b


# Hormones

# Hormones

Hormones are organic substances, produced in small amounts by specific tissues (endocrine glands), secreted into the blood stream to control the metabolic and biological activities in the target cells. Hormones may be regarded as the chemical messengers involved in the transmission of information from one tissue to another and from cell to cell. The major endocrine organs in human body are depicted in the figure (A).

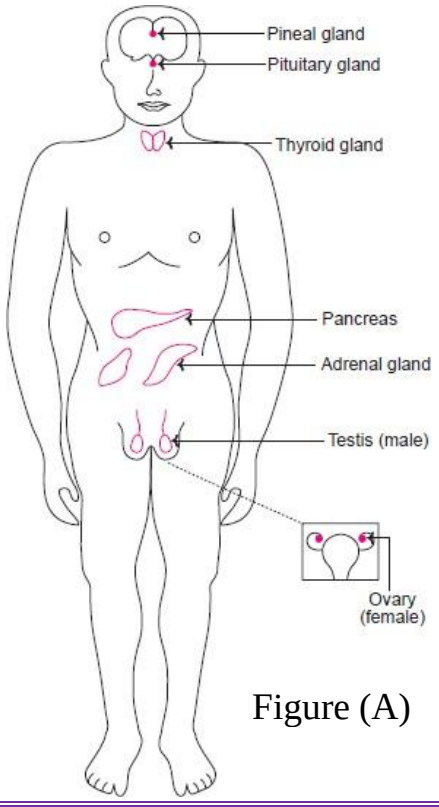



Figure (A)

## Classification of hormones

Hormones may be classified in many ways based on their characteristics and functions. Two types of classification are discussed here.

### I. Based on the chemical nature

The hormones can be categorized into three groups considering their chemical nature.

1. **Protein** or **peptide hormones** e.g. insulin, glucagon,

antidiuretic hormone, oxytocin.

2. **Steroid hormones** e.g. glucocorticoids, mineralocorticoids, sex hormones.

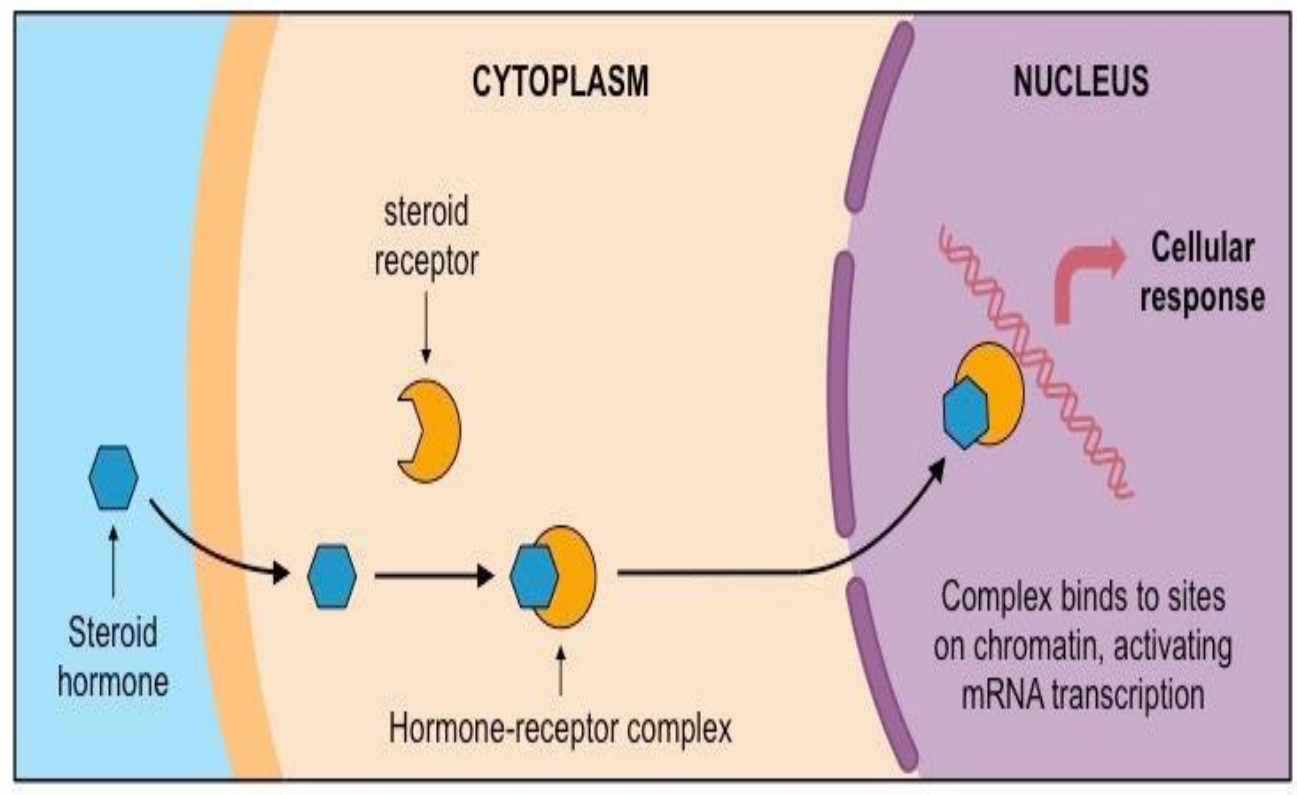
3. **Amino acid derivatives** e.g. epinephrine, norepinephrine, thyroxine (T4), triiodothyronine (T3).

## II. Based on the mechanism of action

Hormones are classified into two broad groups (I and II) based on the location of the receptors to which they bind and the signals used to mediate their action.

1. **Group I hormones:** These hormones **bind to intracellular receptors** to form receptor hormone complexes (the intracellular messengers) through which their biochemical functions are mediated. Group I hormones are lipophilic in nature and are

mostly derivatives of cholesterol (exception—T3 and T4). e.g. estrogens, androgens, glucocorticoids, calcitriol.



2. **Group II hormones:** These hormones bind to **cell surface (plasma membrane)** receptors and stimulate the release of certain molecules, namely the **second messengers** which, in turn, perform the biochemical functions. Thus, hormones themselves are the first messengers. Group II hormones are subdivided into three categories based on the chemical nature of the second messengers.

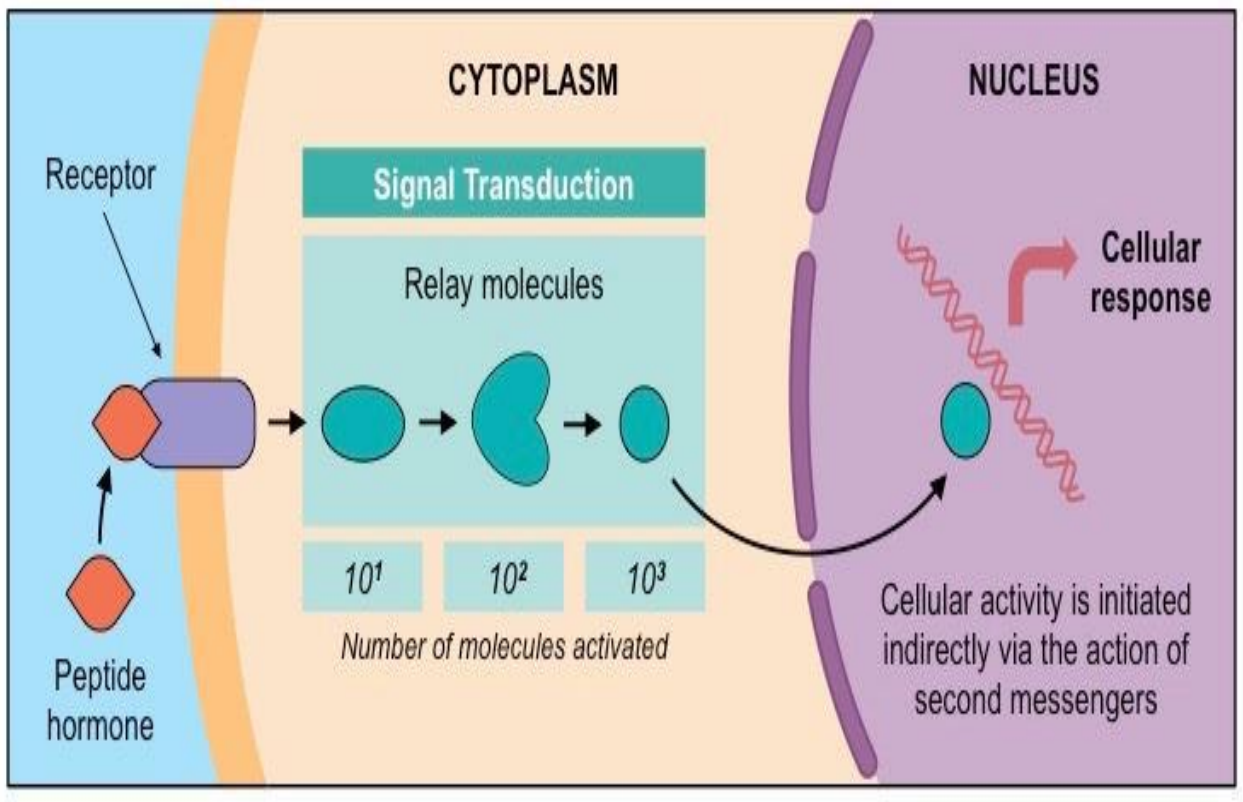
(a) The second messenger is **cAMP** e.g. ACTH, FSH, LH, PTH, glucagon,

calcitonin.

(b) The second messenger is **phosphatidylinositol/ calcium** e.g. TRH, GnRH, gastrin, CCK.

(c) The second messenger is **unknown** e.g. growth hormone, insulin, oxytocin, prolactin.

The principal human hormones, their classification based on the mechanism of action, and major functions are given in Table below.




| Hormone(s) | Origin | Major function(s) |
|---|---|---|
| **Group I. hormones that bind to intracellular receptors** | | |
| Estrogens | Ovaries and adrenal cortex | Female sexual characteristics, menstrual cycle. |
| Progestins | Ovaries and placenta | Involved in menstrual cycle and maintenance of pregnancy. |
| Androgens | Testes and adrenal cortex | Male sexual characteristics, spermatogenesis. |
| Glucocorticoids | Adrenal cortex | Affect metabolisms, suppress immune system. |
| Mineralocorticoids | Adrenal cortex | Maintenance of salt and water balance. |
| Calcitriol (1, 25–DHCC) | Kidney (final form) | Promotes absorption of Ca2+ from intestine, kidney and bone. |
| Thyroid hormones (T3, T4) | Thyroid | Promote general metabolic rate. |

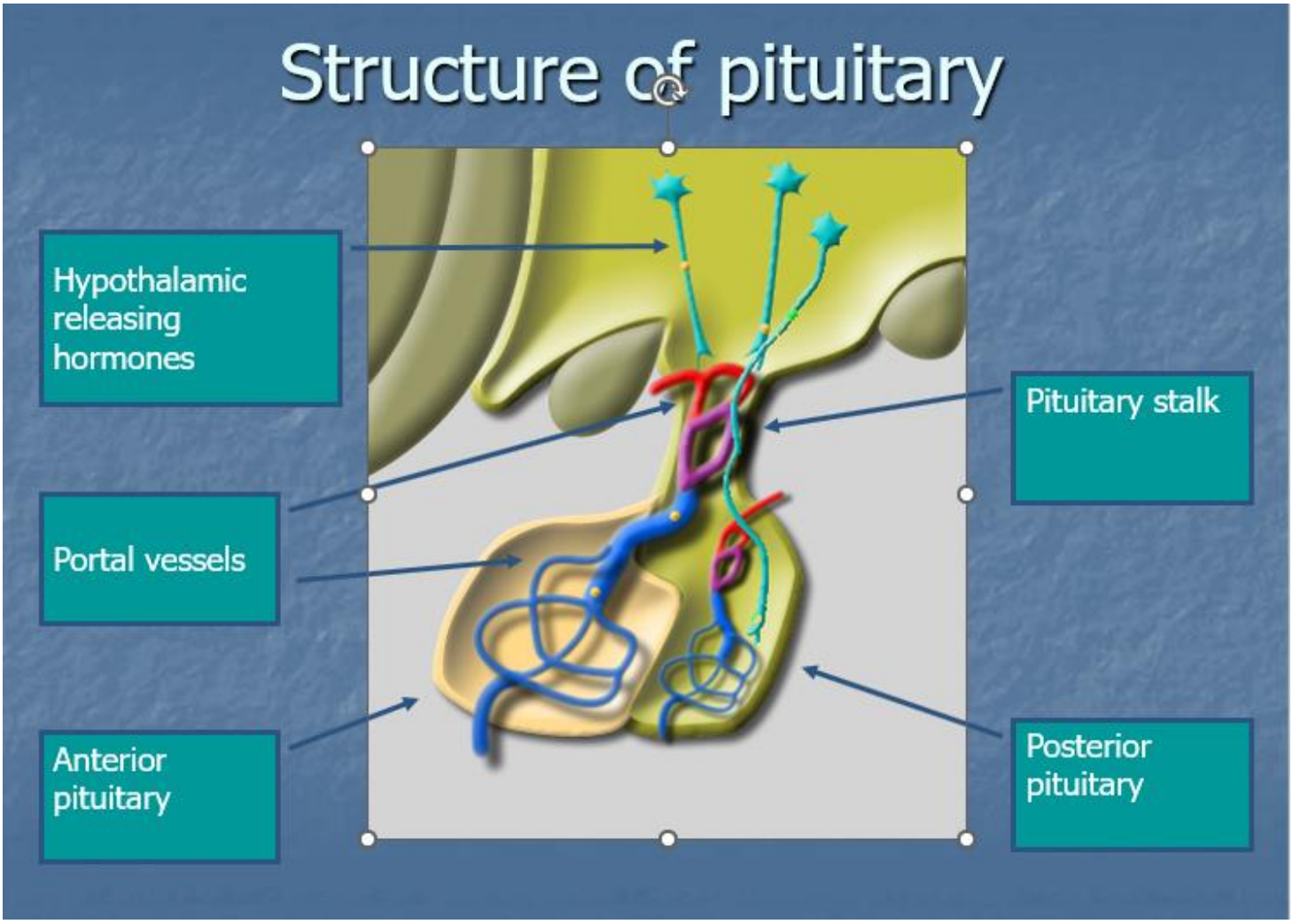
| Hormone(s) | Origin | Major function(s) |
|---|---|---|
| **Group II. Hormones that bind to cell surface receptors** | | |
| **A. The second messenger is cAMP** | | |
| Adrenocorticotropic hormone (ACTH) | Anterior pituitary | Stimulates the release of adrenocorticosteroids. |
| Follicle stimulating hormone (FSH) | Anterior pituitary | In females, stimulates ovulation and estrogen synthesis. In males, promotes spermatogenesis. |
| Luteinizing hormone (LH) | Anterior pituitary | Stimulates synthesis of estrogens and progesterone and causes ovulation. Promotes androgen synthesis by testes. |
| Chorionic gonadotropin (hCG) | Anterior pituitary | Stimulates progesterone release from placenta |
| Thyroid stimulating hormone (TSH) | Anterior pituitary | Promotes the release of thyroid hormones (T3, T4). |
| β-Endorphins and enkephalins | Anterior pituitary | Natural endogenous analgesics (pain relievers). |
| Antidiuretic hormone (ADH) | Posterior pituitary (stored) | Promotes water reabsorption by kidneys |
| Glucagon | Pancreas | Increases blood glucose level, stimulates glycogenolysis and lipolysis. |
| Parathyroid hormone (PTH) | Parathyroid | Increases serum calcium, promotes $Ca^{2+}$ release from bone. |
| Calcitonin | Thyroid | Lowers serum calcium. Decreases $Ca^{2+}$ uptake by bone and kidney. |
| Epinephrine | Adrenal medulla | Increases heart rate and blood pressure. Promotes glycogenolysis in liver and muscle and lipolysis in adipose tissue. |
| Norepinephrine | Adrenal medulla | Stimulates lipolysis in adipose tissue. |

| Hormone(s) | Origin | Major function(s) |
|---|---|---|
| **Group II. Hormones that bind to cell surface receptors** | | |
| **B. The second messenger is phosphatidyl inositol/calcium** | | |
| Thyrotropin-releasing hormone (TRH) | Hypothalamus | Promotes TSH release. |
| Gonadotropin-releasing hormone (GnRH) | Hypothalamus | Stimulates release of FSH and LH |
| Gastrin | Stomach | Stimulates gastric HCI and pepsinogen secretion. |
| Cholecystokinin (CCK) | Intestine | Stimulates contraction of gall bladder and secretion of pancreatic enzymes. |
| **C. The second messenger is unknown/unsettled** | | |
| Growth hormone (GH) | Anterior pituitary | Promotes growth of the body (bones and organs). |
| Prolactin (PRL) | Anterior pituitary | Growth of mammary glands and lactation. |
| Oxytocin | Posterior pituitary (stored) | Stimulates uterine contraction and milk ejection |
| Insulin | Pancreas | Lowers blood glucose (hypoglycemic effect), promotes protein synthesis and lipogenesis. |
| Somatomedins (insulin-like growth factors, IGF-I, IGF-II) | Liver | Growth related functions of GH are mediated. growth factors, IGF-I, IGF-II) Stimulates growth of cartilage. |

## Hypothalamic and Pituitary hormones

The pituitary gland or hypophysis is located below the hypothalamus of the brain. It consists of two distinct parts—the anterior pituitary (adenohypophysis) and the posterior pitutitary (neurohypophysis).

**Hypothalamus** is a specialized center in the brain that functions as a **master coordinator of hormonal action**. In response to the stimuli of central nervous system, hypothalamus liberates certain releasing factors or hormones. These factors stimulate or inhibit the release of corresponding tropic hormones from the anterior pituitary Tropic hormones stimulate the target endocrine tissues to secrete the hormones they synthesize.



Hypothalamus produces at least six releasing factors or hormones as following:

### 1. Thyrotropin-releasing hormone (TRH)

TRH stimulates anterior pituitary to release thyroid stimulating hormone (TSH or thyrotropin) which, in turn, stimulates the release of thyroid hormones ($T_3$ and $T_4$).

### 2. Corticotropin-releasing hormone (CRH)

It stimulates anterior pituitary to release adrenocorticotropic hormone (ACTH) which in turn, acts on adrenal cortex to liberate adrenocorticosteroids. CRH contains 41 amino acids.

### 3. Gonadotropin-releasing hormone (GnRH)

It is a decapeptide. GnRH stimulates anterior pituitary to release **gonadotropins**, namely luteinizing hormone (LH) and follicle stimulating hormone (FSH).

### 4. Growth hormone-releasing hormone

**(GRH)** with 44 amino acids stimulates the release of growth hormone (GH or somatotropin) which promotes growth.

### 5. Growth hormone release-inhibiting hormone (GRIH)

It contains 14 amino acids and is also known as **somatostatin**. GRIH inhibits the release of growth hormone from the anterior pituitary.

### 6. Prolactin release-inhibiting hormone (PRIH)

It is believed to be a dopamine and/or a small peptide that inhibits the release of prolactin (PRL) from anterior pituitary.

## Anterior pituitary hormones

Anterior pituitary or adenohypophysis is truly the **master endocrine organ**. It produces several hormones classified into three categories.

I. The growth hormone-prolactin group.

II. The glycoprotein hormones.

III. The pro-opiomelanocortin peptide family.

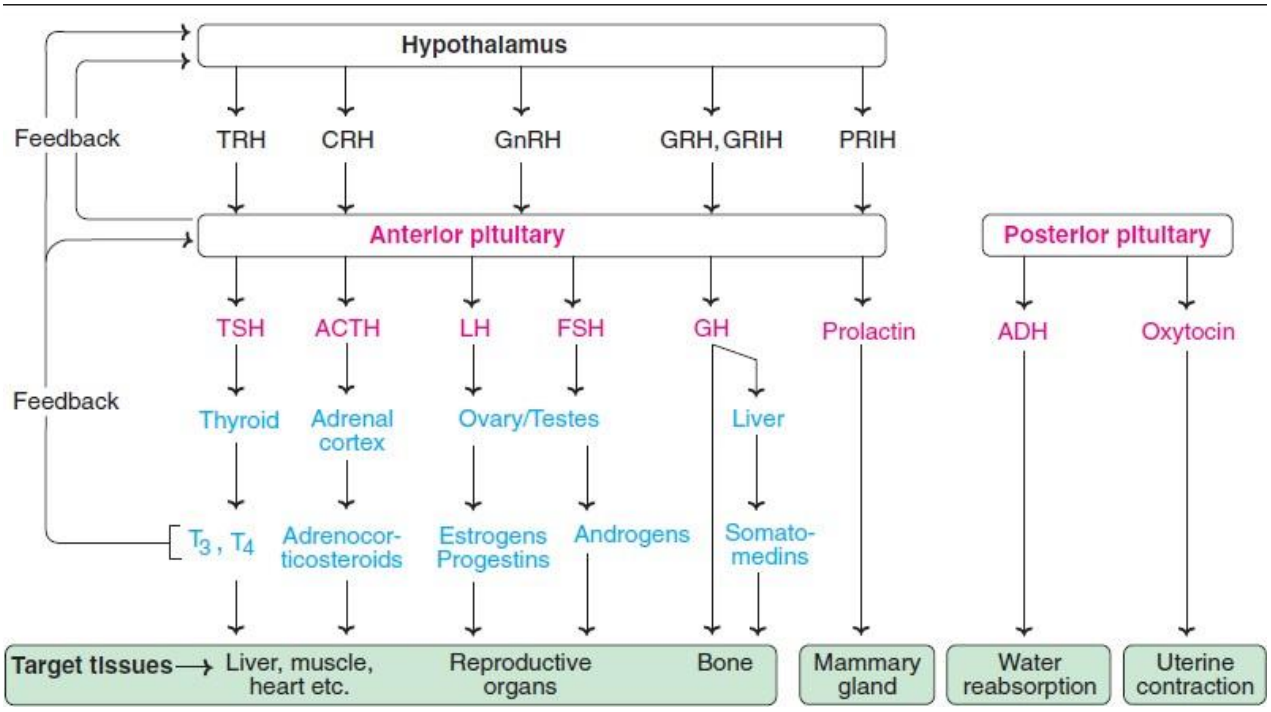
## I. The growth hormone-prolactin group

### Growth hormone (GH)

Growth hormone production is influenced by many factors such as sleep, stress (pain, cold, surgery), exercise, food intake etc. It is observed that the largest increase in the production of GH occurs after the onset of sleep. This supports the **adage "If you don't sleep, you won't grow."**

**Biochemical functions of GH :** Growth hormone promotes growth, and also influences the normal metabolisms (protein, carbohydrate, lipid and mineral) in the body.

The Figure below represents the hormonal heirarchy relationships between hypothalamus and pituitary with other endocrine glands.



## Prolactin

Prolactin (PRL) is also called lactogenic hormone, luteotropic hormone, mammotropin or luteotropin.

### Biochemical functions of PRL :

a) Prolactin is primarily concerned with the initiation and maintenance of lactation in mammals.
b) increases the levels of several enzymes involved in carbohydrate and lipid metabolism.
c) promotes HMP shunt, increases lipid biosynthesis and stimulates lactose production in mammary glands.
d) promotes the growth of corpus luteum (hence also known as luteotropic hormone) and stimulates the production of progesterone.

## II. The glycoprotein hormones

The following four hormones are glycoprotein in nature and possess certain structural similarities, despite their functional diversity.

1. Thyroid stimulating hormone (TSH)
2. Follicle stimulating hormone (FSH)
3. Luteinizing hormone (LH)
4. Human chorionic gonadotropin (hCG).

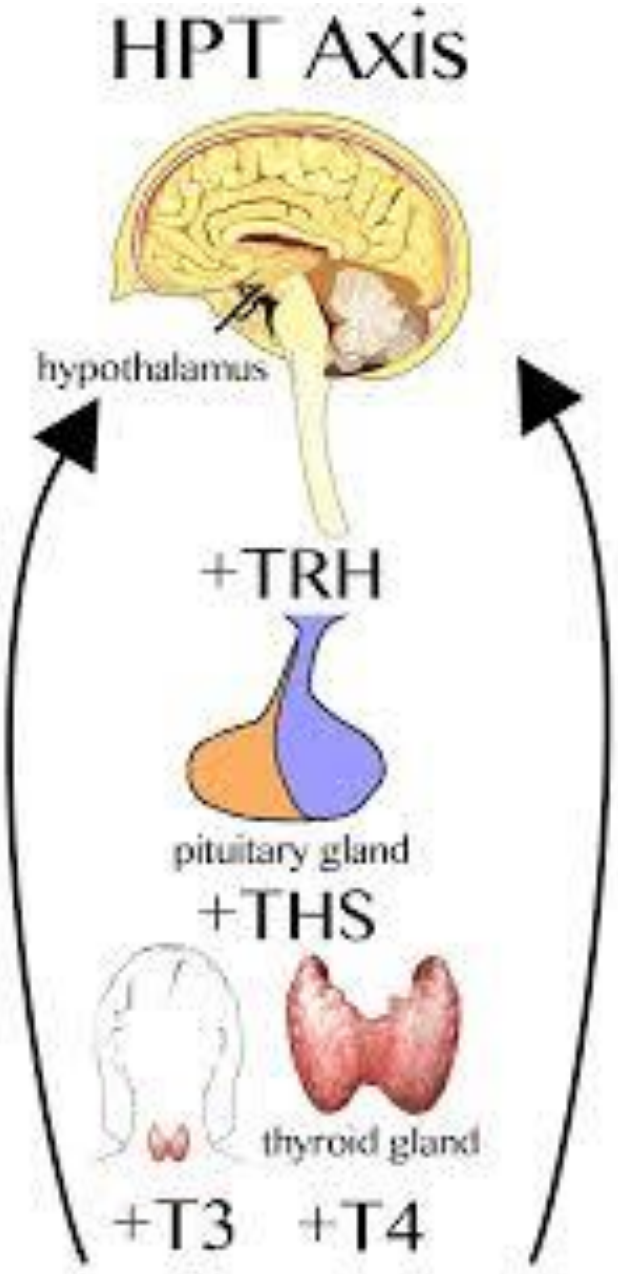
### 1. Thyroid stimulating hormone (TSH)

TSH is a dimer (αβ) glycoprotein with a molecular weight of about 30,000.

### Functions of TSH:

a) Promotes the uptake of iodide (iodide pump) from the circulation by thyroid gland.
b) Enhances the conversion of iodide (I–) to active iodide (I+), a process known as organification.
c) Increases the proteolysis of thyroglobulin to release T3 and T4 into the circulation.

d) increases the synthesis of proteins, nucleic acids and phospholipids in thyroid gland.




## 2- Gonadotropins:

The follicle-stimulating hormone (**FSH**), luteinizing hormone (**LH**) and human chorionic gonadotropin (**hCG**) are commonly known as gonadotropins. All three are glycoproteins.

### Biochemical functions of FSH:

In females, FSH stimulates follicular growth, increases the weight of the ovaries and enhances the production of estrogens.

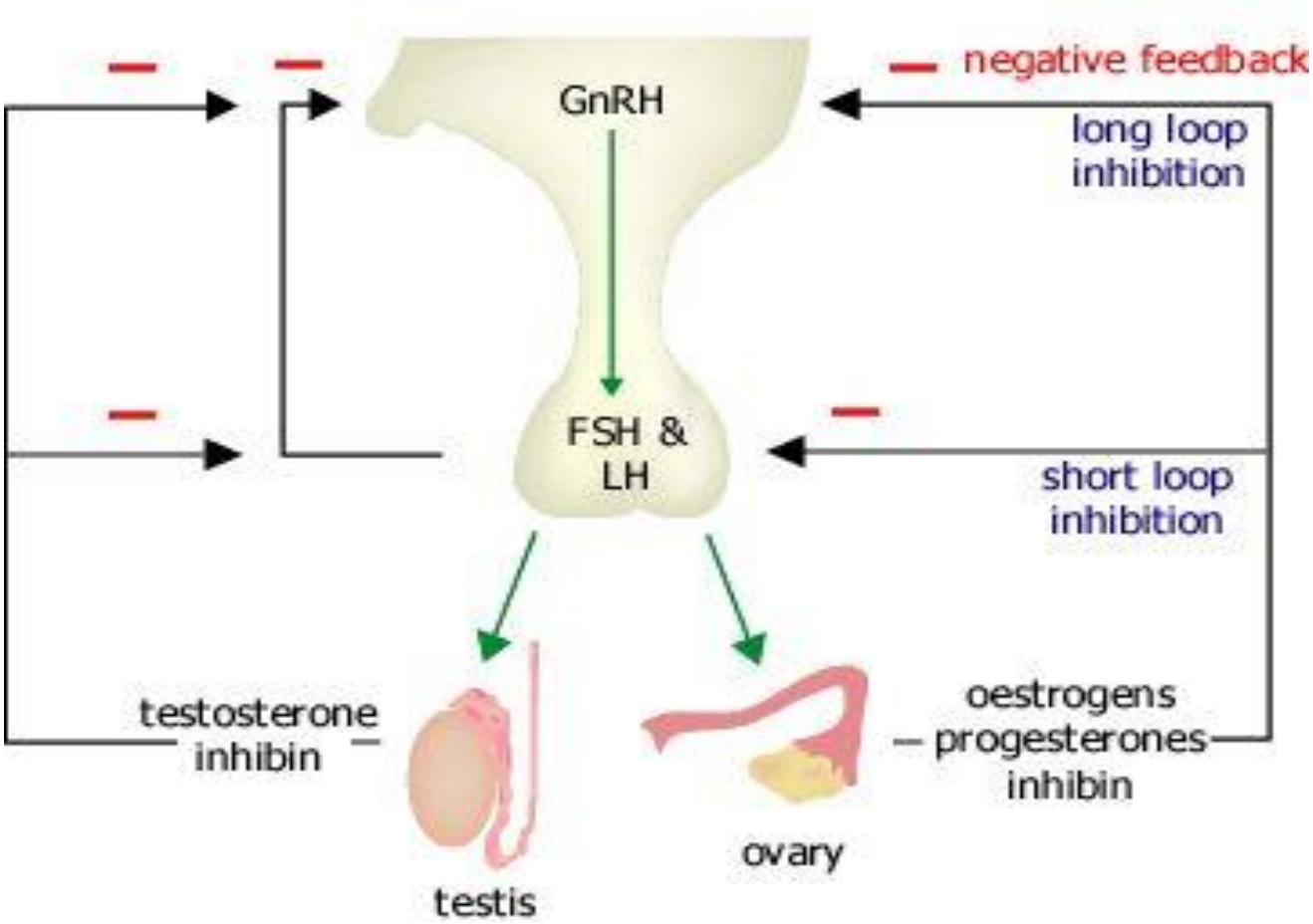
In males, FSH stimulates testosterone production, required for spermatogenesis. FSH also promotes growth of seminiferous tubules.

**Biochemical functions of LH:**

Luteinizing hormone stimulates the production of progesterone from corpus luteum cells in females and testosterone from Leydig cells in males. LH and FSH are collectively responsible for the development and maintenance of secondary sexual characters in males.

**Human chorionic gonadotropin (hCG) :**

The levels of hCG in plasma and urine increase almost immediately after the implantation of fertilized ovum. The detection of **hCG in urine** is conveniently used for the **early detection** (within a week after missing the menstrual cycle) **of pregnancy**.




## III. The pro-opiomelanocortin (POMC) peptide family

This family consists of the hormones

- Adrenocorticotropic hormone (**ACTH**),
- Lipotropin (**LPH**)
- Melanocyte stimulating hormone (**MSH**) and several (about 24) neuromodulators

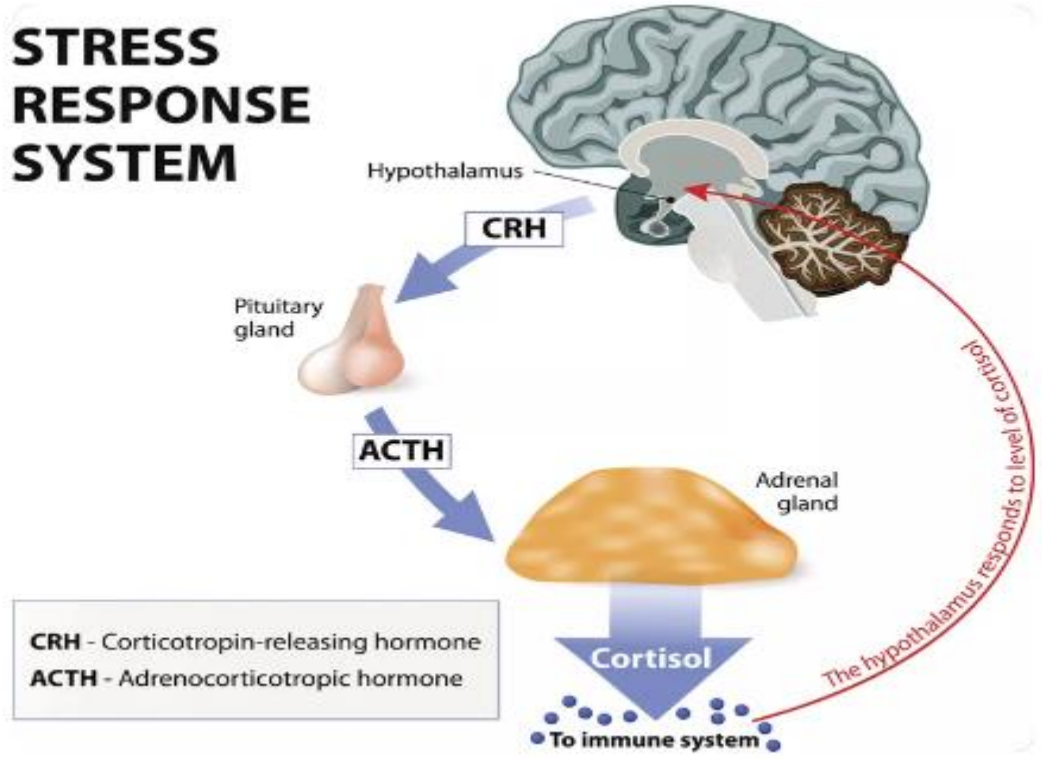
such as endorphins and enkephalins.

a) promotes the conversion of cholesterol to pregnenolone in the adrenal cortex.

b) enhances RNA and protein synthesis and thus promotes adrenocortical growth.

c) increases lipolysis by activating lipase of adipose tissue.

- ❖ Overproduction of ACTH causes a Cushing's syndrome which characterized by hyperpigmentation and increased production of adrenocorticosteroids.




## Biochemical functions of β-LPH

It promotes lipolysis and increases the mobilization of fatty acids. The most important function of β-LPH is its precursor role for the formation of β-endorphin and enkephalins.

## Biochemical functions of Melanocyte stimulating hormone (MSH)

MSH promotes the synthesis of skin pigment melanin (melanogenesis) and disperses melanin granules that ultimately leads to darkening of the skin. In humans, MSH does not appear to play any role in melanin synthesis.

# Posterior pituitary hormones

Two hormones namely **oxytocin** and **antidiuretic hormone** (ADH, vasopressin) are produced by the posterior pituitary gland (neurohypophysis).

## Oxytocin

The release of oxytocin from posterior pituitary gland is caused by the neural impulses of nipple stimulation. The other stimuli responsible for oxytocin release include vaginal and uterine distention.

### Biochemical functions of oxytocin

a) Oxytocin causes the contraction of pregnant uterus (smooth muscles) and induces labor.

b) In mammals, oxytocin causes contraction of myoepithelial cells (look like smooth muscle cells) of breast. This stimulates the squeezing effect, causing milk ejection from the breast.

c) Oxytocin synthesized in the ovary appears to **inhibit the synthesis of steroids**.

## Antidiuretic hormone (ADH)

The release of ADH (also called **vasopressin**) is mostly controlled by osmoreceptors (of hypothalamus) and baroreceptors (of heart). Any increase in the osmolarity of plasma stimulates ADH secretion.

### Biochemical functions of ADH:

ADH is primarily concerned with the regulation of water balance in the body. It stimulates kidneys to retain water and, thus, increases the blood pressure.

- **Diabetes insipidus:** This disorder is characterized by the excretion of large volumes of dilute urine **(polyuria)**. It may be due to insufficient levels of ADH or a defect in the receptors of target cells.

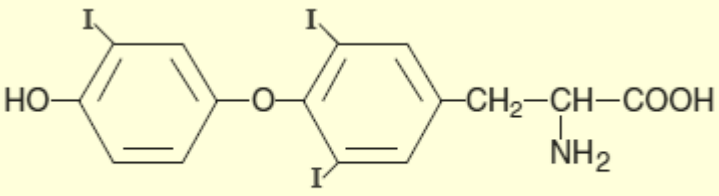
## Thyroid hormones

Thyroid gland (weighs about 30 g in adults) is located on either side of the trachea below the larynx. It produces two principal hormones:

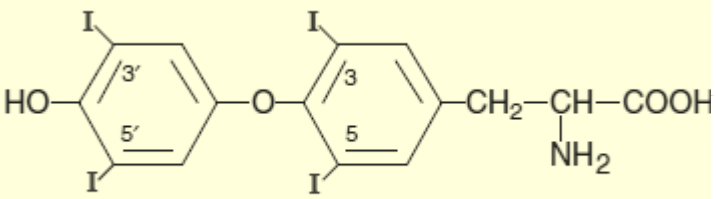
**Thyroxine** (T4; 3,5,3’,5’-tetraiodothyronine) and **3,5,3’-triiodothyronine** (T3)

which regulate the metabolic rate of the body. Thyroid gland also secretes calcitonin, a

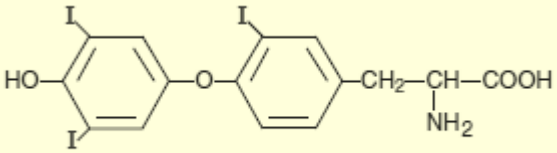
hormone concerned with calcium homeostasis.




**3,5,3′-Triiodothyronine** ($T_3$)

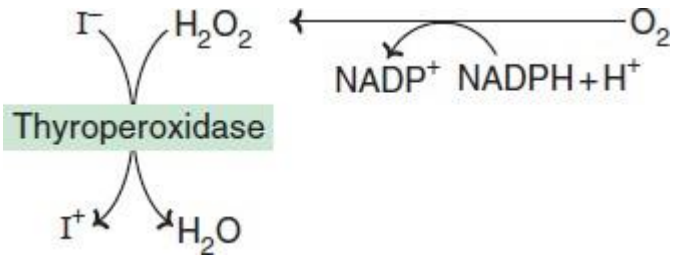



**3, 5, 3′, 5′-Tetraiodothyronine** (thyroxine, $T_4$)




**3, 3′, 5′-Triiodothyronine** (reverse $T_3$, $rT_3$)

**Formation of active iodine:** The conversion of iodide ($I^-$) to active iodine ($I^+$) is an essential step for its incorporation into thyroid hormones. Thyroid is the only tissue that can oxidize $I^-$ to a higher valence state $I^+$. This reaction requires $H_2O_2$ and is catalysed by the enzyme thyroperoxidase.




## Biochemical functions of thyroid hormones

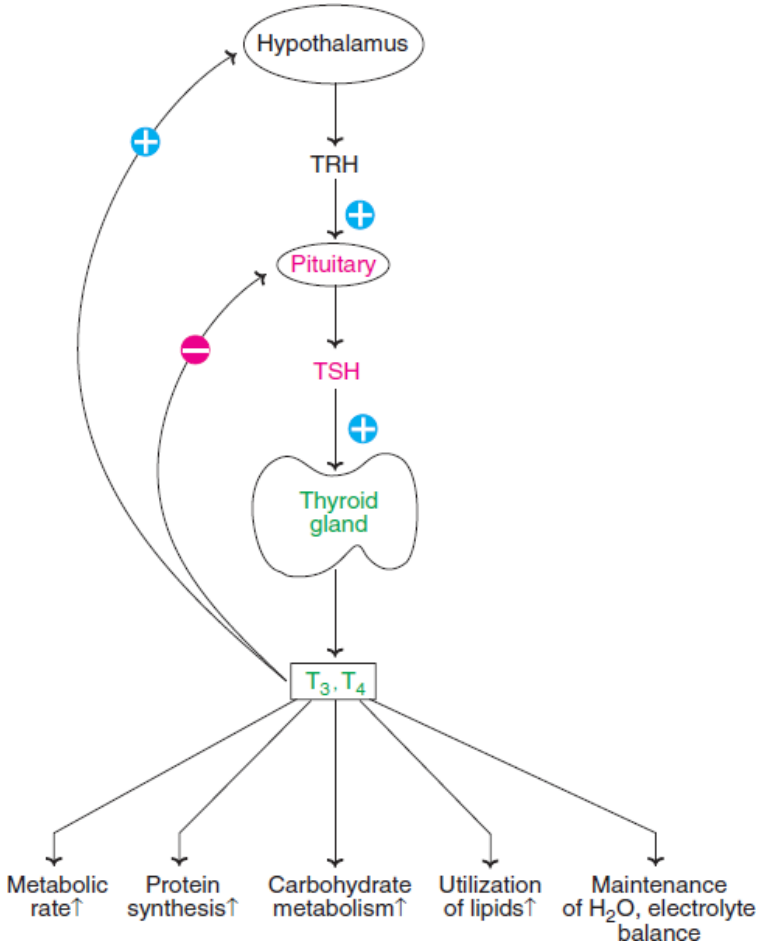
The following are the biochemical functions attributed to thyroid hormones (T3 and T4).

a) stimulate the metabolic activities and increases the oxygen consumption in most of the tissues of the body (exception—brain, lungs, testes and retina).
b) Thyroid hormones act like steroid hormones in promoting protein synthesis by acting at the transcriptional level (activate DNA to produce RNA). Thyroid hormones, thus, function as anabolic hormones and cause positive nitrogen balance and promote growth and development.
c) promote intestinal absorption of glucose and its utilization. These hormones increase gluconeogenesis and glycogenolysis, with an overall effect of enhancing blood glucose level (hyperglycemia).
d) Lipid turnover and utilization are stimulated by thyroid hormones. Hypothyroidism is associated with elevated plasma cholesterol levels which can be reversed by thyroid hormone administration.

### Regulation of T3 and T4 synthesis

The production of thyroid stimulating hormone (TSH) by pituitary, and thyrotropin releasing hormone (TRH) by hypothalamus are inhibited by T3 and, to a lesser degree,

by T4. The increased synthesis of TSH and TRH occurs in response to decreased circulatory levels of T3 and T4 as shown in figure below.



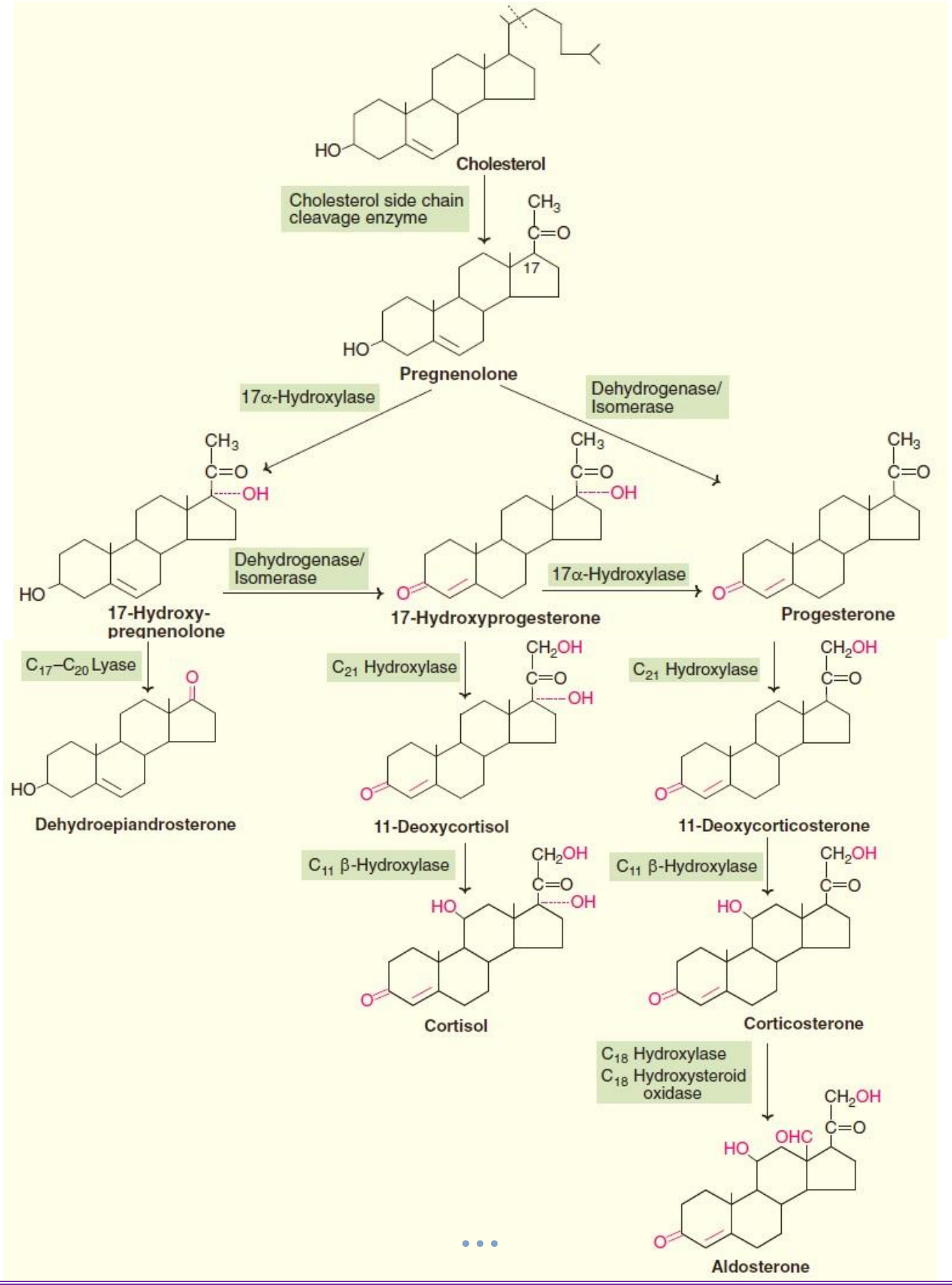

## Hormones of adrenal cortex

**Adrenocorticosteroids** are classified into three groups according to their dominant biological action.

1. **Glucocorticoids:** These steroids hormones affect glucose, amino acid and fat metabolism in a manner that is opposite to the action of insulin. **Cortisol** (also known as hydrocortisone) is the most important glucocorticoid in humans.

2. **Mineralocorticoids:** These hormones regulate water and electrolyte balance. **Aldosterone** is the most prominent mineralocorticoid.

3. **Androgens and estrogens:** These hormones affecting sexual development and functions are mostly produced by gonads. Dehydroepiandrosterone— a precursor for androgens—is synthesized in adrenal cortex.



## Biochemical functions of adrenocorticosteroids

1. **Glucocorticoid hormones :** The important glucocorticoids are—**cortisol**, **cortisone** and **corticosterone**. They bring about several biochemical functions in the body.

(a) promote the synthesis of glucose (gluconeogenesis).

(b) increase the circulating free fatty acids.

(c) Glucocortiocoids exhibit both catabolic and anabolic effects on protein and nucleic acid metabolism. They promote transcription (RNA

synthesis) and protein biosynthesis in

liver.

(d) The influence of glucocorticoids on water metabolism is mediated through antidiuretic hormone (ADH). Deficiency of glucocorticoids causes increased production of ADH. ADH decreases glomerular filtration rate causing water retention in the body.

(e) Glucocorticoids (particularly cortisol), in high doses, suppress the host immune response. The steroid hormones act at different levels—damaging lymphocytes, impairment of antibody synthesis, suppression of inflammatory response etc.

(f) Glucocorticoids are involved in several physiological functions.

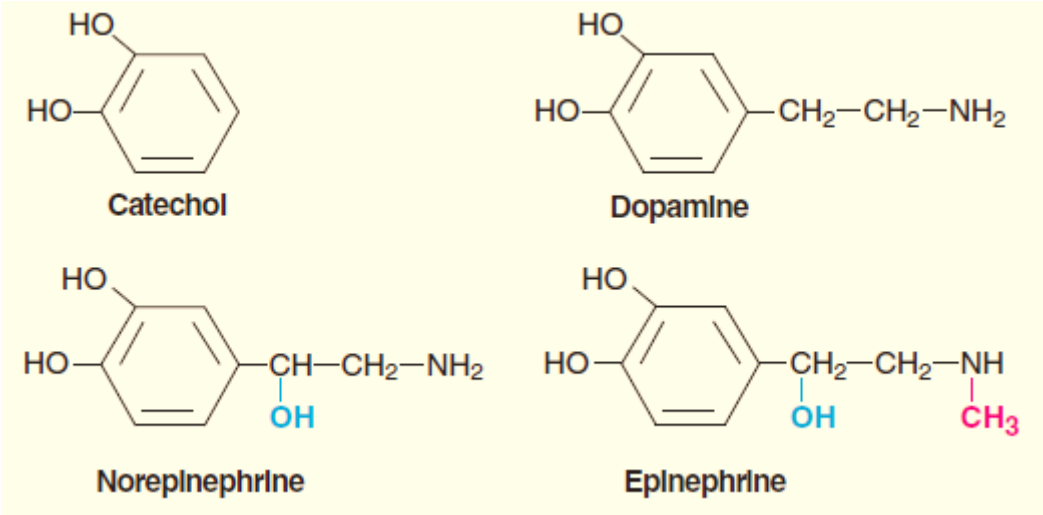
(i) Stimulate the fight and flight response (to face sudden emergencies) of catecholamines.

(ii) Increase the production of gastric HCI and pepsinogen.

(iii) Inhibit the bone formation, hence the subjects are at a risk for osteoporosis.

## Hormones of adrenal medulla

Adrenal medulla is an extension of sympathetic nervous system. It produces two important hormones—**epinephrine** (formerly adrenaline) and **norepinephrine** (formerly noradrenaline). Both these hormones are catecholamines compounds.




## Biochemical functions of catecholamines

Catecholamines cause diversified biochemical effects on the body. The ultimate goal of their action is to mobilize energy resources and prepare the individuals **to meet emergencies** (e.g. shock, cold, low blood glucose etc.).

1. Epinephrine and norepinephrine in general increase the degradation of glycogen (glycogenolysis), synthesis of glucose (gluconeogenesis) and decrease glycogen formation (glycogenesis). The overall effect of catecholamines is to elevate blood glucose levels and make it available for the brain and other tissues to meet the emergencies.

2. Both epinephrine and norepinephrine enhance the breakdown of triacylglycerols (lipolysis) in adipose tissue.

3. catecholamines (most predominantly epinephrine) increase cardiac output, blood pressure and oxygen consumption.

## Hormones of gonads

The gonads (testes in males, ovaries in females) perform closely related dual functions.

1. Synthesize sex hormones.

2. Produce germ cells.

The sex hormones are categorized into three groups

1. **Androgens** or male sex steroid hormones.

2. **Estrogens** or female sex steroid hormones.

3. **Progesterone** is a steroid hormone produced during the luteal phase of menstrual cycle and also during pregnancy.

## Physiological and biochemical functions of androgens

1. **Sex-related physiological functions:** The androgens, primarily DHT and testosterone, influence:

1) Growth, development and maintenance of male reproductive organs.
2) Sexual differentiation and secondary sexual characteristics.
3) Spermatogenesis.
4) Male pattern of aggressive behavior.

2 .**Biochemical functions**: Many specific biochemical effects of androgens that ultimately influence the physiological functions stated above are identified. Androgens are anabolic in nature.

1) Androgens promote RNA synthesis (transcription) and protein synthesis (translation). Androgens cause positive nitrogen balance and increase the muscle mass.
2) Androgens increase glycolysis fatty acid synthesis and citric acid cycle.
3) Androgens promote mineral deposition and bone growth before the closure of epiphyseal cartilage.

## Physiological and biochemical functions of androgens

**1. Sex-related physiological functions:**

1) Growth, development and maintenance of female reproductive organs.
2) Maintenance of menstrual cycles.

3) Development of female sexual characteristics.

2 . **Biochemical functions:** Estrogens are involved in many metabolic functions.

1) Lipogenic effect : Estrogens increase lipogenesis in adipose tissue and, for this reason, women have relatively more fat (about 5%) than men.
2) Hypocholesterolemic effect : Estrogens lower the plasma total cholesterol. The LDL fraction of lipoproteins is decreased while the HDL fraction is increased.
3) Anabolic effect : Estrogens in general promote transcription and translation.
4) Effect on bone growth : Estrogens like androgens promote calcification and bone growth.
5) Effect on transhydrogenase: Transhydrogenase is an enzyme activated by estrogen. It is capable of transferring reducing equivalents from NADPH to NAD+.

### Biochemical functions of progesterone

1 . Progesterone is essentially required for the implantation of fertilized ovum and maintenance of pregnancy.

2. It promotes the growth of glandular tissue in uterus and mammary gland.

3. Progesterone increases the body temperature by 0.5–1.5 F°.

## Gastrointestinal (or gut) hormones

The digestion and absorption of nutrients is a complicated process which is regulated by the autonomic nervous system. This occurs in association with peptide hormones of gastrointestinal tract (GIT).

1. Gastrin. 2. Secretin. 3. Cholecystokinin (CCK). 4. Gastric inhibitory peptide (GIP)

## Other hormones

Besides the hormones discussed above, there are a few other important hormones such as **Insulin, glucagon, parathyroid hormone and calcitonin**