16 ENDOCRINE SYSTEM

There are two types of glands in the body : (1) Exocrine glands and (2) Endocrine glands. Exocrine glands possess the ducts through which secretions are poured externally via ducts. Salivary glands, lachrimal glands, gastric glands etc. are the examples of the exocrine glands.

Endocrine glands are the ductless glands which pour their secretions directly into the blood. These glands are richly supplied with blood and their secretions are named as hormone (*Endo* = inside; *Crinos* = secretions). Endocrine system forms a part of the communication system of the body and provides an alternative method of communication with the nervous system.

Hormones are the chemical messengers, secreted in small amounts by the endocrine glands which travel all over the body via blood to affect distant organs. Chemically, hormones may be peptides (anterior pituitary hormones, insulin and glucagon), steroids (adrenocortical and gonadal hormones), amines (adrenaline and noradrenaline) or derivatives of aminoacids (thyroxine).

Characteristics of hormones :

1. *Action in low concentration :* Hormones act in very low concentrations, like the vitamins.

2. *Storage, metabolism and excretion :* Hormones are usually synthesized and stored in the gland itself (except for posterior pituitary hormones which are synthesized in hypothalamus but stored in posterior pituitary gland). They are rapidly destroyed after their functions are over and hence, they do not have any cumulative action.

3. They never produce new action but modify the physiological functions of the body. In other words, they have a *regulatory role* on the physiological functions.

4. *Distant target organs :* Hormones usually produce their effects at the target organs in the body situated far away from the glands.

Various established endocrine glands and their hormones are summarised in Table 16.1

Mode of action of different hormones : Actual mechanisms by which hormones produce the effects are not very clear, however, various mechanisms of action have been proposed. Most hormones bind to their specific protein receptors on plasma membranes of target cells. Steroids form complexes with cytoplasmic proteins which attach to nuclear receptors.

Thyroid hormone penetrates the cell to adhere to nuclear receptors. These hormones which bind to nuclear receptors affect the synthesis of proteins. The effect may be an increase or decrease in the synthesis of proteins.

Hormones that bind to the receptors on plasma membranes may alter protein synthesis, cellular permeability or the production of secondary messengers. The common second messenger involved is cyclic adenosine 3'-5' monophosphate (cAMP). This is a nucleotide which is formed by the activation of membrane bound enzyme adenylate cyclase when certain hormones bind to cell membrane receptors. Increase in cAMP activates

Table 16.1 : Endocrine glands and their hormones

Endocrine gland	Hormonal secretions
1. Pituitary (Anterior)	Growth hormone (GH)
	Prolactin
	Thyrotrophic hormone (TSH)
	Follicle Stimulating hormone (FSH)
	Leutenizing hormone (LH)
	Adrenocorticotrophic hormone (ACTH)
Pituitary (Intermediate)	Melanocyte stimulating hormone (MSH)
Pituitary (Posterior)	Oxytocin
	Vasopressin
2. Thyroid	Tri-iodo-l-thyronine (T_3)
	Thyroxine (T_4)
	Calcitonin
3. Parathyroid	Parathormone
4. Adrenal or suprarenal	Glucocorticoids e.g. cortisone
	Mineralocorticoids eg. aldosterone
	Sex-steroids e.g. progesterone, estrogen and androgens
	Adrenaline
5. Pancreas	Glucagon
	Insulin
	Somatostatin
6. Testis	Testosterone
7. Ovary	Estrogen
	Progesterone

protein kinase in the nucleus or cytoplasm, producing metabolic and physiological responses. These include the degradation of protein, fat and glycogen, the relaxation of smooth muscles in various organs and contraction of cardiac muscles. Some hormones bind to receptors which cause an increase in cGMP (cyclic guanine monophosphate) to produce opposite effects.

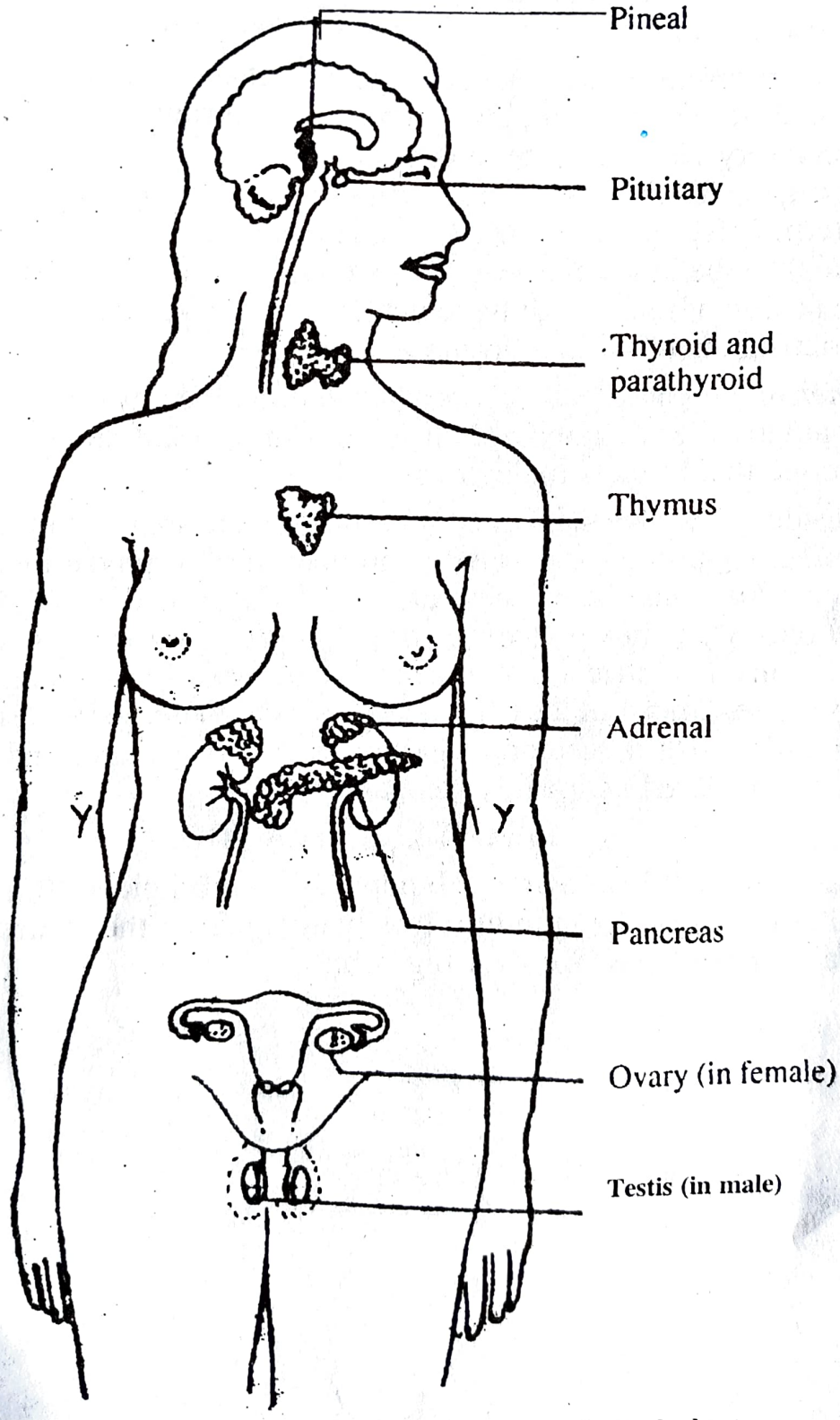


Fig. 16.1 : Endocrine glands and their location in the body

The term hormone is often confused with various other related substances like local hormones, neurohormones, pheromones, neurotransmitters etc.

Neurohormones are the chemical agents that are synthesized by special neurons and function like gland cells. Such neurons are often called neurosecretory cells. Examples of neurohormones are oxytocin, vasopressin (or antidiuretic hormone) and various hormone releasing factors produced by neurosecretory cells of hypothalamus in the brain.

Neurotransmitters are chemical agents that are synthesized by neurons and stored in their terminals. Here, the neurons do not work like neurosecretory cells and the substances released, may act locally or at distant organs. Examples are noradrenaline (at adrenergic or sympathetic nerve terminals), acetylcholine (at parasympathetic or cholinergic nerve terminals), dopamine, and GABA (γ-aminobutyric acid). Adrenaline is synthesized in adrenal medulla which is not a nerve ending, so it is not a neurotransmitter but it is a hormone.

Pheromones are chemical agents that affect the physiology of animals in a population. For example, female dogs in heat are known to release a pheromone that attracts male dogs.

Besides the above mentioned substances, there are substances produced locally in response to a stimulus and produce various physiological actions in very minute quantities. These are popularly termed as local hormones or autacoids. Histamine, 5-hydroxytryptamine or serotonin, prostaglandins, prostacyclins, leucotrienes, angiotensin, renin, bradykinin, kalidin etc. are the common examples of local hormones. Besides these, some gastrointestinal secretions like gastrin, secretin, enterogastrin, cholecystokinin and enterokinin are also considered as local hormones.

PITUITARY GLAND

Anatomy : It is known as Hypophysis-cerebri gland. It is situated in the sella-turcica of the cranium. It is hanging from the centre of base of the brain. It is of the size of a big bean.

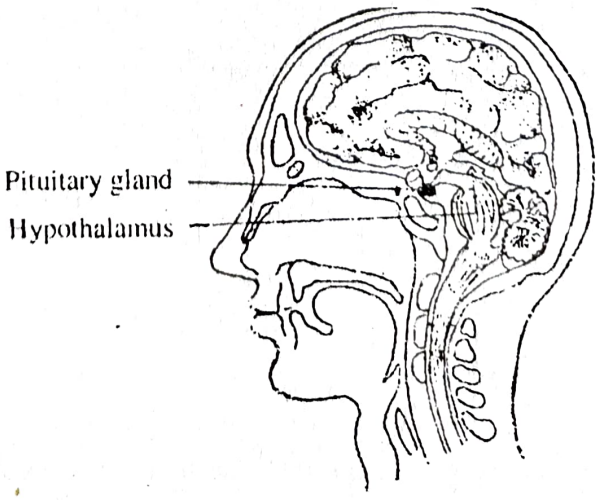


Fig. 16.2 : The location of pituitary gland

The pituitary gland is divided into three parts :

1. Pars anterior or Anterior pituitary
2. Pars intermedia.
3. Pars posterior or Posterior pituitary.

Pars-anterior or Anterior pituitary : It consists of three types of cells :

1. *Acidophilic cells :* These cells are stained with the acidic dyes and secrete growth hormone or somatotrophin and prolactin.

2. *Basophilic cells :* These cells are stained with the basic dyes. They secrete Thyrotrophic or Thyroid Stimulating Hormone (TSH) and the Gonadotrophic hormones namely Follicle Stimulating Hormone (FSH) and Leutenising hormone (LH).

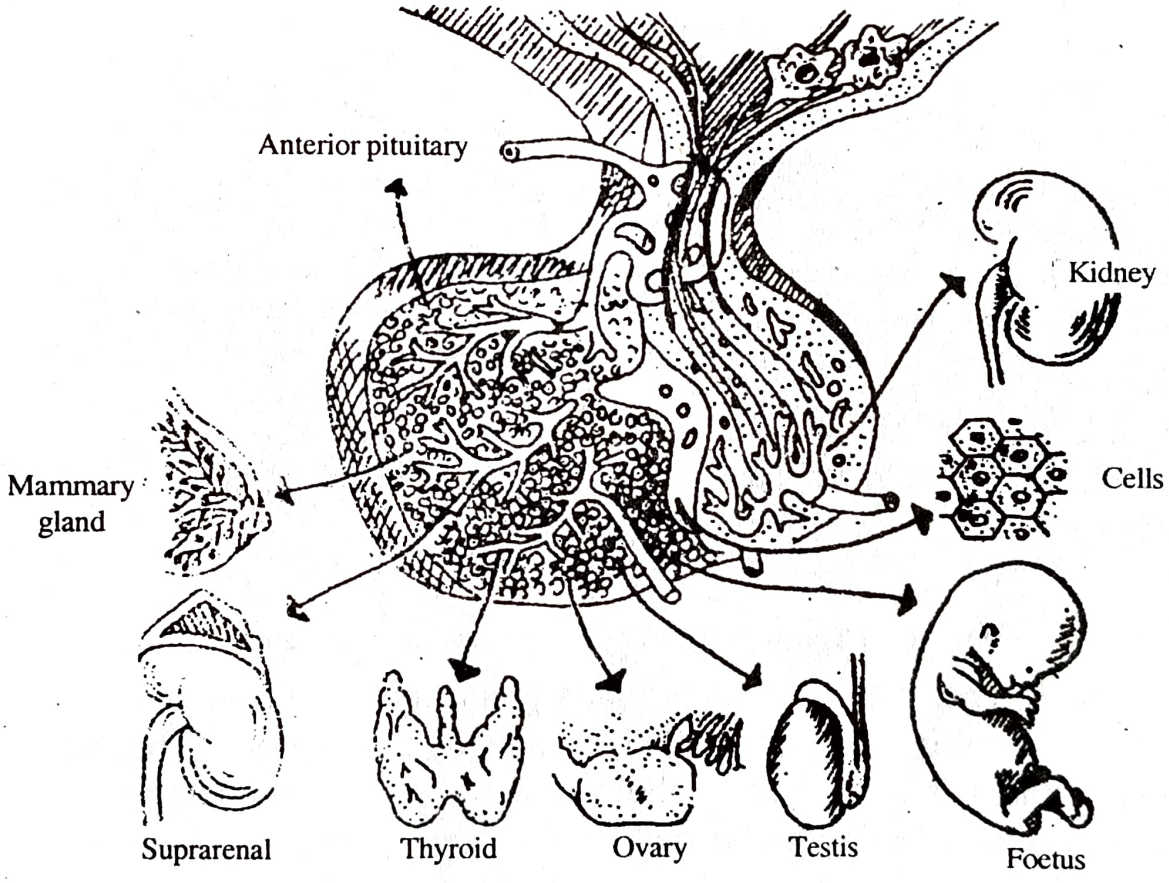


Fig. 16.3 : Pituitary gland and its control on other endocrine glands

3. *Chromophobe cells :* These cells do not take up any stain. They secrete Adrenocorticotrophic hormone or adrenal-cortex stimulating hormone (ACTH).

Regulation of hormonal secretion : The feed-back Mechanism

The anterior pituitary hormones besides controlling growth and metabolism of protein, fat and carbohydrates, control the other endocrine glands. The pituitary gland is thus described as the *'master-gland'*.

Any fall of the hormone level (e.g. thyroid hormone) in the blood, stimulates the hypothalamus which secretes the respective releasing factor (e.g. growth hormone releasing factor, thyrotrophic releasing factor. This is turn stimulates the pituitary gland to secrete the trophic hormone (viz. thyrotrophic hormone) which finally stimulates the gland to increase the release of that particular hormone. This process of stimulation of a particular endocrine gland in response to decrease in the hormone level in the blood is known as *Positive Feed-Back Mechanism* (Fig. 16.4).

The processes are reversed when there is rise of a particular hormone. The process of inhibition of a particular endocrine gland (Fig. 16.4) in response to increase in the hormone level in blood is described as *Negative Feed-back mechanism.*

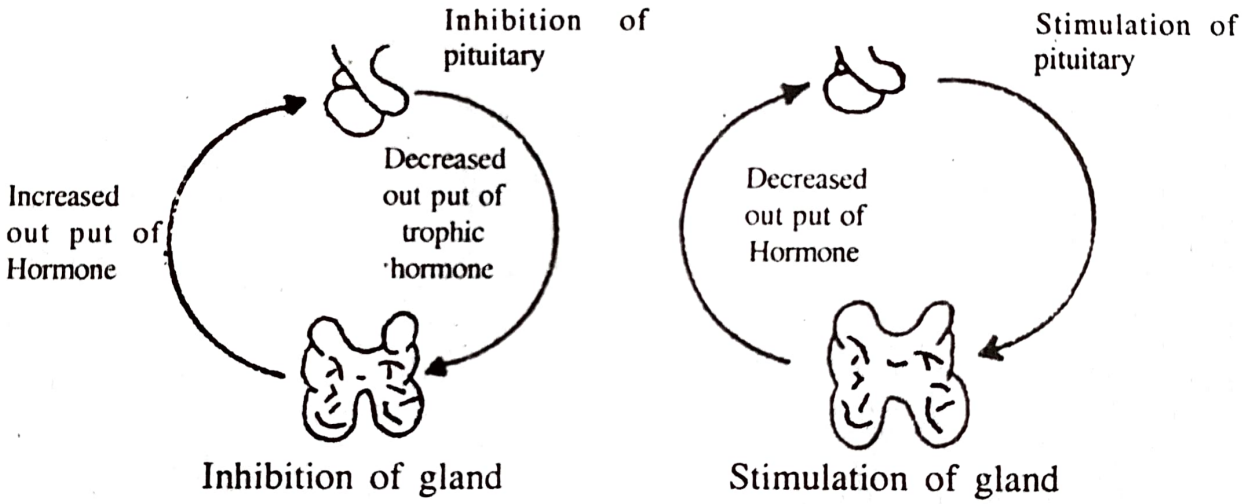


Fig. 16.4 : The negative and positive feed-back mechanisms

Thus, although the anterior pituitary gland controls the other endocrine glands, it is ultimately controlled by the hypothalamus. The anterior pituitary gland is described as the 'orchestra' and hypothalamus as the 'queen of the endocrine orchestra.'

Growth hormone or Somatotrophic hormone (GH or STH) :

It is secreted by acidophil cells of anterior pituitary gland and is proteinous in nature. The main function of growth hormone is to increase the body growth in general. It stimulates the multiplication of epiphyseal cartilage and thus increases the length of the cartilage. Growth of skeletal muscles and thymus gland is also stimulated. It increases the secretion of milk during lactation.

Besides the general effect on growth of the body, GH also produces its effects on metabolism.

Protein metabolism : GH increases nucleic acid and protein synthesis, decreases nitrogen excretion in the urine and causes retention of nitrogen. In other words, GH produces anabolic effects. These effects of growth hormone are brought about through insulin.

Fat metabolism : GH causes mobilization of peripheral depot of fat to the liver. The free fatty acid level in plasma rises and the oxidation of fat is increased by GH. This provides more energy for the utilization of aminoacids in the protein synthesis.

Carbohydrate metabolism : GH produces increase in blood sugar level. This leads to over production of insulin which finally may get exhausted resulting in the status of diabetes mellitus.

Ion and mineral metabolism : GH increases intestinal absorption of calcium as well as its excretion. It also causes retention of sodium, potassium, magnesium, phosphate and chloride.

Regulation of growth hormone secretion : As mentioned above (under feed back mechanism) secretions of all hormones are regulated by hypothalamus. Decrease in GH in blood, hypoglycaemia, exercise, fasting, protein meal, infusion of aminoacids specially arginine, increase in glucagon, pyrogen, or deep sleep are the stimuli which cause hypothalamus to release growth hormone releasing factor (GHRF). This stimulates anterior pituitary gland to release its growth hormone. Increase in GH in blood, causes inhibition of the release of GH by negative feed back mechanism.

Dysfunction of acidophilic cells of anterior pitutary : Hypersecretion of GH in the young causes *'Gigantism'* whereas, in adults, it causes *Acromegali.* Hyposecretion of GH in young causes *Dwarfism* and in adults *'Acromicra'* (Fig. 16.5)

In 'gigantism', the patient is very tall (7-8 ft). The development of muscles and viscera is proportionally greater. Patient has hyperglycemia, glycosuria, with increased B.M.R. and sweating. Gigantism starts from adolescence.

Fig. 16.5 : Gigantism and Acromegali

In 'Acromegali' there is overgrowth of the two jaws, the molar bones, the supraorbital ridges etc. Hands and feet are also enlarged and there is bowing of the spine. There is increase in the amount of subcutaneous tissue of the hand, feet, scalp, nose, lips and skin. The tongue is also enlarged. Metabolism is also increased and the patient shows hyperglycemia, glycosuria, increased B.M.R. and sweating. Acromegali starts after puberty.

Dwarfism is characterised by decrease in the height of the patient (about 3 ft or less). The sex organs may not grow but intelligence is normal and proportionate to age. The metabolism is also normal.

In 'acromicra' the bones of hands, face and feet are small. There is loss of hair and sexual functions. This condition however, is very rare.

Prolactin or Lactogenic hormone or Luteotrophic hormone :

It is a peptide hormone secreted by acidophil cells. This hormone is responsible for lactation in the post partum state of women. During last phase of pregnancy for milk secretion the breast are prepared by estrogen and progesterone. GH helps in initiation and the maintenance of milk secretion. Prolactin also stimulates the proliferation of glandular element of the mammary glands during pregnancy. It also helps in maintenance of secretory activity of corpus luteum.

Like GH, the secretion of prolactin is also controlled by hypothalamus through prolactin releasing factor.

Thyrotrophic hormone or Thyorid stimulating hormone (TSH) :

It is chemically glycoprotein and as the name suggests it controls the activity of thyroid gland. The release of thyrotrophic hormone in turn is controlled by thyroxine level in the blood through TSH releasing factor secreted from the hypothalamus.

Adrenocorticotrophic hormone (ACTH) :

It is a polypeptide hormone secreted by chromophobe cells of pituitary gland. As the name suggests, it controls the secretions of adrenal cortex. The action of ACTH is mediated through cAMP. The secretion of ACTH is controlled by ACTH releasing factor. Condition of stress also controls ACTH secretion.

Gonadotrophic hormone :

Basophil cells of anterior pituitary gland, secrete two principle hormones namely follicle stimulating hormone (FSH) and luteinising hormone (LH) in females and males both or interstitial cell stimulating hormone (ICSH) in males. They are chemically glycoproteins.

FSH stimulates the Graffian follicles for oogenesis and secretion of estrogen in females. In males, it stimulates spermatogenesis.

LH is responsible for the complete development of follicles to secretory stage and secretion of estrogen. In addition, it also stimulates the formation of corpus luteum. In males, LH stimulates the interstitial cells of the testes to secrete testosterone.

Both FSH and LH are essential for the rupture of follicles and ovulation.

Pars intermediate is not much understood. It secretes the melanocyte stimulating hormone (MSH) in animals. This hormone does not seem to have specific role in human beings.

Pars posterior or posterior pituitary gland is nervous in nature. It does not produce any hormone but stores and releases two hormones synthesized in the hypothalamus. These hormones reach the posterior pituitary gland through hypophyseal portal system. The hormones are 1. Vasopressin or Antidiuretic hormone and 2. Oxytocin

Antidiuretic hormone (ADH) or Vasopressin

It is a polypeptide hormone released from posterior pituitary. Its main actions are : (1) Constriction of capillaries and blood vessels to raise blood pressure and (2) Retention of Na^+ and thus reducing the urine volume. Due to rise in blood pressure it causes cardiac slowing and hyperpnoea with occasional apnoea by reflex mechanism. The intestinal muscles are also stimulated by vasopressin.

Decrease in plasma volume increases osmotic pressure of the blood. This causes release of vasopressin. Other stimuli for vasopressin release are pain, stress and hypoxia. Decrease in plasma volume or osmotic pressure of blood and stimulation of atrial receptors inhibits the release of vasopressin through hypothalamus.

Oxytocin : It is a polypeptide hormone of posterior pituitary gland. The main action of oxytocin is contraction of uterus. In addition, it also causes contraction of myoepithelial cells in the ducts of glands to expell the accumulated milk from the mammary glands. It facilitates transport of sperms in non-pregnant female genital tract. Oxytocin also stimulates contraction of gall bladder, intestine and urinary bladder.

THYROID GLAND

Anatomy : Thyroid gland is situated on the thyroid cartilage, in centre of the neck and in front of the trachea. It has one lobe on each side with a linking isthmus in the centre. Sometimes, an accessory gland is also found. Shape of thyroid gland resembles a butterfly. On its back, there are two beads like structures on each side, the parathyroid glands.

Histologically thyroid gland is composed of a mass of hollow spheres or follicles. Each follicle has a lining of one cell thickness and contains a jellylike colloid. (Fig. 16.7)

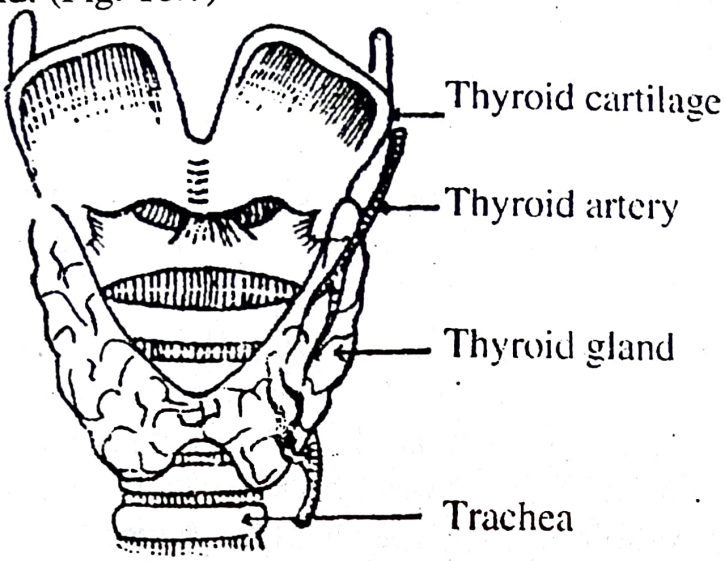


Fig. 16.6 : Location and gross structure of thyroid gland

Biosynthesis, storage and transport of thyroid hormones :

The lining cells of thyroid follicles have a remarkable ability to extract iodide from the blood. This process is known as *iodine trapping*. This is an active transport mechanism and it is stimulated by thyrotropic hormone from anterior pituitary gland.

The trapped iodide is converted into iodine in the thyroid follicles. This iodine combines with the aminoacid tyrosine to form monoiodotyrosine (MIT) and di-iodotyrosine (DIT). Iodination takes place at 3rd and 5th positions of tyrosine. The next step is coupling or condensation of MIT and DIT. Two molecules of DIT from tetraiodothyronine or thyroxine (T_4), whereas, one molecule of DIT and other molecule of MIT combines to form tri-iodothyronine (T_3). The intermediate compounds, T_3 and T_4 and are stored in the colloid of the follicles. They are bound to thyroglobulin which is a high molecule protein.

T_3 and T_4 are released in the blood from thyroglobulin by lysozymes. The released T_3 and T_4 are bound to other proteins in plasma namely thyroxine binding alpha globulin and thyroxine binding pre-albumin. T_4 is bound much more firmly than T_3 and hence T_3 is quickly acting and short lasting whereas, T_4 is slow but long acting.

Since T_3 is more active than T_4, it is also derived from T_4 by removal of one iodine molecule through the enzyme deiodinase. In fact, it is the major source of T_3 in the body. Both T_3 and T_4 are metabolised in the liver and peripheral tissues by deamination and decarboxylation to form

triodothyroacetic acid and tetraiodothyroacetic acid and are excreted in urine.

Functions of thyroid gland :

1. Calorigenic : Thyroid hormones increase oxygen uptake, calorie production and basal metabolic rate (BMR).

2. Metabolism : They stimulate the carbohydrate and protein metabolism and mobilise Ca^{+2} and PO_4^{-3} from the bone.

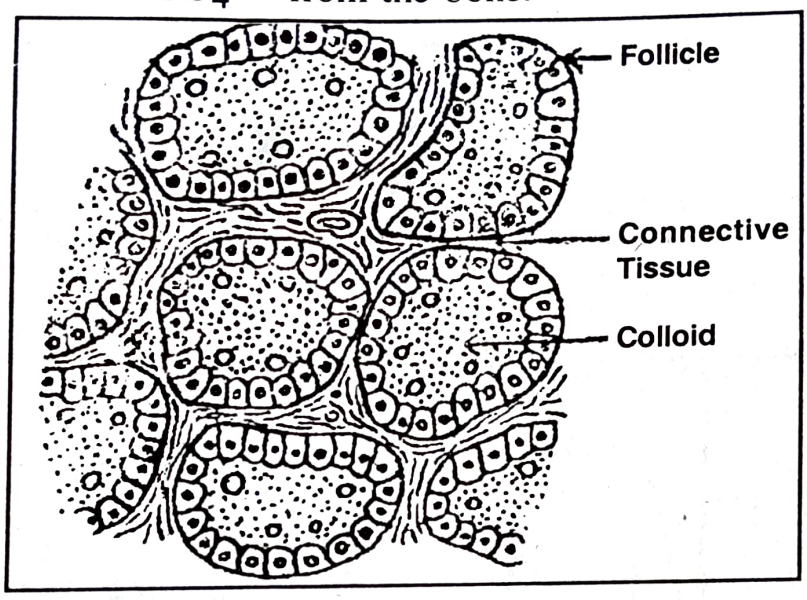


Fig. 16.7 : T.S. of thyroid gland

3. Growth : Thyroid hormones also stimulate growth.

4. Mammary Glands : Milk-secretion and fat-content are increased by thyroid hormones.

5. Heart : Heart rate is increased by direct action of these hormones. Hence, tachycardia and palpitation are the common signs of hyperthyroidism.

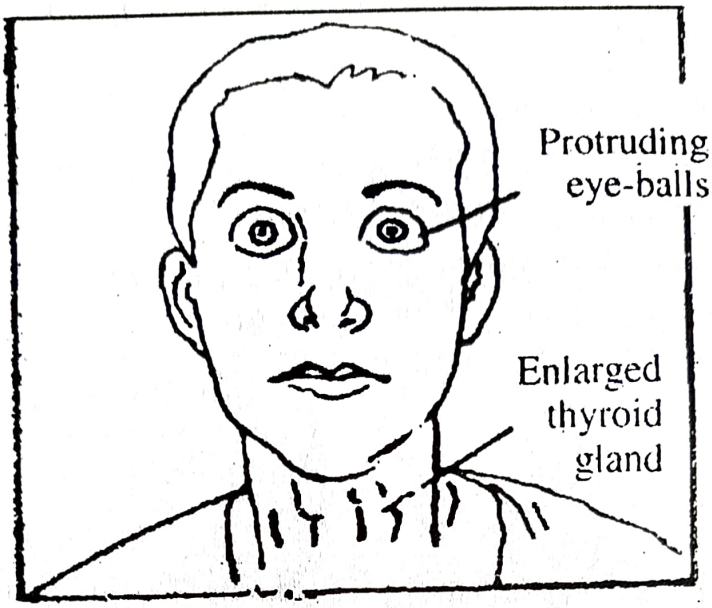
6. Kidney : Thyroid hormones act as diuretic and excrete nitrogenous end products like creatinine and salts by stimulating metabolism.

7. Release of Calcitonin : It is a polypeptide hormone produced by the para follicular cells of thyroid gland. It lowers the concentration of calcium ions in the blood and causes deposition of calcium in bones.

Thyroid Dysfunctions : These are Hypothyroidism and Hyperthyroidism.

A. Hypothyroidism : It develops due to deficiency of thyroid hormone. It is called 'Cretinism' in children and 'Myxoedema' in adults. In addition there may be colloidal goitre.

1. Cretinism : The child is stunted in growth and height. Its face is bloated and the child remains idiotic. BMR is low. If pregnant women is suffering from hypothyroidism, child born may have abnormalities. Hence, it is advised that pregnant women must take iodized salt to prevent hypothyroidism and its consequences on to the new-born.



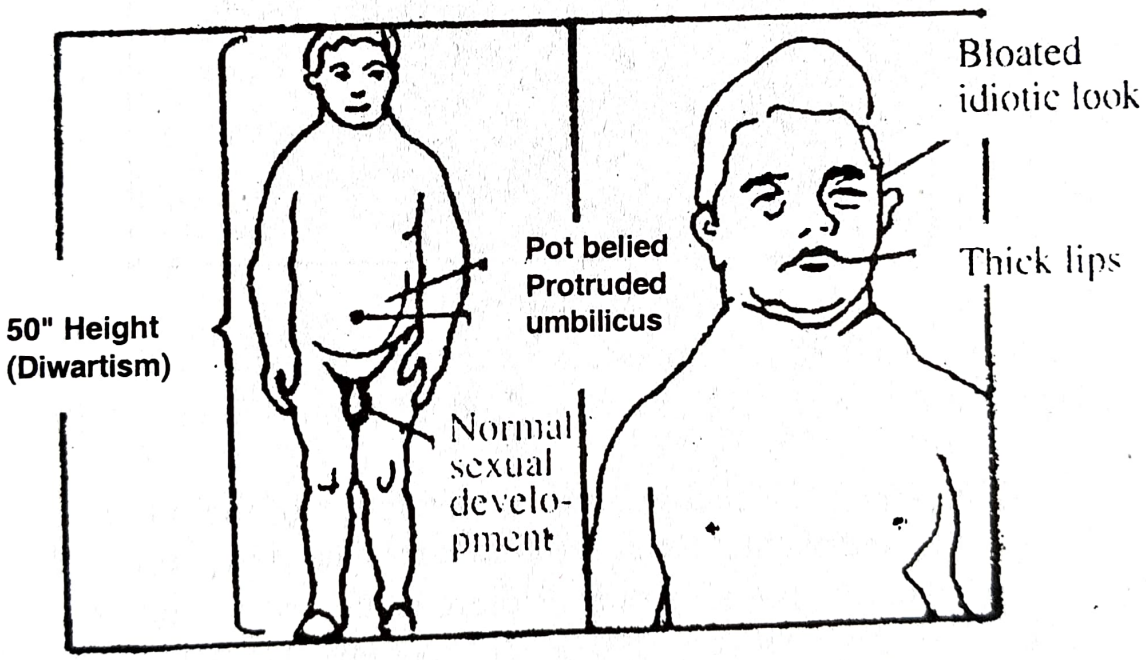


Fig. 16.8 : (b) Cretinism or hypothyroidism in child

2. *Myxoedema :* In this condition the patients have puffy face with filter-paper like dry skin, scanty hair, slow speech, decreased intelligence, amenorrhoea (in females), slow pulse and low B.M.R.

3. *Goitre :* It is the condition of hypothyroidism in which the neck gets swollen with colloid due to iodine deficiency. This disease is found in Alps and Himalayas where water does not contain iodine.

B. Hyperthyroidism : It is called 'Grave's disease' and also "Exophthalmic goitre". So named because the eyes seem to be bulging out in the patient. Really, the eyelids are drawn up, due to sympathetic stimulation and eyes therefore, look staring. The weight is rapidly lost, mind is anxious and sharp, skin is soft and red, heart beats fast, muscles show tremors and urine contains sugar. BMR is very high. Picture of hyperthyroidism is like a fast burning human mail train engine.

PARATHYROID GLAND

There are four parathyroid glands which are normally found on the posterior surface of the thyroid gland. Each gland consists of a closely packed mass of two types of cells. One of these types of cells secrete the hormone parathormone.

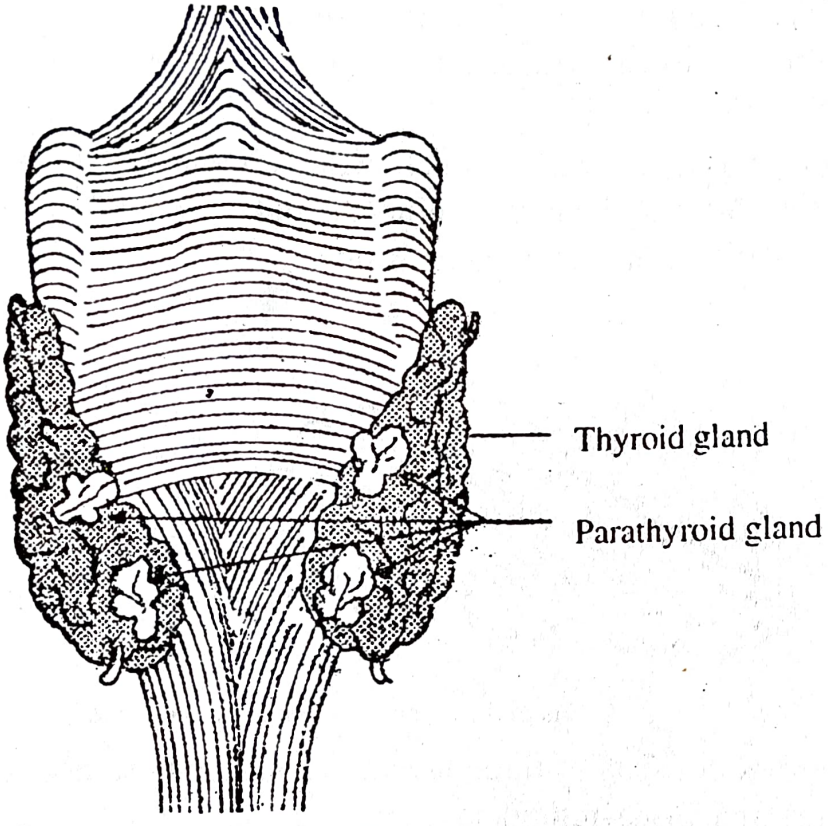


Fig. 16.9 : The parathyroid glands (Posterior view) (4 in number)

Parathormone is a polypeptide hormone concerned with control of calcium ion concentration in the blood. It is secreted in response to a fall in calcium ion concentration and it tends to raise it.

Parathormone produces its effect by :

1. *Mobilisation of calcium ions* from the bones by stimulating the bone cells.
2. *Prevention of loss of calcium ions* in the urine, by promoting reabsorption of calcium ions from the tubules back into the blood;
3. *Increasing the absorption of calcium* from the gut. It is however, much less important than vitamin D in this respect. Parathyroid hormone (parathormone), calcitonin and vit. D are the chief hormones regulating the calcium ion concentration of blood. Calcitonin and Vit. D work synergistically to increase the deposition of calcium in the bone and decrease the calcium level in blood. Parathormone has opposite or antagonistic effect to calcitonin and

Vit. D. It produces increase in calcium level in blood by mobilizing calcium from the bones. (For the details of calcium regulation refer fig 12.12)

ADRENAL OR SUPRARENAL GLAND

There are two adrenal glands, situated on the top of each kidney. It is therefore, also named as suprarenal gland. They fit like a cap on each kidney.

Structurally as well as functionally adrenal gland is divided into two parts, the cortex and medulla. Whole gland is covered by connective tissue capsule which sends trabeculae inside.

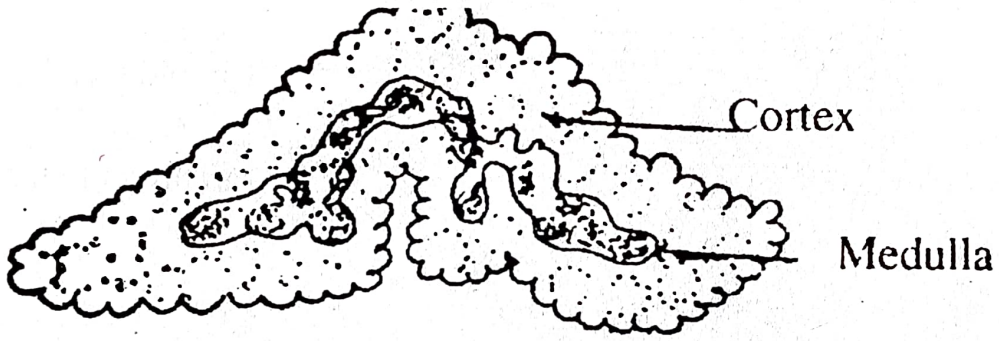


Fig. 16.10 : Adrenal or Suprarenal gland

Cortex consists of three layers : Zona-glomerulosa, Zona-fasciculata (radiata) and Zona-reticulata.

Zona glomerulosa consists of 2-3 layers of columnar cells arranged parallel to the surface, in the alveoli form. This layer secretes, *mineralocorticosteroids*-aldosterone.

Zona fasciculata or radiata comprises of polyhedral cells arranged in perpendicular rows. This layer secretes *glucocorticosteroids*-cortisone, corticosterone, 11-dehydro- or 17-hydrocorticosteroids. This layer occupies the largest part.

Zona reticulata is an irregular network of rows of cells. The meshwork of cells is filled with sinusoids lined by reticuloendothelial cells. This layer secretes various sex *hormones :* progesterone, estrogen, and androgens.

Adrenal medulla lies in central part of the gland. The cells are larger and more deeply staining than the cortex. Cells are arranged in groups or clusters and between them are large and small blood sinusoids. The secretion of adrenal-medulla is *adrenaline.*

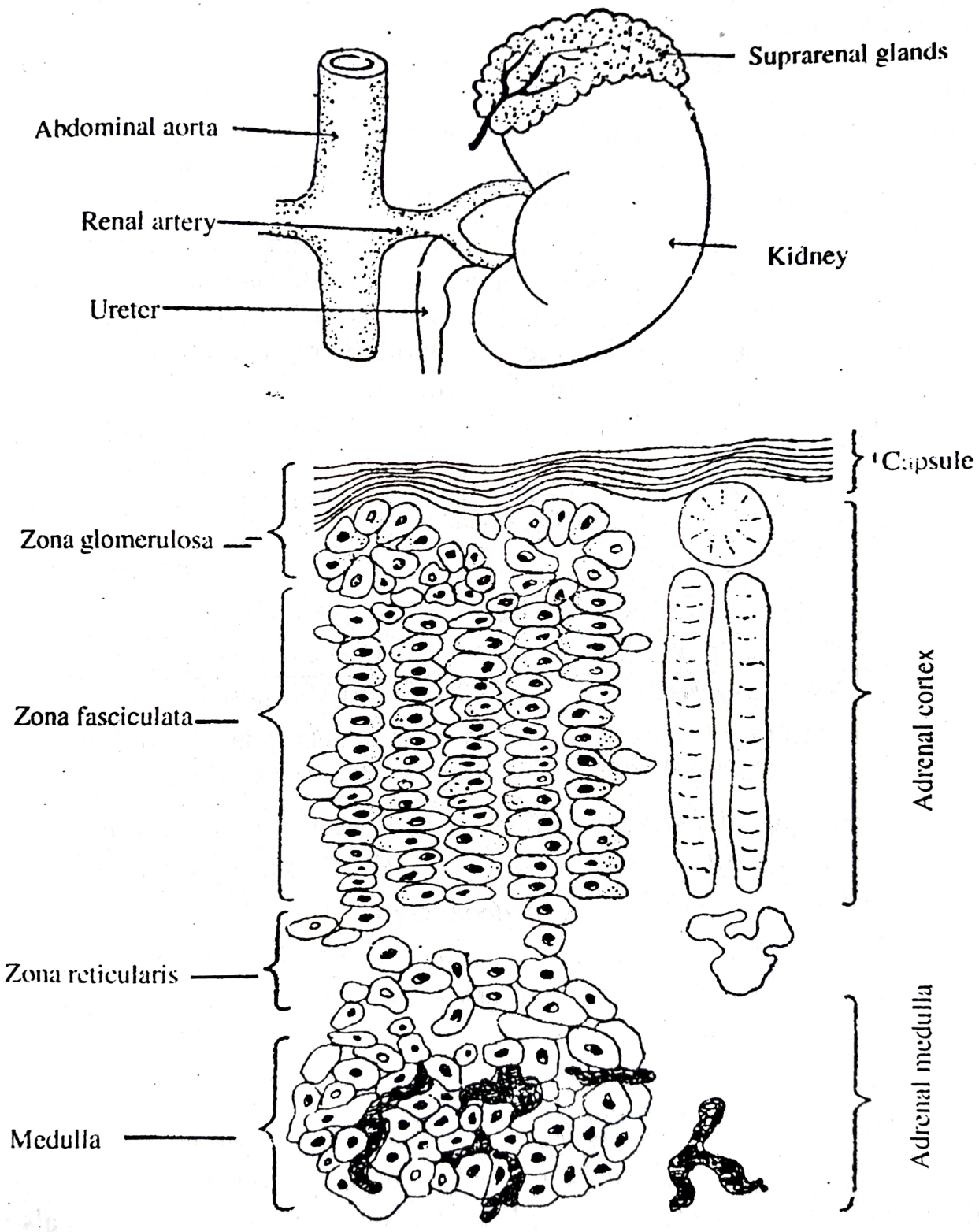


Fig. 16.11 : Anatomy and histology of adrenal (suprarenal) gland

Biosynthesis, transport and metabolism of adrenocortical hormones :

All the hormones of adrenal cortex have a common basic structure-cyclopentanoperhydrophenanthrene or steroid ring. Cholesterol is the major precursor of all steroid hormones. It is formed from acetate. Cholesterol under the influence of ACTH is converted into pregnenolone after hydroxylation and side chain clevage. Pregnenolone after dehydrogenation is converted into progesterone. It may also be converted into 17-hydroxypregnenolone by the enzyme 17- ∝-hydroxylase.

From progesterone, 11-deoxycorticosterone and corticosterone are formed. Corticosterone may be converted into aldosterone. In another pathway, 17-hydroxpregnenolone is converted into 17-hydroxyprogesterone and cortisol, (a glucocorticoid). From 17-hydroxypregnenolone, androgens and estrogen, the sex steroids are formed.

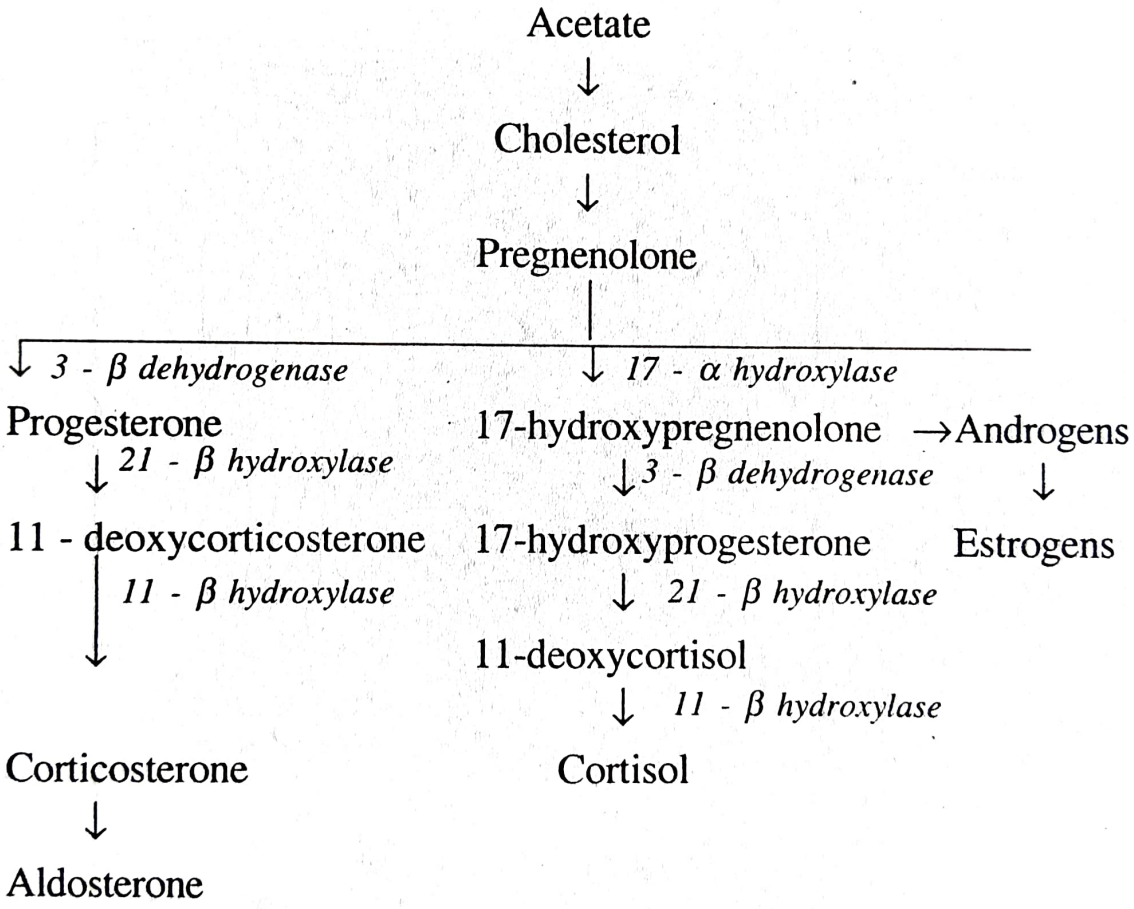


Fig. 16.12 : Major pathways for the synthesis of various steroid hormones.

Cortisol is the main glucocorticoid in human blood. It is transported after being bound to a specific ∝-globulin transcortin. Aldosterone is also present in plasma in very small quantity. It is mainly bound to albumin. Estrogen and progesterone are also bound to albumin. Steroids are metabolised in liver and excreted in urine.

Physiological actions of glucocorticosteroids :

(1) Carbohydrate metabolism : Glucocorticoids produce their main actions on carbohydrate metabolism and hence are called glucocorticoids.

They produce both insulin like as well as anti-insulin effects. Like insulin, they stimulate the formation of glycogen in liver and muscles and increase gluconeogenesis in liver, specially of proteins. However, unlike insulin they depress glucose uptake and its oxidation by tissues. Glucocorticoids help in absorption of sugar from intestine and from renal tubules. Glycosuria and hyperglycemia are the major effects of glucocorticoid excess.

2. Protein Metabolism : Glucocorticoids increase the rate of deamination and break down of tissue proteins to amino acids. Thus, body proteins are lost, increasing nitrogen excretion. They also decrease protein synthesis by interfering with nucleic acid metabolism. Thus, excess of glucocorticoids result in wasting of muscles, osteoporosis, dissolution of lymphoid tissue and increased excretion of creatinine and uric acid in the urine.

3. Fat metabolism : Glucocorticoids stimulate fat absorption from the intestine and mobilise fat from the depot and disintegrate to form ketone bodies in the liver. Excess of cortisol may cause redistribution of fat in the body and hyperlipidemia. They also depress synthesis of fat from carbohydrates.

4. Other metabolisms : Glucocorticoids have minimal action on mineral metabolism causing sodium and water retention and increased excretion of K^+ and PO_4. It stimulates BMR (basal metabolic rate).

5. Blood and cardiovascular system : Glucocorticoids produce anti-lymphocytic and anti-eosinophilic action causing lymphopenia and eosinopenia in blood and involution of thymus, lymph glands spleen etc. This may reduce the resistance power of the body. Hypotension is found in deficiency of adrenal cortex and is corrected after the administration of cortisol.

6. Central nervous system : Hypofunctioning of adrenal cortex causes derangement of functions of central nervous system. Glucocorticoids protect the body against stress.

7. Anti-inflammatory and immunosuppressive effects : Glucocorticoids possess anti-inflammatory activity. They retard migration of leucocytes into traumatised areas. They also possess antiallergic and immunosuppressant activity. Persons with hyperfunctioning of adrenal cortex is more prone to infections.

8. Miscellaneous effects : Chronic treatment of glucocorticoid causes increased secretion of HCl and pepsinogen from the stomach and trypsinogen by the pancreas. Mental, physical and physiolological stress is resisted by glucocorticoids. This is known as *Dr. Seyele's General Adaptation Syndrome* (GAS). Glucocorticoids also stimulate melanin pigment causing darkening of the skin.

Adrenal cortex is very rich in vitamin C. There is about 200 mg of vit. C per 100g. of cortical tissue. Stimulation of adrenal cortex for secretion of corticosteroids by ACTH (adrenocorticotrophic hormone) of pituitary gland results in depletion of vitamin C. This effect is utilised for the bioassay of ACTH.

Physiological actions of mineralocorticoids (Aldosterone) :

Aldosterone has potent effect on mineral and water metabolism (and hence known as mineralocorticoid). It produces retention of NaCl and water, thereby increases blood-volume and blood pressure. In addition, it also increases the excretion of K^+ and PO_4^{-3}. Aldosterone increases blood pressure by vasoconstriction.

Aldosterone may also produce other effects as produced by glucocorticoids, however, it is less potent in those effects.

The secretion of aldosterone is regulated through the renin angiotensin system. Refer page 138 Adrenocorticotrophic hormone (ACTH) also regulates to some extent, the release of aldosterone.

Physiological actions of Sex-steroids :

Sex differentiation in foetus is controlled by sex hormones of the corticosteroids. It also affects sex-development and growth, as well as secondary sex characteristics. Attraction for opposite sex i.e. libido, is also due in part to the sex hormone of corticosteroids. The details of the individual sex hormones are described in chapter 17.

Relationship of Adrenal Medulla with Autonomic Nervous System (ANS) :

Adrenal medulla is many a times wrongly described as the part of ANS. This is of course due to adrenaline that is released from this gland and most physiological actions of adrenaline are similar to the stimulation of sympathetic Nervous System. Adrenal medulla is an endocrine gland is rather innervated by parasympathetic nerves.

Physiological actions of Adrenaline :

Adrenaline is the principal secretion of the adrenal medulla of the suprarenal gland. A minute trace of noradrenaline is also secreted along with it. It produces a number of physiological effects on the body, especially the cardio-vascular system.

Cardio-vascular System : It increases the force (inotropic) and frequency (chronotropic) of the heart. As a result, the cardiac output is increased. All minute blood vessels such as capillaries and arterioles are constricted except the coronary vessels and vessels supplying the skeletal muscles which are dilated. Thus, systolic blood pressure is increased but diastolic pressure falls a little. The mean blood pressure is increased.

Respiratory System : Bronchioles are relaxed and the mucus secretion is decreased by adrenaline. Therefore, it finds a therapeutic use in

bronchial asthma. With an increase in adrenaline level, the respiration stops for a while in animals. This is called "Respiratory apnoea."

Endocrine System : Anterior pituitary is stimulated so as to increase the ACTH and blood glucose level.

Liver : Glycogen from the liver is converted into glucose by adrenaline.

Blood : Adrenaline hastens blood coagulation. Blood volume, RBC, total WBC count and Hb percentage are increased temporarily. Adrenaline also produces splenic contraction. Blood lactate is also increased whereas blood K^+ level falls.

Metabolism : Basal metabolism is raised, RQ increases and glycogenolysis increases the blood glucose level. Fat metabolism is stimulated to liberate free fatty acids.

Skin : In humans, adrenaline causes sweating but in animals sweating is a cholinergic phenomenon. Adrenaline causes the hair to stand on the edge as a result of contraction of erector-pilorum muscle fibres attached to the hair roots. It is a nature's device to produce heat by erector-pili contractions thereby to combat cold.

Smooth Muscles : Adrenaline produces contraction of gall bladder and sphincters of the gastrointestinal tract. However, secretion and movements are inhibited. It increases thick salivary secretion. Adrenaline contracts the spleen whereas, urinary bladder relaxes and its sphincters constrict. Pupil of the eye dilates and intraocular tension increases. Uterine contraction is inhibited somewhat during labour and for a week thereafter.

Noradrenaline : This is secreted in minute amount along with adrenaline. It is mainly a neurotransmitter released from postganglionic sympathetic nerve endings. Actions are similar to adrenaline however, it differs in some respects. Noradrenaline does not increase the heart rate but raises the blood pressure by acting on the minute blood vessels. It raises both the systolic and diastolic pressure. Unlike adrenaline, it has no action on fat metabolism but blood sugar is slightly raised.

Disorders of adrenal cortex :

Addison's disease : It is the disorder of hypofunctioning of the adrenal cortex. The major symptoms are hypoglycemia, loss of body water, fall in blood pressure, severe muscular weakness, anorexia, nausea, vomiting, pigmentation of skin, delayed wound healing etc. Severe loss of sodium chloride in urine occurs in this condition.

Cushing's syndrome : It is the disorder of hyperfunctioning of the adrenal cortex. The major symptoms are hyperglycemia, water retention, increased blood pressure, increased fat deposition in trunk, abdomen and buttocks, increased appetite etc.

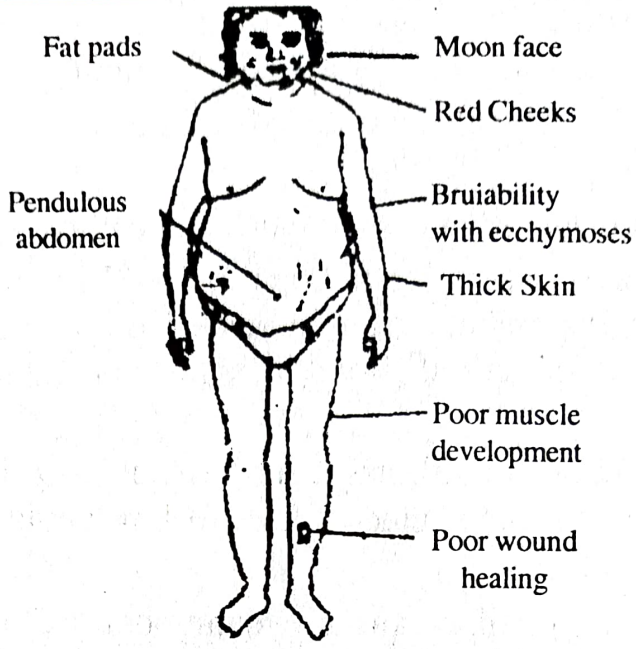


Fig. 16.13 : Cushing's syndrome

Disorders of adrenal medulla

Pheochromocytoma : It is the cancer of adrenal medulla leading to increased adrenaline and noradrenaline secretion. All the actions of adrenaline are exaggerated during this disorder. Severe hypertension is the characteristic symptom.

THYMUS

Anatomy : Thymus normally exists only upto puberty but rarely it persists. It is situated on the trachea, below the thyroid gland. Structurally, it is made up, partly of endocrine areas and partly of lymphoid tissue, characterised by presence of Hassal's corpuscles.

It is subdivided into cortex and medulla. The gland contains small lymphocyte-like structure, small granular cells and Hassal's corpuscles. These Hassal's cells are typical of thymus. They look like a transverse section of onion with concentrically arranged flat cells with hyaline in the centre.

Functions : (1) Formation of lymphocytes, (2) Related to growth of sex glands and development of puberty. Thymus involutes as puberty ensues. (3) A substance, depressing muscular contraction is likely to be secreted by the gland. (4) It aids the deposition of mineral salts in the bone.

Anterior pitutary, thyroid, and adrenal cortex, control the thymus functions to some extent. Thymus gland atrophies at the time of pubery.

PANCREAS

It is a mixed type of gland consisting of two parts : exocrine part and the endocrine part.

The bulk of the pancrease consists of glandular acini which secrete a

powerful digestive juice into the gut. This is the exocrine part of the pancreas. Scattered amongst the acini are tiny clumps of cells known as the *islets* of *Langerhans*. This is the endocrine part of the pancreas. There are two types of cells in the islets of Langerhans.

(i) The large and peripheral alpha (α) cells which secrete the polypeptide glucagon.

(ii) The smaller beta (β) cells which are clumped around capillaries and secrete the insulin. It increases with rise in glucose levels in the blood.

(iii) In addition to α and β cells there are so called δ (delta) cells which contain less dense granules and whose function is still not known.

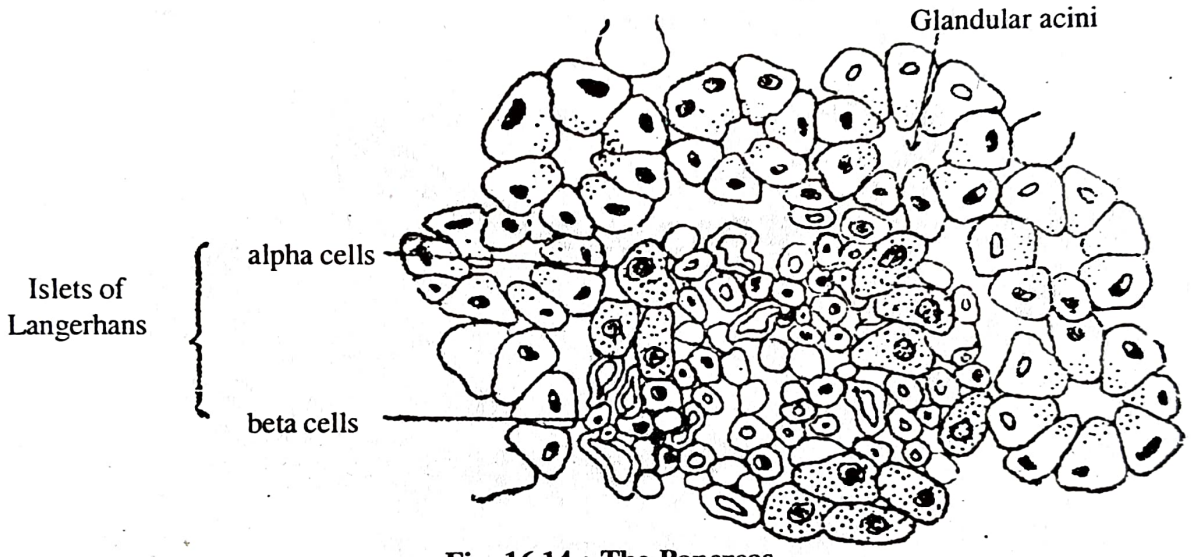


Fig. 16.14 : The Pancreas

Glucagon and insulin are the principal hormones controlling the blood sugar level. Glucagon increases the blood sugar (glucose) level whereas, insulin decreases the blood sugar level.

Glucagon is chemically polypeptide containing 29 amino-acids with a molecular weight of 3450. It raises blood glucose level by (i) promoting glucogenolysis (break-down of glycogen into glucose) and by (ii) stimulating glyconeogenesis (formation of glucose from non-carbohydrate source). Glucagon activates adenylate cyclase to form cyclic AMP and accelerates deamination of amino acids. It also has a calorigenic action. Glucagon does not produce any action on either muscle glycogen or on the peripheral utilization of glucose. It promotes lipolysis in adipose tissue and liver and enhances ketogenesis.

The main stimulus for the secretion of glucagon is a fall in blood glucose level. The rise in blood glucose inhibits secretion of glucagon. During starvation, glucagon and growth hormone maintain the blood glucose level. A rise in plasma free fatty-acids provides extra energy for most tissues, but the glucose level in the blood must be maintained to provide the brain with adequate amounts of energy, since glucose is the only substance which the brain can utilize for energy production.

Insulin is also a polypeptide hormone containing 51 amino acids

arranged in two chains-the chain A, containing 21 amino acids and the chain B, containing 30 amino acid residues. These two chains are cross-linked by two sulphur bridges between cysteine residues. Insulin is formed by proteolytic cleavage of its 84 amino acid precursor proinsulin.

Insulin circulates in the blood plasma, bound to a β-globulin. It is inactivated in the body by the enzyme glutathion insulin transhydrogenase which breaks up the bisulfide bridges to form two peptide chains A and B.

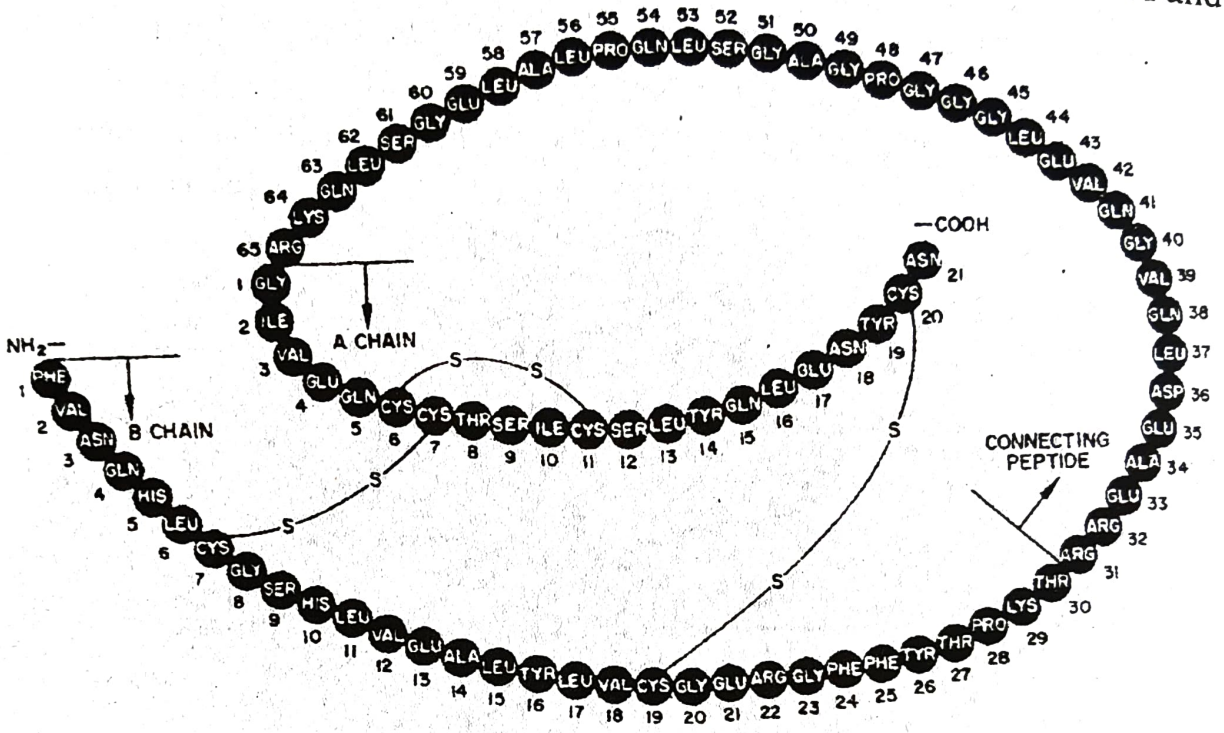


Fig. 16.15 : Structure of proinsulin

A normal man secretes about 50 units of insulin daily. The total insulin content of pancreas is about 200 units. Insulin secretion is continuous but its rate of secretion is influenced by a variety of factors.

Table 16.2 : Factors influencing insulin secretion

Factors Stimulating insulin secretion	Factors inhibiting insulin secretion
Glucose	Adrenaline
Fructose, Mannose	Noradrenaline
Aminoacids	Insulin
Glucagon	Starvation
Ketones	∝-mannoheptulose
Growth hormone	2-deoxyglucose
Secretin	Diazoxide
Sulfonylureas	Vagotomy
Cyclic AMP	Somatostatin
Pancreozymin	
Vagal stimulation	
Estrogen	

Physiological actions of Insulin

1. Carbohydrate metabolism : Insulin increases the oxidation of sugar in the tissues and stimulates transport of glucose into the cells. It increases glycogen synthesis in muscle and liver. The net result is hypoglycemia (decrease in blood sugar level.) Gluconeogenesis (formation of glucose from non-carbohydrate source) is also decreased.

2. Protein metabolism : Insulin 'stimulates protein synthesis and growth. It increases synthesis of messenger RNA and decreases gluconeogenesis. It also increases amino acid uptake in the muscle.

3. Lipid metabolism : In adipose tissues insulin increases fatty acid synthesis, glycerol phosphate synthesis and triglyceride deposition. It also activates lipoprotein-lipase. There may be decrease in breakdown of triglycerides.

4. Miscellaneous actions : Insulin prevents ketone body formation and increases potassium uptake. It increases ketone uptake.

DISORDERS RELATED TO PANCREAS DYSFUNCTION

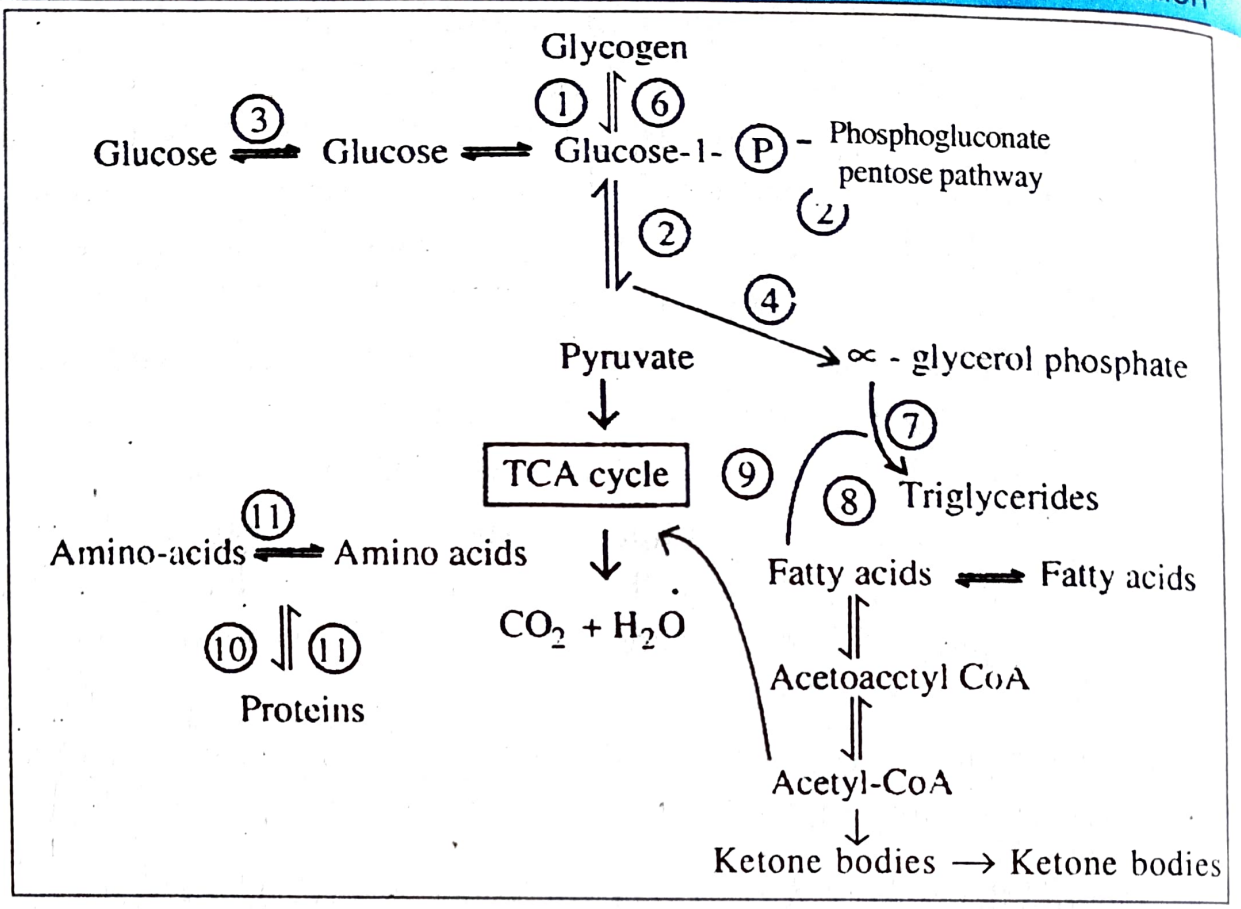
Hypoglycaemia : Increased secretion of insulin causes severe hypoglycemia. Normal blood sugar level ranges from 80 to 120 mg%. If blood sugar level falls below 70 or 50 mg% symptoms of hypoglycemia appear. They are : (1) A feeling of fatigue, weakness and hunger. (2) Extreme anxiety and irritability. (3) Abnormal behaviour. (4) Tremors. Later on vasomotor disturbances such as flushing and perspiration may start. Finally the patient may manifest convulsions, or coma.

Diabetes - mellitus

Diabetes mellitus is a chronic endocrine disorder characterized by deranged secretion of insulin and/or glucagon with extensive disturbances of carbohydrate, protein and lipid metabolism. There is generalized thickening of capillary basement membranes throughout the body mainly due to hyperglycaemia. Long term complications include cataract (eye), nephropathy (kidney), neuropathy (peripheral nervous system), atherosclerosis and cardiomyopathy (cardiovascular system).

Symptoms of diabetes mellitus can be sumarized in Table 16.3

All the symptoms are mainly consequences of decreased insulin secretion/effects (Fig 16.17).



EFFECTS OF INSULIN ON CARBOHYDRATE PROTEIN AND FAT METABOLISM

Tissues	Carbohydrate Metabolism	Protein Metabolism	Fat Metabolism
Liver Cells	↑ (1) Glycogenesis ↑ (2) Glycolysis ↓ (5) Gluconeogenesis ↓ (6) Glycogenolysis	↑ (10) Protein synthesis ↓ (12) Protein breakdown	↑ (7) Lipogenesis
Fat Cells	↑ (3) Glucose uptake ↑ (4) Glycerol synthesis	–	↑ (8) Synthesis of triglycerides ↑ (9) Fatty acid synthesis
Muscle	↑ (1) Glycogenesis ↑ (2) Glycolysis ↑ (3) Glucose Uptake	↑ (10) Protein Synthesis ↑ (11)Aminoacid uptake	–

Fig 16.16 : Illustration of the effects of insulin on metabolism

Table 16.3 : Signs and Symptoms of Diabetes

	Early Phase :	
	TYPE I (IDDM)	**TYPE II (NIDDM)**
a)	Fatigue	a) Fatigue
b)	Weight Loss	b) Impotence
c)	Polyuria, nocturia	c) Perhaps Type 1 symptoms
d)	Thirst, (polydipsia)	
e)	Increased appetite (polyphagia)	
f)	Pruritis (itching)	
g)	Impotence (erectile dysfunction)	
h)	Infections (urinary tract, tuberculosis, oral and vulvovaginal candidiasis)	
	Late Manifestations : (Types I and II)	
a)	Ocular (retinopathy, cataracts)	
b)	Renal (proteinuria)	
d)	Neuropathies (leading to ulceration or gangrene of the feet)	
e)	Cardiomyopathy (heart failure in the absence of arterial disease)	
f)	Hypertension	

There are mainly two types of Primary diabetes mellitus : (1) Juvenile onset or insulin dependent diabetes mellitus (IDDM) and (2) Maturity onset diabetes or non-insulin dependent diabetes mellitus (NIDDM).

Juvenile-onset diabetes or insulin dependent diabetes mellitus (IDDM). This is Type I diabetes-mellitus. It usually occurs in young age. It is characterised by rapid onset and speedy progression to ketoacidosis and coma. Insulin levels are decreased and may finally even stop. Patient then depends only on exogenous insulin. It occurs in 5-10% of the cases. This type of diabetes may be due to genetic disorder or viral infection, or abnormal immunological response.

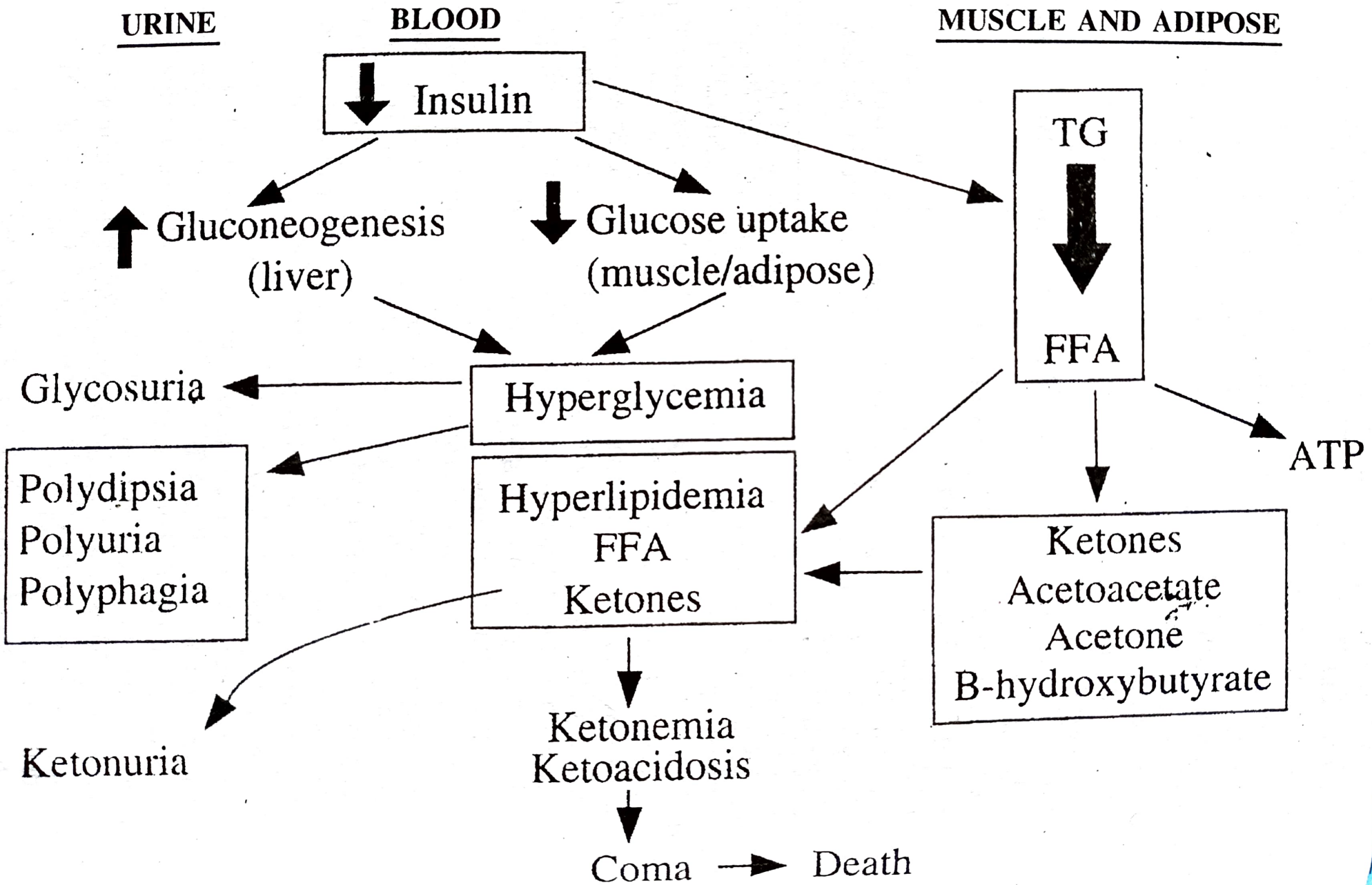
Maturity onset or non-insulin dependent diabetes mellitus : This is type II diabetes-mellitus. Other name of this type of diabetes are ketosis resistant or stable diabetes. It is more common than juvenile type. It is usually mild, ketoacidosis is rare and is associated with obesity in over two-third of the cases. The β-cells respond normally and plasma insulin levels are normal or raised. It occurs in about 90-95% of diabetics.

Other forms (Secondary) diabetes-mellitus are as follows :-

Impaired glucose tolerance : It is asymptomatic, chemical latent or borderline type of diabetes mellitus. Blood glucose levels remain between normal and that of primary diabetic patients. Renal or retinal complications are not seen in this type of diabetes-mellitus.

Gestational diabetes : It occurs during pregnancy. Glucose intolerance is transitory and have tendency to be converted into primary Type II diabetes-mellitus.

Diabetes associated with other complications such as Cushing's syndrome, pheochromocytoma or stress.



16.17 : Consequences of insulin deficiency.