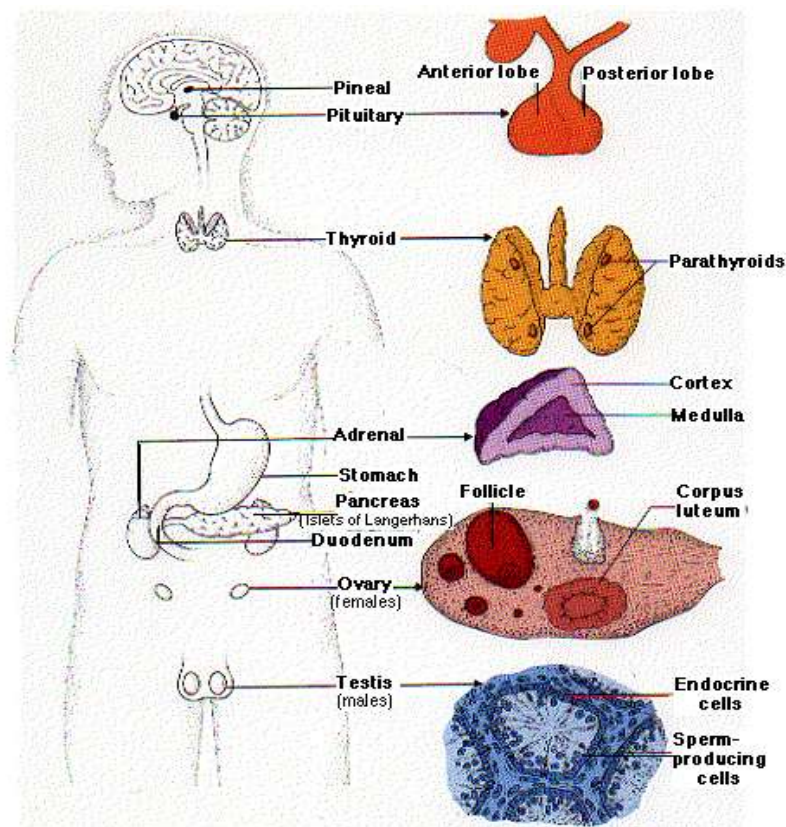


## ENDOCRINE SYSTEM

The regulating systems of body are nervous system & endocrine system, which consists of endocrine glands that secrete chemicals called hormones (Hs).

- Glands are – group of specialized cells that produce secretions.
- Exocrine glands: secrete through a duct.
- Endocrine glands: ductless, secrete Hs directly into blood stream.
- Hormones: regulate activities of cells & other organs.
- Target tissue: specific tissue acted upon by a hormone.
- Some Hs, such as insulin & thyroxine, have many target organs. Other Hs, such as calcitonin & some pituitary gland Hs, have only one or a few target organs.
- **CHEMISTRY OF HORMONES**
- Hs are classified into three groups:
  - 1. **Amines**—these simple Hs are structural variations of amino acid tyrosine. This group includes thyroxine & epinephrine.
  - 2. **Proteins**—these Hs are chains of amino acids; e.g Insulin, growth H, & calcitonin. Short chains of amino acids called **peptides**. E.g Antidiuretic H & oxytocin, Hs.
  - 3. **Steroids**—cholesterol is the precursor for steroid Hs, which include cortisol & aldosterone, estrogen & progesterone, & testosterone.



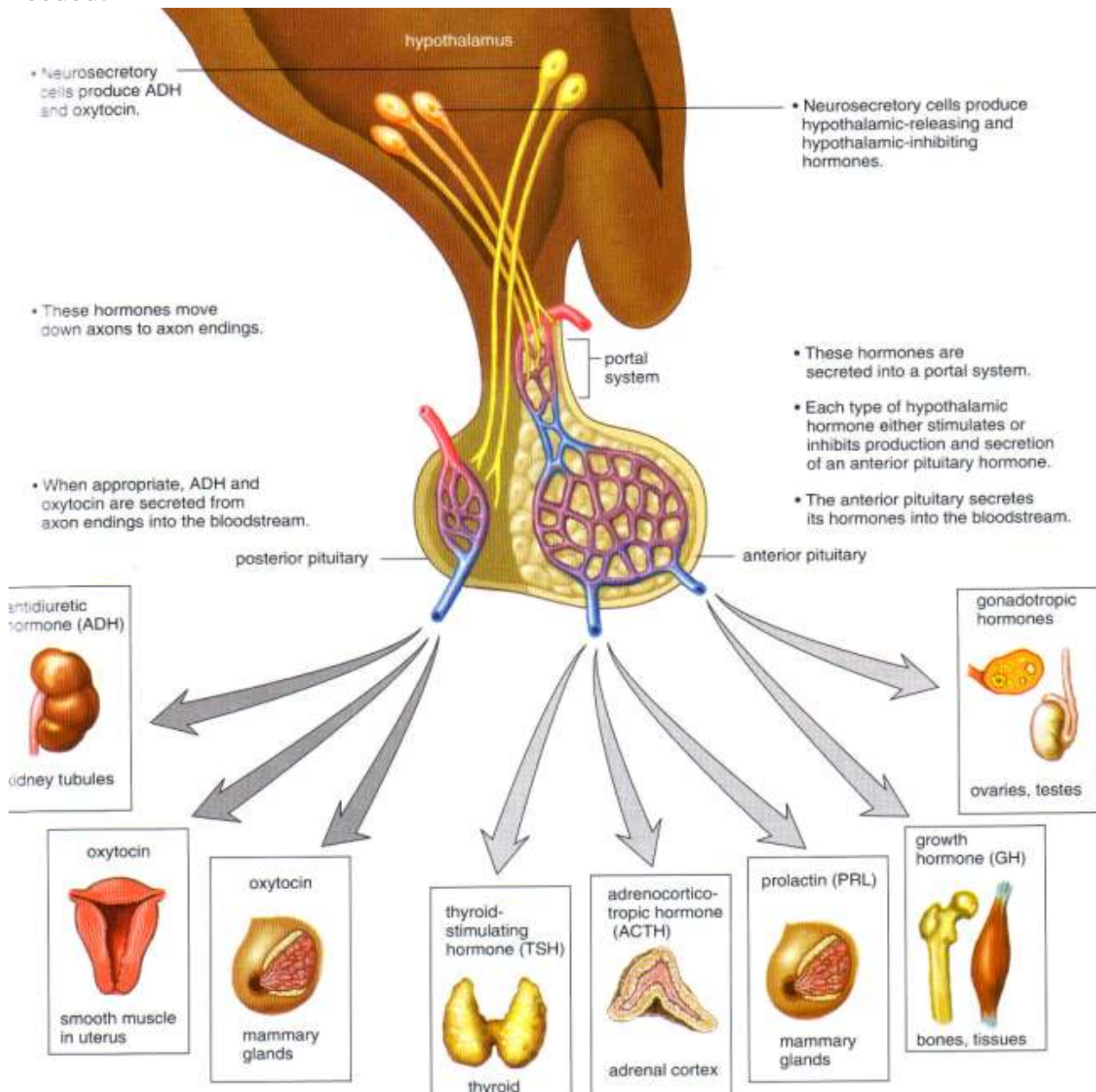
**PITUITARY GLAND** (or **hypophysis**) = PG

Despite its small size, PG regulates many body functions. Its two major portions are;

- ❖ posterior PG (**neurohypophysis**), an extension of nerve tissue of hypothalamus.
- ❖ anterior PG (**adenohypophysis**), which is glandular tissue.

**POSTERIOR PITUITARY GLAND**

- Hs of posterior PG are synthesized in cell bodies of supraoptic & paraventricular nuclei & transported down axons to their endings in posterior lobe, where they are secreted in response to electrical activity from hypothalamus.
- So, Oxytocin & vasopressin are typical **neural hormones** that are produced by hypothalamus & stored in posterior PG until needed.



### Antidiuretic Hormone(ADH, also called vasopressin)

#### ➤ **Function** ;

- ❖ ↑water reabsorption by kidney tubules (water returns to blood).
- ❖ ↓sweating.
- ❖ Vasoconstriction (in large amounts).

#### ➤ **Regulation** of secretion;

- ❖ ↓water content in the body (alcohol ingestion inhibits ADH secretion).

- Any type of dehydration stimulate secretion of ADH to conserve body H<sub>2</sub>O. If much H<sub>2</sub>O loss,(diarrhea), **osmoreceptors** in hypothalamus detect ↑saltiness in body fluid, transmits impulse to post. PG→↑ ADH.

- In severe hemorrhage, ADH is released in large amounts →vasoconstriction.

### Oxytocin

#### ➤ **Function**

- ❖ Promotes contraction of myometrium of uterus during labor;

- As labor begins, uterine cervix stretched→ sensory impulse to hypothalamus → stimulates posterior PG to release oxytocin→ myomaterial contraction.

- ❖ Promotes release of milk from mammary glands.

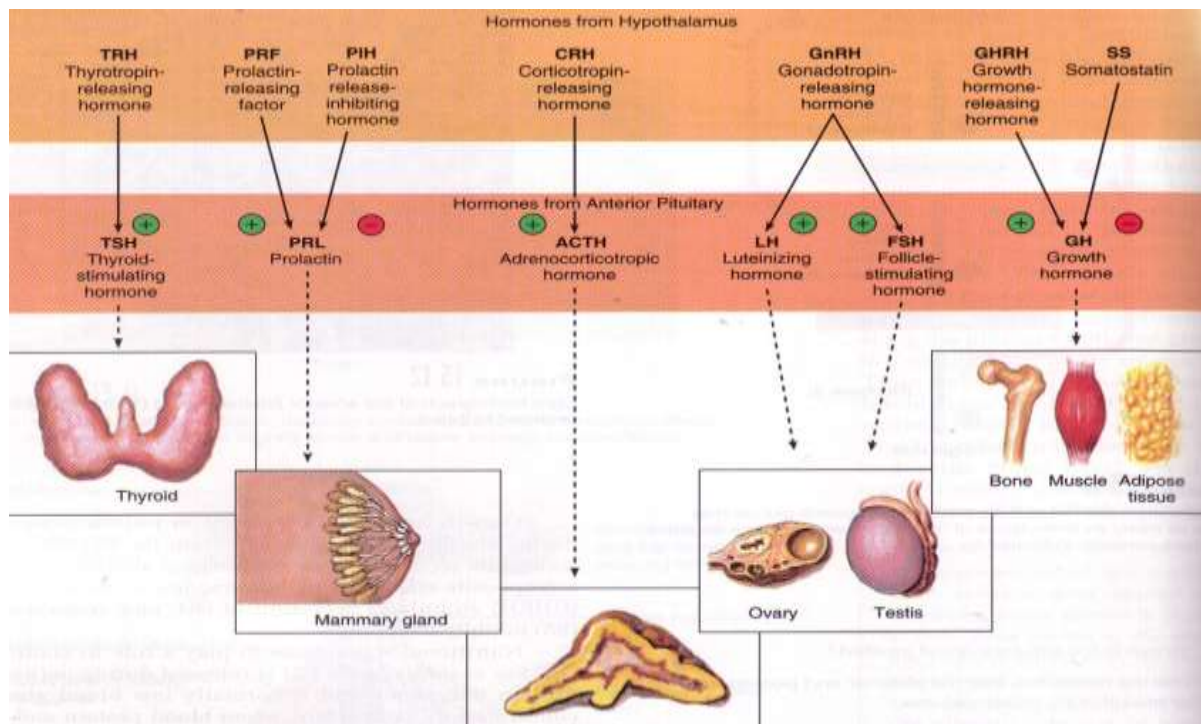
- “*milk let-down*” reflex; When a baby is breast-fed, sucking of baby stimulates sensory impulses from mother’s nipple → hypothalamus → posterior PG→ release of oxytocin → contraction of smooth muscle cells around mammary ducts.

#### ➤ **Regulation** of secretion ;

- ❖ Nerve impulses from hypothalamus.

- ❖ Secretion from placenta at end of gestation— stimulus unknown

- Secretion of oxytocin is one of few +ve feedback mechanisms within the body.



## ANTERIOR PITUITARY GLAND

- Hypothalamus secrete **releasing Hs**, which pass through **hypophyseal portal** vein to another capillary network in ant. PG→ stimulate secretion of anterior PG Hs.
- **hypophyseal portal** is small, specialized pathway of circulation, permits releasing Hs to rapidly stimulate ant. PG, without having to pass through general circulation.

## GROWTH HORMONE (GH) also called **somatotropin**:

- Insulin-like growth factors (IGFs); intermediary molecule that bring about GH functions.

### ➤ **Function:**

- 1- ↑ transport of amino acids(a.a) into cells, & ↑ rate of protein synthesis.
  - Excess a.a are changed to carbohydrates (CHO) or fat, for energy storage).
  - GH ensures that a.a will be used for protein synthesis is necessary, before a.a can be changed to CHO.
- 2- Stimulates cell division in tissues capable of mitosis.
  - These functions(protein synthesis & cell division) contribute to body growth during childhood, especially growth of bones & muscles.
- 3- Stimulates release of fat from adipose tissue (for energy production).
  - This is important any time we go for fasting, no matter what our ages.

### • **Does GH is secreted in adults?**

Answer is yes. The use of a.a for protein synthesis is still necessary, because some tissues will require new proteins for repair or replacement.

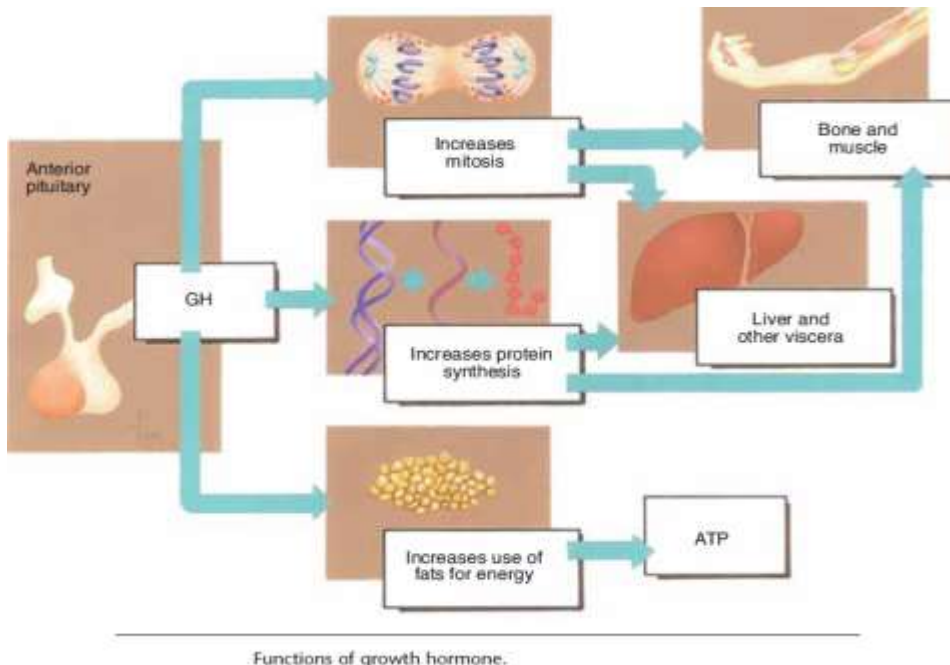
### ➤ **Regulation** of Secretion of GH is by two Hs from hypothalamus:

- 1- Growth H–releasing H (GHRH), ↑ secretion of GH, produced during;

- Hypoglycemia .
  - Exercise.
  - High blood level of a.a.
- 2- Growth H inhibiting H (GHIH)(also called **Somatostatin**)→↓ secretion of GH.
- It is produced during hyperglycemia.

#### Disorders of GH secretion.

- **Acromegaly** hypersecretion of GH in adult, caused by pit. tumor. Long bones can't grow because epiphyseal discs are closed, but growth of other bone is stimulated.
- **pituitary dwarfism** Hyposecretion of GH in childhood, person may attain a final height of 3-4 feet but will have normal body proportions.
- **Giantism** :Hypersecretion of GH in childhood→ long bones grow excessively & person attain a height of 8 feet.



Functions of growth hormone.

#### **THYROID STIMULATING HORMONE (TSH)** (also called Thyrotropin),

- Its target organ is thyroid gland (TG).
- **Function**: It stimulates normal growth of TG & secretion of thyroxine (T4) & triiodothyronine (T3).
- **Regulation** of Secretion of TSH by TRH from hypothalamus.
  - When ↓metabolic rate (↓energy production) → TRH is produced.

#### **ADRENOCORTICOTROPIC H (ACTH)**

- **Function**: It stimulates secretion of cortisol & other Hs by adrenal cortex.
- **Regulation** of secretion by CRH from hypothalamus.
  - CRH is produced in any physiological stress (exercise or hypoglycemia - hungry).

#### **PROLACTIN**

- **Function**: It stimulates milk production by mammary glands.(responsible for lactation).

- **Regulation** of secretion; # PRH (from hypothalamus) stimulates secretion of prolactin.  
# PIH (from hypothalamus) inhibits secretion of prolactin.
- After delivery of the baby; prolactin secretion is  $\uparrow$  → milk production.

### FOLLICULAR STIMULATING HORMONE (FSH)

- It is one of gonadotropic Hs; that is, it has its effects on gonads: ovaries or testes.
- **Function in women:**
  - ❖ Initiates growth of ova in ovarian follicles.
  - ❖  $\uparrow$  Secretion of estrogen by follicle cells.
- **Function In men:**
  - ❖ Initiates sperm production in the testes
- **Regulation** of secretion is
  - ❖ GnRH (hypothalamus) stimulates secretion of FSH.
  - ❖ Inhibin (H produced by ovaries or testes) → inhibits secretion of FSH.

### LUTEINIZING HORMONE (LH)

- It is another gonadotropic H.
- **Function In women:**
  - ❖ Causes ovulation.
  - ❖ Causes the ruptured ovarian follicle to become corpus luteum.
  - ❖ Increases secretion of progesterone by corpus luteum.
- **Function in men:**
  - ❖  $\uparrow$  secretion of testosterone by interstitial cells of testes.
- **Regulation** of secretion: by GnRH (from hypothalamus)

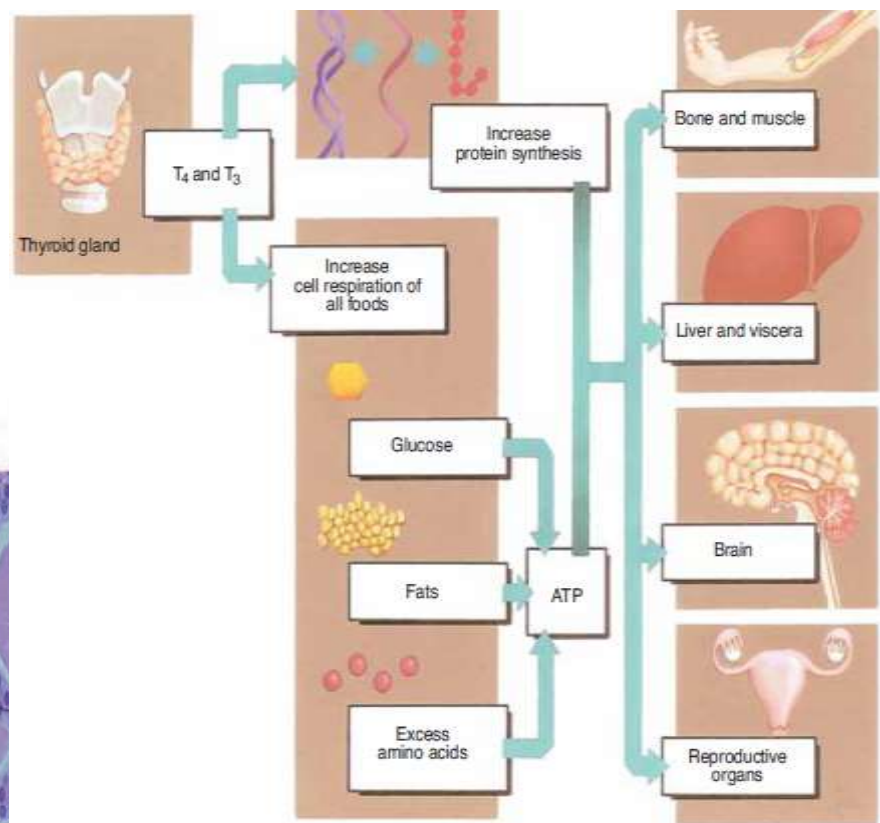
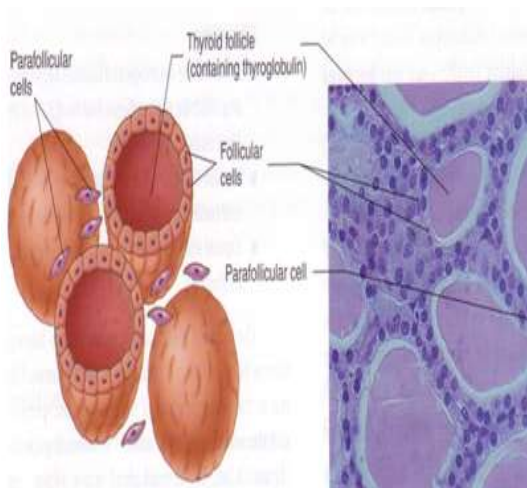
### THYROID GLAND (TG)

- Structural units of TG are thyroid follicles.
- TG produce the following hormones:
  - **Thyroxine (T4-** contain 4 atoms of iodine) ← secreted by follicular cells.
  - **Triiodothyronine (T3-** contains 3 atoms of iodine). ↙
  - **Calcitonin**, which is secreted by parafollicular cells.

### THYROID HORMONES

- Follicular cells require iodine salts (iodides) to produce T4 & T3 .such salts are normally obtained from foods, absorbed from intestine → blood carry some of them to TG.
  - An efficient active transport protein (iodine pump) moves iodide into follicular cells, with a.a tyrosine, are used to synthesize thyroid Hs.
  - Follicular cells synthesize a protein (thyroglobulin) which is rich in tyrosine molecules, many of which have already had iodide attached by an enzymatic reaction.
  - Once in blood, Hs combine with blood protein ( $\alpha$  globulins) & transported to body cells.
- T3 is 5 times more potent, but T4 accounts for 95% of circulating thyroid Hs.
- T4 & T3 have the same **functions** which are :
  - ❖  $\uparrow$  Energy & heat production from all food types.

- ❖ ↑ Rate of protein synthesis within cells.
- Normal production of T<sub>4</sub> & T<sub>3</sub> is essential for ;
  - physical growth
  - normal mental development.
  - maturation of reproductive system.
- Although T<sub>4</sub> & T<sub>3</sub> are not vital Hs, in that they are not crucial to survival, their absence greatly diminishes physical & mental growth & abilities.
- **Regulation** of Secretion by **TSH** .
  - When ↓ metabolic rate (energy production)→ detected by hypothalamus → secretes TRH→ secrete TSH→ release T<sub>4</sub> & T<sub>3</sub>→↑ metabolic rate by ↑ energy production.
  - This -ve feedback mechanism, shuts off TRH from hypothalamus until metabolic rate ↓.

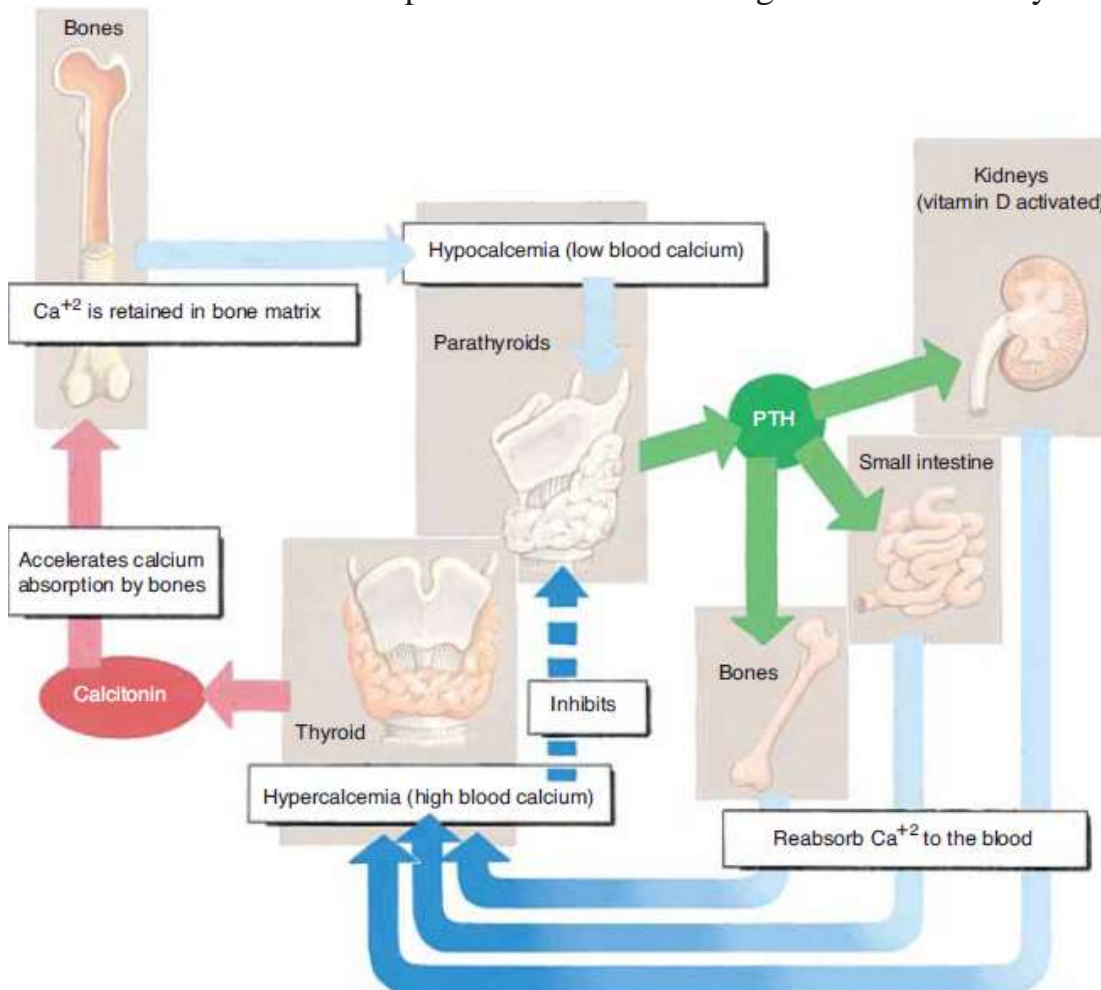
Functions of thyroxine and T<sub>3</sub>.

## CALCITONIN

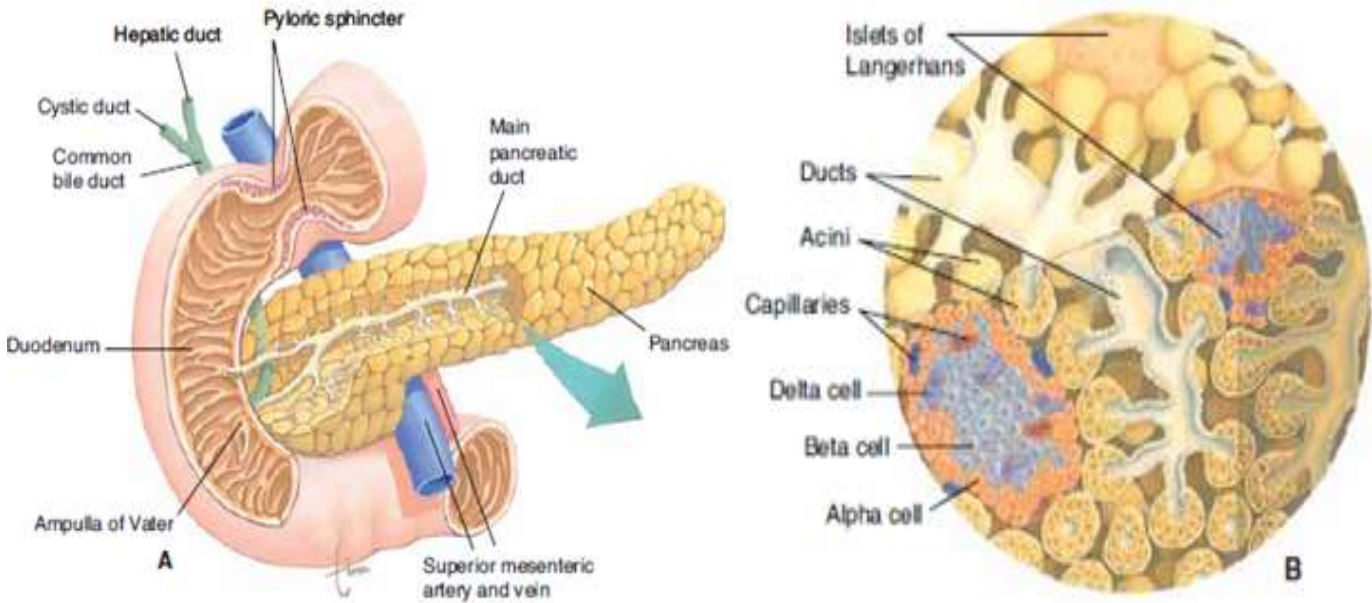
- **Function;** ↓ reabsorption of Ca<sup>2+</sup> & phosphate from bone to blood → ↓ their blood level.
- So, it helps maintain normal blood level of Ca<sup>++</sup> & phosphate & also helps maintain a stable, strong bone matrix.
- Calcitonin exerts its most important effects during childhood, when bones are growing.
- **Regulation** for secretion is **hypercalcemia**.
- When ↑ blood Ca<sup>++</sup> , calcitonin ensures that no more Ca<sup>++</sup> will be removed from bones until there is a real need for more Ca<sup>++</sup> in blood.

## PARATHYROID GLANDS

- There are 4 parathyroid glands, produce parathyroid H (PTH)
- Target organs of PTH are bones, small intestine, & kidneys.
- **Function:**
  1. ↑ Reabsorption of  $\text{Ca}^{+2}$  & phosphate from bones to blood → ↑ their blood levels.
  2. ↑ Absorption of  $\text{Ca}^{+2}$  & phosphate in small intestine, which also requires vitamin D.
  3. In kidneys;
    - ❖ Stimulates activation of vitamin D.
    - ❖ ↑ reabsorption of  $\text{Ca}^{+2}$  & excretion of phosphate.
- Therefore, overall effect of PTH is to ↑ blood  $\text{Ca}^{++}$  level & ↓ blood phosphate.
- **Regulation** of secretion is stimulated by *hypocalcemia* & inhibited by *hypercalcemia*.
- PTH & calcitonin are of antagonistic effects; they maintain blood  $\text{Ca}^{+2}$  within a normal range  
 $\text{Ca}^{+2}$  in blood is essential for process of blood clotting & normal activity of neurons & muscle.





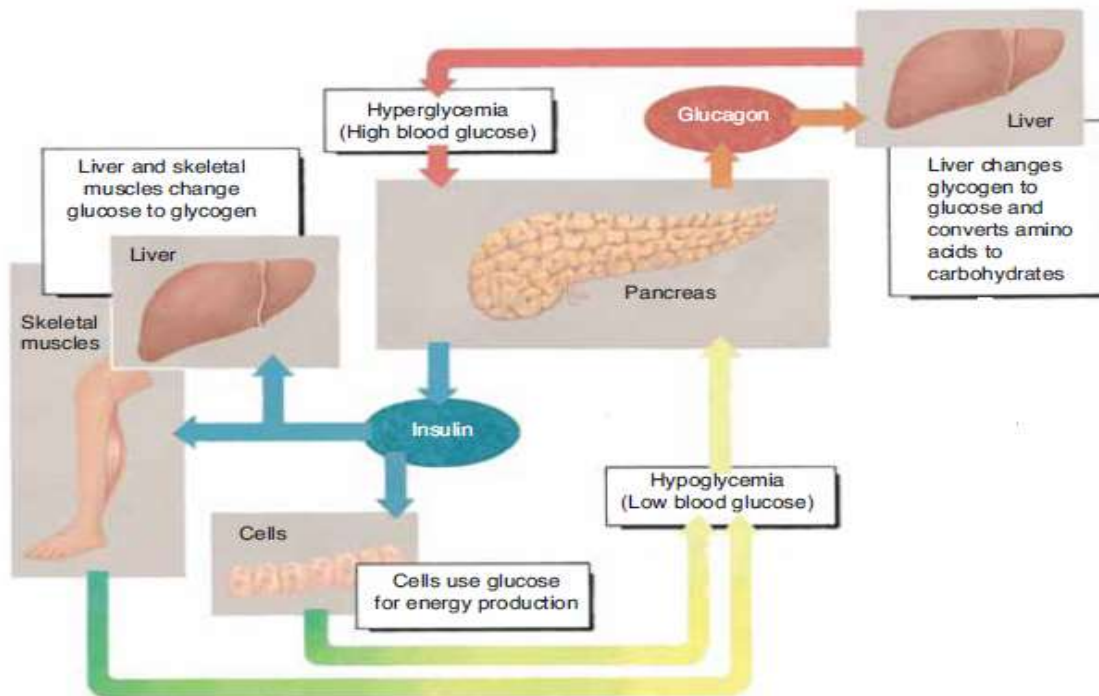


## PANCREAS

- Although pancreas is both an exocrine (digestive) gland & endocrine gland.
- The endocrine hormone-producing cells of pancreas are called **islets of Langerhans** (pancreatic islets); they contain  **$\alpha$  cell** that produce glucagon &  **$\beta$  cells** that produce insulin, & **Delta** cells that produce somatostatin.

## GLUCAGON

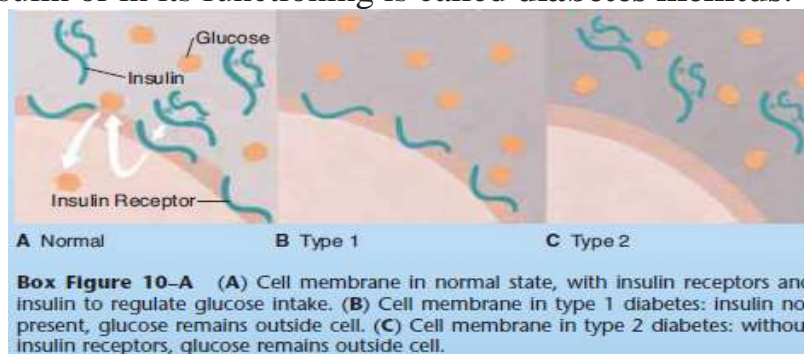
- **Function** ( $\uparrow$  blood glucose level & to make all types of food for energy production) by;
  - ❖  $\uparrow$  Conversion of glycogen to glucose in liver (*Glycogenolysis*).
  - ❖  $\uparrow$  Use of fats & excess a.a for energy production.
- **Regulation** of secretion is stimulated by **hypoglycemia**; which may occur between meals or during physiological stress situations such as exercise.



## INSULIN

### ➤ **Function;**

- 1) ↑ glucose transport into cells by ↑ permeability of cell membranes to glucose.
  - 2) ↑ conversion of excess glucose to glycogen in liver & muscles
  - 3) ↑ a.a & F.a transport into cells, & their use in synthesis of protein & lipid.
- Brain, liver, & kidney cells, are not dependent on insulin for glucose intake.
  - Without insulin, blood levels of lipids tend to rise & cells accumulate excess f.a.
  - So, it is vital H; we cannot survive for very long without it.
  - **Regulation** of secretion; it is stimulated by **hyperglycemia**, after eating, especially meals of high CHO. At the same time, excess glucose will be stored in liver & muscles as glycogen.
  - A deficiency of insulin or in its functioning is called **diabetes mellitus**.



## Somatostatin

- It is produced by Delta cells,
- It is identical to GHIH from hypothalamus.
- **Function**; It acts locally to;

- ❖ Inhibit secretion of insulin & glucagon.
- ❖ Slow absorption of nutrients in small intestine.

### ADRENAL GLANDS (*suprarenal glands*)

- The two **adrenal glands** are located one on top of each kidney.
- Each adrenal gland consists of two parts:
  - ❖ Inner adrenal medulla.
  - ❖ Outer adrenal cortex.

### ADRENAL MEDULLA

- Secrete epinephrine & norepinephrine, called **catecholamine (sympathomimetic)**.
- Secretion of both Hs is stimulated by sympathetic impulses from hypothalamus, & their functions duplicate & prolong those of sympathetic division of ANS

### Epinephrine (Adrenalin ) & Norepinephrine (noradrenalin) (E & NE)

- They are both secreted in stress situations & help prepare body for “fight or flight.”
- **NE** is secreted in small amounts, & its significant *function* is;
  - ❖ Vasoconstriction in skin, viscera, & skeletal muscles.
- **E**, secreted in larger amounts & *function*;
  - ❖ ↑ heart rate & force of contraction.
  - ❖ Dilates bronchioles.
  - ❖ ↓ peristalsis.
  - ❖ ↑ conversion of glycogen → glucose in liver.
  - ❖ vasodilation in skeletal muscles & vasoconstriction in skin & viscera.
  - ❖ ↑ use of fats for energy
  - ❖ ↑ rate of cell respiration.
- Responding to stress is so important that body acts redundantly & has both a nervous mechanism & a hormonal mechanism.
- E is more effective than symp. stimulation, because H ↑energy production & cardiac output to a greater extent.

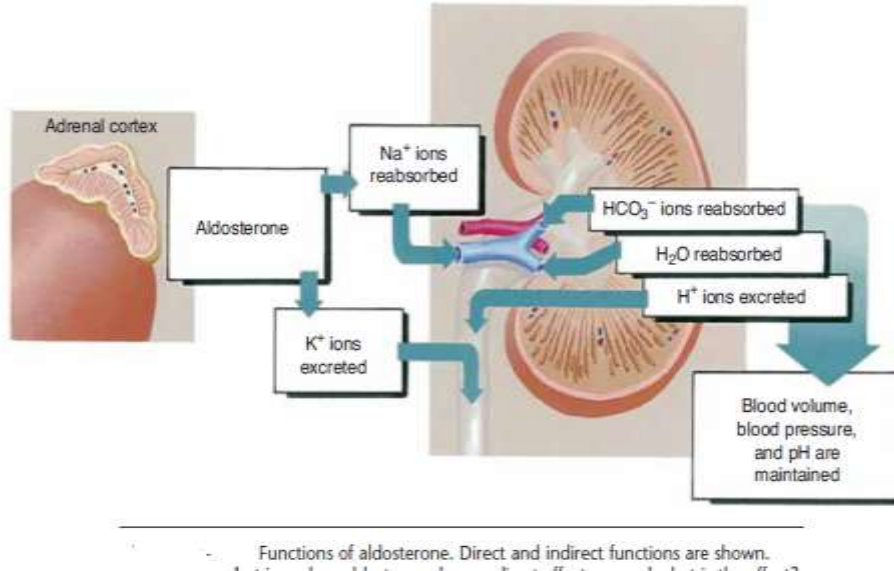
### ADRENAL CORTEX

- It secretes 3 types of steroid Hs: mineralocorticoids, glucocorticoids, & sex Hs.
- Sex Hs, “female” estrogens & “male” androgens, are produced in very small amounts.

### ALDOSTERONE

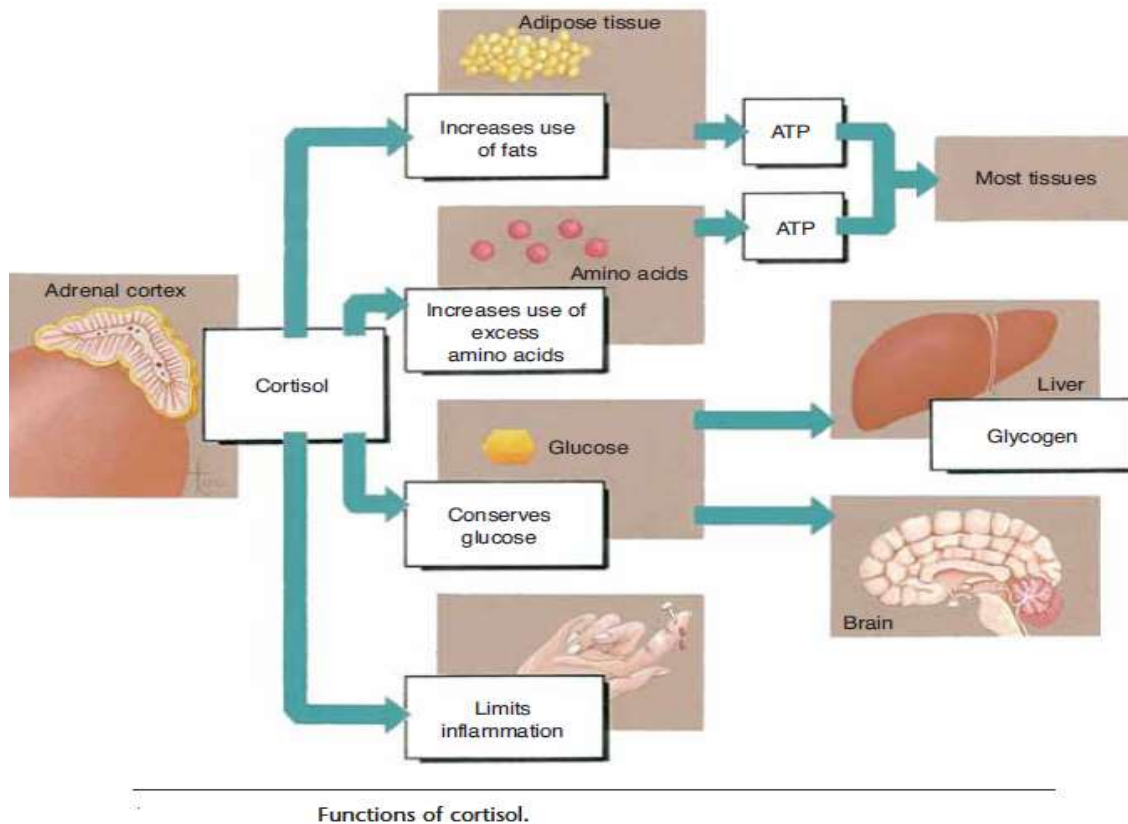
- **It** is the most abundant of **mineralocorticoids**,
- Target organ is kidney, but there are important secondary effects. Its *function*;
  - ❖ ↑ Reabsorption of Na ions by kidneys to blood.
  - ❖ ↑ Excretion of K ions by kidneys in urine.
- As Na ions are reabsorbed;
  - hydrogen ions (H<sup>+</sup>) may be excreted in exchange.
  - -ve ions such as Cl<sup>-</sup> & HCO<sub>3</sub><sup>-</sup> – follow Na ions back to blood.

- H<sub>2</sub>O follows by osmosis (important to maintain normal blood volume & BP).this is indirect effect of aldosterone.
- **Regulation** of Secretion of aldosterone.
  - ❖ Low blood Na<sup>+</sup> level
  - ❖ Low blood volume or BP
  - ❖ High blood K<sup>+</sup> level
- ↓BP or blood volume activates **renin-angiotensin mechanism** of kidneys→ formation of angiotensin II.( Angiotensin II →vasoconstriction & stimulates secretion of aldosterone).



## CORTISOL

- It is responsible for most of actions of glucocorticoids groups.
- **Function:**
  - ❖ ↑ Use of fats & excess a.a for energy (gluconeogenesis).
  - ❖ ↓ Use of glucose for energy. (except for brain) called glucose sparing effect, & it is important because it conserves glucose for use by brain.
  - ❖ ↑ conversion of glucose to glycogen in liver.
  - ❖ Anti-inflammatory effect: stabilizes lysosomes & blocks effects of histamine.
    - During inflammation, histamine from damaged tissues makes capillaries more permeable, & lysosomes of damaged cells release their enzymes, which help break down damaged tissue & destruction nearby healthy tissue.
    - Too much cortisol→↓ immune response( body susceptible to infection) & slowing healing of damaged tissue.
- It is secreted in any physiological stress: physical injury, fear or anger, exercise & hunger.
- Although most body cells easily use f.a & excess a.a in cell respiration, brain cells do not, so they must have glucose.
- **Regulation** of secretion is **ACTH** during physiological stress.



## OVARIES

Hs produced are steroids (estrogen & progesterone, & protein inhibin).

## ESTROGEN

- It is secreted by follicle cells of ovary;
- **Regulation** of secretion is stimulated by **FSH**.
- **Function;**
  - ❖ Promotes maturation of ovum in ovarian follicle.
  - ❖ Stimulates growth of blood vessels in endometrium of uterus prepared for a possible fertilized egg.
  - ❖ Develop *2ry sex characteristics in ♀* which are (growth of duct system of mammary glands, growth of uterus, & deposition of fat subcutaneously in hips & thighs).
  - ❖ Promote long bones to grow (beginning at puberty), however it stimulate ossification of epiphysial disks, & consequently they stop bone lengthening.
    - Effect of estrogens on disks is stronger than that of androgens. For this reason ♀ reach their maximum height earlier than males.
  - ❖ ↓ blood levels of cholesterol & triglycerides.
    - It is benefit for ♀ before menopause, as it ↓ risk of atherosclerosis & coronary disease.
- Estrogen has effects on many organs, including brain, heart, & blood vessels.
  - In brain, testosterone from testes or adrenal cortex can be converted to estrogen, which may be important for memory, especially for older people.

## PROGESTERONE

- When a mature ovarian follicle releases an ovum, follicle becomes **corpus luteum** & begins to secrete progesterone in addition to estrogen.
- **Function;**
- ❖ Promotes storage of glycogen.
- ❖ Promote the further growth of blood vessels in endometrium, which thus becomes a potential placenta.
- ❖ Develop secretory cells of mammary glands.
- **Regulation;** it is stimulated by LH.

## INHIBIN

- It is secreted by corpus luteum.
- **Function:** helps ↓ secretion of FSH & GnRH by hypothalamus.

## TESTES

It secrete Two Hs, testosterone & inhibin.

### TESTOSTERONE

- It is a steroid H secreted by interstitial cells of testes;
- **Function:**
- ❖ Promote maturation of sperm in seminiferous tubule of testes; this process begins at puberty & continues throughout life.
- ❖ Stimulate development of ♂ *2ry sex characteristics* at puberty (growth of reproductive organs, facial & body hair, larynx & deepening of voice & growth (protein synthesis of skeletal muscles)).
- ❖ Brings about closure of epiphyses of long bones.
- **Regulation** for secretion; stimulated by LH.

### INHIBIN

- Secreted by sustentacular cells of testes.
- **Function;** ↓ secretion of FSH.
- **Regulation** for secretion; stimulated by ↑ed testosterone.

## PINEAL GLAND

- It is located at the back of 3<sup>rd</sup> ventricle of brain, & produce hormone **Melatonin**.
- Secretion is greatest in darkness & ↓ when light enter eye & retina signals hypothalamus.
- Retina also produce melatonin (eyes & pineal gland work with biological clock of hypothalamus).
- For people, melatonin definitely stimulates onset of sleep & ↑ its duration.
- In other mammals, it helps regulate seasonal reproductive cycles, but does pineal gland have a similar function for control of reproduction in humans? The answer is unknown. However, some of tumors occur in region of pineal gland secrete excessive quantities of pineal H, whereas others press on pineal gland to destroy it.

- Both types of tumors are associated with hypogonadal or hypergonadal function. So perhaps pineal gland plays a role in controlling sexual drive & reproduction in human.

✚ **Other organs that produce Hs** have only one or a few target organs. For example;

- Stomach & duodenum produce Hs that regulate aspects of digestion & appetite.
- Adipose tissue produces appetite-suppressing H **leptin**.
- Thymus gland produces Hs necessary for normal function of immune system.
- Kidneys produce H that stimulates RBC production.

### PROSTAGLANDINS (PGs)

- They are made by all cells from phospholipids of their cell membranes.
- They differ from other Hs in that, they exert their effects locally where they are produced & do not circulate in blood to target organs.
- There are many types of PGs, as in PGA, PGB, so on.
- **Function**; Involved in inflammation, pain, blood clotting, vasoconstriction & dilation, uterine contraction, reproduction, secretion of digestive glands & nutrient metabolism.
- E.g;
  - ❖ In minor pain as in headache, people take aspirin which inhibits synthesis of PGs involved in pain mechanisms.
  - ❖ People with rheumatoid arthritis, take aspirin to diminish pain & inflammation. They may bruise easily because of impaired blood clotting process.

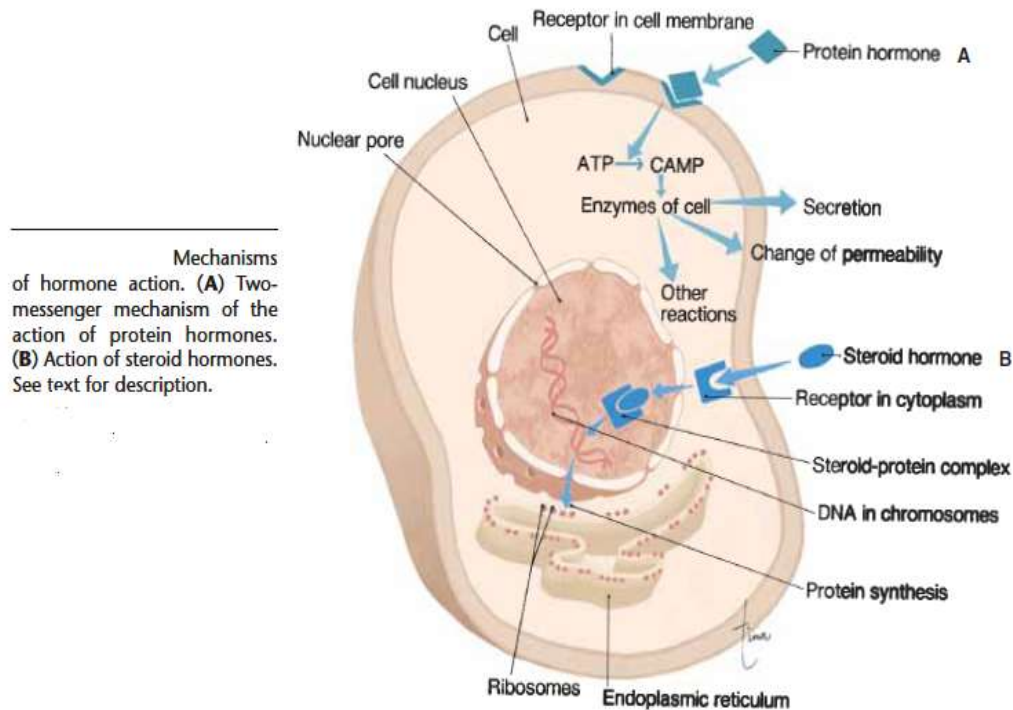
### MECHANISMS OF HORMONE ACTION

- Cells respond to certain Hs & not to others because of presence of specific receptors (proteins).
- Receptors may be part of cell membrane or within cytoplasm or nucleus of target cells.
- Bone cells have receptors for GH, PTH, & calcitonin.
- Cells of ovaries & testes do not have receptors for PTH & calcitonin, but do have receptors for FSH & LH.

### THE TWO-MESSENGER MECHANISM— PROTEIN HORMONES

- Two-messenger mechanism of H action involves *messengers* that make stimulate reactions.
- Protein Hs bond to receptors of cell membrane, & H is called 1<sup>st</sup> messenger.
- H –receptor bonding activates enzyme adenyl cyclase on inner surface of cell membrane.
- Adenyl cyclase synthesizes a substance called cyclic adenosine monophosphate (**cAMP**) from ATP,( cAMP is the 2<sup>nd</sup> messenger).
- cAMP activates specific enzymes within cell, which bring about cell's characteristic response to H; which include;
  - ❖ a change in permeability of cell membrane to a specific substance.
  - ❖ ↑ Protein synthesis.

- ❖ Activation of other enzymes.
- ❖ Secretion of a cellular product.



### ACTION OF STEROID HORMONES

- They are soluble in lipids of cell membrane & diffuse easily into a target cell.
- Once inside cell, they combine with a receptor in cytoplasm, this (steroid-protein complex) enters nucleus & activates specific genes, which begin process of protein synthesis.

### AGING & ENDOCRINE SYSTEM

- Most of endocrine glands ↓ their secretions with age, but normal aging usually do not lead to serious H deficiencies.
  - ↓ Secretion of GH → ↓ in muscle mass & ↑ in fat storage.
  - A lower basal metabolic rate is common in elderly as TG slows its secretion of thyroxine.
  - Unless specific pathologies develop, endocrine system continues to function in old age.
- 
-