CHAPTER

8

Endocrine System and Homeostasis

Introduction

- A system of glands which pour their secretions *ie*, **hormones** directly into venous blood or lymph which pass to different body organs in order to control their functioning, metabolism, growth and stress conditions is called **endocrine system**.
- **Thomas Addison** (1793-1863) is known as **Father of Endocrinology**.

Types of Glands

Exocrine gland	**Endocrine gland** (Ductless gland)	**Heterocrine gland**
(Pours its secretion on the surface or into a particular region by means of ducts) **Example** : Sebaceous glands, sweat glands, salivary glands, intestinal gland.	(Pours its secretion into venous blood or lymph for reaching the target organ without ducts) **Example** : Pituitary, thyroid, parathyroid, thymus, adrenal glands.	(Endocrine as well as exocrine in nature or mixed gland) **Example** : Pancreas.

- Endocrine and nervous systems are collectively called as **neuroendocrine system.** Both the systems are essential for **homeostasis** (keeping internal environment of the body constant).

Hormones

- Secretory products of endocrine glands are known as **hormones**. These are the organic compounds, secreted in small amount which can inhibit or modify the cellular activities of the body.
- The term hormone was given by **Hippocrates** (460–377 BC).
- **Baylis** and **Starling** extracted the first hormone from secretory cells of duodenal mucosa and named it **secretin**.

Chemical Nature of Hormones

(a) Steroid hormones
- These are made up of **cholesterol,** which is a lipid derivative, synthesized by the liver cells.
- These hormones are lipid soluble, that is why, their molecules pass freely through the lipid bilayer of the cell membrane *eg*, corticotropin, aldosterone, testosterone, oestrogen, progesterone etc.

(b) Peptide hormones
- These are made up of amino acids. The number of amino acids greatly vary from hormone to hormone.
- These are lipid insoluble hormones, due to which, they can not pass freely through the cell membrane *eg*, oxytocin, prolactin, somatotropin, insulin, glucagon, secretin, relaxin etc.

(c) Amino acid derivative hormones
- These are smallest hormones, derived from histidine, tryptophan and tyrosine amino acids *eg*, epinephrine, nor-epinephrine and thyroxine hormone.

Mechanism of Hormone Action

- Hormones produce response only in those specific target cells which have **receptor molecules** on the membrane or within the cytoplasm.
- Based on the binding of receptors, mechanism of hormone action can be either membrane bound receptor hormone or cytoplasm bound receptor hormone action mechanism.

(a) Membrane bound receptor hormone action mechanism

- Amino acid and peptide hormones have very large structure due to which they do not pass through plasma membrane directly. These hormones first bind with receptor molecules present in the plasma membrane of target cells.
- The binding of a hormone to a receptor triggers an increase in the conversion of ATP to cyclic AMP. Thus, the hormone behaves as a first messenger that causes the release of a **second messenger** *ie*, **cyclic-AMP**.
- The second messengers activate enzymes that cause the cell to alter its functioning, since many molecules of cyclic-AMP may be manufactured after a single hormone molecule has bound, the message is amplified, perhaps many thousands of times.

(b) Cytoplasm bound receptor hormone action mechanism

- Steroid hormones are lipid soluble so they can pass freely across the lipid bilayer of plasma-membrane. After getting entrance in the cytoplasm, molecules of steroid hormones bind to receptor molecules, located within the cytoplasm of the target cell and thus a **hormone receptor complex** is formed. Now this complex moves into the nucleus of the cell and activates specific genes which ultimately produce specific proteins.

Endocrine Glands of Man

Pituitary Gland

- Pituitary gland is also called master endocrine gland/chief executive gland.
- It has two parts/lobes *ie*, **adenohypophysis** (anterior and intermediate lobes) and **neurohypophysis** (posterior lobe).

Table 8.1 Pituitary Hormones : Summary of Regulation and Effects

Hormone (Chemical structure and cell type)	Regulation of release	Target organ and effects	Effects of hyposecretion ↓ and hypersecretion ↑
Anterior Pituitary Hormones			
Growth Hormone (GH) (Protein, somatotrope)	**Stimulated** by GHRH* release which is triggered by low blood levels of GH as well as by a number of secondary triggers including oestrogens, hypoglycemia, increases in blood levels of amino acids, low levels of fatty acids, exercise and other types of stressors	Liver, muscle, bone, cartilage, and other tissues : anabolic hormone; stimulates somatic growth, mobilizes fats, spares glucose	↓ Pituitary dwarfism in children ↑ Gigantism in children, acromegaly in adults
	Inhibited by feedback inhibition exerted by GH and IGFs, and by hyperglycemia, hyperlipidemia obesity, and emotional deprivation, all of which elicit GHIH* (somatostatin) release	Most effects mediated indirectly by IGFs	
Thyroid-Stimulating Hormone (TSH) (Glycoprotein, thyrotrope)	**Stimulated** by TRH* and indirectly by pregnancy and cold temperature		↓ Cretinism in children, myxedema in adults, ↑ Graves' disease, exophthalmos
	Inhibited by feedback inhibition exerted by thyroid hormones on anterior pituitary and hypothalamus and by GHIH*	Thyroid gland : stimulates thyroid gland to release thyroid hormone	
Adrenocorticotropic Hormone (ACTH) (Polypeptide, 39 amino acids, corticotrope)	**Stimulated** by CRH* , stimuli that increase CRH release include fever, hypoglycemia, and other stressors		↓ Rare ↑ Cushing's disease

Hormone (Chemical structure and cell type)	Regulation of release	Target organ and effects	Effects of hyposecretion ↓ and hypersecretion ↑
	Inhibited by feedback inhibition exerted by glucocorticoids	Adrenal cortex : promotes release of glucocorticoids and androgens (mineralocortucoids to a lesser extent)	
Follicle-Stimulating Hormone (FSH) (Glycoprotein, gonadotrope)	**Stimulated** by GnRH* **Inhibited** by feedback inhibition exerted by oestrogen in females and testosterone and inhibin in males	Ovaries and testes : in females, stimulates ovarian follicle maturation and oestrogen production; in males, stimulates sperm production	↓ Failure of sexual maturation ↑ No important effects
Luteinizing Hormone (LH)	**Stimulated** by GnRH*		As for FSH
(Glycoprotein, gonadotrope)	**Inhibited** by feedback inhibition exerted by estrogen and progesterone in females and testosterone in males	Ovaries and testes; in females, triggers ovulation and stimulates ovarian production of oestrogen and progesterone, in males, promotes testosterone production	
Prolactin (PRL) (Protein, lactotrope)	**Stimulated** by PRH*; PRH release enhanced by estrogens, birth control pills, opiates, and breast-feeding **Inhibited** by PIH* (dopamine)	Breast secretory tissue : promotes lactation	↓ Poor milk production in nursing women ↑ Inappropriate milk production (galactorrhoea); cessation of menses in females; impotence and breast enlargement (gynecomastia) in males
Posterior Pituitary Hormones (made by hypothalamic neurons and stored in posterior pituitary)			
Oxytocin (Peptide, neurons in paraventricular nucleus of hypothalamus)	**Stimulated** by impulses from hypothalamic neurons in response to cervical/uterine stretching and suckling of infant at breast		Unknown
	Inhibited by lack of appropriate neural stimuli	Uterus : stimulates uterine contraction, initiates labor breast : initiates milk ejection	
Antidiuretic Hormone (ADH) or **vasopressin** (Peptide, neurons in supraoptic nucleus of hypothalamus)	**Stimulated** by impulses from hypothalamic neurons in response to increased osmolarity of blood or decreased blood volume; also stimulated by pain, some drugs, low blood pressure		↓ Diabetes insipidus ↑ Syndrome of inappropriate ADH secretion (SIADH)
	Inhibited by adequate hydration of the body and by alcohol	Kidneys : stimulates kidney tubule cells to reabsorb water	

* Indicates hypothalamic releasing and inhibiting hormones: GHRH = growth hormone-releasing hormone; GHIH = growth hormone-inhibiting hormone; TRH = thyrotropin-releasing hormone; CRH = corticotropin-releasing hormone; GnRH = gonadotropin-releasing hormone; PRH = prolactin-releasing hormone; PIH = prolactin-inhibiting hormone.

Thyroid Gland

- It is the largest endocrine gland situated in the neck region extending from thyroid cartilage of larynx to fourth tracheal cartilage.
- It is a brownish H-shaped, bilobed gland. These two lobes are connected with each other by a straight structure, called **isthmus.**

Table 8.2 Hormonal Sources other than the Mammalian Hypothalamus and Pituitary

Source	Its secretion (s)	Main targets	Primary actions
Adrenal cortex	Glucocorticoids (eg, cortisol)	Most cells	Raise blood sugar level, help control lipid, protein metabolism, mediate responses to stress
	Mineralocorticoids (including aldosterone)	Kidney	Promote sodium reabsorption, control salt, water balance
	Sex hormones (including testosterone)	General	Influence sexual characteristics, general growth
Adrenal medulla	Epinephrine (adrenalin)	Muscle, adipose tissue	Raises blood sugar level by stimulating glucose production, raises blood levels of fatty acids, increases heart rate, force of contraction
	Norepinephrine	Smooth muscle in walls of blood vessels	Promotes vasoconstriction or vasodilation
Thyroid	Tri-iodothyronine, thyroxine	Most cells	Regulates carbohydrate, lipid metabolism; contributes to growth, development (including brain development, function)
Parathyroids	Parathyroid hormone (or parathormone)	Bone, kidney, gut	Elevates calcium levels in blood by stimulating calcium reabsorption from bone, kidneys, and absorption from gut
Gonads testis (in males)	Testosterone (an androgen)	General	Has key roles in spermatogenesis, development of genital tract, and maintenance of accessory sex organs and secondary sex traits, influences growth, development
Ovary (in females)	Oestrogens	General	Have key roles in oogenesis, stimulate thickening of uterine lining for pregnancy; other actions same as above
	Progesterone	Uterus, breasts	Prepares, maintains uterine lining for pregnancy, stimulates breast development
Pancreatic islets	Insulin	All cells except most neurons in brain and red blood cells	Lowers blood sugar by stimulating glucose uptake by cells, fat storage, protein synthesis
	Glucagon	Liver	Raises blood sugar by stimulating glucose production
	Somatostatin	Insulin-secreting cells in pancreas	Influences carbohydrate metabolism
Endocrine cells of gastrointestinal epithelium	Gastrin, cholecystokinin, secretin and others	Stomach, pancreas, gall bladder	Influences activity of stomach, pancreas, liver, gall bladder
Liver	Somatomedins	Most cells	Stimulates overall growth, development
Kidney	Erythropoietin*	Bone marrow	Stimulates red blood cell production
	Angiotensin*	Adrenal cortex, arterioles	Helps control blood pressure and aldosterone secretion
	Vitamin D_3 (an active from)	Bone, gut	Enhances calcium resorption from bone; enhances calcium uptake from gut
Heart	Atrial natriuretic hormone	Kindney, blood vessels	Increases sodium excretion, lowers blood pressure
Thymus	Include thymosin	Lymphocytes, plasma cells	Promote development of infection-fighting abilities and lymphocyte function in immune responses
Pineal	Melatonin	Gonads (indirectly, perhaps via hypothalamus)	Influences daily biorhythms, sexual activity and sexual development

* These hormones are not produced in the kidney but are formed when enzymes produced in kidneys activate specific plasma proteins.

Disorders of thyroid gland

(i) ***Graves's disease*** Hypersecretion of thyroxin causes enlargement of the gland. This results in increase in heart beat, nerve activities and muscles movements. This disease is known as Grave's disease or toxic goitre.

(ii) ***Exophthalmic goitre*** In some cases hypersecretion leads to protrudance of eyeballs from their orbits. This condition is known as exophthalmic goitre (exophthalmia).

(iii) ***Cretinism*** It is the result of thyroid malfunctioning from a very early stage of development. Hyposecretion of thyroxine can retarded the physical, sexual and mental development and slow metabolic rate. Such children are stunted and also shows other symptoms such as slow BMR, heart beat, bone growth, low intelligence and protruding tongue.

(iv) ***Myxoedema*** or ***Gull's disease*** This disorder appears in adults. In this, mucus becomes stored in subcutaneous tissue which holds water and gives a puffy appearance to the skin *ie*, Myxoedema.
The patient affected by myxoedema shows symptoms like greying and falling of hairs, dryness and paleness of skin, low metabolic rate, intelligence, blood pressure, heart beat, body temperature and sexual development.

(v) ***Goitre*** This disease is common in hilly areas and is caused due to genetic defect or iodine deficiency in the food or the low level of thyroxin secretion. For solving this problem, the thyroid gland becomes enlarge and causes a collar-like front swelling in the neck, called **goitre**. This may lead to cretinism in the young and myxoedema in adults.

(vi) ***Hashimoto's disease*** This is also called as autoimmune thyroiditis or suicide of the thyroid. In this disorder, the immune system of the body becomes affected and starts forming antibodies, which attach and destroy the thyroid gland itself.

Parathyroid Glands

- These glands consist of four separate glands located on the posterior surface of the lobes of the thyroid gland.
- They are present in all vertebrates except fishes.
- They contain two kinds of cells **chief cells** or **principal cells** and **oxyphils cells** or **eosinophil cells.**
- Chief cells are the major synthesizers of **Parathormone** or **Para Thyroid Hormone** (PTH) or **Collip's hormone.**
- PTH regulates the amount of calcium and phosphate in ECF (Extra Cellular Fluid).
- Parathyroids are under the **feed back control** of blood calcium level. A fall in blood calcium stimulates them to secrete parathormone while a rise in blood calcium inhibits parathormone secretion from them.
- The functions of oxyphil cells are unknown.
- **Hypoparathyroidism** *ie*, deficiency of PTH causes **parathyroid tetany** or **hypocalcaemic tetany**.
- **Hyperparathyroidism** *ie*, excess of PTH causes **osteitis fibrosa cystica** or **osteoporosis.**

Hypothalamus

- Hypothalamus links with anterior part of pituitary gland by means of hypothalamo-hypophysial portal vein and with the posterior lobe of pituitary gland by means of axons of it's neurosecretory cells.
- The hormones of hypothalamus influence the functioning of the pituitary gland.
- The neurosecretory cells (neurons) of hypothalamus secrete hormones called **neurohormones**.

Hormones of hypothalamus

(i) **Thyrotropin Releasing Hormone (TRH)** It stimulates the anterior pituitary for the release of thyrotropin or thyroid stimulating hormone.

(ii) **Adrenocorticotropic Releasing Hormone (ARH)** It stimulates the anterior pituitary part for the release of Adrenocorticotropic Hormone (ACTH).

(iii) **Gonadotropin Releasing Hormone (GnRH)** It stimulates the anterior pituitary part for secretion of Luteinising Hormone (LH) and Follicle Stimulating Hormone (FSH).

(iv) **Prolactin Inhibiting Hormone (PIH)** It retards the anterior pituitary part for the release of prolactin hormone.

(v) **Growth Inhibiting Hormone (GIH) or Somatostatin (SS)** It retards the anterior pituitary part for the release of growth hormone (GH).

(vi) **Prolactin Releasing Hormone (PRH)** It helps in secretion of prolactin from anterior lobe of pituitary gland.

(vii) **Somatotropin Releasing Hormone (SRH)** It helps in secretion of Growth Hormone (GH) from anterior lobe of pituitary gland.

(viii) **Melanocyte Releasing Hormone (MRH)** It stimulates anterior pituitary part for release of Melanocyte Stimulating Hormone (MSH).

(ix) **Melanocyte Inhibiting Hormone (MIH)** It retards the release of MSH from anterior part of pituitary gland.

Adrenal Glands (Glands of Emergency)

- These are paired structures located on the top of the kidneys, hence, called **"Suprarenals."**
- Adrenal glands are also known as 4S gland.
- Each adrenal gland is divided into two parts outer **adrenal cortex** and inner **adrenal medulla.**
- **Adrenal cortex** secretes the three types of steroid hormones **Mineralocorticoids**, **Glucocorticoids** and **Gonadocorticoids**.
- **Adrenal medulla** secretes two hormones **Noradrenaline** (nor epinephrine) and **Adrenaline** (epinephrine).
- Both adrenaline and noradrenaline act on the cells of skeletal, cardiac and smooth muscles, blood vessels and fat cells.

Disorders of adrenal glands

(i) **Addison's disease** It is caused by the deficiency of mineralocorticoids and glucocorticoids.

(ii) **Cushing's disease** It is caused by excess of cortisol which may be due to a tumour of the adrenal cortex.

(iii) **Virilism** Appearance of male characters in female is called virilism. Excessive production of male sex corticoids (androgens) produces male secondary sexual characters like beard, moustache, hoarse voice in woman.

(iv) **Gynecomastia** It is the development of enlarged mammary glands (breasts) in the males. It is due to excessive secretion of female sex hormones (oestrogen) in males.

Pineal Gland

- Pineal gland is an endocrine organ, it is located in the posterior portion of the roof of third ventricle.
- Pineal gland in man starts to degenerate at about age 7 years, in adult it is largely fibrous tissue.
- Pineal gland creates three hormones namely **melatonin, serotonin** and **adrenoglomerulotropin.**
- Pineal gland functions as a **biological clock** and neurosecretory transducer, converting neural information.

Thymus Gland

- Thymus is a bilobed lymphoid organ situated in front of the heart in the upper part of sternum.
- Thymus is called "the throne of immunity" or training school of T-lymphocytes.
- Thymus is active in young ones but gradually becomes inconspicuous after sexual maturity.
- Thymus gland secretes a hormone, **thymosin** which promotes immuno competence in young T-lymphocytes.

Pancreas

- Pancreas is a **mixed** (exocrine as well as endocrine) **gland.**
- The tissue of pancreas has groups of cells called **islets of Langerhans,** which contains four types of cells.
  - (i) **Alpha or A-cells** Secrete **glucagon** hormone.
  - (ii) **Beta or B-cells** Secrete **insulin** hormone.
  - (iii) **Delta or D-cells** Secrete **somatostatin.**
  - (iv) **F-cells or PP-cells** Secrete **pancreatic polypeptide**.
- **Insulin Dependent Diabetes Mellitus** (IDDM) is caused by a failure of the Beta-cells to produce adequate amounts of insulin (*ie*, hyposecretion of insulin).
- Insulin decreases blood sugar level by promoting liver glycogen formation.
- **Banting** and **Best** (1921) extracted insulin from pancreas.

Gonads

- The main function of gonads (ovaries and testes) is to produce gametes (ova and sperm) but they also secrete sex hormones.
- Sex hormones are mostly steroids.
- Female, **ovaries** secrete hormones **oestrogens**, **progesterone**, **relaxin** and **inhibin/actin**.
  - *(a) Oestrogens*
    - These are secreted by the cells of Graafian follicles.
    - These stimulate the development of female secondary sexual characters during puberty and maintains them through the reproductive years of adult life.
  - *(b) Progesterone*
    - It is secreted by **corpus luteum.**
    - Progesterene is responsible for growth and maintenance of foetus.
  - *(c) Relaxin*
    - It is secreted by the **corpus luteum** only during later stage of pregnancy.
    - It helps to softens ligaments at the time of child birth.
  - *(d) Inhibin/Actin*
    - Inhibin/actin is secreted by **corpus luteum.**
    - Inhibin hormone inhibits and actin hormone activates the FSH and GnRH production.
- In males, testes contains small clusters of endocrine cells called **interstitial cells** or **Leydig's cells** which secrete various **male sex hormones** called **androgens.**
- The principal androgen is **testosterone** which is responsible for puberty in man.

Prostaglandins

- Prostaglandins were discovered from human semen in 1930.
- The name prostaglandin was introduced by **Von Euler** in 1937.
- The common prostaglandins are PGA_1, PGA_2, PGE_1, PGE_2, PGF etc.

Pheromones

- The term pheromone was proposed by **Karlson.**
- Pheromones are chemical messengers produced by animals and released outside the body, hence, called **"ectohormones."**
- **Bombycol**, a pheromone produced by silk moth was the pheromone studied first.