



Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial

# COLLEGE OF PHARMACY

(An Autonomous College)

BELA (Ropar) Punjab



Name of Unit	Endocrine system
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## Learning Outcome of Module-4

LO	Learning Outcome	Course Outcome Code
1	To understand anatomy of endocrine glands.	BP201.5
2	To focus the mechanism of hormones and their functions.	BP201.5
3	To focus on regulation of endocrine glands and its related hormones.	BP201.5

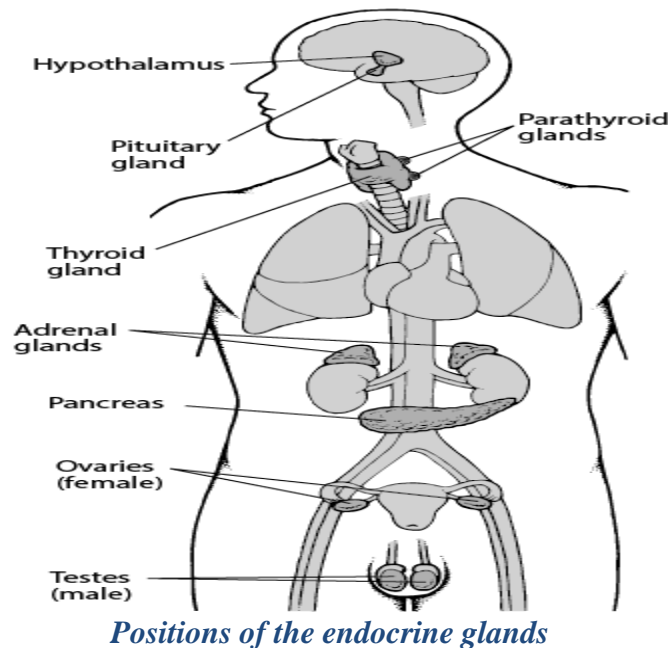
**Content Table**

**Topic**

- Classification of hormones, mechanism of hormone action
- Structure and functions of pituitary gland, thyroid gland, parathyroid gland, adrenal gland, pancreas, pineal gland, thymus and their disorders.
- Hormones related disorders

## ENDOCRINE SYSTEM

The endocrine system consists of glands widely separated from each other with no physical connections. Endocrine glands are groups of secretory cells surrounded by an extensive network of capillaries that facilitates diffusion of hormones (chemical messengers) from the secretory cells into the bloodstream. They are also referred to as ductless glands because hormones diffuse directly into the bloodstream. Hormones are then carried in the bloodstream to target tissues and organs that may be quite distant, where they influence cell growth and metabolism.



### Classification of endocrine glands

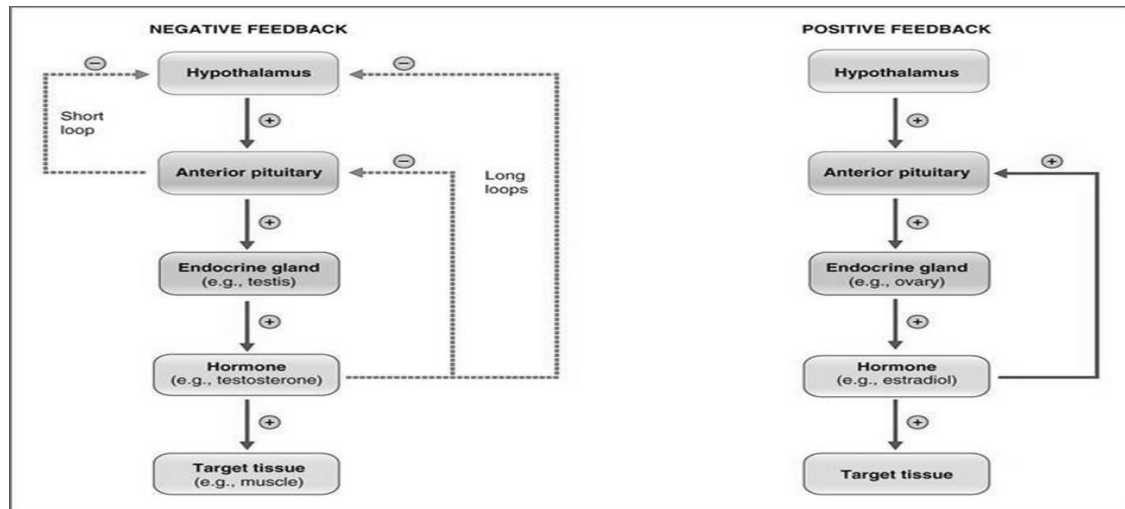
There are three general classes of hormones:

1. Proteins and polypeptides, including hormones secreted by the anterior and posterior pituitary gland, the pancreas (insulin and glucagon), the parathyroid gland (parathyroid hormone), and many others.
2. Steroids secreted by the adrenal cortex (cortisol and aldosterone), the ovaries (estrogen and progesterone), the testes (testosterone), and the placenta (estrogen and progesterone).
3. Derivatives of the amino acid tyrosine, secreted by the thyroid (thyroxine and triiodothyronine) and the adrenal medullae (epinephrine and norepinephrine). There are no known polysaccharides or nucleic acid hormones.

### Mechanisms of Action of Hormones

The first step of a hormone's action is to bind to specific receptors at the target cell. The receptors for some hormones are located on the target cell membrane, whereas other hormone

receptors are located in the cytoplasm or the nucleus. When the hormone combines with its receptor, this usually initiates a cascade of reactions in the cell, with each stage becoming more powerfully activated so that even small concentrations of the hormone can have a large effect.



## *Regulation of hormone*

### **Regulation of hormone**

Negative feedback prevents over activity of hormone systems. Although the plasma concentrations of many hormones fluctuate in response to various stimuli that occur throughout the day, all hormones studied thus far appear to be closely controlled. In most instances, this control is exerted through negative feedback mechanisms that ensure a proper level of hormone activity at the target tissue. After a stimulus causes release of the hormone, conditions or products resulting from the action of the hormone tend to suppress its further release. In other words, the hormone (or one of its products) has a negative feedback effect to prevent over secretion of the hormone or over activity at the target tissue.

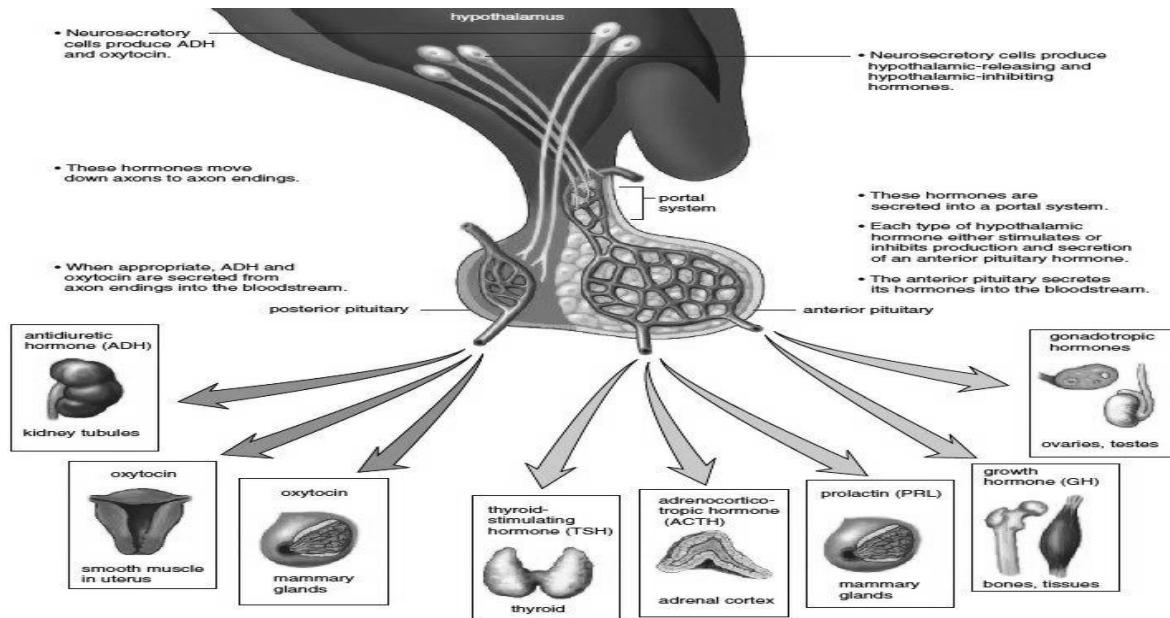
The controlled variable is often not the secretory rate of the hormone itself but the degree of activity of the target tissue. Therefore, only when the target tissue activity rises to an appropriate level will feedback signals to the endocrine gland become powerful enough to slow further secretion of the hormone.

Feedback regulation of hormones can occur at all levels, including gene transcription and translation steps involved in the synthesis of hormones and steps involved in processing hormones or releasing stored hormones.

### **Pituitary gland and Hypothalamus**

The pituitary gland and the hypothalamus act as a unit, regulating the activity of most of the other endocrine glands. The pituitary gland lies in the hypophyseal fossa of the sphenoid bone

below the hypothalamus, to which it is attached by a stalk. It is the size of a pea, weighs about 500 mg and consists of two main parts that originate from different types of cells. The anterior pituitary (adenohypophysis) is an upgrowth of glandular epithelium from the pharynx and the posterior pituitary (neurohypophysis) a downgrowth of nervous tissue from the brain. There is a network of nerve fibres between the hypothalamus and the posterior pituitary.



*Structure of lobes of the pituitary gland and their relationship with the hypothalamus*

## Anterior pituitary

The anterior pituitary is supplied indirectly with arterial blood that has already passed through a capillary bed in the hypothalamus. This network of blood vessels forms part of the pituitary portal system, which transports blood from the hypothalamus to the anterior pituitary where it enters thin-walled sinusoids that are in close contact with the secretory cells. As well as providing oxygen and nutrients, this blood transports releasing and inhibiting hormones secreted by the hypothalamus.

These hormones specifically influence secretion and release of other hormones formed in the anterior pituitary. Some of the hormones secreted by the anterior lobe stimulate or inhibit secretion by other endocrine glands (target glands) while others have a direct effect on target tissues. Secretion of an anterior pituitary hormone follows stimulation of the gland by a specific releasing hormone produced by the hypothalamus and carried to the gland through the pituitary portal system. The whole system is controlled by a negative feedback mechanism. That is, when the level of a hormone in the blood supplying the hypothalamus is low it produces the appropriate releasing hormone that stimulates release of a trophic hormone by the anterior

pituitary. This in turn stimulates the target gland to produce and release its hormone. As a result the blood level of that hormone rises and inhibits secretion of its releasing factor by the hypothalamus.

## **Hormones and functions of pituitary gland**

### **Growth hormone (GH)**

This is the most abundant hormone synthesised by the anterior pituitary. It stimulates growth and division of most body cells but especially those in the bones and skeletal muscles. Body growth in response to the secretion of GH is evident during childhood and adolescence, and thereafter secretion of GH maintains the mass of bones and skeletal muscles. It also regulates aspects of metabolism in many organs, e.g. liver, intestines and pancreas; stimulates protein synthesis, especially tissue growth and repair; promotes breakdown of fats and increases blood glucose levels.

### **Thyroid stimulating hormone (TSH)**

The release of this hormone is stimulated by thyrotrophin releasing hormone (TRH) from the hypothalamus. It stimulates growth and activity of the thyroid gland, which secretes the hormones thyroxine (T4) and tri-iodothyronine (T3). Release is lowest in the early evening and highest during the night. Secretion is regulated by a negative feedback mechanism, i.e. when the blood level of thyroid hormones is high, secretion of TSH is reduced, and vice versa

### **Adrenocorticotrophic hormone (ACTH, corticotrophin)**

Corticotrophin releasing hormone (CRH) from the hypothalamus promotes the synthesis and release of ACTH by the anterior pituitary. This increases the concentration of cholesterol and steroids within the adrenal cortex and the output of steroid hormones, especially cortisol.

### **Prolactin**

This hormone is secreted during pregnancy to prepare the breasts for lactation (milk production) after childbirth. The blood level of prolactin is stimulated by prolactin releasing hormone (PRH) released from the hypothalamus and it is lowered by prolactin inhibiting hormone (PIH, dopamine) and by an increased blood level of prolactin.

Prolactin, together with oestrogens, corticosteroids, insulin and thyroxine, is involved in initiating and maintaining lactation. Prolactin secretion is related to sleep, rising during any period of sleep, night or day.

## Gonadotrophins

Just before puberty two gonadotrophins (sex hormones) are secreted in gradually increasing amounts by the anterior pituitary in response to luteinising hormone releasing hormone (LHRH), also known as gonadotrophin releasing hormone (GnRH). Rising levels of these hormones at puberty promotes mature functioning of the reproductive organs. In both males and females the hormones responsible are:

1. Follicle stimulating hormone (FSH)
2. Luteinising hormone (LH).

**In both sexes:** FSH stimulates production of gametes (ova or spermatozoa) by the gonads.

**In females:** LH and FSH are involved in secretion of the hormones oestrogen and progesterone during the menstrual cycle. As the levels of oestrogen and progesterone rise, secretion of LH and FSH is suppressed.

**In males:** LH, also called interstitial cell stimulating hormone (ICSH) stimulates the interstitial cells of the testes to secrete the hormone testosterone.

## Posterior pituitary

The posterior pituitary is formed from nervous tissue and consists of nerve cells surrounded by supporting glial cells called pituicytes. These neurones have their cell bodies in the supraoptic and paraventricular nuclei of the hypothalamus and their axons form a bundle known as the hypothalamohypophyseal tract. Posterior pituitary hormones are synthesised in the nerve cell bodies, transported along the axons and stored in vesicles within the axon terminals in the posterior pituitary. Oxytocin and antidiuretic hormone (ADH, vasopressin) are the hormones released from axon terminals within the posterior pituitary. These hormones act directly on non-endocrine tissue.

## Oxytocin

Oxytocin stimulates two target tissues during and after childbirth (parturition): uterine smooth muscle and the muscle cells of the lactating breast. During childbirth increasing amounts of oxytocin are released from the posterior pituitary into the bloodstream in response to increasing stimulation of sensory stretch receptors in the uterine cervix as the baby's head progressively dilates it. Sensory impulses are generated and travel to the control centre in the hypothalamus, stimulating the posterior pituitary to release more oxytocin.

In turn this stimulates more forceful uterine contractions and greater stretching of the uterine cervix as the baby's head is forced further downwards. This is an example of a positive feedback

mechanism which stops soon after the baby is delivered when distension of the uterine cervix is greatly reduced.

The process of milk ejection also involves a positive feedback mechanism. Suckling generates sensory impulses that are transmitted from the breast to the hypothalamus. The impulses trigger release of oxytocin from the posterior pituitary. On reaching the lactating breast, oxytocin stimulates contraction of the milk ducts and myoepithelial cells around the glandular cells, ejecting milk. Suckling also inhibits the release of prolactin inhibiting hormone (PIH), prolonging prolactin secretion and lactation.

### **Antidiuretic hormone (ADH, vasopressin)**

The main effect of antidiuretic hormone is to reduce urine output (diuresis is the production of a large volume of urine). ADH acts on the distal convoluted tubules and collecting ducts of the nephrons of the kidneys. It increases their permeability to water and more of the glomerular filtrate is reabsorbed. ADH secretion is determined by the osmotic pressure of the blood circulating to the osmoreceptors in the hypothalamus.

As osmotic pressure rises, for example as a result of dehydration, secretion of ADH increases. More water is therefore reabsorbed and the urine output is reduced. This means that the body retains more water and the rise in osmotic pressure is reversed. Conversely, when the osmotic pressure of the blood is low, for example after a large fluid intake, secretion of ADH is reduced, less water is reabsorbed and more urine is produced.

The thyroid gland is situated in the neck in front of the larynx and trachea at the level of the 5th, 6th and 7<sup>th</sup> cervical and 1st thoracic vertebrae. It is a highly vascular gland that weighs about 25 g and is surrounded by a fibrous capsule. It resembles a butterfly in shape, consisting of two lobes, one on either side of the thyroid cartilage and upper cartilaginous rings of the trachea. The lobes are joined by a narrow isthmus, lying in front of the trachea.

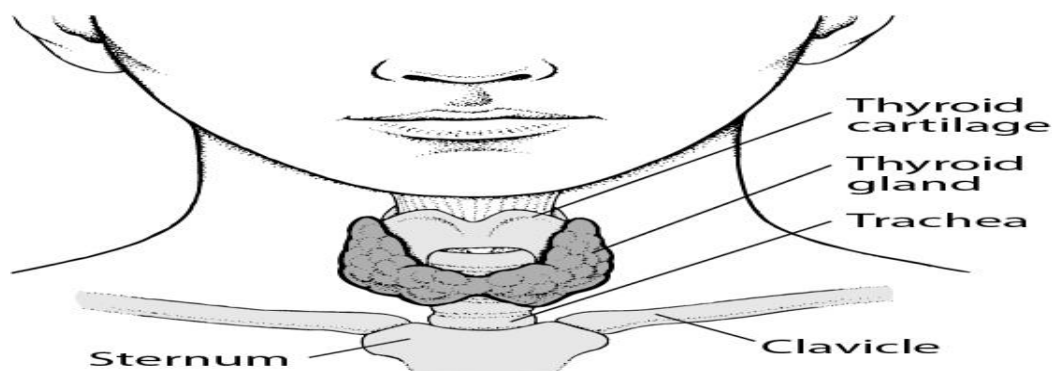
The lobes are roughly cone shaped, about 5 cm long and 3 cm wide. The arterial blood supply to the gland is through the superior and inferior thyroid arteries. The superior thyroid artery is a branch of the external carotid artery and the inferior thyroid artery is a branch of the subclavian artery. The venous return is by the thyroid veins, which drain into the internal jugular veins.

### **Thyroid gland**

The recurrent laryngeal nerves pass upwards close to the lobes of the gland and, especially on the right side; lie near the inferior thyroid artery. The gland is composed of largely spherical follicles formed from cuboidal epithelium. These secrete and store colloid, a thick sticky protein



material. Between the follicles are other cells found singly or in small groups: parafollicular cells, also called C-cells, which secrete the hormone calcitonin



*Structure of position of the thyroid gland and its associated structures*

## **1. Thyroxine and tri-iodothyronine**

Iodine is essential for the formation of the thyroid hormones; thyroxine (T<sub>4</sub>) and tri-iodothyronine (T<sub>3</sub>), so numbered as these molecules contain four and three atoms of the element iodine respectively. The main dietary sources of iodine are seafood, vegetables grown in iodine-rich soil and iodinated table salt. The thyroid gland selectively takes up iodine from the blood, a process called iodine trapping.

Thyroid hormones are synthesised as large precursor molecules called thyroglobulin, the major constituent of colloid. The release of T<sub>3</sub> and T<sub>4</sub> into the blood is stimulated by thyroid stimulating hormone (TSH) from the anterior pituitary.

## **Regulation and functions of Thyroid hormone**

Secretion of TSH is stimulated by thyrotrophin releasing hormone (TRH) from the hypothalamus and secretion of TRH is stimulated by exercise, stress, malnutrition, low plasma glucose levels and sleep. TSH secretion depends on the plasma levels of T<sub>3</sub> and T<sub>4</sub> because it is these hormones that control the sensitivity of the anterior pituitary to TRH. Through the negative feedback mechanism, increased levels of T<sub>3</sub> and T<sub>4</sub> decrease TSH secretion and vice versa. Dietary iodine deficiency greatly increases TSH secretion causing proliferation of thyroid gland cells and enlargement of the gland (goitre).

Thyroid hormones enter the cell nucleus and regulate gene expression, i.e. they increase or decrease protein synthesis. They enhance the effects of other hormones, e.g. adrenaline (epinephrine) and noradrenaline (norepinephrine). T<sub>3</sub> and T<sub>4</sub> affect most cells of the body by:

1. Increasing the basal metabolic rate and heat production
2. Regulating metabolism of carbohydrates, proteins and fats.

T3 and T4 are essential for normal growth and development, especially of the skeleton and nervous system. Most other organs and systems are also influenced by thyroid hormones. Physiological effects of T3 and T4 on the heart, skeletal muscles, skin, digestive and reproductive systems are more evident when there is underactivity or overactivity of the thyroid gland and can be profound in childhood.

## 2. Calcitonin

This hormone is secreted by the parafollicular or C-cells in the thyroid gland. Calcitonin lowers raised blood calcium ( $\text{Ca}^{2+}$ ) levels. It does this by acting on:

1. Bone cells promoting their storage of calcium
2. Kidney tubules inhibiting the reabsorption of calcium.

Its effect is opposite to that of parathyroid hormone, the hormone secreted by the parathyroid glands. Release of calcitonin is stimulated by increased blood calcium levels. This hormone is important during childhood when bones undergo considerable changes in size and shape.

## Parathyroid glands

There are four small parathyroid glands, each weighing around 50 mg, two embedded in the posterior surface of each lobe of the thyroid gland. They are surrounded by fine connective tissue capsules that contain spherical cells arranged in columns with sinusoids containing blood in between them.

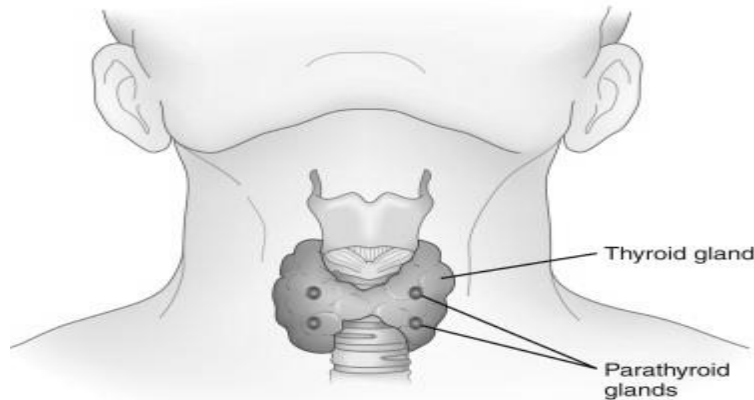
## Parathyroid Hormone

Parathyroid hormone provides a powerful mechanism for controlling extracellular calcium and phosphate concentrations by regulating intestinal reabsorption, renal excretion, and exchange between the extracellular fluid and bone of these ions. Excess activity of the parathyroid gland causes rapid absorption of calcium salts from the bones, with resultant *hypercalcemia* in the extracellular fluid; conversely, hypofunction of the parathyroid glands causes *hypocalcemia*, often with resultant tetany.

## Anatomy of the Parathyroid Glands:

Normally there are four parathyroid glands in humans; they are located immediately behind the thyroid gland—one behind each of the upper and each of the lower poles of the thyroid. Each parathyroid gland is about 6 millimeters long, 3 millimeters wide and 2 millimeters thick and has a macroscopic appearance of dark brown fat. The parathyroid glands are difficult to locate

during thyroid operations because they often look like just another lobule of the thyroid gland. For this reason, before the importance of these glands was generally recognized, total or subtotal thyroidectomy frequently resulted in removal of the parathyroid glands as well.



*Structure and positions of the parathyroid glands*

## **Functions of Parathyroid Glands**

**1. Effect of Parathyroid Hormone on Calcium and Phosphate Concentrations in the Extracellular Fluid:** Parathyroid Hormone Increases Calcium and Phosphate Absorption from the Bone PTH has two effects on bone in causing absorption of calcium and phosphate. One is a rapid phase that begins in minutes and increases progressively for several hours. This phase results from activation of the already existing bone cells (mainly the osteocytes) to promote calcium and phosphate absorption. The second phase is a much slower one, requiring several days or even weeks to become fully developed; it results from proliferation of the osteoclasts, followed by greatly increased osteoclastic reabsorption of the bone itself, not merely absorption of the calcium phosphate salts from the bone.

**2. Rapid Phase of Calcium and Phosphate Absorption—Osteolysis:** When large quantities of PTH are injected, the calcium ion concentration in the blood begins to rise within minutes, long before any new bone cells can be developed. Histological and physiologic studies have shown that PTH causes removal of bone salts from two areas in the bone: (1) from the bone matrix in the vicinity of the osteocytes lying within the bone itself and (2) in the vicinity of the osteoblasts along the bone surface.

### 3. Parathyroid Hormone Decreases Calcium Excretion and Increases Phosphate Excretion by the Kidneys:

Administration of PTH causes rapid loss of phosphate in the urine owing to the effect of the hormone to diminish proximal tubular reabsorption of phosphate ions.

PTH also increases renal tubular reabsorption of calcium at the same time that it diminishes phosphate reabsorption. Moreover, it increases the rate of reabsorption of magnesium ions and hydrogen ions while it decreases the reabsorption of sodium, potassium, and amino acid ions in much the same way that it affects phosphate. The increased calcium absorption occurs mainly in the *late distal tubules*, the *collecting tubules*, the early collecting ducts, and possibly the ascending loop of Henle to a lesser extent. Parathyroid hormone increases intestinal absorption of calcium and phosphate at this point.

These glands secrete parathyroid hormone (PTH, parathormone). Secretion is regulated by blood calcium levels. When they fall, secretion of PTH is increased and vice versa.

The main function of PTH is to increase blood calcium levels. This is achieved by increasing the calcium absorption from the small intestine and reabsorption from the renal tubules. If these sources provide inadequate supplies then PTH stimulates osteoclasts (bone-destroying cells) and calcium is released from bones into the blood.

Parathormone and calcitonin from the thyroid gland act in a complementary manner to maintain blood calcium levels within the normal range. This is needed for:

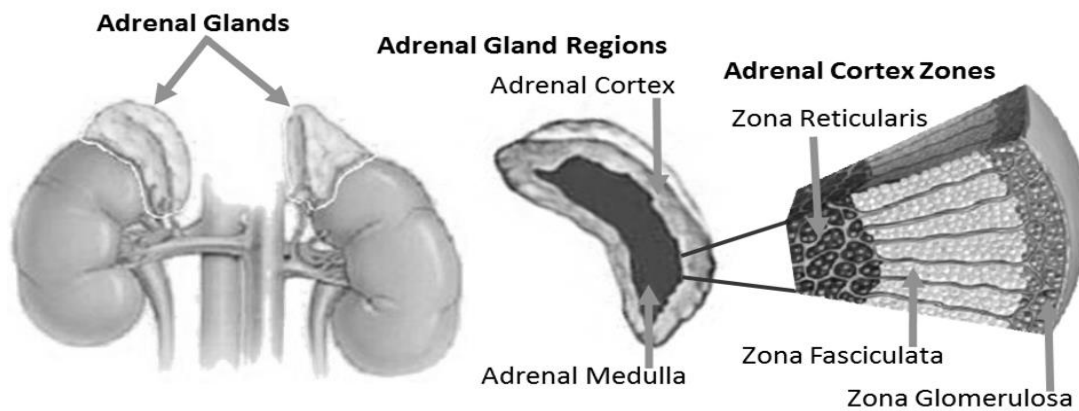
1. Muscle contraction
2. Transmission of nerve impulses
3. Blood clotting
4. Normal action of many enzymes.

### Control of Parathyroid Secretion by Calcium Ion Concentration

Even the slightest decrease in calcium ion concentration in the extracellular fluid causes the parathyroid glands to increase their rate of secretion within minutes; if the decreased calcium concentration persists, the glands will hypertrophy, sometimes fivefold or more. For instance, the parathyroid glands become greatly enlarged in *rickets*, in which the level of calcium is usually depressed only a small amount; also, they become greatly enlarged in *pregnancy*, even though the decrease in calcium ion concentration in the mother's extracellular fluid is hardly measurable; and they are greatly enlarged during *lactation* because calcium is used for milk formation.

Conversely, conditions that increase the calcium ion concentration above normal cause decreased activity and reduced size of the parathyroid glands. Such conditions include (1)

excess quantities of calcium in the diet, (2) increased vitamin D in the diet, and (3) bone absorption caused by factors other than PTH (for example, bone absorption caused by disuse of the bones)



*Location and structure of adrenal glands*

## Adrenal glands

The two adrenal (suprarenal) glands are situated on the upper pole of each kidney enclosed within the renal fascia. They are about 4 cm long and 3 cm thick. The arterial blood supply is by branches from the abdominal aorta and renal arteries.

The venous return is by suprarenal veins. The right gland drains into the inferior vena cava and the left into the left renal vein.

The glands are composed of two parts which have different structures and functions. The outer part is the cortex and the inner part the medulla.

## Adrenal cortex

The adrenal cortex produces three groups of steroid hormones from cholesterol. They are collectively called adrenocorticoids (corticosteroids). The groups are:

1. Glucocorticoids
2. Mineralocorticoids
3. Sex hormones (androgens).

The hormones in each group have different characteristic actions but as they are structurally similar their actions may overlap.

### 1. Glucocorticoids

Cortisol (hydrocortisone) is the main glucocorticoid but small amounts of corticosterone and cortisone are also produced. Commonly these are collectively known as 'steroids'; they are

essential for life, regulating metabolism and responses to stress. Secretion is controlled through a negative feedback system involving the hypothalamus and anterior pituitary. It is stimulated by ACTH from the anterior pituitary and by stress.

Cortisol secretion shows marked circadian variation peaking between 4 a.m. and 8 a.m. and being lowest between midnight and 3 a.m. When the sleeping waking pattern is changed, e.g. night shift working, it takes several days for ACTH/cortisol secretion to readjust. Glucocorticoid secretion increases in response to stress, including infection and surgery.

Glucocorticoids have widespread metabolic effects generally concerned with catabolism (breakdown) of protein and fat that makes glucose and other substances available for use. These include:

1. Hyperglycaemia (raised blood glucose levels) caused by breakdown of glycogen and gluconeogenesis (formation of new sugar from, for example, protein)
2. Lipolysis (breakdown of triglycerides into fatty acids and glycerol for energy production) raising circulating levels of free fatty acids
3. Stimulating breakdown of protein, releasing amino acids, and increasing blood levels. Amino acids are then used for synthesis of other proteins, e.g. Enzymes, or for energy production.
4. Promoting absorption of sodium and water from renal tubules (a weak mineralocorticoid effect).

In pathological and pharmacological quantities glucocorticoids also have other effects including:

- a) Anti-inflammatory actions
- b) Suppression of immune responses
- c) Delayed wound healing.

When corticosteroids are administered in the treatment of common disorders, e.g. asthma, the high circulating levels exert a negative feedback effect on the hypothalamus and pituitary and can completely suppress natural secretion of CRH and ACTH respectively.

## **2. Mineralocorticoids (aldosterone)**

Aldosterone is the main mineralocorticoid. It is involved in maintaining water and electrolyte balance. Through a negative feedback system it stimulates the reabsorption of sodium ( $\text{Na}^+$ ) by the renal tubules and excretion of potassium ( $\text{K}^+$ ) in the urine. Sodium reabsorption is also accompanied by retention of water and therefore aldosterone is involved in the regulation of blood volume and blood pressure too.

Blood potassium levels regulate aldosterone secretion by the adrenal cortex. When blood potassium levels rise, more aldosterone is secreted. Low blood potassium has the opposite

effect. Angiotensin also stimulates the release of aldosterone.

**Renin–angiotensin–aldosterone system:** When renal blood flow is reduced or blood sodium levels fall, the enzyme renin is secreted by kidney cells. Renin converts the plasma protein angiotensinogen, produced by the liver, to angiotensin 1. Angiotensin converting enzyme (ACE), formed in small quantities in the lungs, proximal kidney tubules and other tissues, converts angiotensin 1 to angiotensin 2, which stimulates secretion of aldosterone. Angiotensin 2 causes vasoconstriction and increases blood pressure closing the negative feedback loop.

## **Sex hormones**

Sex hormones secreted by the adrenal cortex are mainly androgens (male sex hormones) although the amounts produced are insignificant compared with those secreted by the testes and ovaries in late puberty and adulthood.

## **Adrenal medulla**

The medulla is completely surrounded by the adrenal cortex. It develops from nervous tissue in the embryo and is part of the sympathetic nervous system. When stimulated by extensive sympathetic nerve supply, the glands release the hormones adrenaline (epinephrine, 80%) and noradrenaline (norepinephrine, 20%).

## **Adrenaline (epinephrine) and noradrenaline (norepinephrine)**

Noradrenaline is the postganglionic neurotransmitter of the sympathetic division of the autonomic nervous system. Adrenaline and some noradrenaline are released into the blood from the adrenal medulla during stimulation of the sympathetic nervous system. The action of these hormones prolongs and augments stimulation of the sympathetic nervous system. Structurally they are very similar, which explains their similar effects. Together they potentiate the fight or flight response by:

- a) Increasing heart rate
- b) Increasing blood pressure

Diverting blood to essential organs, including the heart, brain and skeletal muscles, by dilating their blood vessels and constricting those of less essential organs, such as the skin

- a) Increasing metabolic rate
- b) Dilating the pupils.

Adrenaline has a greater effect on the heart and metabolic processes whereas noradrenaline has



more influence on blood vessel diameter.

When the body is under stress homeostasis is disturbed. To restore it and, in some cases, to maintain life there are immediate and, if necessary, longer-term responses. Stressors include exercise, fasting, fright, temperature changes, infection, disease and emotional situations. The immediate response is sometimes described as preparing for 'fight or flight'. This is mediated by the sympathetic nervous system.

In the longer term, ACTH from the anterior pituitary stimulates the release of glucocorticoids and mineralocorticoids from the adrenal cortex providing a more prolonged response to stress.

## **Pancreatic islets**

The pancreas is a pale grey gland weighing about 60 grams. It is about 12–15 cm long and is situated in the epigastric and left hypochondriac regions of the abdominal cavity. It consists of a broad head, a body and a narrow tail. The head lies in the curve of the duodenum, the body behind the stomach and the tail lies in front of the left kidney and just reaches the spleen. The abdominal aorta and the inferior vena cava lie behind the gland.

The pancreas is both an exocrine and endocrine gland.

## **The exocrine pancreas**

This consists of a large number of lobules made up of small acini, the walls of which consist of secretory cells. Each lobule is drained by a tiny duct and these unite eventually to form the pancreatic duct, which extends along the whole length of the gland and opens into the duodenum. Just before entering the duodenum the pancreatic duct joins the common bile duct to form the hepatopancreatic ampulla. The duodenal opening of the ampulla is controlled by the hepatopancreatic sphincter (of Oddi) at the duodenal papilla.

The function of the exocrine pancreas is to produce pancreatic juice containing enzymes, some in the form of inactive precursors that digest carbohydrates, proteins and fats. As in the alimentary tract, parasympathetic stimulation increases the secretion of pancreatic juice and sympathetic stimulation depresses it.

## **The endocrine pancreas**

Distributed throughout the gland are groups of specialised cells called the pancreatic islets (of Langerhans). The islets have no ducts so the hormones diffuse directly into the blood. The endocrine pancreas secretes the hormones insulin and glucagon, which are principally concerned with control of blood glucose levels.

1.  $\alpha$  (alpha) cells, which secrete glucagon

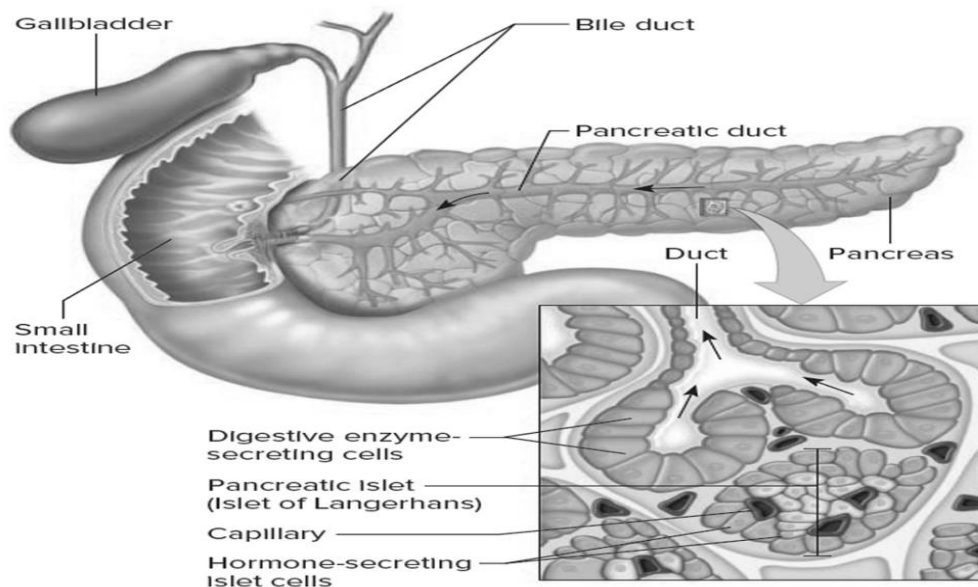


2.  $\beta$  (beta) cells, which are the most numerous, secrete insulin
3.  $\delta$  (delta) cells, which secrete somatostatin (GHRIH)

The normal blood glucose level is between 3.5 and 8 mmol/litre (63 to 144 mg/100 mL).

Blood glucose levels are controlled mainly by the opposing actions of insulin and glucagon:

1. Glucagon increases blood glucose levels
2. Insulin reduces blood glucose levels.



*Structure of pancreas*

## Insulin

Insulin is a polypeptide consisting of about 50 amino acids. Its main function is to lower raised blood nutrient levels, not only glucose but also amino acids and fatty acids. These effects are described as anabolic, i.e. they promote storage of nutrients. When nutrients, especially glucose, are in excess of immediate needs insulin promotes their storage by:

1. Acting on cell membranes and stimulating uptake and use of glucose by muscle and connective tissue cells
2. Increasing conversion of glucose to glycogen (glycogenesis), especially in the liver and skeletal muscles
3. Accelerating uptake of amino acids by cells, and the synthesis of protein
4. Promoting synthesis of fatty acids and storage of fat in adipose tissue (lipogenesis)
5. Decreasing glycogenolysis (breakdown of glycogen into glucose)
6. Preventing the breakdown of protein and fat, and gluconeogenesis (formation of new sugar from, e.g., protein).

Secretion of insulin is stimulated by increased blood glucose levels, for example after eating a meal, and to a lesser extent by parasympathetic stimulation, raised blood amino acid and fatty

acid levels, and gastrointestinal hormones, e.g. gastrin, secretin and cholecystokinin.

Secretion is decreased by sympathetic stimulation, glucagon, adrenaline, cortisol and somatostatin (GHRH), which is secreted by the hypothalamus and pancreatic islets.

## Glucagon

Glucagon increases blood glucose levels by stimulating:

1. Conversion of glycogen to glucose in the liver and skeletal muscles (glycogenolysis)
2. Gluconeogenesis.

Secretion of glucagon is stimulated by low blood glucose levels and exercise, and decreased by somatostatin and insulin.

## Somatostatin (GHRH)

This hormone, also produced by the hypothalamus, inhibits the secretion of both insulin and glucagon in addition to inhibiting the secretion of GH from the anterior pituitary.

## Gonads

The female reproductive organ especially the ovaries secretes estrogen, progesterone, relaxin, inhibit.

The male reproductive organ especially the testes secretes testosterone and inhibit.

## Pineal gland

The pineal gland is a small body attached to the roof of the third ventricle and is connected to it by a short stalk containing nerves, many of which terminate in the hypothalamus. The pineal gland is about 10 mm long, reddish brown in colour and surrounded by a capsule.

The gland tends to atrophy after puberty and may become calcified in later life.

## Functions

For as long as the pineal gland has been known to exist, myriad functions have been ascribed to it, including its

- Being the seat of the soul
- Enhancing sex
- Staving off infection
- Promoting sleep
- Enhancing mood
- Increasing longevity (as much as 10 to 25 per cent).

It is known from comparative anatomy that the pineal gland is a vestigial remnant of what was a

third eye located high in the back of the head in some lower animals. Many physiologists have been content with the idea that this gland is a nonfunctional remnant, but others have claimed for many years that it plays important roles in the control of sexual activities and reproduction, functions that still others said were nothing more than the fanciful imaginings of physiologists preoccupied with sexual delusions.

## **Melatonin**

This is the main hormone secreted by the pineal gland. Secretion is controlled by daylight and darkness; levels fluctuate during each 24-hour period, the being highest at night and the lowest around midday. Secretion is also influenced by the number of daylight hours, i.e. there may be seasonal variations. Although its functions are not fully understood, melatonin is believed to be associated with:

1. Coordination of the circadian and diurnal rhythms of many tissues, possibly by influencing the hypothalamus
2. Inhibition of growth and development of the sex organs before puberty, possibly by preventing synthesis or release of gonadotropin.

The pineal gland is controlled by the amount of light or “time pattern” of light seen by the eyes each day. For instance, in the hamster, greater than 13 hours of darkness each day activates the pineal gland, whereas less than that amount of darkness fails to activate it, with a critical balance between activation and nonactivation. The nervous pathway involves the passage of light signals from the eyes to the suprachiasmatic nucleus of the hypothalamus and then to the pineal gland, activating pineal secretion.

Second, the pineal gland secretes melatonin and several other, similar substances. Either melatonin or one of the other substances is believed to pass either by way of the blood or through the fluid of the third ventricle to the anterior pituitary gland to decrease gonadotropic hormone secretion. Thus, in the presence of pineal gland secretion, gonadotropic hormone secretion is suppressed in some species of animals, and the gonads become inhibited and even partly involuted. This is what presumably occurs during the early winter months when there is increasing darkness. But after about 4 months of dysfunction, gonadotropic hormone secretion breaks through the inhibitory effect of the pineal gland and the gonads become functional once more, ready for a full springtime of activity.

**Questions Bank**

1. What do you mean by endocrine gland? Name endocrine glands locate in human body.
2. Why pituitary gland is called master gland?
3. Name the hormones from pituitary gland and mention their functions.
4. Give structure and functions of thyroid gland?
5. Write thyroid hormones and its production and regulation process.
6. Name the hormones from adrenal gland and mention their functions.
7. Write the functions of insulin, glucagon and, somatostatin?
8. Write the function of pineal gland.

