SAWA UNIVERSITY

Clinical Endocrinology

Adrenal Gland

Sawa University

College of health and medical techniques

Department of Medical Laboratories

جامعـــــة ســـــاوة الاهلية

كليـــة التقنيـــات الصحيـة والطبيـة

قسم تقنيات المختبرات الطبية

المرحلـــــــــــة الثالـثة

الجانب النظري

.Third . Stage

محاضرة رقم 12

Lecture No. 12 Theoretical

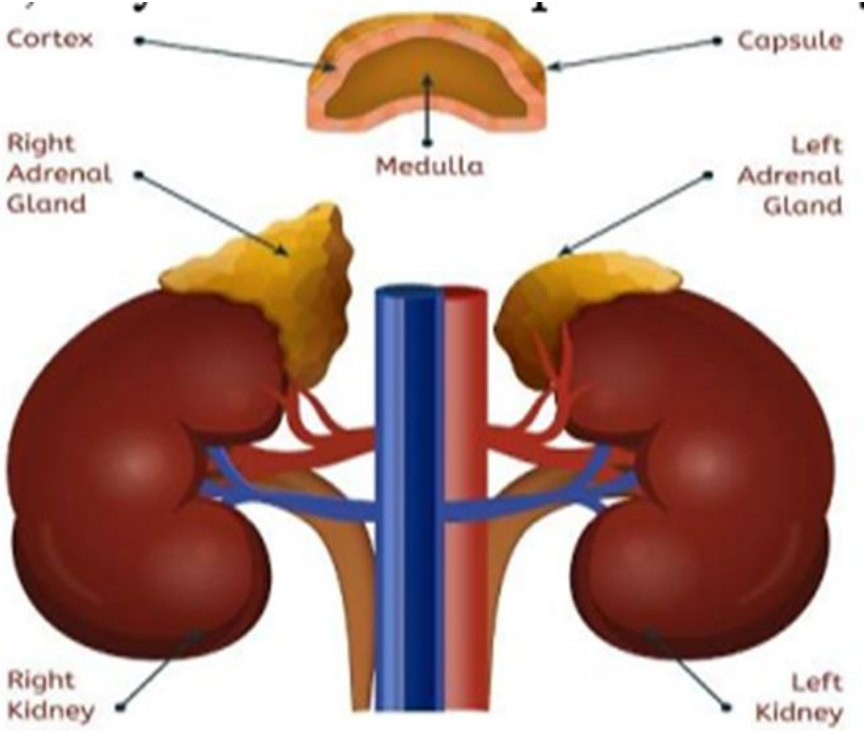
تدريسي المادة : م.م عقيل محمد رسول

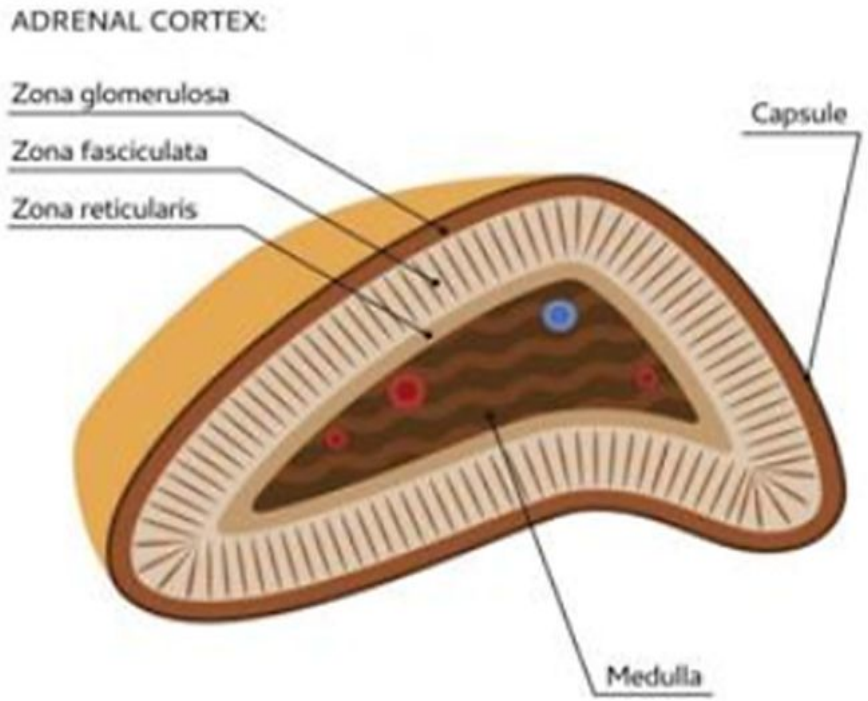
Hormones Of Adrenal Cortex

The adrenal glands are **two small organs** (each **weighing** about 10 g), located above the kidneys. Each adrenal consists of **two distinct tissues**—an **outer cortex (with 3 zones) and inner medulla**. As many as **50 steroid hormones** (namely **adrenocorticosteroids**), **produced by adrenal cortex**, have been identified. However, only **a few** of them possess **biological activity.**

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

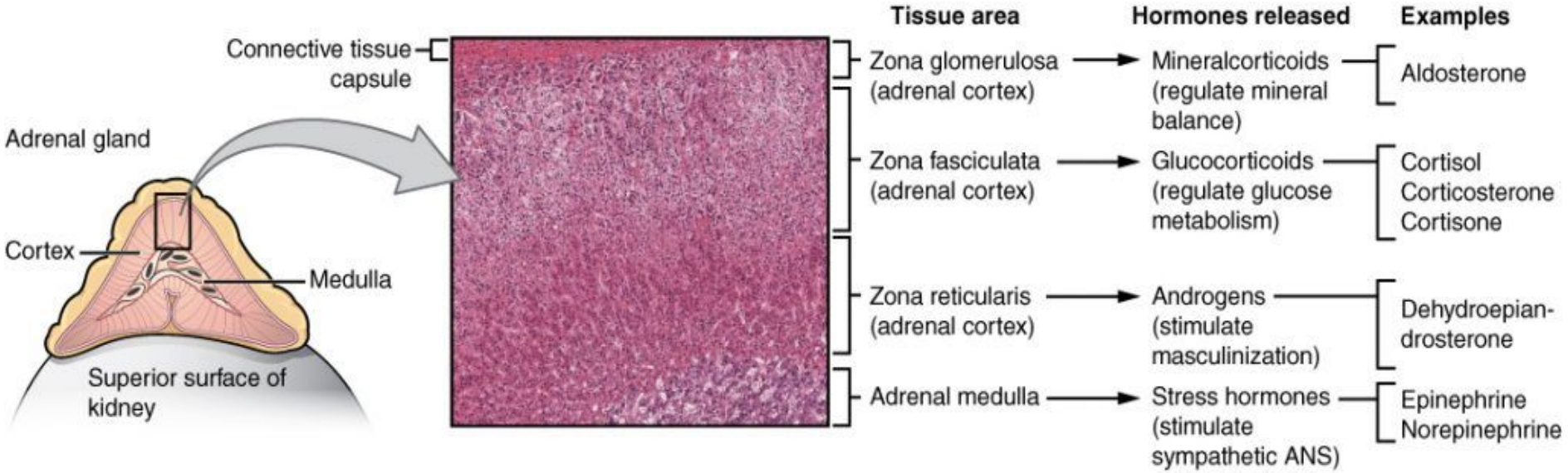
1. **Glucocorticoids:** These are **21-carbon steroids**, **produced** mostly by **zona fasciculata**. They **affect** glucose (**hence the name**), amino acid and fat metabolism in a manner that is **opposite** to the **action of insulin**. Cortisol (also known as hydrocortisone) is the **most important glucocorticoid** in humans. Corticosterone is predominantly found in rats.


Cortex
Capsule
Medulla
Right Adrenal Gland
Left Adrenal Gland
Right Kidney
Left Kidney


ADRENAL CORTEX:
Zona glomerulosa
Zona fasciculata
Zona reticularis
Capsule
Medulla

2. **Mineralocorticoids**: These are also **21- carbon** containing **steroids produced** by **zona glomerulosa**. They **regulate** **water and electrolyte balance**. **Aldosterone** is the most **prominent mineralocorticoid.**

3. **Androgens and estrogens**: The innermost **adrenal cortex zona reticularis** produces small quantities of **androgens (19-carbon) and estrogens (18-carbon).** These hormones **affecting** **sexual development and functions** are mostly *produced by gonads*.



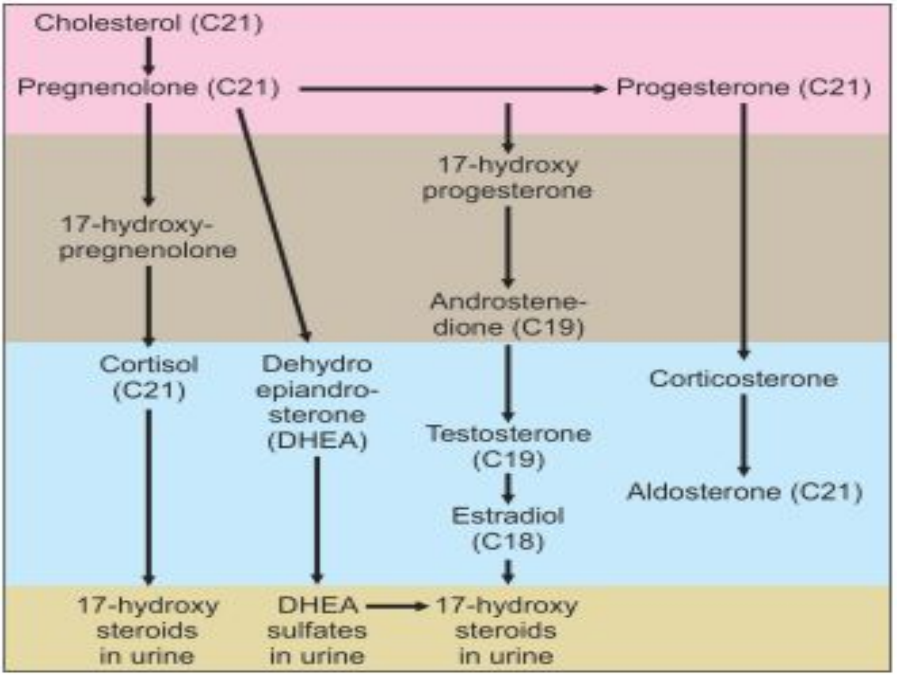
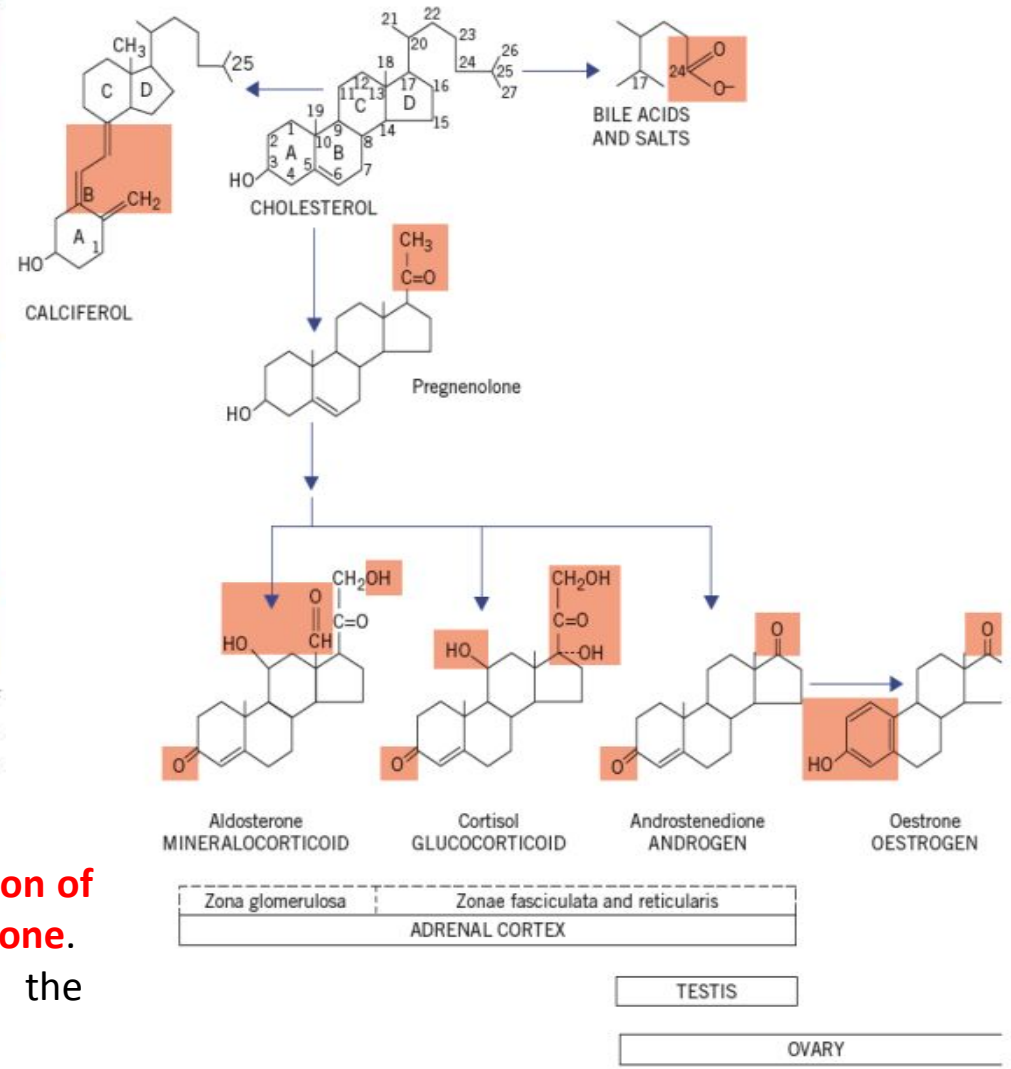


Fig. 52.5: Summary of major pathways for production of glucocorticoids, mineralocorticoids and sex steroids. Precursors in red box; intermediaries in gray box; hormones in blue box; excretory products in brown box



Synthesis of adrenocorticosteroids

Cholesterol undergoes cleavage with an **elimination of a 6-carbon fragment** to form **pregnenolone**. **Pregnenolone** is the common **precursor** for the **synthesis of all steroid hormones.**

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) Effects on carbohydrate metabolism: Glucocorticoids **promote** the **synthesis of glucose** (**gluconeogenesis**). This is brought about by **increasing the substrates** (particularly **amino acids**) and **enhancing** the **synthesis of phosphoenolpyruvate carboxykinase**, the **rate limiting** enzyme in **gluconeogenesis.** The **overall influence** of glucocorticoids on carbohydrate metabolism is to ***increase blood glucose concentration***. The *biological actions of glucocorticoids generally* ***oppose*** *that of* ***insulin.***

(b) Effects on lipid metabolism: Glucocorticoids **increase** the **circulating free fatty acids**. This is caused by two mechanisms.

(i) Increased breakdown of storage triacylglycerol (**lipolysis**) in adipose tissue.

(ii) Reduced utilization of plasma **free fatty acids** for the synthesis of triacylglycerols.

c) Effects on protein and nucleic acid metabolism: Glucocortiocoids **exhibit** both **catabolic and anabolic effects** on protein and nucleic acid metabolism. They **promote transcription (RNA synthesis) and protein biosynthesis in liver**. These **anabolic effects** of glucocorticoids are **caused by** the ***stimulation*** *of specific genes*. Glucocorticoids (particularly at high concentration) **cause catabolic effects** in **extrahepatic tissues** (e.g**. muscle, adipose tissue, bone etc**.). This results in **enhanced degradation of proteins.**

(d) Effects on water and electrolyte metabolism: 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) Effects on the immune system: 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) Other physiological effects of glucocorticoids: 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 HCl and pepsinogen.**

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

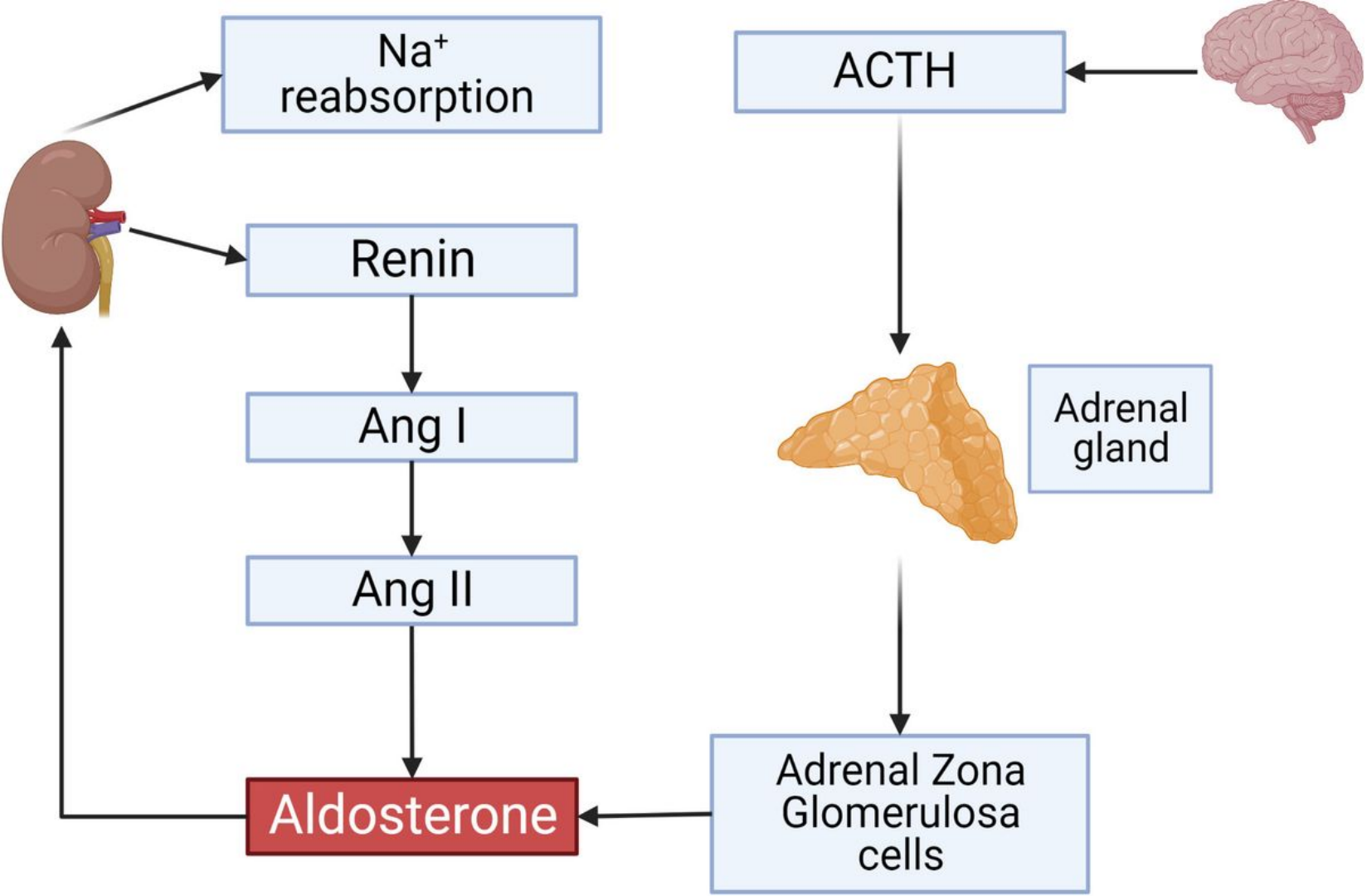
Mechanism of action of glucocorticoids: Glucocorticoids bind to specific receptors on the target cells and bring about the action. These hormones mostly **act at** the transcription level and control the protein synthesis.

2. Mineralocorticoid hormones: The most active and potent mineralocorticoid is **aldosterone**. It **promotes** **Na+ reabsorption at the distal convoluted tubules** of kidney. **Na+ retention** is **accompanied by** corresponding excretion of K+, H+ and NH4+ ions.

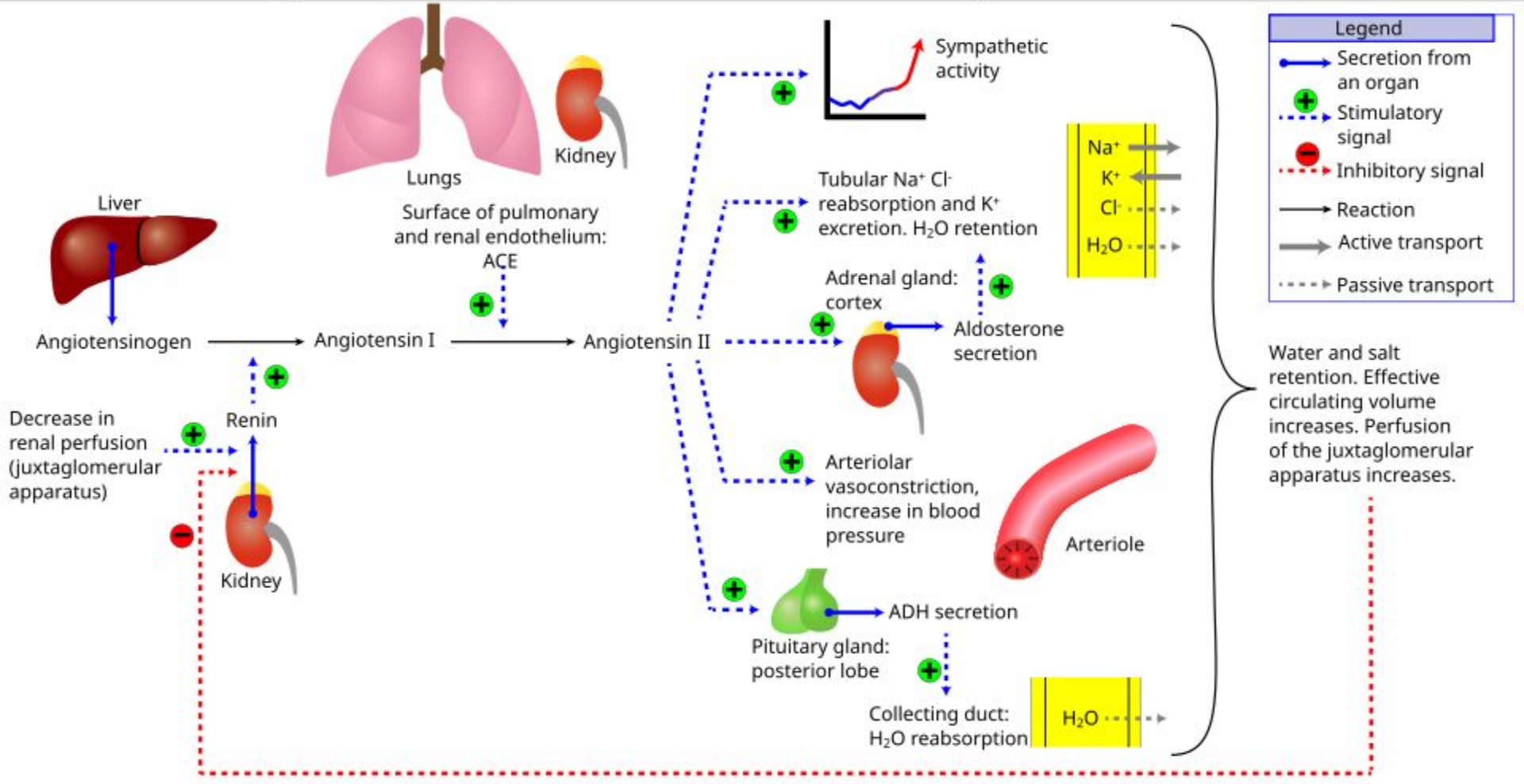
Regulation of aldosterone synthesis: The production of aldosterone is **regulated** by **different mechanisms**. **Mechanism of aldosterone action**: Aldosterone acts like other steroid hormones. It binds with specific receptors on the target tissue and promotes transcription and translation.

These include renin-angiotensin, potassium, sodium and ACTH.

Metabolism of adrenocorticosteroids: The steroid hormones are **metabolized in the liver and excreted in urine as conjugates of glucuronides or sulfates**. The **urine contains** mainly **two steroids— 17- hydroxysteroids and 17-ketosteroids**, derived from the metabolism of glucocorticoids and mineralocorticoids. **Androgens synthesized** by **gonads** also **contribute** to the formation of 17-ketosteroids. **Urinary 17-ketosteroids estimated** in the laboratory are expressed in terms of dehydroepiandrosterone and their normal excretion is in the range **of 0.2–2.0 mg/day.**


Na+ reabsorption
ACTH
Renin
Ang I
Ang II
Adrenal gland
Aldosterone
Adrenal Zona Glomerulosa cells

Renin–angiotensin–aldosterone system



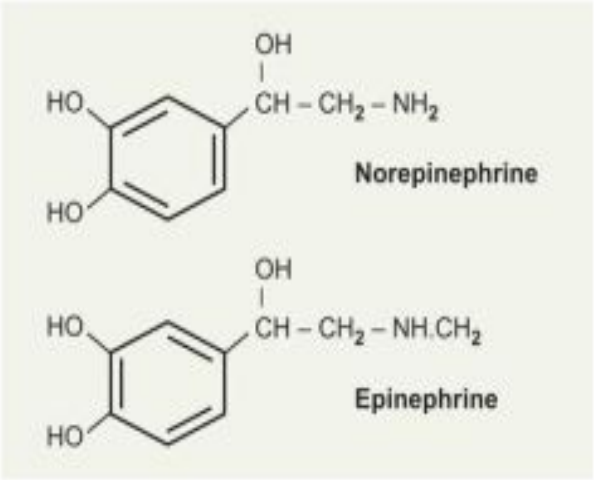
Abnormalities of adrenocortical function

Addison's disease: **Impairment in adrenocortical function** results in Addison's disease. This disorder is **characterized by** decreased **blood glucose level** (**hypoglycemia**), loss of weight, loss of appetite (anorexia), muscle weakness, impaired cardiac function, low blood pressure, decreased Na+ and increased K+ level in serum, increased susceptibility to stress etc.

Cushing's syndrome: Hyperfunction of adrenal cortex may be due to **long term pharmacological use of steroids or tumor of adrenal cortex or tumor of pituitary**. Cushing's syndrome is **characterized by hyperglycemia** (due to **increased gluconeogenesis**), fatigue, muscle wasting, edema, osteoporosis, negative nitrogen balance, hypertension, moon-face etc.

Hormones Of Adrenal Medulla

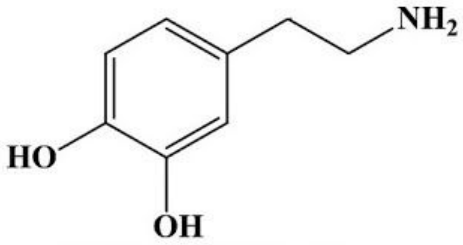
Adrenal medulla is an **extension** of sympathetic nervous system. It **produces** two important hormones—**epinephrine** (formerly **adrenaline**) and **norepinephrine** (formerly **noradrenaline**). Both these hormones are **catecholamines** since they are **amine derivatives of catechol nucleus** (**dihydroxylated phenyl ring**). **Epinephrine** is a methyl derivative of norepinephrine. **Dopamine** is **another catecholamine**, **produced as** an **intermediate** during the **synthesis of epinephrine**. **Norepinephrine and dopamine** are *important neurotransmitters in the brain and autonomic nervous system.*



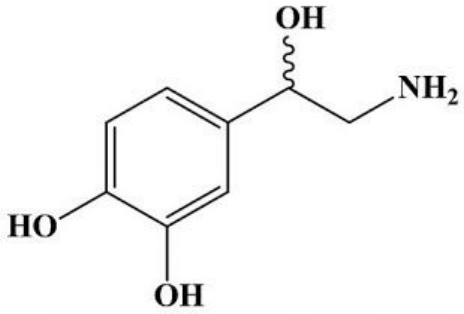
Synthesis of catecholamines

The amino acid **tyrosine is the precursor** for the synthesis of catecholamines. **Catecholamines** are **produced** in **response to fight, fright and flight**. These include the **emergencies like** shock, cold, fatigue, emotional conditions like anger etc

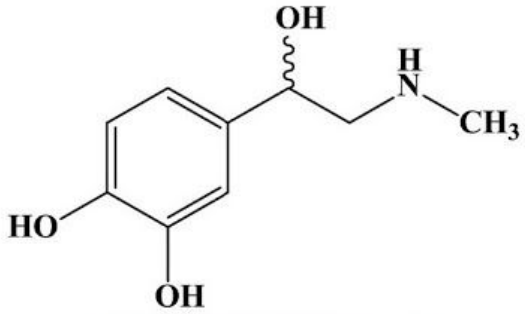
Metabolism of Catecholamines



Dopamine



Norepinephrine
(Noradrenaline)



Epinephrine
(Adrenaline)

Enzymes

MAO: Mono Amine Oxidase

AD: Aldehyde Dehydrogenase

COMT: Catechol O-Methyl Transferase

RxPA
Mr. Ramrao

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.).

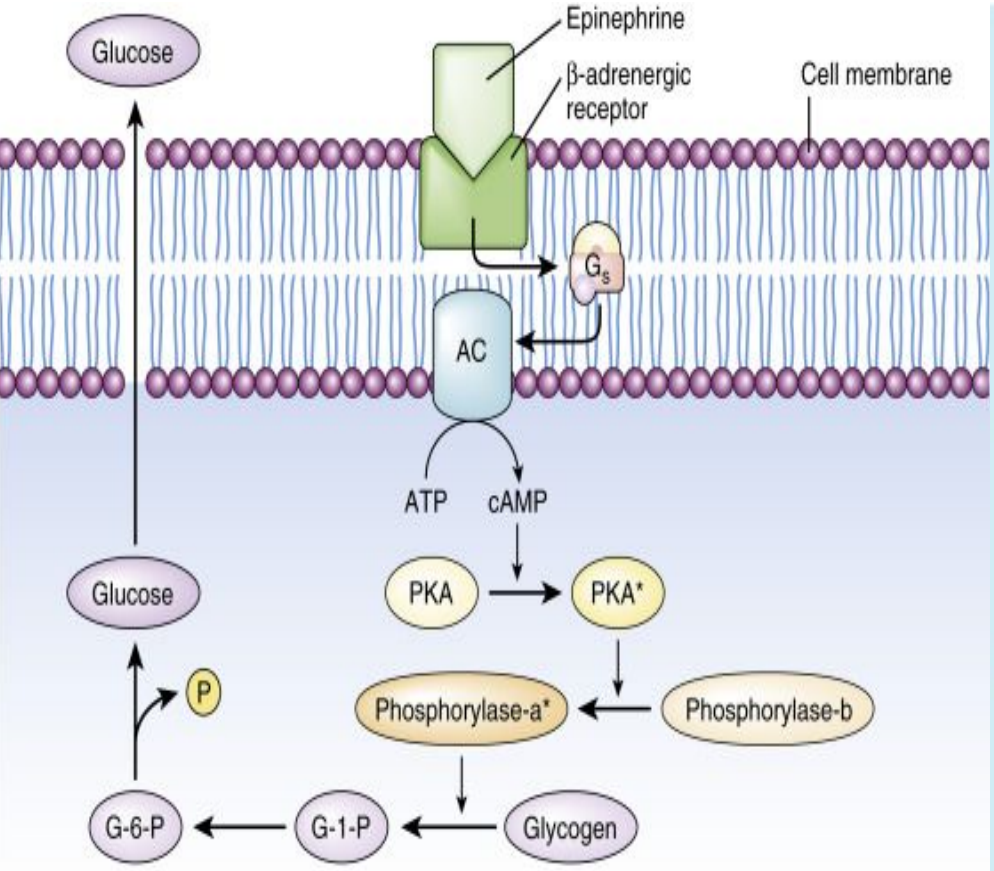
1. Effects on carbohydrate metabolism: Epinephrine and norepinephrine in general **increase** the degradation of glycogen (**glycogenolysis**), synthesis of glucose (**gluconeogenesis**) and **decrease glycogen formation** (**glycogenesis**). The **overall effect** of catecholamines is to **elevate blood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

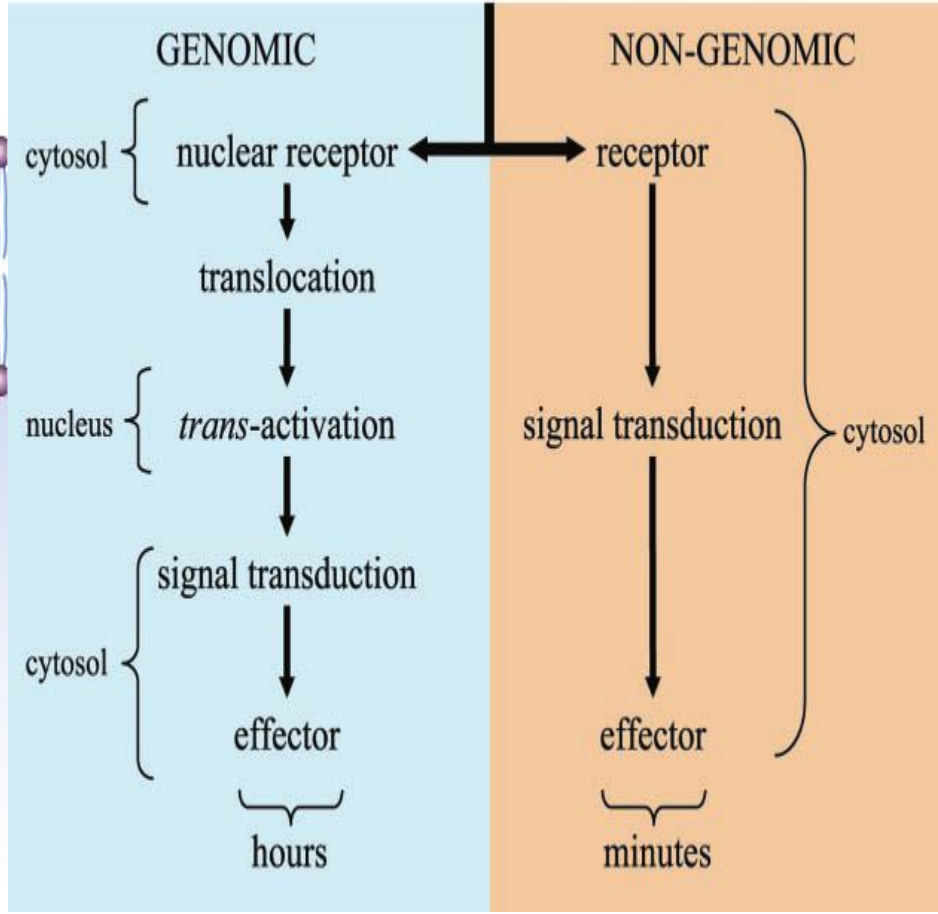
2. Effects on lipid metabolism: Both epinephrine and norepinephrine **enhance** the **breakdown of triacylglycerols** (**lipolysis**) in adipose tissue. This causes **increase** in the **free fatty acids** in the circulation which are **effectively utilized *by the heart and muscle as fuel source.***

The **metabolic effects** of catecholamines are mostly related to the **increase in adenylate cyclase activity causing elevation in cyclic AMP levels.**

3. Effects on physiological functions: In general, catecholamines (most predominantly **epinephrine**) **increase cardiac output, blood pressure and oxygen consumption**. They **cause** *smooth muscle relaxation in bronchi, gastrointestinal tract and the blood vessels supplying skeletal muscle*. **On the other hand**, catecholamines **stimulate** *smooth muscle contraction of the blood vessels* **supplying skin and kidney**. **Platelet aggregation is inhibited** by catecholamines.

Abnormalities of catecholamine production Pheochromocytomas: These are the **tumors** of **adrenal medulla**. The **diagnosis of pheochromocytoma** is possible only when there is an **excessive production** of epinephrine and norepinephrine that **causes severe hypertension**. In the individuals affected by this disorder, **the ratio of norepinephrine to epinephrine is increased**. The **measurement of urinary VMA** (**normal <8 mg/day**) is helpful in the diagnosis of pheochromocytomas.


Glucose
Epinephrine
β-adrenergic receptor
Cell membrane
G_s
AC
ATP
cAMP
PKA
PKA*
Phosphorylase-a*
Phosphorylase-b
Glucose
P
G-6-P
G-1-P
Glycogen


GENOMIC
NON-GENOMIC
cytosol
nuclear receptor
translocation
nucleus
trans-activation
signal transduction
cytosol
effector
hours
receptor
signal transduction
effector
minutes
cytosol

Questions :

1. Which of the following is not a primary function of gonads?
2. Androgens are classified as:

a. C-18 steroids b. C-21 steroids c. C-19 steroids

d. Peptide hormones e. Amino acid

3. Androgens are primarily produced by:

a. Ovarian follicles b. Corpus luteum c. Leydig cells of the testes

d. Placenta e. Adipose tissue

Learning Resources for Hormone Mechanisms

Here are excellent sources to deepen your understanding of this topic:

Medical Textbooks:

"Harper's Illustrated Biochemistry" (Chapter on Hormones & Signal Transduction): Provides a detailed, yet clear, biochemical perspective on second messenger systems.

"Guyton and Hall Textbook of Medical Physiology" (Chapter 74: Introduction to Endocrinology): Excellent for understanding the physiological principles of hormone-receptor interactions and signaling.

"Greenspan's Basic & Clinical Endocrinology": A comprehensive resource that links basic mechanisms to clinical practice.

YouTube Channels:

Armando Hasudungan: His detailed drawings are fantastic for visualizing signal transduction pathways.

Dr. Najeeb Lectures: Provides extremely detailed lectures on the entire process.