CHEMICAL CO-ORDINATION & INTEGRATION

To maintain homeostasis, the functions of the organs/organ systems in our body must be coordinated. This coordination and integration of all the activities of the organs is provided by neural system and endocrine system jointly. The neural system provides a point to point rapid co-ordination among organs. This response is rapid but short lived. For example, the nerve impulse causes the skeletal muscle to respond only in milliseconds. As all the cells of the body are not innervated by neurons, the cellular functions are continuously coordinated and integrated by the endocrine system through hormones.

Endocrine glands and hormones:

The study of endocrine glands and hormones in animals is called endocrinology.

The name hormone was first used by the British physiologists W.M.Baylis and E.H. Starling in 1905.The first hormone discovered is secretin. The endocrine glands are called ductless glands. Because they lack ducts. Hormones are defined as non-nutrient chemicals. Which act as intercellular messengers and are produced in trace amounts. Hormones arose early is evolution as they are found in all five kingdoms and many of them are similar in different kingdoms. Invertebrates possess very simple endocrine systems with few hormones where as vertebrates possess a large number of hormones.

Endocrine glands:

(G.K. endo= within, krinein= to secrete)

Secrete hormones: (=To excite) into the blood which then transport these to target tissues located away from the site of secretion. Endocrine system generally control, long term activities of target organs as well as physiological activities such as digestion, metabolism, growth, development and reproduction.

Human Endocrine system:

The endocrine system constitutes endocrine glands and hormone producing diffused tissues/cells located in different parts of the body. The endocrine system consists of organized endocrine bodies such as pituitary, pineal, thyroid, adrenal, pancreas, parathyroid, thymus and gonads. In addition, some other organs eg: liver, heart, kidney, gastrointestinal tract also produce hormones.

Hypothalamus: Hypothalamus is the basal part of diencephalon, forebrain.

It consists of several groups of neurosecretory cells called nuclei. They produce two types of hormones.

1) The releasing hormones and

2) The inhibiting hormones

The releasing hormones stimulate the secretion of pituitary hormones. For example the synthesis and release of gonadotropins from the pituitary is stimulated by gonadotropin releasing hormone (GnRH) secreted by hypothalamus the inhibiting hormones inhibit the secretion of pituitary hormones. For example somatostatin from hypo thalamus inhibits the release of growth hormone (somatotropin) from the pituitary. These hormones secreted by the hypothalamic neurons, pass through the axons and released into the portal circulatory system through which they reach the anterior pituitary (adenohypophysis) the posterior pituitary (neurohypophysis) is under the direct neural regulation of hypothalamus.

The Pituitary gland: The pituitary gland lies in sella turcica of the basisphenoid bone present on the ventral side of parietal region of cranium anatomically, it is divided into an adenohypophysis and a neurohypophysis. Adenohypophysis consists of pars distalis (anterior pituitary) and pars intermedia. Adenohypophysis develops as an out growth of ectoderm (Rathke's pouch) from the roof of the buccal cavity (stomodaeum). Anterior pituitary (pars distalis) secretes six protein hormones where as pars intermedia secrete one protein hormone. In humans pars intermedia is almost merged with pars distalis.

Neurohypophysis (pars nervosa) also known as posterior pituitary develops as an ectodermal out growth of hypothalamus (floor of diencephalon). It stores and releases two hormones called oxytocin and vasopressin, which are actually synthesized by the hypothalamus and transported neurohypophysis through hypophyseal portal system.

The anterior pituitary secrets six protein hormones. Out of which five are tropic hormones (except GH).

1. Growth hormone (GH) or somatotropin:

This hormone stimulates growth and development of all the tissues by accelerating protein synthesis and decreasing catabolism of proteins.

Disorders:

a) Gigantism: Over secretion (hyper secretion) prior to Puberty leads to gigantism. It is typical by abnormal increase in the length of bones.

b) Acromegaly: Over secretion during adulthood leads to acromegaly. It is characterized by the over growth of the bones of hands, feet and is particular the jaws, cheeks and face.

1. Pituitary dwarfism:

Hyposecretion during the growth years leads to pituitary dwarfism. The hypophyseal dwarfs are frequently immature sexually. At adult age they may attain a height of 3 or 4 feet.

2. Prolactin (PRL): Regulates the growth of mammary glands during pregnancy and formation of milk after child birth. Its function is not known is males.

3. Thyroid stimulation hormone (THS): Stimulates the synthesis and secretion of thyroid hormones from the thyroid gland.

4. Adrenocorticotropin hormone (ACTH): Stimulates the synthesis and secretion of steroid hormones called glucocorticoids from the adrenal cortex.

5. Gonadotropins: Luteinizing hormone (LH) and follicle stimulating hormone (FSH) are collectively referred to as gonadotnopins as they stimulate gonadal activity.

In males LH or interstitial cell stimulating hormone (ICSH) stimulate the interstitial cells (leydig cells) in the testis to secrete androgens. In males, FSH and androgens regulate spermatogenesis. In females, LH stimulates ovulation and maintains corpus luteum.

In females FSH stimulates growth and development of ovarian follicles.

Hormone of pars intermedia: It secretes a single protein hormone called melanocyte stimulating hormone (MSH). It acts on melanocytes and regulates pigmentation of the skin. In hormones the pars inter media is merged with pars distalis.

Hormones of Neurohypophysis: It stores and releases two peptide hormones.

1. Oxytocin: It causes uterine contraction during child birth and milk injection after delivery. It also causes general contraction of smooth muscles and stimulates adenohypophysis to secrete LTH. Its function is not clearly known in males and non pregnant females.

2. Vasopressin: It stimulates the reabsorption of water and electrolytes by the distal tubules of the kidney and reduces the loss of water through urine (diuresis). Hence it is also called ant diuretic hormone (ADH). It causes contraction of arterioles and capillaries (in general) while only capillaries (in humans) It reduces heart rate and helps in micturition. Hypo secretion of this hormone causes diabetes insipidus leading to excessive excretion of dilute urine (about 20 liters a day). This causes dehydration, extreme thirst and polydipsia.

The pineal gland: It is small gland locates on the dorsal side of the third ventricle of the brain. It is an amine hormone derived from the amino acid tryptophan. It regulates diurnal rhythm of the body (E.g. sleep wake cycle) It also influences metabolism, body temperature pigmentation (makes the skin pale is amphibians) the menstrual cycle as well as our defense capability. It is antagonistic to MSH.

Thyroid gland: This is the largest endocrine gland located on either side of the trachea. It consists of two tubes connected with a thin flap of connective tissue called isthmus. Each lobe consists of follicles and stromal tissue. The follicular cells secretes amine hormones derived form tyrosine, (eg. tetraiodothyronine(T4) or thyroxine and triiodothyronine (T3). These hormones increases basal metabolic rate (BMR) support RBC formation, controls metabolism of carbohydrates, balance, affects growth and they are essential for metamorphosis in amphibians. Thyroid gland also secretes a protein hormone called thyrocalcitonin (TCT) which regulates blood calcium levels.

Disorders of thyroid gland:

1. Hypothyroidism:

In sufficient secretion of T3 and T4 causes cretinism in children and myxedema in adults. Cretins are characterized by stunted growth, low intelligence quotient, abnormal skin, and deaf mutism and sterile. A hallmark of myxedema is oedema that causes the facial tissue to look puffy. The hypothyroidism caused due to inadequate dietary iodine intake results is the enlargement of thyroid gland commonly called goitre.

2. Hyperthyroidism: It is due to cancer of thyroid gland or due to development of nodules of the thyroid gland. The most common form of hyperthyroidism is Graves ‘ disease which is an autoimmune disorder in which the person produces anti bodies that mimic the action of TSH Graves patients often have a peculiar oedema behind the eyes called exophthalmos.

Parathyroid gland: There are four parathyroid glands partially embedded in thyroid lobes dorsally. They secrete a peptide hormone called parathyroid hormone (PTH) The secretion of PTH is regulated by the circulating levels of calcium ions. PTH is a hypercalcemic hormone that increases the blood Ca^{2+}. It stimulates bone resorption by increasing the activity of osteoclasts. It stimulates reabsorption of Ca^{2+} by the renal tubules. It increases Ca^{2+} absorption from the digested food by promoting the formation of calcitriol, the active form of vitamin D.

Parathyroid gland disorders: Hypoparathyroidism leads to deficiency of Ca^{2+} which leads to tetany (sustained contraction) of skeletal muscles. Hypercalcemia which causes excessive resorption of bone matrix. The symptoms include stones (kidney stones) bones (bones related complications) groans (gastro intestinal symptoms moans (effects on central nervous system)

Thymus: It is a lobular structure located on the dorsal side of heart and the aorta. It is degenerated in the old individuals resulting in the decreased production of thymosin.

This gland secrete the peptide hormones called thymosins. Thymosins promote differentiation of T-lymphocytes, which provide cell, mediated immunity and also promote production of antibodies, which provide humoral immunity.

Adrenal glands or suprarenal glands: There is a pair of adrenal glands, one at the anterior part of each kidney. The gland is differentiated into an outer cortex that develops from mesoderm and a central medulla that develops from ectoderm. The adrenal cortex can be subdivided into three layers called zona glomerulosa (outer layer) zona -fasciculata (middle layer) and zona reticularis (inner layer). The adrenal cortex secretes many hormones collectively called corticosteroids.

Mineralocorticoids: - They are corticoids which regulate the balance of water and electrolytes in our body. The main mineralocorticoid is aldosterone. It stimulates the reabsorption of Na+ and water and excretion of K+ and phosphate ions in the renal tubules and thus helps in the maintenance of electrolytes, body fluid volume osmotic pressure and blood pressure.

Glucocorticoids: They are corticoids involves in carbohydrate metabolism. The main glucocorticoid is cortisol. Glucocorticoids stimulate, gluconeogenesis, lypolysis and proteolysis and inhibit cellular uptake and utilization of aminoacids. They have antiinflamatory effect and supress immune response. Cortisol stimulates the production of RBC.

Androgenic steroids: They are secreted in small amounts which play a role in the growth of axial hair, pubic hair and facial hair during puberty.

Hormones of adrenal medulla:

Adrenal medulla secretes two hormones called adrenaline or epinephrine and noradrenaline or norepinephrine which are commonly called catecholamines. These hormones are called emergency hormones or hormones of fight because they are secreted in response to stress and during emergency conditions. The functions of these hormones are closely allied to those of the sympathetic part of autonomic nervous system. These hormones are not essential for life because of the presence of sympathetic neurons in other parts of the body. These hormones increase alertness pupilary dilation piloerection (raising of hairs) sweating, increase the heart beat, the strength of heart contraction, rate of respiration, stimulate the breakdown of glycogen lipids and proteins. Thus they increase blood levels & glucose and fatty acids.

Disorders of adrenal glands:

1. Cushing's syndrome: It is caused due to the hyper secretion of glucocorticoids (cortisol). This hyper secretion is due to a tumor of the adrenal gland that secretes glucocorticoids or due to a tumor in the pituitary that secretes ACTH. This may also be due to prolonged therapeutic use of ACTH or glucocorticoids -for instance, to prevent rejection of a transplanted organ. It is characterized by protein catabolism and redistribution of body fats, resulting in spindly arms and legs accompained by a rounded moon face buffalo hump on the back, and pendulus (hanging) abdomen. Excessive gluconeogenesis causes hyperglycemia and glycosuria. The other symptoms are susceptibility to infection, insomnia, excitability, euphoria, psychotic depression,

osteoporosis, hypertension menstrual disturbances and arrest of growth in children.

Addison's disease: This is caused due to hyposecretion of all adrenal cortex hormones. The major cause for the hyposecretion is auto immune disorders in which the antibodies cause the destruction of adrenal cortex on block binding of ACTH to its receptors.

The out standing effects of this disease are hypoglycaemia, dehydration, increased pigmentation of the skin (bronzed appearance) hypotension decreased cardiac output arrhythmias, mental confusion, menstrual disturbances, elevated potassium and decreased sodium in the blood.

Pancreas: pancreas act as both exocrine and endocrine gland (mixed gland).The exocrine part of pancreas consists of ‘acini’ that produce digestive enzymes. The endocrine part of pancreas consists of Islets of langerhans (1to 2 million Islets of langerharns in normal human pancreas. Each pancreatic islet contains 4 types of cells. They are alpha cells, beta cells, delta cells and F- cells or p.p. cells.

Hormones of pancreas:

1. Glucagon: It is a hyperglycemic hormone that stimulates glycogenolysis and gluconeogenesis is hepatocytes. Glucagon reduces the cellular glucose uptake and utilization.

2. Insulin: It is peptide hormone secreted by beta cells. It is a hypoglycemic hormone that stimulates glycogenesis in the target cells. It enhances cellular glucose uptake and utilization. It accelerates lipogenesis (synthesis of fatty acids) and protein synthesis and slows down glycogenolysis and gluconeogenesis. Thus it maintains homeostasis of blood glucose and promotes other metabolic activities that are anabolic.

3. Somatostatin: It is secreted by delta cells. It inhibits the secretion of insulin and glycogon.

4. Pancreatic polypeptide :

It secreted by f cells or pp cells. It inhibits somatostatin secretion gallbladder contraction and secretion of digestive enzymes in the pancreas.

Disorders of pancreatic islets:

Diabetes mellitus: It is caused due to deficiency or absence of insulin causing impaired carbohydrate fat and protein metabolism. It is associated with glucosuria or glycosuria (loss of glucose in urine) Polyuria (excessive urine production), Poly dipsia (excessive thirst) and Polyphagia (excessive eating) and formation of harmful compounds known as Ketone bodies.

Diabetes mellitus is of two types.

1. Type I Diabetes: It is caused due to lack of insulin secretion or little secretion of insulin. It is also called insulin dependent diabetes mellitus (IDDM) because insulin injections are required to treat.

2. Type II Diabetes: it is caused by decreased sensitivity of target tissues to insulin.

Diabetes mellitus is the most common endocrine disorder.

Testis: Testis performs dual functions as primary sex organ as well as an endocrine gland. The leydig cells or interstitial cells which are present in the intertubular spaces produce a group of hormones called androgens mainly testosterone.

Androgens are responsible for the development of penis, scrotum, prostate gland. epididymis, vas deferens, seminal vesicles, urethra etc. These hormones stimulate muscular growth, growth of facial and axillary hair, aggressiveness low pitch of voice etc. They influence male sexual behavior and produce anabolic effects on protein and carbohydrate metabolism. They stimulate spermatogenesis.

Ovary: Ovary performs dual functions as primary sex organ as well as endocrine gland. Ovary consists of ovarian follicles and stromal tissues. It produces two groups of steroid hormones called estrogen and progesterone.

Estrogen or Estradiol: It is mainly secreted by the growing ovarian follicles. Estrogens are responsible for the development of female secondary sex organs, ovarian follicle,

Female secondary sex characters (e.g. high pitch of voice etc) mammary gland development estrogens also regulate female sexual behavior.

Progesterone: It is secreted by a structure called corpus luteum which is formed from the ruptured follicle after ovulation. Progesteron prepares uterus for pregnancy and inhibits ovulation and menstrual cycle during pregnancy. It acts on mammary glands and stimulates the formation of alveoli (sac like structures which store milk) and milk secretion.

Relaxin: It is a polypeptide hormone secreted by ovary placenta and corpus luteum. It helps in pubic symphysis relaxation and uterine contractions at parturition.

Hormones of heart, kidney gastrointestinal tract:

1. Atrial natriuretic factor (ANF): It is a peptide hormone secreted by atrial wall of heart it decreases blood pressure by causing the dilution of blood vessels

2. Erythropoietin: It is a peptide hormone secreted by the juxtaglomerular cells of the kidney. It Stimulates Erythropoiesis (formation of RBC)

3. Growth factors: They are secreted by non-endocrine tissues which are essential for normal growth of tissues and their repairing or regeneration.

Hormones of gastro-intestinal tract:

The endocrine cells present in different parts of gastrointestinal tract secrete four major peptide hormones, namely gastrin, secretin, cholecystokinin (CCK) and gastric inhibitory peptide (GIP)

1. Gastrin: It stimulates the gastric glands to secrete hydrochloric acid and pepsinogen.

2. Secretin: It stimulates the exocrine pancreas to secrete water and bicarbonate ions.

3. Cholecystokinin (CCK): It acts on pancreas and gall bladder and stimulates the secretion of pancreatic enzymes and bile juice, respectively.

4. Gastric inhibitory peptide: It inhibits gastric secretion and motility.

Mechanism of hormone action:

Hormones affect only specific target cells by binding to specific proteins called hormone receptors located in the target cells only. Some hormones (e.g. growth hormone and thyroxin) affect many cells of different types as all of these cells possess receptors for these hormones. But receptors are specific because each receptor is specific to one hormone only.

Hormone receptor is of two types

1) Membrane bound receptors

2) Intracellular receptors

Membrane bond receptors: - They are presentation the cell membrane of the target cells. Water soluble hormones (protein hormones, peptide hormones and catecholamines) binds to the membrane bound receptors. This causes the generation of second messengers (e.g. cyclic AMP, IP3, Ca++ etc) which in turn activates a cascade of enzymes and regulate cellular metabolism.

2. Intracellular receptors: They are mostly nuclear receptors. Lipid soluble hormones (e.g.steroid hormones idothyromines, etc) bind to introcellular receptors and form a hormone- receptor complex. The activate hormone receptor complex mostly regulate gene expression or chromosome function.

Classification of hormones:

On the basis of their chemical nature hormones are divided into four types.

1. Peptide, polypeptide, protein hormones. Peptide hormones consists of chains of 3 to 49 amino acids (e.g. ADH and oxytocin) protein hormones consists of 50 to 200 amino acids (e.g. GH, TSH and insulin)

2. Steroids: They derived from cholesterol (e.g. cortisol, testosterone, estradiol and progesterone)

3. Iodothyronines: They are derived from the amino acid tyrosine and contains iodine (e.g. thyroid hormones)

4. Amino-acid derivatives: They are derived from a single amino acid. The catecholamines (e.g. epinephrine, norepinephrine) are derived from the amino acid tyrosine. Melatonin is derived from the amino acid tryptophan.