CHAPTER 6

The Endocrine System

CHAPTER OUTLINE

STUDY OBJECTIVES

- ✓ To discuss the different types of glands in the body.
- ✓ To define hormones and describe the mechanism of hormone action.
- ✓ To describe the structure of the hypothalamus and pituitary glands and discuss the various hormones secreted by the hypothalamus and the anterior pituitary and posterior pituitary glands.
- ✓ To describe the anatomical structure and function of various hormones secreted by the pineal, thyroid and parathyroid glands.
- ✓ To describe the anatomical structure of adrenal gland and discuss the various hormones secreted from the adrenal cortex and the adrenal medulla.
- ✓ To describe the anatomical structure and function of various hormones secreted by pancreas, gonads and the gastrointestinal system.

INTRODUCTION

Endocrine system (Greek word: *endon*: within, *krinien*: to separate) works in coordination with the nervous system to maintain homeostasis and to perform the basic functions of internal communication and regulation of all body systems. However, there are some basic differences between the two controlling systems. The nervous system stimulation provides immediate response to the stimuli by transmitting nerve impulses, whereas the endocrine system releases mediator molecules called *hormones* (Greek word: *hormaein*: to excite), and their response is usually slow but more prolonged.

To summarize, the nervous and endocrine systems share a unique partnership to coordinate the body functions. Therefore, the two systems are often collectively called the *neuroendocrine* system. This chapter mainly emphasizes the endocrine system, the various major endocrine glands and their role in coordinating body activities. The study of endocrine glands and the role of their secretions is called *endocrinology*.

The body contains the following two types of glands (Fig. 6.1):

1. **Exocrine glands**
   - These glands secrete their products into ducts that carry these secretions into body cavities, into lumen of an organ or to the outer surface of the body.
   - Exocrine glands include sebaceous (oil), sweat, salivary and gastric glands.

DO YOU KNOW

- The endocrine system produces almost 30 hormones in our body.
- The hormone melatonin controls the sleep cycle of our body and is produced by the pineal gland.
- The hypothalamus gland in our body triggers the sense of thirst and hunger.
- The thyroid gland is responsible for activities such as overactivity or sluggishness of an individual.
- The endocrine system significantly influences the behaviour and the characteristics of a person.

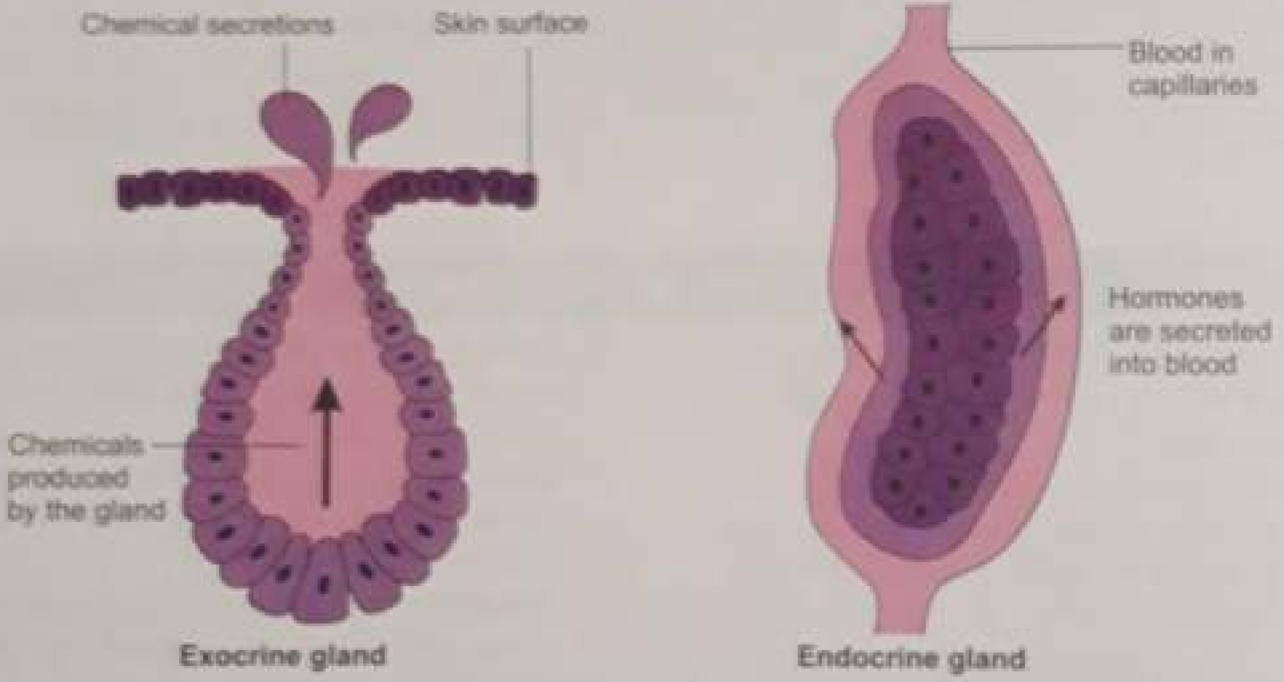

Figure 6.1 Exocrine and endocrine glands.

Medical Terminology

- **Antidiuretic**: It is a drug that limits the formation of urine.
- **Circadian rhythm**: It is the 'internal body clock' that regulates the (roughly) 24-hour cycle of biological processes.
- **Corpus luteum**: It is a yellow body that forms in the ovary on the site where an egg has been released and that produces progesterone to facilitate a pregnancy.
- **Glands**: It is a cell, a tissue or an organ that secretes certain chemical compounds useful for our body.
- **Homeostasis**: It is the body's ability to physiologically regulate its inner environment to ensure its stability in response to fluctuations in the outside environment and the weather.

2. **Endocrine glands or ductless glands**
   - These glands lack ducts and therefore secrete their products directly into the bloodstream. The blood circulatory system then carries these products to the target organs.
   - The secretions of these glands are known as *hormones*, and these are secreted in response to changes in the external or internal environment.
   - Endocrine glands include the pituitary, thyroid, parathyroid, adrenal and pineal glands.

Although there are many endocrine glands located throughout the body, only major endocrine glands are discussed in this chapter.

Figure 6.2 shows the location of major endocrine glands.

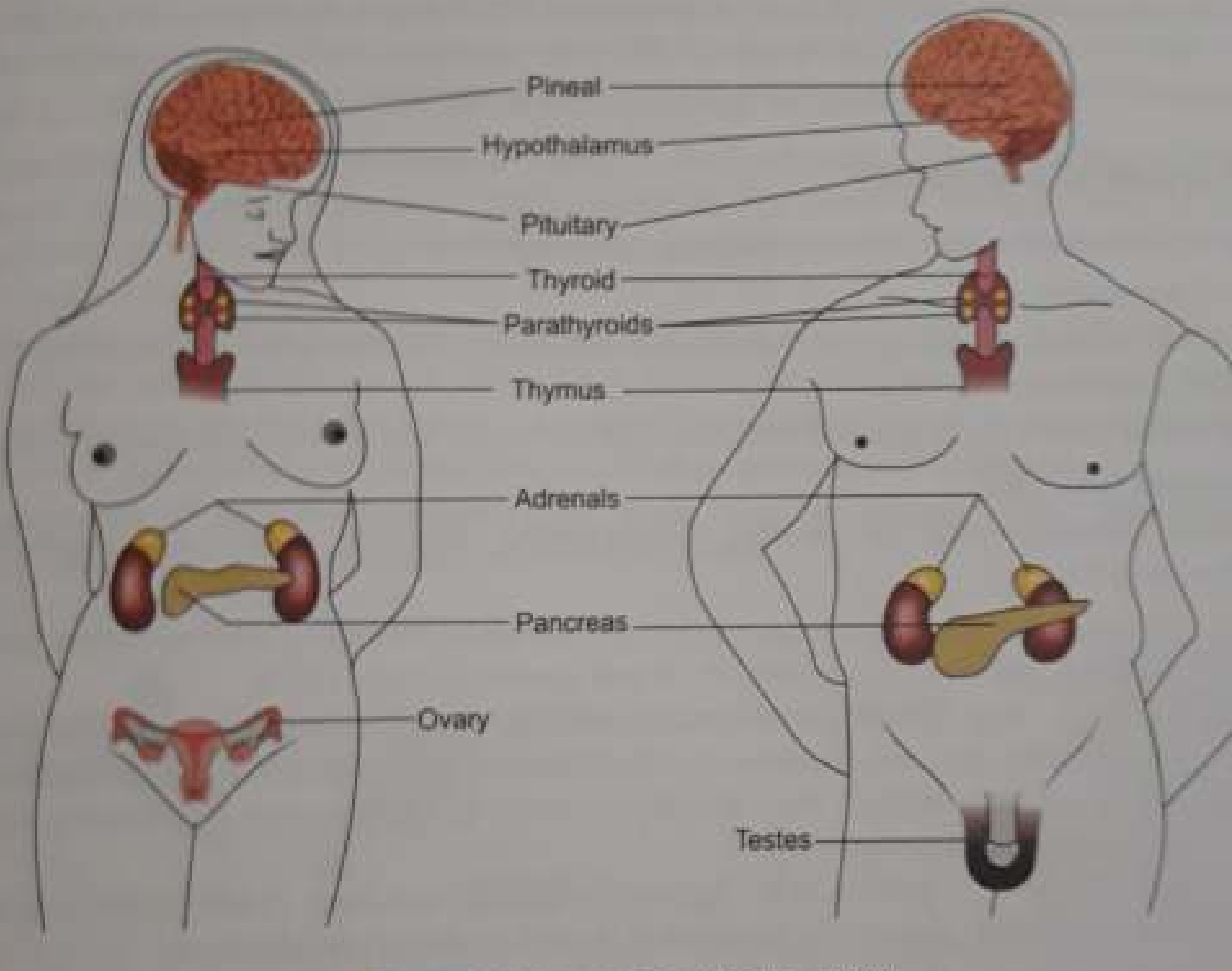

Figure 6.2 The major endocrine glands.

Medical Terminology

- **Nerve impulse**: It is the electrical discharge that travels along a nerve fibre.
- **Osmoreceptors**: It is a specialized nerve cell responsible for monitoring the osmotic pressure of the blood and extracellular fluid.
- **Ovulation**: It is the process in a female's menstrual cycle by which a mature ovarian follicle ruptures and discharges an ovum.
- **Receptors**: It is a structure on the surface of a cell (or inside a cell) that selectively receives and binds a specific substance.

HORMONES

Hormones are the chemical messengers secreted by endocrine glands that regulate the physiological processes in the body.

The first hormone was discovered in 1903 by two physiologists: William M. Bayliss and Ernest H. Starling. The term *hormone* was coined by Starling in 1905.

The hormones secreted by the endocrine gland travel throughout the body, but they affect only the *target cells* because only the target cells for a given hormone have receptors that bind and recognize that hormone. The nontarget cells lack these receptors and therefore they do not respond to the circulating hormones.

The hormone binds to the receptor on the target cell and changes the shape of the receptor. The receptor's new shape sets up certain changes in the cell—such as alteration in permeability, enzyme activity or gene transcription—which results in physiological responses in the target cells.

Classification of hormones

The hormones can be classified into the following two categories:

1. **Steroid hormones**
   - These hormones are derived from cholesterol and include the hormones from the adrenal cortex, testes, ovaries and placenta.
   - Examples include oestrogen, aldosterone, hydrocortisone, testosterone and progesterone.
2. **Nonsteroid hormones**
   - These hormones may be proteins (polypeptides), peptides, amino acid derivatives or glycoproteins.
     (a) *Proteins*: They include adrenocorticotropic hormone (ACTH), calcitonin, insulin, glucagon, prolactin, parathyroid hormone (PTH) and growth hormone (GH).
     (b) *Peptides*: They include gonadotropin-releasing hormone, thyrotropin-releasing hormone, somatostatin, oxytocin, melanocyte-stimulating hormone and antidiuretic hormone.
     (c) *Amino acid derivatives*: They include epinephrine, norepinephrine, melatonin, thyroxine (T_4) and triiodothyronine (T_3).
     (d) *Glycoproteins*: They include thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and chorionic gonadotropin.

In addition to the above classification, the hormones can also be classified into two groups according to the distance between the site of production and target site:

Circulating hormones: Hormones that are secreted into the blood and act on distant target cells are called *circulating hormones*.

Local hormones: These hormones act locally without first entering the bloodstream. Among local hormones are those that act on neighbouring cells, called *paracrines* (*para*: near), and those that act on the same cell that secreted them, are termed *autocrines* (*auto*: self).

Mechanism of hormone action

The mechanism of hormonal action differs in different categories of hormones. For example, catecholamines (adrenaline and noradrenaline) and pancreatic (protein) hormones are lipid insoluble and thus cannot diffuse through the lipid bilayer of the plasma membrane. On the other hand, steroid hormones and thyroid hormones are lipid soluble and thus readily pass through the plasma membrane of target cells to enter the cytoplasm.

Thus, the molecular mechanism of hormone action can be described by the following two ways.

1. Mode of hormone action through extracellular receptors

The lipid-insoluble hormones such as catecholamines and pancreatic hormones cannot enter the target cell, and therefore they bind to the specific receptor molecules present on the surface of the cell membrane. In this case, the hormone acts as the first messenger and causes the production of a second messenger inside the cell, where specific responses takes place. The examples of second messenger are cyclic adenosine monophosphate (cAMP), inositol triphosphate (IP_3), diacyl glycerol (DAG), calcium ions (Ca^+) and cyclic guanosine monophosphate (cGMP) (Fig. 6.3a).

The various steps of the mechanism of hormonal action are as follows:

1. **Formation of the hormone–receptor complex**: The lipid-insoluble hormone binds to the receptor present at the surface of the target cell's membrane. The hormone–receptor complex activates a membrane protein called a *G protein* that causes the releases of an enzyme *adenylate cyclase* from the receptor site.
2. **Formation of second messenger**: Adenylate cyclase converts ATP into cAMP, which activates the protein kinases present in the cell. [Protein kinases are the enzymes that phosphorylates (adds a phosphate group) the other cellular proteins.] The activated protein kinases phosphorylate the cellular proteins and trigger the reactions that produce physiological responses.
3. **Inactivation of second messenger**: After some time, an enzyme called *phosphodiesterase* inactivates cAMP, resulting in the inhibition of response.

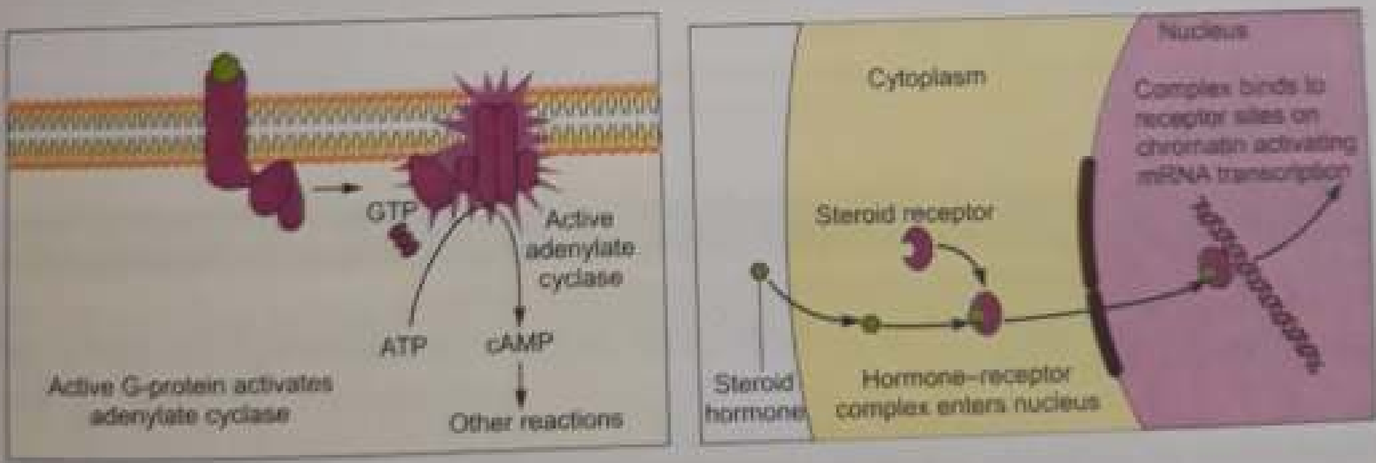

Figure 6.3 Hormone action by (a) extracellular and (b) intracellular receptors.

Hormones that bind to the plasma membrane receptors can induce their effects at very low concentration as they initiate a cascade of chain reaction.

For example: Binding of a single epinephrine molecule to the receptor activates hundreds of G proteins, each of which activates an adenylate cyclase molecule. Each adenylate cyclase produces around 1000 cAMP, and each cAMP may act on thousands of substrate molecules. Thus, the response is the result of the amplification of signal.

- **Synergistic effect**: When the effect of two hormones acting together is greater or extensive than the effect of each hormone acting alone, the two hormones are said to have the synergistic effect.
- **Antagonistic effect**: When one hormone opposes the actions of the other hormone, the two hormones are said to have the antagonistic effect.

2. Mode of hormone action through extracellular receptors

The lipid-soluble hormones, such as steroid hormone and thyroid hormone, bind to receptors within target cells (Fig. 6.3b).

Their mechanism of action is as follows:

1. The lipid-soluble hormone diffuses through the cell membrane and binds to the receptor located in the cytoplasm or nucleus.
2. The receptor–hormone complex then alters gene expression by activating certain genes.
3. The activated genes transcribe the mRNA, which directs the synthesis of a new protein (often an enzyme) on the ribosomes.
4. The new protein promotes the metabolic reactions in the cell and alters the cell activity.

HYPOTHALAMUS

ANATOMICAL STRUCTURE

The hypothalamus is a small part of the diencephalon and is composed of a number of groups of nerve cells. It is situated below and in front of the thalamus and immediately above the pituitary gland and serves as the major link between the nervous system and the endocrine system. For more details, see Chapter 5.

HORMONES

Hypothalamus is connected to the pituitary gland through a funnel-shaped stalk called the *infundibulum* (also called as *pituitary stalk*) through which it sends neural and chemical signals to the pituitary gland. Hence, it controls the secretion of hormones from the pituitary gland.

The influence of the hypothalamus on the release of hormones is different in the anterior and posterior lobes of the pituitary gland.

Regulation of anterior pituitary hormones

The hypothalamus contains some specialized nerve cells called *neurosecretory cells* that synthesize and secrete certain releasing and inhibitory hormones. These hormones are immediately taken into a complex network of blood vessels that form the hypophyseal portal system, which transports these hormones from the hypothalamus into the infundibulum and then directly to the anterior pituitary.

These releasing and inhibitory hormones either stimulate or inhibit the release of a particular hormone from the anterior pituitary gland.

The releasing and inhibitory hormones secreted by the hypothalamus are summarized in Table 6.1.

Table 6.1 Hypothalamic hormones

Hypothalamic hormones	Functions
Thyrotropin-releasing hormone (TRH)	Triggers the release of thyroid-stimulating hormone (TSH) or thyrotropin from anterior pituitary
Prolactin-releasing hormone (PRH)	Triggers the release of prolactin from the anterior pituitary
Prolactin-inhibiting hormone (PIH)	Inhibits the release of prolactin from the anterior pituitary
Growth hormone–releasing hormone (GHRH)	Triggers the release of growth hormone (GH) from the anterior pituitary
Somatostatin /Growth hormone–inhibiting hormone (SS/GHIH)	Inhibits the release of GH from anterior pituitary
Gonadotropin-releasing hormone (GnRH)	Triggers the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary
Corticotropin-releasing hormone (CRH)	Triggers the release of adrenocorticotropic hormone (ACTH) or adrenocorticotropin from the anterior pituitary

Regulation of posterior pituitary hormones

The hormones secreted by the posterior lobe of the pituitary gland are actually synthesized by specialized neurons of the hypothalamus. These hormones are transported to the posterior pituitary through the nerve fibres of the hypothalamohypophyseal tract by means of axonic flow and then stored in the vesicles within the axon terminals in the posterior pituitary.

Nerve impulses from the hypothalamus trigger their release from the posterior pituitary by exocytosis.

To summarize, the hypothalamus is linked to the posterior lobe of the pituitary gland by nerve fibres and to the anterior lobe by a complex system of blood vessels. This hypothalamic-pituitary system plays an important role in homeostasis as it regulates the activities of most of the other endocrine glands (Fig. 6.4).

PITUITARY GLAND

The pituitary gland, or hypophysis, was initially called the *master* endocrine gland because it secretes several hormones that control other endocrine glands. However, now, it is clear that the pituitary gland itself is regulated by the hypothalamus.

ANATOMICAL STRUCTURE

The pituitary is a small, pea-shaped gland, about 1.2–1.6 cm in length, located in the depression of the sphenoid bone below the hypothalamus. It is attached to the hypothalamus of the brain through a stalk or infundibulum.

The pituitary gland is divided into the following two lobes:

1. **Anterior lobe or pars anterior**: It is also called *adenohypophysis* (adeno gland).
2. **Posterior lobe or pars nervosa**: It is also referred to as *neurohypophysis*.

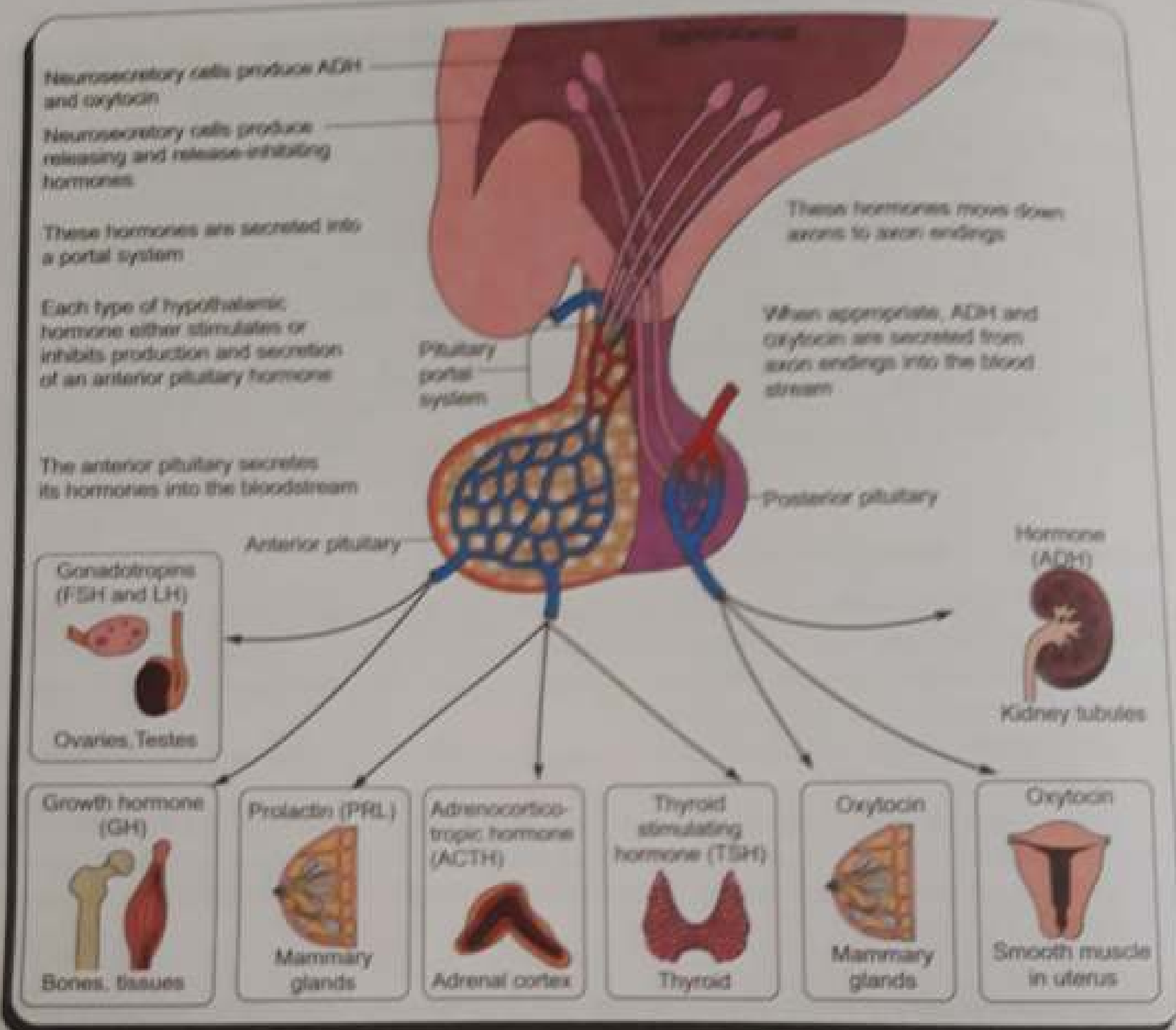

Figure 6.4 Hypothalamic–pituitary system.

(a) Between these two lobes, there is an intermediate lobe that atrophies during human fetal development and does not exist as a separate lobe. Its role in humans is not known.

(b) The anterior pituitary develops as an upwards growth from the pharyngeal epithelium, and the posterior pituitary is the downgrowth of nervous tissue from the brain.

ANTERIOR PITUITARY

Anterior pituitary consists of the following five types of secretory cells that secrete various hormones:

1. **Somatotrophs**: These secretory cells secrete GH or somatotropin (*somato*: body; *tropin*: change).
2. **Thyrotrophs**: These secretory cells secrete TSH or thyrotropin.
3. **Corticotrophs**: These secretory cells secrete ACTH or corticotrophin.

4. **Gonadotrophs**: These secretory cells secrete two hormones: FSH and LH.
5. **Lactotrophs**: These secretory cells secrete prolactin.

Most of the hormones of the anterior pituitary are *tropic hormones* or *tropin* (i.e. the hormones that stimulate other endocrine glands). The FSH and LH are collectively called *gonadotropins* as they specifically regulate the functions of the gonads. Thyrotropin stimulates the thyroid gland and the corticotrophin acts on the cortex of the adrenal gland.

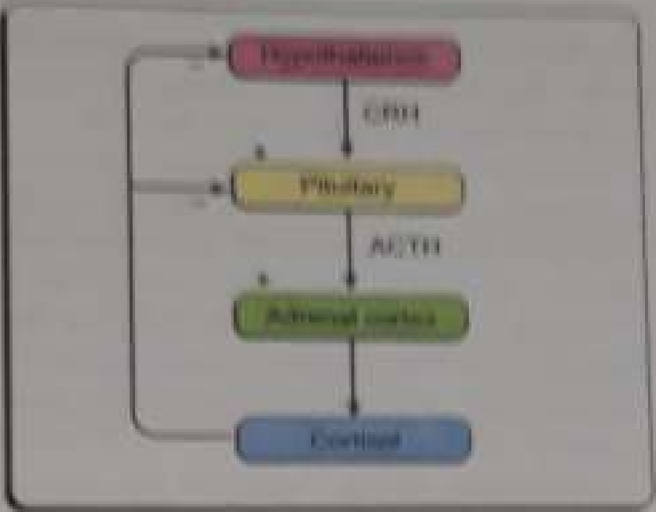

Figure 6.5 Negative feedback system.

Note: Increased cortisol secretion inhibits the hypothalamus and pituitary to secrete CRH and ACTH, respectively.

As discussed previously, the release of anterior pituitary hormones is regulated by the secretion of releasing and inhibitory hormones from the hypothalamus. This whole system is controlled by a *negative feedback system*, that is when the concentration of a particular hormone reaches a certain level in the body, it inhibits the gland to release further hormones, and later when the concentration falls below normal, the inhibition on the gland ceases and it begins to release the hormones again. This system helps regulate the concentration of hormones in our body. Figure 6.5 shows an example of the negative feedback system.

Hormones of anterior pituitary

The anterior pituitary lobe secretes the following hormones:

- Growth hormone (GH)
- Prolactin
- Thyroid-stimulating hormone (TSH)
- Adrenocorticotropic hormone (ACTH)
- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)

Growth hormone (GH)

- It is the most abundant hormone synthesized by anterior pituitary and is responsible for the general growth of the body.
- Body growth in response to GH secretion is evident during childhood and adolescence, and thereafter, secretion of GH maintains the mass of bones and skeletal muscles.
- GH stimulates the liver to secrete small protein hormones called *insulin-like growth factors (IGFs)*, or *somatomedins*, that stimulate the growth of the body by:
  - Stimulating growth and division of most of the body cells, especially of bones and skeletal muscles
  - Increasing protein synthesis by enhancing the uptake of amino acids into cells and increasing transcription and translation

- Promoting mobilization of fats from adipose tissue and accelerating their catabolism, which results in the release of free fatty acids that can be used for ATP production by body cells
- GH also increases blood glucose levels by decreasing glucose uptake, which decreases the use of glucose for ATP production in the cells
- The release of GH is stimulated by growth hormone-releasing hormone (GHRH) and suppressed by growth hormone-inhibiting hormone (GHIH), both of which are secreted by the hypothalamus. The secretion of GH is greater during periods of sleep, exercise and fasting (hypoglycaemia). The secretion is also inhibited by increased levels of GH itself through the negative feedback mechanism.
- The deficiency of GH in children causes stunted growth leading to *dwarfism*, whereas the excessive secretion of GH causes enormous growth of the body leading to *gigantism*. The excessive secretion of GH may also cause *diabetogenic effect* (i.e. condition of diabetes mellitus due to persistent hyperglycaemia).
- **Diabetogenic effect**: Persistent hyperglycaemia due to excessive GH stimulates the pancreas to secrete insulin continually. Such excessive stimulation for prolonged periods may cause *beta cells burnout* (i.e. decreased capacity of beta cells of pancreas to secrete insulin, resulting in the condition of *diabetes mellitus*).

Prolactin

- It is also known as *luteotrophic/lactogenic hormone*.
- It promotes the development of mammary glands during pregnancy and stimulates *lactation* (milk production) after parturition (childbirth).
- The release of prolactin is stimulated by the prolactin-releasing hormone (PRH) from the hypothalamus and the suckling action of a nursing infant. The secretion is lowered by prolactin-inhibiting hormone (PIH, or dopamine) and by an increased blood level of prolactin (negative feedback). In non-nursing mothers and males, PIH secreted by hypothalamus inhibits the production of prolactin hormone.

Thyroid-stimulating hormone (TSH)

- It stimulates and maintains the growth and development of the thyroid gland. It also stimulates the thyroid gland to secrete thyroid hormones—T_4 and T_3.
- The release of TSH is stimulated by thyrotropin-releasing hormone (TRH) from the hypothalamus and is suppressed by increased levels of T_3 and T_4 through the negative feedback mechanism.

Adrenocorticotropic hormone (ACTH)

- ACTH promotes and maintains the growth of the adrenal cortex and stimulates the adrenal cortex to secrete glucocorticoids (mainly cortisol) and mineralocorticoids.
- ACTH secretion is stimulated by corticotrophin-releasing hormone (CRH) produced by the hypothalamus and is suppressed by the negative feedback mechanism when the blood level of ACTH rises.

Follicle-stimulating hormone (FSH)

- In females, FSH stimulates the development of the follicles in the ovaries of females. It also stimulates follicular cells to secrete *oestrogens* (female sex hormones).
- In males, it promotes the development of testes and stimulates spermatogenesis (production of sperms).

- The release of FSH is stimulated by gonadotropin-releasing hormone (GnRH) from the hypothalamus and is suppressed by the negative feedback mechanism by oestrogen (in females) and testosterone (in males).

Luteinizing hormone (LH)

- In females, LH functions as follows:
  - Stimulates ovulation and forms corpus luteum in the ovary. It also stimulates the secretion of progesterone from corpus luteum.
  - FSH and LH together stimulate the secretion of oestrogen by ovarian cells.
- In males, LH is also known as interstitial cell-stimulating hormone (ICSH) because it stimulates the interstitial cells of Leydig in testes to synthesize and secrete the male sex hormone *testosterone*.
- Secretion of LH, similar to that of FSH, is regulated by GnRH from the hypothalamus.

POSTERIOR PITUITARY

Posterior pituitary is formed from nervous tissue and consists primarily of nerve cells surrounded by specialized neuroglial cells called *pituicytes*. These neurons in the posterior pituitary have their cell bodies in the supraoptic and paraventricular nuclei of the hypothalamus, and their axons form the hypothalamo-hypophyseal tract, which begins in the hypothalamus and ends in the posterior pituitary.

Posterior pituitary hormones are synthesized in the nerve cell bodies of the hypothalamus and are transported along the axons to be stored within the axon terminals in the posterior pituitary. Thus, posterior pituitary only stores the hormones and releases them when stimulated by nerve impulses from the hypothalamus.

Hormones of posterior pituitary

The posterior pituitary lobe stores and releases the following two hormones:

- Vasopressin/antidiuretic hormone (VP/ADH)
- Oxytocin (OT)

Vasopressin/antidiuretic hormone (VP/ADH)

- It maintains the body's water balance by promoting increased water reabsorption in the distal convoluted and collecting tubules of the nephrons of the kidneys, resulting in decreased urine output. If secreted in large amounts, VP/ADH leads to constriction of blood vessels and thus increased blood pressure; hence, it is also referred to as *vasopressin*.
- The hypothalamus regulates ADH secretion through osmoreceptors that detect changes in the osmotic pressure of body fluids. Conditions such as decreased extracellular fluid (ECF) volume or high osmotic pressure due to dehydration like in diarrhoea, excessive sweating or haemorrhage stimulate osmoreceptors in the hypothalamus, which further stimulate the posterior pituitary to release ADH to prevent fluid loss from the body.
- Conversely, low osmotic pressure of blood (or increased blood volume) due to excessive fluid intake inhibits ADH release by the negative feedback mechanism.

Oxytocin (OT)

- It causes the contraction of the uterine smooth muscles to facilitate labour at the time of childbirth (parturition). Hence, it is popularly known as *birth hormone*.

- It also causes the initiation of the 'milk ejection reflex' upon suckling by baby and stimulates the contraction of cells in the mammary glands, leading to milk ejection. Hence, it is also called *milk-ejecting hormone*.
- Oxytocin is released in response to the stimulation of uterine stretch receptors because of uterine distension during childbirth and suckling by baby after childbirth.

PINEAL GLAND

ANATOMICAL STRUCTURE

Pineal gland is also called as *pineal body*.

It is a small, pine-shaped gland attached to the roof of the third ventricle and is present between the two cerebral hemispheres of the brain.

HORMONES

The hormone secreted by the pineal gland is *melatonin*.

Melatonin regulates the biological clock of the body and affects our circadian (sleep–wake pattern) rhythm. The secretion of melatonin is controlled by daylight, and its levels fluctuate during each 24-h period, being lesser in bright light (day) and higher in darkness (night). This is because the nerve impulses in the retina of eyes send light information to the pineal gland. In dark or dim light, nerve impulses from the eyes decrease, which causes increased melatonin secretion that results in sleepiness.

It also inhibits growth and development of the sex organs before puberty, possibly by inhibiting the secretion of gonadotropin hormones (FSH and LH) from the anterior pituitary gland.

THYROID GLAND

ANATOMICAL STRUCTURE

The thyroid gland is a highly vascular, large endocrine gland weighing about 20–40 gm in an adult. It is situated in the neck just inferior to the larynx and consists of two lobes, one on either side of the trachea, that are connected in the middle by an isthmus (Fig. 6.6).

The thyroid gland is composed of a large number of thyroid follicles. The wall of each follicle consists primarily of cuboidal epithelial cells called *follicular cells*. The follicular cells produce two hormones: T_4 or *tetraiodothyronine* that contains four atoms of iodine and T_3 or *tri-iodothyronine* that contains three atoms of iodine; *the iodine atoms in these hormones indicate that iodine is essential for the formation of thyroid hormones*.

Between the follicles, there are other cells called *parafollicular cells* or *C cells*, which secrete the hormone *calcitonin*.

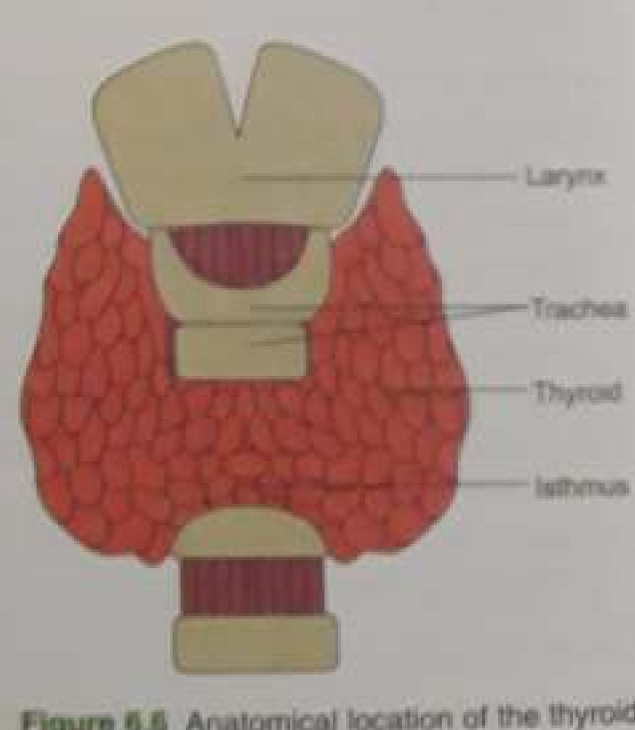

Figure 6.6 Anatomical location of the thyroid gland.

HORMONES

The thyroid gland secretes three hormones: T_3, T_4 and *calcitonin*.

T_4 and T_3

T_4 and T_3 exert their effects throughout the body as most of the body cells have receptors for thyroid hormones. The various actions of thyroid gland include the following:

1. Thyroid hormones increase the basal metabolic rate (BMR) by stimulating the production and oxidation of ATP. When the basal metabolic rate increases, the metabolism of carbohydrates, fats and proteins is also stimulated.
2. Increased BMR and cellular metabolic processes increases the heat production in the body and leads to rise in body temperature. This phenomenon is called as the *calorigenic effect*. In this way, thyroid hormones play an important role in the maintenance of normal body temperature.
3. Thyroid hormones are necessary for normal body growth and development, especially the growth of the nervous system and the skeletal system. They accelerate growth by increasing the use of carbohydrates and lipids for ATP production and by stimulating protein synthesis. Deficiency of thyroid hormones during fetal development, infancy or childhood causes severe mental retardation and stunted bone growth.

The secretion of thyroid hormones is controlled by the anterior pituitary through the feedback mechanism. Anterior pituitary secretes thyroid-stimulating hormone (TSH) under the influence of thyrotropin-releasing hormone (TRH) from the hypothalamus. TSH stimulates thyroid to release the thyroid hormones in conditions of stress, malnutrition, cold, pregnancy, high altitude and low thyroid hormone levels. Conversely, TSH and TRH secretions are inhibited in response to high thyroid hormone levels by the negative feedback mechanism.

Calcitonin

Calcitonin controls the calcium and phosphorus balance and lowers the concentration of calcium and phosphorus in the blood by:

1. Inhibiting bone resorption (breakdown of the bone extracellular matrix) by osteoclasts and facilitating the deposition of calcium and phosphorus in bones
2. Increasing the excretion of calcium and phosphorus by the kidneys

It acts antagonistically to parathormone (PTH), the hormone released by the parathyroid gland.

Release of calcitonin is stimulated by an increase in the blood calcium level and vice versa.

PARATHYROID GLANDS

ANATOMICAL STRUCTURE

Parathyroids are small, round and flattened glands present on the posterior surface of the thyroid gland. These are usually four in number, two in each lobe of the thyroid (Fig. 6.7).

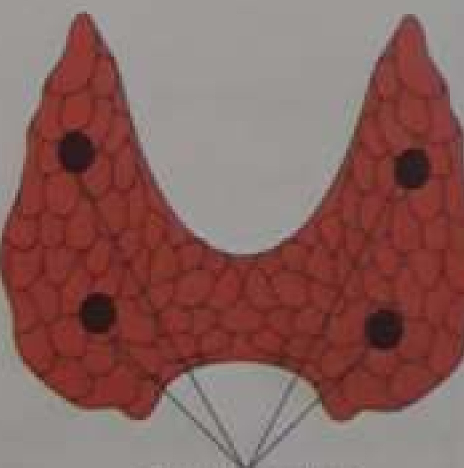

Figure 6.7 Anatomical location of parathyroid glands.

At the cellular level, parathyroid glands contain two kinds of epithelial cells: chief cells and oxyphil cells. The chief cells secrete parathormone (PTH), whereas the function of oxyphil cells is not known.

HORMONES

The parathyroid glands secrete *PTH*.

The primary action of PTH is to increase the calcium levels in the blood (*Fig. 6.8*). This is achieved as follows:

1. It increases the number and activity of osteoclasts and thus elevates bone resorption that releases calcium and phosphate ions into the blood.
2. It enhances active reabsorption of calcium and magnesium from kidneys.
3. It also increases the excretion of phosphate ions in the urine and thus lowers the blood phosphate levels.
4. It promotes formation of calcitriol (active form of vitamin D) in the kidneys, which increases the rate of absorption of calcium and phosphate ions from the gastrointestinal tract into the blood.

The secretion of PTH is regulated directly by the calcium levels in the blood. Decrease in the blood calcium level stimulates the secretion of PTH and vice versa.

PTH and calcitonin act in a complementary manner to maintain blood calcium levels within a narrow range. This maintenance of blood calcium levels is very essential for muscle contraction, blood clotting and transmission of nerve impulse.

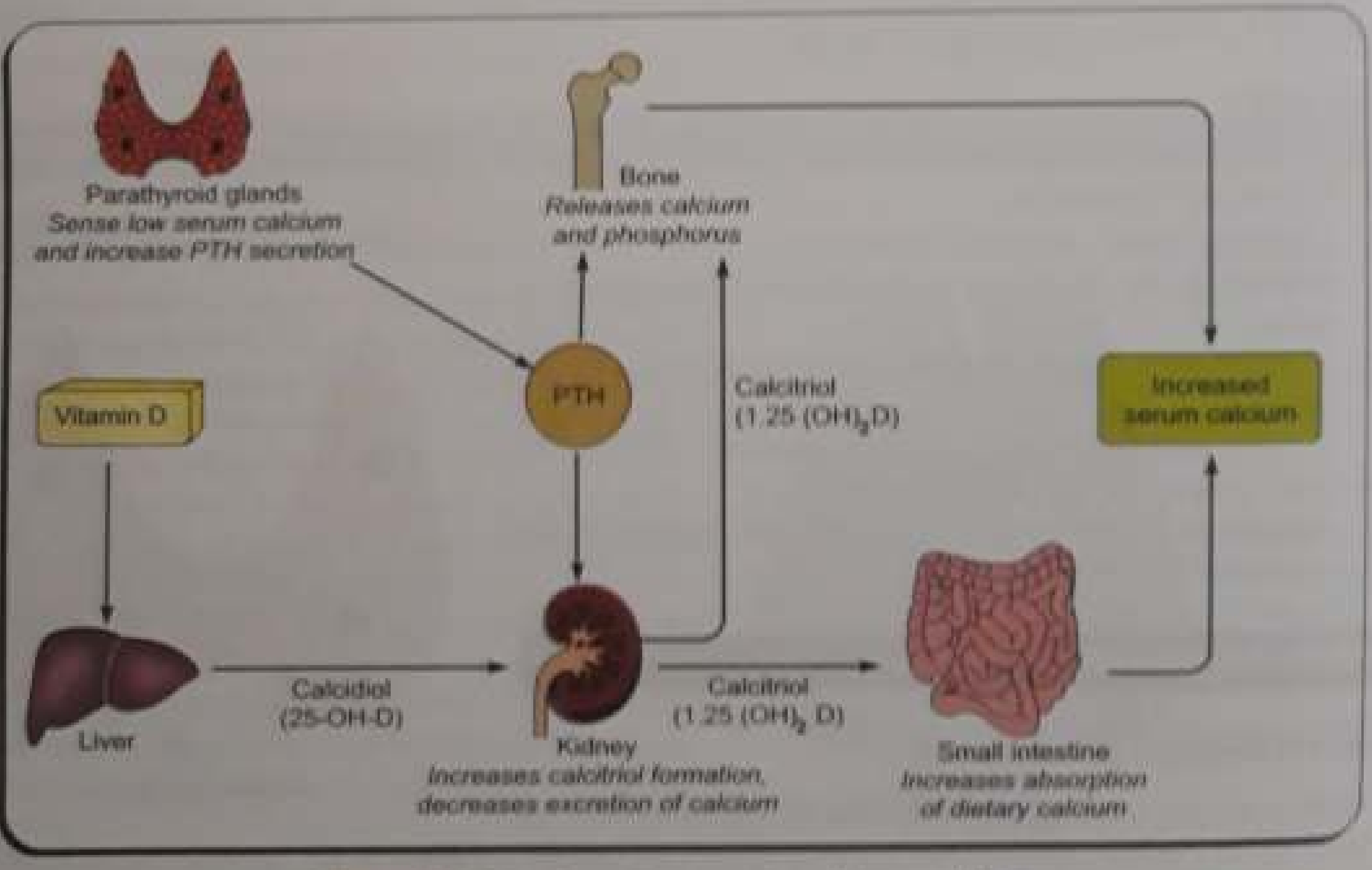

Figure 6.8 Role of parathormone in calcium regulation.

ADRENAL GLANDS

ANATOMICAL STRUCTURE

Adrenal glands are also known as the suprarenal glands. There are two adrenal glands situated on the upper pole (top) of each kidney.

Each gland is made of two parts: *adrenal cortex*—the outer part—and *adrenal medulla*—the inner part. These two parts are structurally and functionally different from each other (Fig. 6.9).

ADRENAL CORTEX

The adrenal cortex is subdivided into three zones: *zona glomerulosa*—the outer zone, *zona fasciculata*—the middle zone and *zona reticulata*—the inner zone.

Each of these zones secretes different hormones: the outer zone, the zona glomerulosa, secretes hormones called mineralocorticoids; the middle zone, the zona fasciculata, secretes mainly glucocorticoids; and the inner zone, the zona reticulata, secretes mainly gonadocorticoids (sex hormones).

The adrenal cortex is essential for life. The damage or destruction of the adrenal cortex may lead to death due to electrolyte imbalances and dehydration.

Hormones of the adrenal cortex

The hormones of the adrenal cortex are collectively known as *adrenocortical hormones* or *corticosteroids*. All adrenocortical hormones are steroid in nature and are synthesized mainly from the cholesterol.

The adrenocortical hormones include *mineralocorticoids*, *glucocorticoids* and *gonadocorticoids* (sex hormones).

Mineralocorticoids

The major mineralocorticoid is *aldosterone*, and it is very essential for life. Thus, it is usually called *life-saving hormone*.

The major function of aldosterone involves regulation of the water and electrolyte balance and blood volume in the body. It regulates this balance by increasing the reabsorption of sodium and water from renal tubules to reduce their loss from the body. It also stimulates the kidneys to increase the secretion of K^+ and H^+ into the urine.

The increased water reabsorption by kidneys causes persistent increase in blood volume, which finally leads to increase in blood pressure.

The secretion of aldosterone from the adrenal cortex is regulated by the following factors:

1. **The blood potassium level**: The increase in the blood potassium level increases the aldosterone secretion and vice versa.
2. **The renin–angiotensin–aldosterone system (RAAS)**
   - The decrease in the sodium ion concentration or blood volume stimulates the *juxtaglomerular cells* in the kidneys to secrete *renin*.
   - Renin converts *angiotensinogen*, produced by the liver, to *angiotensin I*, which is further converted to *angiotensin II* by *angiotensin-converting enzyme (ACE)*.
   - Angiotensin II stimulates the adrenal cortex to secrete aldosterone. It also causes vasoconstriction and increases the blood pressure. (For more details, see chapter The Urinary System.)

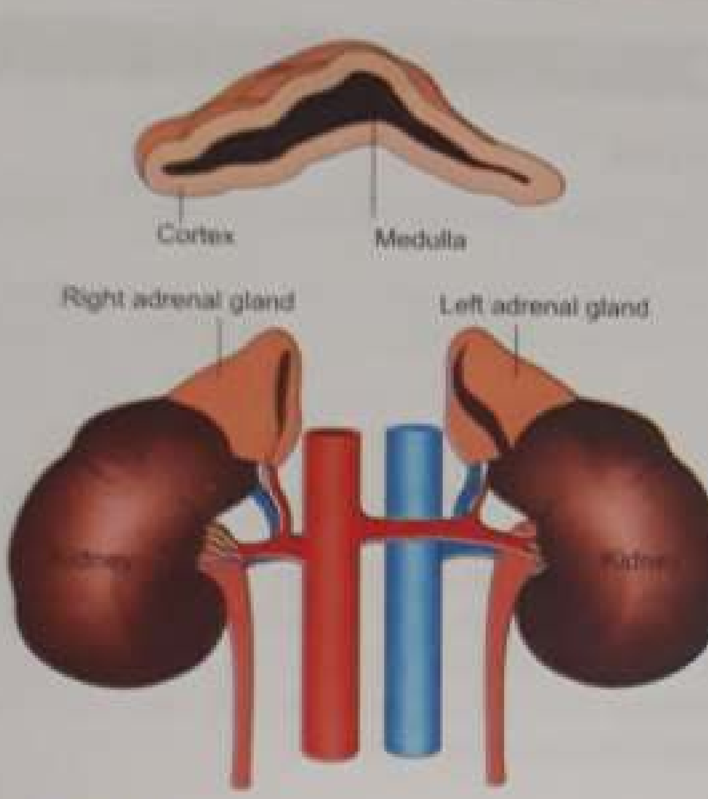

Figure 6.9 Anatomical location of adrenal glands.

Glucocorticoids

Glucocorticoids include cortisol (or hydrocortisone), corticosterone and cortisone. The major and most abundant of them is *cortisol*, which is usually referred to as *life-protecting hormone*. They are very essential for life as they regulate the metabolism of carbohydrates, proteins and fats and also help withstand stress and trauma.

The various effects of glucocorticoids include the following:

1. **Glucose formation**: The glucocorticoids increase the blood glucose level by promoting gluconeogenesis in the liver from amino acids and by inhibiting glucose uptake and utilization by peripheral cells.
2. **Metabolism of proteins and lipids**: The glucocorticoids stimulate the breakdown of proteins and lipids to release amino acids and fatty acids, respectively, into the bloodstream. The amino acids can be used by body cells to synthesize new proteins (e.g. enzymes). Both amino acids and fatty acids may also be taken up by tissues for ATP production as a quick source of energy.
3. **Resistance to stress**: The glucocorticoids provide resistance to stress in many ways: the fatty acids released from cells and glucose in liver cells serve as a quick source of energy during stressful conditions such as exercise, fasting, infection, trauma and disease. In case of excessive bleeding, glucocorticoids constrict blood vessels to counterbalance the drop in blood pressure due to blood loss.
4. **Anti-inflammatory effects**: Glucocorticoids prevent the inflammatory changes in the cells caused by injury or infection. They inhibit the migration of leukocytes (white blood cells) to the affected area and prevent the rush of blood to the injured area by causing vasoconstriction. By these effects, glucocorticoids also retard tissue repair and slow down wound healing.

5. **Immunosuppressive effects**: Glucocorticoids suppress the immune system of the body by decreasing the number of T-lymphocytes. Thus, they are used to prevent tissue rejection during organ transplantation.

The secretion of glucocorticoids is regulated through the negative feedback mechanism involving the hypothalamus and anterior pituitary. The stressful conditions and the low level of cortisol stimulate the hypothalamus to secrete *CRH*. CRH, in turn, stimulates the secretion of *ACTH* from the anterior pituitary. ACTH flows towards adrenal cortex through blood, where it stimulates glucocorticoid (cortisol) secretion. Conversely, high levels of cortisol inhibit the release of corticotropin-releasing hormone (CRH) from the hypothalamus and ACTH from the anterior pituitary.

Gonadocorticoids (sex hormones)

Most of the gonadocorticoids secreted by the adrenal cortex are male sex hormones (androgens). They are secreted in very small amounts in both males and females, and the major androgen secreted is *dehydroepiandrosterone (DHEA)*. The androgens, in general, are responsible for the development of male sexual characteristics, but the amount of androgens secreted by the adrenal cortex is usually so low that their effects are insignificant.

They stimulate the growth of pubic and axillary hair in both males and females. They also promote libido (sex drive) and are converted to oestrogens by other body tissues.

ADRENAL MEDULLA

Medulla is the inner part of the adrenal gland. It mainly consists of the hormone-producing cells called *chromaffin cells* that release the hormones after stimulation by the sympathetic division of the autonomic nervous system (ANS).

Hormones of adrenal medulla

Unlike the hormones of the adrenal cortex, the medullary hormones are not essential for life as they only intensify the responses of the sympathetic nervous system.

The two major hormones synthesized by adrenal medulla include *epinephrine* (or *adrenaline*) and *norepinephrine* (or *noradrenaline*). Both these hormones are structurally very similar and thus also have similar effects.

Effects of epinephrine and norepinephrine

Epinephrine and norepinephrine prepare our body for stressful situations such as injury, exercise, trauma, anger, fear, pain and danger; hence, they are commonly referred to as *fight or flight hormones*.

The various actions of these hormones include the following:

1. Increase in heart rate and force of contraction that leads to increased cardiac output and blood pressure
2. Increased blood flow to essential organs including the heart, liver, brain and skeletal muscles by dilating their blood vessels and constricting those of less-essential organs, such as skin
3. Increased metabolic rate and increased breakdown of glycogen (glycogenolysis) and lipids (lipolysis) to release glucose and fatty acids in the bloodstream for ATP synthesis
4. Increased rate and force of respiration

All these changes prepare our body to either fight or flee the stressful situation and thus these responses are collectively termed as *flight or fight responses*.

The release of these hormones is regulated by the hypothalamus and stressful situations that cause the stimulation of the sympathetic nervous system to further stimulate the adrenal medulla to release epinephrine and norepinephrine.

Response to stress

Stressful conditions such as infection, emotional disturbance, fasting and exercise stimulate an immediate response called short-term response' by the release of flight or fight hormones. However, in the longer term, ACTH from the anterior pituitary stimulates the release of glucocorticoids and mineralocorticoids from the adrenal cortex, resulting in longer term response to stress.

PANCREAS

ANATOMICAL STRUCTURE

The pancreas is a flattened, elongated organ located in the epigastric and hypochondriac (left) regions of the abdomen. (For more details, see the chapter The Digestive System).

Pancreas mainly consists of lobules or acini that secrete the pancreatic juice, which flows into the gastrointestinal tract through a network of ducts (exocrine function of pancreas). Interspersed at random among the acini are tiny clusters of endocrine tissues called *pancreatic islets* or *islets of Langerhans* that secrete the pancreatic hormones directly into the bloodstream (endocrine function of pancreas) (Fig. 6.10).

HORMONES

The islets of Langerhans consist of the following four main types of cells:

- Alpha cells, which secrete the hormone *glucagon*
- Beta cells, which secrete the hormone *insulin*
- Delta cells, which secrete the hormone *somatostatin*
- PP cells, which secrete the hormone *pancreatic polypeptide (PP)*
- Insulin and glucagon are the important pancreatic hormones and have antagonistic effects on *blood glucose levels*; glucagon increases blood glucose levels and insulin lowers them.

Insulin

The various functions of insulin are as follows:

1. **Increased glucose uptake**: Insulin accelerates the transport of glucose into cells by increasing the permeability of cell membrane to glucose. It enhances the uptake and use of glucose by all the tissues, especially by the liver, skeletal muscle and adipose tissue.
2. **Increased glycogenesis**: Insulin promotes the rapid conversion of glucose into glycogen (glycogenesis), especially in the muscles and liver.
3. **Increased lipogenesis**: Insulin promotes the synthesis of fatty acids and storage of fats in adipose tissue.

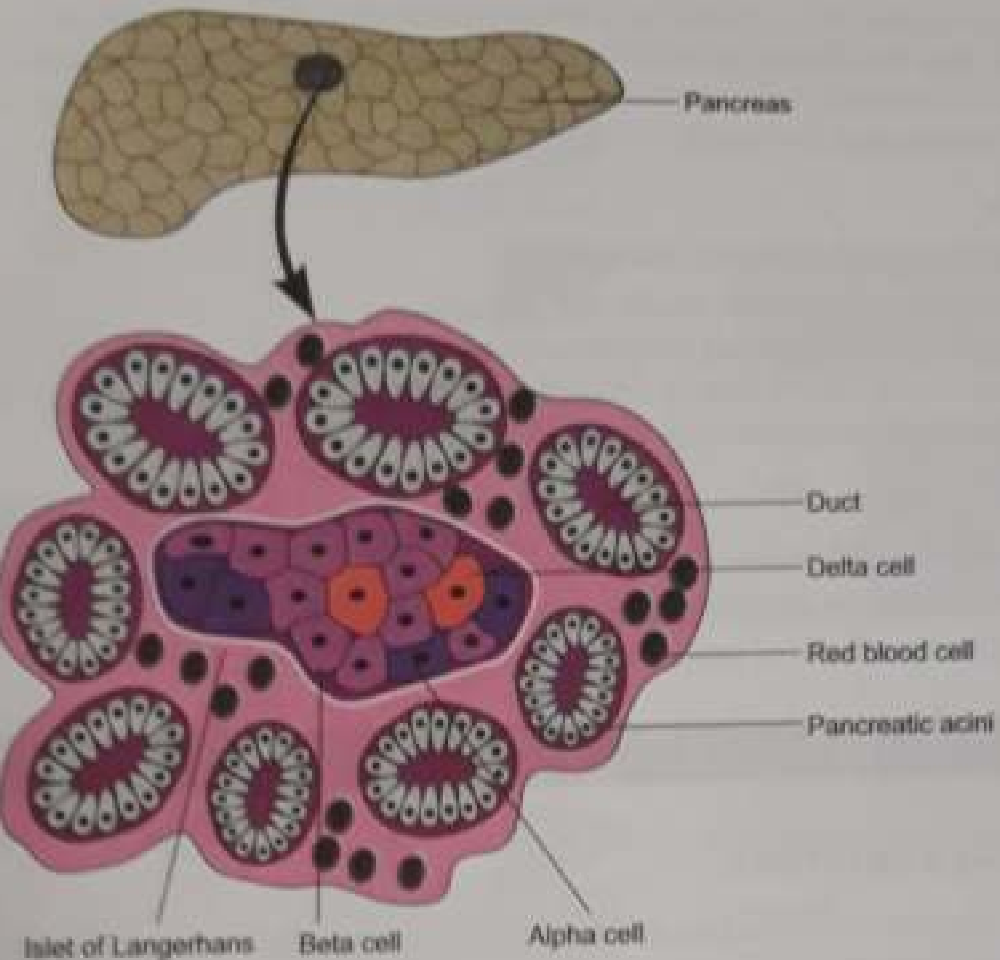

Figure 6.10 Anatomical structure of pancreas (close-up view of an islet of Langerhans).

4. **Increased protein synthesis**: Insulin accelerates the uptake of amino acids by cells and stimulates protein synthesis.
5. **Decreased proteolysis, lipolysis and gluconeogenesis**
   - Insulin prevents the breakdown of proteins and fats and inhibits gluconeogenesis (i.e. formation of glucose from nonsugar substrates such as proteins).
   - Insulin also inhibits glycogenolysis (i.e. breakdown of glycogen into glucose in the muscles and liver).

Secretion of insulin is stimulated by increased blood glucose level, increased blood amino acid and fatty acids levels, parasympathetic stimulation (acetylcholine) and gastrointestinal hormones (e.g. gastrin, secretin and cholecystokinin). Secretion is inhibited by glucagon, sympathetic stimulation (adrenaline) and somatostatin.

Glucagon

Glucagon increases the blood glucose levels and is released when the blood glucose level falls drastically.

The effects of glucagon in increasing the blood sugar level are as follows:

1. It accelerates the breakdown of glycogen into glucose in the liver (*glycogenolysis*), which is released into the bloodstream.
2. It promotes gluconeogenesis (i.e. the formation of glucose from nonsugar substrates such as proteins and fats).

3. It promotes lipolysis (i.e. breakdown of fats to provide an alternative energy source).

Thus, glucagon and insulin are part of a feedback system that maintains the correct blood glucose level (Fig. 6.11). Secretion of glucagon is stimulated by low blood glucose level and exercise, and it is decreased by somatostatin and insulin.

Somatostatin

Somatostatin performs the following functions:

1. It inhibits the secretion of both insulin and glucagon.
2. It inhibits the release of GH and TSH from the anterior pituitary.
3. It also decreases the smooth muscle contractions and flow of blood in the intestine. Thus, it decreases the rate of nutrient absorption from the gastrointestinal tract.

Pancreatic polypeptide (PP)

The principal actions of PP include the following:

1. It inhibits somatostatin secretion and gall bladder contraction.
2. It also inhibits the release of pancreatic juice.

GONADS

ANATOMICAL STRUCTURE

Gonads are the structures that produce gametes—sperm in males and oocyte in females. The anatomical structures of male (testes) and female gonads (ovaries) are discussed in the chapter The Reproductive System.

HORMONES

The hormones secreted by the gonads include the following:

- Testosterone (secreted by testes)
- Oestrogen (secreted by ovaries)
- Progesterone (secreted by ovaries)
- Relaxin (secreted by ovaries)

Testosterone

- Testosterone is the male sex hormone.
- It is responsible for the development of male reproductive structures, and at puberty, for the enlargement of testes and penis.
- It stimulates the formation of sperms (spermatogenesis) in the seminiferous tubules.
- It also promotes the development of accessory male sexual characters such as growth of facial and chest hair, deepening of the voice, muscular development and bone growth.

Oestrogen

- Oestrogen is the female sex hormone.
- It is responsible for the development and growth of female reproductive structures: the uterus, vagina and fallopian tubes.

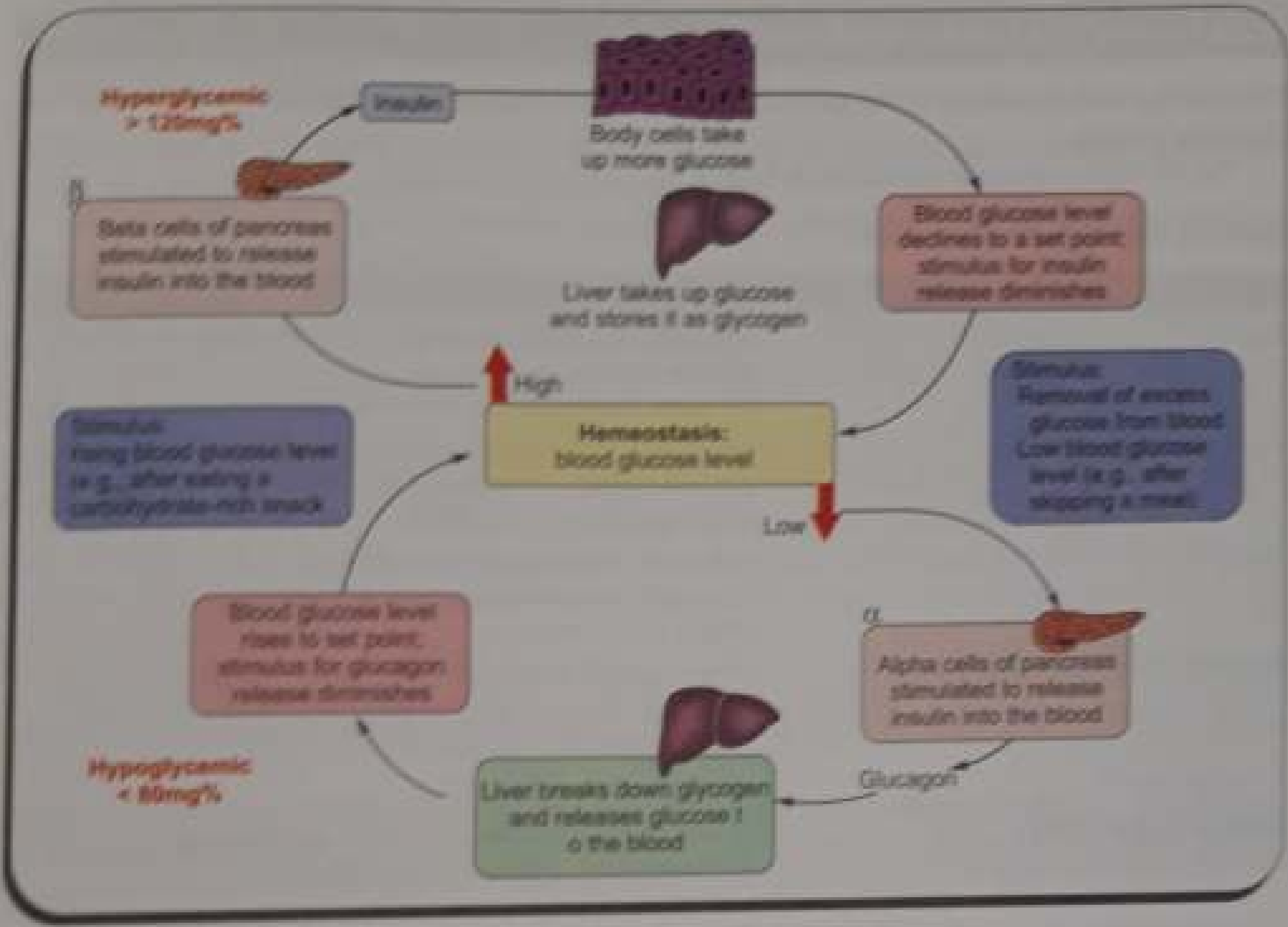

Figure 6.11 Regulation of pancreatic hormones insulin and glucagon.

- It stimulates the differentiation of ova (oogenesis) in the ovary.
- It promotes the development of accessory female sexual characters such as enlargement of breasts, growth of pubic and axillary hair, deposition of fat in the thighs and onset of menstrual cycle.

Progesterone

- Progesterone is also called *hormone of pregnancy*.
- It plays a major role in implanting the fetus to the uterine wall, forming the placenta and regulating the development of fetus in the uterus.

Relaxin

Relaxin is believed to increase the flexibility of pubic symphysis during pregnancy and widen the pubic symphysis at the time of birth.

All the hormones produced by gonads are discussed in details in the chapter The Reproductive System.

GASTROINTESTINAL HORMONES

The anatomy and physiology of the gastrointestinal (GI) system have been discussed in the chapter The Digestive System.

The GI hormones are summarized in Table 6.2.

Table 6.2 Gastrointestinal hormones

Agent	Effect
Gastrin	Stimulates HCl gastric secretion Stimulates mucosal cell growth Stimulates contractions of oesophageal sphincter and stomach
Cholecystokinin (CCK)	Stimulates contraction of gall bladder; inhibits gastric emptying Stimulates pancreatic secretion of enzymes Inhibits gastric secretion of HCl
Secretin	Stimulates pancreatic secretion of fluid Stimulates bile-salt-independent biliary secretion Inhibits gastric emptying
Gastric-inhibitory polypeptide (GIP)	Inhibits gastric secretion of HCL Stimulates intestinal secretion of Cl^- Inhibits intestinal absorption of Na^+
Enteroglucagons	Inhibit gastric secretion of HCl
Pancreatic polypeptide	Inhibits pancreatic secretion of HCO_3^- and enzymes Increases gastric and intestinal motility

OTHER ENDOCRINE GLANDS

Some other organs, which also perform glandular function, are listed in Table 6.3.

Table 6.3 Other endocrine glands

S. no.	Hormone	Principal actions
1.	**Heart** Atrial natriuretic peptide (ANP)	Decreases blood pressure
2.	**Placenta** Human chorionic gonado-tropin (HCG)	Stimulates the corpus luteum in the mother's ovary to continue the secretion of oestrogen and progesterone to maintain preg-nancy
3.	**Thymus gland** Thymosin	Promotes the maturation of T-lymphocytes
4.	**Kidney** (a) Renin (b) Erythropoietin	(a) Converts angiotensinogen to angiotensin that raises blood pressure by vasoconstriction and aldosterone secretion (b) Increases the rate of RBC production

DISORDERS ASSOCIATED WITH THE ENDOCRINE SYSTEM

ADDISON'S DISEASE

Addison's disease is a chronic endocrine disorder in which the adrenal glands produce insufficient steroid hormones—glucocorticoids and mineralocorticoids.

The most common cause is autoimmune disorder in which antibodies destroy the adrenal cortex or block the binding of ACTH to its receptors.

The most common symptoms include fatigue, mental lethargy, anorexia, muscle weakness, fever, weight loss and gastrointestinal disturbances including nausea, vomiting and diarrhoea.

Treatment consists of replacing glucocorticoids and mineralocorticoids and increasing sodium in the diet.

DIABETES MELLITUS

Diabetes mellitus is a very common disorder manifested by high blood sugar (glucose). The classical symptoms of diabetes mellitus include polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger).

There are two main types of diabetes as follows:

- **Type 1 diabetes** or **IDDM (insulin-dependent diabetes mellitus)**: It occurs due to the deficiency or absence of insulin.
- **Type 2 diabetes** or **NIDDM (non-insulin-dependent diabetes mellitus)**: It is the most common form of diabetes that occurs due to insulin resistance, a condition in which cells fail to use insulin properly. It usually develops after 40 years due to genetic factors, obesity or sedentary lifestyle.

DIABETES INSIPIDUS

Diabetes insipidus is the most common abnormality associated with the dysfunction of the posterior pituitary and mainly occurs due to deficiency of antidiuretic hormone (ADH).

The symptoms include excretion of large amounts of severely diluted urine, resulting in excessive thirst and dehydration.

Treatment involves mainly hormone replacement therapy.

GOITRE

This is enlargement of thyroid gland that leads to the swelling of the neck or larynx. It is caused by reduced levels of T_3 and T_4 that stimulate the secretion of TSH, resulting in hyperplasia of the thyroid gland.

The main reason of goitre is low dietary intake of iodine, which results in inadequate synthesis of thyroid hormones.

HYPERTHYROIDISM

Hyperthyroidism is also known as thyrotoxicosis and refers to the increased thyroid hormones (T_4 and/or T_3) in the blood.

The symptoms of hyperthyroidism include nervousness, irritability, anxiety, thinning of the skin, fine brittle hair and muscular weakness.

The causes of hyperthyroidism include Grave's disease (autoimmune disorder in which an antibody functions similar to TSH and results in increased release of T_4 and T_3) or toxic nodular goitre (the nodules of gland secrete excess T_4 and T_3).

HYPOTHYROIDISM

Hypothyroidism refers to the deficiency of thyroid hormone and occurs due to an abnormality in the thyroid gland or, less commonly, the pituitary gland or hypothalamus.

Cretinism is a form of hypothyroidism occurring in infants. Its symptoms include poor muscle tone (muscle hypotonia), fatigue, dry, itchy and puffy skin, especially on the face and abnormal menstrual cycles.

Myxoedema is the condition of hypothyroidism in adults and results in an abnormally low metabolic rate.

ACROMEGALY

Acromegaly is a syndrome in which the pituitary gland produces excess GH after the epiphyseal plate closure at puberty.

It mostly affects adults in middle age and results in severe disfigurement of the body parts, especially the face, enlarged tongue and excessive large hands and feet.

The treatment for acromegaly includes irradiation, radioisotope implantation or surgical removal of the tumour or pituitary gland.

GIGANTISM

Gigantism is a condition manifested by abnormal excessive growth and height that is significantly above average.

It is caused by an overproduction of human GH, usually by a hormone-secreting pituitary tumour.

The treatment for gigantism includes surgical removal of the tumour or the pituitary gland (hypophysectomy).

PITUITARY DWARFISM

Pituitary dwarfism is the condition characterized by hyposecretion of GH during the growth years.

It leads to the slowing of bone growth and closure of the epiphyseal plates before normal height is reached.

The symptoms include small body, but normally proportioned; mild obesity with lack of appetite; tender, thin skin.

The treatment includes GH injections.

CUSHING'S DISEASE

Cushing's disease is characterized by the increased secretion of ACTH from the anterior pituitary.

Its symptoms include rapid weight gain, moon-like face, shape of back and neck resembles a buffalo hump, hyperhidrosis (excess sweating), telangiectasia (dilation of capillaries) and thinning of the skin.

Its treatment includes surgical removal of portions of the pituitary gland or adrenal glands, irradiation and hormone replacement therapy.

GRAVE'S DISEASE (THYROTOXICOSIS)

Grave's disease is characterized by hyperthyroid secretion (excessive secretion by the thyroid gland).

Its symptoms include loss of weight, rapid pulse, warm and moist skin, increased appetite, increased BMR, tremor, goitre, exophthalmos (bulging eyes) and muscular weakness.

Its treatment includes removal of a portion of the thyroid gland, radioiodine and antithyroid drugs.

MYXOEDEMA

Myxoedema is characterized by hypothyroid secretion (insufficient secretion of the thyroid gland) in adults.

Its symptoms include weight gain, slow pulse, dry and brittle hair, decreased BMR, lack of energy, sensation of coldness, diminished perspiration and weakness.

Its treatment includes thyroid hormone (T3 and T4) administration.

CRETINISM

Cretinism is characterized by hypothyroid secretion (severe insufficiency of thyroid gland secretion) in infants and children.

Its symptoms include stunted growth, thickened facial features, large and protruding tongue, abnormal bone growth, mental retardation, decreased BMR and general lethargy.

Its treatment includes thyroid hormone administration.

Summary of major hormones

Major hormones, alongwith their position and functions, are listed in Table 6.4.

Table 6.4 Summary of major hormones

S.no.	Gland	Position	Hormones and their nature	Functions
1.	Thyroid	In the neck inferior to larynx	i) Thyroxine (T_4) ii) Triiodothyronine (T_3) iii) Calcitonin (CT) (peptide)	i) Increase basal metabolic rate; excess of the hormone causes Grave's disease; deficiency produces cretinism in children and myxoedema in adults. iii) Calcitonin controls the calcium and phosphorus balance.
2.	Parathyroids	In the back of thyroid	i) Parathormone (PTH) (peptide)	i) Regulates the calcium-phosphorus balance in blood; deficiency causes cramps and convulsions; excess of the hormone weakens bones.
3.	Adrenals a) Cortex	On top of kidneys	i) Glucocorticoids, e.g. cortisol (steroid) ii) Mineralocorticoid, e.g. Aldosterone (steroid) iii) Sex corticoids (steroids)	i) Regulates carbohydrate, fat and protein metabolism; controls the electrolyte and water balance; deficiency causes Addison's disease. ii) Produces accessory sex characters; excess in early life causes early abnormal sexual maturity. iii) Prepare the body for emergency by increasing heart beat, blood pressure, respiratory rate, blood sugar level, etc.
	b) Medulla		i) Adrenaline (amine) ii) Noradrenaline (amine)	
4.	Hypothala-mus	Base of diencephalon	i) Releaser hormones (peptides) ii) Inhibiting hormones (peptides)	i) Stimulate anterior pituitary to secrete hormones. ii) Inhibit anterior pituitary to secrete hormones.
5.	Pituitary a) Anterior lobe	Beneath brain	i) Follicle-stimulating hormone (FSH) (protein) ii) Luteinizing hormone LH (protein) iii) Growth Hormone (GH) (protein) iv) Prolactin (protein) v) Adrenocorticotrophin (ACTH) (peptide) vi) Thyrotrophin (TSH) (protein)	i) Stimulates spermatogenesis in males and growth of ovarian follicle in female; promotes ovulation and secretion of oestrogen and progesterone in females; induces testosterone secretion in males iii) Regulates protein metabolism and growth of bones; deficiency causes dwarfism; excess hormones leads to gigantism in young and acromegaly in adults. iv) Controls the development of milk glands. v) Stimulates secretion of hormones of the adrenal cortex. vi) Stimulates secretion of thyroid hormones.

S. no.	Gland	Position	Hormones and their nature	Functions
	b) Posterior lobe		i) Oxytocin (peptide) ii) Vasopressin/ADH (peptide)	i) Regulates uterine contractions and release of milk ii) Reduces loss of water in urine
6.	Pineal	Roof of brain	i) Melatonin (amine)	i) Regulates sleep-awake pattern.
7.	Pancreas	Below stomach	i) Insulin (protein) ii) Glucagon (protein) iii) Somatostatin (SS) iv) Pancreatic polypeptide	i) Controls carbohydrate metabolism, increases glucose uptake, lipogenesis, glycogenesis and protein synthesis; its deficiency causes diabetes mellitus. ii) Increases the blood sugar level. iii) Inhibits secretion of both insulin and glucagon. iv) Inhibits the release of pancreatic juice.
10.	Gonads a) Testes	In scrotal sacs	i) Testosterone (steroid)	i) Develops male reproductive organs and accessory sexual characters.
	b) Ovaries	Lower abdomen	i) Oestrogen or oestradiol (steroid) ii) Progesterone (steroid) iii) Relaxin (protein)	i) Develops female genital organs and accessory sexual characters. ii) Attaches fetus to uterine wall. iii) Widening of pelvis at birth.