mediate hormone action within the cell.

Mode of action of peptide hormones

- The molecules of hormones that are amino acid derivatives, peptides or proteins are large and insoluble in lipids, and cannot enter the target cell. Therefore, they act at the cell surface.
- They bind to **specific receptor molecules** located on the surface of the cell membrane.
- The **hormone-receptor complex** activates G protein associated with the cytoplasmic C-terminal which initiate the release of an enzyme **adenyl cyclase** from the receptor site.
- Adenyl cyclase enzyme forms in the cell, cyclic adenosine monophosphate (cAMP) from ATP. The cAMP activates the existing enzyme system of the cell. This accelerates the metabolic reactions in the cell.

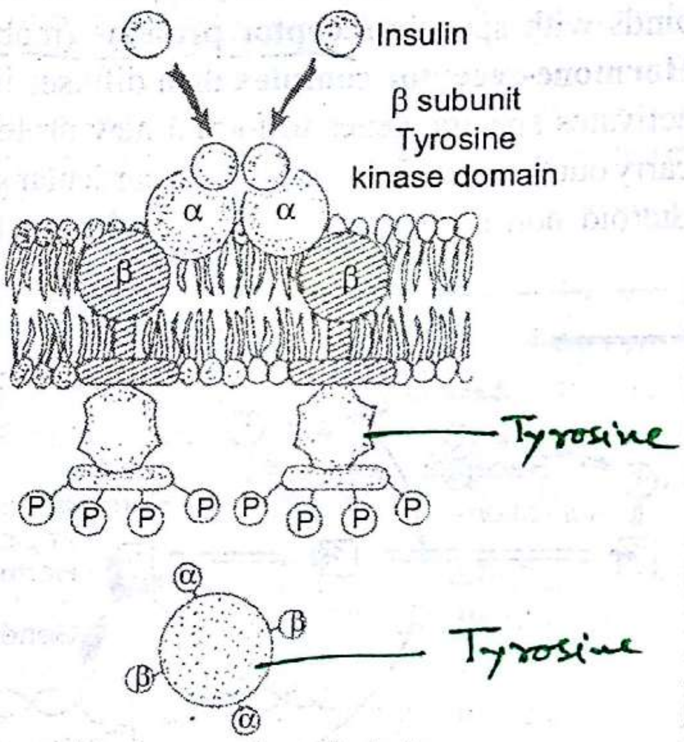

Fig.: Insulin - Hormone - Receptor complex.

- The hormone is called the **first messenger** and the cAMP is termed the **second messenger**.
- The role of cAMP as second messenger in hormonal action was first described by **Earl Sutherland. in 1965.**
- Insulin provides a good example to explain the mode of action of **peptide hormone**.
- Insulin is a polypeptide hormone, not soluble in lipids. It operates through extracellular membrane – bound receptor,

a **heterotetrameric protein** on the target cell. It consists of four subunits : two α – subunits and two β – subunits. The two α – subunits project out of the surface of cell membrane and possess insulin-binding sites. The two β – subunits project into the cytoplasm of the target cell.

- Insulin molecules (first messenger) bind at the binding - sites of outer two α – subunits of the receptor protein to form **hormone-receptor complex.** This binding results in conformational changes in the β – subunits of the receptor protein. Activated β – subunits become an activated **kinase** (tyrosine kinase) which then promotes addition of phosphate groups (phosphorylation) on the tyrosine residues projecting in the cytoplasm of target cells.
- Activated β – subunits of tyrosine kinase then activate **G - protein**. The latter activates an enzyme **phosphodiesterase**. This activated enzyme results in degradation of PIP_2 (phosphatidylinositol 4, 5 - biphosphate) into two mediators namely, **inositoltriphosphate (IP_3)** and **diacylglycerol (DG).** These act as **intracellular-secondary messengers** responsible for amplification of signal.
- IP_3 and DG now amplify a hormonal signal by initiating various events involving **cascade effect** in the target cell.
- In cascade effect, every activated molecule in turn activates many molecules of inactive enzyme of next category and this process is repeated a number of times.

Mode of action of steroid hormones

- Steroid hormones, being hydrophobic molecules, diffuse freely into all cells and act within the cell.
- 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 carry out the specific response for a particular steroid hormone.
- Steroid hormones are related to **cholesterol.**

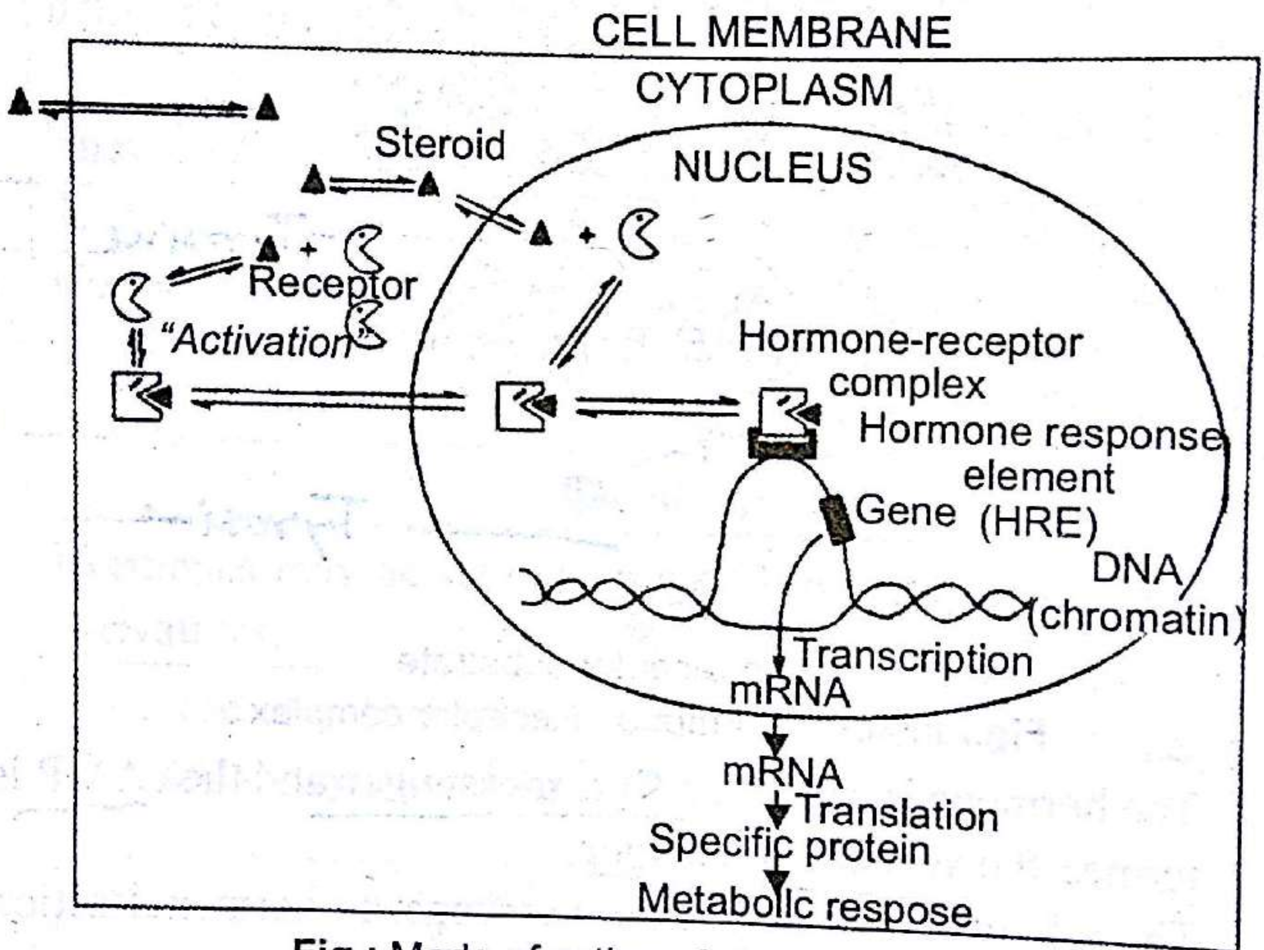

Fig.: Mode of action of steroid hormone.

ENDOCRINE GLANDS

- The mammalian endocrine system consists of the following organs and tissues: **hypothalamus, pituitary, thyroid**, four

(xii) ... different from ... it is synthesized.

Classification of hormones

The hormones may be classified into four categories :

(i) **Amino acid derivative hormones** - The hormones **epinephrine** (adrenaline), **norepinephrine** (noradrenaline) and **thyroxine** are derived from the amino acid tyrosine.

(ii) **Peptide hormones** - The hormones **oxytocin** and **vasopressin** (= ADH) are composed of peptides.

(iii) **Protein (Polypeptide) hormones** - The **somatotropic, thyrotropic** and **gonadotropic hormones, insulin, glucagon, parathormone, human chorionic gonadotropin, human chorionic somatomammotropin** (HCS) and **relaxin** are made up of proteins.

(iv) **Steroid hormones** - The hormones secreted by the adrenal cortex, testes and ovaries are composed of steroids. Placental estradiol and progesterone are also steroid hormones.

Role of hormones in homeostasis

- **Homeostasis** means keeping the internal chemical environment of the body constant. Hormones help maintain homeostasis by their integrated action and feedback control.

Negative feedback control

- In this, synthesis of a hormone slows or halts when its level in the blood rises above normal. *e.g.*, blood-glucose homeostasis. Secretion of hormone may be under the negative feedback control of a metabolite.
- For instance, increase in blood-glucose level on eating a carbohydrate-rich meal, stimulates pancreas to secrete insulin. The latter stimulates the target cells to take up glucose, which is utilized in cell respiration or is stored as glycogen. This lowers the blood-glucose level to normal.
- With fall in blood glucose level, insulin secretion decreases. This checks the further fall in the blood-glucose level.
- In this manner insulin maintains blood-glucose homeostasis.

Positive feedback control

- In the positive feedback control, an accumulating biochemical increases its own production.
- For example, uterine contraction at the onset of labour stimulates the release of the hormone oxytocin, which intensifies uterine contractions.
- The contractions further stimulate the production of oxytocin. The cycle of increase stops suddenly after birth of the baby.

Mode of action of hormones

- The secretion of hormone from an endocrine gland is controlled by its circulating level in the blood.

the hypothalamus packaged in secretory granules and transported down the axons to be stored for release by the posterior lobe.

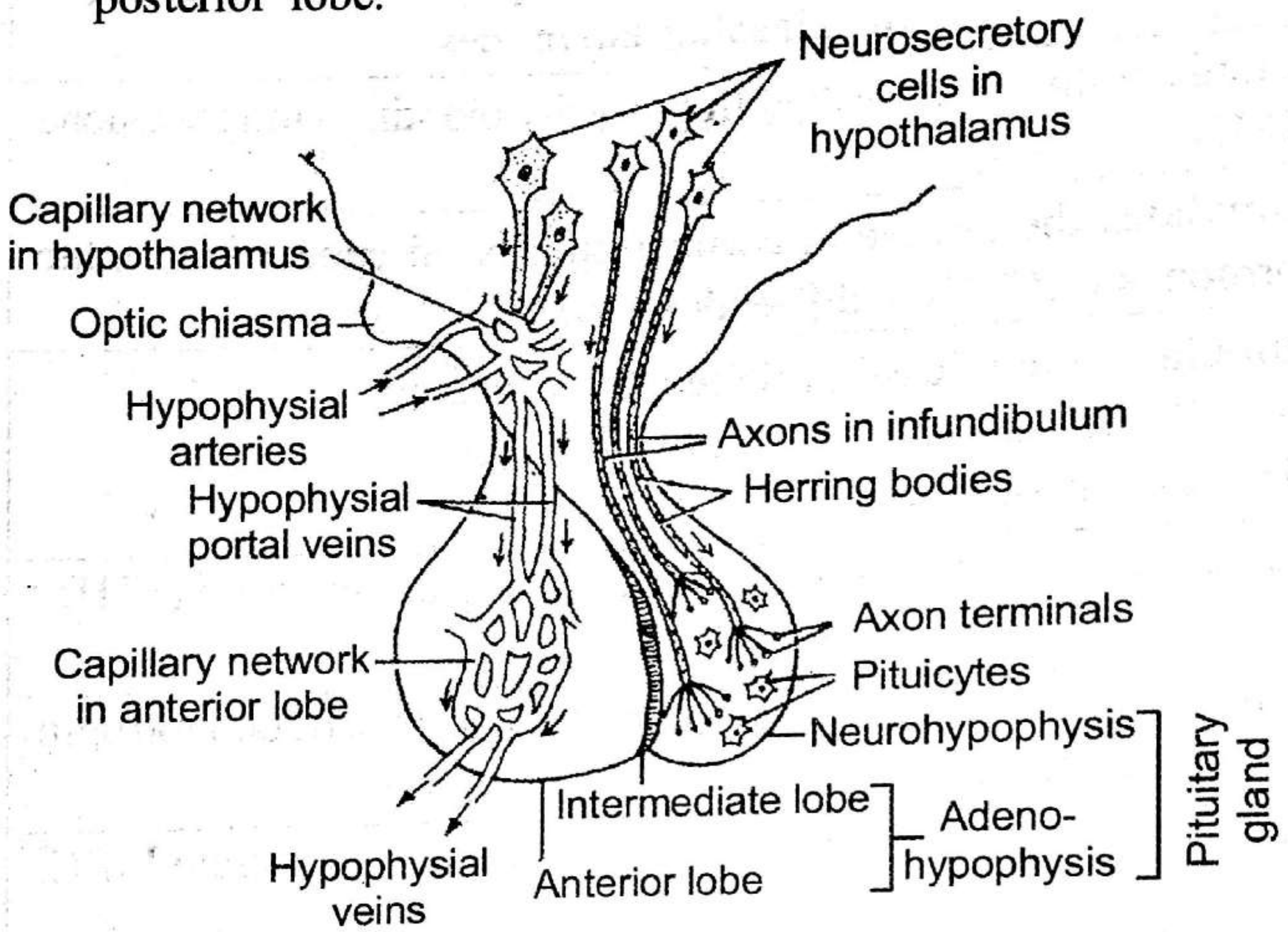

Fig.: Neurosecretory cells (neurons) of hypothalamus discharging their neurohormones into hypophysial portal veins and into neurophypophysis (posterior lobe) of pituitary gland.

- Hence, **hypothalamic - pituitary system** is a direct proof of coordination between the hormonal and nervous system. It regulates most of physiological activities of body and maintains homeostasis inside the body.

Pituitary gland

- Pituitary gland or hypophysis is a small pea shaped gland situated below the hypothalamus and connected to the brain by a stalk.
- It lies in the cavity called **sella turcica or hypophysial fossa** of sphenoid bone of skull above the roof of the nasal cavity.

Parts of pituitary gland

Mode of action of Hormones :—

- Action of hormones are carried via the blood throughout the entire body, yet they affect only certain cells.
- The specific cells that respond to a given hormone have receptors sites for that hormones. This is a sort of lock and key mechanism.

1. Mode of Action of Peptide hormones :—

- The molecules of hormones that are amino acid derivatives, peptides or proteins, catecholamines are large and insoluble in lipids and cannot enter to the target cells. Therefore, they act at the cell surface.
- Such hormones circulating in tissue fluid, come in contact with the external domain of the extracellular receptor present on the surface of the cell.
- The hormone binds to the receptor and forms a Hormone-receptor complex which brings about conformational changes in the cytoplasmic part of the receptor
- The cytoplasmic part of the receptor then produces second messengers such as Ca^{++}, cAMP, IP_3 etc — which activates the existing enzyme system of the cell and accelerates the biochemical reactions in the cell. This way the cellular metabolism is regulated.
- The hormone is called the First messenger and cAMP, IP_3, Ca^{++} are called 2nd/secondary messengers.

Note:—
- The hormone-receptor complex activates G-protein associated with the cytoplasmic C-terminal which initiates the release of an enzyme (Adenyl cyclase) from the receptor site.
- [Adenyl cyclase is the enzyme that synthesizes cAMP from ATP.]
- cAMP functions as a secondary messenger to relay extracellular signals to intracellular effectors, particularly protein Kinase A.

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- Regulation of intracellular concentrations of cAMP is under the control of Adenyl cyclase.
- The role of cAMP as a secondary messenger in hormonal action was first described by — Earl Sutherland in 1965.

Mode of Action of peptide hormone, e.g. Insulin:

- Insulin is a peptide hormone, not soluble in lipids. It operates through extracellular membrane-bound receptor, a heterotetrameric protein on the target cell.

↓

- It consist of two β-subunits and two α-subunits.
- The two α-subunits project out of the surface of cell membrane and possess insulin-binding sites.
- The two β-subunits project into the cytoplasm of target cell.

↓

- Insulin molecules (1st messenger) bind at the binding-sites of outer two α-subunits of receptor protein to form hormone-receptor complex.

↓

- This binding results in conformational changes of β-subunits of receptor protein. (Activated)

↓

- Activated β-subunits become an Activated Kinase (Tyrosine Kinase) - which then promotes addition of phosphate group (phosphorylation) on Tyrosine residues projecting in the cytoplasm of target cells.

↓

- Activated β-subunits of tyrosine kinase then activates G-protein.

↓

- G-protein then activates an enzyme phosphodiesterase.

↓

- phosphodiesterase enzyme degrades PIP_2 (Phosphatidyl-inositol 4,5-biphosphate) into two mediators — namely - IP_3 (Inositol triphosphate) and DAG (Diacyl-glycerol).

↓

- These IP_3 and DAG act as intracellular secondary messengers responsible for amplification of signals.

⇓

- IP_3 and DAG (/DG) now amplify a hormonal signal by initiating various events involving Cascade effect in the target cell.

— x —

NOTE:–

(G-Protein):– • G-proteins are so-called because they bind the Guanine nucleotides GDP and GTP.

- They are (heterotrimers) (i.e. made of 3 different subunits) associated with the inner surface of the plasma membrane and transmembrane receptors of hormones etc → these are called G-Protein-coupled receptors (GPCRs).

⊞ Mode of Action of Steroid Hormones:–

- Steroid hormones are hydrophobic and Lypophilic i.e. lipid-soluble. Therefore, they are able to cross the lipid-bilayer of plasma membrane and hence they move inside the target cell without any difficulty.
- (Steroid hormones) and (iodothyronines) (T3, T4) – shows same mode of action.
- 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 carry out the specific response for a particular steroid hormone.
- Steroid hormones are slower but long lasting in response to the water soluble hormones.

Classification of Hormones

1. Steroid Hormones :-

- The hormones secreted by the Adrenal cortex [eg- Aldosterone (Mineralocorticoids), cortisol (Glucocorticoid)]
- Hormones of Testes :— Testosterone
- Hormones of Ovaries :— Estrogen, Progesterone
- Placental Hormones (some) :— eg- Oestrogen and Progesterone

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- The study of endocrine glands is called **Endocrinology**.
- Father of endocrinology is **Thomas Addison**.
- Endocrine glands pour their secretion directly into the blood or body fluid. Such secretions are not carried through ducts. The endocrine gland are, therefore, also known as **ductless glands.**

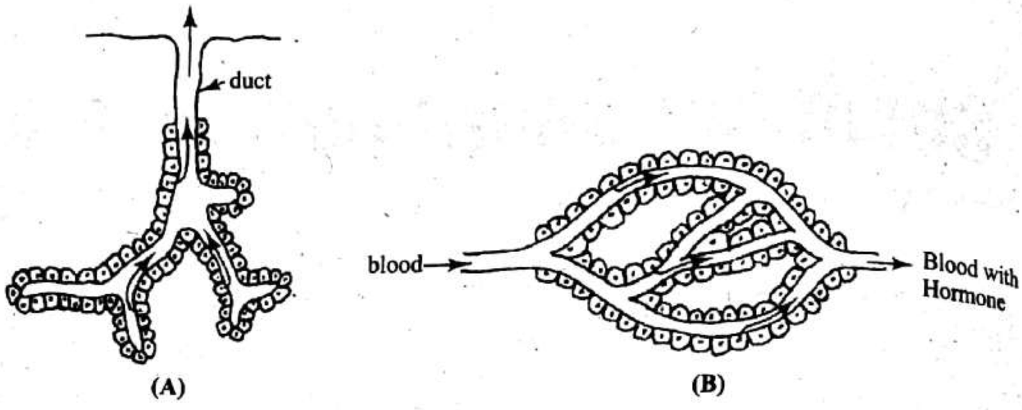

Fig. 22.1 (A) Exocrine gland, (B) Endocrine gland

- The secretions of endocrine glands are called hormones, means to excite or stimulate.
- **Secretin** was the first hormone, discovered by **Bayliss** and **Starling** (1902).
- The term 'hormone' was coined by **Starling** (1905).

PARAHORMONES/ LOCAL HORMONES

- Parahormones are short-lived chemicals which are produced from almost all body cells (except mammalian RBCs).
- These chemicals affect the functioning of either the neighbouring cells **(Paracrine hormones)** or the same cells from which they are secreted (**Autocrine hormones**).
- Most of the local hormones are paracrine type and include *Prostaglandins, Neurotransmitters* and *Interferons* etc.

(a) Prostaglandins

- They were discovered by **Von Euler** (1935) in the semen of human and were thought to be the secretion of Prostate glands, and hence named so.
- They are derivatives of polyunsaturated fatty acids (eg. **Arachidonic acid**).
- They regulate BP by contraction and relaxation of smooth muscles of blood vessels.
- These chemicals also regulate Peristalsis and secretion of the digestive juices.
- They cause pain at injury site and induce fever. They also promote inflammation. (*The pain killers inhibit the secretion of prostaglandins*).
- Prostaglandins also cause contraction of uterine muscles, vas deferens and oviduct etc.

(b) Neurotransmitters/ neuro-regulators

- These chemicals are peptides and are synthesized in the nerve cells.
- They help in transmitting nerve impulses to muscles/glands or across the synapses.
- Neuro-regulators are of two types,
  1. Excitatory - eg. Acetylcholine, Nor-epinephrine, Serotonin and Dopamine etc.
  2. Inhibitory– eg. Glycine, Gamma Amino Butyric Acid (GABA), Endorphins and Nitric Oxide (NO) etc.

- They are low molecular weight proteins secreted by virus infected cells and provide resistance to the neighbouring cells (*For details please* refer *'Immune system'*)

...ONES or ECTO HORMONES/ SEMIOCHEMICALS

- The term 'pheromone' was given by **Karlson**.
- The pheromones are volatile and odorous.
- They travel through air and alter the functioning of the other members of the same species. The **'confusion technique'** is based upon the use of pheromones.
- The important examples of pheromones are *bombycol, geradioal* and *muskone.*
- Bombycol is secreted by *Bombyx mori* (Silkmoth) as a sex attractant for mating. This was the first pheromone discovered. Geradiol is secreted by honey bees for aggregation and muskone is secreted from musk deer.

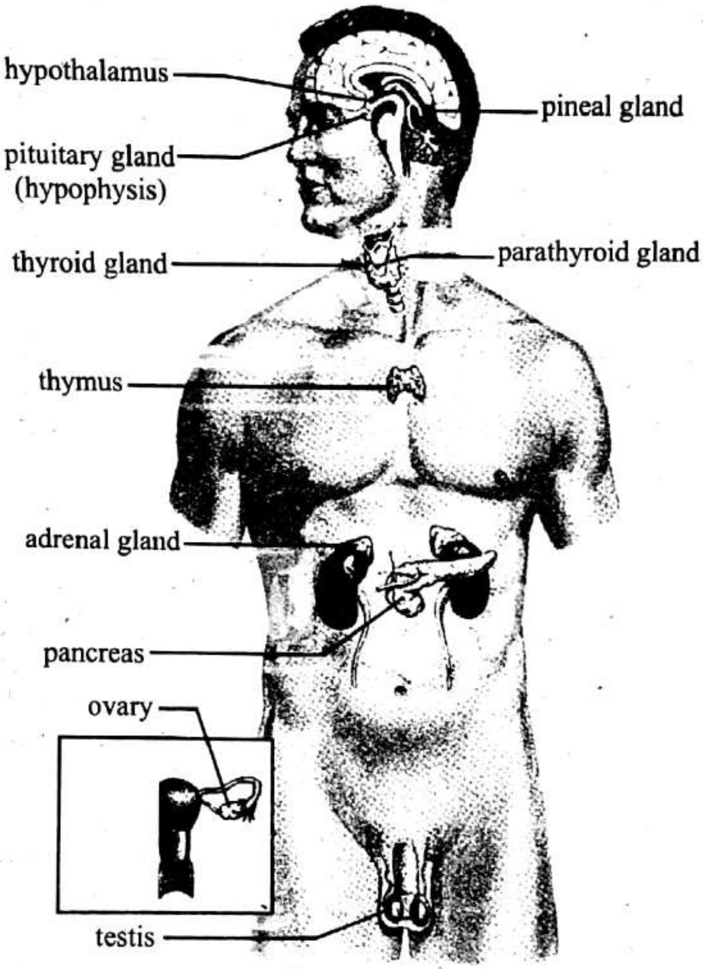

Fig. 22.2 Human endocrine glands

ENDOCRINE GLANDS

Chemical nature of hormones -

1. *Amino acid derivatives -*

   eg. Thyroxine, adrenaline (both *tyrosine* derivatives) and melatonin (*tryptophan* derivative).

2. *Steroids (lipids) –*

   They are cholesterol derivative. eg. Estrogen and progesterone (from ovary and placenta) testosterone (from testis) and hormones of adrenal cortex (Corticoids).

3. *Peptides/ proteins –*

   The maximum of the hormones are peptides or proteins. Some are glyco-proteins (FSH, LH, TSH & hCG) while others are pure proteins, eg. Hormones of Pancreas, Parathyroid, Pituitary and thymus.

(1) Pituitary Gland

- It is called **master gland** (master of endocrine orchestra) as it regulates the functioning of other endocrine glands like thyroid, Adrenal cortex, testes and ovaries etc. However, the secretions of pancreas, thymus and pineal body are not regulated by the hormones of pituitary.
- Pituitary is a single or unpaired gland weighing about 0.5 gm.

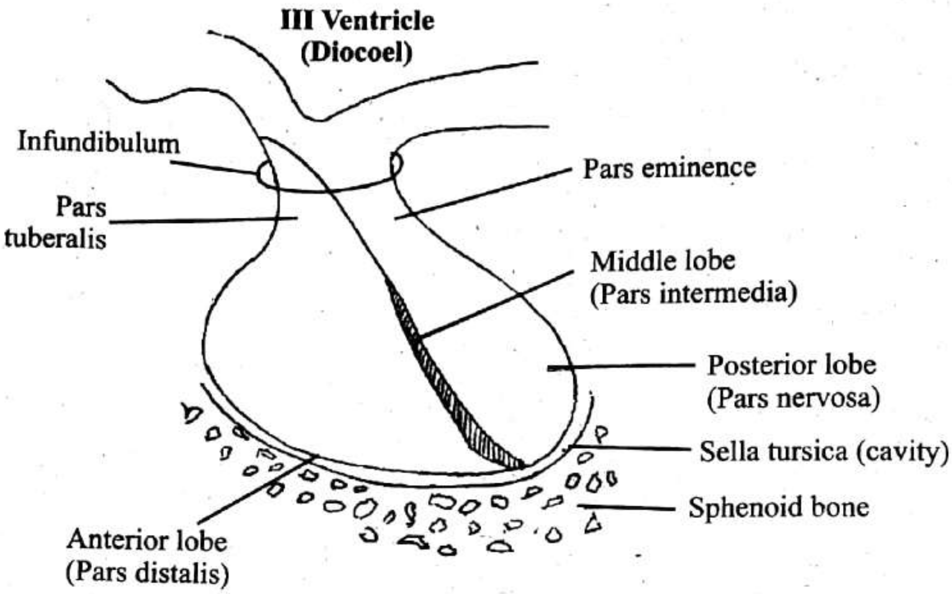

Fig. 22.3 Pituitary Gland

- It is present in the **'Sella tursica'** cavity of Basi-sphenoid bone, and is attached to the floor of Diencephalon (*hypothalamus*) of fore brain through a stalk called *Infundibulum*.
- As it is present below diencephalon of fore-brain it is also known as **Hypophysis cerebri**.
- In mammals it is *ectodermal in origin.*
- It consists of two-parts - (1) Adenohypophysis, and (2) Neurohypophysis

(1) Adenohypophysis -

It develop from *Rathke's pouch*, a diverticulum of buccal cavity and includes (i) Anterior lobe (*pars distalis*) and (ii) Middle lobe (*pars intermedia*)

(2) Neurohypophysis -

It is directly connected to the Hypothalamus (diencephalon) part of the forebrain. It includes posterior lobe (*pars nervosa*)

(A) Anterior lobe - 6 hormones

(i) Growth hormone or somatotrophic hormone (STH)
(ii) Prolactin (PRL) or mammotropin or LTH (Leuteotropic Hormone)
(iii) Adreno corticotropic hormone (ACTH)
(iv) Thyroid stimulating hormone (TSH)
(v) Follicle stimulating hormone (FSH)
(vi) Leutinizing hormone (LH)

[STH & PRL are secreted from Acidophilic (40%) cells; ACTH is secreted from chromophobic cells, while rest three, TSH, FSH & LH are secreted from Basophilic (10%) cells.]

- Last three hormones, TSH, FSH and LH, are glycoproteins while the first three are peptides/ proteins.
- Except prolactin all other hormones of anterior pituitary are **Tropic hormones** because they stimulate other endocrine glands. Prolactin hormone stimulates mammary glands which are not endocrine but exocrine in nature.

Growth Hormone (STH)

- It is anabolic hormone and stimulates protein synthesis. The catabolism of proteins and amino acids is decreased.
- *It stimulate lipolysis,* i.e. break down of lipids for energy production.
- It decreases the use of glucose for energy production and conserves carbohydrates as glycogen.
- It reserves calcium and phosphate and causes the elongation of bones.

Hyposecretion of STH-

In children – **Dwarfism**, producing *'Midgets'* with stunted growth

In adults – **Simmond's disease** (protein synthesis is decreased and lactation, in females, is reduced)

Hypersecretion of STH–

In children – **Gigantism** (over growth of the body)

In adults – **Acromegaly**, i.e. gorilla appearance (free ends or extremities like fingers, toes, chin etc. are elongated). The affected person develops Osteoarthritis, Gynecomastia and Hirsutism (showing presence of coarse & pigmented hair on chest-back etc.

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(ii) Prolactin (PRL)

- It stimulates mammary glands for the synthesis of milk.
- It is a non-tropic hormone.

(iii) Adreno corticotropic hormone (ACTH)

- It stimulates the secretion of corticoids from Adrenal cortex.
- It also regulates melanin pigment in human skin.

(iv) Thyroid stimulating hormone (TSH)

- It stimulates the growth of thyroid follicles.
- It also promotes the utilization of iodine by the gland, for the synthesis of thyroxine.

(v) Follicle stimulating hormone (FSH)

- It is commonly called **Gametogenic hormone** as it regulates Spermatogenesis in males and Oogenesis in females.
- In females it also stimulates ovarian follicles for the secretion of estrogen hormone.

(vi) Leutinizing hormone (LH)

- It is responsible for **ovulation**, i.e. release of female gamete from the ovary.
- It also helps in the formation of **Corpus luteum**.
- It stimulates corpus luteum for the synthesis of mainly progesterone hormone.
- In males, this hormone stimulates interstitial cells or **Leydig cells**, for the synthesis of '*testosterone*' and is, therefore, called as **Interstitial cells stimulating hormone (ICSH).**

Hypothalamic control over Anterior Pituitary –

The chemical factors, released from hypothalamus affect the secretions of anterior pituitary through the **hypophyseal portal system**. Following are the six releasing factors or hormones.

(1) *Growth hormone releasing factor (hormone) – GRH*
It stimulates the secretion of growth hormone from anterior pituitary.

(2) *Growth hormone release inhibiting hormone – GIH*
It is also known as **Somatostatin** and inhibits the secretion of growth hormone from anterior pituitary.

(3) *Thyrotropin releasing hormone – TRH*
It stimulates the secretion of thyroid stimulating hormone (TSH or thyrotropin)

(4) *Corticotropin releasing hormone - CRH*
It stimulates the secretion of ACTH.

(5) *Gonadotropin releasing hormone – Gn RH*
It stimulates anterior pituitary for the secretion of FSH and LH

(6) *Prolactin inhibitory hormone – PIH*
[The production of prolactin releasing hormone (PRH) is doubtful in human.]

(B) Middle lobe -

(i) **Intermedin hormone -**

- It is secreted in fishes, amphibians and reptiles.
- It causes darkening of skin by dispersing pigmented cells (**Chromatophores**).

(ii) **Melanocyte stimulating hormone - MSH**

- It is secreted in birds and mammals.
- It also causes darkening of skin by synthesizing more melanin and by causing dispersal of melanocytes.

  In human the middle lobe is rudimentary and *MSH is either vestigial or is not secreted in adults.* The dispersal of melanocytes or the skin pigmentation in human is regulated by ACTH

(C) Posterior lobe –

The hormones of posterior lobe of pituitary are actually *produced from the axons of neurons of hypothalamus.* These hormones are, therefore, called *Neurohormones*. There are two neurohormones secreted (released) from posterior pituitary.

(i) **Oxytocin (Pitocin) -**

- It is a small peptide of 9-amino acids.
- It causes contraction of smooth muscles, mainly of mammary glands and uterus.
- The contraction of mammary glands causes release of milk and the hormone is, therefore, called as **'Milk-let-down factor'.**
- The contraction of smooth muscles of uterus during matured pregnancy causes expulsion of child (**parturition**). This hormone is therefore, also known as **'Birth-hormone'**.

(ii) **Vasopressin (Pitressin) -**

- It causes constriction of blood vessels and raises blood pressure.
- It also helps in absorption of water from glomerular filtrate in uriniferous tubules of kidney. Thus, it reduces the amount of water in urine and hence concentrates it.
- This hormone is commonly called as **Anti-diuretic hormone (ADH)**

  Hyposecretion of ADH –

  In such a condition the water absorption is reduced and the amount of water in urine is increased. This condition of diluted urine (Diuresis), without sugar or glucose, is called **Diabetes insipidus**.

  *(It is different from **Diabetes mellitus** in which sugar/glucose passes with urine).*

(2) Pineal Gland

- It is ectodermal in origin.
- It is unpaired (Single) and is *attached to epithalamus of diencephalon*. It is therefore, also known as *Epiphysis cerebri* (Pituitary, attached to hypothalamus, is called *Hypophysis cerebri*)
- It is considered to be the *'seat of soul'*.
- In human it starts degenerating at the age of 7-8 years.
- The calcium and magnesium salts are deposited in this gland at later stages and the structure is then known as '*brain sand*'.
- This gland produces single hormone **melatonin** which is biogenic amine.

Melatonin –

- It is derivative of amino acid – *Tryptophan*
- It causes lighting of skin and is *antagonistic to MSH.*
- It delays sexual maturity by influencing the development of gonads and release of gonadotropin hormones from pituitary. Its secretion is increased during darkness.
- As it delays puberty, It is also known as **anti-ageing hormone** (the pacemaker for ageing is, however, *Thymus gland*).
- It maintains *biological clock* in human body. It also maintains diurnal variations (*circadian rhythm*) in animals and decides the breeding season in them.

- It is single, bilobed and endodermal.
- It lies close to heart.
- It is differentiated into outer-cortex and inner-medulla. The medulla contains two onion shaped **Hassel's corpuscles.**
- It is highly developed at puberty and later degenerates with the advancement of age.
- It is *lymphatic organ as well as an endocrine gland.*
- It produces T-lymphocytes and is *related to immune system.*
- The hormone of this gland is called **Thymosin** or **Thymitin.**

  [Do not confuse this hormone with ***Thymine*** *(a nitrogenous base) and* ***Thiamine*** *– Vitamin* B_1*.]*
- It is peptide and stimulates the production of lymphocytes from other lymphatic tissues.

Gonads

A. Testis -

It contains large number of seminiferous tubules. In between seminiferous tubules the endocrine cells, called **Leydig cells** or **Interstitial cells** are present. Inside seminiferous tubules, there are non-dividing , diploid and supporting cells, called **Sertoli cells**. Besides nourishing the developing sperms, the sertoli cells also secrete hormones. Two hormones, released from testes, are -

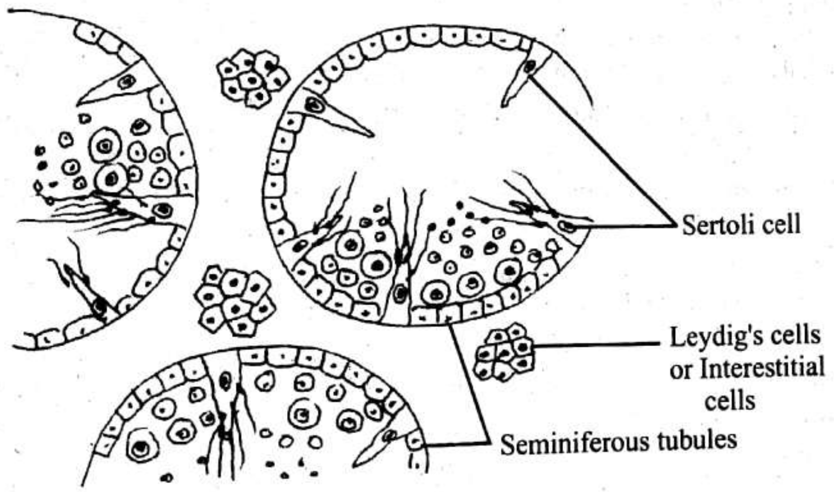


Fig. 22.4 C.S. Testis

(1) Testosterone –

- It is steroid (cholesterol-derivative) in nature.
- It is secreted from **Leydig's cells** under the influence of interstitial cell stimulating hormone (ICSH) of anterior pituitary.
- It promotes the development of reproductive organs in males. *(Before birth, it stimulates descent of testes into scrotum).*
- It also helps FSH of anterior pituitary in spermatogenesis process.
- It is responsible for the development of *secondary sexual characters* also, like beard, moustaches, low pitch voice and body musculature, in males.

(2) Inhibin –

- This is secreted from *sertoli cells* under the influence of FSH from anterior pituitary. The Sertoli cells also secrete *Androgen Binding Protein* (ABP) that concentrates testosterone hormone in seminiferous tubules.
- Excess of inhibin hormone, by feed back mechanism, inhibits the secretion of FSH.
- Inhibin is also secreted in females by *granulosa cells.*

B. Ovary -

It contains a large number of **Graafian follicles** (the term, used for ovarian follicles in mammals). The connective tissue of ovary is called **Stroma.** Following hormones are secreted from ovary.

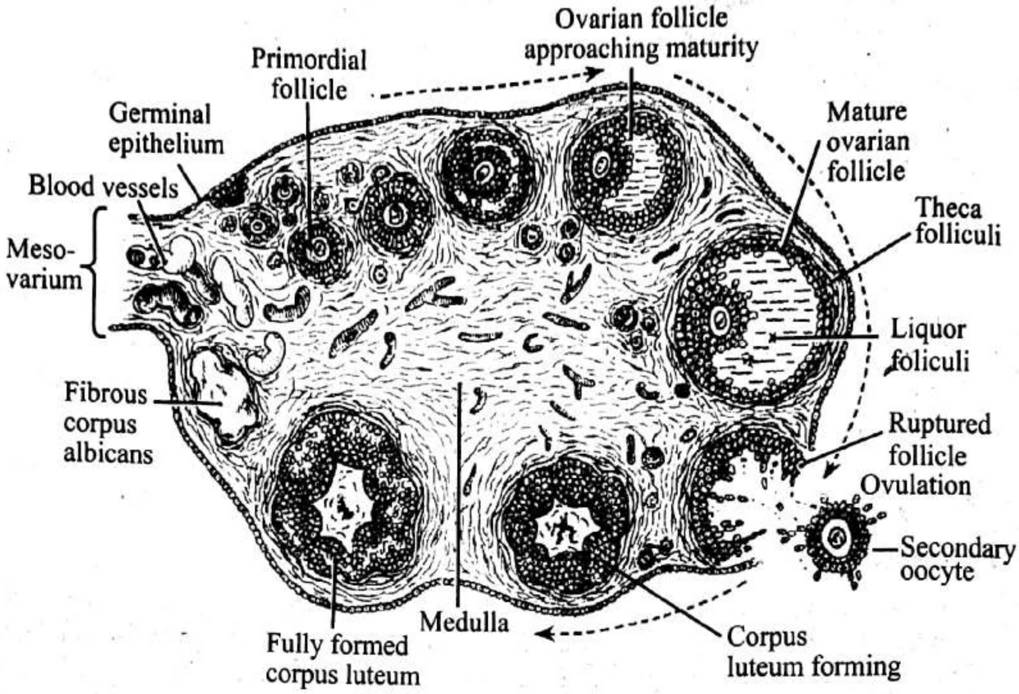


Fig. 22.5 C.S. of Mammalian ovary

(1) Estrogen *(Steroid)*-

- It is secreted from the cells of *Stratum granulosum*. The *granulosa cells* or follicular cells form internal coating to theca folliculi.
- FSH of anterior pituitary stimulates the secretion of this hormone. (*Estrogen is also secreted from corpus luteum*).
- Estrogen stimulates the development of reproductive organs like oviduct, uterus, vaginal tube etc.
- It stimulates the development of *secondary sexual characters* also, i.e. high pitch voice, female body musculature, development of breasts and pattern of pubic hair distribution.
- It also helps in Oogenesis process and regulates menstrual cycle.

(2) Progesterone *(Steroid)* -

- This hormone is secreted from **Corpus luteum** (means *yellow body*).
- It is responsible for implantation of embryo and maintenance of pregnancy.
- It also stimulates mammary glands for storing and secreting milk.
- It is commonly called **Pregnancy hormone**.
- Progesterone inhibits ovulation, maturation of Graafian follicles and abortion.

(3) Relaxin *(Peptide)* -

- It is also secreted from corpus luteum.
- It dilates or relaxes pubic symphysis and cervix to help in parturition (child birth) at the end of pregnancy.

  (Relaxin hormone is also produced from prostate glands in males and placenta, mammary glands and uterus in females)

Following conditions may arise from *abnormal functioning of gonadal hormones* (and/or the sex hormones of Adrenal gland)

(1) *Sexual pseudoprecocity* -

- This developes due to *hypersecretion of sex hormones*.
- In male children (boys) it is due to excess of *testosterone* hormone. It causes enlargement of penis and early appearance of pubic and axillary hair, faster body growth and masculinisation. *The spermatogenesis, however, does not occur.*

- In female children (girls) this arises from increased amount of *estrogen* hormone. The secondary sexual characters develop but *ovulation does not start.*
- In case of true sexual precocity or ***Precocious puberty*** the gonads are matured earlier and production of gametes also starts. In females this may begin by the age of 9 years and in males by 10 years.

(2) *Eunuchoidism*

- It develops due to failure of testosterone secretion. The accessory sexual organs like penis, prostate glands and seminal vesicles remain infantile or smaller in size. *The secondary sexual characters of males fail to develop.*

(3) *Gynaecomastia*

- It is due to disturbance of 'estrogen to androgen' ratio.
- The amount of circulating estrogen (from adrenal gland) increases in males. This causes development of breasts.
- The decrease in the amount of testosterone in later life of males can also produce such symptoms.

(5) Placenta

In females the placenta acts as a temporary endocrine gland during pregnancy. It secretes following hormones–

(i) Human chorionic gonadotropin (hCG) -

- Chemically it is a glycoprotein.
- It passes out through urine and can be used for *Gravi-index test*, commonly called pregnancy test.
- This hormone prolongs the life of *corpus luteum*, which in turn secretes progesterone for maintaining pregnancy.

(ii) Human chorionic somatomammotropin (hCS) -

- It is a peptide hormone which has growth-stimulating and lactogenic activity.
- The structure of this hormone is very similar to human growth hormone, and therefore it is inappropriate to call it *prolactin* or *chorionic mammotropin*.

(iii) Relaxin -

- It is a peptide hormone and softens the connective tissue of pubic symphysis. It is not significant in human.

(iv) Chorionic thyrotropin -

- Its function is similar to TSH.

(v) Chorionic corticotropin -

- It is also a peptide hormone and is similar in function to ACTH of anterior pituitary.

(vi) Estrogen (Steroid) and **Progesterone** (Steroid) -

These hormones are also secreted from placenta. The amount of hCG decreases after the initial rise but estrogen and progesterone secretion increases until just before parturition. The function of these hormones is similar to the hormones of ovary.

(6) Gastro-Intestinal Tract (GIt)

The endocrine cells of gut together form a mass bigger than any other endocrine gland of the body. It secretes following hormones.

(i) Gastrin -

- It is secreted from mucosa of pyloric stomach.
- It stimulates the secretion of gastric juice and HCl.

(ii) Enterogastrone –

- It is secreted from duodenal mucosa.
- It inhibits the secretion of gastric juice and also regulates the mobility of food in gut.

[Two other hormones, **GIP** (Gastric inhibitory polypeptide) and **VIP** (Vasoactive Intestinal polypeptide) have also been known to inhibit gastric secretion].

(iii) Secretin -

- It is also secreted from duodenal mucosa.
- It stimulates Pancreas for the secretion of bicarbonates and fluid in *pancreatic juice*. It, thus, increases the amount of pancreatic juice.

(iv) Cholecystokinin (CCK or Pancreozymin)-

- It is also secreted from duodenal mucosa.
- It stimulates pancreas for the *secretion of enzymes* in pancreatic juice.
- It also causes *contraction of gall bladder* for the release of bile juice.

(v) Hepatokinin -

- It is also secreted from duodenal mucosa.
- It stimulates liver for the *synthesis of bile juice.*

(vi) Enterocrinin -

- It is secreted from the mucosa lining of ileum.
- It stimulates intestinal glands for the secretion of intestinal juice *(Succus entericus)*

(7) Pancreas

It lies in the coil of duodenum. It is about 15 cm. long and weighs about 80 g. It is a mixed **(composite heterocrine)** gland. Its exocrine part includes **Acini** and produces pancreatic juice. Its endocrine part consist of a large number of cell – groups, called **Islets of Langerhans** (identified and named by Paul Langerhans, 1869).

The islets of Langerhans contain three types of cells.

1. Alpha (α) cells = 10-20%
2. Beta (β) cells = 70-80%
3. Delta (δ) cells = ~5%

(i) α-Cells -

- They are acidophilic cells and secrete **Glucagon** hormone.
- This hormone is peptide in nature (consists of 29 amino acids).
- It was 1st Isolated in pure crystalline form by Kimbell and Murlin (1923).
- It is glycogenolytic (*in liver, not in muscles*) and causes breakdown of glycogen into glucose

$$\text{Glycogen} \xrightarrow{\text{Glucagon}} \text{Glucose}$$

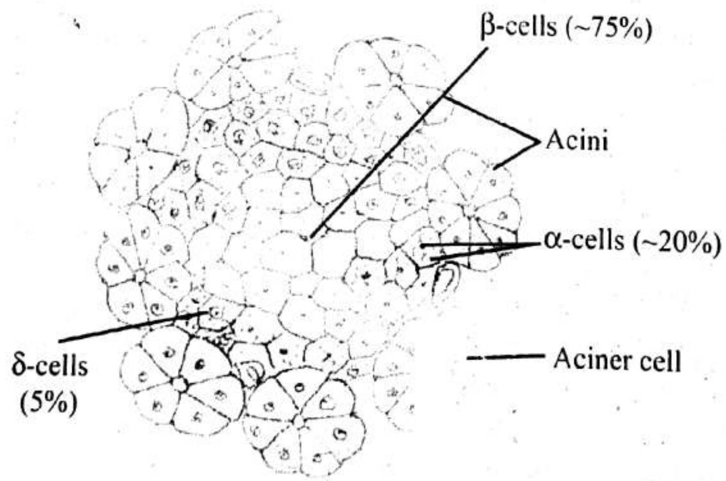


Fig. 22.6 C. S. pancreas

- It increases the amount of glucose in blood and is therefore called **hyperglycemic factor**.
- It is **gluconeogenetic** also and produces glucose from non-carbohydrate sources, like amino acids and fatty acids.

- It also reduces the uptake and utilization of glucose by the cells.
- It is **lipolytic** and **ketogenic.**
- The α-cells are damaged by **Cobalt chloride.**

(ii) β-Cells -

- These cells secrete another peptide hormone, i.e. **Insulin**.
- Insulin contains *zinc* and *sulphur*
- It was first isolated in pure, crystalline form by **Banting and Best** (1922), and they were awarded Nobel prize for this discovery.
- The molecular structure of insulin was discovered by **F. Sanger**, (was awarded Nobel prize).
- Each molecule of insulin consists of 2-polypeptide chains (1 α–chain, having 21 amino acids, and one β-chain. having 30 amino acids.)
- It is *glycogenic* (causes **glycogenesis**), i.e. converts glucose into glycogen in liver as well as muscle cells.
- It is **hypoglycemic factor**, i.e. it decreases the amount of glucose in blood. The insulin is, therefore, antagonistic to glucagon.
- Insulin increases the permeability of plasma membrane of the cells to increase the diffusion of glucose into cells to produce energy. It prevents break down of lipids and proteins.
- *It is lipogenic* and helps in synthesis of fat from glucose. It also inhibits the break down of glucose (*glycolysis*).

Hyposecretion of insulin -

- It causes **hyperglycemia** as the amount of glucose is increased in blood. As the permeability of the plasma membrane is decreased the cells can not utilize this glucose for energy production. The glucose, therefore, passes with urine (glycosuria). Moreover. there is accumulation of **Ketone bodies** in blood.
- The passing of glucose in urine due to deficiency of insulin in called **Diabetes mellitus** (*compare it from* **Diabetes incipidus**). It is more a disease of lipid metabolism than carbohydrate break down.
- The person feels more thirst (**polydypsia**) and consumes more food (**polyphagia**).
- The break down of muscular tissue produces loss of weight and tiredness.
- Retinal damage begins.
- The healing is also delayed.

  Alloxan damages β-cells and produces the symptoms of Diabetes mellitus

Hypersecretion of insulin -

- It causes **hypoglycemia** (The amount of blood glucose is decreased)
- The other symptoms of hypersecretion are irritability, double vision and sweating.
- Hypoglycemia may produce **Coma** in certain cases.

(iii) δ-Cells -

- These cells secrete *somatostatin* hormone, also known as 'growth hormone-release-inhibiting-hormone' (GHRIH).
- It acts as paracrine factor to inhibit the secretions of α–cells and β–cells.
- It also stimulates collagen formation.

Connecting Concepts

✦ Both, STH of anterior pituitary and insulin, are anabolic hormones which conserve carbohydrates and stimulate protein synthesis. But *STH is lipolytic while insulin in lipogenic.*

Connecting Concepts

✦ **Ketone bodies** (Ketosis) —

✦ When there is excess *Acetyl-CoA* in the body, some of it gets converted in to *acetoacetyl-CoA* which in *liver* (unlike other tissues) changes to *Acetoacetate* (free form).

✦ *The Free acetoacetate* (β-Keto acid) is converted to *β-Hydroxybutyrate* and *acetone*. These compounds, i.e. *Acetoacetate, β-hydroxybutyrate* and acetone are called **'Ketone bodies'**.

✦ *(These compounds metabolize in liver with difficulty and diffuse into circulation. The other tissues, however, transfer CoA from succinyl-CoA to acetoacetate and then metabolize 'active' acetoacetate to CO_2 and H_2O via citric acid cycle.*

✦ The normal ketone level in human is 1 mg/100 ml. of blood. The ketone bodies are normally metabolized as rapidly as they are formed. But if the entry of acetyl CoA into citric acid cycle is depressed because of decreased supply of glucose products, or if the entry of acetyl-CoA into CAC doesn't increase with its increased production, the acetyl Co-A accumulates and more acetoacetyl - CoA is formed, and more free acetoacetate is produced in the liver.

✦ Three conditions lead to deficient supply of intracellular glucose : *Starvation, Diabetes mellitus and high fat - low carbohydrate diet.* The ketone bodies in blood (Ketosis) produces acidosis and dehydration, resulting into coma, in Diabetes mellitus.

(8) Thyroid Gland

- It is single and bilobed gland present on either side of trachea below larynx The 2-lobes remain connected by a non-glandular tissue called **Isthmus.**
- It is endodermal in origin
- It is the largest endocrine gland in the body (weighing ~35gm)

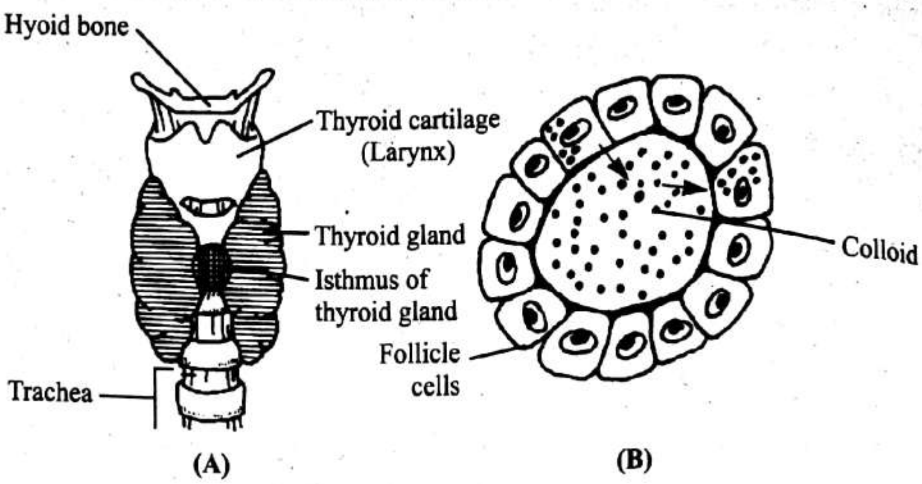


Fig. 22.7 (A) Thyroid gland, (B) Thyroid follicle

Hormones – 3-important hormones are secreted from thyroid gland, i.e. Calcitonin, T_3 and thyroxine (T_4).

(i) Calcitonin (or Thyrocalcitonin) –

- It is proteinaceous and non-iodinized hormone (Iodine absent).
- It is secreted from C (clear) – cells or *Parafollicular cells* (outside thyroid follicles)
- It is **hypocalcimic factor** and decreases the amount of Ca^{2+} in the blood.
- It is angonistic to PTH (Para-thyroid hormone).

(ii) Thyroxine (T_4)–

- It is **Tetra-ido-thyronine** and is secreted from the cells of thyroid follicles. T_4 with T_3 are stored as a *colloidal material* in the follicles.
- Thyroxine regulates basic metabolic rate (BMR) - stimulating heart beat, breathing rate etc.
- It causes demineralization of bones in adults (by stimulating **osteoclasts** - the bone eating cells).
- It causes hyperglycemia by stimulating *glycogenolysis* and *Gluconeogenesis*.
- It causes nervous excitation also.
- It is *lipolytic*, and can also be used for reducing body weight.
- It is catabolic in nature and increases heat production/energy production. It is also known as *pace-setter of the body.*
- In frog it causes *metamorphosis in tadpole.*

Hyposecretion –

Children – **Cretinism**

- In this disorder the physical growth, mental growth and sexual growth in the children is retarded. Such a dwarf and sterile child is called **cretin**.
- A cretin child shows pot-belly, Pigeon-chest and protruded tongue.

Adults – **Myxoedema**

- This disease also known as **Gull's disease.**
- Due to hyposecretion of thyroxine, the fat and protein metabolism is reduced and they get accumulated under the skin of the face to make it fluffy.
- Such persons are lethargic (due to less energy production) and sensitive to cold (due to less heat production).

Hypersecretion –

- BMR increases to produce restlessness.
- The body becomes lean and thin (**Emaciation**).
- The disorder is called thyrotoxicosis or *Grave's disease**. Besides, there is bulging of eyes, called **exophthalmic goiter**.

Grave's disease is actually an autoimmune disease in which person produces *antibodies that mimic the action of TSH* and stimulate the secretion of thyroxine. This effect is not regulated by feed back mechanism.

(iii) Tri-ido-Thyronine (T_3)–

- It is secreted in very small amount (~2% of T_4). A major amount of this is formed by deiodination of T_4.
- It is more potent than T_4 and is the principal feed back regulator of TSH.
- It has short life span.
- It acts with T_4. It is mainly responsible for thermoregulation in the body. The thyroid gland is therefore, also known as *thermostat of the body.*

Simple Goiter –

- It is not because of hypo or hypersecretion of thyroxine, but is due to the deficiency of iodine in food.
- It is endemic in hilly areas.
- The number of thyroid follicles or the size of thyroid gland increases due to increased amount of TSH.
- Sea food and onion are rich sources of iodine. Now-a-days the common salt is also being iodized to prevent the occurrence of such goiters.

(4) Parathyroid Gland

- These glands are four in number and are embedded, 2-in each lobe, in the thyroid gland.
- They are endodermal in origin.
- The hormone of these glands is called **Parathyroid hormone** (PTH) or **Parathormone** or *Collip's hormone* (Isolated by Collip).

Parathormone (PTH) –

- Chemically it is a protein/peptide.
- It regulates calcium and phosphate metabolism.
- It inhibits the synthesis of collagen by osteoblast, and bone resorption by osteoclasts.
- It also helps in absorption of dietary calcium from the intestine and renal tubules.
- It makes the bones and teeth healthy.
- It is **hypercalcemic factor** (increases the amount of calcium in blood) and is antagonistic to Calcitonin.

Hyposecretion of PTH – Tetany

- It shows restlessness, haemorrhage in tissues and spasmic contraction, twitches and convulsions in muscles (*The neurons become depolarized even in the absence of stimuli*).
- Heart beat and breathing rate increases. (Deficiency causes excitatory effect on nervous system).

Hypersecretion of PTH – Osteoporosis

- The amount of calcium, at the cost of bones, increases in the blood (**Hypercalcemia**).
- The bones become spongy due to removal of calcium phosphate (demineralization of bones). Such bones are easily fractured and deformed.
- Ca^{++} prolongs systole. Therefore, hypercalcemia may cause cardiac arrest at this stage.
- If hyperparathyrodism is not treated for a long, it may lead to the deposition of fibrous tissues in the cavities formed in the bones. This disorder is known as **Osteitis fibrosa cystica**.

(10) Adrenal Gland

- It is also known as *Supra-renal gland* and is formed by the fusion of two different tissues. The outer tissue is Cortex (~70%) and inner medulla (~30%). The cortex is mesodermal and medulla is ectodermal in origin. The adrenal gland is thus, **meso-ectodermal** in origin.

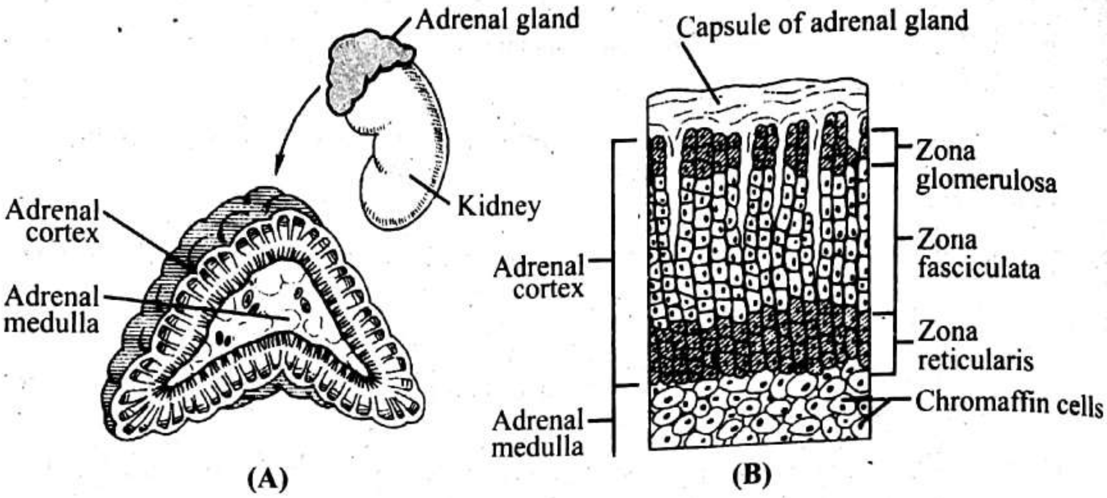


Fig. 22.8 (A) Adrenal gland, (B) V. S. Adrenal gland

I. Adrenal Cortex (Hormones – Steroids)

- The cortex of adrenal gland consists of three zones.
  (i) Zona glomerulosa (outermost) -- It produces mineralocorticoids.
  (ii) Zona fasciculata (Middle) – It produces glucocorticoids.
  (iii) Zona reticularis (Inner most) – It produces sex corticoids.

(A) Mineralocorticoids :

1. **Aldosterone**

- It is the most potent mineralocorticoid.
- It regulates mineral (sodium) metabolism.
- It is commonly called as **hypernatrimic factor** since it increases the amount of **Natrium (Na^+)** in blood.
- Its secretion is regulated by *Rennin-Angiotensin-system*, and not by ACTH of anterior pituitary.
- It promotes the absorption of sodium (Na^+) from DCT and collecting tubules of nephrons.

*(For details of Renin-Angiotensin – Aldosterone-system, **RAAS**, please refer 'Excretion', Chapter 15)*

Hypersecretion – Conn's disease

- Amount of sodium increases in blood.
- BP increases and hypertension develops.
- As the amount of sodium increases in blood the potassium passes out through urine causing kidney failure in later stages.

(B) Glucocorticoids :

2. **Cortisol**

- It is the most potent glucocorticoid in the body.
- It is **hyperglycemic factor** and converts glycogen into glucose. *(synergistic to Glucagon and antagonistic to Insulin).*
- It also causes **gluconeogenesis** (conversion of non-carbohydrates into carbohydrates or glucose).

- It is anti-stress and anti-inflammatory.
- It is anti-allergic and anesthetic also.
- It suppresses immune system.
- It prevents deposition of collagen fibres and relieves arthritis.
- It also stimulates RBC - production.

Hypersecretion – Cushing's syndrome

- Blood glucose level rises (**hyperglycemia**).
- Glucose starts passing through urine (**glycosuria**).
- Due to fat deposition in the back it shows *buffalo-hump*-condition..

Connecting Concepts

✦ The over-dose of cortisol is used for suppressing immune activity for preventing the rejection during organ transplantation.

(C) Sex-corticoids :

3. **Androgens and Estrogens.**

- These hormones are generally secreted before sexual maturity, when the testes and ovaries are not fully developed.

Hypersecretion of androgens – Adrenal virilism

- It is sex reversal, 'from female to male', due to excess of androgens (testosterone).
- The facial hair and secondary sexual characters of males develop in females.

Hypersecretion of estrogens – Gynaecomastia

- It is sex reversal, 'from male to female'.
- Female-like mammary glands (breasts) develop in males.

(Please refer 'gonadal hormones' also, for virilism and gynaecomastia).

Hyposecretion of corticoids – Addison's disease

- This disorder develops due to atrophy or hypotrophy of adrenal cortex.
- Amount of both, sodium and glucose decreases in the blood.
- There is **Bronzing of skin** due to hypersecretion of ACTH.

(In human the skin colour is governed by ACTH and not MSH, as in other mammals.)

II. Adrenal Medulla -

- It is called *emergency gland* and secretes **adrenaline** (Epinephrine) and **nor-adrenaline** (nor-epinephrine) hormones.
- Hormones of medulla are chemically **Catecholamines** which are derivatives of *Tyrosine* (amino acid).

Adrenaline (epinephrine) -

- It is commonly called as **'emergency hormone'** or 3F – hormone (For fear, fight & flight).

  Its secretion is regulated by SNS, and not by pituitary as in case of adrenal cortex.
- It stimulates sweating, heart beat and breathing rate. It causes the dilation of coronary artery (supplying blood to the heart muscles), bronchioles (for increasing inspiratory volume) and pupil (for better vision)
- It is hyperglycemic, i.e. increases the amount of glucose in blood.
- It increases blood supply to brain and skeletal muscles also.
- It also stimulates **erythropoesis** (production of RBCs).

Check Point

1. Name the hormone that -
   (i) Promotes loss of sodium in urine.
   (ii) Is secreted during emergency.
   (iii) Stimulates red bone marrow for RBC-production.
   (iv) Is responsible for Conn's disease.
   (v) Is catecholamine.
   (vi) Is secreted from Leydig cells
   (vii) Is secreted from β- cells of pancreas
   (viii) Provides cell mediated immunity
   (ix) Is secreted from C- cells of thyroid
   (x) Regulates calcium metabolism

- It also causes alertness and piloerection (goose flesh), heart beat and breathing rate etc.
- It promotes blood clotting for preventing excessive loss of the blood during injury/ emergency.
- It inhibits the functions related to the alimentary canal, e.g. it reduces the secretion of saliva, gastric juice, bile juice, pancreatic juice and intestinal juice. It also slows peristalsis and inhibits food absorption.

  (*All above activities are related to emergency conditions in the body.*)
- Nor-adrenaline is vasoconstrictor and saves blood from excessive loss. It constricts peripheral blood vessels for raising BP also.

(11) Kidney

It secretes **erythropoietin** and **renin**.

(i) Erythropoietin -

- This hormone is secreted from *peritubular capillary-network* of uriniferous tubules (nephrons) of kidney.
- It stimulates red bone marrow for the *production of RBCs* **(Erythropoesis)**

(ii) Renin -

- It is primarily an enzyme, and is secreted from 'Juxta Glomerular Cells' of **Juxta glomerular apparatus (JGA).**
- It converts plasma protein – **Angiotensinogen** into **Angiotensin-I,** which changes into **Angiotensin–II**. The Angiotensin II stimulates adrenal cortex for the secretion of Aldosterone.

(12) Heart

The heart is primarily a blood-pumping organ, but its atrial wall also secretes a hormone, called **Atrial Natriuretic Factor (ANF).**

ANF -

- It promotes the loss of *Natrium* (Na^+ - Sodium) in urine.
- It inhibits absorption of sodium chloride (NaCl) from collecting ducts.
- It also inhibits the release of **renin**, which through RAAS *(Refer Chapter 15)* increases the amount of sodium in blood.
- It is secreted when the osmolarity of the blood, or the blood pressure, rises.

HORMONAL ACTION

Hormonal action affects metabolic changes in the target cells in three different ways

1. By altering permeability of the plasma membrane
2. Through intracellular (IInd or IIIrd) messengers
3. By altering activity of genes.

   On the basis of types of receptors used, the hormones fall into three categories.

1. Peptide / protein-hormones and catecholamines

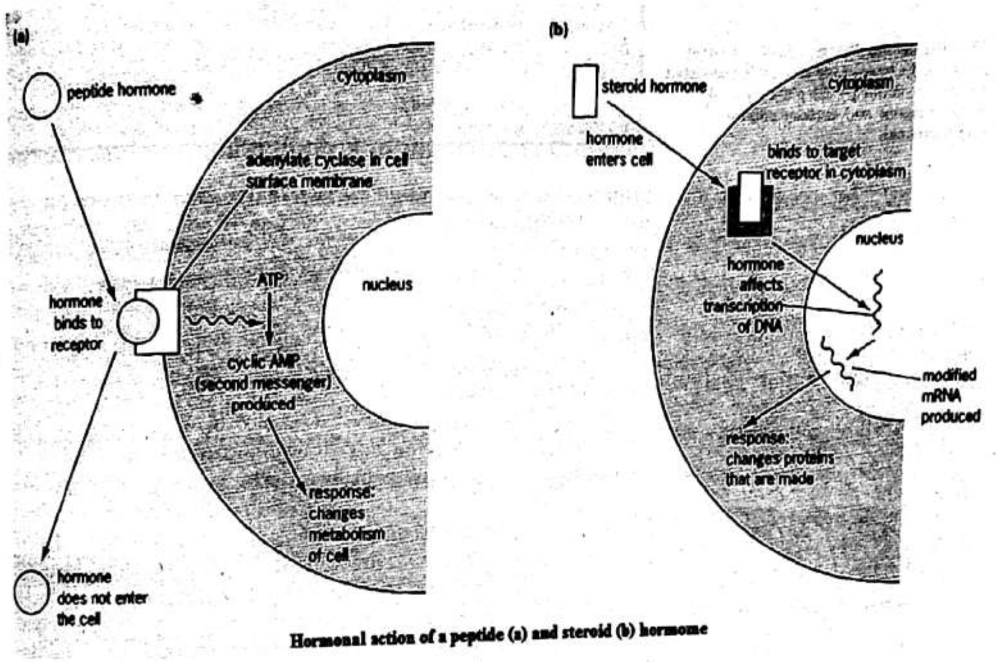
- Insulin, glucagon, growth hormone and parathyroid hormones etc. are peptides while Adrenaline (epinephrine) is a catecholamine.
- Such hormones are insoluble in lipids/fats and can not enter through bilipid-plasma membrane.
- The 'receptors' for such hormones are *present in plasma membrane.*

2. Steroid hormones

- The examples of steroid hormones are estrogen, testosterone and corticoids like aldosterone and cortisol etc.
- These are fat soluble and can pass through bilipid layer of cell membrane to reach the cytoplasm.
- The receptors for such hormones are, therefore, *present* intracellularily.

3. Thyroid hormones (T_3 & T_4)

- These hormone can also pass through plasma membrane as they are also fat-soluble.
- Their receptors are *present inside the nucleus.*



Hormonal action of a peptide (a) and steroid (b) hormome

Fig. 22.9 Functioning of peptides and steroid hormones

I. Steroids and thyroid hormones

- They readily pass through plasma membrane into the cytoplasm of target cells.
- Inside cytoplasm steroids bind to intracellular receptor proteins in the presence of Ca^{++} and form a complex, which enters into the nucleus and binds to regulatory sites on the chromosomes.
- The binding of the complex alters the pattern of gene expression, by initiating or suppressing the transcription of certain genes to produce specific types of mRNA.
- The thyroid hormones directly affect transcription of the genes as their receptors are present in the nucleus itself.
- The action of lipid soluble hormones is slower but long lasting.

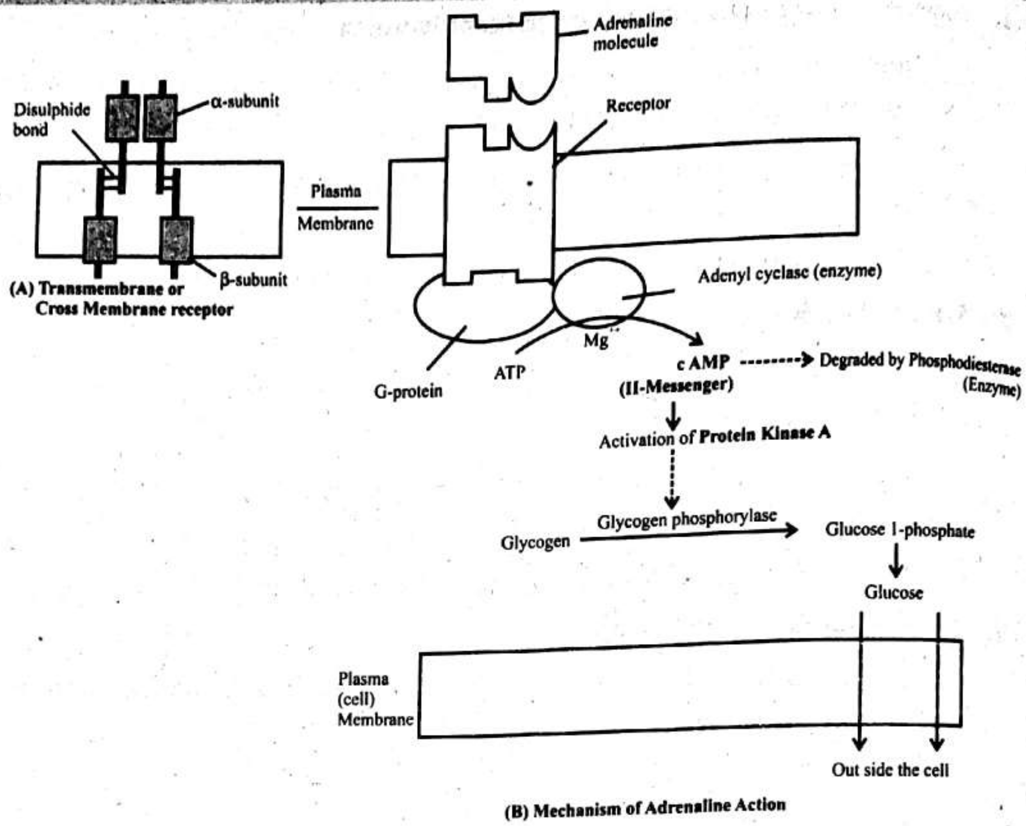


Fig. 22.10 Functioning of Catecholamine hormones

B. Peptide and catecholamines

- The receptors for such hormones are **Transmembrane-proteins** in the plasma membrane of the target cells. These receptors undergo conformational change when they bind with the hormone.
- This receptor is a tetramer, made up of 2α and 2β glycoprotein subunits, bound to each other by disulphide bonds.
- The α-subunits are extra cellular and bind with the hormone, whereas β-subunits are present across the membrane. The intracellular portion of β–subunit has tyrosine kinase activity.

I. In case of Adrenaline the binding of hormone triggers the tyrosine kinase activity of β-subunits producing auto-phosphorylation.

- Due to activity of β-subunit the G proteins (α-type) are activated.
- Each stimulated molecule of G-protein activates the neighboring molecule of enzyme **Adenyl cyclase**, suspended in the inner layer of plasma membrane. *(see figure)*
- Active Adenyl cyclase, in the presence of Mg^{++} catalyses hydrolysis of ATP molecules (in cytosol) into **Cyclic AMP (cAMP)**. The cyclic AMP acts as a **II-messenger** for hormonal action.
- Increased number of cAMP molecules in cytoplasm stimulate the molecules of a special category of metabolic enzymes, i.e. **Protein kinases A.**
- Active molecules of Protein kinases A activate *phophorylase kinases* which further modify the activity of other enzymes for required metabolic processes.
- An enzyme **phosphodiesterase** degrades the additional molecule of cAMP to bring their number to the normal. This stops the effect of the hormone on the target cell.

In case of adrenaline following is the chain of enzymatic reactions :

(i) 1 mol of *Adenyl cyclase* produces 10^2 **mols.** of cAMP (cAMP activates protein kinase A).

(ii) 1 mol. of *protein kinase A* activates 10^2 **mols.** of phosphorylase kinases.

(iii) 1 mol. of *Phosphorylase kinase* activates 10^2 **mols.** of Glycogen phosphorylases.

(iv) 1 mol. of *Glycogen phosphorylase* produces 10^2 **mols.** of glucose-1-phosphate, which finally produce glucose.

From 1 mol. of adrenaline hormone the net-production of glucose mols., is

$$= (10^2 \times 10^2 \times 10^2 \times 10^2) = \mathbf{10^8}\ \textbf{mols.}$$

II. In case of insulin the stimulated receptor molecule activates several molecules of G-proteins, found at the inner surface of the plasma membrane.

- These G proteins activate the enzyme (phosphodiesterase) which converts *phosphoetidyl-inositol 4.5-biphosphate* (PIP_2) into **Diacylglycerol** (DG) and **Inositol tri-phosphate** (IP_3). Both act as IInd messengers.
- The **IP_3** is water soluble and enters into cytoplasm. There it stimulates endoplasmic reticulum for the release of **Ca^{++}**, the **IIIrd messenger**, which activates a chain of reactions.
- **DG**, another II-messenger, is insoluble in water and stays in plasma membrane. Here it activates **Protein Kinases C,** which bring out many metabolic changes in the cytoplasm.

The following compounds may act as IInd, and some even III-messengers, in hormonal action :

(i) Cyclic Adenosine Monophosphate (cAMP)

(ii) Cyclic Guanosine Monophosphate (cGMP)

(iii) Diacyl glycerol (DAG or DG)

(iv) Inositol triphosphate (ITP or IP_3)

(v) Calcium (Ca^{++})

Heart muscles use 2-types of II-messengers. The cAMP is the II-messenger for adrenaline and stimulates heart beat. The cGMP is the II-messenger for acetylcholine and slows down the heart beat.