Physiology team

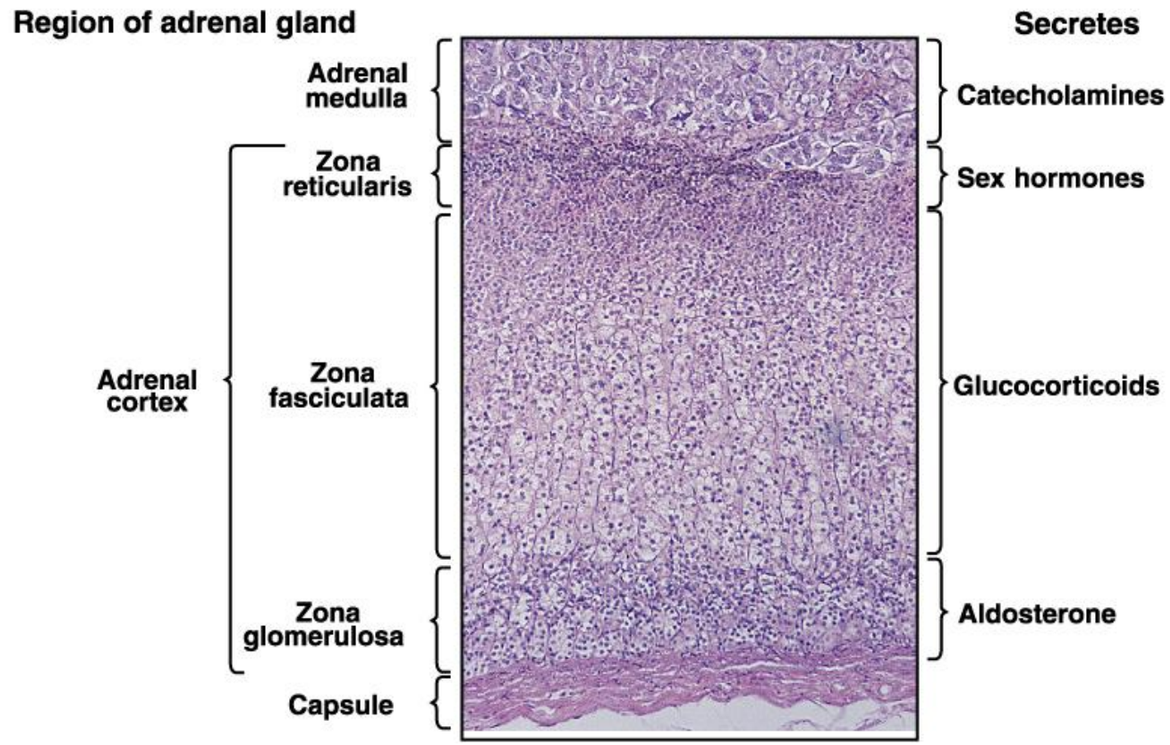
10 Mineralocorticoids

MED 433 Teams

Sources:
Guyton

Hormones of Adrenal gland

- **Cortex: (Secretes steroid hormones)**
  - Glucocorticoids. (from zona fasciculata)
  - **Mineralocorticoids. (from zona glomerulosa)**
  - Androgens.(from zona reticularis)
- **Medulla (Amino acid secretions)**
  - Catecholamines (from adrenal medulla)



Aldosterone

Chemical structures	A steroid hormone.
Location of binding to receptor	Cytoplasm of principle cells in renal tubules
Source	Zona glomerulosa
Activity	exerts the 90% of the mineralocorticoid activity “the rest by other types of mineralocorticoid”
Peak and lowest secretion level	diurnally—**highest concentration being at 8 AM**, **lowest at 11 PM** in parallel to cortisol rhythms.
Metabolize in	Liver “by conjugation to glucuronic acid and sulfate”

Actions of Aldosterone

1- Na+ reabsorption:

- in the **distal tubule** and the **cortical collecting duct** by binding to target cells are called "principal (P) cell"
- In **sweat, salivary and intestinal cells** by stimulates synthesis of more Na/K-ATPase pumps.

2- Maintain extracellular volume.

3- Active secretion of K+: from the distal tubular cell into the urine.

4- Stimulates secretion of H+ by the kidney.

Regulation of aldosterone secretion

Direct stimulation

- High plasma potassium level
- ACTH (Due stress)

Aldosterone Inhibited by **ANP** that released from Heart in response to **increase in blood pressure**

Indirect stimulation

Angiotensin II (RAAS): this system is activated by:

1-low blood pressure and renal ischemia **(Juxtaglomerular cells)**

2-low Na+ concentration **(at macula densa)**

ACTH & Aldosterone releasing

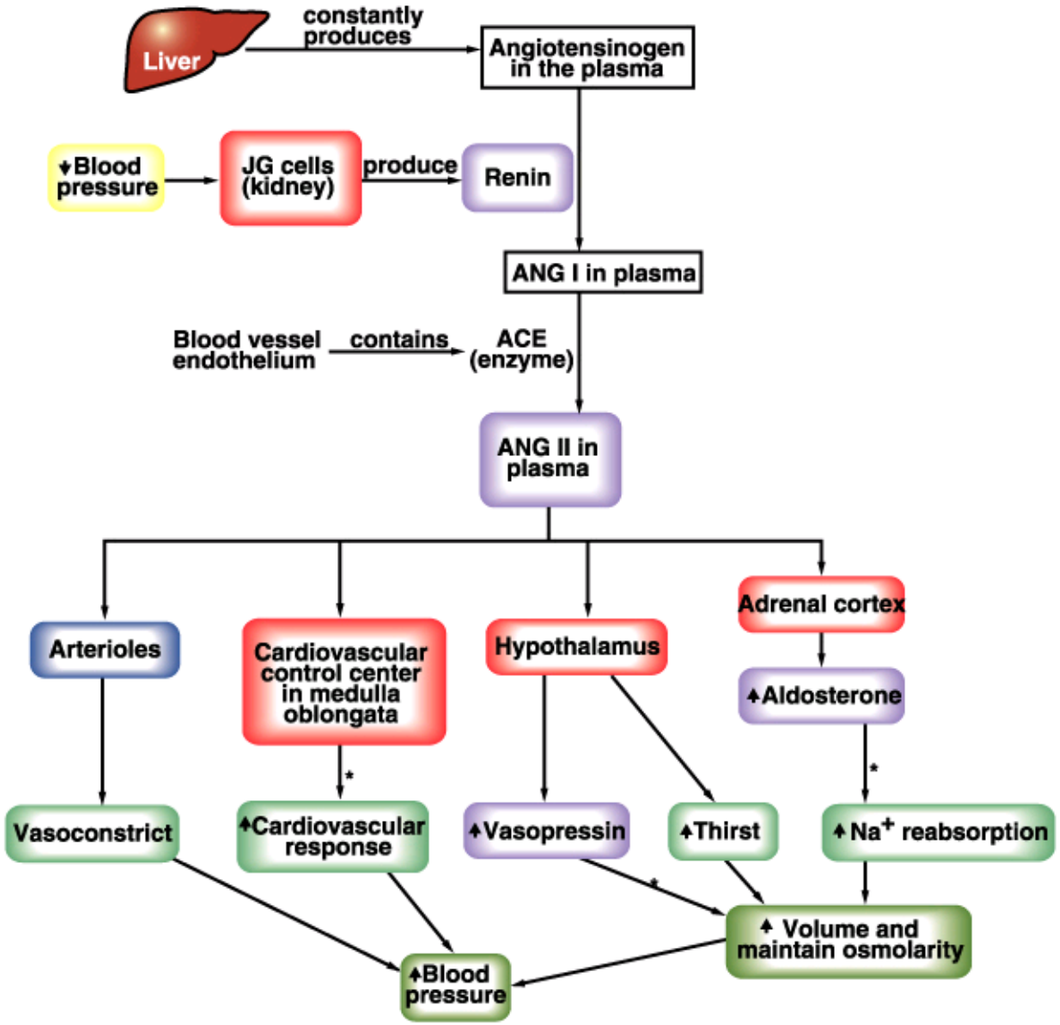
ACTH also stimulates aldosterone synthesis.
However the ACTH stimulation **is more transient** than the other stimuli and is **diminished within several days.**

High levels of potassium & Aldosterone releasing

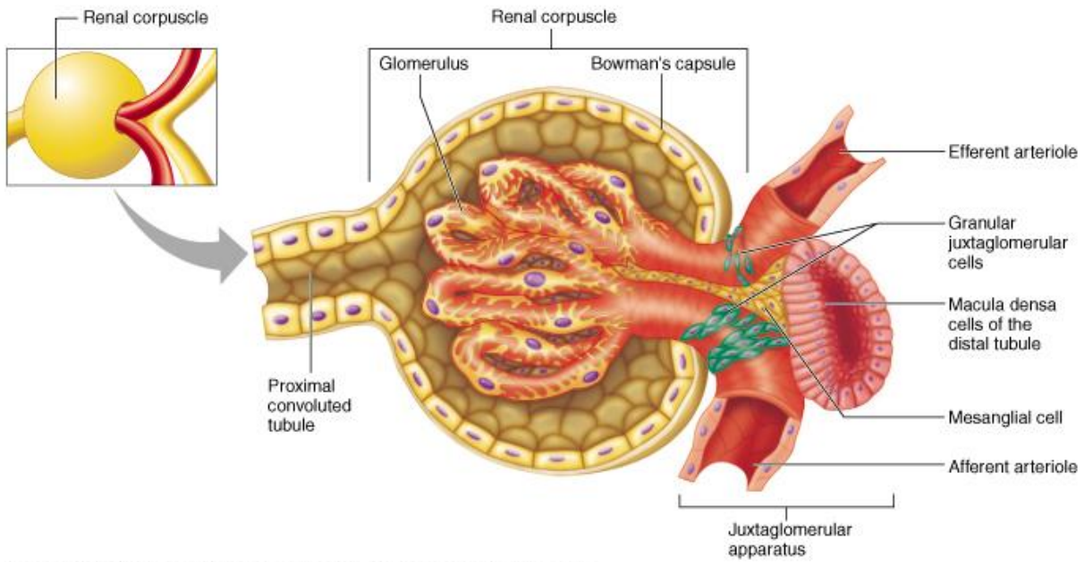
increased potassium intake induces greater potassium excretion mediated by aldosterone Potassium stimulates aldosterone synthesis by **depolarizing zona glomerulosa cell membranes**

Angiotensin II & Aldosterone releasing

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



Juxtaglomerular apparatus (JGA)



Macula densa cells:
Specialized **chemoreceptor** cells in the wall of the distal convoluted tubule

respond to changes in solute concentration (especially sodium levels) in the tubular fluid.

Information is conveyed to the juxtaglomerular cells which will adjust their output of renin accordingly.

Juxtaglomerular cells:
Specialized **smooth muscle cells** which act as **mechanoreceptors .**

They are stretched in response to increases in the blood pressure of the afferent arteriole

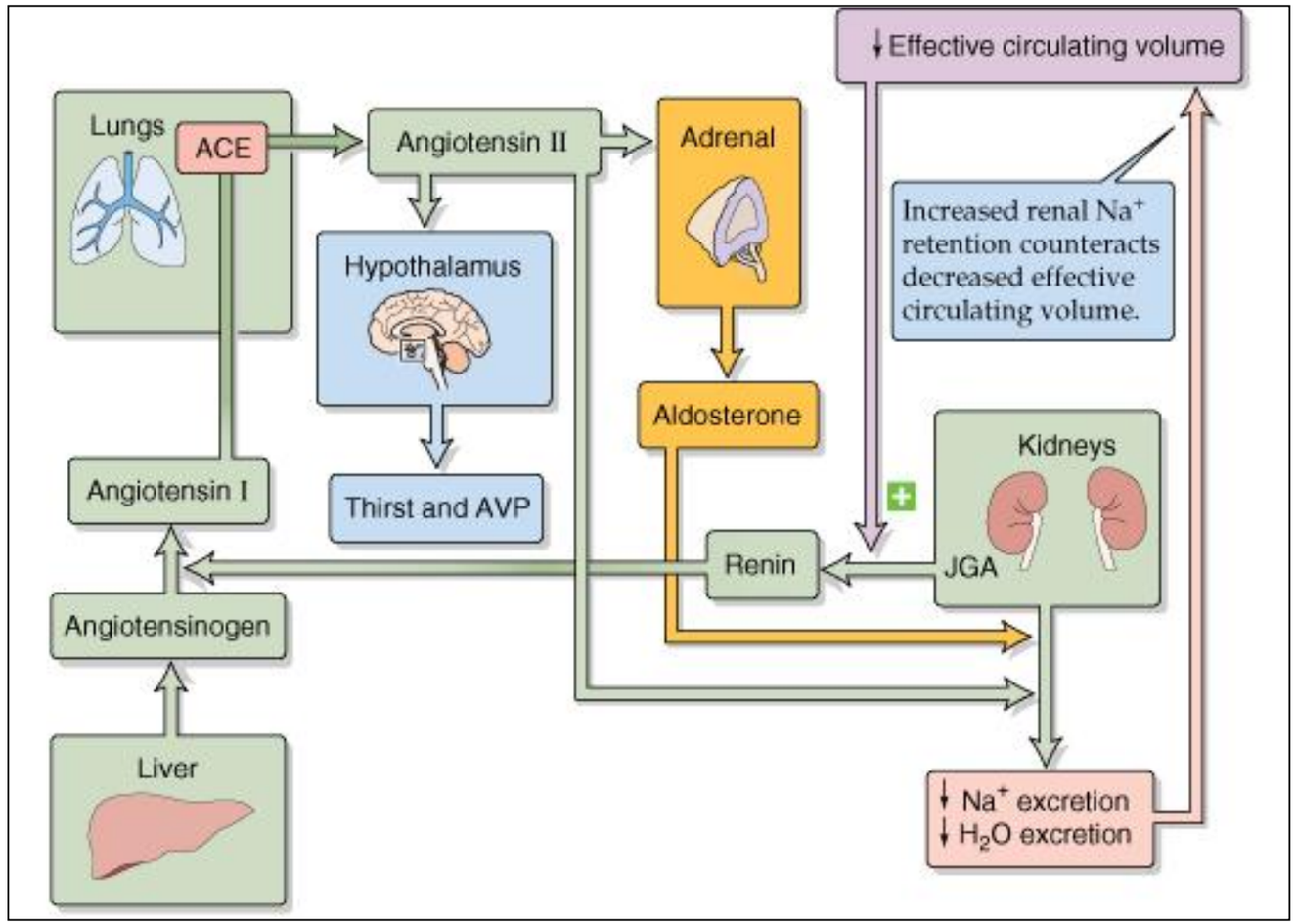
synthesize and secrete renin

Renin-angiotensin-aldosterone axis

Principal factor controlling Ang II levels is renin release.

Decreased circulating volume stimulates renin release via:

- **Decreased Blood pressure** (sympathetic effects on JGA).
- **Decreased [NaCl] at macula densa** (“NaCl sensor”)
- **Decreased renal perfusion pressure** (“renal” baroreceptor)



Angiotensinogen: by liver

Renin: by Juxtaglomerular cells to **convert Angiotensinogen to angiotensin I**

ACE enzyme: by lungs to **convert Angiotensin I to Angiotensin II**

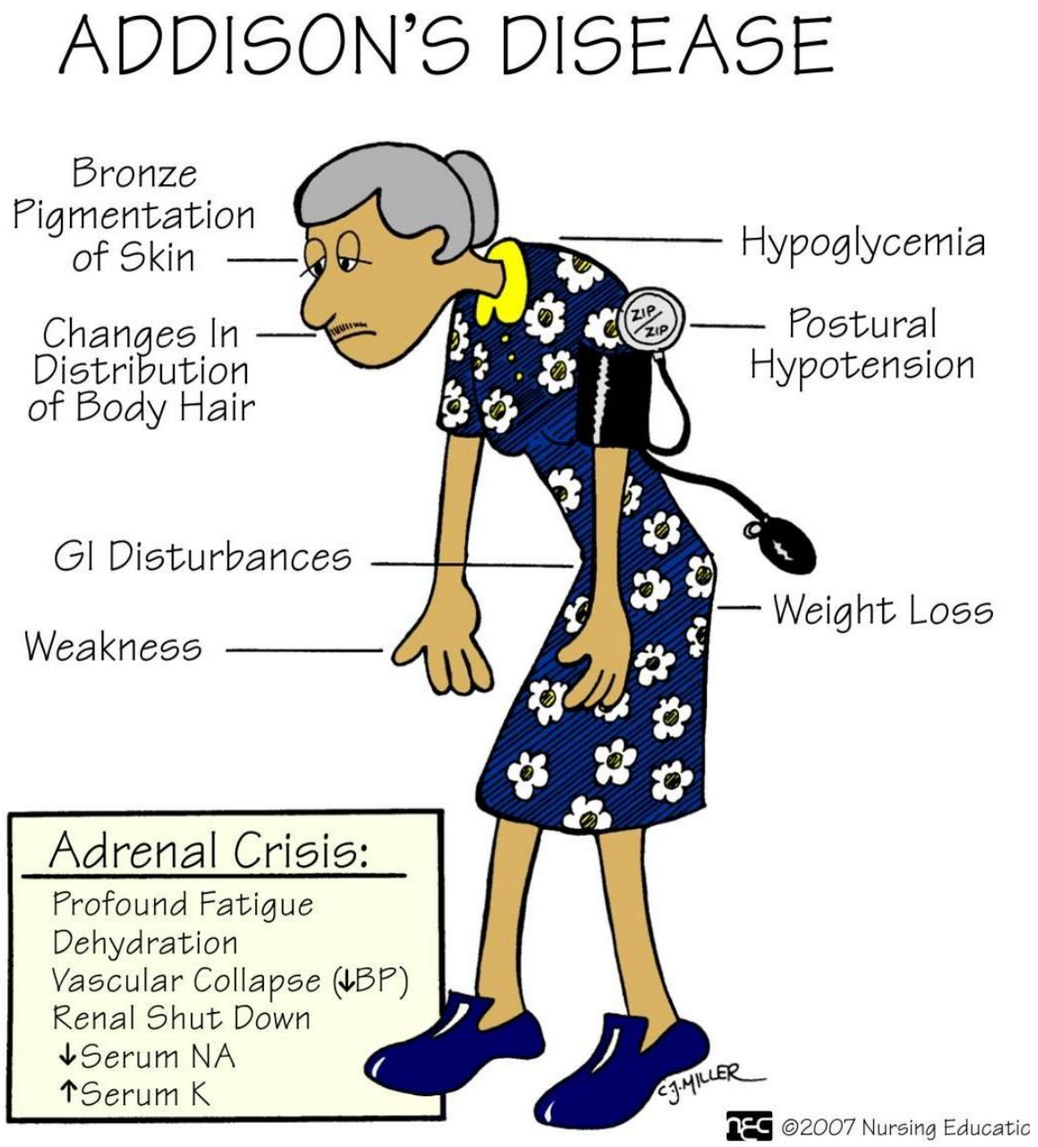
Adrenal insufficiency

Addison's Disease:

Inadequate amounts of adrenocortical hormones due to **bilateral destruction of adrenal cortices.**

Causes:

Autoimmunity – TB – Radiation - Malignancy.



Lack of aldosterone:

- Increased loss of sodium, chloride, water:
Decrease ECF volume.
- Decrease secretion of K+
Hyperkalemia
- Decrease secretion of H+:
Mild acidosis
- Decrease reabsorbation of sodium:

- lead to circulatory collapse.
- Decrease cardiac output
- shock
- death within 4 days to a 2 weeks if not treated.

Hyperaldosteronism

Primary **overproduction of aldosterone** in conditions such as **Conn's syndrome.**

Clinical Features of Primary Aldosteronism:

- Hypertension.
- Nocturnal polyuria & polydipsia
- Neuromuscular manifestations
- weakness, paresthesia
- intermittent paralysis

- Increased K+ secretion:

- Hypokalemia

- Increased H+ secretion:

- mild alkalosis.

Hyperaldosteronism—Conn's syndrome

- is caused by an aldosterone-secreting tumor.
- is characterized by the following:

(1) **Hypertension** (because aldosterone increases Na^+ reabsorption, which leads to increases in ECF volume and blood volume)
(2) **Hypokalemia** (because aldosterone increases K^+ secretion)
(3) Metabolic alkalosis (because aldosterone increases H^+ secretion)
(4) ↓ **renin** secretion (because increased ECF volume and blood pressure inhibit renin secretion by negative feedback)

Tests Confirming the Diagnosis of Primary Aldosteronism:

- Plasma supine aldosterone at 0800h > 15 ng/dl
- Urinary aldosterone metabolites
  - 18-Monoglucuronide > 20 ug/24h
  - Tetrahydroaldosterone > 65 ug/24h
- NaCl infusion/ suppression test > 10 ng/dl

Summery

Aldosterone secretion (see Chapter 3 VI B)

- is under tonic control by ACTH, but is separately regulated by the renin–angiotensin system and by potassium.

(1) Renin–angiotensin–aldosterone system

(a) Decreases in blood volume cause a decrease in renal perfusion pressure, which in turn increases renin secretion. **Renin,** an enzyme, catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to **angiotensin II** by **angiotensin-converting enzyme (ACE)**.

(b) Angiotensin II acts on the zona glomerulosa of the adrenal cortex to **increase the conversion of corticosterone to aldosterone.**

(c) Aldosterone increases renal Na^+ reabsorption, thereby restoring extracellular fluid (ECF) volume and blood volume to normal.

(2) Hyperkalemia increases aldosterone secretion. Aldosterone increases renal K^+ secretion, restoring blood $[K^+]$ to normal.

Actions of mineralocorticoids (aldosterone) [see Chapters 3 and 5]

a. ↑ **renal Na^+ reabsorption** (action on the principal cells of the late distal tubule and collecting duct)

b. ↑ **renal K^+ secretion** (action on the principal cells of the late distal tubule and collecting duct)

c. ↑ **renal H^+ secretion** (action on the α-intercalated cells of the late distal tubule and collecting duct)

Disorder	Clinical Features	ACTH Levels	Treatment
Addison's disease (e.g., primary adrenocortical insufficiency)	Hypoglycemia Anorexia, weight loss, nausea, vomiting Weakness Hypotension Hyperkalemia Metabolic acidosis Decreased pubic and axillary hair in women Hyperpigmentation	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoids and mineralocorticoids

MCQs

1- From which part of adrenal the aldosterone are secreted :

A- Zone fasciculata

B- Zona reticularis

C- Zona glomerulosa

D- adrenal medulla

2- Aldosterone will bind to receptor that located in:

A- Cytoplasm

B- Nucleus

C- Plasma membrane

D- Golgi Complex

3-Which of the following is action of aldosterone:

A- Na+ secretion.

B- H+ secretion.

C- K+ reabsorbation.

4-Which of the following is indirect stimulus of aldosterone:

A- Release of Angiotensin II.

B- High plasma level of Na+.

C- ACTH.

D-High plasma level of K+.

5- Which of the following stimulus for aldosterone releasing has the weakest effect:

A- High K+ level

B- Angiotensin II

C- Low Na+ level

D- ACTH

6-Which of the following cells responsible of synthesis of Renin:

A- Hepatocytes

B- Lung cells

C- Juxtaglomerular cells

D- Macula densa cells

7- Which of the following enzyme converts Ang I to Ang II:

A- Renin

B- ACE

C- ANP

D- ACTH

8-Symptoms of Addison disease:

A- Hyperpigmentation.

B- Hypoglycemia.

C- All above

1- C 2- A 3- B 4- A 5- D 6-C 7- B 8-C

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Endocrine Block