CHEMICAL COORDINATION AND INTEGRATION

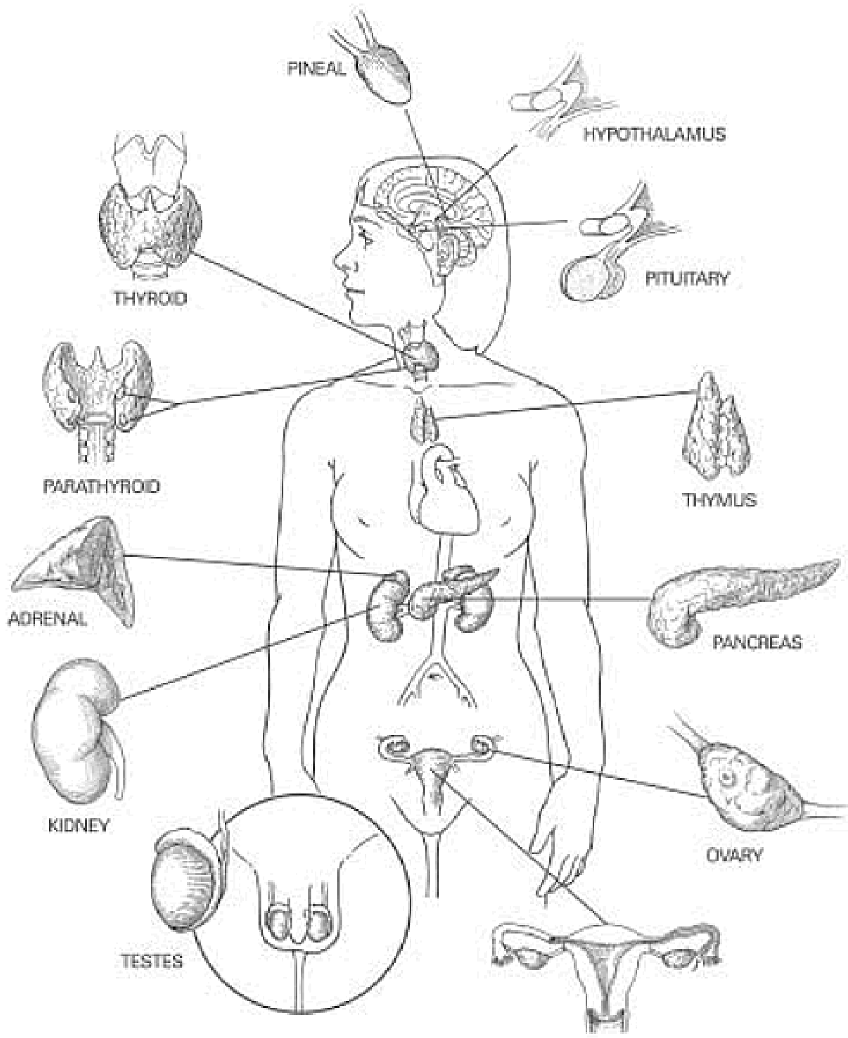
Contents

7. Chemical Coordination and Integration
7.1 Introduction
- In multicellular animals, homeostasis involves chemical messengers that act over longer periods and more slowly than the neurotransmitters.
- These messengers called hormones, constitute second great communication system.
- The hormones are secreted by endocrine glands of ductless glands as they release their products directly into the blood stream.
- The term hormone means to excite or to arouse, coined by British physiologist E.H. Starling, who, in association with Bayliss, discovered the hormone secretin in the wall of intestine.
- However, it was later known that hormones not only excite but some hormones inhibit the target organs.
- It is formed of all endocrine glands of body which along with nervous system of body, controls and coordinates the body functions and maintains a homeostasis (constancy of body fluids) inside the body.
- So, both endocrine and nervous systems collectively form neuro-endocrine system of body.
- The combined study of these two systems is called Neuroendocrinology because the regulation of body functions and maintenance of a homeostasis inside the body requires not only the constant modulation and integration of nervous system but also, chemical control by the endocrine system.
- Need of endocrine control arises because the nerve fibres do not innervate al the cell of the body.
- Though different endocrine glands are different in embryonic origin are isolated from the another but these interact with one another so collectively from an endocrine system.
- Some of these are highly organized glands example- liver, kidney, heart, gastrointestinal tract, etc.

7.2 Endocrine Glands and Hormones
- Greek word *endon* means inside and *krinein* means to separate.
- These are endogenously located glands which lack the ducts (so also called ductless glands) and generally secrete their secretions into the blood for their transportation to target organs (sites of action).
- The branch dealing with the study of endocrine glands and actions of their hormones is called Endocrinology.
- Types of Glands –
  - Endocrine
  - Exocrine
  - Heterocrine Glands

Differences between Endocrine, Exocrine and Heterocrine glass

Endocrine glands	Exocrine glands	Heterocrine glands
These lack ducts.	These have ducts.	Partly exocrine with duct and partly endocrine without duct.
These secrete hormones generally in blood. Example- Thyroid, Pituitary, Hypothalamus, Adrenal, etc.	These secrete their secretions in ducts to carry them either on the body surface or to some internal body part. Example- Sweat and oil glands of skin, salivary glands, liver, etc.	Exocrine part release secretion in duct, while endocrine part releases hormones in blood. Example- Pancreas and gonads.



Various Endocrine Glands of Human Being

- Greek word *Hormaein* means to excite.
- Term hormone was coined by Starling (1905) from Greek word *hormain* means to excite or to arouse activity.
- Hormones, also called chemical messengers or information molecules, are the non-nutrient organic compounds secreted in the trace amounts by endogenously located endocrine glands of body, generally released in the blood stream (except a few local hormones like Gastrin) and have specific effect (excitatory or inhibitory) on the specific organs, called target organs, generally located distantly from endocrine glands so act as inter cellular messengers.
- Local hormones work upon the adjoining tissue and reach there by diffusion example- Gastrin, Enterocrinin, etc.
- Though hormones are released in general blood circulation but each hormone stimulates only a specific target organ to initiate a specific response. It is so because of the presence of specific protein only in the specific target cell.
- First hormone discovered was secretin (secreted by duodenal mucosa and stimulating the secretion of pancreatic juices). It was discovered by two English physiologists: William M. Bayliss and Ernst H. Starling in 1903.

- It is a misnomer because a number of hormones are known to have inhibitory effect on target organs, example- Somatostain.
- Hormones, on the bases of their chemical composition, are classified into three categories-
  - Amine hormones-These are derived from tyrosine amino acid and have amino (-NH_2) group, example- Thyroxine (Thyroid gland); Epinephrine (adrenaline) and Norepinephrine (nor-adrenaline) of Adrenal medulla.
  - Steroids-These are fat-soluble and have sterol group. These are derived from cholesterol, example- hormones of adrenal cortex (cortisol, aldosterone, cortisone, corticosterone, etc.), testes (testosterone, androstenedione etc. and ovaries (estrone, estradiol, progesterone etc.).
  - Proteinous and peptide hormones-These are formed of 3-200 amino acids interlinked by peptide bonds and are water soluble example-
    - Proteinous and peptide like STH, TSH, FSH, LH etc. from anterior lobe of pituitary gland. Out of these, LH and FSH hormones are glycoproteinous.
    - Long peptide hormones like insulin and glucagon (pancreas), ACTCH (anterior lobe of pituitary gland), Parathormone (parathyroid) etc.
    - Short peptide hormones formed of a few amino acids like Oxytocin and ADH (posterior lobe of pituitary gland), MSH (intermediate lobe of pituitary gland).
- Both hormonal and nervous systems control and coordinate the body functions and work in coordination to maintain a steady state condition, called homeostasis. But two types of controls differ in some important characters -

Differences between Nervous and Hormonal information

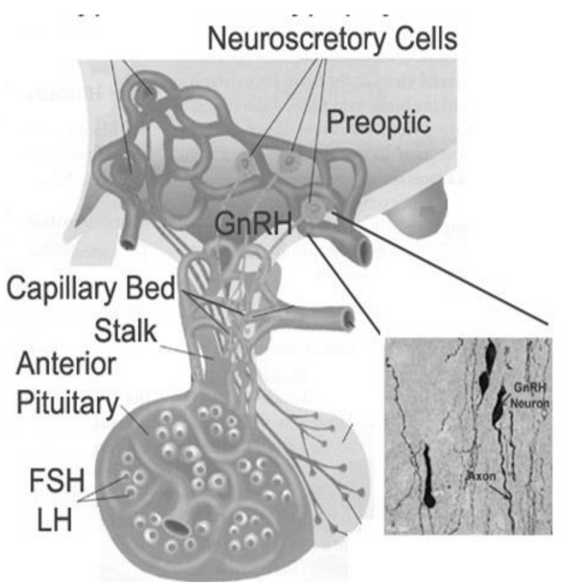
Characters	Nervous information	Hormonal information
Speed of action	Always quick acting.	May be quick acting or acting with a lag period.
Mode of trans-mission of information.	As electrochemical nerve impulses.	As chemical messengers.
Path of trans-mission.	Through nerve fibres.	Through blood.
Direction of the information.	Towards a specific direction (effectors organ or CNS).	Released in general blood circulation from where taken by specific receptor.
Suitability	For quick reactions like reflexes.	For long-term changes example- maintenance of pregnancy.
Durability	Short time effect.	Long lasting.

7.3 Human Endocrine System

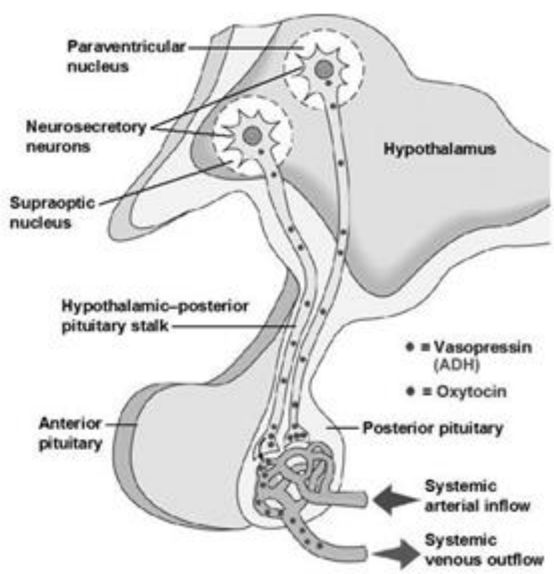
- The endocrine glands and hormone producing diffused tissues or cells located in different parts of our body constitute the endocrine system.
- Pituitary, pineal, thyroid, adrenal, pancreas, parathyroid, thymus and gonads i.e. testes in males and ovary in females are the organized endocrine bodies in our body.
- In addition to these, some other organs, example gastrointestinal tract, liver, kidney, heart also produce hormones.
- A brief account of the structure and functions of all major endocrine glands and hypothalamus of the human body is as follows-
  - Partly Endocrine Glands of Man
  - Those glands which secrete only hormones. These are of following types-

7.3.1 The Hypothalamus

- Hypothalamus is the floor of diencephalon.
- It is formed of masses of grey matter, called hypothalamic nuclei, containing neurosecretory cells.
- It is connected with anterior pituitary lobe by blood capillaries of hypophyseal portal system and with the posterior pituitary lobe by axons of its neurons, both passing through the pituitary stalk.
- Neurosecretory cells of hypothalamus secrete neurohormones called releasing factors (RF-which stimulate the secretion of pituitary hormones) or inhibiting factors (IF-which inhibit the secretion of pituitary hormones).
- These neurohormones are carried by hypophyseal portal system to adenohyophysis (primary target organ) and stimulate or inhibit the release of trophic hormones from adenohyophysis.
- For each releasing hormone secreted by hypothalamus, there is a corresponding trophic hormone synthesized by the anterior lobe of the pituitary.
- These neurohormones are proteinous in nature and formed of 3-20 amino acids.
- The hypothalamic-pituitary (hypothalamohypophyseal) system is a direct proof of coordination between the hormonal and nervous system.
- These neurosecretory cells are also known to synthesize two more hormones.
- Oxytocin and Vasopressin, which are stored in their axons extending in the posterior lobe of pituitary gland.
- The posterior pituitary is under the direct regulation of hypothalamus.



Hypothalamus-Hypophyseal Axis



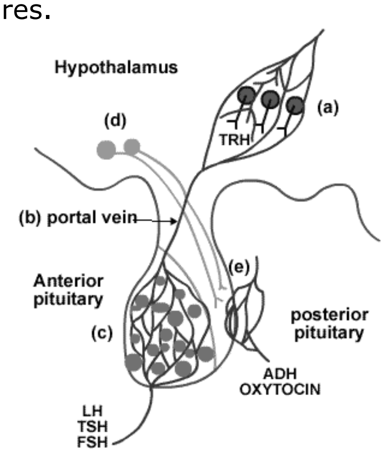
Relationship between Hypothalamic Neurons and Posterior Pituitary Cells

Neurohormones and their physiological effects

Neurohormones	Physiological effects
TSH-RF or TRF (Thyroid Stimulating Hormone-Releasing Factor)	Increased TSH secretion from adenohyophysis.
ACTH-RF or CRF (Adrenocorticotrophic Hormone-Releasing Factor)	Increased ACTH secretion from adenophypophysis.
STH-RF or GHRF (Somatotrophic Hormone-Releasing Factor or Growth Hormone Releasing Factor)	Increased STH secretion from adenohyophysis.
Somatostatin (Growth Inhibiting Hormone)	Decreased STH secretion from adenohyophysis.
Gn TH-RF or GnRF (Gonadotropic Hormone-Releasing Factor) (i)FSH-RF (Follicular Stimulating Hormone-Releasing Factor) (ii) LH-RF (In female) (Luteinizing Hormone-Releasing Factor)	Increased FSH secretion from adenohyophysis. Increased LH secretion from adenohyophysis.
ICSH-RF (In male) (Interstitial Cells Stimulating Hormone-Releasing Factor)	Increased ICSH secretion from adenohyophysis.
Prolactin-Releasing hormone (P-IH)	Increased secretion of prolactin or leutotrophic hormone.
Prolactin-Inhibiting hormone (P-IH)	Inhibits the secretion of prolactin or leutotrophic hormone.
MSH-RF or MRF (Melanophore Stimulating Hormone-Releasing Factor)	Increased MSH release from intermediate pituitary lobe.
MIF (Melanophore Inhibiting Factor)	Decreased release from intermediate pituitary lobe.

7.3.2 Pituitary Gland

- It is a small sized, (about 1.3 cm in diameter) pinkish-coloured, pea-seed shaped gland present below the hypothalamus, so it is also called hypothalamus cerebri.
- It lies in a depression called sella turcica, in the sphenoid bone of cranium of skull.
- It is connected to hypothalamus by an infundibular stalk formed of connective tissue with blood capillaries and nerve fibres.

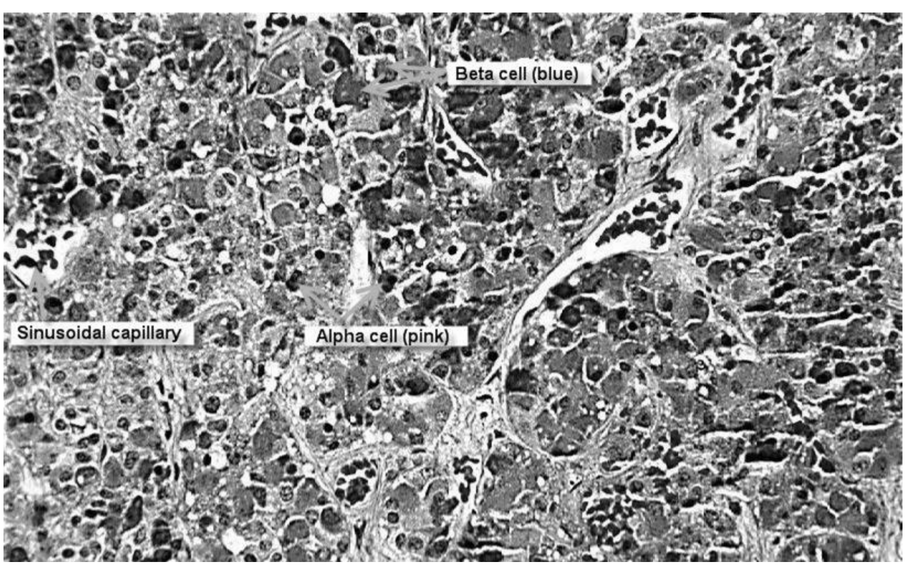


Relationship between Hypothalamic Neurons and Anterior and Posterior Pituitary Cells

- Anatomically, the pituitary gland is formed of two parts-
  - Adenohypophysis develops as an outgrowth of pharynx, called Rathke's pouch, and is formed of three parts- the pars distalis, the pars tuberlis and the pars intermedia (Intermediate lobe). Pars distalis and pars tuberlis together are known as anterior lobe of pituitary.
  - Neurohypophysis develops as a downgrowth of hypothalamus and forms pars nervosa, which forms the posterior lobe of pituitary.

7.3.2.1 Hormones of Adenohypophysis

- Adenohypophysis secrets 7 hormones, all being proteinous in chemical composition.
- Most of these are trophic in function (so are called tropins) and exert important regulatory actions on other endocrine glands, called secondary target organs of hypothalamus, to increase or inhibit their secretion (secondary target organs of hypothalamus).
- So pituitary gland is also called "Master Gland" or "Master of endocrine orchestra;. So is the most important endocrine gland.
- Some of these control the growth of the body as a whole.
- But now it has been proved that the pituitary acts as an "Executive officer" of the hypothalamus and simply carries the instructions of the hypothalamus to other endocrine glands of body.
- Secretion of these trophic hormones is controlled by releasing or inhibiting hormones of hypothalamus through a feedback mechanism which operates either at gene level or at enzyme level.
- Histologically, adenohyophysis is formed of 5 types of endocrine cells which secret seven types of hormones.
- There are somatotropes (30%-40% and secrete STH or Growth hormone); Corticotropes (about 20% and secrete ACTH); Thyrotropes (secrete TSH); Gonadotropes (secrete FSH, LH and ICSH) and Lactotropes (secrete prolactin).
- The hormones of adenohyophysis with their physiological effects and disorders caused due to their imbalanced level are listed in



Pituitary gland

Hormones of adenohyophysis, their physiological effects and disorders due to their imbalanced level

Region	Hormone	Chemistry	Physiological effects	Disorders
Pars distails	TSH (Thyroid Stimulating Hormone) or Thyrotropin	Glycoproteins	Increased iodine uptake, synthesis of thyroxine and breakdown of colloid of thyroid follicles to release thyroxine.	
	ACTH (Adrenocortico-trophic Hormone)	Polypeptide	Increased secretion corticoids, especially glucocorticoids from adrenal cortex.	
	STH or hGH (Somatotrophic Hormone or Human Growth Hormone) (Gr. Soma = body; (Gr. Soma = body; trophe = nourishment)	Proteinous	Stimulates growth of body by • Increased growth of bones by increased, absorption of calcium from intestine. • Increased lipolysis in adipose tissue. • Increased amino acid uptake and protein synthesis. • Increased glucose level in blood by decreased secretion of insulin. • Increased cell division. • Decreases use of blood glucose for ATP production.	• Dwarfism characterised by retarded physical growth (3- 4 fit) caused by deficiency of STH in children but patient has normal brain. • Acromicria (Simmond's disease): due to hyposecretion by smaller hands, feets and face, premature ageing. • Gigantism. Characterized by abnormal increased height (7-8 ft) and long bones due to over secretion of STH from childhood. • Acromegaly characterised by abnormal elongation of limbs and lower jaw, giving gorilla like appearance

				and, kyphosis protruding bony ridges over the eyes. It occurs due to over secretion of STH in adult.
	Lactogenic or Prolactin Hormone (PRL) or Mammotrophin (MTH) or Luteotrophic hormone (LTH). 5 & 6. Gonadotrophins or Gonadotrophic Hormones (Gn TH). • FSH (Follicular Stimulating Hormone) in both sexes. • LH (Luteinizing Hormone in female) • Or ICSH (Interstitial cells stimulating hormone in male).	Peptide Glycoproteinous	• Proliferation of mammary glands and formation of milk after the birth of baby. • In birds like pigeon, dove etc. it stimulates formation of crop glands. Regulate the growth and functioning of gonads. Also called Gametokinetic factor • Gametogenesis in gonads (Tests and Ovaries) to form gametes (sperms and ova). In males, stimulates spermatogenesis while in females, stimulates growth of ovarian follicles. • Stimulates secretion of estrogens from the ovaries. • Ovulation from ovary. • Formation of corpus luteum. Stimulates interstitial cells of testes to secrete male sex hormone, testosterone (androgens) which controls development of secondary sex organs and secondary sexual characters.	
Pars inter-media	MSH (Melanophore Stimulating Hormone) or Intermedin.	Polypeptide	Controls the synthesis and dispersal of melanin granules in the chromatophores (pigment cells) in the skin of fishes, amphibians and some reptiles (poikilothermal animals). So it causes darkening of skin. It is non-functional in man.	

7.3.2.2 Hormones of Neurohypophysis

- Neurohypophysis (Pars nervosa or posterior lobe) is with two types of groups of neurosecretory cells, called nuclei which secrete nonpeptide hormones-oxytocin and vasopressin.
- These are stored in the end knobs of the axons present in posterior lobe of pituitary and are released in blood when required, so these are also called Neurohypophyseal hormones.

Neurohypophyseal hormones and their physiological effects

Hormone	Physiological effects
Oxytocin or Pitocin (Gr. Oxytocin = Quick birth) (Secreted by Paraventricular nucleus of hypothalamus)	• Contraction of smooth muscles of myometrium of uterus during parturition (child birth) for normal delivery, so also called 'birth hormone'. So its secretion is more near the end gestation period. Sometime synthetic oxytocin is given to pregnant woman to induce labour contractions during delivery. • Contraction of smooth muscles surrounding the alveoli of mammary glands in lactating females during sucking of nipples by the infant, so releasing milk. It is also called "milk-ejection hormone".
Vasopressin or Anti Diuretic Hormone (ADH) or Pitressin. (Secreted by supraoptic nucleus of hypothalamus)	• Contraction of smooth muscles of arterioles, so exerts pressure effect and increases blood pressure so is called vasopressin. • Controls the permeability of wall of collecting tubules and DCT of renal tubules to water, so controls the osmoregulation (water balance in the body fluids). • Its secretion is stimulated by rise in osmotic pressure of blood due to loss of water. Increase in osmotic pressure stimulates osmoreceptors. It increase facultative reabsorption of water and decreases urine output and conserves the body fluid, called antidiuretic effect, so is called antidiuretic hormone (ADH). Its secretion is more in desert mammals like camel, kangaroo rat, etc. Deficiency of ADH causes decreased reabsorption of water from collecting tubules. This causes Diabetes insipidus (Gr. Incipit = tasteless) characterized by diuresis (10 liters urine/day) polydipsia (increased thirst) but urine has no sugar.

Differences between Cretinism and Dwarfism

Characters	Cretinism	Dwarfism
Cause	Deficiency of thyroxin in childhood.	Deficiency of STH in childhood.
Symptoms	Decreased BMR, stunted growth, mentally retarded and late puberty.	Decreased BMR, stunted growth so dwarf but mentally normal.

Difference between FSH and LH

Characters	FSH	LH
Occurrence	In both the sexes.	Only in female.
Primary function	Controls, gametogenesis, so called Gametokinetic hormone.	Controls ovulation.
Other functions	No effect on corpus-luteum but stimulates secretion of estrogens.	Stimulates formation and secretion from corpus luteum.

Differences between Somatotrophin and Somatostain

Characters	Somatotrophin	Somatostatin
Source	Secreted by anterior lobe of pituitary.	Secreted by hypothalamus.
Function	Stimulates body growth.	Decreases the secretion of growth hormone from the anterior pituitary.

Differences between Gigantism and Acromegaly

Characters	Gigantism	Acromegaly
Cause	Over secretion of STH or Growth hormone from the childhood period.	Over secretion of STH or Growth hormone in adult.
Symptoms	Abnormal height (about 7-8) and long bones but the body parts are proportionate.	Abnormal elongation of only some body parts like arms, legs, jawbones, bony ridges over the eyes, etc. so giving gorilla like appearance.

Differences between Diabetes mellitus and Diabetes insipidus

Characters	Diabetes mellitus	Diabetes insipidus
Causes	Deficiency of insulin.	Deficiency of Vasopressin (ADH).
Blood testing	Hyperglycemia, ketonaemia, acidosis (6.8 pH)	No such symptoms.
Urine testing	Glycosuria, Ketonuria, diuresis.	Only diuresis. No Glycosuria and Ketonuria.

Difference between Vasopressin and Oxytocin

Characters	Vasopressin	Oxytocin
Source	By neutrons of supraoptic nucleus of hypothalamus.	By neurons of Paraventricular nucleus of hypothalamus.
Functions	• Helps of osmoregulation. • Increases blood pressure.	• Contraction of uterine muscles so helps in child birth. • Release of milk from mammary glands.

7.3.4 Pineal Body

- It is a small (8 $\times$4 mm), knob-like body present at the top of pineal stalk on the dorsal side of superior coliculi of mid brain. It is small, reddish-grey, pine-cone shaped, and solid endocrine gland formed of parenchymal and neuroglial cells.
- It was considered vestigial of 3rd eye earlier but now has been confirmed to be endocrine gland. It secretes melatonin hormone.
    - It controls development and concentration of melanin in melanocytes of skin of frog (lower vertebrates). So it makes the skin lighter in colour.

- It plays important regulatory role in sexual and reproductive function. It inhibits the ovarian functions.
- It regulates the 24-hour (diurnal rhythm) of the body like sleep-wake cycle, body temperature, etc.

7.3.5 Thyroid (Gr. Thyreo = shield; eidos =shaped)

- It is largest endocrine gland (5×2 cm) and 25 gm in weight.
- It lies on ventral and lateral sides of upper part of the trachea in the neck.
- It is brownish red, shield-shaped, bilobed and butterfly-shaped gland.
- Two lobes are interconnected by a transverse glandular bland, called isthmus so is H-shaped.
- Histologically, it consists of about 3 million, small, oval or rounded thyroid follicles held together by stromal tissue and enclosed by a white fibrous capsule.
- Each follicle is lined by a cuboidal glandular follicular epithelium of acinal cells and surrounds a gelatinous material, called colloid which is inactive glycoproteinous thyroglobulin.
- Scattered in connective tissue and between the thyroid follicles, there are groups of endocrine cells, called parafollicular or G-cells.
- Thyroid gland secrets two hormones-
  - Thyroxine and Thyrocalcitonin (TCT). Secretion of Thyroid gland is regulated by TSH of anterior pituitary lobe.
  - Thyroxine-It is an iodine containing (65% iodine) amine hormone which is derived from tyrosine amino acid. Chemically thyroxine is tetra-iodothyroniene though also found as tri-iodothyroniene. These hormones perform following functions.
    - These regulate Basal Metabolic Rate (BMR) of the body as control rate of cell respiration and energy production in mitochondria. So these control physical, mental and sexual growth of body.
    - These control tissue differentiation and metamorphosis of tadpole larva into adult frog. It is evident from the fact that a thyroidless larva fails to undergo metamorphosis.
    - These control working of renal tubules of kidneys so control urine output.
    - These help in homeothermy in warm blooded animals.
    - Promote the protein synthesis.
    - Influence the maintenance of water and electrolyte balance in the body.
- Hypothyroidism (Decreased secretion of Thyroxine from Thyroid Gland). It may be due to following reasons:
  - Decreased TSH stimulation.
  - Hypoacitivity of acinal cells of thyroid gland.
  - Decreased I_2 intake in the diet.
- It leads to the following diseases-
  - Cretinism -It is a disease of infants, called Cretin. It is characterized by Decreased BMR (50% than normal); stunted growth; retarded mental development so low I.Q. delayed puberty; decreased body temperature, heart rate, pulse rate, blood pressure and cardiac output; reduced urine output; decreased sugar level in blood, dry skin, deaf-mutism, lethargy, constipation, pigeon's chest (chest bulging forward in sterna region). Cretinism can be congenital (absence of thyroid due to

genetic defect) or endemic (absence of iodine in diet. It can be correct by thyroxine administration.

- Myxoedema - It occurs due to deficiency of thyroxine in adults. Like cretinism, it also has low BMR (by 30-40&); low body temperature; reduced heart rate, pulse rate, blood pressure and cardiac output; low sugar and iodine level in blood etc. But the peculiar feature of myxoedema is that face and hands become swollen due to deposition of albuminous myxomatous tissue. In females, it also causes irregular menstrual cycle.
- Endemic or Simple Goitre or Colloid goitre-It occurs due to deficiency of iodine in drinking water. It is non-genetic (Sporadic goitre is a genetic disease) It is characterized by enlargement of thyroid gland due to increase in number and size of acinal cells of thyroid gland. It is more common in people of hilly region. To prevent goitre, the table salt is being iodised these days.
- Hashimoto's disease -It is also called autoimmune thyroiditis and occurs due to age-factor or injury to thyroid gland causing hyposecretion of thyroxine. When thyroxine secretion falls upto minimal limit, the antibodies are formed which destroy the thyroid gland.

- Hyperthyroidism-It occurs due to cancer of thyroid gland and is characterized by increased secretion of thyroxine causes exophtalmic goitre. Main symptoms of this disorder are-enlargement of thyroid gland (2-3 times more than normal size); increased BMR (double than normal rate); increased hear rate, pulse rate and cardiac output; increased body temperature, reduced body weight due to rapid oxidation of even stored food; osteoporosis due to loss of Ca and P from bones etc. Peculiar symptom is a peculiar oedema behind the eyes so causing bulging eyeballs with starting look and less blinking. It can be corrected by removing a part of the gland.
- Thyrocalcitonin (TCT)-It is a long peptide hormone secreted by parafollicular cells of thyroid gland. Its secretion is regulated by increased plasma level of calcium by feedback mechanism. TCT is hypocalcaemia factor so lowers calcium level in blood to normal by-
  - Increasing calcium deposition of calcium from urine so checks osteoporosis.
  - Decreasing reabsorption or calcium from urine, so increasing excretion of Ca^{2+}.
  - So it prevents hypercalcaemia.

Differences between Exophthalmic goitre and Iodine-deficiency goitre

Characters	Exophthalmic goitre	Iodine-deficiency goitre
Size of Thyroid gland	Increase in size	Increases in size (about 15 times).
Cause	Hypersecretion of thyroxine.	Less secretion of thyroxine.
BMR	Increases	Decreases
Other symptoms	Faster heart beat, pulse and blood pressure.	Slower heart beat, pulse and blood pressure.
Effect on eyes	Bulging outward.	No effect.

7.3.6 Parathyroid Glands

- These are four pea-shaped glands which are wholly or partially embedded in the dorsal surface of the thyroid gland, two glands in each lobe of thyroid gland.
- Each is oval-shaped, small sized (5 $\times$ 5 mm) and yellow coloured.
- Histologically, a parathyroid gland is formed of masses of polygonal cells arranged in cords. Endocrine cells are called chief cells.
- Hormone. Active hormone secreted by parathyroids is Parathormone (PTH), also called Collip's.
- It is a polypeptide hormone. Its secretion is stimulated by low level of calcium in blood than normal level through feedback control.
  - PTH is a hypercalcaemia factor so increases calcium level to normal by following actions:
    - Increases activity of Osteoclasts which separate calcium from the bones called bone resorption.
    - It reduces excretion of calcium in urine as increases reabsorption of calcium.
    - Increases absorption of calcium from intestine. Normal Calcium/Phosphorus balance helps in normal growth of bones and teeth; blood clogging; normal muscle contraction and nerve impulse conduction.
  - Hyperparathyroidism (Hyposecretion of Parathormone due to accidental damage to the parathyroids) leads to parathyroid or hypocalcaemictetany which is characterized by marked fall in calcium level in blood (6 mg/100 ml) and causes muscle-twiches, painful spasmodic contraction of muscles of face, hands, feet and larynx; and increased neuro-excitation.
  - Hyperparathyroidism (Hypersecretion of parathormone due to tumour in the parathyroids). It causes osteitis fibrosa cystic, which is characterized by increased separation of calcium from bones so causing osteoporosis, softening and bending of bones, areas of damaged bones are replaced by cavities, high calcium level in blood and loss of calcium in urine. Sometimes, calcium is deposited in kidney tubules leading to kidney stones and decreased urine output.

7.3.7 Thymus

- Thymus is a soft, pinkish, bilobed mass of lymphoid tissue present just above the heart. It is large sized and active in the young child, grows to maximum size at puberty and then atrophies gradually. Histologically, it is formed of outer cortex and central medulla. Internally, it is formed of many labules held together by connective tissue.
- Thymus secrets one or more stimulatory factors, collectively called thymic hormones (most important being thymosine-a polypeptide hormone).
  - Thymus is the site of differentiation of T-lymphocytes of immune system.
  - Thymosine increases the activity of T-lymphocytes which provide cell-mediated immunity.
  - It also has Hassall's corpuscles which act as phagocytes.
  - It increases the rate of cell division so controls the rate of growth early life.
  - It increases the production of antibodies from B-lymphocytes so provides humoral immunity.

7.3.8 Adrenal Glands

- Adrenal glands, also called supra-renals, are one pair of yellowish coloured, tricon-shaped, small sized (4×3 cm) glands present on the upper border of kidneys.
- Histologically, an adrenal gland consists of two distinct portions, viz. outer adrenal cortex (80-90%) and inner adrenal medulla (10-20%) which differ structurally, functionally and embryologically from each other.

Differences between Adrenal cortex and Adrenal medulla

Characters	Adrenal cortex	Adrenal medulla
Position	Outer part of adrenal gland.	Central part of adrenal gland.
Colour	Pale yellowish pink.	Dark reddish brown.
Percentage	From 80% of adrenal gland.	From 20% of adrenal gland.
Origin	Mesodermal.	Ectodermal.
Differentiation	Differentiated into three zones: zona glomerulosa, zona fasciculate and zona reticularis.	Not differentiated into zones.
Nature of hormones	Steroid hormones.	Amine hormones.
Type of hormones	Mineralocorticoids, glucocorticoids and sex corticoids.	Adrenalin and noradrenalin.
Control	Under ACTH of pituitary.	Under sympathetic nerve fibres.
Association with sympathetic nervous system	No.	Yes.

7.3.8.1 Hormones of Adrenal Cortex

- Adrenal cortex is mesodermal in origin, formed of three peculiar zones of cells (Zona glomerulosa, Zona fasciculate and Zona reticularis) and secretes 40 different steroid hormones, collectively called Adrenocorticoids.
- All these corticoids are synthesized through the modifications of cholesterol.
- Corticoids are divided in three categories on the basis of their functions.
  - Mineralocorticoids-These include Aldosterone, 11-Deoxycorticosterone etc. These are secreted by zona glomerulosa of adrenal cortex. Their secretion is stimulated by decrease in sodium level of increase in potassium level in blood. Secretion of aldosterone is stimulated by ACTH and angiotensin.
    Mineralocorticoids maintain hypernatraemia (high Na^+ level in blood) and sodium reabsorption from nephric filtrate and decreased loss of sodium in sweat, so Aldosterone is also called salt-retaining hormones. Increased sodium concentration increases sat concentration of interstitial fluid which increases water reabsorption and blood sugar, excretion of Na^+ and water in urine (dehydration), nervous depression, nausea, vomiting, weakness, low blood pressure and diarrhea.
    Excess of aldosterone causes Aldosteronism characterized by hypernatraemia, hypokalaemia, increased blood volume and blood pressure. This causes irritation in nervous tissue.
  - Glucocorticoids-These include Cortisol, (main Glucocorticoid), Cortisone, Corticosterone, Dehydrocorticosterone etc. These are secreted by the zona fasciculate of adrenal cortex.

- Glucocorticoids are primarily meant for carbohydrate metabolism. Their chief physiological functions are:
  - Increased rater of gluconeogenesis (conversion of proteins in liver into sugars.)
  - Decrease in peripheral utilization of glucose.
  - These have anti-inflammatory and anti-allergic actions. These also depress immune response. So these are used against the problems like rheumatoid arthritis, asthma, organ transplantation, conjunctivitis, autoimmune diseases etc.
  - These act as vasoconstrictor in case of excessive bleeding to counter the drop in blood pressure.
- Over secretion of cortisol (Glucocorticoid) causes cushing syndrome which is characterized by high sugar level in blood; loss of sugar in urine; loss of weight as large number of amino acids changed into sugars; high Na^+/low K^+ concentration in the plasma; rise in blood volume and blood pressure and swollen face, neck, hands etc. due to deposition of fats below the skin of these body parts.

Differences between Glucocorticoids and Mineralocorticoids

Characters	Glucocorticoids	Mineralocorticoids
Source	Secreted by zona fasciculate of adrenal cortex.	Secreted by zona glomerulosa of adrenal cortex.
Functions	These regulate carbohydrate metabolism and increase the sugar level of blood.	These regulate Na^+/K^+ level in blood.
Examples	Cortisol.	Aldosterone.

- Sex corticoids (Gonadocorticoids) - These include Androstenedione, Androsterone, Dehydroepiandrosterone etc. These are secreted by zona reticularis of the adrenal cortex. These also include small amounts of female sex hormones like estrogens and progesterone.
- These stimulate the development of secondary sexual characters of male type distribution of axillary, public and facial hair, deepening of voice etc. Estrogens stimulate the appearance of female secondary sexual characters like breast enlargement, beginning of menstruation, etc.
- Over secretion of sex corticoids in female causes Adrenal virilism or pseudohermoaphroditism in which male type secondary sexual characters like facial hair, hoarse voice etc. appear in the female while it cause gynaecomastia (enlarged breasts) in males.

7.3.8.2 Hormones of Adrenal Medulla

- Adrenal medulla is central part of adrenal gland and is derived from nervous tissue (ectodermal in origin).
- Glandular cells of adrenal medulla are called chromaffin cells which secrete two hormones.
- 80% Adrenalin (epinephrine) and 20% Noradrenalin (nor-epinephrine).
- Both these hormones are amine hormones and are derivatives of catechol, so collectively called cateholamines.
- Adrenalin is a sympathomimetic hormone because it has same biological effects as of sympathetic nervous system.
  - Increase the rate of heart beat and cardiac output, so increases blood pressure.
  - Increases the rate of tissue oxidation so increases BMR (20% more than normal rate).

- Increases sugar level in blood by stimulating glycogenolysis in liver.
- Increases respiration rate as dilates trachea.
- Increases lipolysis in adipose tissue to increase level of fatty acids in blood.
- Dilation of pupil of eye.
- Increased blood supply to heart, skeletal muscles and brain as acts as vasodilator.
- Stimulates the contraction of spleen to release the stored blood.
- Goose flesh due to contraction of arrector pili muscles to erect the body hair called piloerection.

- In general, adrenalin prepares the body to face emergency conditions of physical and emotional stress like fall in blood pressure, muscular exertion, pain, cold, injury, anger, fear etc. so epinephrine is also called emergency hormone or hormones of 'Fight or Flight' and adrenal glands are called Glands of Emergency.
- Hyperactivity of adrenalin causes hypertension which may cause death.
- Nor-adrenalin (nor-epinephrine) more or less resembles adrenalin in its biological effects that it operates during normal state, exercise lesser effect on cardiac activity and produces greater constriction of blood vessels in the muscles.

Summary of Hormones of Adrenal Glands and their Action on the Target Cell

Adrenal Gland Hormones	Principal Action	Target Tissue
Mineralocorticoids example-aldosterone (mainly), deoxy-corticosterone	Control electrolyte and water metabolism, increase blood levels of Na^+ and water, decrease blood levels of K^+ by stimulating kidney tubules to reabsorb more Na^+, Cl^- and water and less K^+.	Kidney
Glucocorticoids	Raise blood glucose level; promote liver glycogen formation; breakdown of plasma protein; increase availability of amino acids for enzyme synthesis; general resistance to long-term stress by inflammatory and allergic responses.	Liver
Gonadocoricoids	Development of secondary sexual characteristics, particularly those of the male; concentrations secreted by adults are so low that their effects are usually insignificant.	Gonads
Adrenaline	Stimulates elevation of blood glucose by converting liver glycogen to glucose; rise in blood pressure; acceleration of rate and force of heart beat; constriction of skin and visceral smooth muscle capillaries; dilation of arterioles of heart and	Skeletal muscles, cardiac muscles, smooth muscles, blood vessel, fat cells.

	skeletal muscles; increase in breakdown of lipids; increase in oxygen consumption; erection of hairs (goose flesh); dilation of pupils; initiates stress responses.	
Nor-adrenaline	Stimulates reactions similar to those produced by adrenaline.	

7.3.9 Pancreas

- It is an elongated, yellow coloured, second largest gland (12-15 cm), about 85 gm in weight, located in the loop of duodenum
- Pancreas is a heterocrine gland or composite gland.
- The endocrine part is formed of about 1 to 2 million groups of epithelial cells, called islets of Langerhans (discovered by Langerhans, 1869), scattered in the connective tissue between acini (exocrine part) of the pancreas .
- Endocrine part forms about 1-2% of the pancreatic mass. Each islet of Langerhans has about 3,000 cells.
- An islet of Langerhans is formed of three types of cells:
  - (Alpha) α cells (also called Oxyphils). These secrete glucagon hormone.
  - (Beta) β cells. These secrete insulin hormone.
  - (Gamma) γ cells. These are precursor of (α) and (β) and (β) cells.
- All the pancreatic hormones are polypeptides.
  - Insulin-It is earliest known hormone. It is also called Hypoglycemic or antidiabetic factor, as it decreases glucose level in blood and prevents occurrence of diabetes. It is secreted by β-cells of the islets of Langerhans. Secretion of insulin is stimulated by higher glucose level (60-100 mg/ 100 ml of blood) or rise in amino acid concentration. Insulin acts on three target tissues - hepatocytes of liver, muscles and adipocytes of adipose tissue. It performs following functions:
    - Stimulates utilisation of glucose as respiratory fuel in body cells.
    - Stimulates glycogenesis (conversion of glucose into glycogen) in muscle and liver cells.
    - Prevents gluconeogenesis (conversion of amino acids into sugars).
    - Spares amino acids for protein synthesis.
    - Conversion of excess of glucose into fats.
    - Prevents formation of ketone bodies in blood as reduce the respiratory breakdown of fats.
  - Hypoacitivity (rise in sugar level in the blood about 3 times and is more than 150 mg/100 ml of blood), diuresis (10 times more urine output), polydipsia, (increased thirst), glycosuria (sugar in urine – 100 gm/24 hours), ketonaemia (ketone bodies like acetoacetic acid, butyric acid in blood due to increased oxidation of fats), ketoneuria (ketones in urine), decreased glycogen in liver and muscles, increased cholesterol level in the blood, delayed healing, blurred vision, acidosis (pH of blood decreased from 7.4 to 6.8), diabetic coma and death.

Controlled dose of insulin and sugar free diet are best preventive measures to diabetes melitus. There is another more common type called insulin-independent diabetes in which insulin level is normal but it cannot move glucose for storage or its use as respiratory fuel. So a person is not able to use insulin.

Difference between Insulin-dependent and Non-insulin-dependent diabetes mellitus

Cause	Insulin-dependent diabetes mellitus (IDDM) –(Type-)	Non-insulin-dependent diabetes mellitus (NIDDM)- (Type-II)
Cause	Degeneration of β-cells of islets of Langerhans. So there is severe insulin deficiency.	Deficiency of insulin-receptors on the plasma membrane of liver cells. There is mild insulin deficiency.
Symptoms	Ketoacidosis is common but weight is normal.	Ketoacidosis is rate but patient is generally obese.
Period of occurrence	Generally below 20 years.	Generally after the age of 30 years.

Summary of Hormones of Pancreas and their Actions on Target Cells

Endocrine Cells of Pancreas	Hormone	Principle Action	Target Tissue
α cells	Glucagon (polypeptide)	Raise blood glucose level by- • Accelerating breakdown of glycogen into glucose (Glycogenolysis) in liver; • Promoting conversion of other nutrients, such as amino acids and lactic acid, into glucose (Gluconeogenesis) in liver; • Enhancing release of glucose into blood.	Liver, adipose tissue.
β cells	Insulin (polypeptide)	Lowers blood glucose level by: • Stimulating transport of glucose from blood to muscle and adipose cell and indirectly causing the liver to take up glucose; • Promoting both oxidation of glucose(Glycolysis) and conversion of glucose into glycogen (Glycogenesis) in muscles as well as liver cells; • Inhibiting metabolic breakdown of stored glycogen in liver and	Liver, muscle, adipose tissue

		muscle cells; • Promoting synthesis of fats from glucose by adipose tissue and also inhibiting metabolic breakdown of fat; • Promoting uptake of amino acids by liver and muscle cells, and stimulating protein synthesis while inhibiting protein breakdown.	
γ cells	Somatostain (polypeptide)	Inhibits secretion of glucagon and insulin; decrease secretion, motility and absorption in the digestive tract.	Pancreas, intestine.

- Glucagon. It is a hyperglycemic or diabetogenic polypeptide hormone secreted by α-cells of islets of Langerhans. Its secretion is stimulated by low blood sugar level.
- Glucagon is antagonistic to insulin. (Antagonistic hormones are those which work against each other). Glucagon increases sugar level in blood b promoting glycogenolysis in liver cells, increasing gluconeogenesis and inhibiting conversion of glucose to lactic acid.
- Islets of Langerhans also have another type called delta cells which secrete Somatostatin (SS). It is a polypeptide hormone and inhibits the secretion of glucagon and insulin.

7.3.10 Gonads

- Gonads (Testes in male and ovaries in female) are both exocrine (porduce gametes) as well as endocrine in function.
- Their hormones control reproductive activities and are secreted from the attainment of puberty.

7.3.10.1 Tests

- The endocrine part of testes is formed of groups of cells, called interstitial cells or Leydig's cells, scattered in connective tissue between the sperm-producing seminiferous tubules of the testes.
- Interstitial cells of testes are stimulated to secrete male sex hormones, called androgens, by ICSH of anterior pituitary by a feedback mechanism.
- Four main types of androgens are -Testosterone, Androsterone, Epiandrosterone and Dehydro- epiandrosterone.
- Out of these, testosterone is main androgen and is a steroid hormone.
  - Controls the growth and development of male secondary sex organs like epididymis, prostate glands, seminal vesicles and penis.
  - Stimulates the development of male secondary sexual characters like beard, moustaches, deepening of voice, broadening of shoulders, increased height due to elongation of bones and increased development of limbs.
  - It is responsible for sex-urge for a female partner.
  - Androgens produce anabolic (synthetic) effects on protein and carbohydrate metabolism.

- Stimulates spermatogenesis and maturation of sperms. It also increase the fertilizing power of the sperm.

- Eunuchoidism - The failure of testosterone secretion may be due to hypofunctioning of Leyding cells or sertoli cells or both before puberty. It causes eunuchoidism and person suffering from eunuchoidism is called eunuch or neuter. It is characterized by reduced secondary sex organs (like prostate gland, seminal vesicles, male musculature, and penis), failure of development of secondary sexual characters of male (like beards, moustaches, low-pitch voice, etc.) and failure of spermatogenesis so is sterile.

7.3.10.2 Ovaries

- Just like testes, the ovaries are cytogenic as well as endocrine in function. Ovaries secrete three types of female hormones.
  - Estrogens-These are a group of steroid hormones mainly secreted by follicular epithelial cells of membrane granulose of Graafian follicle though these are also produced by the adrenal cortex and placenta. These include β-estradiol, estrone, estriol etc. out of which most important estrogen is β-estradiol. Secretion of estrogens is stimulated by LH (Luteinizing hormone) of anterior lobe of pituitary gland.
    - Stimulate the growth and normal functioning of female secondary sex organs like fallopian tubes, uterus, vagina etc.
    - Control the development of female secondary sexual characters like breast-enlargement, broadening of pelvis, growth of pubic and auxiliary hair, and beginning of menstrual cycle.
    - Regulate the female sexual behavior.
    - Decrease the secretion of FSH while increase the secretion of LH .
    - Hypogonadism in female- It occurs due to hyposecretion of estrogens or hyposecretion of gonadotrophic hormones (FSH and LH) of pituitary gland. It causes ovary failure and cessation of reproductive cycles so leading to sterility.
  - Progesterone- It is also a steroid hormone secreted by a yellow endocrine gland, corpus luteum, formed from empty Graafian follicle during the pregnancy small amount of progesterone is stimulated by LH of anterior lobe of pituitary gland.
    - Stimulates proliferation of endometrium of uterus and prepares it for implantation.
    - Desensitizes the uterine muscles to the action of oxytocin.
    - Helps in implantation, placenta formation and normal development of the foetus in the uterus.
    - Suspends ovulation during pregnancy as decreases the secretion of LH.
    - Stimulates proliferation of mammary glands and enlargement of breast.
  - Relaxin-It is a proteinous hormone secreted by the corpus albicans formed from the corpus luteum at the end of gestation period. If softens the public symphysis so helps in parturition (child birth).
  - Placements is a mechanical and physiological connection between the developing embryo and the maternal tissue. Its primary function is support and nourishment of the developing embryo, but also acts as endocrine gland during pregnancy. The chronic villi of placenta secret several Gonadotrophins like estrogens, progesterone and HCG (Human Chorionic Gonadotrophins). HCG is a glycoproteinous hormone whose primary function is to maintain the corpus luteum for continued secretion of progesterone so as maintain the pregnancy. It also controls the normal development of foetus in the mother's womb.

Difference between Estrogens and Progesterone

Characters	Estrogens	Progesterone
Source	Follicular cells of Graafian of ovary.	Luteal cells of corpus luteum.
Under the control of	FSH of anterior pituitary.	LH of anterior pituitary.
Functions	• Functioning of secondary sex organs of female. • Development of secondary sex characters in female. • Sex desire for male.	• Proliferation of endometrium of uterus. • Implantation, placentation and normal maintenance of pregnancy.

Summary of hormones regulating reproduction

Endocrine gland	Hormones	Principal action
Ovarian follicle	Estrogen	Stimulates development and maintenance of female sexual characteristics like high pitch, female voice and female pattern of body hair distribution at puberty; together with gonadotropic hormones of the anterior pituitary gland, they also regulate the menstrual cycle.
Corpus luteum	Progesterone and Estrogen	Stimulate uterine lining for embryo implantation to maintain pregnancy (foetal development); prepare the mammary glands for lactations and regulate oogenesis, progesterone inhibits ovulation.
	Relaxin	Relaxes pubic symphysis and helps dilate uterine cervix near the end of pregnancy.
	Inhibin/actin	Inhibition/activation of FSH and GnRH production.
Testes	Testosterone	Stimulates the descent of tests in scrotal sacs and male pattern of development (before birth); stimulates development and maintenance of male sexual characteristics and expression of secondary characteristics, such as beards, moustache and low-pitch voice; starting of puberty; stimulation of spermatogenesis; growth spurt.
	Inhibin/actin	Activation/inhibition of LH and FSH production.
Placenta	Human Chronic Gonadotropin	Stimulates progesterone release from the corpus luteum and maintains it.
	Human Placental Lactogen	Stimulates mammary growth.

Hormones of Heart, Kidneys and Gastrointestinal Tract

- Certain endocrine tissues are not organised to form compact endocrine glands but are presented isolated in certain body parts example-
  - Endocrine cells present in the atrial wall of heart secrete a polypeptide hormone called Atrial natriuretic factor (ANF) which decreases the blood pressure so is secreted in case of increased blood pressure. ANF causes vasodilation which reduces the total peripheral resistance and the blood pressure.
  - Erythropoietin-It is a glycoproteinous hormone secreted by juxtaglomerular cells of the afferent arteriole of the kidney in response to reduces RBC count i.e. anaemia. It stimulates erythropoeisis (RBC formation) in the bone marrow.
  - Gastro-Intestinal hormones- Explain in "Regulation of Digestion" in Chapter 16 of this book.

Feedback Control and Hormonal Secretion

- Homeostasis (Gk. Homeo = same; stasis = state) is the phenomenon which helps in maintaining a constant internal environment in a living system. Term homeostasis was coined by Water B. Cannon. It is also called physiological equilibrium. This internal optimal called physiological equilibrium is the outcome of "feed-back mechanisms" which states that a metabolite will be produced (switched on) only when its level is below than required level while its amount reaches the required level. This "switch on" or "switch off" mechanism operates either at gene level (operon concept) or at the enzyme level.
- Examples of feedback control on secretion of hormones
  - Regulation of thyroxine secretion from thyroid gland - Thermal changes (low body temperature) and increased food intake act as stimulate and stimulate the neurosecretory cells of hypothalamus to secrete a releaser hormone called Thyrotrophic releasing factor (TSH.RF) which, in turn, stimulates the Thyrotropes of adenohypophysis to secrete a thyrotrophic hormone (TSH). TSH (molecular weight = 28,000) stimulates the acinal cells of thyroid follicles to secrete amine-hormone thyroxine in the blood by increased proteolysis of thyroglobin, increased activity of iodide pump, increased synthesis of thyroglobulin, increased activity of iodide pump, increased synthesis of thyroxine, etc. When the thyroxine level of blood plasma reaches at required level, then thyroxine exerts a negative feedback (or feedback-inhibition) on the hypothalamus and anterior pituitary lobe to inhibit or decrease the secretion of TSH-RF and TSH respectively. When the rate of thyroxine secretion falls essentially to zero. But when thyroxine level of blood plasma falls below the normal required level, it exerts positive Feedback on the hypothalamus and anterior pituitary lobe which stimulate the thyroid gland to secrete more thyroxine and so on. So it is evident that secretion of thyroxine from thyroid gland is controlled by the level of thyroxine hormone in blood through a feedback mechanism.
- Feedback relationship between osmotic concentration and ADH secretion- When the osmotic concentration of ECF increases due to deficiency of water in the body fluids, then osmoreceptors (modified neurons) of the hypothalamus are stimulated and appropriate signals are initiated which stimulate and appropriate signals are initiated which stimulated the hypothalamus to increase ADH secretion and increased release of ADH from the posterior pituitary. ADH is transported by the blood to the kidneys where it increases the permeability of the collecting tubules to water so most of water is reabsorbed from the nephric filtrate. It restores the normal osmotic concentration of blood. Reverse occurs

when extracellular fluid becomes too dilute due to excess of water. Therefore, a feedback control is available to control the osmotic concentration of the body fluids.

- Other examples of feedback control
  - Feedback control of secretion of calcium (Fig. 22.26). Secretion of Thyrocalcitonin of calcium parafollicular cells of thyroid gland is stimulated by increased plasma level of calcium (normal calcium level of blood is 8.5-10.5 mg/100 ml of blood) by the feedback mechanism. Similarly secretion of Parathormone (PTH) from the chief cells of parathyroids is stimulated by a decrease in calcium level in the blood from normal level.
  - Feedback control of secretion of Aldosterone. Secretion of Aldosterone (main Mineralocorticoids) from the endocrine cells of zona glomerulosa of adrenal cortex is regulated by sodium level in the blood by feedback mechanism. Low level of sodium or high level of potassium increases the secretion of aldosterone.
  - Feedback control of secretion of Insulin (Fig. 22.27). Secretion of insulin from the β-cells as well as secretion of glucagon from the α-cells of Islets of Langerhans is regulated by the glucose level of blood. Higher glucose level of blood plasma than the normal level (60-100 mg/100 ml of blood) stimulates the secretion of insulin while lower glucose level of blood plasma stimulates the secretion of glucagon.

Types of Endocrine Glands On The Basis of Mode of Action

- These are of two types-

Quick acting hormones- Those hormones which when secreted from endocrine glands initiate immediate and specific response from their target cells. Their receptor is always located on the outer surface of plasma membrane of target cells because these are large sized and not lipid-soluble, so cannot enter their cells through the bilipid layer of plasma membrane. Generally, this extracellular receptor is a glycoprotein. Hormone receptor complex activates a membrane-enzyme adenylcylase which hydrolyses ATP into cyclic AMP which acts as secondary messenger or intracellular hormonal mediator. c-AMP activates an inactive enzyme system by Cascade effect. So their mode of action is called second messenger hypothesis. These include proteinous (example- STH), peptide (example- Insulin) and amine (example- Epinephrine) hormones.

Differences between Quick acting and Lag period hormones

Characters	Quick acting hormone	Lag period hormone
Period of response	Immediately (within a few seconds) after secretion.	After certain lag period (may be in hours or years).
Size	Large sized and lipid-insoluble so are not diffusible through cell membrane of target cells.	Small sized and lipid-soluble so are diffusible.
Hormone receptor	On the cell membrane of target cells.	In the cytosol of target cells.
Mode of action	Though cascade effect.	Through m-RNA synthesis.
Second messenger	c-AMP.	Hormone-receptor complex.
Longevity	Longer.	Shorter.
Examples	Proteinous hormones	Steroid hormones.

- Hormones acting with a lag period. Those hormones in case of which, there is a time period between their secretion from the endocrine glands and the physiological response from their target cells. These are small sized and lipid-soluble so are diffusible through the plasma membrane of their target cells. These bind their proteinous receptor present in the cytosol. These always operate through de novo synthesis of m-RNA by activation certain genes. M-RNA controls the synthesis of specific intracellular proteins which initiate specific cellular functions. So their mechanism of action is called m-RNA hypothesis. These include steroid hormones of testes (example- Testosterone), ovaries (example- Estrogens) and adrenal cortex (example- Aldosterone).

Mechanism of Action of Quick Acting Hormones

- Cateholamines include epinephrine and nor-epinephrine of adrenal medulla.
- These are amine hormones and are derivatives of catechol. E.W.Sutherland (1950s) proposed second messenger hypothesis for their action on liver cells. It involves following steps.
  - Epinephrine acts as first messenger and binds to specific hormone receptor present on outer surface of the liver cells to form epinephrine-receptor complex.
  - The receptor undergoes conformational changes to activate another enzyme, called adenyl cyclase, present on inner surface of cell membrane of liver cells.
  - Activated adenyl cyclase hydrolyses cytoplasmic ATP into C-AMP (cyclic-Adenosine monophosphate) and pyrophosphate in the presence of Mg^{++} as cofactor A.
- Single molecule of activated adenyl cyclase can produce about 100 molecule of C-AMP which rapidly increases in concentration from 10^{-10} to 10^{-6} M and acts as second messenger.
  - Four molecules of C-AMP bind to an active protein-kinease complex to form active protein-kinase A enzyme which starts the casede effect.
  - Each molecule of active protein kinase-A enzyme activates several (about-100) molecules of inactive phosphorylase kinase enzyme by phosphorylation in the phosphate-donor ATP and Ca^{2+} as cofactor.
  - Each activated molecule of phosphorylase kinase enzyme activates several molecule of inactive phosphorylase-b into phosphorylase-a enzyme by phosphorylation in the presence of ATP and Ca^{++}.
  - Each active molecule of phosphorylase-a enzyme degrades the glycogen into glucose-1 phosphate in the presence of phosphate donor phosphoric acid.
  - Glucose-1-phosphate changes into its isomer glucose-6-phosphate in the presence of enzyme phosphoglucomutase.
  - Glucose-6-phosphate dissociates into glucose and phosphate in the presence of glucose-6-phosphatase.
- Due to cascade effect, a single molecule of epinephrine may lead to release of as many as 100 million molecules of glucose within 1 or 2 minutes. This increases the glucose level in the blood.

Mechanism of Action of Insulin

- Insulin is a polypeptide hormone.
- It is not soluble in lipids so is a quick acting hormone and operates through extracellular membrane-bound receptor.
- Its receptor is a heterotetrameric protein formed of four subunits of two types –
  - Two α-subnits which project outside the surface of cell membrane and have insulin-binding sites;
  - Two β-subunits which extend across the cell membrane and project into the cytoplasm. Such insulin-receptors are maximum in the cell membrane of liver cells and may be as many as 100,000 per liver cell.
- Mechanism of action of Insulin involves following steps:
  - Formation of Hormone-receptor complex-Insulin hormone acts as the first messenger and binds α-subnits of insulin-receptor to form a complex which induces conformational changes in the β-subunits act as tyrosine kinase enzyme and bind phosphate molecule on the tyrosine resides projecting in the cytoplasm of target cells (liver cells).
  - Formation of second messenger- An intracellular hormonal mediator (Fig. 22.31). Activated β-subunits of insulin activate a transducer G-protein which activates enzyme phosphodiesterase. This activated enzyme degrades phosphatidylionositol 4,5-biphosphate (PIP_2) into two mediators : Ionositoltriphosphate (IP_3) and Diacylglyceroal (DG). IP_3 is water soluble and diffuses in the cytoplasm and stimulates the release of Ca^{++} ions from endoplasmic reticulum of target cells. Ca^{++} ions activate many Ca^{++} -mediated reactions. DG remains in the cell membrane and activates an enzyme called protein kinase-C. IP_3 and DG act as intracellular second messengers which are responsible for amplifications of signals.
  - Amplifying of signal- The intracellular mediators like DG and IP_3 act as second messengers. These act as intermediate compounds and amplify a hormonal signal and initiate a variety of events involving cascade effect within the target cell. In cascade effect, every activated molecule activates several molecules of inactive enzyme of next category and the process is repeated a number of times.

Mechanism of Action of Hormone Acting With A Lag Period

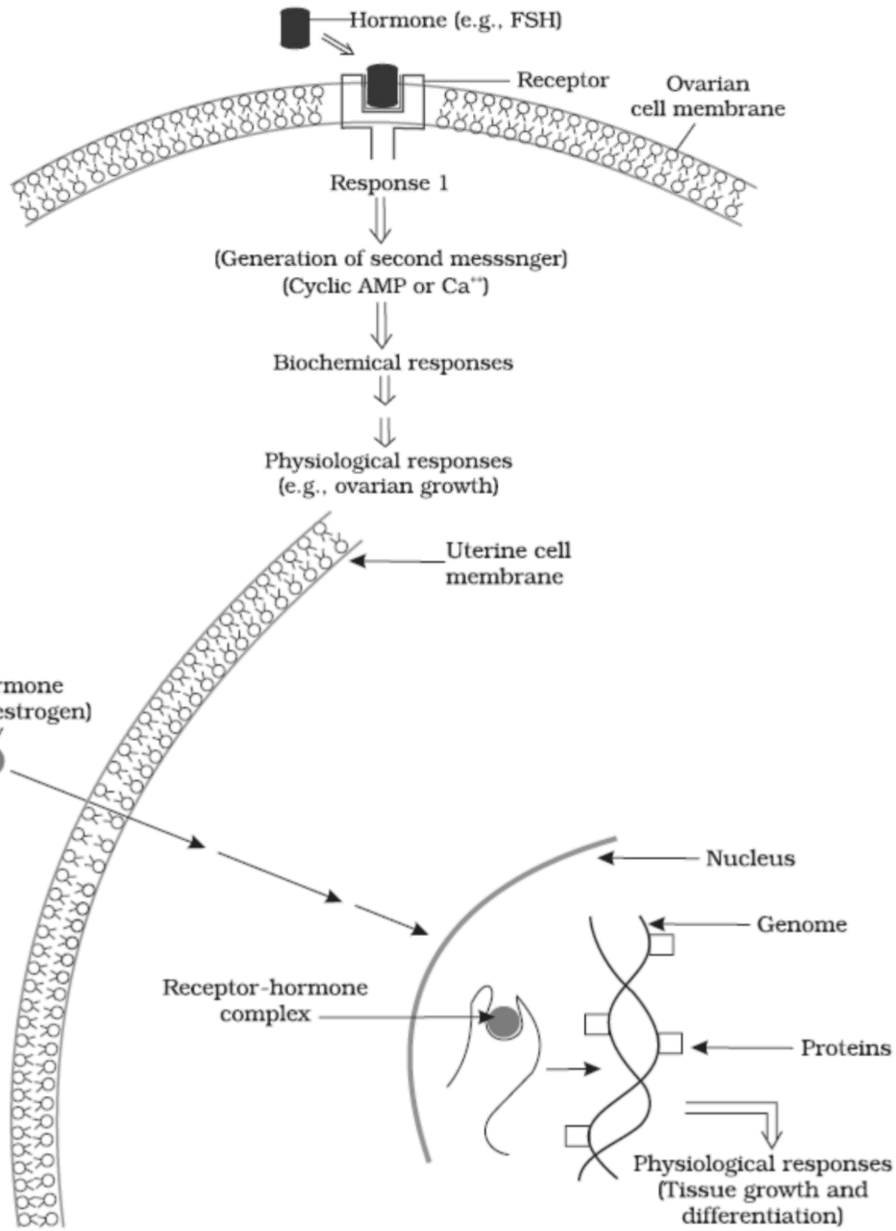
- Steroid hormones are smaller in size and lipid-soluble so can easily pass through the plasma membrane of their target cells to bind hormone-receptors located intracellularly.
- Estrogens are steroid hormones secreted by the follicular cells of the Graafian follicles of ovary β-estradiol is the most important estrogen whose target cells are uterine cells. It shows its biological effect after a lag period of about 20-24 hours.
  - β-estradiol acts as first messenger, diffuses into the cytosol of uterine cells and binds a protein receptor, called estrophillin, to form hormone-receptor complex, called estrophillin-II.
  - Estrophillin –II enters the nucleus binds to specific regulatory and instructs the specific segment of DNA to transcribe a specific mRNA.
  - M-RNA passes out in the cytoplasm and translates specific proteins example- ovallbumin and ovovitellin. These proteins are formed after about 20-24 hours of the release of estrogens from the ovary.
  - These proteins help in growth and division of cells.

7.4 Hormones of Heart, Kidney and Gastrointestinal Tract

- Now you know about the endocrine glands and their hormones.
- However, as mentioned earlier, hormones are also secreted by some tissues which are not endocrine glands.
- For example, the atrial wall of our heart secretes a very important peptide hormone called atrial natriuretic factor (ANF), which decreases blood pressure. When blood pressure is increased, ANF is secreted which causes dilation of the blood vessels.
- This reduces the blood pressure.
- The juxtaglomerular cells of kidney produce a peptide hormone called erythropoietin which stimulates erythropoeisis (formation of RBC).
- Endocrine cells present in different parts of the gastro-intestinal tract secrete four major peptide hormones, namely gastrin, secretin, cholecystokinin (CCK) and gastric inhibitory peptide (GIP).
- Gastrin acts on the gastric glands and stimulates the secretion of hydrochloric acid and pepsinogen.
- Secretin acts on the exocrine pancreas and stimulates secretion of water and bicarbonate ions. CCK acts on both pancreas and gall bladder and stimulates the secretion of pancreatic enzymes and bile juice, respectively.
- GIP inhibits gastric secretion and motility.
- Several other non-endocrine tissues secrete hormones called growth factors.
- These factors are essential for the normal growth of tissues and their repairing/regeneration.

7.5 Mechanism of Hormones Action

- Hormones produce their effects on target tissues by binding to specific proteins called hormone receptors located in the target tissues only.
- Hormone receptors present on the cell membrane of the target cells are called membrane-bound receptors and the receptors present inside the target cell are called intracellular receptors, mostly nuclear receptors (present in the nucleus).
- Binding of a hormone to its receptor leads to the formation of a hormone-receptor complex.
- Each receptor is specific to one hormone only and hence receptors are specific.
- Hormone-Receptor complex formation leads to certain biochemical changes in the target tissue.
- Target tissue metabolism and hence physiological functions are regulated by hormones.
- On the basis of their chemical nature, hormones can be divided into groups :
  - peptide, polypeptide, protein hormones (example- insulin, glucagon,
  - pituitary hormones, hypothalamic hormones, etc.)
  - steroids (example- cortisol, testosterone, estradiol and progesterone)
  - iodothyroniene (thyroid hormones)
  - amino-acid derivatives (example- epinephrine).
- Hormones which interact with membrane-bound receptors normally do not enter the target cell, but generate second messengers (example- cyclic AMP, IP3, Ca^{++} etc) which in turn regulate cellular metabolism.
- Hormones which interact with intracellular receptors (example- steroid hormones, iodothyroniene, etc.) mostly regulate gene expression or chromosome function by the interaction of hormone-receptor complex with the genome.
- Cumulative biochemical actions result in physiological and developmental effects.



Diagrammatic representation of the mechanism of hormone action-
Protein Hormones and Steroid Hormone

7.6 Points to Remember

- There are special chemicals which act as hormones and provide chemical coordination, integration and regulation in the human body.
- These hormones regulate metabolism, growth and development of our organs, the endocrine glands or certain cells.
- The endocrine system is composed of hypothalamus, pituitary and pineal, thyroid, adrenal, pancreas, parathyroid, thymus and gonads (testis and ovary).
- In addition to these, some other organs, e.g., gastrointestinal tract, kidney, heart etc., also produce hormones.
- The pituitary gland is divided into three major parts, which are called as pars distalis, pars intermedia and pars nervosa.

- Pars distalis produces six trophic hormones.
- Pars intermedia secretes only one hormone, while pars nervosa (neurohypophysis) secretes two hormones.
- The pituitary hormones regulate the growth and development of somatic tissues and activities of peripheral endocrine glands.
- Pineal gland secretes melatonin, which plays a very important role in the regulation of 24-hour (diurnal) rhythms of our body (e.g., rhythms of sleep and state of being awake, body temperature, etc.).
- The thyroid gland hormones play an important role in the regulation of the basal metabolic rate, development and maturation of the central neural system, erythropoeisis, metabolism of carbohydrates, proteins and fats, menstrual cycle.
- Another thyroid hormone, i.e., thyrocalcitonin regulates calcium levels in our blood
- by decreasing it.
- The parathyroid glands secrete parathyroid hormone (PTH) which increases the blood Ca^{2+} levels and plays a major role in calcium homeostasis.
- The thymus gland secretes thymosins which play a major role in the differentiation of T-lymphocytes, which provide cell-mediated immunity.
- In addition, thymosins also increase the production of antibodies to provide humoral immunity.
- The adrenal gland is composed of the centrally located adrenal medulla and the outer adrenal cortex.
- The adrenal medulla secretes epinephrine and norepinephrine.
- These hormones increase alertness, pupilary dilation, piloerection, sweating, heart beat, strength of heart contraction, rate of respiration, glycogenolysis, lipolysis, proteolysis.
- The adrenal cortex secretes glucocorticoids and Mineralocorticoids.
- Glucocorticoids stimulate gluconeogenesis, lipolysis, proteolysis, erythropoeisis, cardio-vascular system, blood pressure, and glomerular filtration rate and inhibit inflammatory reactions by suppressing the immune response.
  Mineralocorticoids regulate water and electrolyte contents of the body.
  The endocrine pancreas secretes glucagon and insulin.
- Glucagon stimulates glycogenolysis and gluconeogenesis resulting in hyperglycemia.
- Insulin stimulates cellular glucose uptake and utilisation, and glycogenesis resulting in hypoglycemia.
- Insulin deficiency and/or insulin resistance result in a disease called diabetes mellitus.
- The testis secretes androgens, which stimulate the development, maturation and functions of the male accessory sex organs, appearance of the male secondary sex characters, spermatogenesis, male sexual behaviour, anabolic pathways and erythropoeisis.
- The ovary secretes estrogen and progesterone.
- Estrogen stimulates growth and development of female accessory sex organs and secondary sex characters.
- Progesterone plays a major role in the maintenance of pregnancy as well as in mammary gland development and lactation.
- The atrial wall of the heart produces atrial natriuretic factor which decreases the blood pressure.
- Kidney produces erythropoietin which stimulates erythropoeisis.
- The gastrointestinal tract secretes gastrin, secretin, cholecystokinin and gastric inhibitory peptide.
- These hormones regulate the secretion of digestive juices and help in digestion.