

Endocrine System & Hormonal Co-ordination

Introduction

Endocrine system includes certain glands, principally ductless glands, which secrete the hormones directly into the blood through tissue fluid. These glands are, therefore, called endocrine (*Gr.*, *endon* = within; *krinein* = to secrete) glands.

Study of these glands and their hormones is called **Endocrinology**. Since this system is closely associated with the nervous system in both invertebrates and vertebrates, and hormones may originate from either the endocrine or the neural tissue, a new field, **Neuroendocrinology** has emerged.

11.1 Hormones

(i) **Definition of hormones** : According to Bayliss and Starling (1902) (*Gr. Hormaein* = to excite or stir up, *i.e.*, to arouse to activity, or to set in motion), hormones are biologically highly active organic substances which can be defined as “**chemical messengers**, secreted in some parts of body, and circulated throughout body with blood, to alter the metabolic processes of specific target cells in other parts of body”.

(ii) Properties of hormones :

(a) Hormones are never present in food. These are, therefore, synthesized in the body itself by endocrine cells.

(b) Chemically, hormones fall into two general categories viz **proteinoids** (polypeptides, proteins or amino acid derivatives) which are of neuroectodermal or endodermal origin and **steroids** which are always of mesodermal origin.

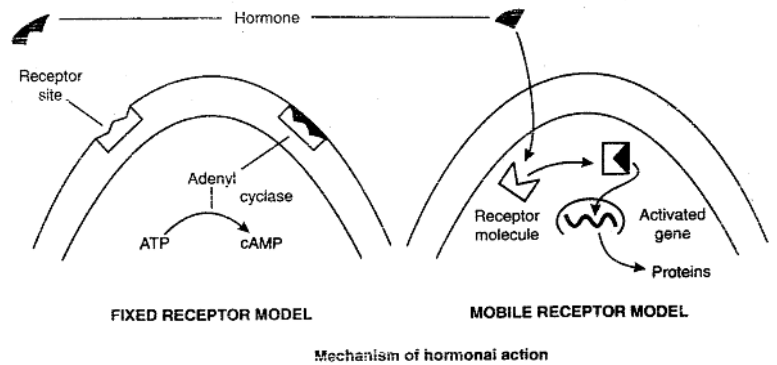
(c) Hormones have relatively small molecules of low molecular weight. These are therefore, soluble in water and easily diffusible through cell membrane.

(d) Hormones are secreted in small amounts, because these have high biological activity. One gram of an adrenal hormone, the **adrenaline**, for example, is sufficient to stimulate the activity of ten million isolated frog hearts. Similarly, one gram of insulin can reduce blood sugar level in 1,25,000 rabbits.

(e) Hormones are released by endocrine cells in response to body requirements. These are not stored in the body. Those not used are quickly excreted in urine, either as such or after being inactivated or degraded, mainly by liver cells. For prolonged effect, therefore, hormones have to be secreted continuously by the concerned glands.

(iii) **Mechanism of hormonal action** : There are two models explaining the mechanism of hormonal action namely fixed receptor model and mobile receptor model.

(a) **Fixed receptor model** : The protein hormones attach on specific receptor sites located on the **cell surface** (plasma membrane). The attachment on the receptor sites increases the activity of **adenyl cyclase**, an enzyme which converts **ATP** to **cAMP** (cyclic adenosine monophosphate). Hormone is called '**first messenger**' and cAMP act as a '**second messenger**'. The role of cAMP as a second messenger in hormonal action was first described by **Earl Sutherland**. Ca^{++} ions act as the '**third messenger**'. These ions activate or inhibit intracellular enzymes.



(b) **Mobile receptor model** : Steroid hormones secreted by adrenal cortex, ovaries and testes do not utilize cAMP to exert their influence. Steroid hormones enter the cytoplasm of a target cell and binds with specific receptor proteins (mobile). Hormone-receptor complex then diffuses into nucleus and activates specific genes to form a new protein. This protein carries out the specific response for a particular steroid hormone. Steroid hormones are related to **cholesterol**.

The most important endocrine glands in man include Pituitary (Hypophysis), Thyroid, Parathyroids, Adrenals (Suprarenals), Pineal gland, Thymus gland, Pancreas, Kidneys, Gonads and Placenta.

11.2 Pituitary gland

Hypothalamus secretes both releasing and inhibitory hormones controlling the secretion of some anterior pituitary hormones. The main function of hypothalamus is thermo-regulation. So, hypothalamus is commonly called as thermo-regulatory centre of body.

Pituitary (hypophysis) regulates so many body activities, it has been nicknamed the '**master gland**' or '**bandmaster of endocrine orchestra**'. Pituitary lies in the **sella turcica** of the sphenoid bone and is attached to the hypothalamus by a short **infundibular stalk**. In man, it normally measures about 1.3 *cm* in diameter and weigh about 0.5 *gram*. It is slightly larger in woman. On the basis of anatomy and embryology, pituitary can be divided into two parts – adenohypophysis and neurohypophysis. It is ectodermal in origin.

Pituitary gland is formed by union of two main lobes of different origin.

(i) **Adenohypophysis** (Anterior lobe) : Originate from Rathke pouch

(ii) **Neurohypophysis** (Posterior lobe) : Originate from floor of fore brain mainly infundibulum.

(i) **Adenohypophysis hormones** :

(a) **Somatotropic hormone (Growth hormone)** : The chief function of GH is to act on the hard and soft tissues to increase the rate of growth. GH is the important hormone for normal growth of body. GH is more effective in the presence of thyroxine. The hyposecretion of GH during the growth years results in the pituitary **dwarfism** (Midget). The hyposecretion of GH in the adult life lead to a rare condition called '**Simmond's disease**'. The patient becomes quite thin and shows signs of premature ageing. The hypersecretion of GH during childhood (before the closure of epiphyseal plates at the ends of the bones) results in **gigantism**. The hypersecretion during adulthood is called **acromegaly** (after the closure of the epiphyseal plates at the ends of the bones). Acromegaly patient has a gorilla-like appearance with huge hands and legs. At cellular level, GH stimulate the synthesis of *mRNA*.

(b) **Thyrotropin** : Thyroid stimulating hormone (TSH) stimulates the synthesis and secretion of hormones produced by thyroid gland.

(c) **Adrenocorticotrophic hormone (ACTH)** : This hormone controls the production and secretion of certain adrenal cortex hormones. If pituitary is surgically removed (hypophysectomy), blood level of sodium falls and potassium rises.

(d) **Follicle stimulating hormone (FSH)** : FSH promotes growth of ovarian follicles in female and stimulates ovaries to secrete estrogens or female sex hormones. FSH stimulates the testis to initiate sperm production.

(e) **Luteinizing hormone (LH)** : LH is called luteotropin in the female and interstitial cell stimulating hormone (ICSH) in the male. In female, together with estrogens, LH stimulates the ovary to release developed ovum and prepares the uterus for implantation of a fertilized ovum. LH also stimulates the formation of the corpus luteum in female. In the male, ICSH stimulates the interstitial cells of Leydig in testis to develop and secrete large amount of testosterone.

(f) **Prolactin** : Prolactin is also known as luteotropic hormone (LTH) or lactogenic or mammatropic (MTH) hormone. Prolactin initiates and maintains milk secretion by mammary glands, a process called lactation.

Melanocyte stimulating hormone (MSH) : MSH increases skin pigmentation by stimulating the dispersion of melanin granules in melanocytes. MSH is also called 'intermedin' in man, it is a vestigial hormone, its secretion is doubtful. MSH is produced in the pars intermedia of the pituitary. MSH induces darkening of the skin of fish and amphibia by expanding the melanophores.

Diseases of adenohypophysis

(1) **Pituitary nanism or dwarfism** : Caused by under secretion of pituitary growth hormone in childhood and aldosterone from the age of 14 to 22 years.

(2) **Pituitary myxodema** : Caused by undersecretion of growth hormone and gonadotropin in adult.

(3) **Gigantism** : Over secretion of growth hormone during childhood. Due to this, over growth of skeleton and entire body to giant size occurs.

(4) **Acromegaly** : Over secretion of growth hormone in adult after growth period causes disproportionate gigantism.

(ii) Neurohypophysis hormones :

(a) **Antidiuretic hormone** : ADH is related with concentration of urine. ADH promotes reabsorption of water from glomerular filtrate. Vasopressin released by pituitary is antidiuretic. Alcohol inhibits secretion of ADH, so increases the urine output. Hyposecretion of ADH results in **diabetes insipidus**. When the amount of ADH decreases in blood, micturition (passing out of urine) increases.

(b) **Oxytocin** : Oxytocin (Pitocin) stimulates the contraction of the smooth muscles of uterus inducing labour pain for child birth. Oxytocin activates smooth muscles of uterus, it is administered to aid parturition (**birth hormone**) In a pregnant woman having prolonged labour pains, if child birth has to be hastened, it is advisable to administer oxytocin which activates smooth muscles of uterus. Oxytocin induces contraction of the mammary gland muscles, help in the flow of milk from mammary glands to mouth of child, hence called '**milk ejection hormone**'.

11.3 Thyroid gland

The name thyroid was introduced by **Thomas Wharton** in 1656. It is derived from Greek '*Thyreos*' a shield. Thyroid gland is a median endocrine gland located below larynx. It is bilobed in birds and mammals (single lobed in reptiles), right and left lobes are connected by a narrow nonglandular median part called isthmus.

(1) Thyroid is the ventral evagination of the floor of pharynx, and is endodermal in origin.

(2) Thyroid gland is homologous to the endostyle of lower chordates. (Protochordates)

(3) In adult, thyroid measures 3-7 cms in length and weigh about 25 gram. It is the largest endocrine gland in the body.

(4) Thyroid is composed of spherical sacs called thyroid follicles. The thyroid hormones are stored in the lumen of follicle, the extracellular space.

(5) The wall of follicles is made of two types of cells, principal cells and parafollicular cells.

(6) The principal cells manufacture the thyroid hormones namely tetraiodothyronine (T₄) and triiodothyronine (T₃).

(7) Thyroxine (T₄) is synthesized from iodine and an amino acid called tyrosine.

(8) The greatest concentration of iodine is found in thyroid.

(9) The iodine content of thyroxine is about 65%.

(10) **Kendall** (1914) was first to prepare crystals of thyroxine.

(11) **Harrington** and **Barger** (1927) worked out the molecular structure of thyroxine.

(12) Secretion of thyroxine is inversely proportional to the blood level of thyroxine (feed back mechanism).

(13) Thyroxine's main function is to control metabolism.

(14) Thyroid regulates the basal metabolic rate.

(15) Thyroid increases catabolism, produces energy and increases the body temperature. This process is called **calorigenic effect**.

(16) Thyroxine also helps to regulate tissue growth and development.

(17) Thyroid initiates, regulates and plays a key role in the metamorphosis of frog's tadpole.

(18) **Gudernatsch** (1912) reported the role of thyroid in the metamorphosis of Amphibia.

(19) Removal of thyroid is called thyroctomy.

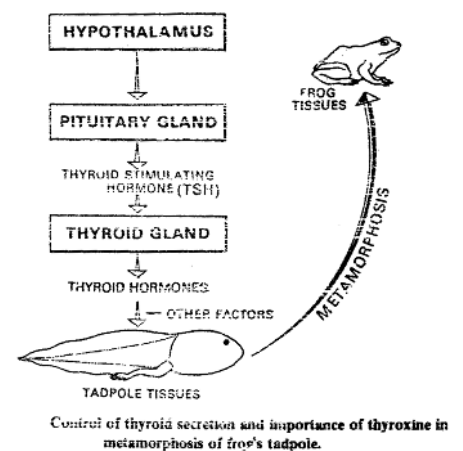
(20) Hyposecretion of thyroxine retards and hypersecretion enhances the rate of metamorphosis.

(21) Addition of thyroxine or iodine in pond water induces and enhances metamorphosis in the tadpoles.

(22) On removing thyroid gland from tadpole, it will remain tadpole throughout life.

(23) **Cretinism** : Hyposecretion of thyroxine during the growth years or birth. It is called childhood hypothyroidism. Two important symptoms are dwarfism and mental retardation.

(24) **Myxoedema (Gulls disease)** : It is adulthood hypothyroidism. Lack of thyroxine causes the body to retain water. Patient suffers from slow heart rate, low body temperature, muscular weakness, etc.



(25) **Simple Goitre** : It is caused by lower intake of iodine through diet. Goitre is the swelling of neck due to enlargement of thyroid. Table salt is often iodised for certain areas to prevent goitre.

(26) **Exophthalmic Goitre (Grave's disease)** : It is hyperthyroidism. Eyeballs protrude due to accumulation of mucus in eye orbits; metabolic rate is abnormally high.

(27) The parafollicular cells(C-cells) of thyroid secrete a noniodised hormone called 'thyrocalcitonin' or calcitonin (TCT).

(28) Calcitonin lowers the amount of calcium and phosphate in the blood.

(29) Calcitonin retards bone dissolution (osteoclastic action) and stimulates excretion of calcium in urine.

(30) Calcitonin lowers calcium in the extracellular fluid (ECF).

(31) **Hashimoto's disease** : It is an autoimmune thyroid disorder discovered by Japanese surgeon **Hakaru Hashimoto**. It is characterized by the production of antibodies in response to thyroid antigens. It is also known as suicide of thyroid.

(32) The thyroid disorders are more frequent in females than in males.

11.4 Parathyroid gland

Parathyroids are two pairs, partially or completely embedded in the dorsal surface of thyroid gland. Parathyroids are present in all vertebrates except fishes.

(1) Parathyroid contains two kinds of cell; **chief cells** and **oxyphil cells**.

(2) Chief cells are the major synthesizer of parathormone or parathyroid hormone (PTH) or **Collip's hormone**.

(3) PTH regulates the amount of calcium and phosphate in ECF. It promotes the absorption of calcium from food in intestine, it accelerates elimination of phosphates in urine.

(4) PTH decreases blood phosphate level and increases blood calcium level.

(5) Parathormone is responsible for regulation of calcium and phosphate metabolism.

(6) Parathormone induces increase in serum calcium level.

(7) **Tetany** : Hypoparathyroidism results in hypocalcemia. Skeletal muscles fail to relax causing tetany.

(8) **Osteoporosis** : Hyperparathyroidism results in osteoporosis, *i.e.*, dissolution of bone and hypercalcemia.

(9) **Osteitis fibrosa cystica** : Hyperparathyroidism also results in Osteitis fibrosa cystica (normal bone is replaced by cysts and fibrous tissue).

11.5 Adrenal glands

Adrenal glands are paired endocrine glands, located superior to kidneys, hence called 'suprarenals'. Adrenal gland is structurally and functionally divided into outer adrenal cortex and inner adrenal medulla. Adrenal gland is also known as 4S gland. Sugar metabolism, Salt retaining, Sex hormone and Stress hormone.

(i) **Adrenal cortex**

(1) Adrenal cortex is derived from **mesoderm**, it is bright yellow in colour constituting 80-90% of gland.

(2) Adrenal cortex is subdivided into 3 zones namely outer **Zona glomerulosa**, middle **zona fasciculatus** and inner **zona reticularis**.

(3) The zona glomerulosa secrete **mineralocorticoids**, zona fasciculatus secrete **glucocorticoids** and zona reticularis synthesize **gonadocorticoids**.

(4) The principle mineralocorticoid is aldosterone commonly called 'salt-retaining hormone'.

(5) Two basic functions of aldosterone are conservation of sodium and water and elimination of potassium.

(6) Low blood pressure stimulates the **Renin-angiotensin** pathway.

(7) Glucocorticoids are a group of hormones concerned with normal metabolism.

(8) Low level of glucocorticoid in the blood stimulates the secretion of ACTH from anterior pituitary.

(9) Adrenal cortex secretes both male and female sex hormones, (gonadocorticoids) estrogens and androgens.

(10) Concentration of sex hormones secreted by normal adult adrenals is usually so low that their effects are insignificant.

(11) All hormones secreted by adrenal cortex are steroids derived from cholesterol.

(12) **Addison's disease (Hypoadrenalism)** : Hyposecretion of glucocorticoids results in Addison's disease.

(13) **Cushing's syndrome (Hyperadrenalism)** : Hypersecretion of glucocorticoids results in Cushing's syndrome. Clinical symptoms are 'Red Moon face' and 'Buffalo hump'.

(14) **Aldosteronism (Conn's disease)** : Hypersecretion of aldosterone results in decrease in body's potassium.

(15) **Adrenogenital syndrome** : The tumours of adrenal cortex result in an excess of adrenal sex hormones. Virilism is development of male characters like growth of beard, deep voice and baldness in a female due to excessive secretion of androgen by adrenal tumours. Gynecomastia is development of mammary glands in a male due to excessive secretion of estrogens by adrenal tumours.

(ii) **Adrenal medulla**

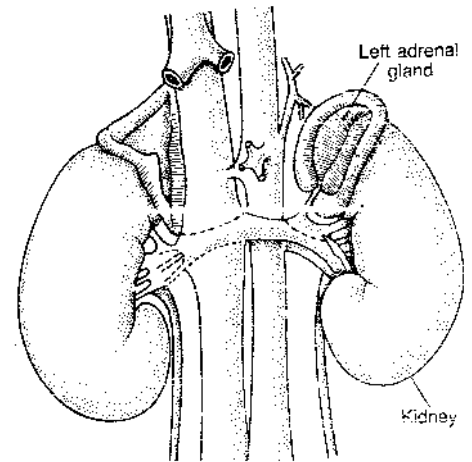
(1) Adrenal medulla is ectodermal in origin and constituting 10-20% of the adrenal gland.

(2) Adrenal medulla contains chromaffin cells secreting two hormones **epinephrine** (adrenaline) and **norepinephrine** (noradrenaline).

(3) Adrenaline is the methylated noradrenaline, both are derived from the amino acid tyrosine.

(4) Catecholamines refer to dopamine, adrenaline and noradrenaline.

(5) The secretion of adrenaline is in direct response to nervous activity (others are pineal and neurohypophysis).



Location of adrenal glands

(6) The secretion of adrenaline is directly controlled by the autonomic nervous systems, but not under the control of pituitary.

(7) Adrenal medulla contributes the **fright, fight** or **flight** reactions which occur in condition of emergency.

(8) Life-saving hormones are secreted by adrenals.

(9) Adrenaline is also called '**emergency hormone**'.

(10) The secretion of adrenaline increases in emotional disturbances.

(11) Adrenaline accelerates the rate of respiration, dilates respiratory passage, decreases the rate of digestion, increases blood sugar level and stimulates cellular metabolism.

(12) Adrenaline increases both the heart beat and blood pressure.

(13) When a person suffers from marked fall in blood pressure, it is helpful to give adrenaline to him.

(14) **Pheochromocytomas** : It is due to tumours of chromaffin cells of adrenal medulla. Hypersecretion of adrenaline causes high blood pressure, high levels of sugar in the blood and urine, high metabolic rate, nervousness and sweating.

11.6 Pineal gland

Pineal gland is an endocrine organ, it is located on the roof of diencephalon. It is **ectodermal** in origin, and is absent in crocodiles. Pineal gland is composed of modified nerve cells called **pinealocytes**. In man starts to degenerate at about age 7 years, in adult it is largely fibrous tissue. Pineal gland secretes three hormones in direct response to nervous activity namely melatonin, serotonin and adrenoglomerulotropin.

(i) Melatonin is a derivative of the amino acid tryptophan and its target cells are melanophores of skin. It is antagonistic to that of melanocyte stimulating hormone (MSH) secreted by pars intermedia of pituitary. Darkness stimulates pineal secretion of melatonin, whereas exposure to light inhibits melatonin secretion.

(ii) Serotonin (5HT) acts as a **vasoconstrictor**, increasing blood pressure.

(iii) Adrenoglomerulotropin stimulates the **zona glomerulosa** of adrenal cortex to secrete aldosterone.

11.7 Thymus gland

Thymus is a bilobed lymphoid organ situated in front of the heart in the upper part of sternum. It is an endocrine gland nearest to heart. Thymus is **endodermal** in origin, at birth weighs 10-12 *gram*, at puberty 20-30 *gram* and at old age it weighs 3-6 *gram*. It is active in young ones but gradually becomes inconspicuous after sexual maturity. According to one of the theories for ageing, the decline and disappearance of thymus gland by late middle age is the primary cause of ageing. Thymus consists of peripheral cortex and central medulla. The medulla contains characteristic thymic (**Hassall's**) corpuscles. The reticular-epithelial cells secrete a hormone, thymosin, which promotes immunocompetence in young T-lymphocytes.

Thymosin (a peptide) produces lymphocytosis. The thymus also secretes a hormone, thymopoeitin (thymine), which inhibits acetylcholine release at motor nerve endings. Thymus gland produces some lymphocytes (T-lymphocytes) and antibodies which keep the young ones immune to some diseases. Like other lymphoid tissue, thymus undergoes atrophy in response to adrenal glucocorticoids.

11.8 Pancreas

Pancreas is **endodermal** in origin, located within the curve of duodenum. The average length of pancreas is 12-15 *cm* and weight is 50-70 *grams*. Pancreas is a mixed gland (heterocrine gland) with both

exocrine and endocrine portions. The exocrine portion of pancreas consists of pancreatic acini (98-99% of gland) which secrete pancreatic juice. The endocrine portion of pancreas consists of clusters of cells called 'Islets of Langerhans' (1-2% of gland). Three kinds of cells are found in islets of Langerhans namely **alpha cells** (15-25%), **beta cells** (70-80%) and **delta cells**.

(i) **Glucagon**

- (1) Glucagon discovered by **Kimball** and **Murlin** (1923) is the product of **alpha cells**.
- (2) Chemically glucagon is a straight-chain polypeptide containing 29 amino acid residues.
- (3) The main physiological activity of glucagon is to increase the blood sugar level.
- (4) Hypersecretion of glucagon causes **hyperglycemia**.

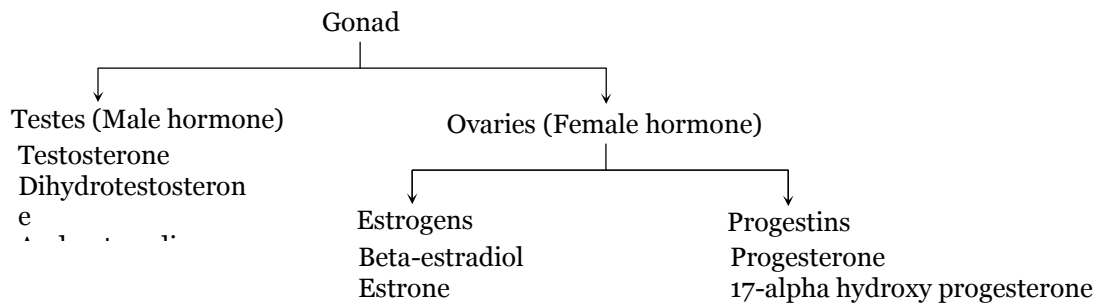
(ii) **Insulin**

- (1) **Insulin** is a hormone, the product of **beta cells**.
- (2) **Banting** and **Best** (1921) extracted insulin from pancreas and showed that it reduced blood sugar in dogs.
- (3) Crystalline insulin was prepared by **Abel** in 1926.
- (4) **Frederick Sanger** (1952) worked out the full chemical structure of insulin.
- (5) Chemically insulin is a protein (large polypeptide). Insulin contains 51 amino acids arranged in two chains, an acidic A-chain containing 21 amino acid residues and a basic B-chain containing 30 residues.
- (6) The A-chain and B-chain are joined by two *S-S* bonds.
- (7) The molecular weight of insulin is 6000.
- (8) For discovering the amino acid sequence in insulin, **F.sanger** was awarded a Nobel prize in 1958. Sanger obtained a second Nobel prize in 1980 for his work on chemical structure of gene. Sanger is the first British scientist to win Nobel prize twice.
- (9) Insulin is the first protein to be synthesized by scientist in the laboratory.
- (10) Insulin is the most important regulator of carbohydrate metabolism.
- (11) Insulin stimulates **glycogenesis** and maintains normal glucose level in the blood, *i.e.*, 100 mg per 100 ml of blood.
- (12) Insulin decreases blood sugar level by promoting liver glycogen formation.
- (13) Hyposecretion (lack) of insulin results in **diabetes mellitus**.
- (14) Insulin is given to patients of diabetes mellitus. Oral insulin is noneffective as it is digested like protein in intestine, so injections of insulin are given.
- (15) Insulin from cattle or sheep may evoke allergic reactions in man, pig insulin resembles more closely to human insulin in structure.
- (16) Patients of diabetes mellitus drink water to eliminate sugar present in the blood.
- (17) High sugar level in the blood is called **hyperglycemia**. The passing of glucose through urine is called **glycosuria**.
- (18) Treatment with **alloxan** and **Streptozocin** destroys beta cells of islets of Langerhans.

(19) Delta cells secrete somatostatin which is growth inhibitor pancreas is also thought to contain 'F' cells which secrete pancreatic polypeptide which inhibit the release of pancreatic juice.

11.9 Gonads

The gonads arise from the mesoderm. Besides producing gametes, the gonads secrete sex hormones from the onset of puberty (sexual maturity) to control the reproductive organs and sexual behaviour. The testes and ovaries secrete different hormones.



(i) Male hormones of gonads

(1) Male hormones called androgens are produced by interstitial cells of Leydig by stimulation from ICSH of anterior pituitary.

(2) The principal male hormone is testosterone. It is responsible for puberty in man.

(3) At puberty by the influence of FSH and ICSH of pituitary, a large amount of testosterone is produced.

(4) Testosterone exerts a feed back inhibitory effect on pituitary LH (ICSH) secretion.

(5) Testosterone is secreted by **Leydig cells**.

(6) Surgical removal of testis is **castration** or **orchidectomy**.

(7) Due to castration, the animal becomes agile and strong.

(ii) Female hormones of gonads

(1) Female hormones are known as **estrogens** and **progestins**.

(2) Estrogens are produced by the theca interna cells of Graafian follicles.

(3) Estrogens regulate growth and development of female accessory reproductive organs, secondary sexual characters and sexual behaviour.

(4) Estrogens suppress the production of pituitary FSH.

(5) The ruptured follicle after ovulation gives rise to a temporary endocrine structure called **corpus luteum** which is the source of the secretion of progesterone.

(6) Progesterone is the hormone responsible for growth and maintenance of foetus.

(7) Progesterone causes the excessive development of endometrium of uterus. It is responsible for the implantation of embryo in uterus and formation of placenta.

(8) The role of progesterone hormone is to thicken uterine wall to increase the blood supply to uterine wall and to build up fat and glycogen in uterine wall.

(9) Progesterone suppresses ovulation and production of pituitary LH.

(10) If pregnancy occurs, corpus luteum is maintained for about three months.

(11) At later stages in pregnancy, the function of corpus luteum will be carried out by placenta through its hormones.

(12) If ovaries of a lady are removed off in 4th month of pregnancy, result will be that the embryo will develop normally till birth.

(13) LH is the hormone present in greatest concentration during ovulation.

(14) Menstruation is the periodic shedding of the endometrium of the uterus in some mammals (primates) with bleeding.

(15) Ovulation occurs usually midway (14th day) during menstrual cycle.

(16) Menarche is the starting of menstruation in girls at about $13\frac{1}{2}$ years.

(17) Menopause (climateric) is the period of life when menstruation naturally stops. It usually occurs between the ages of 45 and 50.

(18) After menopause, ova, corpora lutea and internal secretions of ovary are no longer formed. The woman cannot become pregnant after the age of 50.

(19) After menopause the secretion of both FSH and LH increases but ovaries do not respond to these hormones.

(20) Hormones taken in the form of drugs for contraception are estrogens and progesterone.

11.10 Placenta

A temporary structure with endocrine function is placenta. Placenta secretes many hormones like chorionic gonadotropin, placental lactogen, estrogens, progesterone, relaxin, etc. The presence of HCG (human chorionic gonadotropin) in the urine forms the basis of all pregnancy diagnosis tests. HCG can be detected as early as 14 days after conception. Placental lactogen has functions similar to prolactin and oxytocin. Relaxin secreted by placenta is a polypeptide (molecular weight 8000), it causes relaxation of ligaments of pubic symphysis for easy birth.