate or deactivate enzymes
4. induce secretory activity
5. stimulate mitosis

some hormones bind to receptor molecules on the surface of the target cells.

Steroid hormones (lipid soluble) pass through the cell membrane and generally effect messenger RNA molecules.

In general protein and amine hormones attach to cellular membranes thus increasing the activity of adenyl cyclase. This converts ATP into AMP, a reaction that provides energy for other cellular processes. This membrane binding is necessary because these hormones cannot penetrate the plasma membrane. All of this requires a second messenger system.

The Cyclic AMP signaling system

This system uses three membrane components

1. hormone receptor (1st messenger)
2. Signal transducer (intermediary)
3. Effector enzymes (adenylate cyclase)

Adenylate cyclase generates cAMP from ATP

In this system the hormone binds to the receptor:

This changes the G protein

This in turn acts on adenylate cyclase to convert ATP to cAMP

All of this acts to trigger a cascade of chemical reactions that activate protein kinases.

This system can have a high amplification effect because the G proteins, once activated, go about their business and continue to act as intermediaries.

cAMP is rapidly degenerated by intracellular phosphodiesterase.

PIP Pathway

Some systems use an intracellular calcium ion as a final mediator.

Here hormone binding to the receptor activates a membrane bound phospholipase enzyme that splits PIP_2 (phosphatidylinositol bisphosphate) into diacylglycerol and IP_3 (inositol triphosphate) - both of these then act as second messengers.

Diacylglycerol - activates protein kinases

IP_3 - triggers Ca^{++} release from ER etc. This acts as a third messenger to alter activity of specific enzymes and plasma membrane Ca^{++} channels

OR

IP₃ binds to calmodulin which activates enzymes that amplify cellular responses.

Hormones are under the control of a negative feedback system:

A produces substance B to effect C until C sends a signal back to A telling it that it has enough substance B, in turn A stops producing substance B. Sometimes neural impulses (sympathetic portion of the ANS) cause some endocrine glands (adrenal medulla) to release their hormones.

We will also see a specialized system where a neural impulse causes a release of releasing factors from the hypothalamus.

Pituitary gland: (master gland)

can be divided into two regions:

1. adenohypophysis (anterior pituitary)
2. neurohypophysis (posterior pituitary)

adenohypophysis: develops from ectoderm from the roof of the oral cavity (Rathke's pouch). This gives it a more glandular origin and thus allows it to be the glandular portion of the pituitary gland.

It is subdivided into three regions:

1. pars distalis
2. pars tuberalis (anterior lobe)
3. pars intermedia (atrophies)

Within the adenohypophysis we see 5 principal cell types that are responsible for the secretion of 7 major hormones.

1. somatotrophs
2. thyrotrophs
3. gonadotrophs
4. lactotrophs
5. corticotrophs

Hormones of the adenohypophysis

growth hormone: (GH or hGH or somatotropin) - stimulates growth of body cells, protein anabolism (synthesis), elevation of blood glucose via fat breakdown. Produced by somatotrophs

The secretion of growth hormone is controlled by two releasing hormones from the hypothalamus:

1. growth hormone releasing factor (GRF)

2. growth hormone release inhibiting factor (GRIH)

Insufficient levels (hyoposecretion) of growth hormone during the growing years results in pituitary dwarfism. Excess levels (hypersecretion) during the growth years results in giantism. Excess levels during the adult years results in acromegaly.

thyroid stimulating hormone: (TSH) also know as thyrotropin. Causes the thyroid gland to secrete thyroid hormones. Produced by thyrotrophs.

TSH is triggered by a releasing factor from the hypothalamus, thyrotropin releasing factor (TRF)

follicle stimulating hormone: (FSH) in the female stimulates development of ova and ovarian estrogen production. Produced by gonadotrophs.

In the male it stimulates the testes to produce sperm.

luteinizing hormone: (LH) in the female, along with FSH it stimulates ovulation and thus indirectly the production of progesterone. Produced by gonadotrophs.

In the male it is called interstitial cell stimulating hormone (ICSH) - here it acts on interstitial cells to produce testosterone.

prolactin: (PRL) in females stimulates the mammary glands and thus milk production. Produced in lactotrophs.

In males it may affect (enhance) testosterone production.

production is regulated by prolactin release inhibiting factor (PRIF) from the hypothalamus.

galactorrhea: continued discharge of milk from the breast between feedings and/or after weening. Caused by over production of prolactin in women.

gynecomastia: excessive development of male mammary glands, may see secretion of milk. Caused by over production of prolactin in men. This is common in normal adolescence.

Adrenocorticotropic hormone: (ACTH) acts on the adrenal cortex to cause the release of cortical hormones, mainly cortisol. Produced in corticotrophs.

ACTH also binds to melanocytes in the skin to increase skin pigmentation.

ACTH release is regulated by CRF (corticotropic releasing factor) from the hypothalamus.

melanocyte stimulating hormone: (MSH) acts on melanocytes to synthesize melanin which darkens the skin. Produced in corticotrophs.

release is regulated by releasing factors from the hypothalamus:

MRF - melanocyte releasing factor
MIF - melanocyte inhibiting factor

Neurohypophysis is composed of three regions:

1. median eminence
2. infundibulum (stem)
3. pars nervosa (posterior lobe)

The neurohypophysis is not truly an endocrine gland since it does not synthesize hormones, but simply stores and releases hormones.

The two hormones related to the neurohypophysis are:

1. oxytocin
2. antidiuretic hormone

oxytocin: (OT) is produced in the hypothalamus. It stimulates uterine contraction for childbirth as well as contractions of the ducts in the mammary glands for milk "let down".

antidiuretic hormone: (ADH) is produced in the hypothalamus. It increases water resorption by the kidney tubules resulting in less urine output.

Hyposecretion results in diabetes insipidus which is characterized by output of large amounts of urine and excessive thirst. These people become easily dehydrated.

ADH also causes blood vessels to constrict and so is sometimes called vasopressin.

Thyroid gland: is made up of two cell types:

1. follicular cells
2. parafollicular cells

The **follicular cells** produce **thyroxin** (T4) and **triiodothyronine** (T3)

T3 and T4 both control metabolism and regulate growth and development.

The **parafollicular cells** produce **Calcitonin**. This hormone decreases blood calcium and phosphate levels by inhibiting bone breakdown (osteoclasts) and accelerating calcium absorption into the bone.

Located just inferior to the larynx

Has follicular cells which are under the influence of TSH

The thyroid stores a 100 day supply of thyroid hormones within the colloid of the thyroid follicles.

There are 8 steps for the formation, storage, and release of thyroid hormones

1. Trap iodide ions via active transport from the blood.
2. Make thyroglobulin (TGB)
3. Oxidize iodide so that it can bind to tyrosine and ultimately become colloid (see step 4)
4. Iodinate tyrosine to make T1 and T2
5. Coupling of T1's and T2's to form T3 and T4
6. Pinocytosis and digestion of colloid. Here the colloid is taken back into the follicular cells and digestive enzymes cleave the T3 and T4 from the TGB
7. T3 and T4 are lipid soluble so they diffuse back into the blood stream
8. T3 and T4 once in the blood bind to thyroxine binding globulin (TBG)

Too much iodine in the blood suppresses the release of thyroid hormones

TRH (from the hypothalamus) and TSH (from the anterior pituitary) stimulate the thyroid gland.

High ATP demand, such as hypoglycemia, cold temperatures, high altitude, and pregnancy increase the secretion of thyroid hormones.

Thyroid hormones are important because they regulate oxygen use, basal metabolic rate, cellular metabolism, and growth and development.

Basal metabolic rate (BMR) directly relates to ATP:

1. thyroid hormones increase BMR by stimulating the use of cellular oxygen to produce ATP. This ATP is mainly used by the cells sodium/potassium pumps.
2. Thyroid hormones stimulate the synthesis of more sodium/potassium pumps which use more ATP. This produces heat and raises body temperature.

Thyroid hormones also increase protein synthesis. In addition, glucose and fatty acids are used in greater amounts for ATP production. These hormones also increase lipolysis and enhance cholesterol excretion which decreases blood cholesterol levels.

Thyroid hormones also enhance some actions of catecholamines (epinephrine and norepinephrine) by upregulating Beta receptors. This explains the symptoms of HYPERTHYROIDISM, symptoms such as increased heart rate, increased blood pressure, and forceful heartbeats.

Hyposecretion of thyroid hormones in infancy results in cretinism. Cretinism: stunting of body growth and mental development. In adulthood it results in myxedema (5 times more prevalent in females than in males). Myxedema: 6 different forms. In pituitary myxedema we see a hard edema of the subcutaneous tissue, dryness of skin, loss of hair, subnormal temperature, hoarseness, and muscle weakness.

Hypersecretion of thyroid hormones results in exophthalmic goiter (Graves disease). This is characterized by protruding eyes (due to edema behind the eyeball) and a high energy level. May not always see a goiter. Grave's disease: toxic goiter with diffuse hyperplasia of the thyroid gland. In Grave's disease there are circulating immunoglobulins that bind to thyrotropin receptors in the thyroid gland. This immunoglobulin enhances T4-T3 production which results in hyperthyroidism.

Parathyroid glands Are composed of two cell types:

1. chief (principal) cells
2. oxyphil cells

The **chief cells** produce **parathyroid hormone (PTH)**. This hormone raises blood calcium levels by acting on bones, kidneys, and intestines.

The **oxyphil cells** support the chief cells and may produce some PTH.

Pancreas: has both an endocrine and an exocrine function. Here we will only consider the endocrine function. The endocrine portion of the pancreas is found in the pancreatic islets (islets of Langerhans). Here we see four cell types:

1. alpha cells - produce glucagon
2. beta cells - produce insulin
3. delta cells - produce GHIF or somatostatin
4. F cells - produce a pancreatic polypeptide

glucagon causes the liver to convert glycogen into glucose thus raising blood glucose levels.

insulin decreases blood sugar levels by causing glucose to move through cell membranes into cells. It also stimulates muscle and liver cells to convert glucose to glycogen. This helps amino acids enter cells to aid in synthesizing proteins and fats.

Adrenal gland is divided into two regions:

1. cortex
2. medulla

The cortex is further divided into three zones:

1. outer - zona glomerulosa
2. middle - zona fasciculata
3. inner - zona reticularis

The adrenal cortex is responsible for the production of over 30 hormones called corticosteroids. These are divided into three types:

1. **mineralcorticoids** - are produced in the zona glomerulosa. They regulate the amount or concentration of extracellular electrolytes.

Aldosterone (from the zona glomerulosa) effects the kidneys by regulating the amount of Na⁺ and K⁺ that are eliminated in the urine. At the same time it promotes water resorption and reduces urine output.

2. **glucocorticoids** - are produced mainly in the zona fasciculata. They influence the metabolism of carbohydrates, proteins, and fats.

These also help resist stress, promote vasoconstriction, and are inflammatory.

The most abundant glucocorticoids are Cortisol (hydrocortizone), corticosterone, and cortizone.

3. **gonadocorticoids** - are sex hormones secreted by the zona reticularis. most of these hormones belong to the group referred to as androgens. Some adrenal estrogens and progesterones are also present.

The medulla consists mainly of chromaffin cells. These are arranged around blood vessels. Each cluster of chromaffin cells receives direct sympathetic innervation from the ANS.

The chromaffin cells of the adrenal medulla produce epinephrine and norepinephrine. Note that these are classified as amines (ie. catecholamines) because they consist of amino acids without peptide bonds.

The effect of epinephrine and norepinephrine is similar to that of activating the sympathetic portion of the ANS except that their effects last 10 times longer.

These increase cardiac output and heart rate, dilate coronary vessels, increase mental alertness, increases respiratory rate, and elevate metabolic rate.

Activation of the adrenal medulla prepares the body for the fight or flight response.

A decrease in mineralcorticoid (mainly aldosterone) and glucocorticoids (mainly cortisol) can cause Addison's Disease. Addison's disease: reduced cortical hormones, weakness and lethargy, weight loss and decreased appetite, darkening of skin, abdominal pains accompanied by diarrhea, nausea, and vomiting, and salt craving (to name a few).

An Increase in aldosterone and cortisol cause Cushing's Disease. Cushing's disease: Obesity in the trunk, hump between the shoulders, rounding of face & fullness of neck, muscle weakness and wasting, fatigue, and flushed face. Also may see osteoporosis, diabetes, high blood pressure, and excess hair growth. In men you may see erectile dysfunction. In women you may see absence of menstrual periods.

Gonads: the ovaries and testes

testes - produce testosterone from the interstitial cells (of Leydig). This is responsible for male secondary sex traits and sex drive.

ovaries - produce estrogen from ovarian follicles and from CL. Estrogen is also found in the placenta, adrenal cortex, and the testes.

Estrogen functions to/in:

1. development and function of secondary sex organs
2. menstrual changes of the uterus
3. development of secondary sex characteristics
4. regulation of sex drive

Ovaries also produce progesterone in the corpus luteum. This prepares the uterus for implantation and also aids in the prevention of spontaneous abortion.

Ovaries also produce relaxin, which serves to soften the pubic symphysis and dilate the cervix.

Pineal gland may secrete melatonin. Its function in humans is unknown but is seemingly related to light/dark cycles. It is produced at night (when in the dark) and therefore has been nick named the “Dracula” of hormones.

Thymus: produces T cells for use in the immune system. Also makes thymosin which may stimulate T cells in the body.

Placenta: is a temporary organ. It makes estrogens and progesterones.

Also produces human chorionic gonadotropin (hCG) which is very similar to LH. hCG is the basis for pregnancy tests.

Also produces somatomammotropin which is similar to GH and prolactin.