UNIT 10 COMMUNICATION—II

Structure

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10.1 INTRODUCTION

You would be aware by now that in any multicellular organism, the work done is divided among many different types of cells. These cells must exchange information and work together if the organism is to survive.

In the previous unit we studied one of the two great communication networks—the nervous system, that sends electrical messages via the neurons and nerves to various parts of the body. These messages are transmitted across the synapses in the form of chemicals. In this unit, we shall study the other communication network of chemical messengers — the hormones. The nervous system and the body's chemical messengers work together in coordinating the activities of the different cells of the body.

Originally, hormones were defined as chemicals produced by ductless endocrine glands that travel through the blood to exert their effect at some distance from where they are produced. Now, we know that animals have many other chemical messengers in addition to the hormones produced by endocrine glands. These include the neurotransmitters we encountered in Unit 9; local chemical messengers such as histamine that participate in inflammatory and immune reactions (LSE-01, Unit 15), growth factors that stimulate growth by particular tissues; prostaglandins that are lipids with a variety of effects and pheromones that are chemical signals emitted into the environment that affect the behaviour of other individuals of the same species.

This unit considers general patterns seen in the chemistry and activities of hormones produced by endocrine glands and nervous tissue. You are not expected to remember the chemical structures of different hormones. These structures are included in the text to illustrate the similarities or relationships among several hormones. We shall see how hormones affect the homeostasis and the animal's response to external stimuli and also learn about some of the roles played by pheromones in influencing the behaviour of different individuals of the same species.

Before you begin a study of this unit we suggest that you read Unit 15 of the Cell Biology

Course (LSE–01) again for, we assume your knowledge of certain concepts of hormone action at cellular level.

Objectives

After studying this unit, you should be able to:

- define the terms hormones, endocrine glands and identify sources of hormones other than endocrine glands.
- describe the chemical classification of hormones and compare the hormone action in case of proteins and steroid hormones,
- describe the neuroendocrine relationship and the mechanism by which hypothalamus regulates the secretion from pituitary,
- explain how concentration and action of hormones are regulated by negative feedback mechanism,
- explain the action of insect hormones in controlling metamorphosis,
- describe the role of pheromones in communication and compare it to hormonal action.

10.2 HORMONAL CONTROL SYSTEMS

Throughout the animal kingdom we see that chemical signals transmitted from cell to cell coordinate body function. The three basic modes of chemical signalling are shown in Fig. 10.1.Each involves specific receptor proteins on the surface of the cells that receive the signals. Local chemical mediators are produced by most cells and vary in type and function but they affect the cells in the immediate vicinity only.

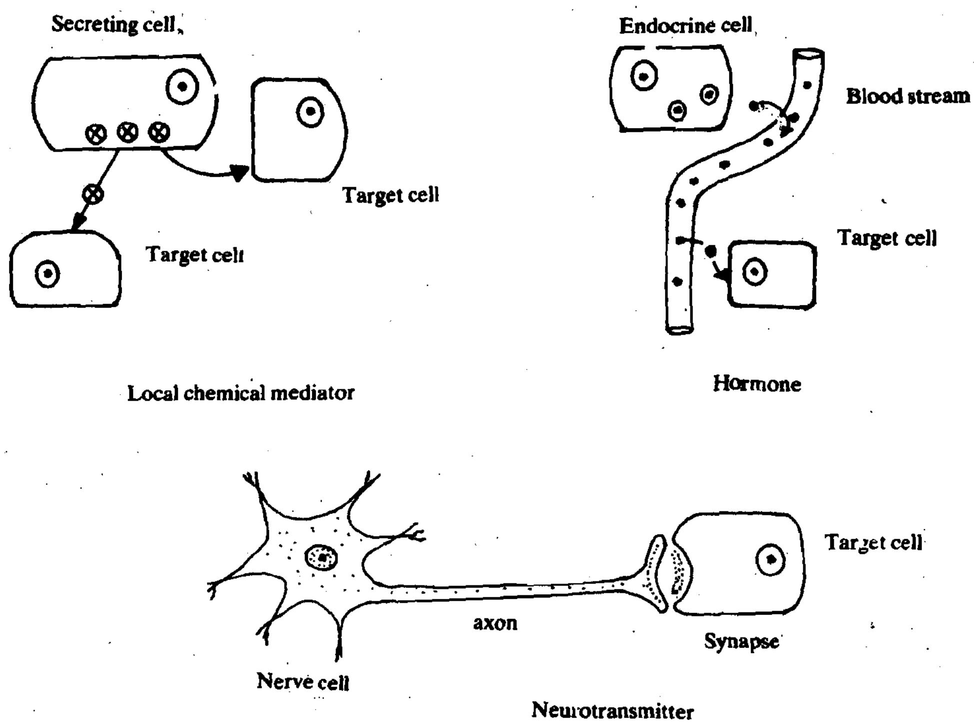

Fig. 10.1: Chemical signalling system.

Hormones in contrast are chemical substances produced by a specific group of cells and released into the blood stream. They may affect distant parts of the body. Even though hormones in blood come in contact with every organ they affect only specific target organs or tissues. These target cells are equipped with receptor cells for a particular hormone or a group of hormones.

The major mammalian endocrine glands are shown in Fig. 10.2 and the most important vertebrate hormones and their functions are listed in Table 10.1. Many of these hormones are almost similar throughout the vertebrate classes; others have specific functions that differ from group to group. For example, prolactin has 365 known effects! Prolactin in mammals stimulates milk secretion, in pigeons it stimulates the formation of crop milk and in fish it affects renal functions and osmotic permeability of the gills.

Fish has maximum hormones, as we go up the evolutionary tree the number of hormones have decreased but specialisation increases.

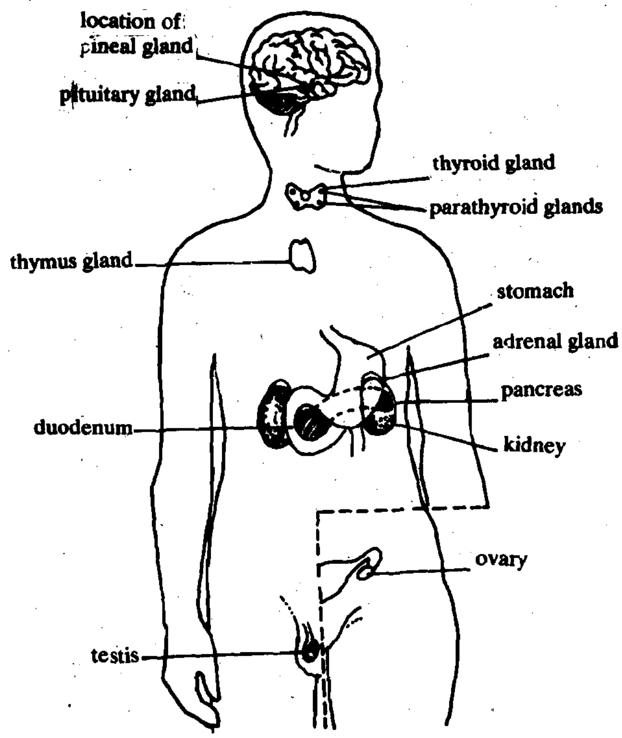

Fig. 10.2: Location of endocrine glands.

Table 10.1 : Some vertebrate hormones grouped according to source and their action (hormones from hypothalamus and pituitary given in Table 10.2 and 10.3)

	Hormones and Source	Chemical Nature	Action.
1)	**Thyroid Gland**		
	Calcitonin	Polypeptide	Decreases blood calcium levels by promoting calcium deposition in bones
	Thyroxine (T_4)	Iodinated tyrosine derivative	1. Growth and metabolism 2. Metamorphosis in amphibians
	Triiodothyronine (T_3)	-do-	
2)	**Parathyroids**		
	Parathormone (PTH)	Polypeptide	Increases blood calcium and phosphorus by releasing calcium stored in bones, decreases excretion of calcium from kidneys
3)	**Pancreas**		
	Insulin (from B-cell)	Polypeptide	Decreases blood glucose, alters protein and lipid metabolism
	Glucagon (from A cell)	Polypeptide	Increases blood glucose by increasing glycogenolysis
	Gastrin (D-cells also found in stomach)	Polypeptide	Secretion of HCl by stomach
4)	**Blood**		
	Erythropoietin	Polypeptide	Increases erythrocyte production in bone marrow
	Angiotensin I Angiotensin II	Small peptide	Stimulate aldosterone synthesis in adrenal cortex
5)	**Small Intestine**		
	Enterogasterone		Inhibits acid secretion in stomach
	Cholecystokinin (CCK)	Polypeptide	Stimulates contraction of gall bladder and release of bile salts; digestive enzymes from pancreas
	Secretin	Polypeptide	Stimulates secretion of water and inorganic salts from pancreas

Table 10.1 Continued

	Hormones and Source	Chemical Nature	Action
6)	**Adrenal Medulla**		
	Epinephrine or adrenalin	Amine	Neurotransmitter, contraction/relaxation smooth muscles
	Norepinephrine or noradrenalin	Amine	Dilation of blood vessels, increase in blood sugar and blood pressure, increases heart rate and cardiac output
7)	**Adrenal Cortex**		
	Glucocorticoids (Corticosterone, Cortisol etc.)	Steroid	Metabolism of carbohydrate, protein and fat in liver; important in fasting or hibernating animals; have anti-inflammatory action; involved in termination of pregnancy
	Minerelocorticoids (Aldosterone)	Steroid	Resorption of K^+ and Na^+ in kidney; sweat, salivary glands, gut, amphibian skin, bladder, fish gills
	Small amounts of sex hormones (androgens and progesterone)	Steriods	Promotes secondary sexual characters predominently male.
8)	**Testes**		
	Androgens (testosterone, 5 α-dihydroxy testosterone)	Steroid	Development and maintenance of male characteristics and behaviour
9)	**Ovaries**		
	Estrogens	Steroid	Development and maintenance of female characteristics and behaviour
10)	**Corpus Luteum**		
	Progesterone	Steroid	Maintenance of uterine endometrium, stimulation of mammary duct formation; acts with estrogens to maintain estrous and menstrual cycle

10.2.1 Chemical Nature

All hormones are chemical compounds that can broadly be grouped as:

1) Those that are synthesised from fatty acid precursors.

2) Those that are synthesised from amino acids or closely related compounds.

Hormones based on fatty acids are relatively small in size and have basically similar structure. All steroid hormones are based on 4 ring structures synthesised from cholesterol (Fig. 10.3).

In invertebrates the ecdysone found in insects is included in the steroid group and in vertebrates the important steroid hormones are estrogens, androgens and corticosteroids. Within each of these groups different hormones are synthesised by addition or removal of oxygen and/or hydrogen (Fig. 10.3b).

The **peptide hormones** or those based on amino acids vary in both size and structure. For example, oxytocin and antidiuretic hormone (ADH) are both small peptide hormones that differ by only two amino acids (Fig. 10.4a) but produce entirely different effects.

Oxytocin is present in all vertebrates but different vertebrate classes have slightly different versions of it. Thyroxine (T_4) which is involved in control of tissue metabolism is derived from the tyrosine residues while growth hormone is composed of 190 amino acids. Most neurotransmitters are essentially modified amino acids (Fig. 10.4b).

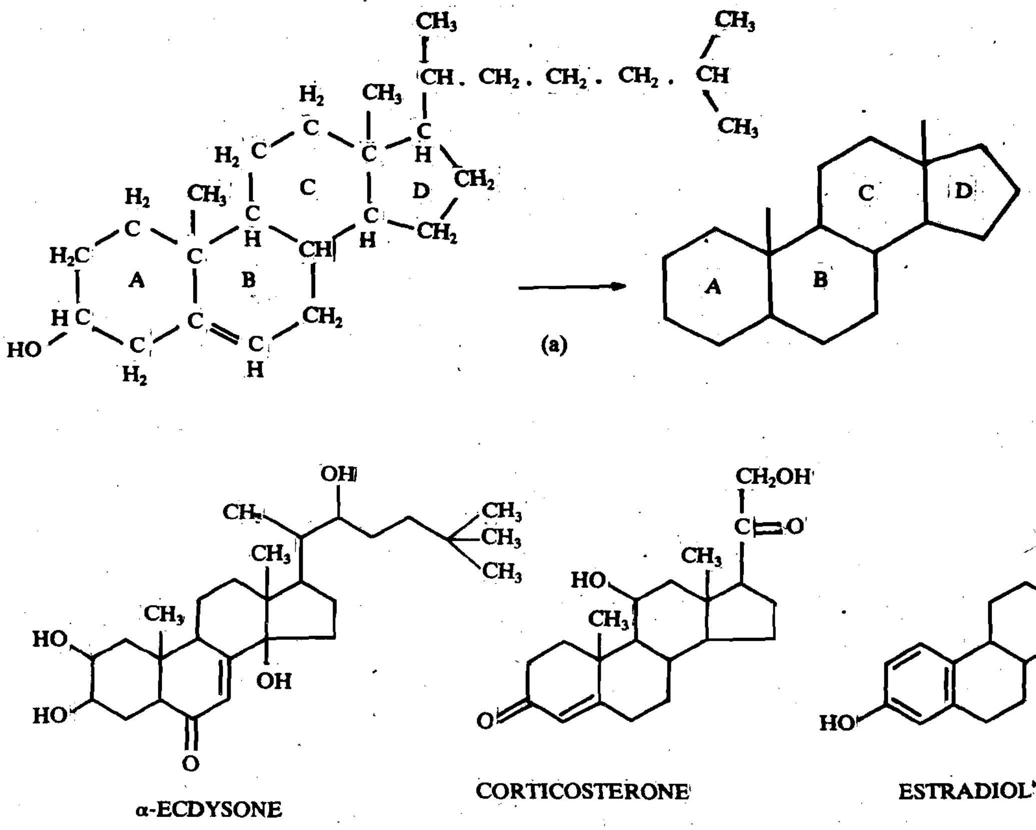

Fig. 10.3 : a) Relationship between cholesterol and basic steroid nucleus. b) All naturally occurring steroids have the basic ring structure of 17 carbon atoms. They differ in the number of carbon, hydrogen and oxygen atoms attached to the basic nucleus

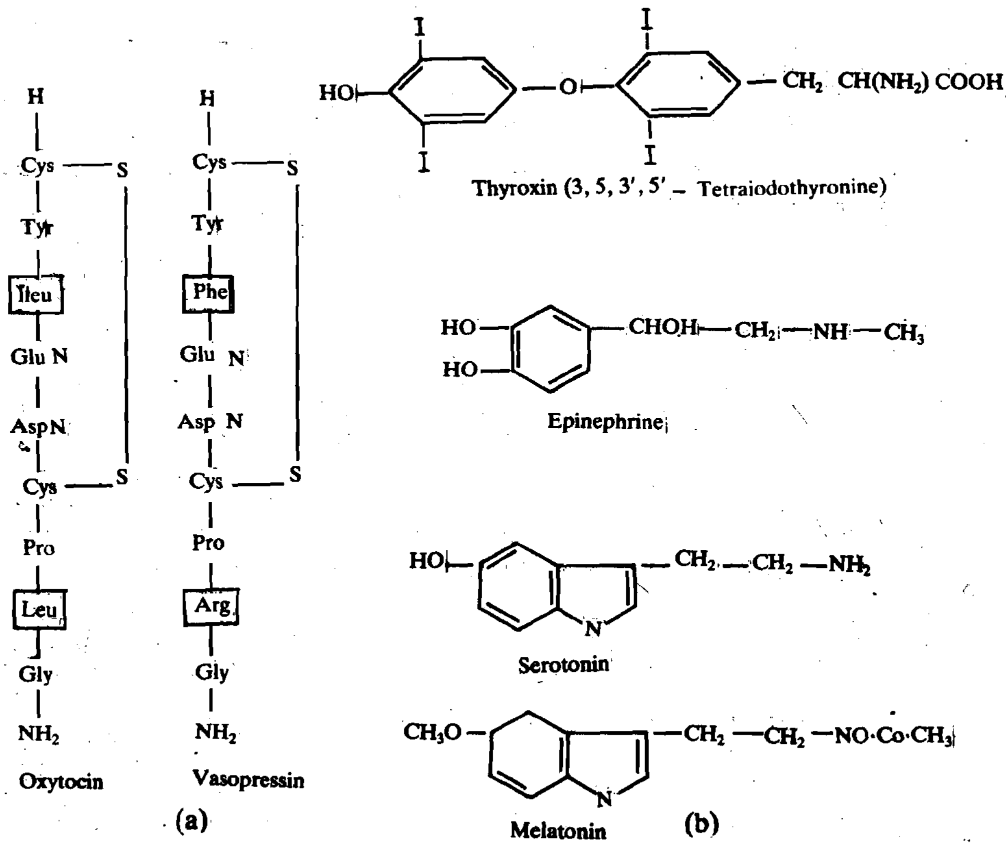

Fig. 10.4 a): Amino acide sequences of oxylocin and vasopressin. b) Amino acid based hormones

10.2.2 Synthesis and Storage

The synthesis and storage of hormone depends on the nature of the hormone. Steroid hormones are secreted in diffuse molecular form and usually accumulate in the cell as clear lipid droplets, or may sometimes be bound to the membrane as lipids-protein aggregate. Hormones based on amino acids are packaged in membrane bound vesicles that are later liberated in extracellular space.

The duration of storage of a hormone within a secretory tissue also varies. Steroid hormones appear to diffuse out of the cells across the membrane (being lipid soluble) in a matter of minutes after synthesis. Secretory residues of most endocrine cells, however, are held till they are given the signal to be released. Thyroid hormone is secreted into extracellular spaces of the cells called follicles and can be stored for several months.

10.2.3 Secretion of Hormones

The secretion of most hormones (except steroid) is by the process of exocytosis. Fig. 10.5 summarises the formation, transport, release and reconstitution of secretory vesicles.

The release of hormones from the endocrine glands is controlled by nervous, hormonal or metabolic stimuli which also control the rate of release into the bloodstream. As with neurotransmitters, Ca^{2+} seems to play an important role in the release of hormones. The secretion is not random but follows a certain pattern. This may be circadian (i.e. approximately a 24 hour cycle) or seasonal or may be periodical (e.g. the human menstrual cycle). Some hormones like the thyroxine or triiodothyronine are secreted continuously by the thyroid gland).

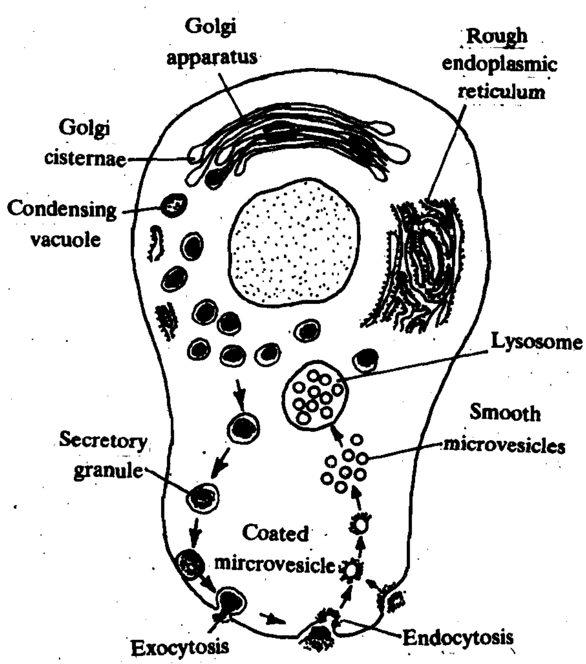

Fig. 10.5 : Formation and secretion of hormones. After their formation in the golgi apparatus secretory vesicles are transported to the site of release. After the release of hormone by exocytosis the new vesicles may form by process of endocytosis

The duration of hormone in the bloodstream is indicated by its 'half life' which varies from a few seconds to almost a week depending on the hormone. The hormone is deactivated in the liver and in the target tissue that break down the hormone, or the hormone may be lost through the kidneys. Hormones of molecular mass of 10,000 or less are selectively filtered from the kidneys and excreted in the urine.

Many hormones are bound to the protein molecules in the blood plasma forming aggregates. This prevents a) the hormones from being excreted out of the body via the kidney, b) rapid destruction of hormones by enzyme. Hormone-protein aggregate is a source of slow release of hormones.

The slow release of hormones occurs because the amount of hormone bound to the plasma protein is always in equilibrium with a small amount of free hormone. Receptor molecules have a greater affinity for hormones than the protein molecules in the plasma. So, free hormones tend to bind to the receptors shifting the equilibrium and more hormone dissociates from the plasma proteins. Because free hormone is also broken down continually by action of enzymes, a steady trickle of hormone is maintained.

Hormone concentrations in the blood are related to the volume of blood, physiological state, metabolic rate and hormone binding capacity of plasma proteins. However, it is seen that hormone levels in blood are always very low in comparison to other substances. Let us take the example of antidiuretic hormone (ADH). Within the blood of rat ADH level is approximately 10^{-11} mole per litre, but if the rat faces dehydration the level increases to 2.5×10^{-10} mole per litre. Hormones like insulin, glucagon that are concerned with maintaining blood glucose levels are in the range of 10^{-9} mole per litre. Sex hormones are in the range of 10^{-7} mole per litre to 10^{-10} mole per litre. Detecting this amount of hormone in blood is equivalent to detecting a teaspoon of sugar in a swimming pool! What does this example illustrate? It shows that receptor molecules must be very sensitive and have a very high affinity for hormone molecules. Therefore we can say that hormones are simply chemicals it is the receptors that makes them hormones.

SAQ 1

Which of the following statements [illegible] and which are [illegible] reasons.

i) Peptide [illegible] are related [illegible] closely to neurotransmitters [illegible] hormones.

ii) All hormones have [illegible] effects on all [illegible]

iii) All steroid hormones [illegible] basically a 4 ring structure [illegible]

iv) Hormone bound to proteins in [illegible] released quickly and [illegible] by [illegible] immediately.

SAQ 2

Fill in the blanks to complete the definition.

A hormone may be defined as [illegible] . . . . produced by one type of cell [illegible] . . . . [illegible] on the activity of another type of [illegible]

10.3 ACTION OF HORMONES

We said earlier that hormones are released into the blood stream or extracellular fluid and therefore, reach most of the cells of the body. However, they are specific and influence only their destined **target cells**. Other cells do not react. For instance, insulin passes throughout the body but only the liver and muscle cells respond to it by taking up glucose. Similarly the target cells respond to the hormones differently at different times. Injections of thyroxine will not make a very young tadpole develop into an adult since the cells cannot respond to the hormones as they will in later life. This suggests that only specific receptor molecules at the target cells recognise and bind to particular hormones, and other cells do not possess these receptor molecules. When the hormone reaches a target cell many changes may occur in the cell.

- The activities of various enzymes may increase or decrease i.e. inactive enzymes are activated..
- permeability of plasma membranes may be altered.
- increase in activity of certain genes may alter the types of messenger RNA and proteins produced by the target cells.

The way in which hormones act upon their target cells is similar to the mechanism involved in the case of neurotransmitters. We must not forget that the 'language' used in both types of communications is chemical. Basically, three steps are involved that have been shown graphically in Fig. 10.6.

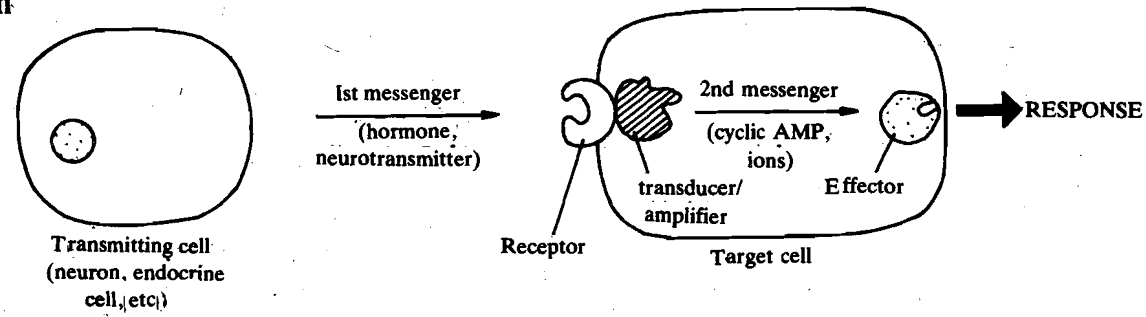

Fig. 10.6: Intracellular communication system involving chemical messengers

The speed with which the hormone acts depends on how it acts. Insulin for example, affects tissues within minutes after it appears in the bloodsteam because it crosses the plasma membrane and acts on the cell's metabolism directly. Other hormones do not enter the cell but bind to receptors on plasma membrane and affect the metabolism and transcription. Hormones that induce genetic activity and protein production are the slowest in their effect.

Hormones can be divided into two groups: 1) those like steroids and other lipid soluble hormones penetrate the surface membrane of the target cells and 2) Proteinaceous hormones and catecholamines that cannot or can poorly penetrate the membrane of the target cell. Let us consider the action of steroid and thyroid hormones first.

In general, the steroid hormones induce the transcription activity of the target cells and proteinaceous hormones affect the membrane permeability and enzyme action.

10.3.1 Steroid and Thyroid Hormones

Cytoplasmic receptors for steroids are proteins with two subunits that bind to the steroid molecules. When both receptor sites are occupied by the steroid then the receptor-steroid complex migrates to the nucleus where one subunit ensures that the complex binds to the specific site on the chromatin. Then the receptor subunits separate and the other subunit interacts directly with the adjacent region of DNA molecule resulting in the transcription of the DNA segment into mRNA (see Box 10.1 and Fig. 10.7a). Thyroid hormone acts in a similar manner (Fig. 10.7b) except that the receptor is located in the nucleus. The major hormone secreted by thyroid is thyroxine (T_4). It travels in blood attached to carrier proteins. Thyroid also secretes a small amount of triiodothyronine (T_3). Carrier proteins have higher affinity for T_4 and very little T_4 is free in the plasma. Only the free T_4 and T_3 enter the cells. The rest of the bound T_4 acts as a reservoir for slow release. The free T_4 that enters the cell is also converted to T_3 enzymatically. Therefore, T_3 is the chemically more potent and active form of thyroid hormone.

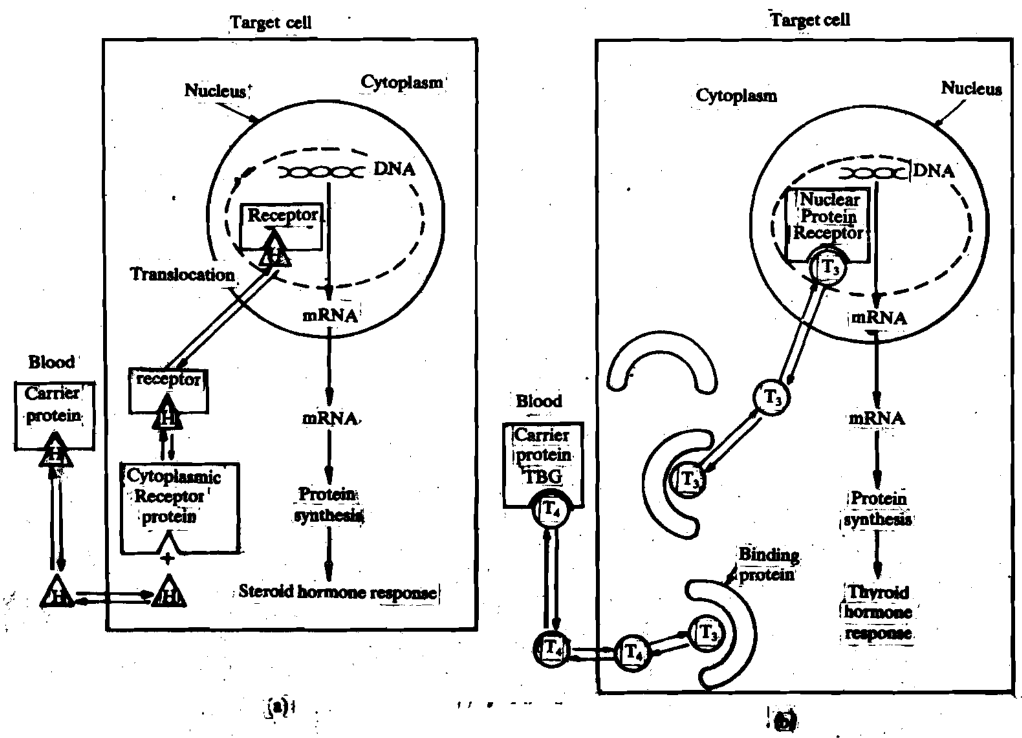

Fig. 10.7 : Molecular action of (a) steroid hormones, (b) thyroid hormone.

The techniques of autoradiography showed that steroid hormones accumulate in the nuclei of target cells but not in the nuclei of other cells. This accumulation occurs very rapidly and remains for some time even after the labelled hormone is removed for circulation. These findings suggested that steroid binding receptors were in the cytoplasm of target cells. By fractionating target tissue (rat uterus) incubated with labelled hormone (estradiol). Roger Gorske (1979) and associates identified the receptor—that was a protein (molecular weight 200,000). This protein binds very strongly to estradiol and was present only in uterine tissue. One significant finding was that substances that have similar hormonal action to that of estradiol are all bound by this protein. This suggests that receptor-steroid complex is an intermediate step in the final action of the hormone. Similar receptor proteins have been identified in target tissues of other steroid hormones.

10.3.2 Peptide Hormones

Protein hormones exert their effect in a different manner than steroid hormones. The hormone does not enter the cell itself but binds to a specific protein receptor on the target cell surface and this results in either

i) stimulation of membrane-bound enzymes or

ii) opening of ion channels in the membrane

In the first system the enzyme activated is **adenylate cyclase** which catalyses the production of cyclic AMP from ATP. A single activated adenylate cyclase can produce about 1000 cyclic AMP molecules per minute so that the enzyme amplifies the interaction of the 1st messenger and receptor (Fig. 10.8). Cyclic AMP operates as the second messenger working inside the cell by activating a set of enzymes known as **protein kinases** which in turn phosphorylate proteins. These proteins can be other enzymes, structural proteins or nuclear proteins and their configuration changes. As a result enzymes may be activated or membrane permeability may change depending on the type of cell.

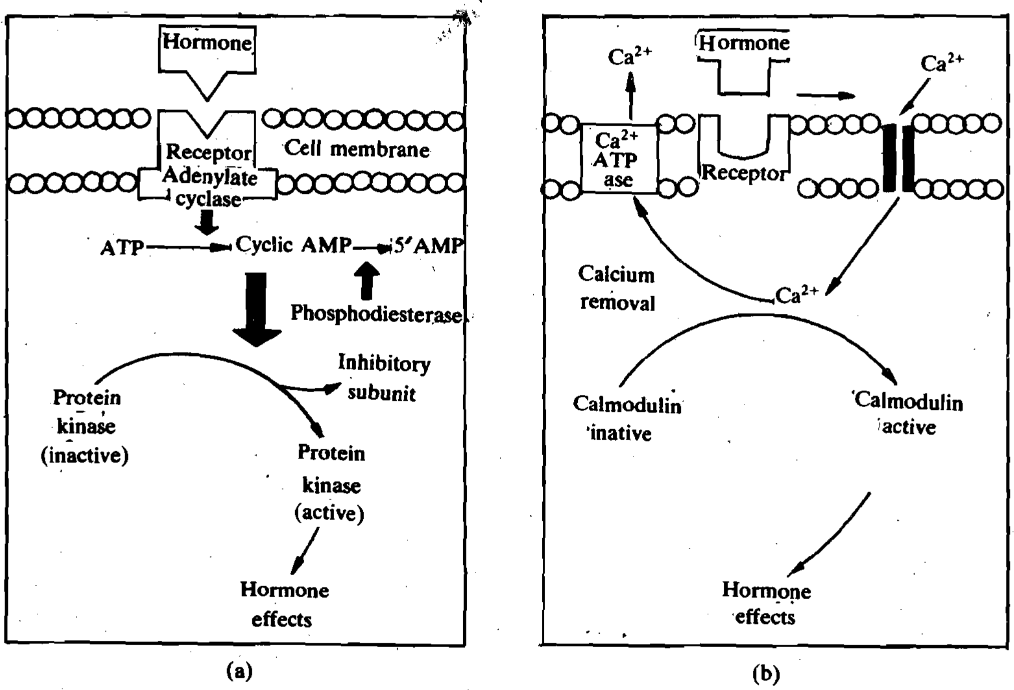

Fig. 10.8: Second messenger concept of hormones
a) By formation of cyclic AMP
b) By Ca-calmodulin system.

In the second system (Fig. 10.8b) the action of receptor and hormone leads to opening of simple ion channels to permit calcium ions (Ca^{2+}) in the membrance. Ca^{2+} enter in and the interaction of 1st messenger and receptor is amplified. Ca^{2+} serves as the second messenger. Many cells produce **calmodulins** (regulatory proteins that depend on calcium) that are analogus to protein kinase. These proteins then produce a wide range of effects depending on the target cell type.

The important feature of these two second messenger systems is that the target cells do not differ in terms of second messenger but in **terms of receptors that are capable of activating the second messenger**. Thus the action of many hormones can be mimicked by raising the level of cyclic AMP or calcium ions by means of various drugs.

In some target cells the Ca^{2+} and cyclic AMP act antagonestically in response to different hormones. For example, Ca^{2+} causes smooth muscles to contract and cyclic AMP causes them to relax. In other situations the two second messengers coordinate or act synergestically (Fig. 10.9 A to D). For example, acetylcholine causes calcium ion gates to open (A) in adrenal medulla to release adrenalin. Medulla cells also have receptors linked to adenylate cylase (B) and a rise in cyclic AMP causes more calcium ions to be released from calcium stores within the cell (C). Thus cyclic AMP acts in coordination with Ca^{2+}. A further rise in cyclic AMP levels increases the synthesis of adrenalin (D).

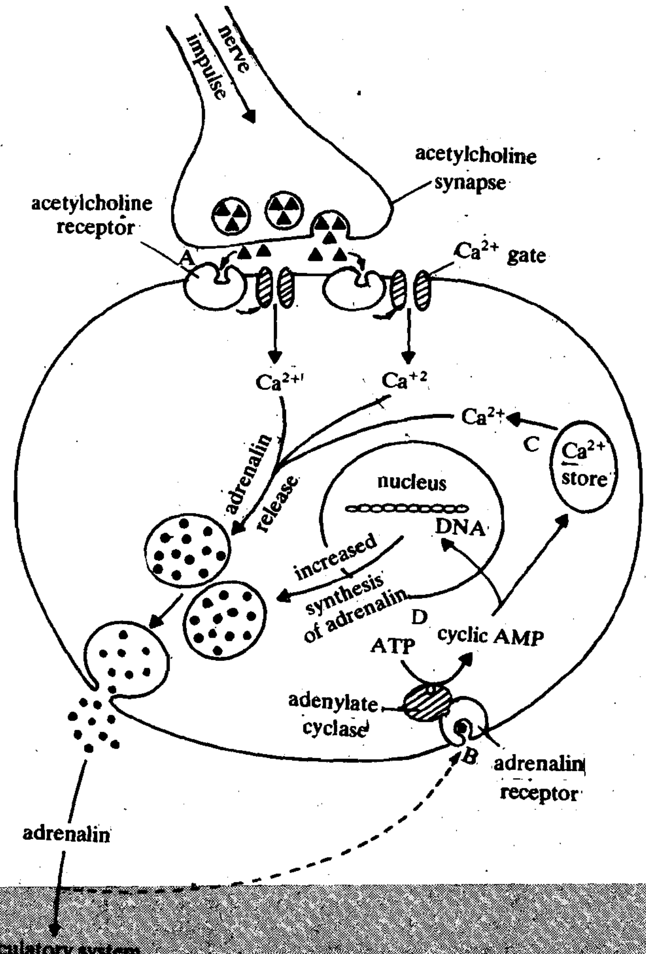

Fig. 10.9 : Factors that affect the synthesis of adrenalin from adrenal medulla (A to D).

SAQ 3

Hormones are known to cause all the following changes in target cells except one:

i) changes in membrane permeability

ii) changes in metabolic rate

iii) increase in AMP concentration inside cells

iv) changes in genetic makeup of cells

v) synthesis of different mRNA and protein.

10.4 NEUROENDOCRINE CONNECTION

Some endocrine glands are part of the central nervous system. There is a close relationship between the neural and endocrine function which we will analyse towards the end of this section.

10.4.1 Hypothalamus and Pituitary

The most obvious neuroendocrine link is between the hypothalamus and pituitary (Box 10.3). The hypothalamus is a part of the brain which is connected to the pituitary gland a small organ situated in the floor of the skull just above the roof of the mouth (Fig. 10.10a)

The pituitary gland was discovered in the 16th century by Vesalius who thought that it was responsible for secretion of pituita (nasal fluid).

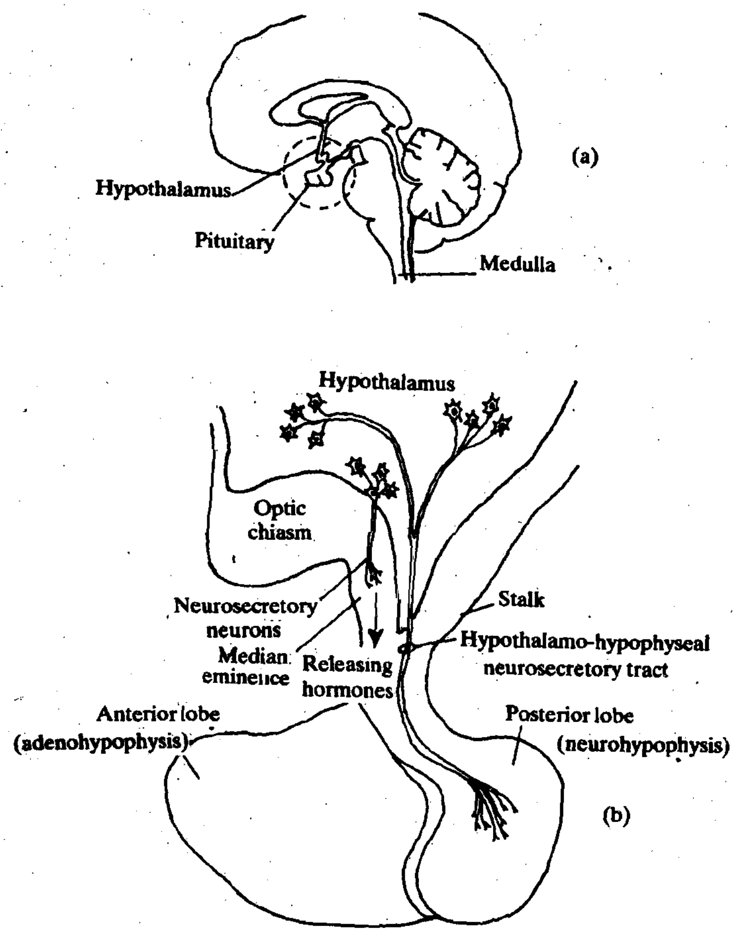

Fig. 10.10: a) Location of pituitary gland and hypothalamus. b) Major components of pituitary-anterior lobe, posterior lobe and stalk. Note the neurosecretary neurous.

Box 10.2

In the 1920s a German scientist Ernst Scharrer observed that the neurons of the hypothalamic region of brain in the bird minnow (*Phoxinus phoxinus*) were: structurally similar to endocrine cells. The axons of these neurons passed out of the hypothalmus, into the pituitary gland. These axons ended into large bulbous swellings that were closely applied to certain blood capillaries passing through the pituitary gland. Scharrer concluded that atleast some of the hormones secreted by pituitary were actually synthesised in the hypothalamus and that pituitary was more of a storage organ. At that time the idea was rejected outright. However, Scharrer and his wife Berta persisted in their studies looking for similar phenomena in other animals. By early 1950s a considerable amount of evidence was collected to support Scharrer's hypothesis in invertebrates. This phenomenon came to be known as **neurosecretion** and the secretory products were called **neurohormones** to indicate their origin in the nervous tissue. The storage organs involved were called **neurohaemal organs** because of the close connection between the blood capillaries and nerve endings in these organs.

The pituitary is also known as **hypophysis**. It is composed of two embryologically distinct tissue. The **anterior pituitary** or **adenohypophysis** is derived from the roof of the mouth and the **posterior pituitary** or **neurohypophysis** is derived from the hypothalamus. Pituitary is joined to the hypothalamus by a slender **stalk** of nervous tissue.

The neurohypophysis consists mostly of **neurosecretory nerve endings** (Fig. 10.10b). The cell bodies of these neurons originate in the hypothalamus. (These were the neurons investigated by Scharrer and his associates). Neurosecretory cells differ from conventional neurons in position and structure of nerve endings. They have more nerve endings so that they secrete greater amounts of neurohormones when stimulated. The size of the neurosecretory granules is also larger (200–500 nm) than those found in other nerve synapses (40–100 nm). These hypothalamic nerve cells synthesise two hormones, vassopressin or **antidiuretic hormone** (ADH) and **oxytocin**. These are transported along the axons, stored and ultimately released from nerve endings, in the posterior pituitary lobe.

The anterior pituitary lobe, however, synthesises and releases atleast 7 peptide hormones. Table 10.2 gives a brief account of their structure and their action on the target tissues.

Table 10.2: Hormones of anterior lobe of pituitary gland

Hormone	Structure	Target Tissue	Action
Adrenocorticotropin (ACTH)	Peptide	Adrenal Cortex	Stimulates synthesis and release of corticosteroids
Thyroid Stimulating Hormone (TSH)	Glycoprotein	Thyroid gland	Stimulates synthesis and release of thyroxin and triidothyronine
Growth Hormone (GH)	Peptide	Liver	Stimulates the liver to produce somatomedins which alter the metabolism of all tissues (liver, muscle, adipose tissue)
Follicle Stimulating Hormone (FSH)	Glycoprotein	Testes and Ovary	Controls development and maturation of germ cells
Luteinizing Hormone (LH)	Glycoprotein	Testes and Ovary	Controls secretion of steroid hormones responsible for male and female sexual characters, also triggers ovulation
Prolactin (PL)	Peptide	Mammary glands	Stimulates milk production
		Corpus luteum	Maintains secretion of estrogens and progesterone
		Liver	Stimulates production of pheromones that control maternal behaviour in some mammals
		Fish gills	Involved in maintenance of salt balance and osmoregulation
Melanocyte Stimulating Hormone (MSH)	Peptide	Pigment cells	Promotes melanin synthesis, (Darkens the skin in lower vertebrates;) controls hair colouration in some mammals; affects activity of some neurons

All except GH and MSH are **tropic hormones** (from Greek for 'to turn' or change) i.e. they stimulate the secretion of other hormones from endocrine glands of the different regions of the body. GH and MSH are direct acting hormones.

The secretory activity of anterior pituitary is regulated by hormones or factors that are secreted by the hypothalamus some are **releasing factors** and some are **releasing-inhibiting factors**. These hormones are all small peptides and named according to their action on the anterior pituitary (Box 10.3). Table 10.3 gives the various factors and there action on anterior pituitary.

Box 10.3

Geoffrey Harris of Oxford University put forward the hypothesis in the 1940s that some neurohormones released in the blood from hypothalmic neurosecretory nerves after electical simulation either inhibit or stimulate the secretion of hormones from the anterior pituitary. This idea was not easily substantiated as it was very difficult to isolate these neurohormones or releasing and release-inhibiting factors.

In 1969, two different groups isolated and chemically identified a releasing factor—the **thyroid-stimulating hormone releasing factor** (TRF) which stimulates the concerned cells of anterior pituitary to release TSH. The two group leaders Roger Guillemin and Andrew Schally were awarded the Nobel Prize for Physiology and Medicine in 1977. According to Guillemin, the cost of isolating the 1st milligram of TRF was stupendous. His group alone extracted 5 million fragments of hypothalmic region from 500 ton of sheep brain over a period of 4 years. The cost was comparable to bringing 1 g of moon rock to earth.

Table 10.3 : Hypothalmic hormones that release or inhibit hormones from anterior pituitary

Hormone	Structure	Action
Corticotropin Releasing Hormone (CRH)	Peptide	Stimulates ACTH release
TSH Releasing Hormone (TRH)	Peptide	Stimulates release of TSH and prolactin
GH Releasing Hormone (GRH)	Peptide	Stimulates GH release
FSH and LH Releasing Hormone or Gonadotropin Releasing Hormone (GrRH)	Peptide	Stimulates release of FSH and LH
GH Inhibiting Hormone (GIH) (somatostatin)	Peptide	Inhibits GH release and interferes with TSH release
Prolactin Release Inhibiting Hormone (PIH) (Tentatives as yet)	Dopamine	Inhibits prolactin release
MSH Release Inhibiting Hormone (MIH)	Peptide	Inhibits MSH release

The releasing factors are carried from the hypothalamus to the anterior lobe via the **porta vessels** (Fig. 10.11 A)

A portal system is a series of blood vessels that carry blood between two sets of capillaries without first returning to the heart.

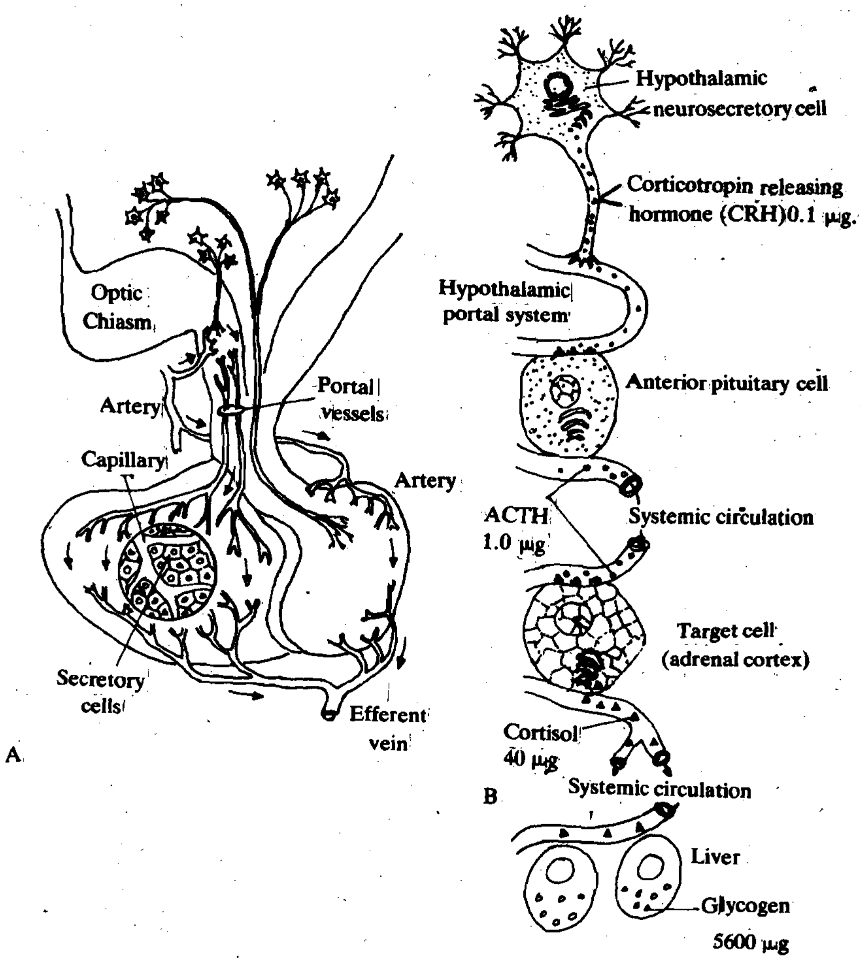

Fig. 10.11 : The hypothalmo-hypophyseal-portal system (A). Amplification in ACTH-endocrine system (B).

By now you would appreciate that the pituitary and hypothalamus are the main centres of physiological control. Unlike the brain, the hypothalamus is not protected by the blood brain barrier hence it detects any changes that take place in the blood stream. Various sensory devices in the hypothalamus also detect any change. Any sensory information from the brain is also routed through the hypothalamus. Thus, it connects the neural and blood borne information and coordinates both sets of inputs to give out and appropriate response. The sequence of hypothalamus ⟶ pituitary ⟶ endocrine gland enables a weak signal to be amplified many times. Examine Fig 10.11 (B) carefully. It shows stepwise, how 0.1 μg of CRF can stimulate the deposition of 5600 μg of glycogen in the liver.

10.4.2 Regulation of Hormone Secretion

The secretion of hormones occurs normally at a basal or 'resting' level. This level is required by the body to regulate the composition of body fluids or the rate of metabolism or other bodily functions. This basal level is raised or lowered by signals acting on the endocrine tissue. The signals may be in the form of neurotransmitters released directly on to the endocine tissue or they may be hormones released from other endocrine tissue.

Endocrine tissues may simply secrete in response to internal or external stimuli without modulation or they may be a part of a **feedback circuit**. You are already familiar with the basic meaning of a feedback circuit (Unit FST-1). The secretion thus is affected by one or more consequences of the secretion.

The secretion from endocrine tissues is generally under **negative feedback control** i.e., the concentration of the hormone itself or a response to that hormone by the target tissue has an inhibitary effect on the further secretion of the hormone. Such negative feedback may be short-looped or long-looped.

Let us take some examples to explain this further. A drop in the calcium level in the blood causes the secretion of parathormone from the parathyroid gland. Parathormone causes the release of calcium from bones, decreases excretion of calcium from kidneys and increases the absorption of calcium from intestines. All these processes increase the calcium concentration in the blood so that it is back to normal within a few hours. The rise in calcium in the blood now inhibits the secretion of parathormone (Fig. 10.12). This is an example of a short-loop negative feedback system. Similar simple feedback loops control hormone secretion from posterior pituitary.

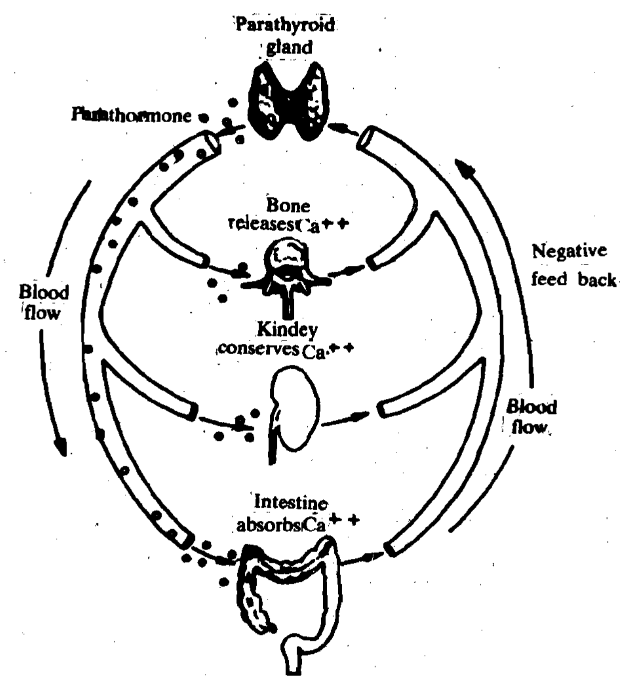

Fig. 10.12 : Feedback control of parathormone secretion

Sometimes inhibition may occur at two sites forming a short and a long loop circuit. Hormone secretion from anterior pituitary is an example of a more complex negative feedback loop (Fig. 10.13).

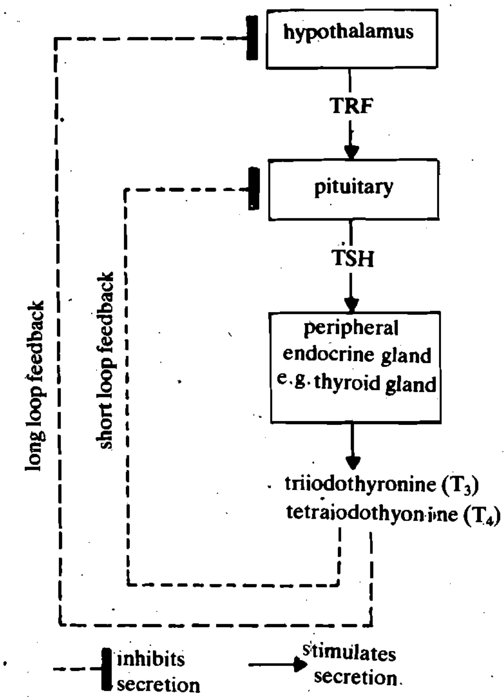

Fig. 10.13 : Feedback control of thyroid hormones as an example of tropic hormones.

A high level of thyroxine in the blood inhibits the release of thyroid stimulating hormone (TSH). This inhibition takes place at the anterior pituitary as well as hypothalamus.

Apart from negative feedback there is also a process of control that feeds upon itself—i.e., the secretion of hormone leads to its increased secretion. This is known as **positive feedback** and occurs in some vertebrate reproductive cycles in which strong response must be built up to a peak relatively quickly.

Upto now we have studied the general principles involved in endocrine functions. Most of the examples used to emphasise a concept have been taken from vertebrates, mammals in particular. In the next section, we shall study the invertebrate hormonal system using some insect hormones.

SAQ 4

a) Given below are some statements that are not entirely incorrect but need to be modified if they are to be precise. Make corrections wherever necessary.

   i) The secretion of hormones from the anterior pituitary lobe is controlled by releasing factors secreted by the brain.

   ii) The cells of the anterior pituitary are connected to the hypothalamus by neurons.

   iii) The secretion of thyroxine is controlled by pituitary.

b) Fill in the blanks with appropriate words from the text.

   Hormone secretion is regulated by a .... control mechanism. A control process that leads to increased secretion of hormone in response to initial secretion levels is known as ....

10.5 INSECT HORMONES

During the last half century, physiologist have seen that many invertebrates too have endocrine systems that approach the complexity of vertebrate endocrine systems. However, there are few similarities in the hormones of both groups of animals.

The principal source of hormones in invertebrates are the neurosecretory cells and their products are secreted directly into the circulation. The most extensively studied group of invertebrates is Insecta hence we shall limit our discussion to hormones found in insects.

Insects being fairly hardy organisms, proved to be ideal subject for the kind of experiments conducted on them (Box 10.4). It has been found that control of development and moulting in insects depends on several major hormones (listed in Table 10.4).

Table 10.4 : Developmental hormones in insects.

Hormone	Tissue of Origin	Structure	Target Tissue	Primary Action
Prothoracicotropin, PTTH (brain hormone)	Neurosecretory cells in brain	Peptide	Prothoracic gland	Stimulates ecdysone release
Ecdysone (molting hormone)	Prothoracic glands, ovarian follicle	Steroid	Epidermis, fat body, imaginal disks	Increases synthesis of RNA, protein, mitochondria, endoplasmic reticulum; stimulates secretion of new cuticle
Juvenile hormone(JH)	Corpus allatum	Terpene derivative	Epidermis, ovarian follicles, accessory sex glands, fat body	In larvae promotes synthesis of larvae structures; inhibits metamorphosis; in adult stimulates yolk protein synthesis and uptake, activates ovarian follicles and accessory sex glands
Bursicon	Neurosecretory cells of CNS	Peptide	Epidermis	Promotes cuticle development; induces tanning of cuticle of newly molted adults
Diapause hormone (silk moth, *Bombyx*)	Neurosecretory cells in subesophageal ganglion	Peptide	Ovaries, eggs	Induces diapause of egg
Eclosion hormone	Neurosecretory cells of brain	Peptide	Nervous system	Induces emergence of adult from puparium

Box 10.4

The first experiments to find whether endocrine secretions control insect development were done by S Kopeč between 1917 and 1922. Kopeč ligated the last instar larvae of a moth at different times during the instar. He found that if the ligation was done before a critical period the insect would develop into an adult anteriorly and remain a larva posteriorly. Cutting the nerve cord was of no effect but if the brain was removed the larvae would not become an adult. Reimplantation of brain, however, allowed pupation to occur. It was ultimately found that a substance secreted from neurosecretory cells of brain induced the prothoracic gland to secrete a hormone that induces moulting. The substance was named **prothoracicotropic hormone** (PTTH).

Fig. 10.14 summarises the role of insect endocrine system in moulting and development.

About a ton of silkworm pupae were required to find out the steroid structure of ecdysone.

1) Neurosecretory cells in the brain synthesise PTTH which is stored in their terminal axons that end in **corpus cardiacum.** The hormone is released into the blood.

2) PTTH in blood activates the prothoracic gland to synthesise the moult-inducing hormone α - **ecdysone** (Fig. 10.3(b)) which is a steroid resembling cholesterol. α-ecdysone is now considered to be a prohormone and is converted to active form β-ecdysone in several target tissues.

3) The corpora allatum contains nonneural endocrine tissue that produce and secrete another hormone-**juvenile hormone (JH)** (Fig. 10.15). This promotes the retention of juvenile characters till larval development is complete.

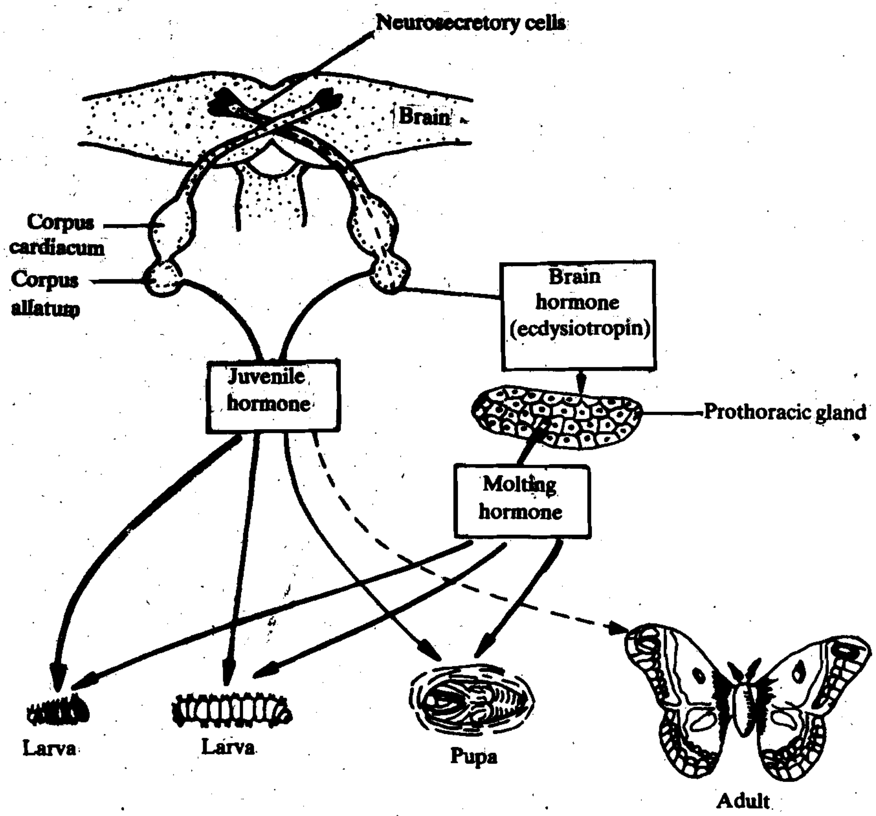

Fig. 10.14 : Role of insect hormones in moulting and development.

The circulating JH level is highest in early larval stage and gradually drops till metamorphosis to adult stage occurs when JH disappears from circulation. The concentration rises again in adult reproductive life. JH promotes development of accessory sexual organs in males of certain insect species and induces yolk synthesis and maturation of eggs in many female insects.

Two additional hormones **eclosion** hormone and **bursicon** regulate the terminal phase of moulting or shedding of the cuticle.

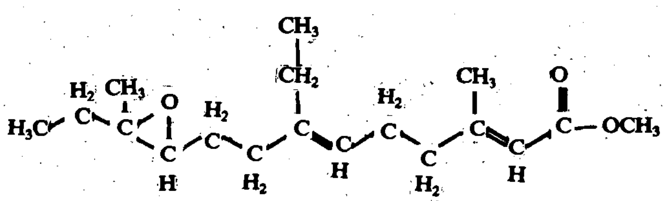

Fig. 10.15 : Structure of juvenile hormone extracted from moth (*Hyalophora cecropia*).

The normal development of an insect depends on precise adjustments in concentration of JH at each stage. Synthetic compounds with juvenile hormone like activities hold great promise as future insecticides. These compounds are effective in very small quantities and if they are applied at the appropriate times, they can prevent the formation of adults and thus reproduction. JH analogs would be a more attractive nontoxic prospect than application of DDT and one against which insects would find it difficult to develop resistance.

SAQ 5

Dysdercus cingulatus, the red cotton bug is a pest on cotton plants. What is the role envisaged for a JH analogue in the control of this pest?

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10.6 PHEROMONES

The word pheromone is derived from Greek word "pherein" meaning to transfer and hormone meaning to excite.

Earlier in the unit we had mentioned about local chemical mediators like histamines, prostaglandins and growth factors. You have read about their mode of action in Unit 15 of LSE-01. You have also studied that both neurotransmitters and hormones are chemical messengers in the body's communication system. While these are chemicals that carry messages inside the body, certain chemicals known as **pheromones** carry information outside the body to other members of the same species.

A pheromone is, therefore, a chemical substance released by an animal into its surroundings which influences the behaviour or development of the individuals of the same species. In many insect species, females release pheromones which function as sex attractants and induce males to come to females to participate in the reproductive behaviour. In honey bee colony, the queen bee produces a chemical called **queen-bee substance** that inhibits development of other queens. Animals of many kinds including protozoa, mammals, fish, amphibian and insects are known to employ pheromones as a primary means of communication, i.e. transmitting information. The pheromonal communication may be used for a variety of purposes in different species: attracting a mating partner, for causing others to stay away when it is appropriate, for directing others to suitable food or resting sites etc.

Mammals in particular use pheromones in urine or faeces or from special scent gland to mark traits and territories. When a dog urinates on a tree, he is depositing a pheromone that will tell other dogs that the tree is a part of his territory. Other large cats such as lions and tigers do the same in the forest. Pheromones also accelerate reproductive maturity in a number of species and permit members of one sex to distinguish which members of the opposite sex are in breeding condition.

The following example will illustrate how pheromones work. Female gypsy moths *Lymantria dispar* emit into a prevailing breeze plumes of a chemical substance known as **gyplure** to "call" male moths that may be hundreds of meters downwind. The male moths are able to recognise the wind-borne pheromone plume by means of receptors located on their antennae. It should be understood that the pheromone emitted by the female contains molecules in a species-specific proportion. The specificity is remarkable since only the males of the particular species will respond to it, and the male will be able to distinguish his species pheromone from another even when many other species are signalling at the same time. The pheromone acts as an odorous (olfactory) stimulus for males. The odor constitutes a message disclosing the presence of conspecific female. Once the male has reached close to the female, male and female exchange another set of messages mediated by chemicals (pheromones), a mating procedure is initiated resulting in copulation. Thus, close-range sexual behaviour is mediated by another set of pheromones. In a few insect species, male insects also produce sex pheromones which facilitate their mating behaviour and may attract females.

Many male animals are known to perform complex courtship displays when near females. For example, male rhesus monkeys continue to groom their sexual partner for quite some time when they smell her sex pheromone. Many male fish perform complex courtship displays when near females, which are caused by pheromones released by female fish. For example, males of the fish *Bathygobius soporator* make rapid fanning and gaping movements and change body colour as courtship behaviour induced by female pheromone.

The pheromones used to mark territories or attract a mate produce immediate effect on the nervous system, physiology and behaviour of the receiving animal.

10.6.1 Neural Basis of Resposes to Sex Pheromones

The ability of insects to detect and discriminate between a variety of pheromones with great sensitivity depends on the presence of specific neural structures in the neuropile of the male antennal lobes. The female antennal lobe lacks these structures. The electrophysiological signals resulting from interaction between pheromonal molecules and antennal olfactory receptors are passed via the olfactory nerve to the specific part of the brain containing specific neural circuitary to decode complex pheromonal signals. The brain then translates pheromonal information into the act of directional locomotion or orientational responses.

There are pheromones that act more slowly and have longer lasting effects. For example, if a newly fertilised female mouse is caged with a strange male, the odor of that male will terminate pregnancy. The pheromone responsible comes from the urine of the male. It is received by the olfactory receptors of the female and triggers activity in the hypothalamus which directs the pituitary to release a hormone that reduces the steroid hormone output of the ovaries. The uterus does not receive adequate hormones for implantation of foetus and the pregnancy aborts.

10.6.2 Phermones Serving Functions Other than Reproduction

Besides sexual responses as described above pheromones mediate several other types of behaviour. **Alarm pheromones** have been found in termites and bees. The termite soldiers liberate alarm pheromones attracting (communicating alarm signals) the aggressive workers that participate in attacking the intrusive individuals. **Trait pheromones** secreted by insects help social integrity during migration of colonies by orienting along an invisible chemical trail that has been laid out by one or more conspecific insects. Both aerial and terrestrial trails are possible. Some species of ants and termites deploy trait pheromones in the recruitment of workers to food sources. **Aggregate pheromones** make it possible for both sexes to aggregate. They are produced by members of both sexes. Pheromone-mediated aggregation help to aggregate insects for feeding, protection, reproduction etc. A pheromone, **2-methoxy-5- ethylaphenol** is produced from faeces of the migratory locust, *Locusta migratoria migratorioides*. The pheromone causes the young hoppers to aggregate and is also associated with the induction of morphological and physiological changes that result in the transformation of the hoppers to the migratory phase. In cockroaches also, the pheromones released from various surfaces of the body and from the faeces cause aggregation. In the protozoan *Dictyostelium discoideum* (amoebae, also known as cellular slime molds) the amoebae release pulses of a pheromone, which has been identified as cyclic 3′–5′ AMP resulting in the aggregation.

10.7 CONCLUSION

Now that you have worked through both Units 9 and 10, you should be able to see clearly the basic principles involved in physiological communication. A stimulus from within or outside the animal triggers the release of chemical messengers that communicate with specific target organs.

In these units we have laid emphasis on the similarities between the action of hormones and nerves not only in their use of chemicals as messengers but also in the way the messengers and receptors interact. But two important differences can be noted:

One related to the speed of action and the other to the size of target. Whenever a quick response is required the nervous system reacts. Nerve impulses move at a speed upto 100 m per second and delay in transmission is hardly more than a few milliseconds. A process regulated by hormones requires that the hormone reach the target organ and this takes place through the blood stream. The minimum response time will be in the magnitude of seconds. Hormones usually control processes that are slow for example the secretion of gastric juices, development of gonads and growth of body.

The second important difference is that action of hormones is diffuse. For instance, hormonal action on liver causes all the cells of the liver to release sugar while neural action permits stimulation of even a single muscle fibre without affecting the others.

However, there is no sharp demarcation between nervous and hormonal control. The nervous system not only regulates the endocrine function it is important in the actual production of hormones. Both systems work hand in hand supervising the animal's complex body functions.

10.8 SUMMARY

In this unit you have studied that :

- Hormones can be broadly subdivided into a) steroids, based on cholesterol structures; and b) polypeptides based on amino acids. The amino acid sequence of a particular polypeptide hormone may vary in different animal species.
- All hormones except steroids are secreted by process of exocytosis; steroids can diffuse through the membrane. Duration of hormone action depends on its longivity and rate of breakdown by liver or excretion from the body. Since receptor cells for hormones are very sensitive and specific, the hormones are required in very minute quantities.
- Steroid hormone receptors lie in the cytoplasm and carry the hormones to the nucleus where it induces transcription activity whereas, receptors for peptide hormones are plasma membrane bound. This results in the formation of a second messenger molecule that interacts with the cellular effectors that may be enzymes, membranes or microfilaments etc. The overall response depends on the particular effector.
- Specialised neurosecretory cells secrete neurohormones into the blood stream which transports them to the target cell. Because of neurosecretory cells, nervous system coordinates the activity of the endocrine system.
- The hypothalamus and pituitary are important centres of physiological regulation. The pituitary gland is divided into two lobes. The anterior lobe which secretes mainly tropic hormones i.e., they regulate the release of hormones from other endocine cells. The hormones of anterior pituitary are in turn regulated by releasing and release-inhibiting factors secreted by neurosecretory cells of hypothalamus. The posterior lobe of pituitary acts as releasing site of hormones produced in hypothalamus.
- The neurosecretory substance → endocrine cell (pituitary) → other endocrine cell arrangement in vertebrates amplifies the original signal. It also forms several feedback loops that finally regulate the whole system.
- Invertebrates also possess endocrine systems. The principal source of hormones are neurosecretory cells. In insects juvenile hormone and ecdysone are the two hormones that control and regulate moulting and development.
- Pheromones are chemical substances that carry information outside the body to other members of the same species and influence their behaviour or development. Pheromones affect the olfactory receptors which transmit the signal to the specific neural circuits to decode the pheromonal signals.
- Communication systems in animals, whether hormonal or nervous basically utilise chemical signals that interact with specific target organs. The two differences, however, are that neural signals are fast acting and can affect even a single cell without affecting others, whereas, hormonal action is slower and diffuse.

10.9 TERMINAL QUESTIONS

1) What are the factors that determine

   a) which target tissue responds to a particular hormone and

   b) duration of response?

   ....

   ....

   ....

2) Compare the action of steroid hormones and protein hormones with respect to

a) structure

b) receptors

c) mechanism of action

....

....

....

3) List the hormones secreted by each of the following endocrine glands and give their action briefly.

a) posterior lobe of pituitary

b) anterior lobe of pituitary

c) adrenal medula

d) β-cells of Pancreas

....

....

....

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4) How does the hypothalamus regulate endocrine activity?

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....

5) Draw a flow chart to illustrate the hormonal control of development in insects.

6) Pheromones are also part of the chemical signal systems in animals. In what way are they different from hormones.

....

....

....

10.10 ANSWERS

Self-assessment Questions

1) i) True. Both neurotransmiter and peptide hormones are composed of amino acids.

ii) False. Hormones in different animal groups may differ slightly in structure so they have different effects on different animals.

iii) True. They are synthesised from cholesterol molecule.

iv) False. Protein-hormone aggregates prevent them from being excreted by kidney. They are a source of slow release of hormones.

2) Chemical messenger; specific regulatory.

3) iv)

4) a) i) Release as well as release-inhibiting factors are secreted by a specific region of the hypothalamus and not the whole brain.

ii) Not by neurons directly but via a portal system in which the neurohormones are released that affect the anterior pituitary.

iii) The hypothalamus is also involved in the feedback loop.

b) negative feedback; positive feedback.

5) Since juvenile hormone suppresses metamorphosis, any compound showing activity similar to its action would result in the larvae retaining their larval characters and never metamorphosise into adults. They are not able to reproduce and increase their population.

Terminal Questions

1) a) Presence of appropriate receptor molecules in the target cells

b) The rate at which the hormone is secreted, the rate at which the hormone is broken down in the liver and the rate at which it is excreted in urine determine the duration of response.

2) Refer to Section 10.3.

3) Refer to Table 10.1 and 10.2.

4) **Hint**: By regulating activity of pituitary gland which in turn stimulates other endocrine glands to secrete hormones. Refer to Section 10.4 for details.

5) a) Neurosecretory cells in brain

↓ PTTH

Corpora cardiacum

↓ PTTH

Prothoracic gland

↓ ecdysone

induces moulting

b) Endocrine tissue in

Corpora allatum

↓ JH

retention of juvenile character.

6) Hormones are chemical signals that carry information **inside the** body while pheromones are chemicals deposited in air or as liquids outside the body that affect the behaviour of other individuals of the same species. Pheromones act on the olfactory receptors which carry the information to the brain which directs an appropriate response.

GLOSSARY

acclimation: the persisting change in a specific function of the body due to prolonged exposure to an environmental condition such as high or low temperature

acclimatisation: the persisting spectrum of changes due to prolonged exposurs to an environmental condition such as high or low temperature

action potential (nerve impulse, spike): an all-or-none electrical event in a neuron or muscle fibre, in which the polarity of the membrane is reversed rapidly, and reestablished

adrenal cortex: the outer part of the adrenal gland derived from embryonic mesoderm. It secretes steroid hormones

adrenal medulla: the inner part of adrenal gland derived from postganglionic sympathetic neurons. Secretes catecholamine hormones

amacrine cells: neurons without axons, found in inner plexiform layer of retina

ambient temperature: surrounding or prevailing temperature

amniotes: any reptile, bird or mammal. Vertebrates whose embryos are enclosed in inner foetal membranes that contain fluid

anaminiotes: vertebrate classes that do not have foetal membranes and fluid surrounding the foetus. Consist of Agntha, fishes and Amphibia

androgens: steroids containing eighteen carbons that have masculinising effects

birth canal: formed by dilation of cervix due to the action of relaxin to facilitate parturation

blastocyst: stage in mammalian development resulting from cleavage. A thin walled hollow sphere containing at one side a knob of cells destined to become embryo proper

blood-brain-barrier: the structure and cells that selectively prevent particular molecules in the plasma from entering the central nervous system.

catecholamines: a group of molecules including epinephrine, norepinephrine, L-dopa, and related molecules that have effects similar to those produced by activation of sympathetic nervous system

circadian rhythms: physiological changes that repeat at about a 24-hour period which are synchronised to changes in external environment such as day-night cycles

corpora allata: nonneural insect glands existing as paired organs or group of cells dorsal and posterior to corpus cardiaca. They secrete juvenile hormone

corpora cardiaca: major insect neurohaemal organs. Paired structures posterior to brain. They liberate brain hormone

estrogens: a family of female sex hormones responsible for producing estrous and female secondary characters

estrous cycle: periodic changes in structure and function of ovaries and female reproductive tract in mammalian species. This is accompanied by a period of receptivity

evaporative cooling: cooling of body by application of saliva which evaporates and lowers the body temperature

GABA: gamma-aminobutyric acid; it is believed to function as inhibitory neurotransmitter in central nervous system

gel state: stiff high-viscosity state of cytoplasm

implantation: attachment of mammalian embryo to lining of uterus preparatory to forming placenta

lordosis: arching of back in female rats in response to handing and when approached by male rats.

lutinisation: formation of corpus luteum and secretion from it

pathological conditions: diseased conditions

puberty: the period of time in an individual's life span when secondary sexual characteristics and fertility develop

secondary sexual characters: characters that distinguish between opposite sexes in animals excluding the gonads, the duct and accessory glands

sol state: low viscosity state of cytoplasm

vaginal smear: scrapings from vaginal wall which is lined by stratified non-glandular epithelium that undergoes cyclic changes

viseral organs: organs lying in abdominal cavity

FURTHER READING

General and Comparative Physiology, William S. Hoar (Third Edition) 1991. Prentice Hall of India Pvt. Ltd., New Delhi.

Dear Student,

While studying the units of this block, you may have found certain portion of the text difficult to comprehend. We wish to know your difficulties and suggestions, in order to improve the course. Therefore, we request you to fill and send us the following questionnaire, which pertains to this block. If you find the space provided insufficient kindly use a separate sheet.

QUESTIONNAIRE

LSE-05
Block-2

Enrolment No.

1) How many hours did you need for studying the units?

Unit Number	6	7	8	9	10
No. of Hours					

2) How many hours (approximately) did you take to do the assignment pertaining to this block?

Assignment Number		
No. of hours		

3) In the following we have listed 4 kinds of difficulties that we thought you might have come across. Kindly tick (√) the type of difficulty and give the relevant page number in the appropriate columns.

Page Number and line Number	Type of difficulties			
	Presentation is not clear	Language is difficult	Diagram is not clear	World/Terms are not explained

4) It is possible that you could not attempt SAQs and TQs. In the following table are listed the possible difficulties. Kindly tick (√) the type of difficulty and the relevant unit and question numbers in the appropriate columns.

Unit No.	SAQ No.	TQ No.	Type of Difficulties			
			Not clearly posed	Cannot answer on basis of information given	Answer given (at end of Unit) not clear	Answer given is not sufficient

5) Where all the difficult terms included in the glossary? If not please list the words in the space given below.

6) Any other suggestion(s) :

To

The Course Coordinator (LSE-05; Physiology; Blocks 1 & 2)
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