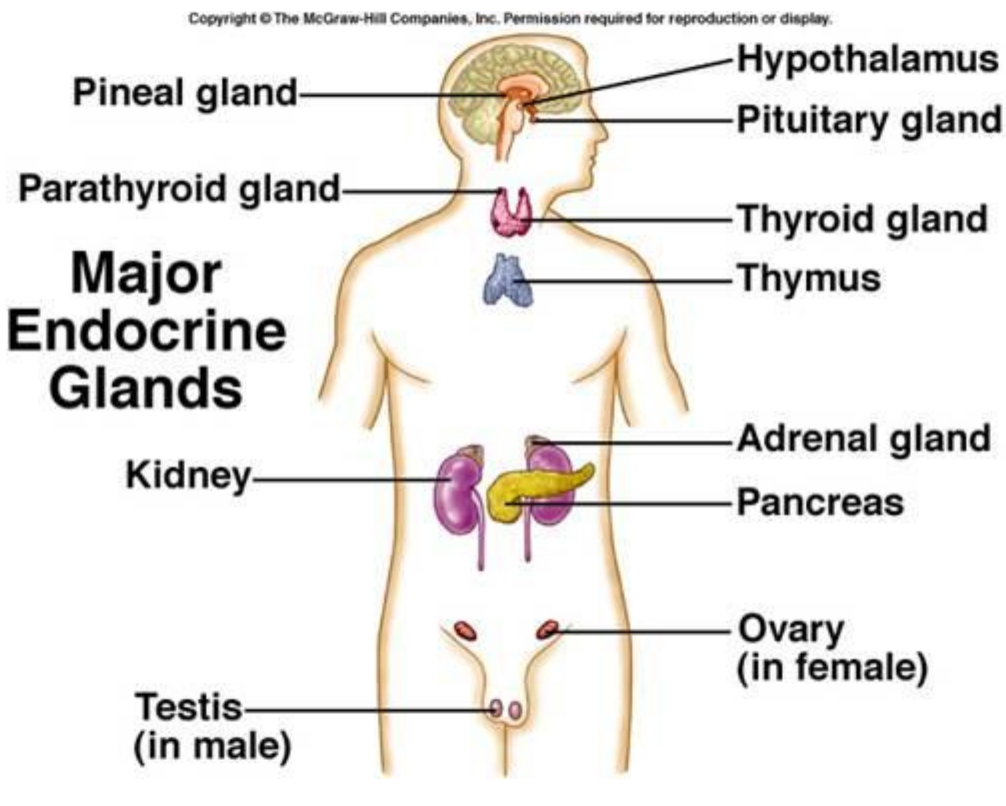
Baida almusawy

The lecture (4) **Human Physiology/The endocrine system**

Introduction

The endocrine system is a control system of ductless glands that secrete hormones within specific organs. Hormones act as "messengers," and are carried by the bloodstream to different cells in the body, which interpret these messages and act on them. The endocrine system provides an electrochemical connection from the hypothalamus of the brain to all the organs that control the body metabolism, growth and development, and reproduction.

There are two types of hormones secreted in the endocrine system: Steroidal and non-steroidal hormones.



Types of Glands

1- Exocrine Glands are those which release their cellular secretions through a duct which empties to the outside or into the lumen of an organ. These include certain sweat glands, salivary and pancreatic glands, and mammary glands. They are not considered a part of the endocrine system.

2- Endocrine Glands are those glands which have no duct and release their secretions directly into the intercellular fluid or into the blood. The collection of endocrine glands makes up the endocrine system.

The main endocrine glands are the pituitary (anterior and posterior lobes), thyroid, parathyroid, adrenal (cortex and medulla), pancreas and gonads.

The pituitary gland is attached to the hypothalamus of the lower forebrain.

The thyroid gland consists of two lateral masses, connected by a cross bridge, that are attached to the trachea. They are slightly inferior to the larynx.

The parathyroid glands are four masses of tissue, two embedded posterior in each lateral mass of the thyroid gland.

One adrenal gland is located on top of each kidney. The cortex is the outer layer of the adrenal gland. The medulla is the inner core.

The pancreas is along the lower curvature of the stomach, close to where it meets the first region of the small intestine, the duodenum.

The gonads are found in the pelvic cavity.

Hormones and Types

A hormone is a type of chemical signal. They are a means of communication between cells.

The endocrine system produces hormones that are instrumental in maintaining homeostasis and regulating reproduction and development. A hormone is a chemical messenger produced by a cell that effects specific change in the cellular activity of other cells (target cells). Unlike exocrine glands (which produce substances such as saliva, milk, stomach acid and digestive enzymes), endocrine glands do not secrete substances into ducts (tubes). Instead, endocrine glands secrete their hormones directly into the surrounding extra cellular space. The hormones then diffuse into nearby capillaries and are transported throughout the body in the blood.

The endocrine and nervous systems often work toward the same goal. Both influence other cells with chemicals (hormones and neurotransmitters). However, they attain their goals differently. Neurotransmitters act immediately (within milliseconds) on adjacent muscle, gland, or other nervous cells, and their effect is short-lived. In contrast, hormones take longer to produce their intended effect (seconds to days), may affect any cell, nearby or distant, and produce effects that last as long as they remain in the blood, which could be up to several hours.

Hormones can be chemically classified into four groups

1. Amino acid-derived: Hormones that are modified amino acids.

2. Polypeptide and proteins: Hormones that are chains of amino acids of less than or more than about 100 amino acids, respectively. Some protein hormones are actually glycoproteins, containing glucose or other carbohydrate groups.

3. Steroids: Hormones that are lipids synthesized from cholesterol. Steroids are characterized by four interlocking carbohydrate rings.

In the following table there are the major hormones, their target and their function once in the target cell

Endocrine Gland	Hormone Released	Chemical Class	Target Tissue/Organ	Major Function of Hormone
Hypothalamus	Hypothalamic releasing and inhibiting hormones	Peptide	Anterior pituitary	Regulate anterior pituitary hormone
Posterior Pituitary	Antidiuretic (ADH)	Peptide	Kidneys	Stimulates water reabsorption by kidneys
	Oxytocin	Peptide	Uterus, mammary glands	Stimulates uterine muscle contractions and release of milk by mammary glands
	Thyroid stimulating (TSH)	Glycoprotein	Thyroid	Stimulates thyroid

Anterior Pituitary	Adrenocorticotropic (ACTH)	Peptide	Adrenal cortex	Stimulates adrenal cortex
	Gonadotropic (FSH, LH)	Glycoprotein	Gonads	Egg and sperm production, sex hormone production
	Prolactin (PRL)	Protein	Mammary glands	Milk production
	Growth (GH)	Protein	Soft tissue, bones	Cell division, protein synthesis and bone growth
Thyroid	Thyroxine (T4) and Triiodothyronie (T3)	Iodinated amino acid	All tissue	Increase metabolic rate, regulates growth and development
	Calcitonin	Peptide	Bones, kidneys and intestine	Lowers blood calcium level
Parathyroids	Parathyroid (PTH)	Peptide	Bones, kidneys and intestine	Raises blood calcium level
Adrenal Cortex	Glucocorticoids (cortisol)	Steroid	All tissue	Raise blood glulose level, stimulates breakdown of protein
	Mineralocorticoids (aldosterone)	Steroid	Kidneys	Reabsorb sodium and excrete potassium
	Sex Hormones	Steroid	Gonads, skin, muscles and bones	Stimulates reproductive organs and brings on sex characteristics
Adrenal Medulla	Epinephrine and norepinephrine	Modified amino acid	Cardiac and other muscles	Released in emergency situations, raises blood glucose level, “fight or flight” response
Pancreas	Insulin	Protein	Liver, muscles, adipose tissue	Lowers blood glucose levels, promotes formation of glycogen
	Glucagon	Protein	Liver, muscles, adipose tissue	Raises blood glucose levels
Testes	Androgens (testosterone)	Steroid	Gonads, skin, muscles and bone	Stimulates male sex characteristics

Ovaries	Estrogen and progesterone	Steroid	Gonads, skin, muscles and bones	Stimulates female sex characteristics
Thymus	Thymosins	Peptide	T lymphocytes	Stimulates production and maturation of T lymphocytes
Pineal Gland	Melatonin	Modified amino acid	Brain	Controls circadian and circannual rhythms, possibly involved in maturation of sexual organs

Endocrine Glands

Pituitary gland

The hypothalamus makes up the lower region of the diencephalons and lies just above the brain stem. The pituitary gland (hypophysis) is attached to the bottom of the hypothalamus by a slender stalk called the infundibulum. The pituitary gland consists of two major regions: the anterior pituitary gland (anterior lobe or adenohypophysis) and the posterior pituitary gland (posterior lobe or neurohypophysis). The hypothalamus also controls the glandular secretion of the pituitary gland. It is divided into two sections: the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis). The Anterior pituitary is involved in sending hormones that control all other hormones of the body.

Posterior pituitary

Communication between the hypothalamus and the posterior pituitary occurs through neurosecretory cells that span the short distance between the hypothalamus and the posterior pituitary. Two hormones: oxytocin and antidiuretic hormone (ADH) are produced and released this way. Decreased ADH release or decreased renal sensitivity to ADH produces a condition known as diabetes insipidus. Diabetes insipidus is characterised by polyuria (excess urine production), hypernatremia (increased blood sodium content) and polydipsia (thirst). The posterior pituitary in effect It does not produce its own hormones, but only stores and releases the hormones oxytocin and antidiuretic hormone. ADH is also known as arginine vasopressin (AVP) or simply vasopressin.

Anterior pituitary

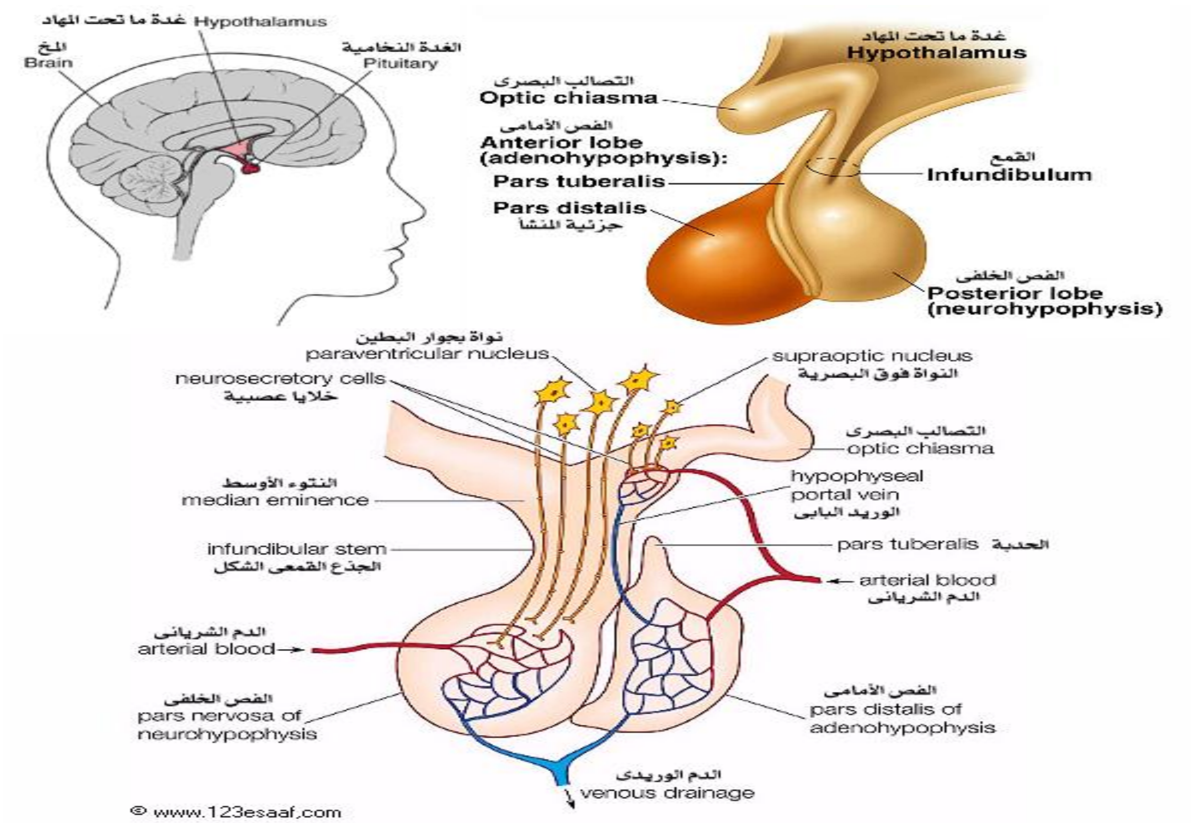
Communication between the hypothalamus and the anterior pituitary occurs through hormones(releasing hormones and inhibiting hormones) produced by the hypothalamus and delivered to the anterior pituitary via a portal network of capillaries. The releasing and inhibiting hormones are produced by specialized neurons of the hypothalamus called neurosecretory cells. The hormones are released into a capillary network or primary plexus and transported through veins to a second capillary network that supplies the anterior pituitary. The hormones then diffuse from the secondary plexus into the anterior pituitary where they initiate the production of specific hormones by the anterior pituitary. The anterior pituitary lobe receives releasing hormones from the hypothalamus via a portal vein system known as the hypothalamic-hypophyseal portal system.

The anterior pituitary secretes:

- thyroid-stimulating hormone (TSH)
- adrenocorticotropic hormone (ACH)
- prolactin
- follicle-stimulating hormone (FSH)
- luteinizing hormone (LH)
- growth hormone (GH)

the anterior lobe. These include:

- thyrotropin-releasing hormone (TRH)
- corticotropin-releasing hormone (CRH)
- dopamine (DA), also called 'prolactin inhibiting factor' (PIF)
- gonadotropin-releasing hormone (GnRH)
- growth hormone releasing hormone (GHRH)



Antagonistic Hormones

Hormones that act to return body conditions to within acceptable limits from opposite extremes are called antagonistic hormones. The two glands that are the most responsible for homeostasis is the thyroid and the parathyroid.

The regulation of blood glucose concentration (through negative feedback) illustrates how the endocrine system maintains homeostasis by the action of antagonistic hormones. Bundles of cells in the pancreas called the islets of Langerhans contain two kinds of cells, alpha cells and beta cells. These cells control blood glucose concentration by producing the antagonistic hormones insulin and glucagon.

Beta cells secrete insulin When the concentration of blood glucose rises such in after eating, beta cells secret insulin into the blood. Insulin stimulates the liver and most other body cells to absorb glucose. Liver and muscle cells convert glucose to glycogen and adipose cells convert glucose to fat. In response glucose concentration decreases in the blood and insulin secretion discontinues through negative feedback from declining levels of glucose.

Alpha cells secrete glucagon when the concentration of blood glucose drops such as during exercise, alpha cells secrete glucagon into the blood. Glucagon stimulates the liver to release glucose. The glucose in the liver originates from the breakdown of glycogen. Glucagon also stimulates the production of ketone bodies from amino acids and fatty acids. Ketone bodies are an alternative energy source to glucose for some tissues. When blood glucose levels return to normal, glucagon secretion discontinues through negative feedback.

Thyroid gland

The Thyroid gland is one of the largest endocrine glands in the body. It is positioned on the neck just below the Larynx and has two lobes with one on either side of the trachea. It is involved in the production of the hormones T3 (triiodothyronine) and T4 (thyroxine). These hormones increase the metabolic activity of the body‘s cells. The thyroid also produces and releases the hormone calcitonin (thyrocalcitonin) which contributes to the regulation of blood calcium levels. Thyrocalcitonin or calcitonin decreases the concentration of calcium in the blood. Most of the calcium removed from the blood is stored in the bones..

The thyroid hormone consists of two components: thyroxine and iodine. This hormone increases the metabolism of most body cells. A deficiency of iodine in the diet leads to the enlargement of the thyroid gland **known** as a simple goiter. Hypothyroidism during early development leads to cretinism. In adults, it produces myxedema, characterized by obesity and lethargy. Hyperthyroidism leads to a condition known as exophthalmic goiter, characterized by weight loss as well as hyperactive and irritable behavior. Usually the patient shows puffy skin, sluggishness and lowered vitality. Other symptoms of hypothyroidism include weight gain, decreased libido, inability to tolerate cold, muscle pain and spasm, insomnia and brittle nails. Hypothyroidism in children, a condition known as cretinism, can result in mental retardation, dwarfism, and permanent sexual immaturity. Sometimes the thyroid gland produces too much thyroxine, a condition known as hyperthyroidism this condition produces symptoms such as an abnormally high body temperature, profuse sweating, high blood pressure, loss of weight, irritability and muscular pain and weakness, It also causes the characteristic symptom of the eyeballs protruding from the skull called exophthalmia.

T3 and T4 Function within the body

The Production of T3 and T4 are regulated by thyroid stimulating hormone (TSH), released by the pituitary gland. TSH Production is increased when T3 and T4 levels are too low. The thyroid hormones are released throughout the body to direct the body's metabolism. They stimulate all cells within the body to work at a better metabolic rate. Without these hormones the body's cells would not be able to regulate the speed at which they performed chemical actions. Their release will be increased under certain situations such as cold temperatures when a higher metabolism is needed to generate heat. When children are born with thyroid hormone deficiency they have problems with physical growth and developmental problems.

Calcitonin

Calcitonin is a 32 amino acid polypeptide hormone. It is an additional hormone produced by the thyroid, and contributes to the regulation of blood calcium levels. Thyroid cells produce calcitonin in response to high calcium levels in the blood. This hormone will stimulate movement of calcium into the bone structure. It can also be used therapeutically for the treatment of hypercalcemia or osteoporosis. Without this hormone calcium will stay within the blood instead of moving into bones to keep them strong and growing.

Parathyroid gland

There are four parathyroid glands. They are small light-colored lumps that stick out from the surface of the thyroid gland. All four glands are located on the thyroid gland. They are butterfly-shaped and located inside the neck, more specifically on both sides of the windpipe. One of the parathyroid glands most important functions is to regulate the body's calcium and phosphorus levels. Another function of the parathyroid glands is to secrete parathyroid hormone (Parathormone) which causes the release of the calcium present in bone to extracellular fluid. PTH does this by depressing the production of osteoblasts, special cells of the body involved in the production of bone and activating osteoclasts, other specialized cells involved in the removal of bone. There are two major types of cells that make up parathyroid tissue:

1- oxyphil cells. Their function is basically unknown.

2- chief cells. Chief cells produce parathyroid hormone.

The structure of a parathyroid gland is very different from that of a thyroid gland. The chief cells that produce parathyroid hormone are arranged in tightly-packed nests around small blood vessels, quite unlike the thyroid cells that produce thyroid hormones, which are arranged in spheres called the thyroid follicles. PTH or Parathyroid Hormone is secreted from these four glands. It is released directly into the bloodstream and travels to its target cells which are often quite far away. It then binds to a structure called a receptor, that is found either inside or on the surface of the target cells. Receptors bind a specific hormone and the result is a specific physiologic response, meaning a normal response of the body. PTH finds its major target cells in bone, kidneys, and the gastrointestinal system. Calcium is important for steps of body metabolism. Blood cannot clot without sufficient calcium. Skeletal muscles require this mineral in order to contract. A deficiency of PTH can lead to tetany, muscle weakness due to lack of available calcium in the blood.

Production of this hormone is directly controlled by the calcium concentration of the extracellular fluid bathing the cells of these glands. Parathormne exerts at least the following five effects:

(1) it increases gastrointestinal absorption of calcium by stimulating the active transport system and moves calcium from the gut lumen into the blood

(2) it increases the movement of calcium and phosphate from bone into extracellular fluid. This is accomplished by stimulating osteoclasts to break down bone structure, thus liberating calcium phosphate into the blood. In this way, the store of calcium contained in bone is tapped

(3) it increases re-absorption of calcium by the renal tubules, thereby decreasing urinary calcium excretion

(4) it reduces the re-absorption of phosphate by the renal tubules

(5)it stimulates the synthesis of 1,25-dihydrixycholecalciferol by the kidney.

Adrenal glands

Adrenal glands are a pair of ductless glands located above the kidneys. Through hormonal secretions, the adrenal glands regulate many essential functions in the body, including biochemical balances that influence athletic training and general stress response. The glucocorticoids include corticosterone, cortisone, and hydrocortisone or cortisol. These hormones serve to stimulate the conversion of amino acids into carbohydrates which is a process known as gluconeogenesis, and the formation of glycogen by the liver. They also stimulate the formation of reserve glycogen in the tissues, such as in the muscles. The glucocorticoids also participate in lipid and protein metabolism. The cortex of the adrenal gland is known to produce over 20 hormones, but their study can be simplified by classifying them into three categories: glucocorticoids, mineralcorticoids, and sex hormones.

Adrenal Cortex: The hormones made by the Adrenal Cortex supply long-term responses to stress. The two major hormones produced are the Mineral Corticoids and the Glucocorticoids. The Mineral Corticoids regulate the salt and water balance, leading to the increase of blood volume and blood pressure. The Glucocorticoids are monitoring the ACTH, in turn regulating carbohydrates, proteins, and fat metabolism. This causes an increase in blood glucose. Glucocorticoids also reduce the body's inflammatory response.

Cortisol is one of the most active glucocorticoids. It usually reduces the effects of inflammation or swelling throughout the body. It also stimulates the production of glucose from fats and proteins, which is a process referred to as gluconeogenesis.

Aldosterone is one example of a mineralcorticoid. It signals the tubules in the kidney nephrons to reabsorb sodium while secreting or eliminating potassium. If sodium levels are low in the blood, the kidney secretes more renin, which is an enzyme that stimulates the formation of angiotensin from a molecule made from the liver. Angiotensin stimulates aldosterone secretion. As a result, more sodium is reabsorbed as it enters the blood.

The renin-angiotensin-aldosterone mechanism can raise blood pressure if it tends to drop. It does this in two ways. Angiotensin is a vasoconstrictor, decreasing the diameter of blood vessels. As vessels constrict, blood pressure increases. In addition, as sodium is reabsorbed, the blood passing through the kidney becomes more hypertonic. Water follows the sodium into the hypertonic blood by osmosis. This increases the amount of volume in the blood and also increases the blood pressure.

Adrenal Medulla The hypothalamus starts nerve impulses that travel the path from the bloodstream, spinal cord, and sympathetic nerve fibers to the Adrenal Medulla, which then releases hormones. The effects of these hormones Human provide a short-term response to stress.

Excessive secretion of the glucocorticoids causes Cushing's syndrome, characterized by muscle atrophy or degeneration and hypertension or high blood pressure. Under secretion of these substances produces Addison's disease, characterized by low blood pressure and stress.

Epinephrine and norepinephrine produce the "fight or flight" response, similar to the effect from the sympathetic nervous system. Therefore, they increase heart rate, breathing rate, blood flow to most skeletal muscles, and the concentration of glucose in the blood. They decrease blood flow to the digestive organs and diminish most digestive processes.

Should there be an insufficient supply of cortical hormones, a condition known as Addison's disease would result. This disease is characterized by an excessive excretion of sodium ions, and hence water, due to lack of mineralcorticoids. Accompanying this is a decreased blood glucose level due to a deficient supply of glucocorticoids. The effect of a decreased androgen supply cannot be observed immediately. Injections of adrenal cortical hormones promptly relieve these symptoms.

Pancreas

The **pancreas** is very important organ in the digestion system and the circulatory system because it helps to maintain our blood sugar levels. The pancreas is considered to be part of the gastrointestinal system. It produces digestive enzymes to be released into the small intestine to aid in reducing food particles to basic elements that can be absorbed by the intestine and used by the body. It has another very different function in that it forms insulin, glucagon and other hormones to be sent into the bloodstream to regulate blood sugar levels and other activities throughout the body.

Insulin acts to lower blood sugar levels by allowing the sugar to flow into cells. Glucagon acts to raise blood sugar levels by causing glucose to be released into the circulation from its storage sites. Insulin and glucagon act in an opposite but balanced fashion to keep blood sugar levels stable. Insulin deficiency leads to the development of diabetes mellitus, specifically type I, juvenile diabetes. As the pancreas does not produce sufficient insulin, it is treated by insulin injections. In type II or maturity onset diabetes, the pancreas does produce enough insulin, but the target cells do not respond to it.

Insulin is secreted by beta cells, which are located in the part of the pancreas known as the islets of Langerhans. These groups of cells, which are located randomly throughout the pancreas, also consist of other secretory cells called alpha cells. It is these alpha cells that secrete glucagon. Glucagon is a hormone that has the following major effects: it increases hepatic synthesis of glucose from pyruvate, lactate, glycerol, and amino acids (a process called gluconeogenesis, which also raises the plasma glucose level); and it increases the breakdown of adipose tissue triglyceride, thereby raising the plasma levels of fatty acids and glycerol. The glucagon secreting alpha cells in the pancreas, like the beta cells, respond to changes in the concentration of glucose in the blood flowing through the pancreas; no other nerves or hormones are involved.

Sex organs

The main hormones from the reproductive organs are:-

Testosterone is more prominent in males. It belongs to the family of androgens, which are steroid hormones producing masculine effects. Testosterone stimulates the development and functioning of the primary sex organs. It also stimulates the development and maintenance of secondary male characteristics, such as hair growth on the face and the deep pitch of the voice.

Estrogen In females, this hormone stimulates the development of the uterus and vagina. It is also responsible for the development and maintenance of secondary female characteristics, such as fat distribution throughout the body and the width of the pelvis.

Male

The testes produce androgens (i.e., "testosterone"). Testosterone is classified as a steroid and is responsible for many of the physical characteristics in males like.

- Broad shoulders
- Muscular body
- Hair

Testosterone increases protein production. Hormones that build up protein are called anabolic steroids. Anabolic steroids are available commercially and are being used by athletes because they help improve their physical ability, however, they do have major side effects such as:

- Liver and kidney disorders
- Hypertension (high blood pressure)
- Decreased sperm count and impotency
- Aggressive behavior
- Acne

Female

The ovaries produce estrogen and progesterone. Estrogen increases at the time of puberty and causes the growth of the uterus and vagina. Without estrogen egg maturation would not occur. Estrogen is also responsible for secondary sex characteristics such as female body hair and fat distribution. Estrogen and Progesterone are responsible for the development of the breast and for the uterine cycle. Progesterone is a female hormone secreted by the corpus luteum after ovulation during the second half of the menstrual cycle. It prepares the lining of the uterus for implantation of a fertilized egg and allows for complete shedding of the endometrium at the time of menstruation. In the event of pregnancy, the progesterone level remains stable beginning a week or so after conception.

Pineal gland

The pineal gland (also called the pineal body or epiphysis) is a small endocrine gland in the brain. It is located near the center of the brain, between the two hemispheres, tucked in a groove where the two rounded thalamic bodies

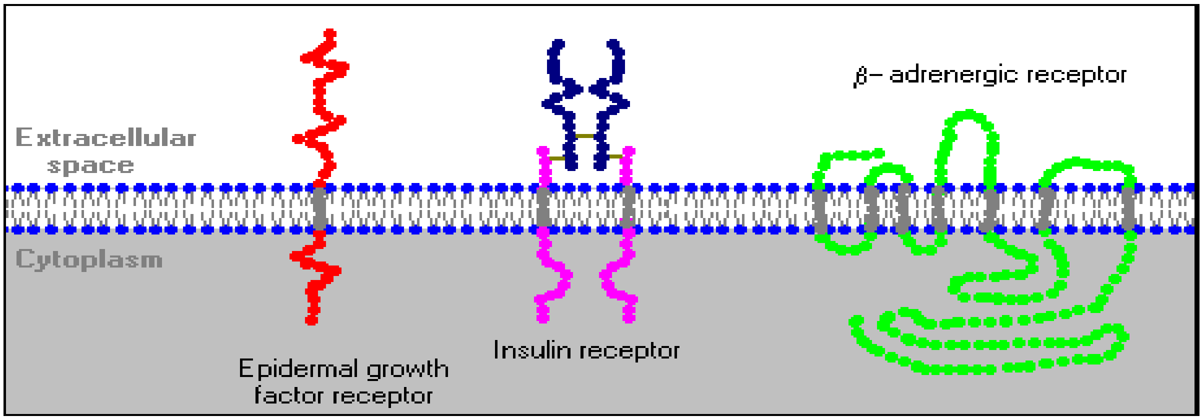
join. The pineal gland is a reddish-gray body about the size of a pea (8 mm in humans) located just rostro-dorsal to the superior colliculus and behind and beneath the stria medullar between the laterally positioned thalamic bodies. It is part of the epithalamus. The pineal gland is a midline structure, and is often seen in plain skull X-rays, as it is often calcified. The main hormone produced and secreted by the pineal gland is melatonin. Secretion is highest at night and between the ages of 0-5.

Mechanism of Action Hormones

Protein and peptide hormones, catecholamines like epinephrine, and eicosanoids such as prostaglandins find their receptors decorating the plasma membrane of target cells.

Binding of hormone to receptor initiates a series of events which leads to generation of so-called second messengers within the cell (the hormone is the first messenger). The second messengers then trigger a series of molecular interactions that alter the physiologic state of the cell. Another term used to describe this entire process is signal transduction.

Several distinctive variations in receptor structure have been identified. As depicted below, some receptors are simple, single-pass proteins; many growth factor receptors take this form. Others, such as the receptor for insulin, have more than one subunit. Another class, which includes the beta-adrenergic receptor, is threaded through the membrane seven times.


β- adrenergic receptor
Extracellular space
Cytoplasm
Epidermal growth factor receptor
Insulin receptor