- The endocrine system is a chemical coordination system in the body comprising of endocrine glands, their hormones and their modes of action. It is directly or indirectly under the control of nervous system so, the two systems are often collectively called as **neuro-endocrine system.**
- **Endocrine glands** are glands of the endocrine system which secrete informational molecules or **hormones** that are poured into venous blood or lymph for reaching the target organ because the glands are not connected with the target organ by any duct. Endocrine gland is, therefore, also called **ductless gland.**
- The **classical definition** of hormone is a chemical produced by endocrine glands and released into the blood and transported to a distantly located target organ. The current scientific definition as follows : "Hormones are non-nutrient chemicals which act as intercellular messengers and are produced in trace amounts." Invertebrates possess very simple endocrine systems with few hormones whereas a large number of chemicals act as hormones and provide coordination in the vertebrates.

HORMONES

- Ernest H. Starling coined the term 'hormone' in 1905. The first hormone to be discovered was 'secretin'. It was discovered by two English physiologists : **William M. Bayliss** and **Ernest H. Starling** in 1903. But the first hormone to be isolated was insulin, by **Banting** and **McLeod.**

Characteristic features of hormones

- Hormones have low molecular weight and are effective in very low concentrations usually in **picogram, nanogram** or **microgram**.
- Hormones do not provide energy or building materials but they do have effects on growth, differentiation and metabolic activities of their target cells.
- They accelerate or inhibit specific physiological processes.
- They are produced in inactive forms **preprohormones** or **prohormones** which are later converted into active hormones.
- Excess or deficiency of hormones lead to **disorders.**

Classification of hormones

- The hormones may be classified into four categories :
  - **Amino acid derivative hormones -** The hormones epinephrine (adrenaline), norepinephrine (noradrenaline) and thyroxine are derived from the amino acid tyrosine.
  - **Peptide hormones -** The hormones oxytocin and vasopressin (= ADH) are composed of peptides.
  - **Protein (Polypeptide) hormones -** The somatotropic, thyrotropic and gonadotropic hormones, insulin, glucagon, parathormone, human chorionic gonadotropin, human chorionic somatomammotropin (HCS) and relaxin are made up of proteins.
  - **Steroid hormones -** The hormones secreted by the adrenal cortex, testes and ovaries are composed of steroids. Placental estradiol and progesterone are steroid hormones.

Role of hormones in homeostasis

- Homeostasis means keeping the internal environment of the body constant. Hormones help in maintaining internal environment of the body.
- When the secretion of hormones is under the control of factors or other hormones it is called **feedback control.** Feedback control is of two types : positive feedback control and negative feedback control.

MODE OF ACTION OF HORMONES

- Most hormones are **steroid-** or **amino acid-based.** Hormones alter cell activity by stimulating or inhibiting characteristic cellular processes of their **target cells.**
- A target cell responds to a hormone because it bears **receptors** for the hormone. **Hormone receptors** are found either exposed on the surface of the cell or within the cell (cytoplasm), depending on the type of hormone. In very basic terms, binding of hormone to receptor triggers a cascade of reactions within the cell that affects function. Cell responses to hormone stimulation may involve changes in membrane permeability; enzyme synthesis, activation, or inhibition; secretory activity; gene activation; and mitosis.

Mode of hormone action through intracellular receptors

- **Steroid hormones** (and thyroid hormones) are lipophilic in nature and can easily pass across the plasma membrane of target cell. They act through the intracellular receptors located either in the cytosol or the nucleus.
- The hormone-receptor complex binds to specific regions on the DNA called **hormone responsive element** (HRE) and causes increased expression of **specific genes.**
- It is believed that the interaction of hormone receptor complex with HRE promotes initiation and, to a lesser extent, elongation and termination of RNA synthesis (transcription).

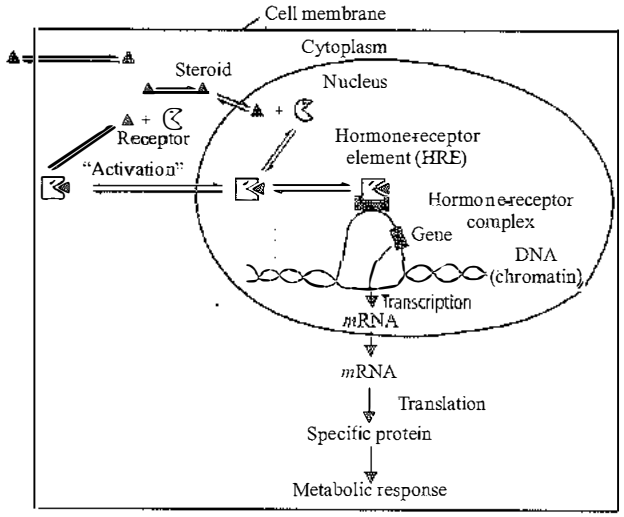


Fig.: Mode of action of steroid hormone

Mode of hormone action through extracellular receptors

- Some hormones bind to cell surface (plasma membrane) receptors and stimulate the release of certain molecules, namely the **second messengers** which, in turn, perform the biochemical functions. Thus, hormones themselves are the **first messengers.** Sometimes second messenger is **cAMP** *e.g.*, ACTH, FSH, LH, PTH, glucagon, calcitonin. At others second messenger is **phosphatidylinositol/ calcium** *e.g.*, TRH, GnRH, gastrin, CCK.

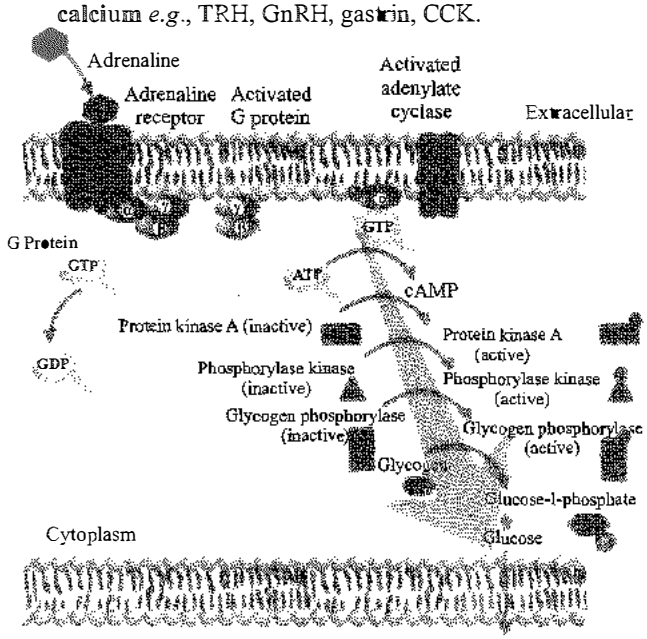


Fig.: Mode of action of hormone through extracellular receptors

HUMAN ENDOCRINE SYSTEM

- Hypothalamus, pituitary, pineal, thyroid, parathyroid, thymus, adrenal, pancreas, testis and ovary are the organized endocrine glands in our body.
- In addition to these, some other organs, *e.g.* gastrointestinal tract, liver, kidney, heart also produce hormones.

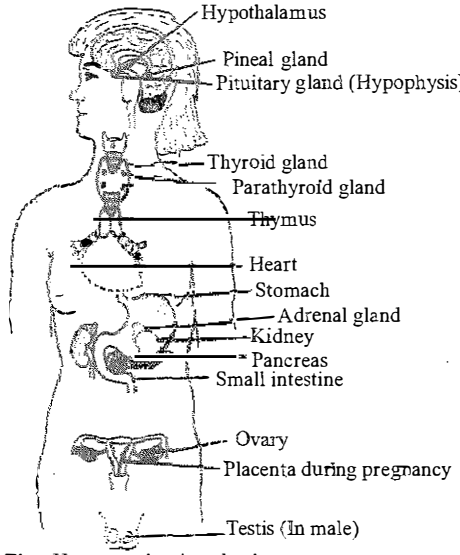


Fig.: Human endocrine glands

Hypothalamus

- It is considered as **supreme commander** of endocrine system. Hypothalamus is the basal part of diencephalon (forebrain) and it regulates a wide spectrum of body functions. It contains several groups of neurosecretory cells called nuclei which produce hormones. These hormones regulate the synthesis and secretion of **pituitary hormones.**
- These hormones are :
  - Thyrotropin releasing hormone (TRH or TSH-RH)
  - Adrenocorticotropin releasing hormone (ARH or ACTH-RH)
  - Gonadotropin releasing hormone (GRH)
  - Somatotropin releasing hormone or growth hormone – releasing hormone (SRH or GH-RH)
  - Somatostatin or growth inhibiting hormone (GIH).
  - Prolactin releasing hormone or luteotropic or lactogenic hormone releasing hormone (PRH, LTH-RH)
  - Prolactin inhibiting hormone and
  - Melanocyte stimulating hormone and melanocyte–inhibiting hormone (MSH or MIH).
- These hormones reach the pituitary gland through a portal circulatory system and regulate the functions of the anterior pituitary. The posterior pituitary is under the direct neural regulation of the hypothalamus.

Pituitary gland

- It is smallest endocrine gland having the weight of about 1-3 gm. Previously it was considered as the **master gland** of the body. Today it is considered as **'Orchestra of endocrine system'.**
- It has two main lobes; anterior lobe or **adenohypophysis** or **pars distalis** and posterior lobe or **neurohypophysis** or **pars nervosa,** and an intermediate lobe or **pars intermedia** at the middle of the two main lobes.
- The pars distalis region of pituitary, commonly called anterior pituitary, produces growth hormone (GH), prolactin (PRL), thyroid stimulating hormone (TSH), adrenocorticotrophic hormone (ACTH), luteinizing hormone (LH) and follicle stimulating hormone (FSH).
- Pars intermedia secretes only one hormone called **melanocyte stimulating hormone** (MSH). However in humans, the pars intermedia is almost merged with pars distalis.
- Neurohypophysis (pars nervosa) also known as posterior pituitary, stores and releases two hormones called oxytocin and vasopressin, which are actually synthesised by the hypothalamus and are transported axonally to neurohypophysis.
- The functions of different pituitary hormones are described below :
  - **GH :** It stimulates body growth .
  - **PRL :** It stimulates secretion of milk from mammary gland after parturition (child birth).
  - **TSH :** It stimulates the synthesis and secretion of thyroid hormones from the thyroid gland.
  - **ACTH :** It stimulates the synthesis and secretion of steroid hormones called glucocorticoids and mineralocorticoids from the adrenal cortex.

- **LH and FSH :** In males, LH stimulates the synthesis and secretion of hormones called androgens from testis. In females, LH induces ovulation of fully mature follicles (Graafian follicles) and maintains the corpus luteum, formed from the remnants of the Graafian follicles after ovulation. FSH stimulates growth and development of the ovarian follicles in females.
- **MSH :** It regulates pigmentation of the skin.
- **Oxytocin (birth hormone or milk ejecting hormone):** It stimulates vigorous contraction of uterus at the time of child birth, and milk ejection from the mammary gland.
- **Vasopressin:** Stimulates resorption of water and electrolytes by the **distal tubules** and thereby reduces loss of water through urine (diuresis). Hence, it is also called as **anti-diuretic hormone (ADH).**

Pituitary disorders

- **Dwarfism :** It is generally due to the deficiency of the growth hormone secretions during childhood.
- **Gigantism :** When large quantities of growth hormone is secreted before adolescence it results in gigantism.
- **Acromegaly :** If an acidophilic tumour occurs causing high GH secretion after adolescence, it causes acromegaly.
- **Diabetes insipidus :** This condition is due to the hyposecretion or inability to produce antidiuretic hormone (ADH) from the posterior pituitary. This condition results in formation of a large volume of dilute urine.

Pineal gland

- The pineal gland is located between the cerebral hemispheres, where it protrudes from the roof of the third ventricle. Pineal secretes a hormone called **melatonin.** Melatonin plays a very important role in the regulation of 24 hour **(diurnal)** rhythm of our body. For example, it helps in maintaining the normal rhythms of **sleep-wake cycle, body temperature.**
- In addition, melatonin also influences metabolism, pigmentation, the menstrual cycle as well as our defense capability.

Thyroid gland

- The thyroid gland is the largest endocrine gland located anterior to the thyroid cartilage of the larynx in the neck. It is bilobed with a connecting **isthmus** (a narrow non-glandular median part).
- The microscopic structure of thyroid gland shows thyroid follicles composed of **cubical epithelium** and filled with a homogenous material called **colloid.** Small amount of loose connective tissue forms **stroma** of the gland. Besides containing blood capillaries, the stroma contains small clusters of specialized **parafollicular cells** or **'C' cells.**
- The thyroid gland secretes three hormones: **Thyroxine** (tetraiodothyronine or T_4) and **triiodothyronine** or T_3 are secreted by the thyroid follicular cells. **Calcitonin** is secreted by the C-cells of the thyroid gland.
- The thyroid gland is the only gland that stores its hormones in large quantity.
- **Iodine** is essential for the synthesis of thyroid hormones.
- Thyroglobulin is a glycoprotein and precursor for the synthesis of T_3 and T_4. T_4 and T_3 contain four and three atoms of iodine respectively, therefore, they are named so. T_3 is secreted in smaller amounts but it is more active and several times more potent than T_4.
- Thyroid hormones stimulate the metabolic activities and increases the oxygen consumption in most of the tissues of the body (exception - brain, lungs, testes and retina).
- Calcitonin is secreted when calcium level is high in the blood. It then **lowers the calcium** level by suppressing release of calcium ions from the bones.

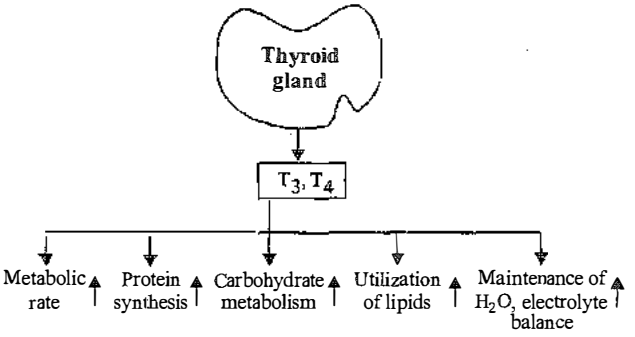
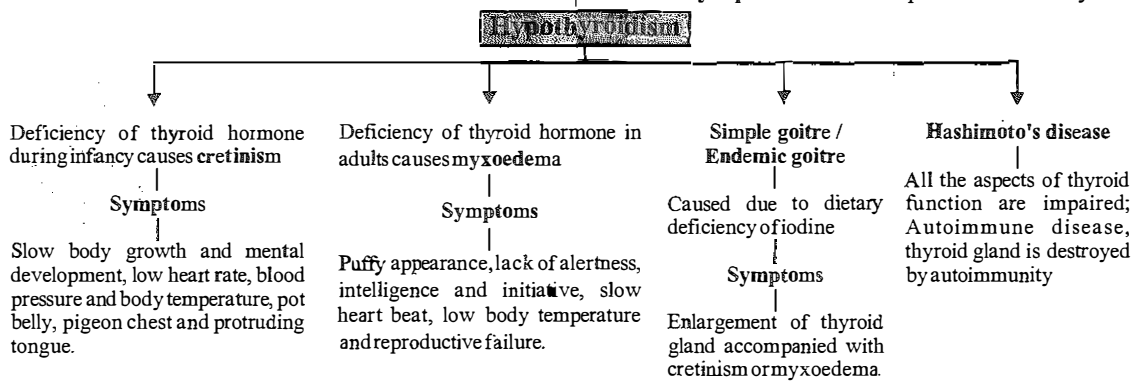


Fig.: Regulation of synthesis and function of thyroid hormones

Hyperthyroidism

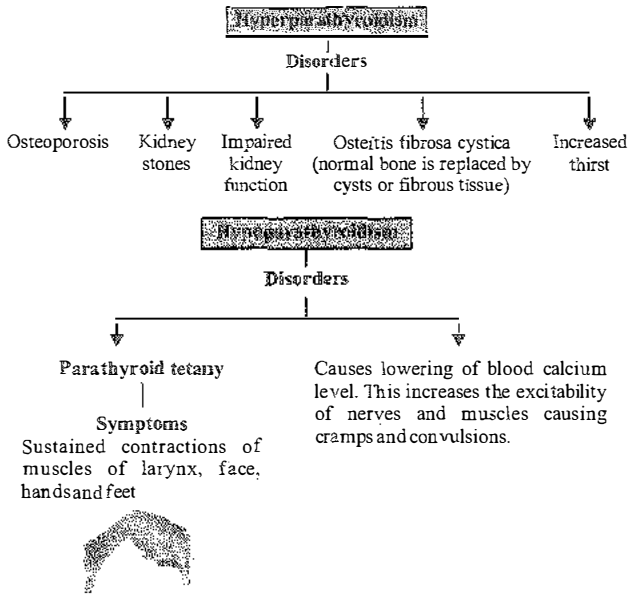
- Grave's disease / Basedow's disease / Parry's disease Exophthalmic goitre is caused due to over secretion of thyroid hormones. It is a disease in which a person produces antibodies that mimic the action of TSH but are not regulated by normal negative feed back control.
- Its **symptoms** include protrusion of eye balls, loss



of weight, rise in body temperature, rapid heart beat, nervousness, tremor and restlessness.

Parathyroid glands

- The parathyroid glands consist of four separate glands located on the posterior surface of the lobes of the thyroid gland. They consist of two types of cells : chief cells (small) and oxyphil cells (large).
- The chief cells secrete **parathormone** or **Collip's hormone** which is synthesised as a preprohormone, and loses 25 amino acids to become the active parathormone.
- This hormone regulates calcium and phosphate balance between the blood and other tissues. The release of parathormone increases blood calcium to normal by drawing calcium from the bones into the plasma, by increasing calcium absorption in the digestive tract, and by reducing loss of calcium in the urine.
- PTH has an effect that **opposes the effect of calcitonin.**



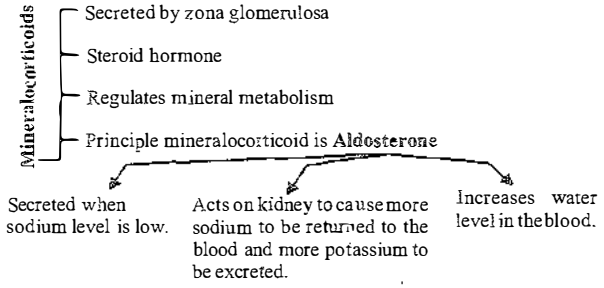
Adrenal glands

- Adrenal glands are paired structures (conical, yellowish bodies) located on the top of the kidneys. Each adrenal gland has two parts : external adrenal cortex and internal adrenal medulla.

Adrenal cortex

- It further shows three concentric zones :
  - **Zona glomerulosa** is the outer zone that constitutes about 15% of the gland and secretes hormones called mineralocorticoids.
  - **Zona fasciculata** is a middle zone that constitutes 50% of the gland and secretes glucocorticoids.
  - **Zona reticularis** is the inner zone that constitutes 7% of the gland and secretes gonadocorticoids.

Mineralocorticoids

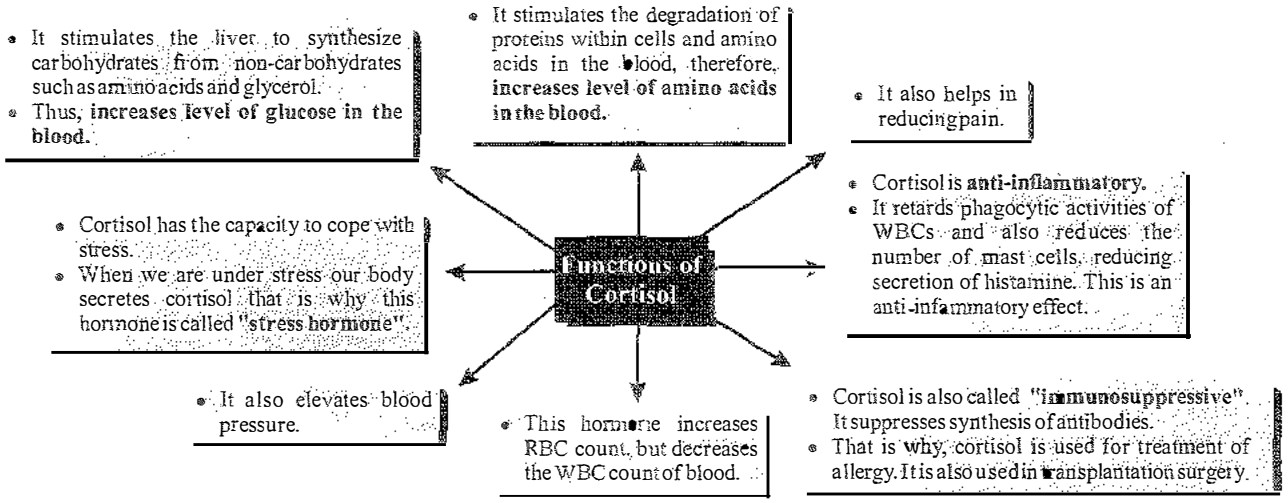


Glucocorticoids

- They affect carbohydrate metabolism, however, they also affect the metabolism of proteins and fats.
- Glucocorticoids include three main hormones: **cortisol** (= hydrocortisone), **corticosterone** and **cortisone.** Of the three, cortisol is the most abundant (about 95%). Cortisol has **anti-insulin affect.**

Gonadocorticoids (sexcorticoids)

- **Sexcorticoids** include small amounts of both male and female sex hormones.
- However, more male sex hormone **(testosterone)** is produced than female sex hormone **(oestrogen).**



Adrenal medulla

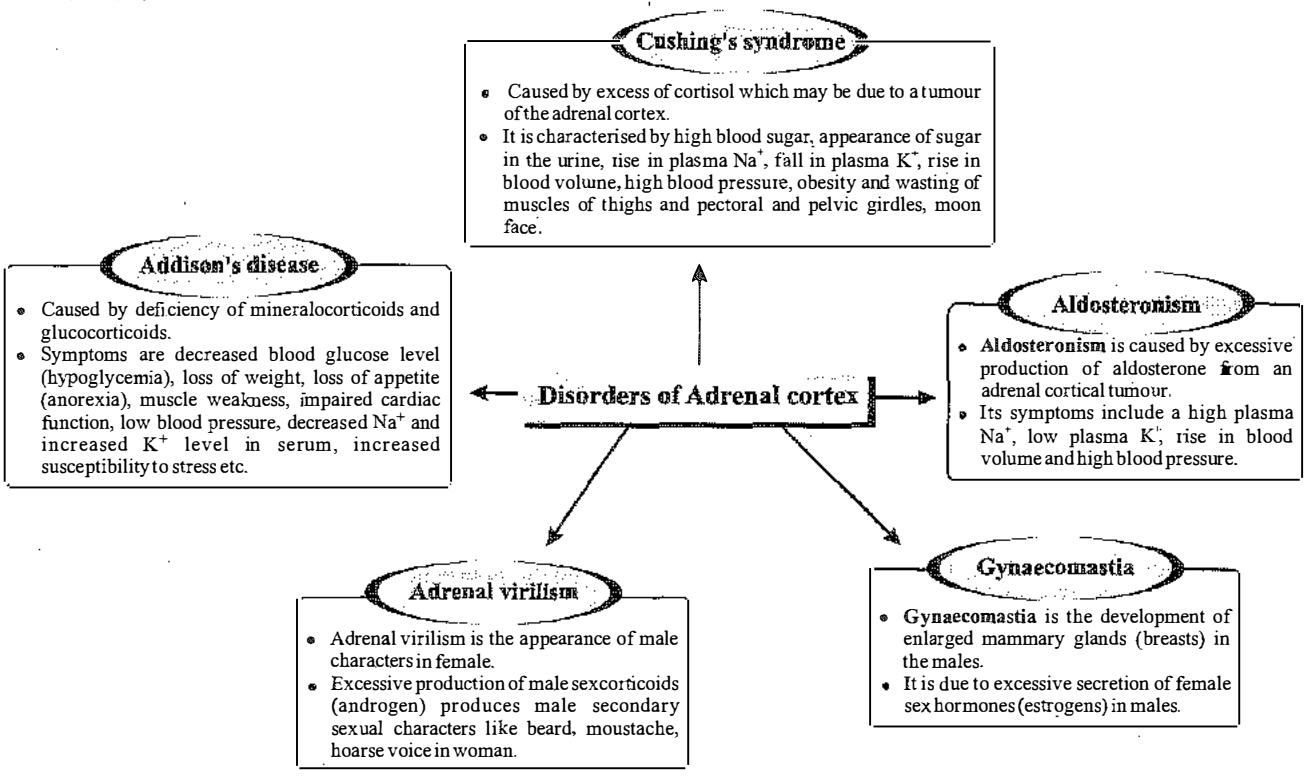
- The adrenal medulla consists of rounded groups of relatively large and granular cells called **chromaffin cells.** These cells are connected with the pre-ganglionic motor fibres of the sympathetic nervous system.
- The adrenal medulla is simply an extension of the sympathetic nervous system. The medulla of the adrenal glands secretes two hormones: norepinephrine (noradrenaline) and epinephrine (adrenaline).
- Both epinephrine and norepinephrine are synthesized from the amino acid tyrosine.
- **Norepinephrine** (noradrenaline) regulates the blood pressure under normal condition. It causes constriction of essentially all blood vessels of the body. It causes increased activity of the heart, inhibition of gastrointestinal tract, dilation of the pupils of the eyes and so forth.
- **Epinephrine** (adrenaline) is secreted at the time of emergency. Hence it is also called **emergency hormone.**

The conversion of tyrosine to epinephrine involves 4 step –
(a) Ring hydroxylation
(b) Decarboxylation
(c) Side chain hydroxylation
(d) N-methylation

Tyrosine
↓ tyrosine hydroxylase
Dopa
↓ dopa decarboxylase
Dopamine (inteimediate product)
(3, 4 dihydroxyphenyl ethanamine)
↓ dopamine β-hydroxylase
Norepinephrine
↓ PNMT (Phenyl ethanolamine N- methyl transferase)
Epinephrine

Called catecholamines

Flow chart : Biosynthetic pathway



- Because of the role of their hormones, the adrenal glands are also called **'glands of emergency'.** The above role of adrenaline and noradrenaline is often called **"fight or flight reaction".** It prepares the body to face stress or danger.

Pancreas

- The pancreas lies inferior to the stomach in a bend of the duodenum. It is both an exocrine and an endocrine gland.
- Pancreas has groups of cells called islets of Langerhans. These produce endocrine secretions. Four kinds of cells have been identified in the islets.

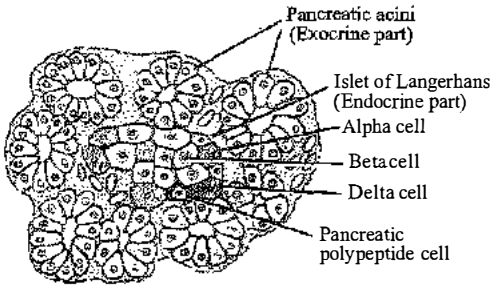
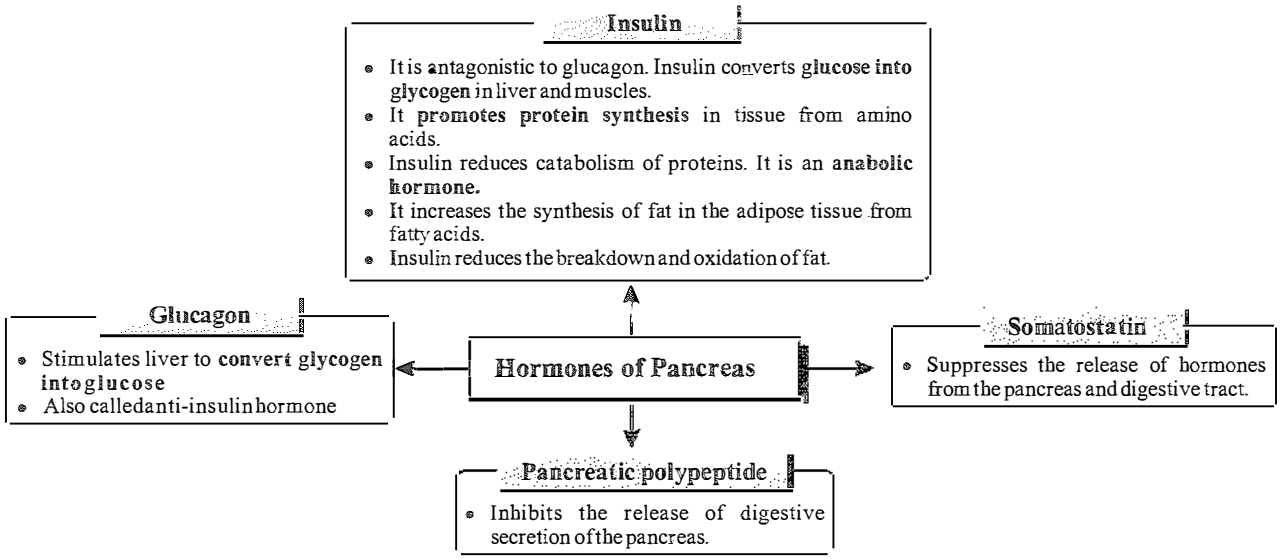


Fig.: Physiological anatomy of the pancreas

- **Alpha cells** or A cells (about 15 %) produce glucagon.
- **Beta cells** or B-cells (about 65 %) produce insulin.
- **Delta cells** or D-cells (about 5 %) produce somatostatin (SS).
- **Pancreatic polypeptide cells** or PP cells or F cells (15 %), produce pancreatic polypeptide (PP).

Disorders of the pancreas

- The most common endocrine disorder of the pancreas is the diabetes mellitus (hyperglycemia), now recognized to exist in two forms – **insulin-dependent and non-insulin-dependent.**
- The insulin-dependent diabetes mellitus (**IDDM**) is caused by a failure of the beta-cells to produce adequate amounts



of insulin while the non-insulin-dependent diabetes mellitus (**NIDDM**) appears to involve failure of insulin to facilitate the movement of glucose into the cells.

Gonads

- The gonads are the sex glands; the ovaries and the testes. They produce ova and sperms respectively but also secrete hormones.
- In females, the ovaries are located in the pelvic cavity in close proximity to the oviducts and the uterus. The hormones produced by ovaries include oestrogens, progesterone, relaxin and inhibin/actin. Oestrogens is secreted by the cells of **Graafian (ovarian) follicles.**
- **Estradiol** is the principle feminizing oestrogen. It stimulates the development of female secondary sex characteristics during puberty and maintains them through the reproductive years of adult life. It also stimulates maturation of ova (in the ovaries) and development of the uterine epithelium and the mammary glands.
- Progesterone is secreted by **corpus luteum.** It brings about most of the pregnancy changes such as development of uterine lining and mammary gland, and also formation of placenta.
- Relaxin is secreted by the corpus luteum only during the later stages of pregnancy and helps to soften ligaments, especially those that hold the pubic symphysis together.
- The connective tissue present between the **seminiferous tubules** in a testis contains small clusters of endocrine cells called **interstitial cells** or **Leydig's cells.** These cells secrete various male sex hormones called androgens. The principal androgen is **testosterone.**
- Testosterone stimulates growth and development of male sex organs and secondary sexual characters like beard, moustache and low pitch voice. It also stimulates formation of sperms and promotes growth of bones and muscles.

Disorders

- **Eunuchoidism :** Failure of testosterone secretion causes eunuchoidism. A eunuch has under developed and non-functional secondary sex organs, lacks accessory sex characters, and does not produce sperms.
- **Male hypogonadism** is due to the deficiency of androgens, deficiency of sperm formation or both, before puberty. As a result male secondary sexual characters and musculature do not develop.
- **Female hypogonadism** is due to deficiency of oestrogens (female sex hormones), pituitary gonadotropins (LH, FSH or both) or can represent primary ovary failure. It results in lack of development of female secondary sexual characters.
- **Precocious puberty** – Early maturation of ovaries and testes with production of ova before the age of 9 years in girls or sperms before 10 years in boys is called sexual precocity.

CONCEPT MAP

Human Endocrine System

Hypothalamus
- Supreme commander of endocrine system.
- Hypothalamic releasing hormones reach the pituitary gland through a portal circulatory system and regulate its secretion.

Pituitary
- Orchestra of endocrine system.
- It has two main lobes; **anterior lobe** or **adenohypophysis** or **pars distalis** and **posterior lobe** or **neurohypophysis** or **pars nervosa** and an intermediate lobe or pars intermedia.

Anterior pituitary
- The anterior pituitary regulates the growth and activity of several other endocrine glands. Hence it is referred to as **master endocrine** gland.

Posterior pituitary
- Neurohypophysis stores and releases oxytocin and vasopressin which are actually synthesized by the hypothalamus and are transported to it.

Pineal
- It secretes **melatonin** which helps in regulating sleep-wake rhythmic cycle.

Thyroid
- It is the largest endocrine gland.
- It secretes two iodine-containing thyroid hormones that control the rate of all metabolic processes.
- It also contains C-cells which secrete calcitonin that lowers the blood calcium level.

Parathyroid
- Two pairs of endocrine glands located behind the thyroid gland.
- They secrete parathyroid hormone (PTH) that controls the amount of calcium in the blood.
- PTH acts in opposition to calcitonin.

Adrenal
- A pair of endocrine gland situated immediately above kidneys.
- It has two parts external adrenal cortex and internal adrenal medulla.
- Adrenal cortex secretes mineralocorticoids (*i.e.*, aldosterone), glucocorticoids (*i.e.*, cortisol, corticosterone and cortisone) and gonadocorticoids (*i.e.*, testosterone and estrogen).
- Adrenal medulla is an extension of sympathetic system. It secretes norepinephrine (noradrenaline) and epinephrine (adrenaline). These hormones prepare the body to face stress or danger

Pancreas
- It contains a group of cells called islets of Langerhans that function as an endocrine gland.
- **α-cells** produce glucagon, **β-cells** produce insulin, **γ-cells** produce somatostatin.

Gonads
- The sex glands, the ovaries and the testes also secrete hormones.
- Ovaries secrete estrogens, progesterone, relaxin and inhibin/actin.
- Testes secrete androgens by cluster of endocrine cells called interstitial cells or Leydig's cells.