

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ



ENDOCRINOLOGY

The Adrenal Gland

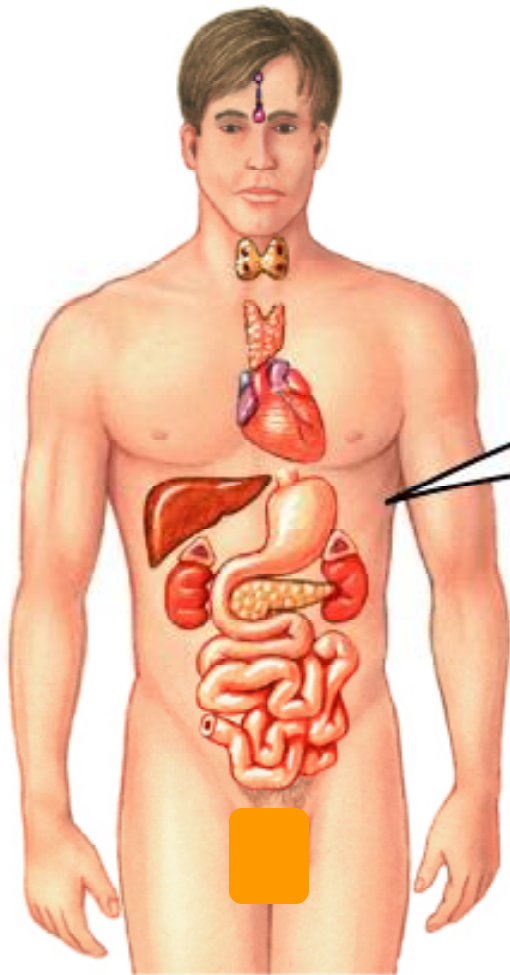
Mineralocorticoids

Dr. Abeer Al-Ghumlas

Objectives

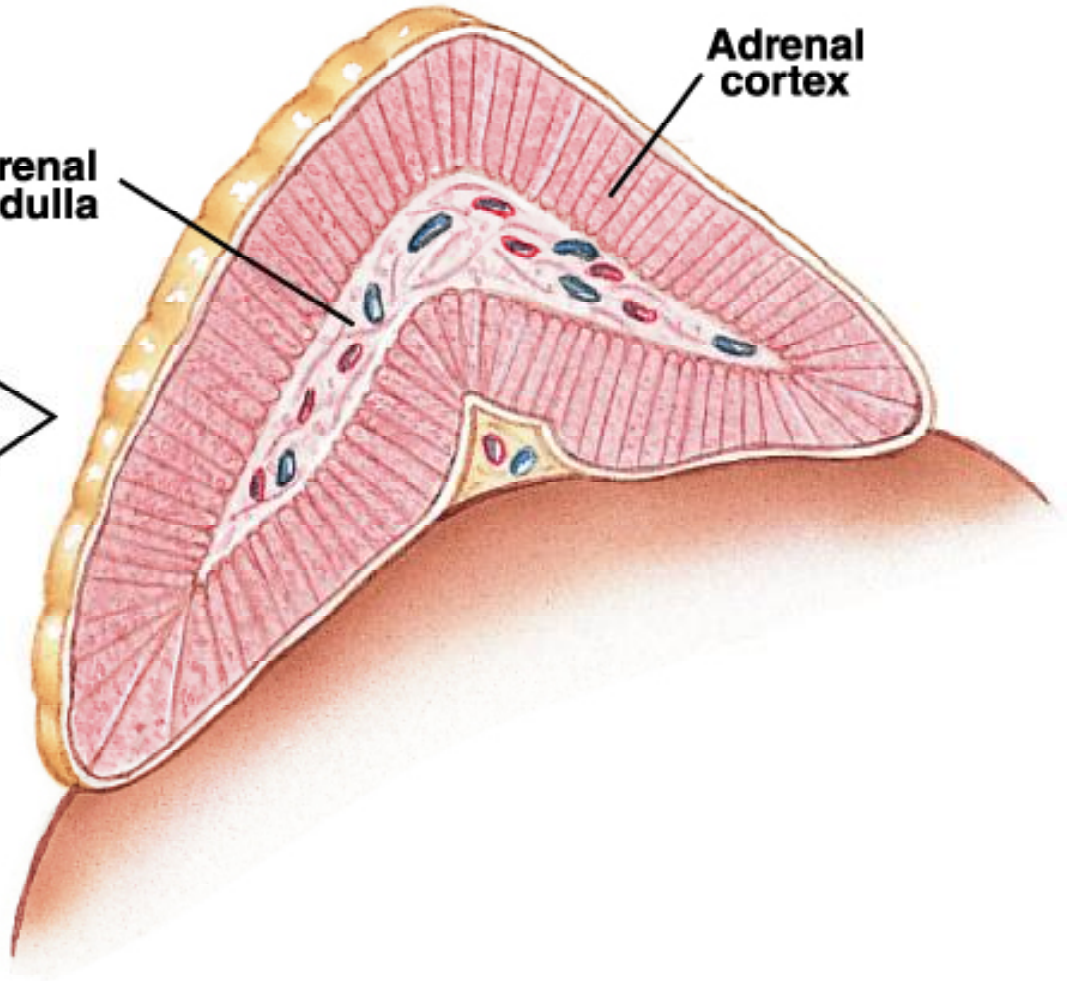
At the end of this lecture student should be able to know:

- The cellular arrangements and functional components of the adrenal gland.
- The hormones secreted by the medulla and cortex of the adrenal gland.
- The synthesis of the adrenocortical steroids.
- The physiological actions of aldosterone.
- The regulation of aldosterone secretion.
- The major stimuli for aldosterone secretion.



Adrenal medulla

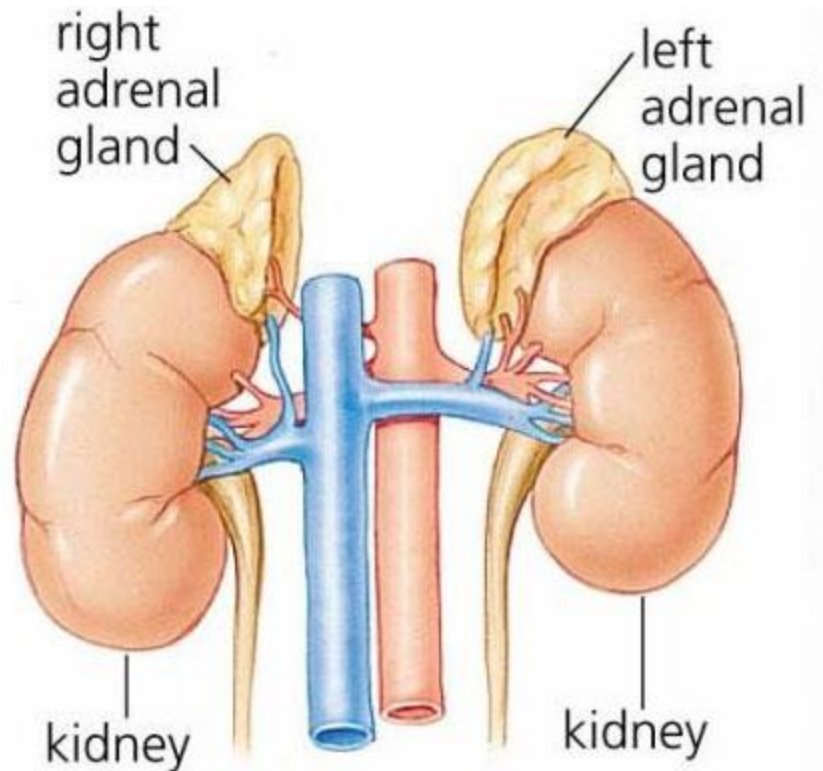
Adrenal cortex



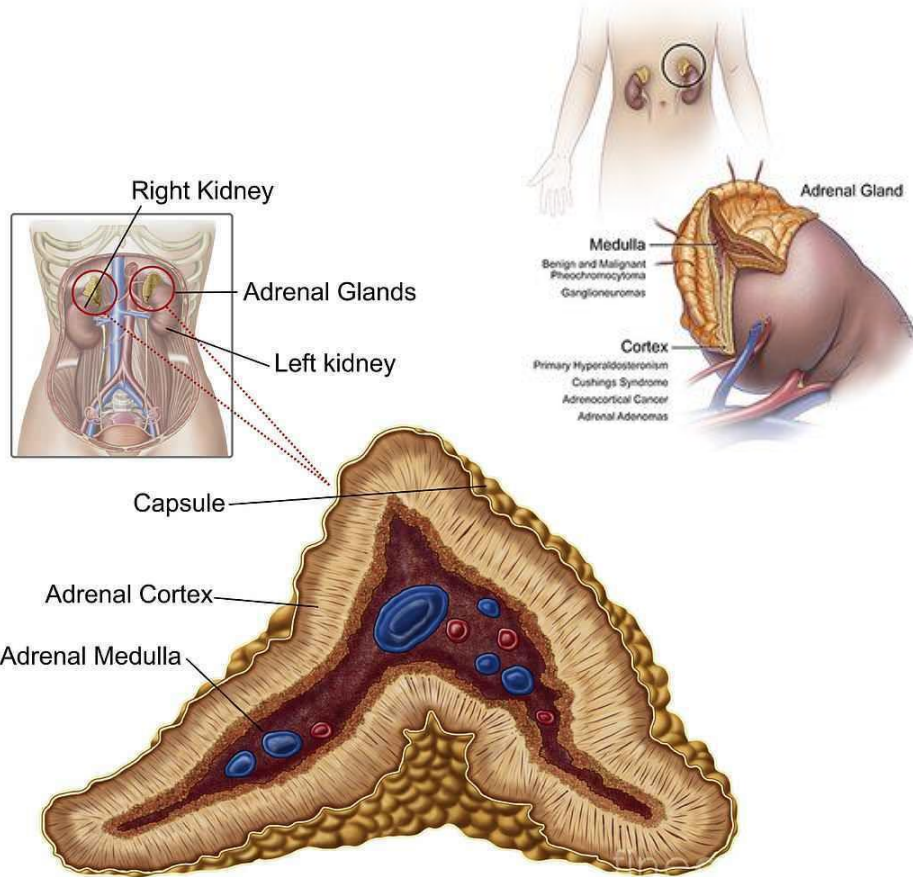
Adrenal Gland

The Adrenal Gland

- There are two adrenal (suprarenal) glands that lie at the superior pole of the two kidneys
- Small, pyramid-shaped
- Weigh 6-10 g

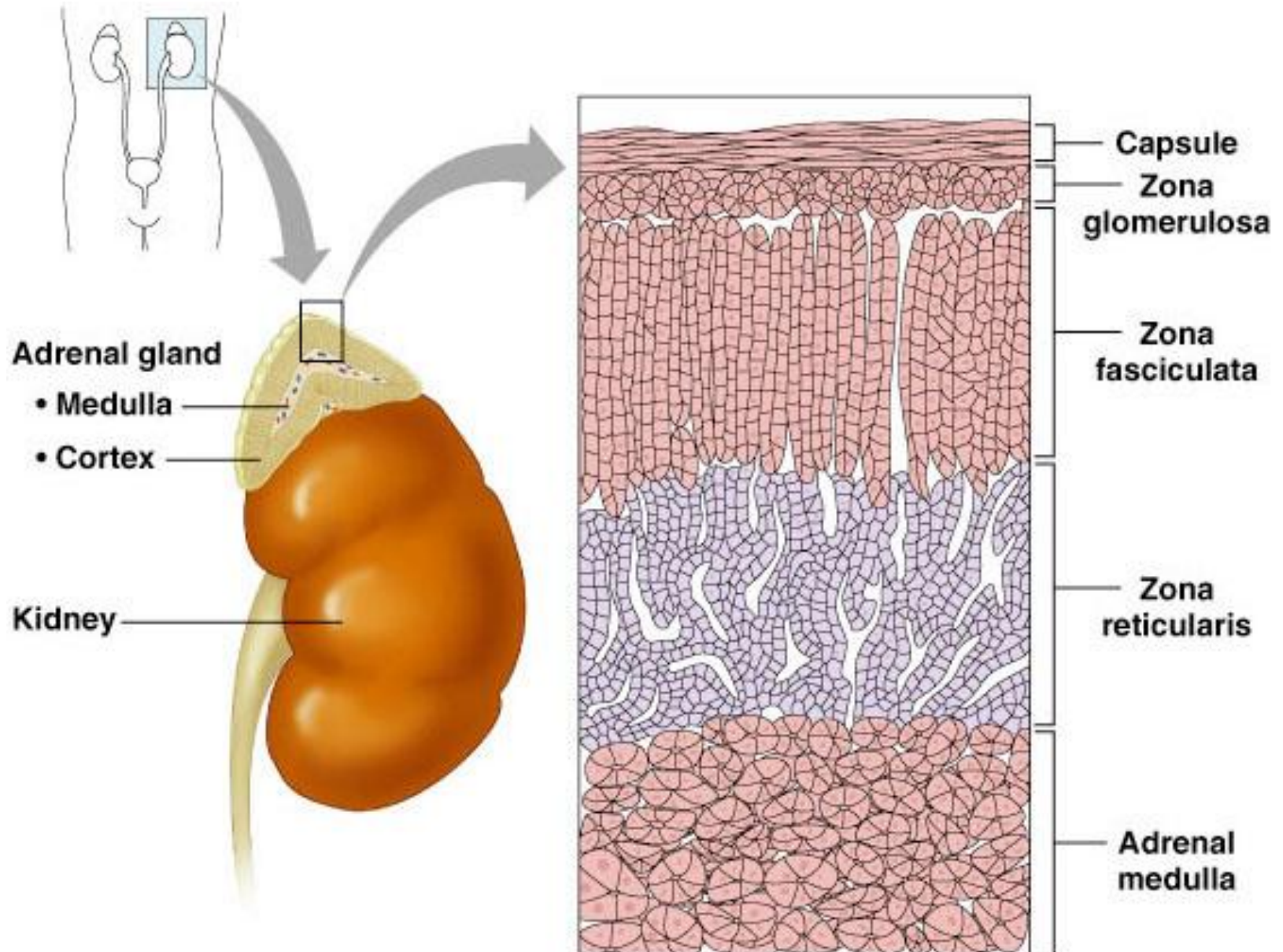


Adrenal Gland



- Divided into two morphologically and distinct regions:
 - Adrenal cortex.
 - Adrenal medulla.

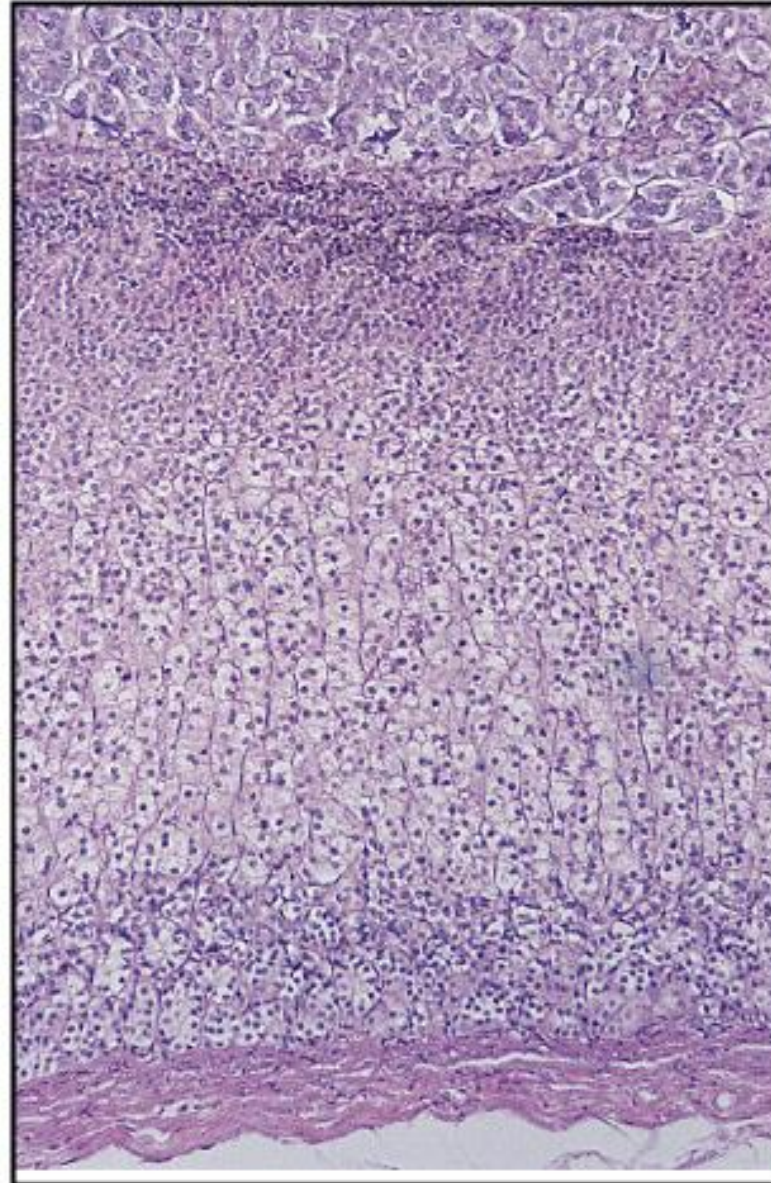
Adrenal Cortex



The Adrenal Gland

Corticosteroid hormones

Region of adrenal gland



Secretes

Catecholamines

Sex hormones

Glucocorticoids
(Cortisol)

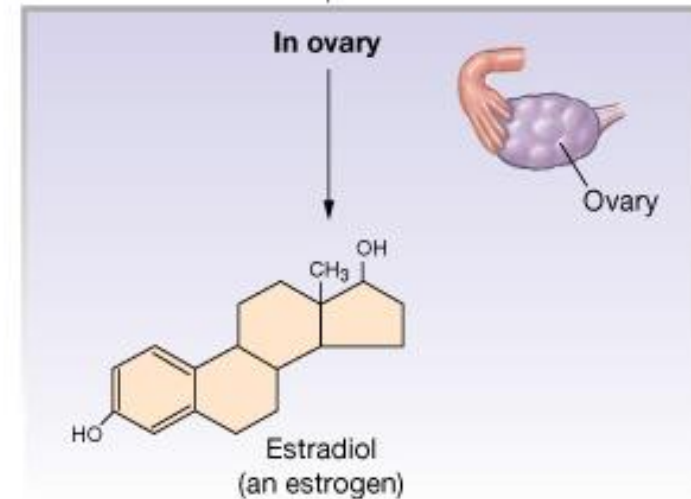
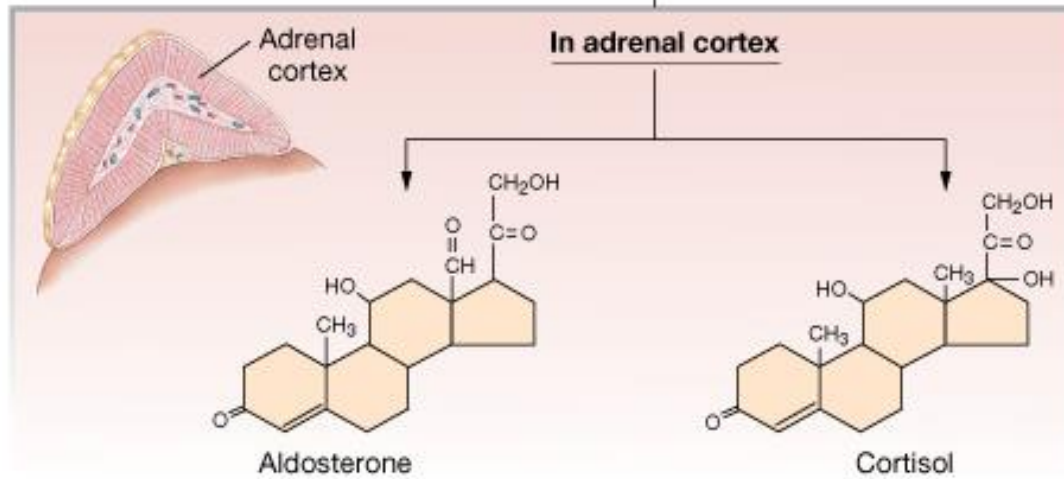
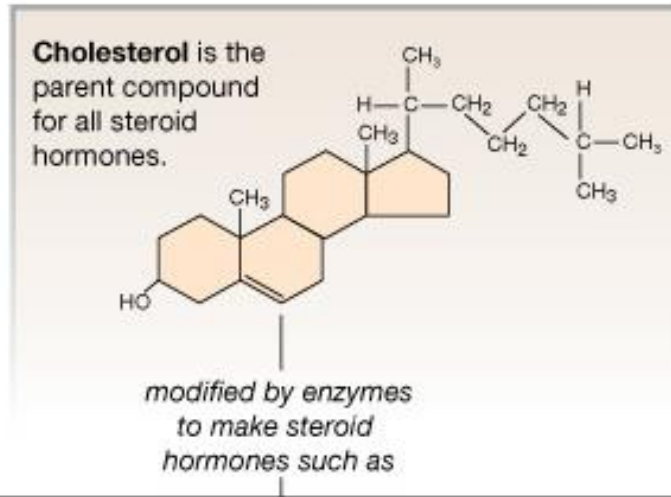
Mineralocorticoids
(Aldosterone)

The Adrenal Gland

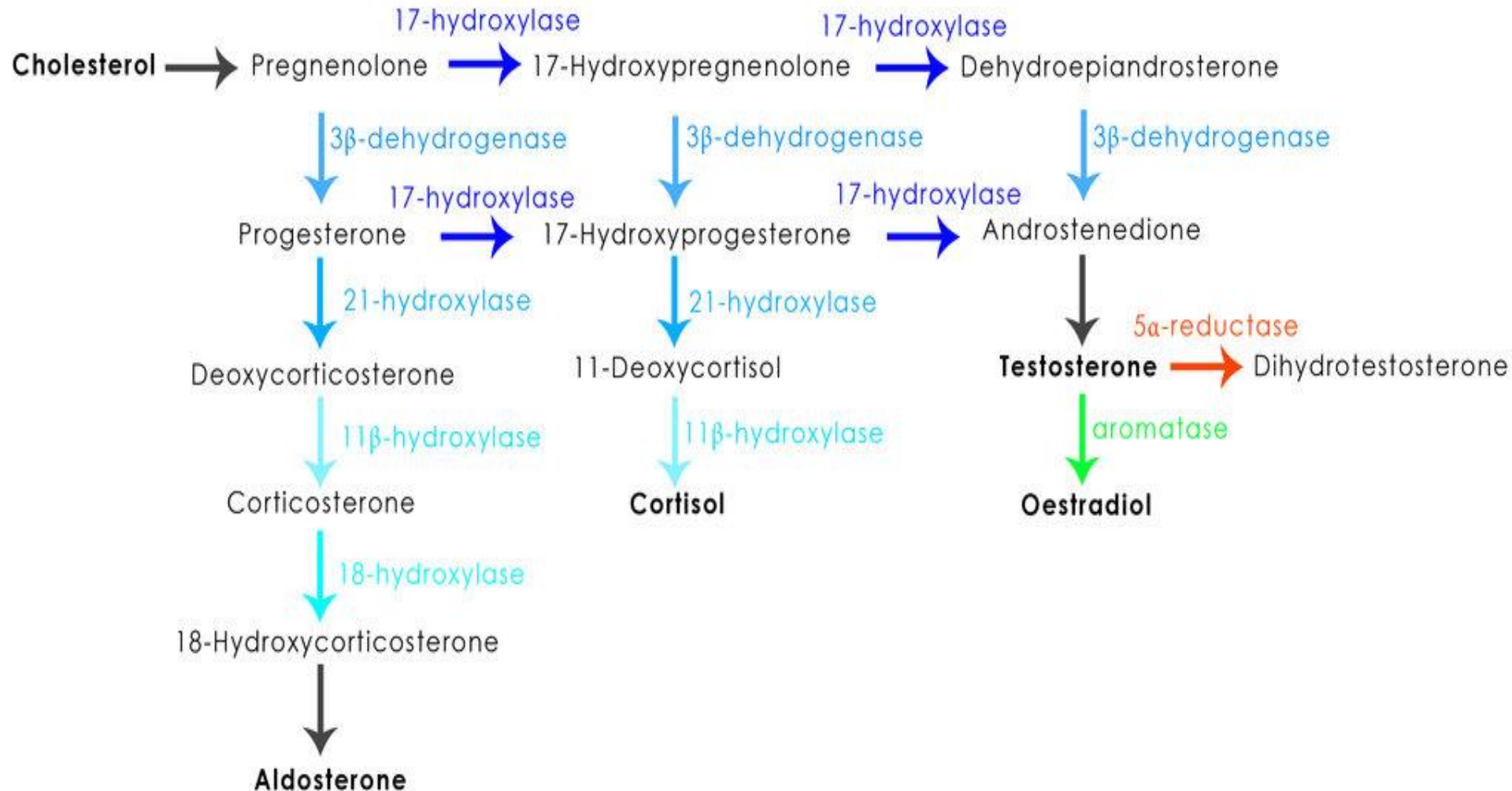
- Adrenal Cortex: Synthesizes and releases steroid hormones (corticosteroids)
- Different corticosteroids are produced in each of the three layers.

Region	Types	Hormones
Zona glomerulosa	Mineralocorticoids	Aldosterone
Zona fasciculata	Glucocorticoids	Cortisol (mainly) Corticosterone Androgens (small amount) Estrogens (small amount)
Zona reticularis	Gonadocorticoids	<u>Androgens:</u> DHEA Androstenedione Estrogen (small amount) <u>Glucocorticoids</u>

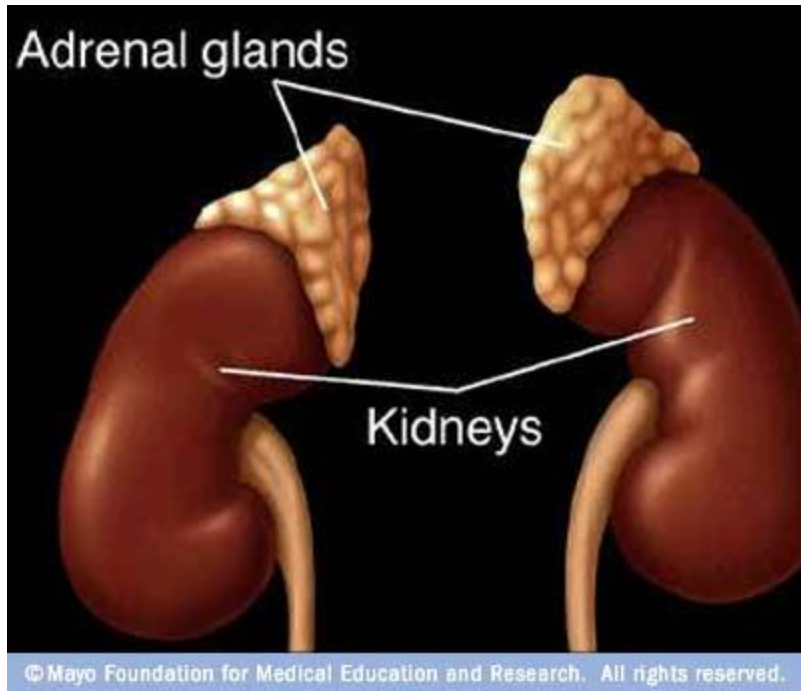
Steroid Hormones: Structure



SYNTHESIS OF STEROID HORMONES



In black are hormones, in colour are enzymes.

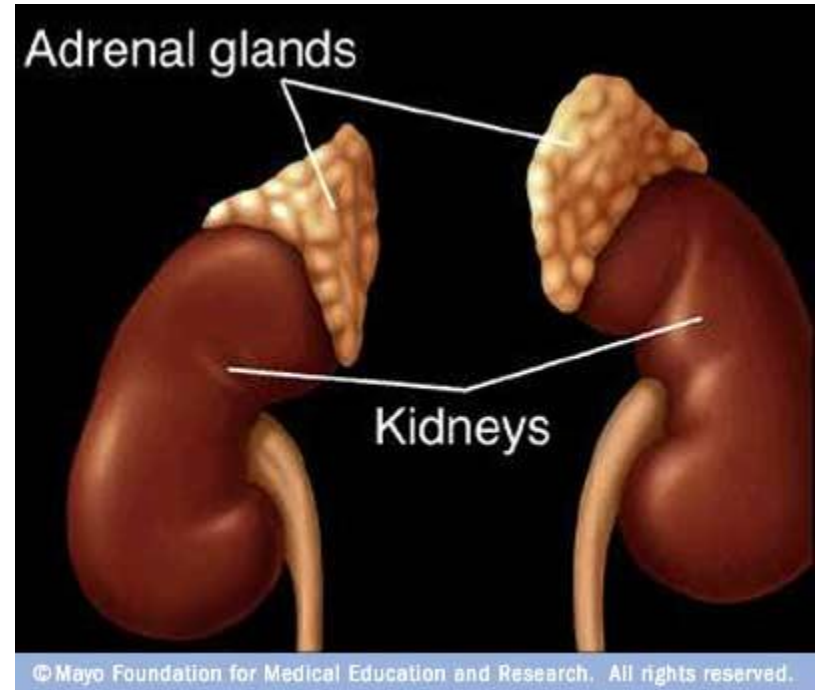


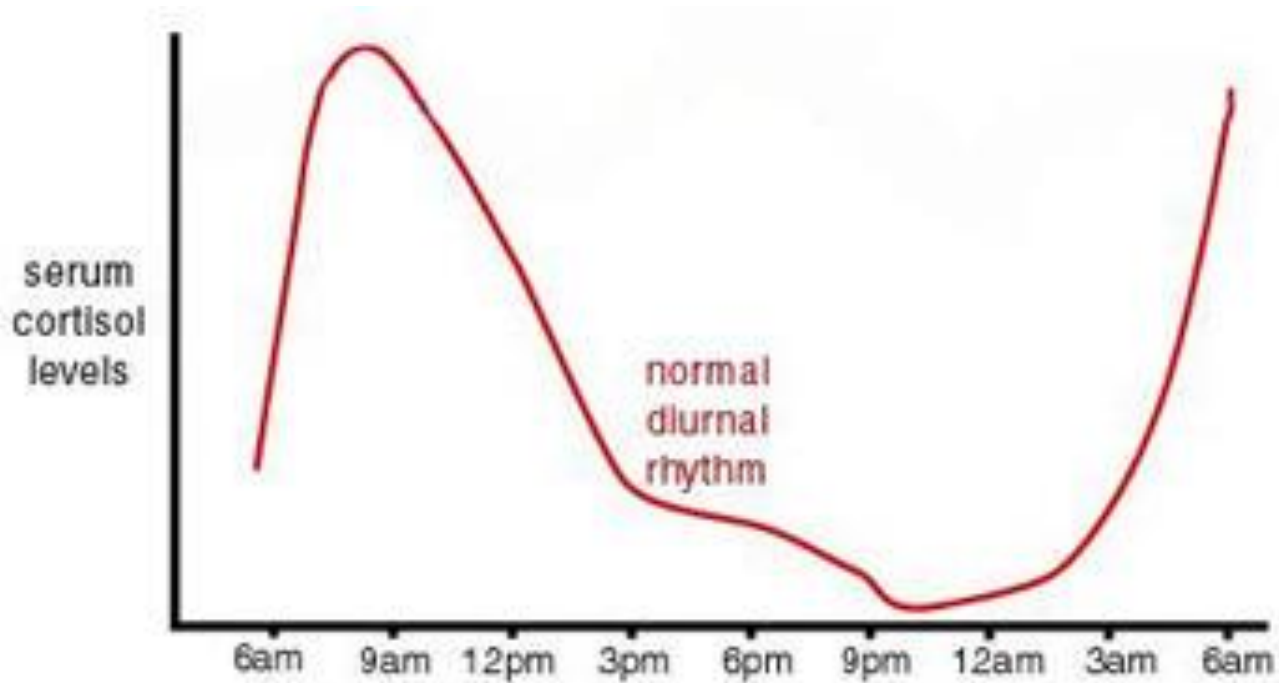
Aldosterone

The main mineralocorticoid produced by the adrenal gland

Mineralocorticoids: Aldosterone

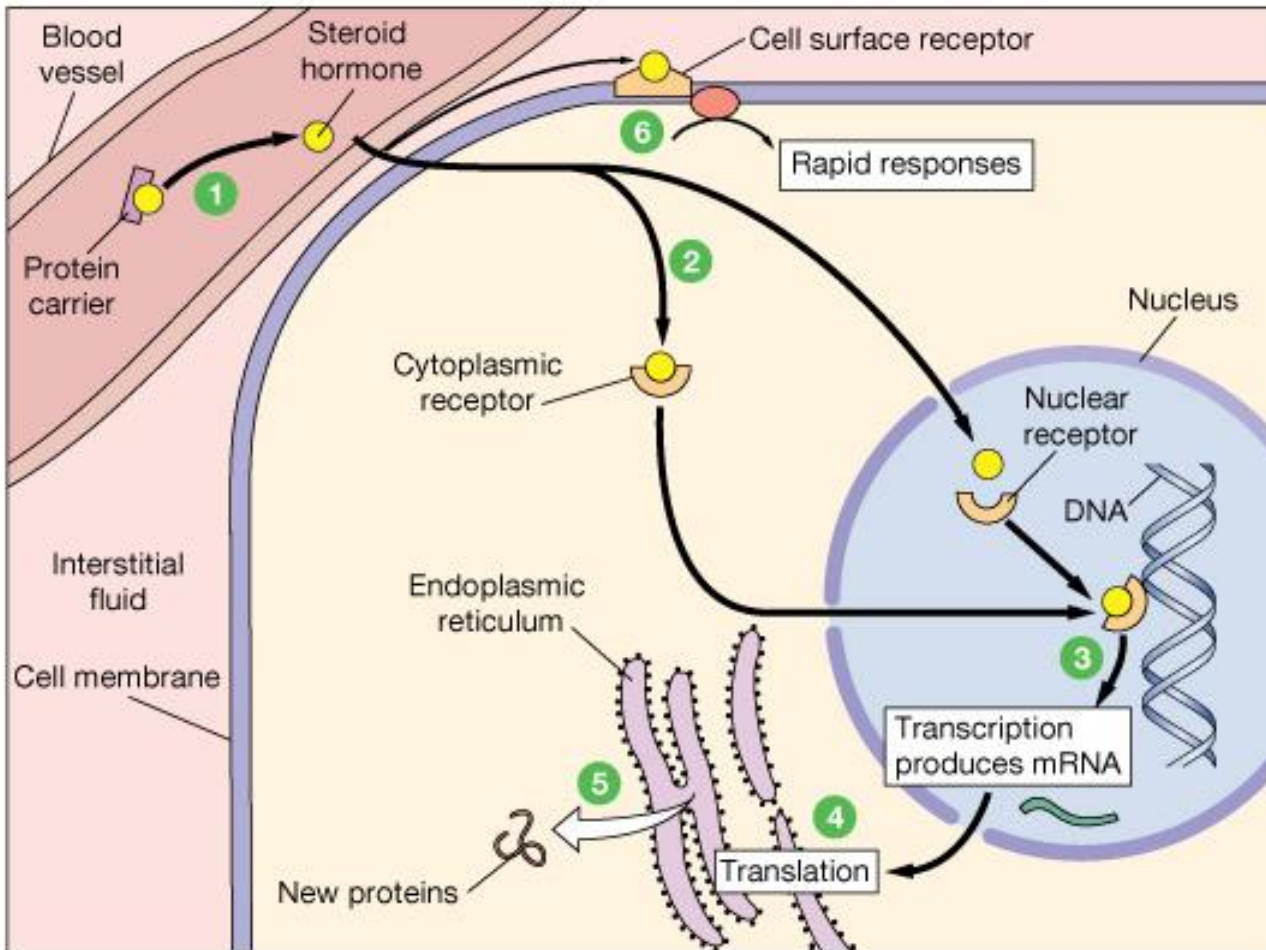
- A steroid hormone.
- Essential for life.
- Synthesized in zona glomerulosa
- Aldosterone exerts 90% of all the mineralocorticoid activity.
- Target cells are called “principal (P) cell”.
- 60% of aldosterone bound to plasma protein...40% is free form.
- Half life: 20 min
- Much of secreted aldosterone is metabolized by the liver and converted to tetrahydroglucuroind derivative.





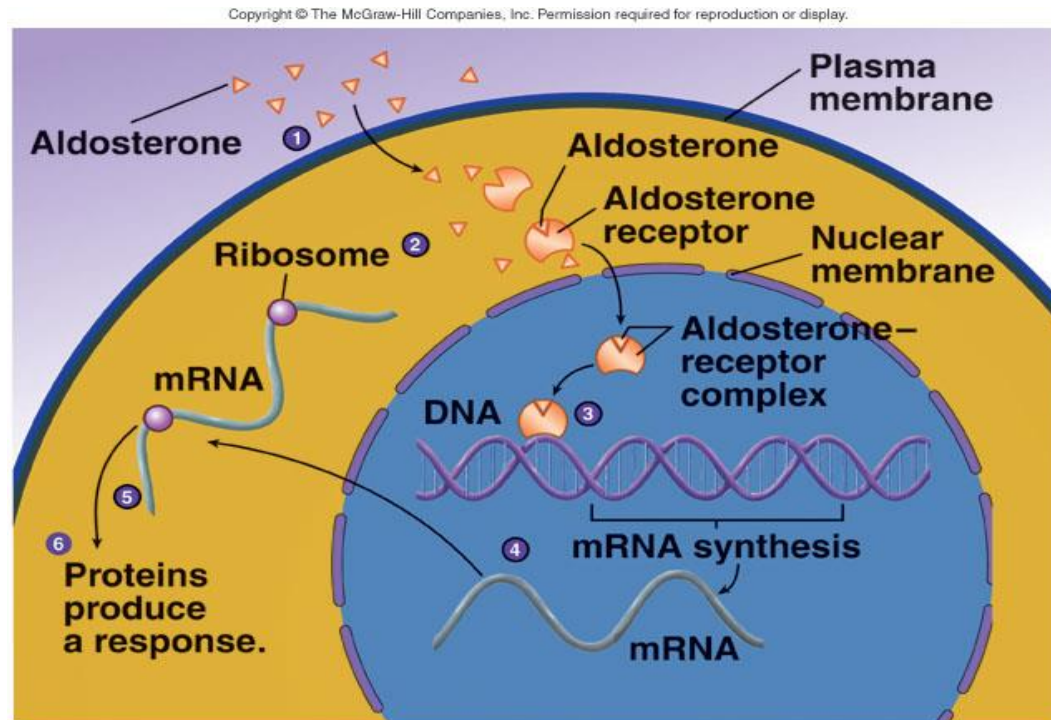
- Aldosterone levels fluctuate diurnally—highest concentration being at 8 AM, lowest at 11 PM, in parallel to cortisol rhythms.

Steroid Hormones: Action



- 1 Most hydrophobic steroids are bound to plasma protein carriers. Only unbound hormones can diffuse into the target cell.
- 2 Steroid hormone receptors are in the cytoplasm or nucleus.
- 3 The receptor-hormone complex binds to DNA and activates or represses one or more genes.
- 4 Activated genes create new mRNA that moves back to the cytoplasm.
- 5 Translation produces new proteins for cell processes.
- 6 Some steroid hormones also bind to membrane receptors that use second messenger systems to create rapid cellular responses.

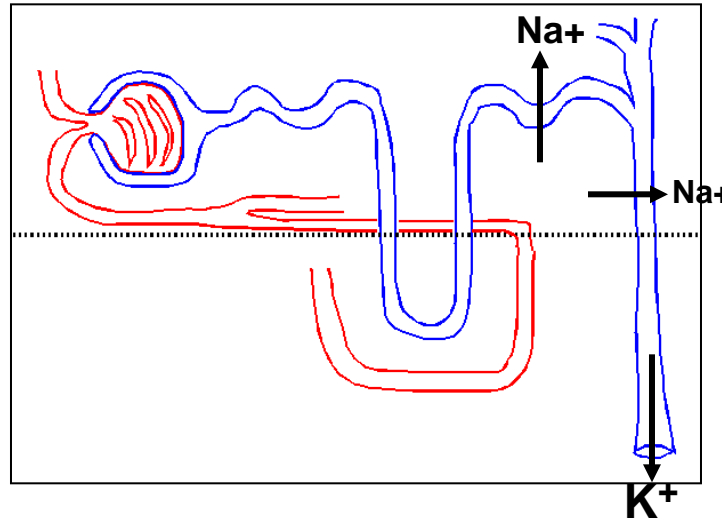
Steroid Hormones: Action



- Increases transcription of Na^+/K^+ pump
- Increases the expression of apical Na^+ channels and $\text{Na}^+/\text{K}^+/\text{Cl}^-$ cotransporter

Actions of aldosterone

Acts mainly on the cells of the collecting ducts and distal tubules.



Increases Renal Tubular Reabsorption of Na^+ and Secretion of K^+ and H^+

1. Renal action:

Aldosterone causes sodium to be conserved in the ECF while increasing potassium excretion in the urine.

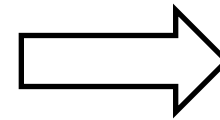
2. Circulatory Actions of Aldosterone:

Increases ECF volume and Arterial Pressure.

3. It also affects Na^+ reabsorption by sweat, salivary and intestinal cells. (Stimulates synthesis of more Na/K-ATPase pumps)

Control of Aldosterone Secretion

- ↑K⁺ concentration in the ECF
- ↓Na⁺ concentration in the ECF
- Increased activity of the renin-angiotensin system
(increased levels of angiotensin II)
- Hypovolemia
- Hypotention
- ACTH: ACTH also stimulates aldosterone synthesis. However the ACTH stimulation is more transient than the other stimuli and is diminished within several days
- stress, surgery,.....

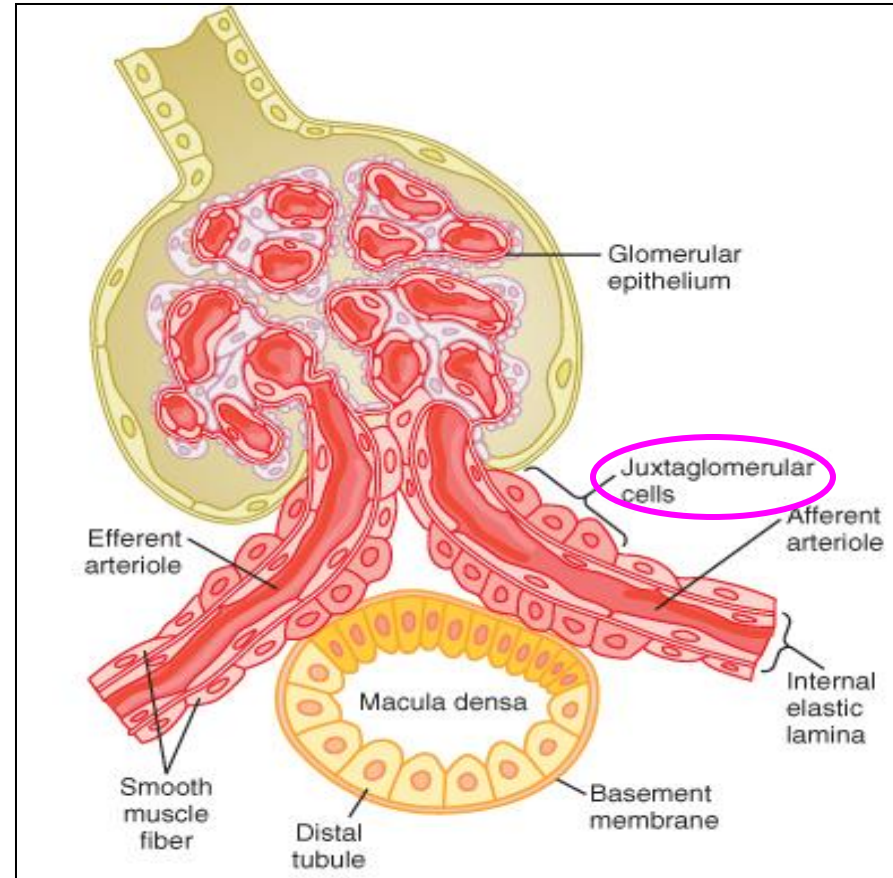


increases aldosterone secretion.

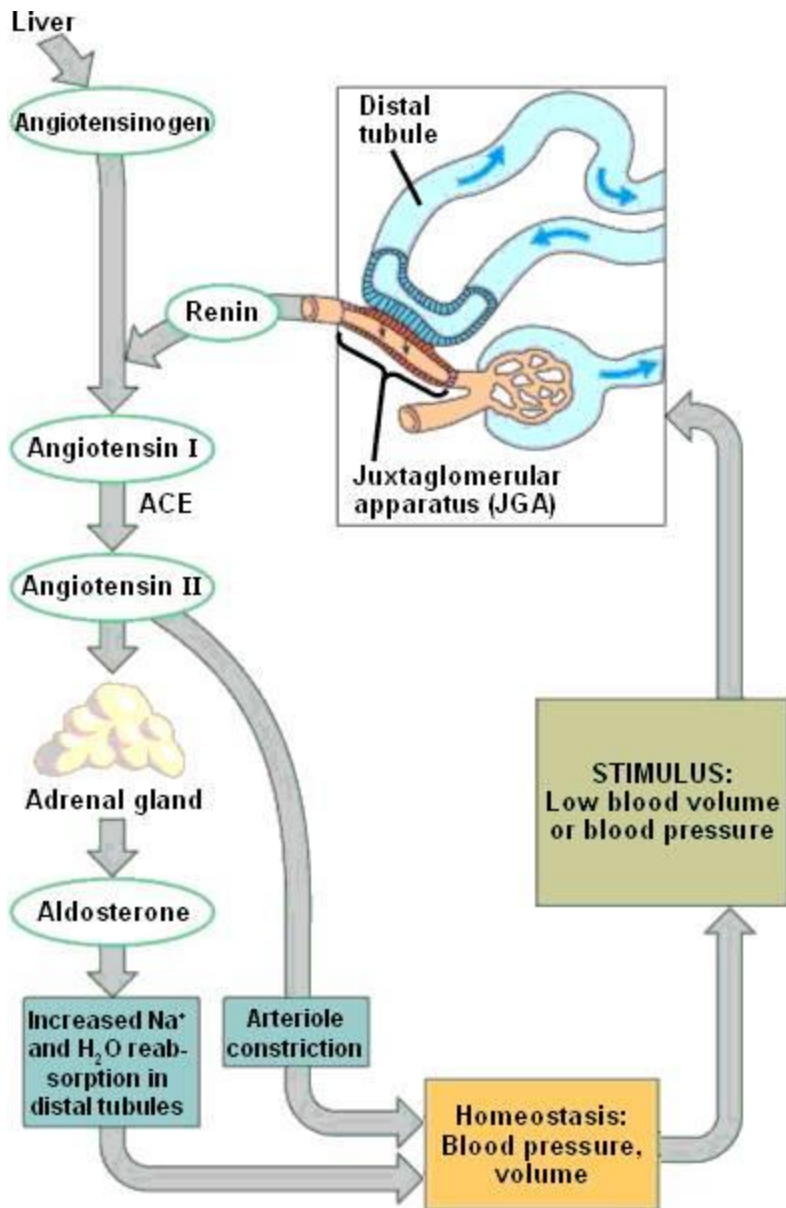
Control of Aldosterone Secretion

Renin :

- is a enzyme released by the kidneys when the arterial pressure falls.
- Renin is synthesized and stored in in the *juxtaglomerular cells (JG cells)* of the kidneys.
- The JG cells are modified smooth muscle cells located *in the walls of the afferent arterioles immediately proximal to the glomeruli*.
- Renin acts on another plasma protein (*angiotensinogen*), to release *angiotensin I* which is converted to *angiotensin II (in the lungs)*.



Control of Aldosterone Secretion



Angiotensin II increases the blood pressure through:

1- Vasoconstriction occurs intensely in the arterioles & much less so in the veins.

Constriction of the arterioles increases the total peripheral resistance, thereby raising the arterial pressure.

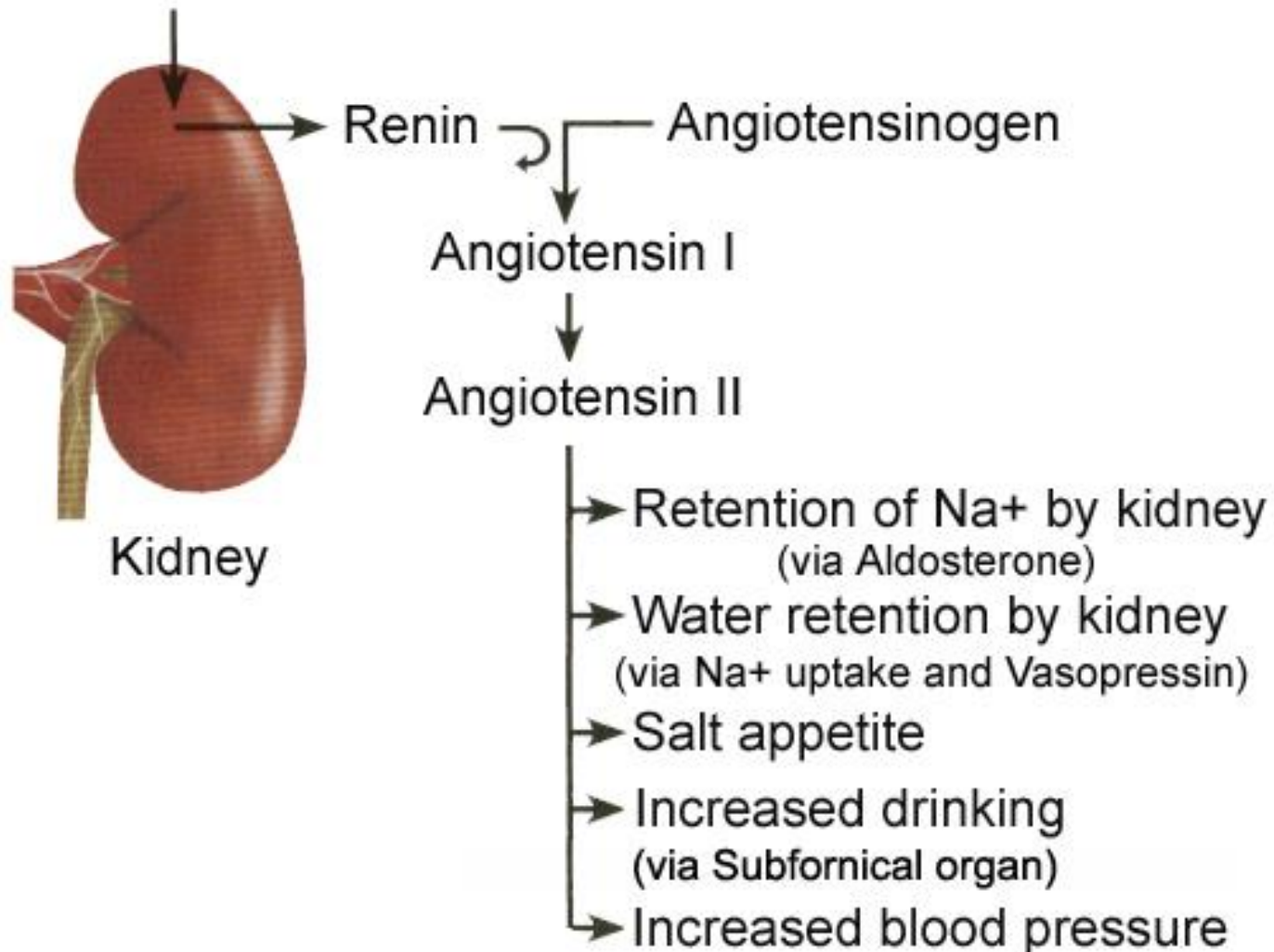
2- decrease excretion of both salt and water by the kidneys.

This slowly increases ECF volume, which then increases the arterial pressure during subsequent hours and days.

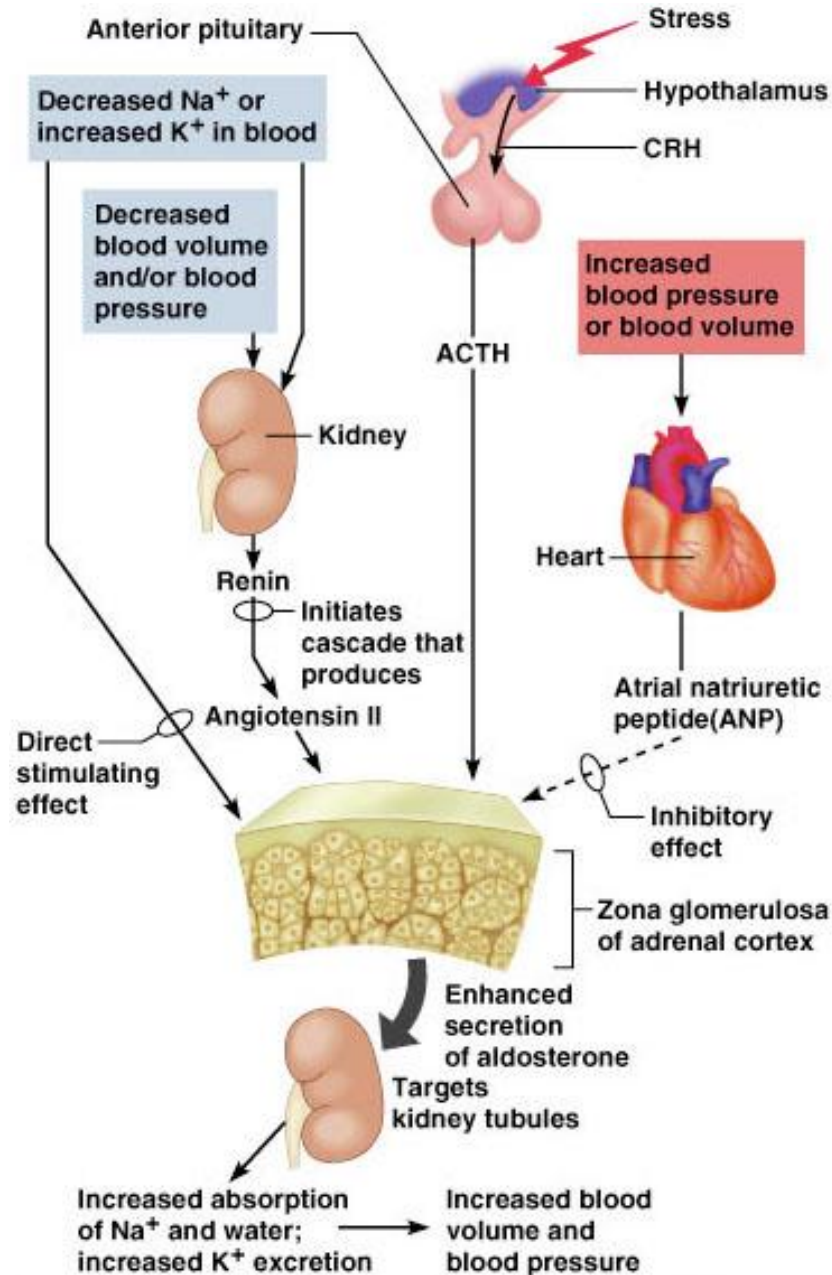
- **Angiotensin II** acts on the zona glomerulosa to stimulate aldosterone synthesis.
- Angiotensin II acts via increased intracellular cAMP to stimulate aldosterone synthesis.

Renin-Angiotensin-Aldosterone System

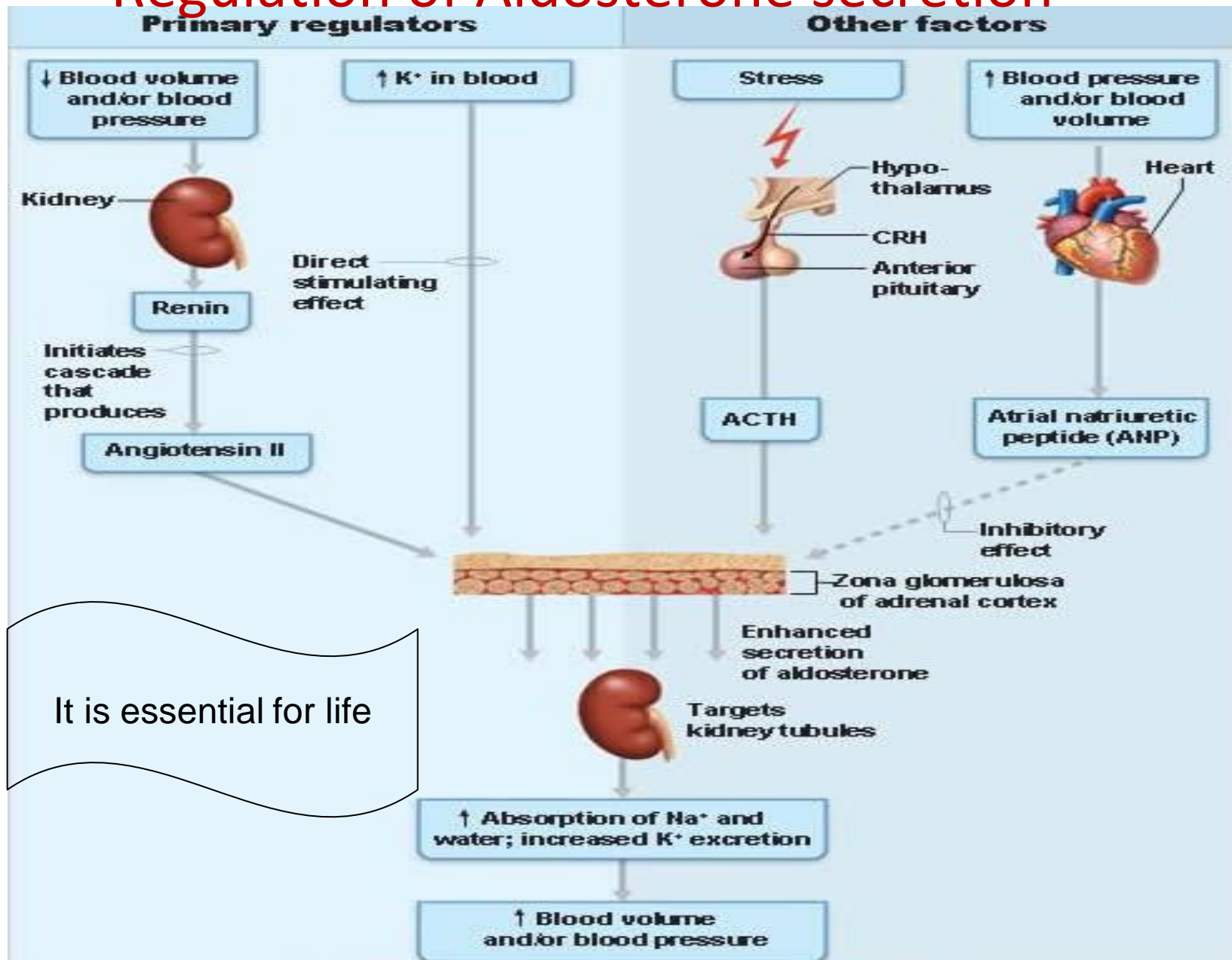
Hypovolemia
(or low blood pressure)



Regulation of Aldosterone secretion



Regulation of Aldosterone secretion



It is essential for life

Hormones of adrenal cortex

	production mg/day	concentr. ng/ml	activity MINERAL.	activity GLUCO.
aldosterone	0.05-0.15	0.15	90%	
deoxycorti- costerone	0.6	0.15	1/15	
corticoste- rone	1-4	2-4	1/50	4%
cortisol	8-25	40-180	1/400	95%
DHEA	7-15	5		

Notes:

Hormones of adrenal cortex

- 1- Cortisol is at 1000 fold higher concentrations than aldosterone
- 2- Corticosterone >>>>aldosterone
- 3- Cortisol binds well to the mineralocorticoid receptor.

Abnormalities

Primary hyperaldosteronism
(increase secretion
of mineralocorticoids)

Conn's Syndrome

Complete failure to
secrete aldosterone

- Dehydration
- Low blood volume
- Low blood pressure

DEATH

Primary Aldosteronism (Conn's Syndrome)

➤ Cause: tumor of the zona glomerulosa cells (adenoma) → secretes large amounts of aldosterone.

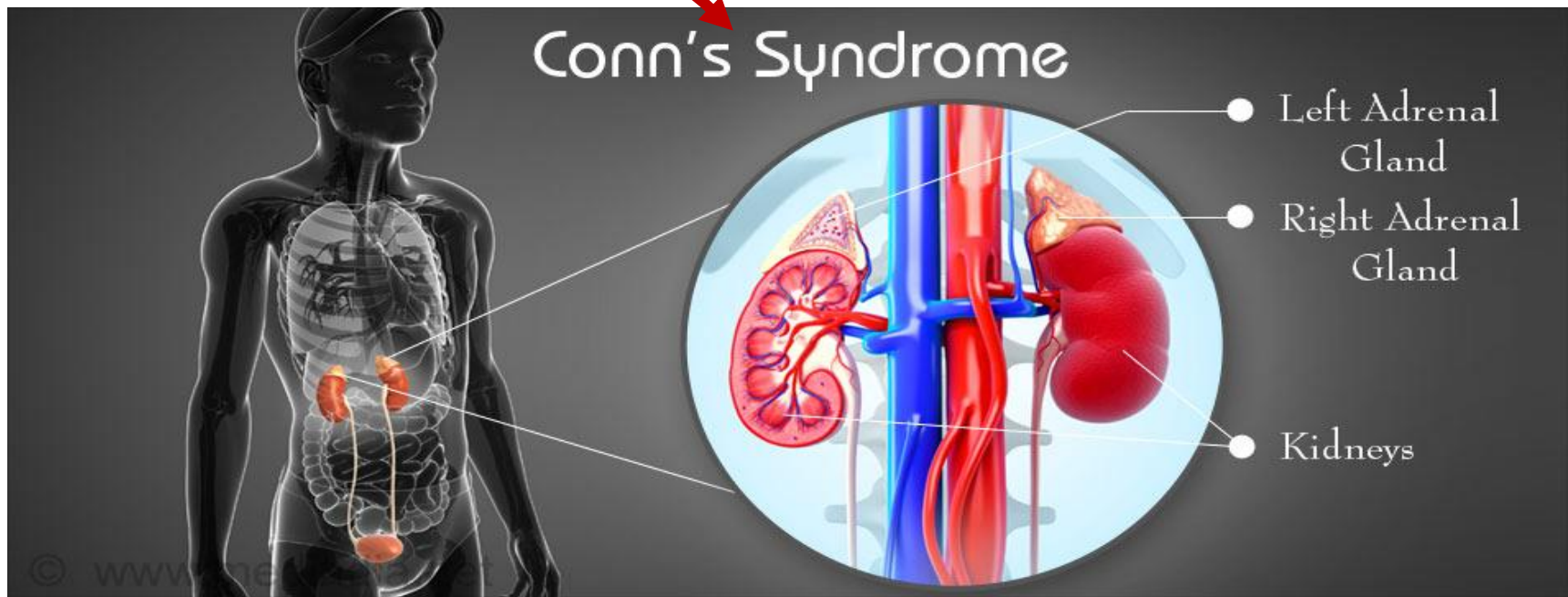
➤ Effects:

The most important effects are:

- hypokalemia.
- slight increase in ECF volume and blood volume.
- very slight increase in plasma sodium concentration.
- almost always, hypertension.
- There are occasional periods of muscle paralysis caused by the hypokalemia.
- decreased plasma renin concentration (from feedback suppression of renin secretion caused by the ↑ aldosterone) or by the excess ECF volume and arterial pressure.

➤ Treatment: usually surgical removal.
Spironolactone

Primary Aldosteronism

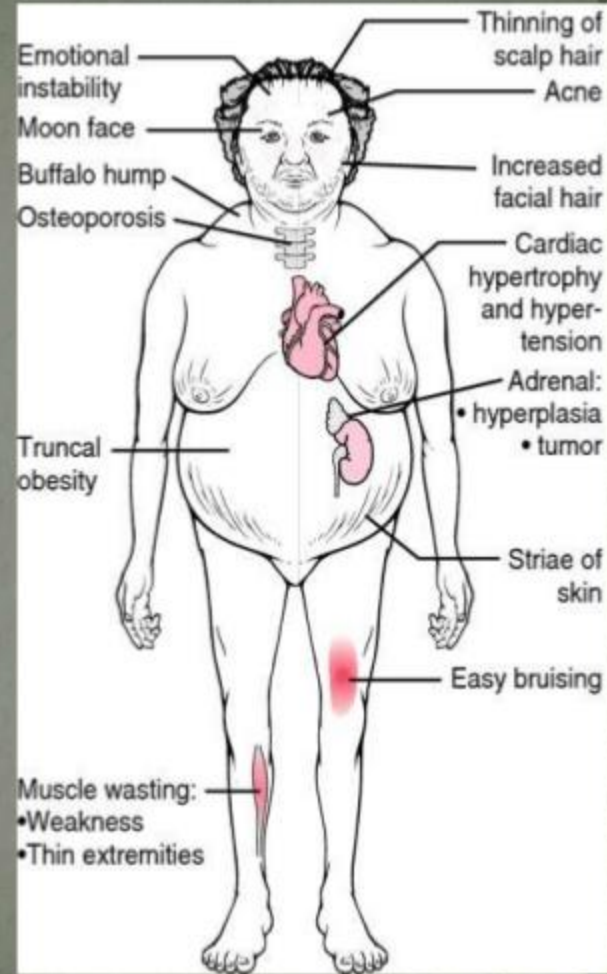




- ❑ Hypertension.
- ❑ Hypokalemia and hypernatremia
- ❑ Nocturnal polyuria & polydipsia
- ❑ Increased tubular (intercalated cells) hydrogen ion secretion, with resultant mild alkalosis.
- ❑ Neuromuscular manifestations
 - ▣ weakness, paresthesia
 - ▣ intermittent paralysis

Conn's Syndrome

Symptoms

- Frequent urination
- Increased thirst
- Weakness and fatigue
- Headache
- Muscle cramps
- Tingling in fingers
- Temporary paralysis
- Heart palpitations
- Hypertension (high blood pressure)



Conn's Syndrome (Primary Hyperaldosteronism)	Secondary Hyperaldosteronism
 plasma Renin	 plasma Renin

Thank you

