Unit Five

Chemistry of Hormones

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Unit 5. Chemistry of Hormones

Definition of Hormones

The classical definition of a hormone is “substances released from ductless or endocrine glands directly to the blood”. A more modern definition of a hormone is that it is synthesized by one type of cells and transported through blood to act on another type of cells or regulating the function of another tissues. Based on mechanism of action, the hormones may be divided into two types:

1. Hormones with cell surface receptors
2. Hormones with intracellular receptors.

Endocrine glands may secrete excessive or deficient amounts of hormone. Abnormalities of target glands may be primary or secondary to dysfunction of the controlling mechanism. Hormone secretion may vary predictably over a 24-h (circadian) or longer period. It may be episodic or may respond predictably to physiological stimuli such as stress.

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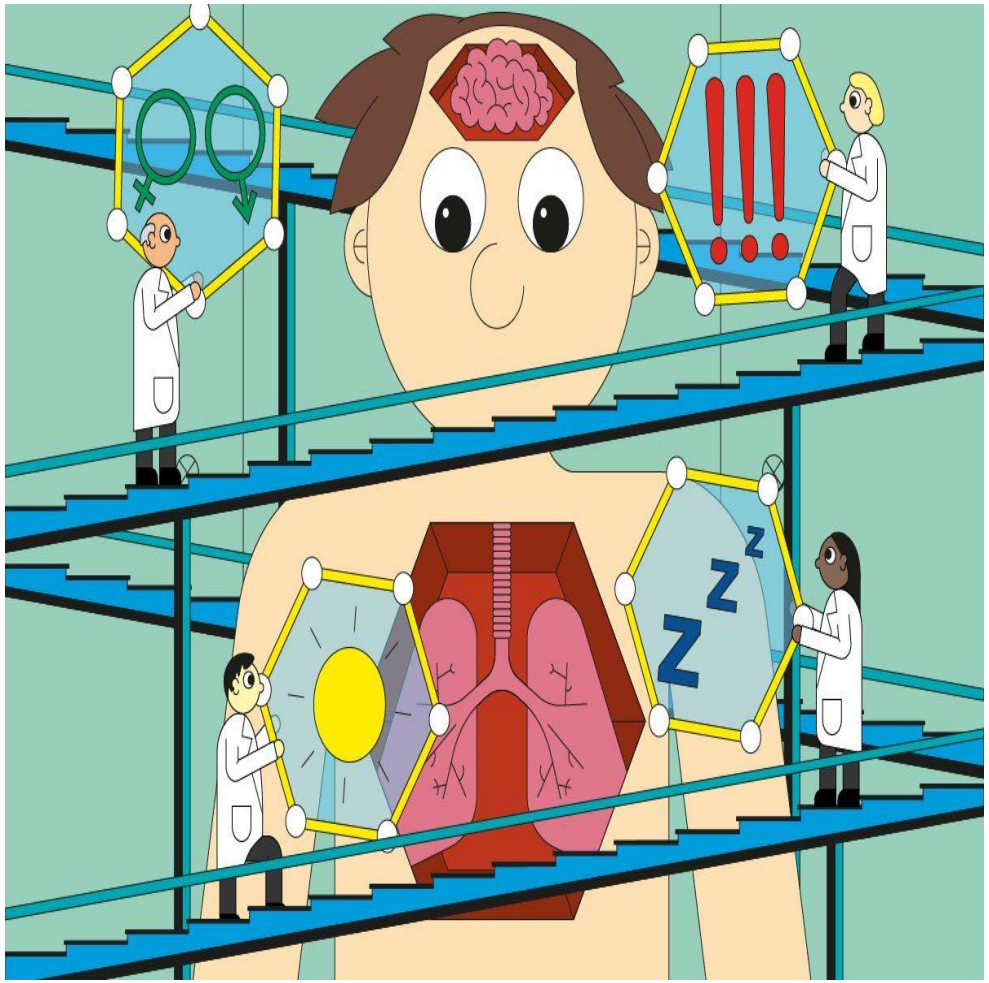
Chemical Classification of Hormones

Hormones are classified to **four** types based on their chemical structures:

1- Hormones derived from Polypeptides & Proteins.
2- Hormones derived from Amino Acids.
3- Hormones derived from Steroids.
4- Hormones derived from Glycoproteins.



Functions of Hormones

1- Regulation of Anabolic and Catabolic bio-reactions for enzymes and proteins inside the cells..
2- Mental and intellectual functions.
3- Regulation of entrance the metabolic materials via the cells.
4- Mediating inflammatory/healing responses.
5- Analgesia effectiveness.

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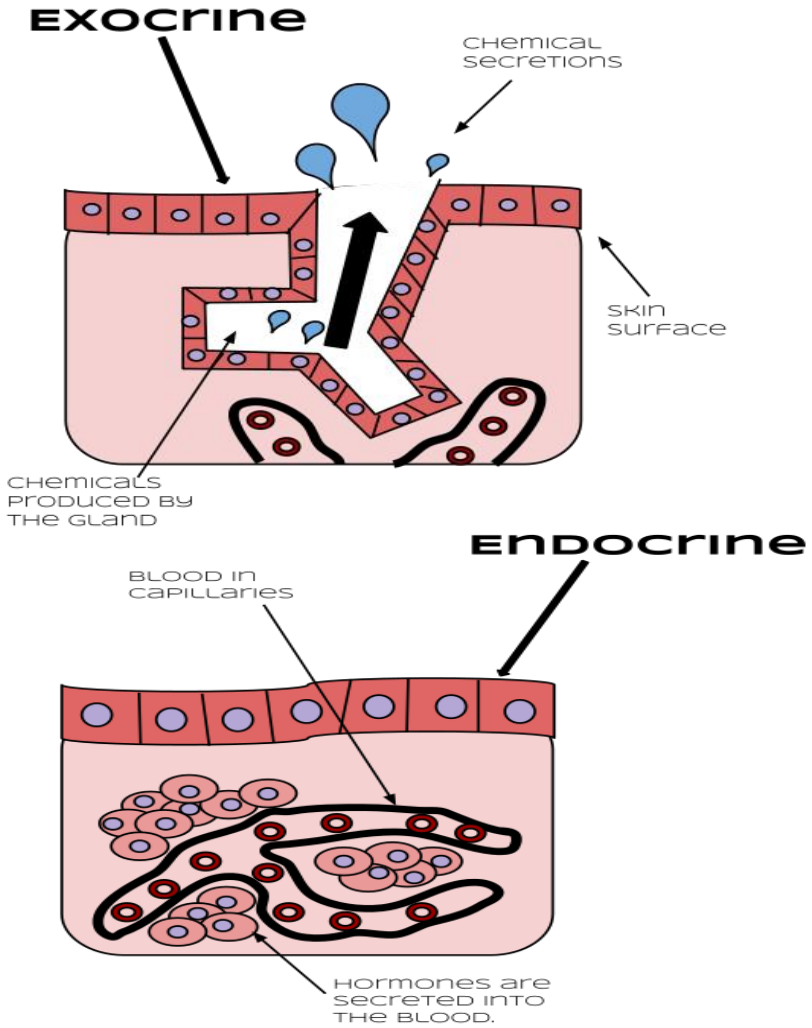
Human Body Glands

There are **two** types of glands in the human body:

1- Exocrine Glands: They are glands that secrete substances onto an epithelial surface by way of a duct. For example; sweat, salivary, mammary, ceruminous, lacrimal, sebaceous, prostate and mucous.

2- Endocrine Glands: They are ductless glands of the endocrine system that secrete their products, hormones, directly into the blood. The major glands of the endocrine system include the pineal gland, pituitary gland, pancreas, ovaries, testes, thyroid gland, parathyroid gland, hypothalamus and adrenal glands. The hypothalamus and pituitary glands are neuroendocrine organs.

The liver and pancreas are both exocrine and endocrine glands; they are exocrine glands because they secrete products—bile and pancreatic juice—into the gastrointestinal tract through a series of ducts, and endocrine because they secrete other substances directly into the bloodstream.



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Hypothalamus Gland

The hypothalamus is a small region of the brain. It's located at the base of the brain, near the pituitary gland. While it's very small, the hypothalamus plays a crucial role in many important functions. The overall function of the hypothalamus is to link the central nervous system to the endocrine system via the pituitary gland. The hypothalamus produces two types of endocrine factors:

1-Hypothalamic Neuropeptides: There are two hormones in this type:

A- Antidiuretic hormone (ADH): It’s called also Vasopressin. Its main action is to prevent diuresis. So it reduces the urine output. The ADH acts on the distal convoluted tubules of the kidney, producing reabsorption of water. Deficiency of ADH results in diabetes insipidus. It is characterized by excretion of large volumes of dilute urine.

B- Oxytocin: The term means “to stimulate birth”. It acts on an estrogen-primed uterus. The synthetic derivative of oxytocin, pitocin, is used to induce labor. It has an effect on the mammary glands. Suckling generates a neurogenic reflex, which stimulates the production of oxytocin. It causes contraction of the myoepithelial cells expelling the milk into milk ducts from the acini.

2-Hypothalamic Releasing Factors: They are neurosecretions and have their effect on the secretion of pituitary hormones such as thyrotropin releasing hormone (TRH), gonadotropin releasing hormone (GnRH), growth hormone releasing hormone (GHRH), prolactin inhibitory factor (PIF) and Somatostatin.

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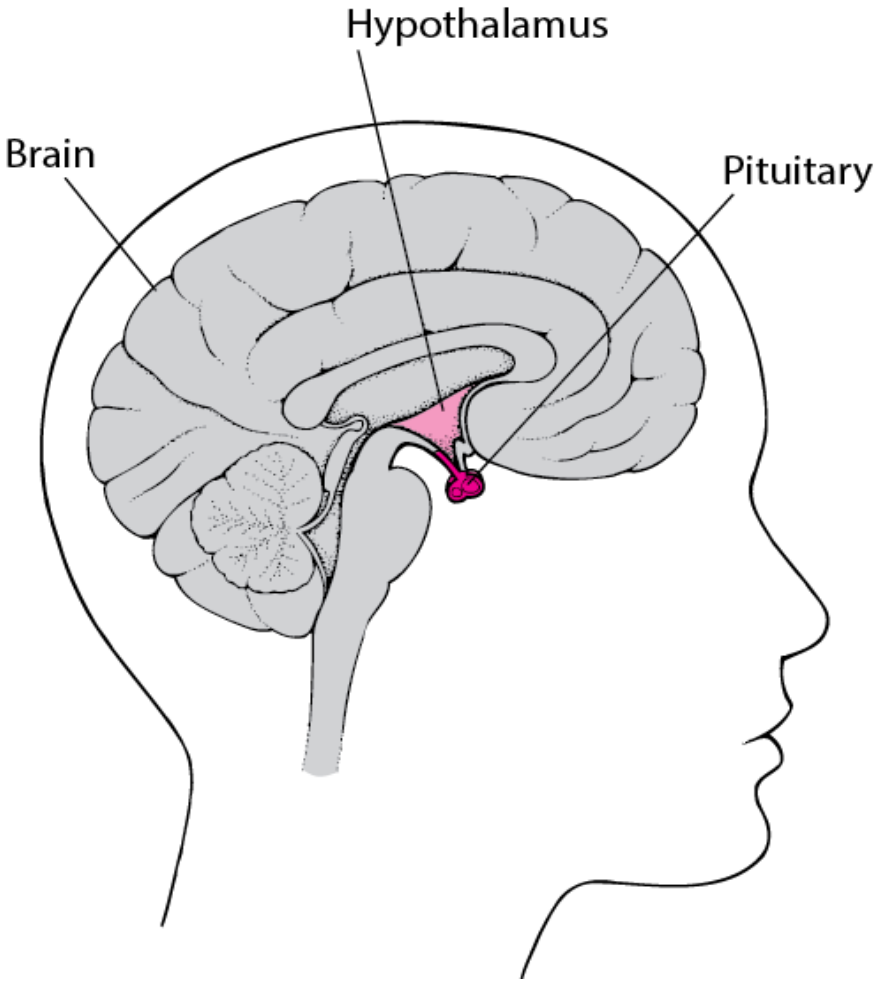
Pituitary Gland

The pituitary gland (also called hypophysis) is an endocrine gland, about the size of a pea and weighing 0.5 grams in humans. It is a protrusion off the bottom of the hypothalamus at the base of the brain. It is composed of two lobes:

1- Anterior Lobe: It regulates several physiological processes, including stress, growth, reproduction, and lactation. Proper functioning of the anterior pituitary and of the organs it regulates can often be ascertained via blood tests that measure hormone levels. The anterior pituitary hormones are tropic in nature which stimulating the secretion of hormones from target organs. Secretions of all these hormones are under the control of hypothalamic releasing or inhibitory factors.

2- Posterior Lobe: In all animals, the glandular anterior pituitary is distinct from the neural composition of the posterior pituitary which may considered as an extension of the hypothalamus gland.



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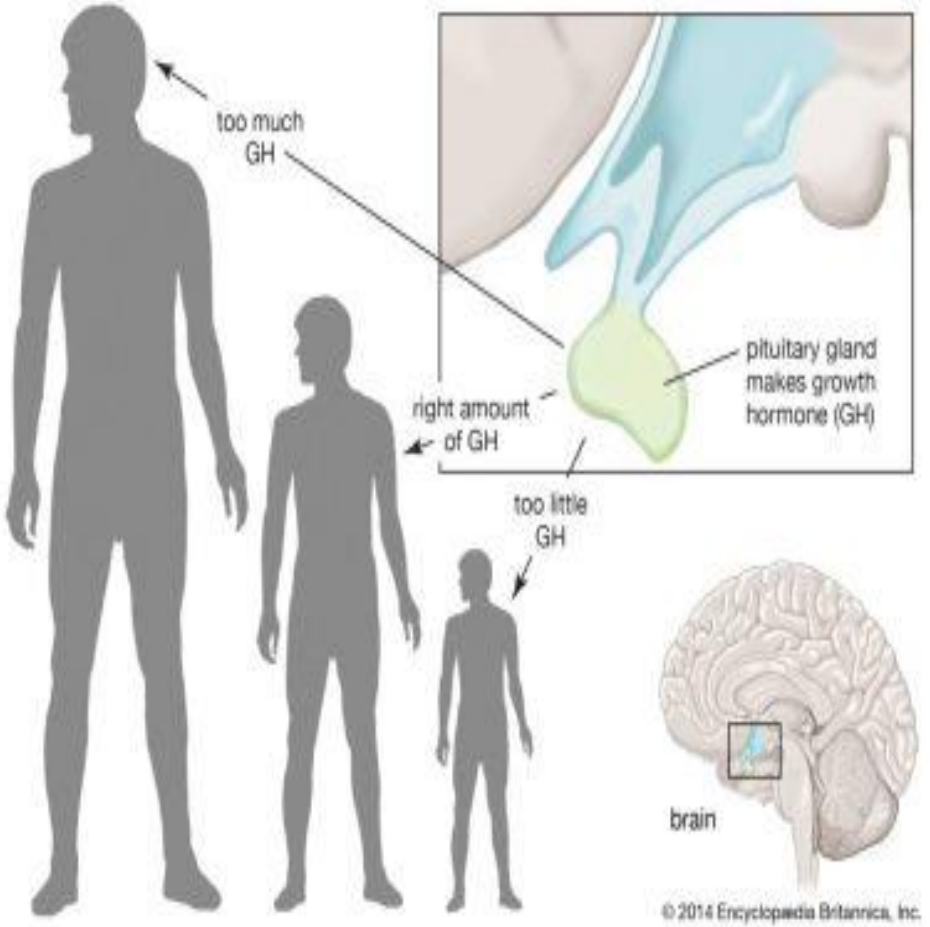
Hormones of Anterior Lobe of the Pituitary Gland

1- Growth Hormone (GH): It is also called Somatotropin. Maximum level of GH is seen during deep sleep. Hypoglycemia stimulates GH secretion, and hyperglycemia suppresses it. Somatostatin inhibits the GH secretion. GH increases the uptake of amino acids by cells; enhances protein synthesis, and produces positive nitrogen balance. The anti-insulin effect of GH causes lipolysis and hyperglycemia. The overall effect of GH is to stimulate growth of soft tissues, cartilage and bone. GH is lipolytic, inducing the breakdown of tissue lipids and thus providing energy supplies. Excess secretion by GH secreting tumor, leads to gigantism in children and acromegaly in adults. Deficiency of GH secretion in early childhood results in pituitary dwarfism. Dwarfism may also result from congenital deficiency of GH due to end organ resistance. It is treated by giving GH produced by recombinant technology.



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2- Adrenocorticotropic Hormone (ACTH): It is released from the pituitary in a pulsatile manner, with a definite diurnal rhythm, the secretion being highest in the early morning, and minimum at midnight. This pattern of secretion is reflected in cortisol also. Factors that increase ACTH secretion include stresses such as pain, cold exposure, acute hypoglycemia, trauma, depression, and surgery. ACTH secreting tumors of pituitary will cause Cushing's disease. Deficiency of ACTH secretion may occur as a part of panhypopituitarism. Dexamethasone suppresses ACTH hormone and cortisol production in normal subjects; but not in patients with Cushing's syndrome.

3- Endorphins: They are responsible for increasing the threshold of pain, especially under conditions of stress. Morphine binds to the receptors for endorphins, by which morphine induces the pain relief.

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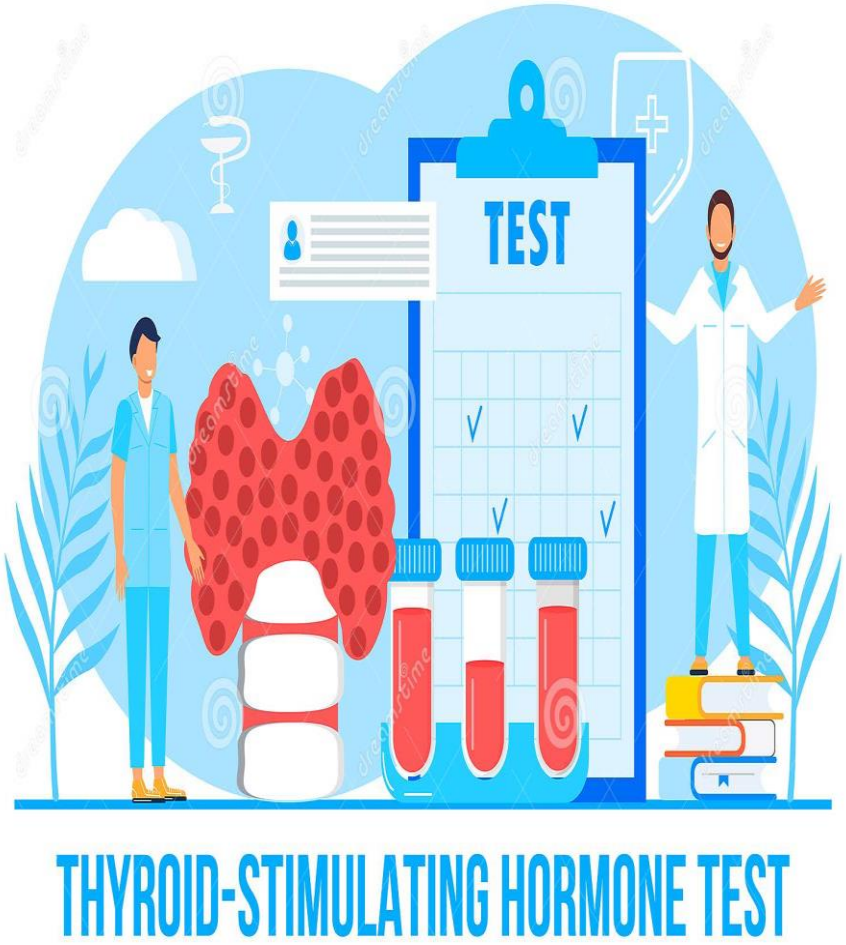
4- Thyroid Stimulating Hormone (TSH): It's also called Thyrotropin. It increases the secretion of thyroid hormones by stimulating all the steps of production of synthesis of thyroxine. High levels of TSH may occur due to primary hypothyroidism and lack of feedback control. Normal TSH level is 0.5–5 microunits per mL. Deficiency may occur as a part of hypopituitarism. Increased serum TSH levels are seen in primary hypothyroidism (3–100 times normal), Hashimoto's thyroiditis, ectopic TSH secretion by tumors (lung, breast), and in thyroid hormone resistance. The TSH is elevated in euthyroid patients during treatment of hyperthyroidism but TSH is low for 4–6 weeks after achieving euthyroid state in treated hyperthyroid patients. Decreased levels are observed in primary hyperthyroidism, secondary hypothyroidism (pituitary origin), tertiary hypothyroidism (hypothalamic), subclinical hyperthyroidism (e.g. toxic multinodular goiter, exogenous thyroid hormone administration, autonomous thyroid hormone secretion) and in euthyroid sick syndrome.



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5- Gonadotropins: They are LH (Luteinizing hormone) and FSH (Follicle stimulating hormone). The FSH stimulates growth of ovarian follicles in females and spermatogenesis (Sertoli cells) in males. The FSH secretion rises during the follicular phase of the menstrual cycle, reaches a peak by the 14th day and starts falling when ovulation occurs. Ovulation occurs as a result of positive feedback effect of estrogen producing the preovulatory LH surge. The level of FSH and LH falls during the postovulatory phase, unless fertilization and implantation occur. High levels of FSH and LH are seen in postmenopausal women. FSH regulates the development, growth, pubertal maturation, and reproductive processes of the body. The FSH levels are normally low during childhood and, in females, high after menopause. High FSH levels are an indication of subfertility and/or infertility. Diminished secretion of FSH can result in hypogonadism. This condition is typically manifested in males as failure in production of normal numbers of sperm. In females, cessation of reproductive cycles is commonly observed. Serum level of FSH is raised in primary gonadal failure, ovarian or testicular agenesis, castration, menopause, orchitis and gonadotropin secreting pituitary tumors. Serum level of FSH is decreased in anterior pituitary hypofunction, hypothalamic disorders, pregnancy, anorexia nervosa, polycystic ovary disease, hemochromatosis, sickle cell anemia, and in hyperprolactinemia. In hypogonadism, if the levels of FSH and LH are lower than normal for the patient's age, it suggests hypothalamic or pituitary disease and if more than normal, indicates gonadal problem. Serum level of LH is raised in primary gonadal dysfunction, polycystic ovary syndrome, postmenopausal women and in pituitary adenoma. Serum level of LH is decreased in pituitary hypothalamic impairment, anorexia nervosa and severe illness.

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6- Human Chorionic Gonadotropin (HCG): The placenta also produces it. It is produced only during pregnancy. Its appearance in the plasma and urine is one of the earliest signals of pregnancy and the basis of many pregnancy tests. The role of hCG during pregnancy is to prevent disintegration of the corpus luteum so as to maintain the synthesis of progesterone by this tissue.

7- **Prolactin (PRL):** It's called also Somatomammotropin. It controls the initiation and maintenance of lactation. The PRL secretion is pulsatile; highest levels during rapid eye movement sleep and peak serum level occurs between 04:00–06:00 hours. Prolactin stimulates lactation on estrogen primed breast. It increases synthesis of milk protein and fat. Hyperprolactinemia is a cause of infertility in females.

8- **Human Placental Lactogen (HPL):** At its height the hormone is secreted at a rate of about 1 g/day, the highest secretory rate of any known human hormone. However, little HPL reaches the fetal circulation. The amount of HPL that is secreted is proportional to the size of the placenta. Low levels of HPL during pregnancy are a sign of placental insufficiency. The biological actions of HPL are similar to those of GH.

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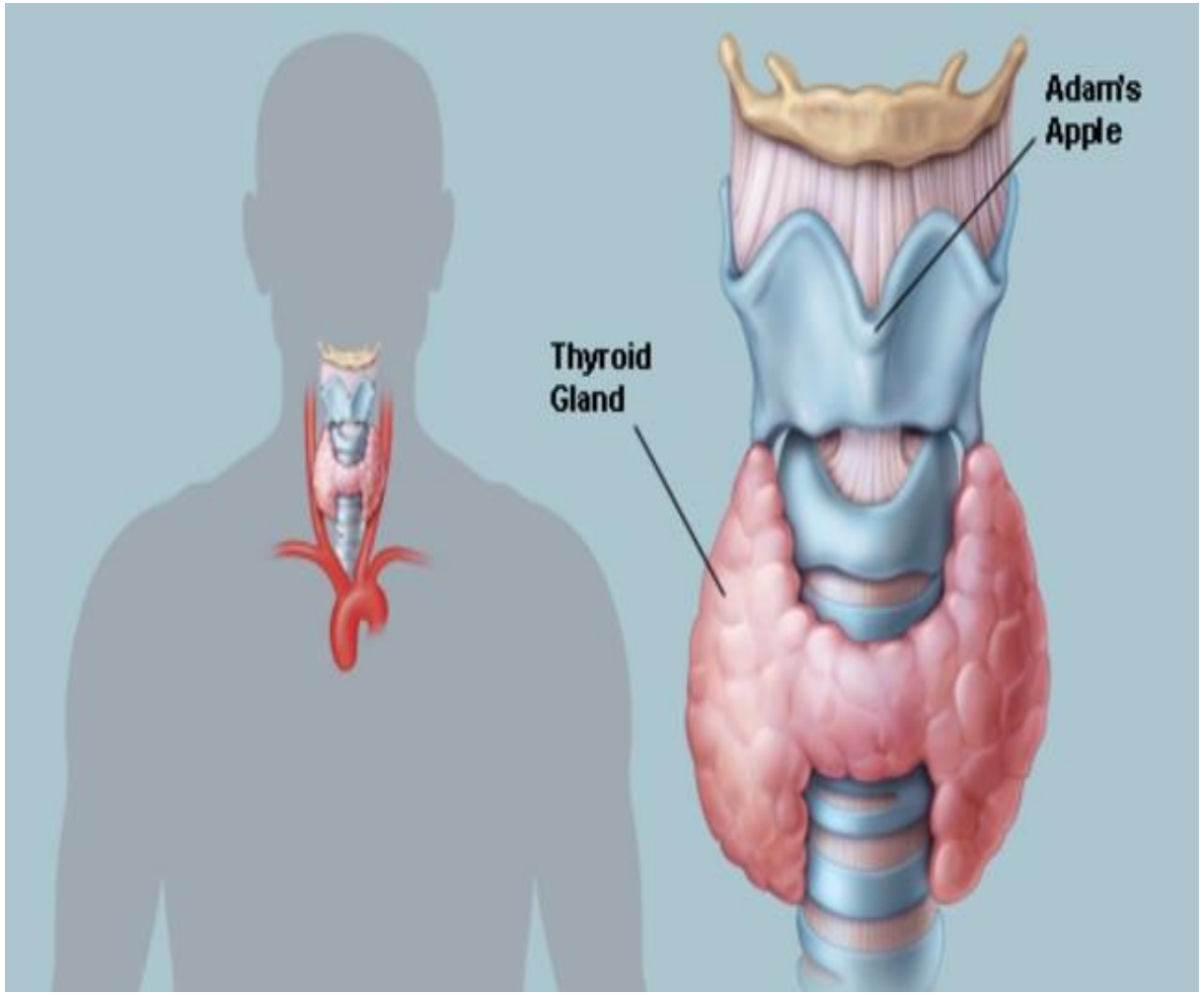
Thyroid Gland

The thyroid, or thyroid gland, is an endocrine gland in the neck consisting of two connected lobes. The thyroid is located at the front of the neck, below the Adam's apple. The thyroid gland secretes three hormones: triiodothyronine (T3), thyroxine (T4) and calcitonin. T3 and T4 influence the metabolic rate and protein synthesis, and in children, growth and development. Calcitonin plays a role in calcium homeostasis. Secretion of T3 & T4 hormones is regulated by TSH which is regulated by TRH. The thyroid gland is unique, in that it is the only endocrine gland to store appreciable amounts of the hormone.



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Metabolic Effects of Thyroid Hormones

T3 attaches to specific nuclear receptors Then the receptor-hormone complex binds to the DNA. The T3 binding results in increase in transcription rate. The hormone exerts action on every cell of the body. Calorigenic effect or thermogenesis is the major effect of thyroid hormone. One milligram of T4 will produce an excess of 1000 kcal. This thermogenic effect is mediated by uncoupling of oxidative phosphorylation. T4increases cellular metabolism. Earliest effect of T4 is stimulation of RNA synthesis and consequent increase in protein synthesis. Higher concentration of T3 causes protein catabolism and negative nitrogen balance. Loss of body weight is a prominent feature of hyperthyroidism. Gluconeogenesis and carbohydrate oxidation are increased. Fatty acid metabolism is increased. Cholesterol degradation is increased and hence cholesterol level in blood is decreased, which is another hallmark of hyperthyroidism.

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Abnormalities of Thyroid Function

The most common types of thyroid diseases are:

1- Hyperthyroidism (excess secretion): It may be due to Effects of autoantibodies, TSH secreting tumors, T4 toxicosis (T4 increase while T3 low) and Graves' disease. Patients have an increased rate of metabolism, weight loss, tachycardia, fine tremors, sweating, diarrhea, emotional disturbances, anxiety and heat sensitivity.

2- Hypothyroidism (decreased secretion): It is due to diseases of thyroid gland. It is seen in autoimmune hypothyroidism (e.g. Hashimoto's thyroiditis), thyroidectomy and radiation therapy. Drugs producing hypothyroidism are lithium, antithyroid drugs and para-aminosalicylic acid.

3- Congenital Hypothyroidism: It is seen in approximately 1 in 4000 newborns. Thyroid hormones are very low or completely absent from birth. Symptoms include puffy face, dullness, thick protruding tongue, which get worsened with time. Infants may have choking episodes, constipation, dry brittle hair, jaundice, floppiness, sluggishness and sleepiness. Treatment consists of oral administration of thyroid hormone, which is simple and cheap. If untreated, child will have mental and growth retardation. Newborn screening helps to totally avoid this condition.

4- Goiter (enlargement of thyroid gland): Goiter may or may not be associated with abnormal function, e.g. euthyroid goiter (diffuse enlargement); nodular goiter which may lead to hyperfunction, or iodine deficiency goiter which may result in hypothyroidism.

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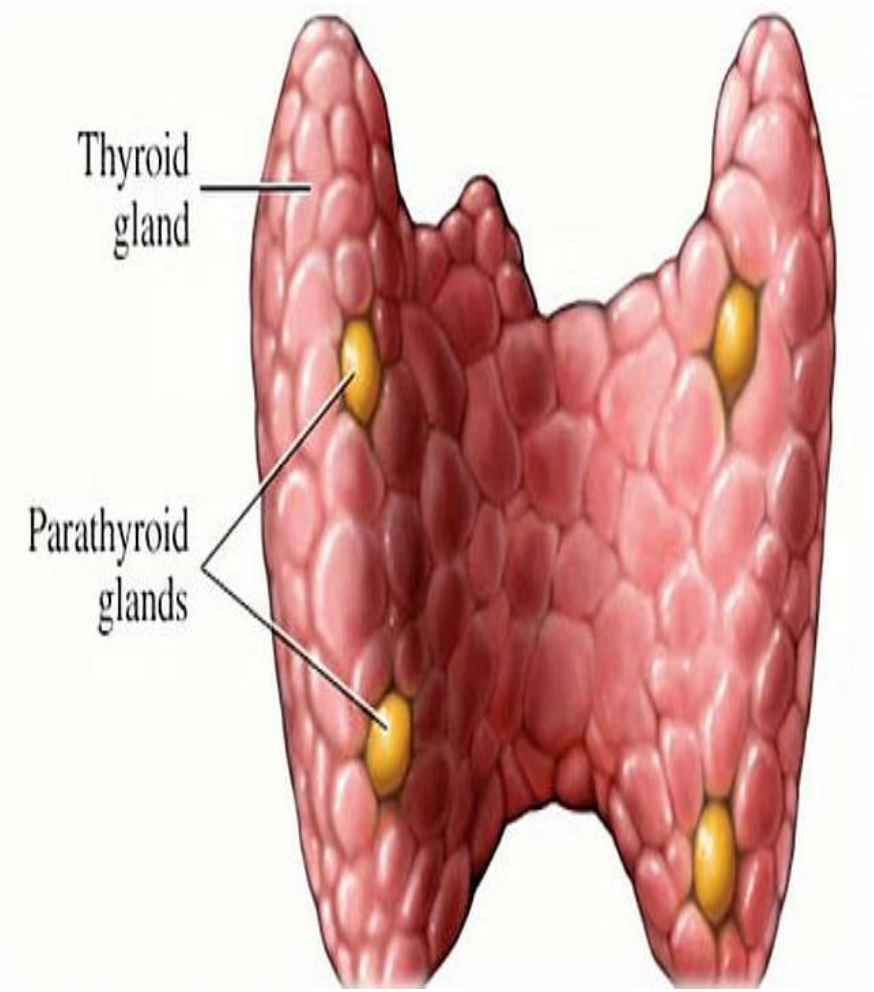
Parathyroid Gland

Parathyroid glands are small endocrine glands in the neck of humans and other tetrapods. Humans usually have four parathyroid glands, located on the back of the thyroid gland in variable locations. The parathyroid gland produces and secretes parathyroid hormone (PTH) in response to a low blood calcium, which plays a key role in regulating the amount of calcium and phosphate in the blood and within the bones. Parathyroid glands share a similar blood supply, venous drainage, and lymphatic drainage to the thyroid glands. Hyperparathyroidism (this may cause bone pain and tenderness due to increased bone resorption) and hypoparathyroidism (associated with damage to the glands or their blood supply during thyroid surgery, it may be associated with rarer genetic syndromes such as DiGeorge syndrome), characterized by alterations in the blood calcium levels and bone metabolism, are states of either surplus or deficient parathyroid function.



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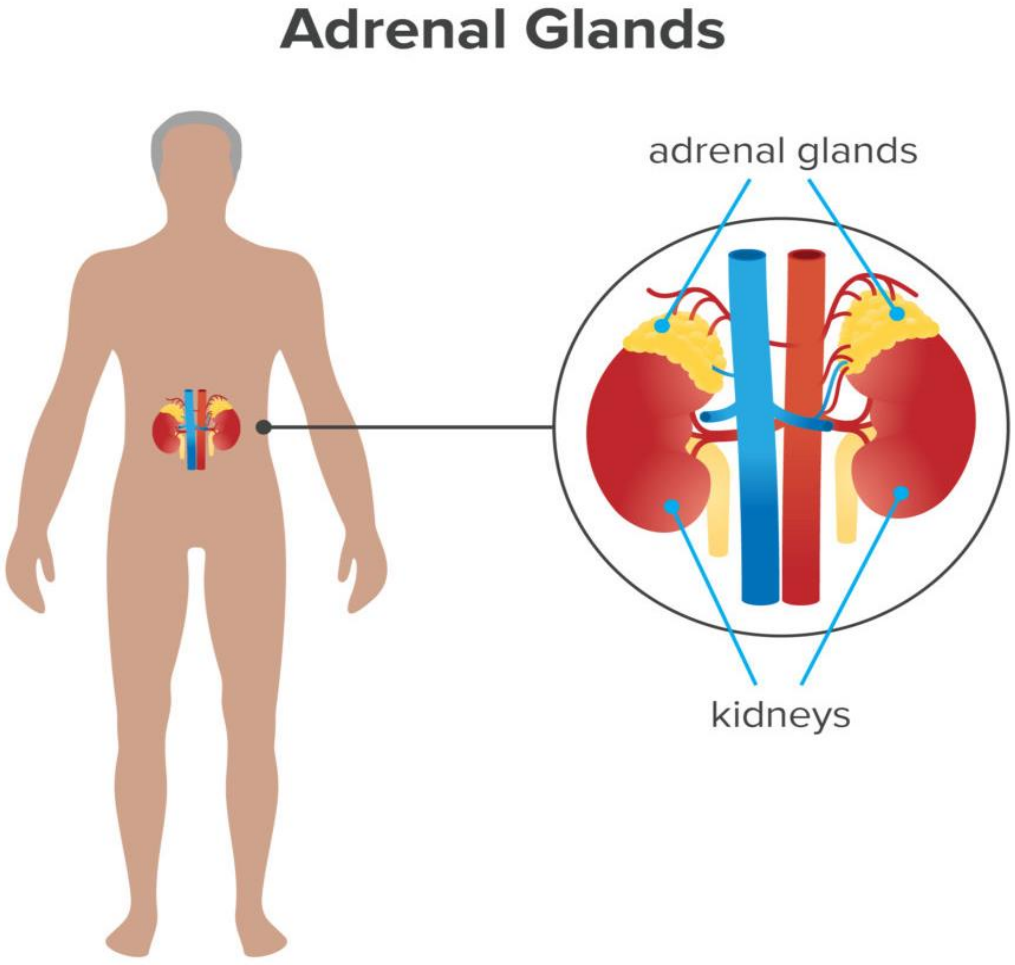
Adrenal Gland

Adrenal glands (also known as suprarenal glands) are endocrine glands that produce a variety of hormones including adrenaline and the steroids aldosterone and cortisol. They are found above the kidneys. Each gland has an outer cortex and an inner medulla. The outer cortex produces steroid hormones (Corticosteroids) such as Mineralocorticoids, Glucocorticoids mainly; and adrenal androgens and estrogens to a lesser extent, and Androgens and Estrogens. Cholesterol is a common precursor for all the steroid hormones. Progesterone is the first steroid hormone formed. Progesterone is further converted into Glucocorticoids, Mineralocorticoids and Sex Steroids. The steroid hormones are metabolized and inactivated by the liver. The major processes are reduction and conjugation.



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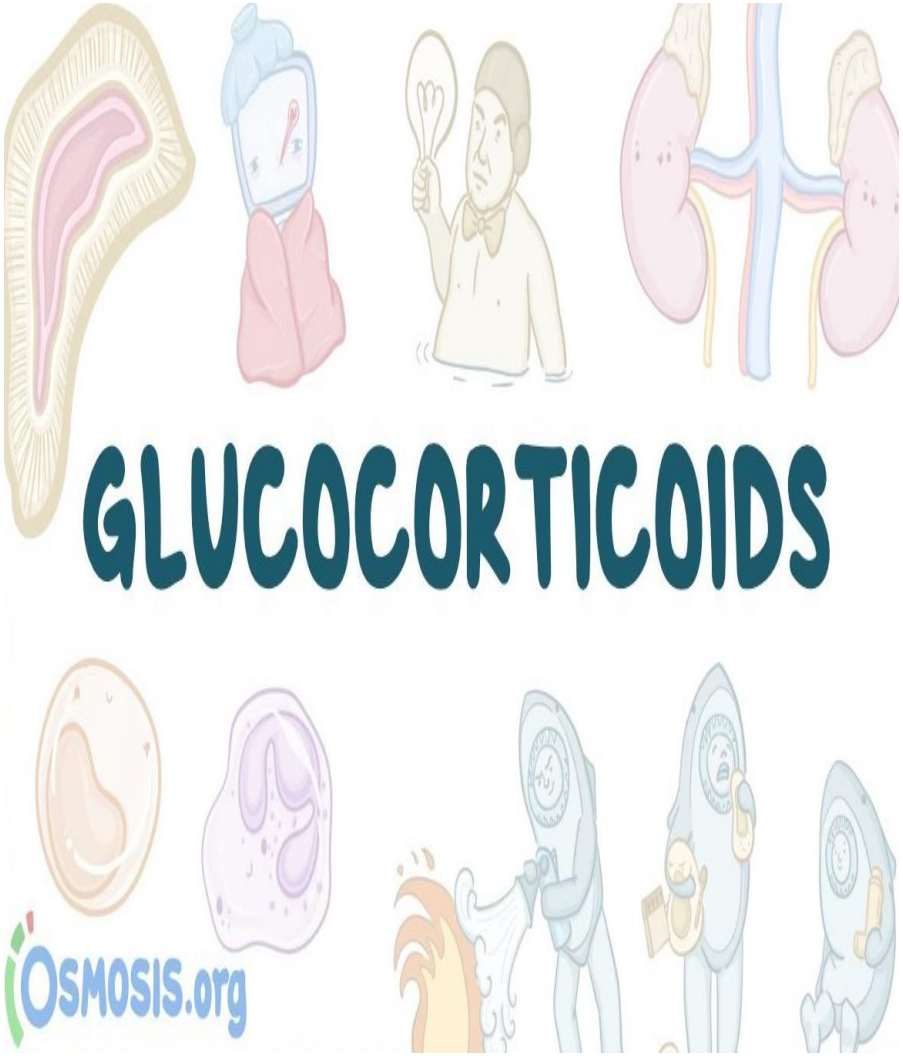
1- Mineralocorticoids: The major Mineralocorticoid is Aldosterone, but 11-deoxycorticosterone and Corticosterone also have significant mineralocorticoid activity. They have effects on water and electrolyte balance. They increases sodium reabsorption from renal tubules, leading to sodium retention and resultant water retention.

2- Glucocorticoids: The major adrenal glucocorticoids are Cortisol, Cortisone and Corticosterone. The diurnal variation of secretion of cortisol (highest values early in the morning and minimum at night). Cortisol is released in response to stress and low level blood sugar. The glucocorticoids, as the name suggests, mainly affect metabolism of glucose, increase lipid mobilization, diverse effects on inflammation and protein synthesis, increased catabolism of proteins and nucleic acids and decrease serum calcium, …etc.



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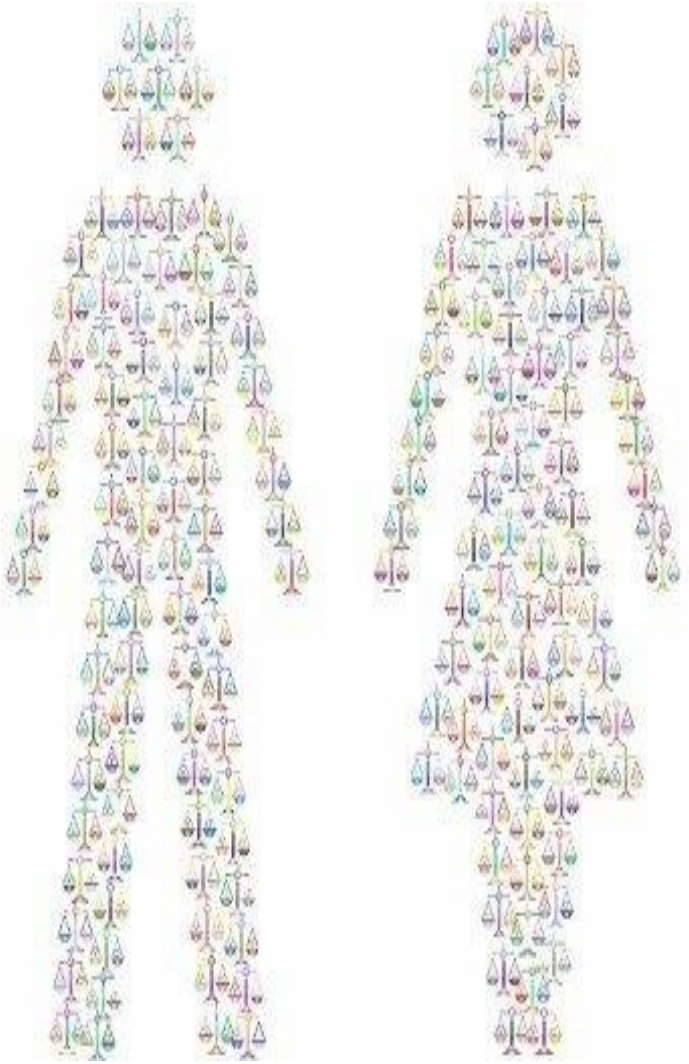
3- Androgens (Sex Hormones): These are secreted by the gonads in response to LH and FSH. They divided to two types:

A- Ovarian Hormones: They are Estrogens and Progesterone which are produced by the ovarian follicles. Estrogen level gradually increases in the second week of the menstrual cycle and perform maintenance of pregnancy. Estradiol is the most important estrogen and make maturation and function of female secondary sex organs. It is converted to estrone by liver and is the predominant sex hormone present in females; however, it is present in males, at lower levels, as well. Estradiol has not only a critical impact on reproductive and sexual functioning, but also affects other organs including the bones. Estradiol enters cells freely and interacts with a cytoplasmic target cell receptor; then, estradiol enters the nucleus of the target cell, and regulates gene transcription. Certain breast cancers, especially in perimenopausal women are estrogen-dependent. In such patients, estrogen receptor antagonists (Tamoxifen) will block the estrogen receptors, and cancer cells tend to die. Progesterone makeImplantation of ovum and maintenance of pregnancy.



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B- Testicular Hormones: The major male hormone in males is Testosterone. Testosterone stimulate spermatogenesis, produce hypertrophy of prostate, seminal vesicles, muscle, bone and kidney cells, So, it is anabolic and maturation and function of male secondary sex organs. The enzyme 5-alpha-reductase is convert testosterone to Dihydrotestosterone (DHT) which is the cause for the benign prostate hypertrophy, that affects more than 75% of men over the age of 60 years. Finasteride can inhibit 5-alpha-reductase, and hence it is used as a treatment for prostate hypertrophy. Prostate cancers are androgen dependent, so androgen ablation is used for treatment of advanced prostate cancer. Androgen receptor (AR) is believed to play critical roles in the development and progression of cancer. Over-expression of proto-oncogenes may be driven by AR.

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4- Catecholamines Hormones: They are epinephrine (adrenaline) and norepinephrine (noradrenaline). The adrenal glands are responsible for most of the adrenaline that circulates in the body, but only for a small amount of circulating noradrenaline. These hormones are released by the adrenal medulla. Adrenaline and noradrenaline act at adreno-receptors throughout the body, with effects that include an increase in blood pressure and heart rate. Actions of adrenaline and noradrenaline are responsible for the fight or flight response, characterised by a quickening of breathing and heart rate, an increase in blood pressure, and constriction of blood vessels in many parts of the body. The major emotion studied in relation to adrenaline is fear.

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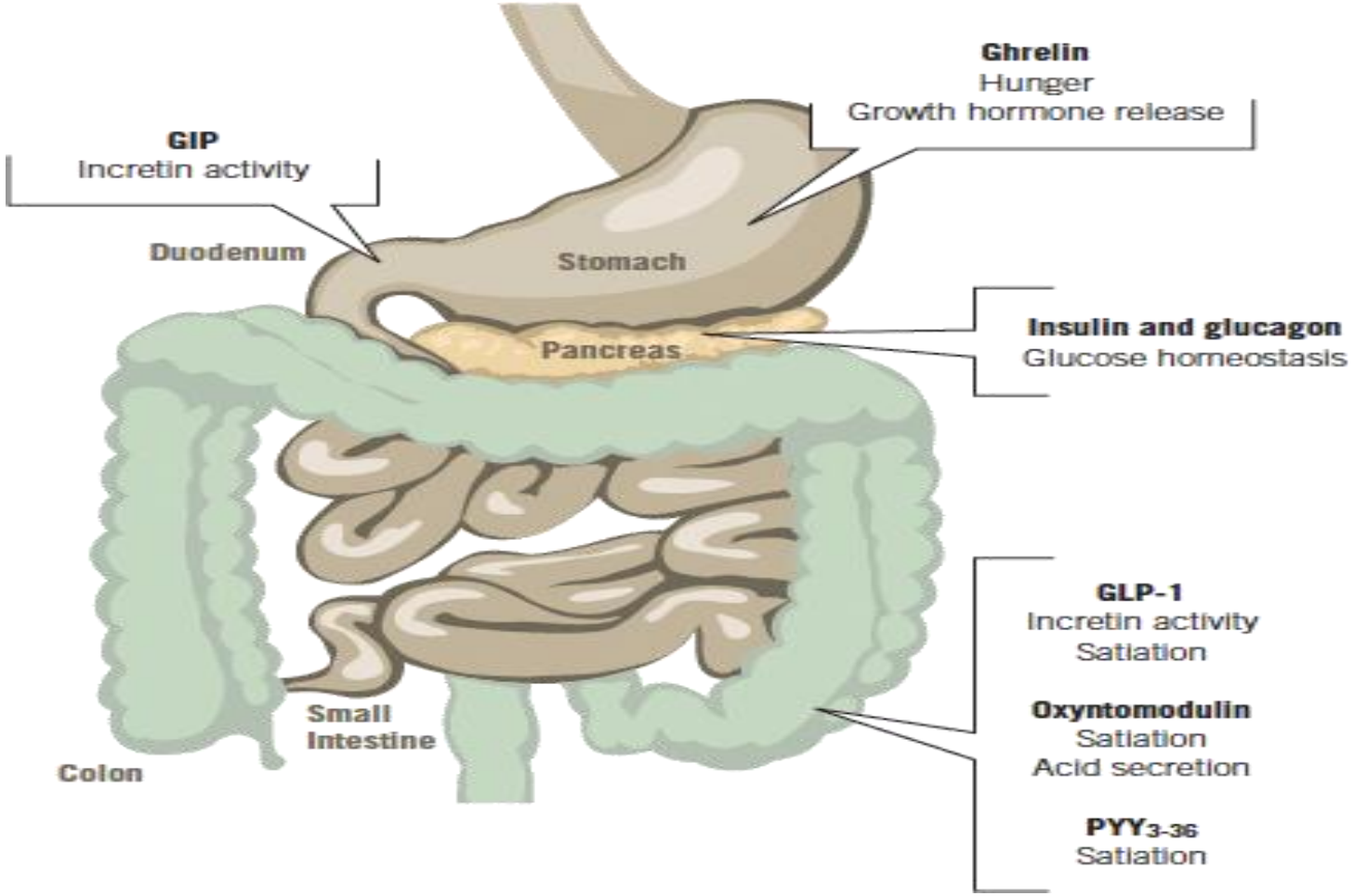
Gut Hormones

There are more than 30 peptides (small proteins) expressed within the digestive tract, making the gut the largest endocrine organ in the body. These are identified as regulatory peptide hormones, peptide neurotransmitters and growth factors. Several of these peptides were first identified in the central nervous system (CNS); and they have subsequently been found in endocrine cells of the gut.



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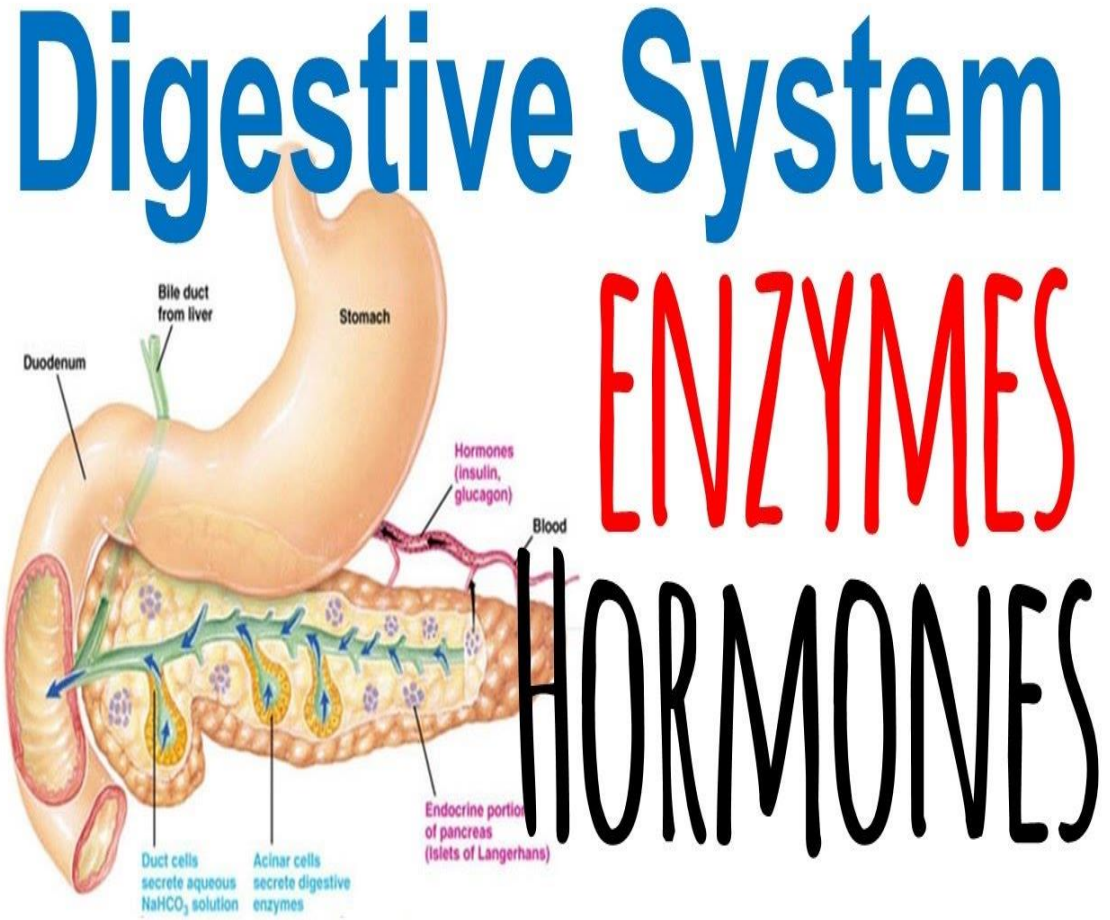
1- Hormones Regulating Digestion of Food

The gastrointestinal peptide hormones are synthesized and secreted in the gastrointestinal tract. Their action is mainly on gastrointestinal secretions, digestion and absorption of nutrients and food intake. These gut hormones are Gastrin, Cholecytokinin, Secretin, Vasoactive intestinal polypeptide (VIP), Insulin, Glucagon, GLP-1, GLP-2, Glicentin, GIP, Pancreatic polypeptide, Neuropeptide Y, Gaunylin and Serotonin. These gastrointestinal hormones are secreted by epithelial endocrine cells. Most of them are small peptides. They regulate the rate of secretion and composition of digestive juices. They are derived from a common precursor peptide and shows sequence homology especially at the C terminal fragment.



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2- Peptide Hormones Regulating Food Intake

The discovery of a group of peptides secreted by the gastrointestinal tract (GIT) which influences food intake has led to the understanding of the relation between hunger and satiety signals in the genesis of obesity. The major peptides included in this group are Ghrelin, glucose-dependent insulinotropic polypeptide (GIP), Somatostatin (SS), Neuropeptide Y and glucagonlike peptide (GLP). The neuroendocrine control of intake of metabolism of nutrients protects a person against starvation and extreme obesity. Upon the entry of nutrients into the small intestine, nutrient sensing mechanisms are activated to allow the body to adapt appropriately to the incoming nutrients. There is an upper intestinal lipid-induced gut-brain neuronal axis to regulate energy homeostasis.

3- Adipose Tissue Derived Hormones

These include peptide hormones like Leptin, Adiponectin and Resistin that can regulate the energy intake, storage and metabolism. Initially these were called adipokines (mediators of endothelial function and inflammation involved in atherosclerosis), but presently they are more often referred to as adipose tissue derived hormones.

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Happiness Hormones

1- Serotonin: Its biological function is complex and multifaceted, modulating mood, cognition, reward, learning, memory, and numerous physiological processes such as vomiting and vasoconstriction.

2- Dopamine: It is a neurotransmitter that plays a major role in the motivational component of reward-motivated behavior.

3- Endorphin: The principal function of endorphins is to inhibit the communication of pain signals. Endorphins may also produce a feeling of euphoria.

4- Oxytocin: It plays a role in social bonding, reproduction, childbirth, and the period after childbirth. Oxytocin is released into the bloodstream as a hormone in response to love and in labor. This helps with birth, bonding with the baby, and milk production.