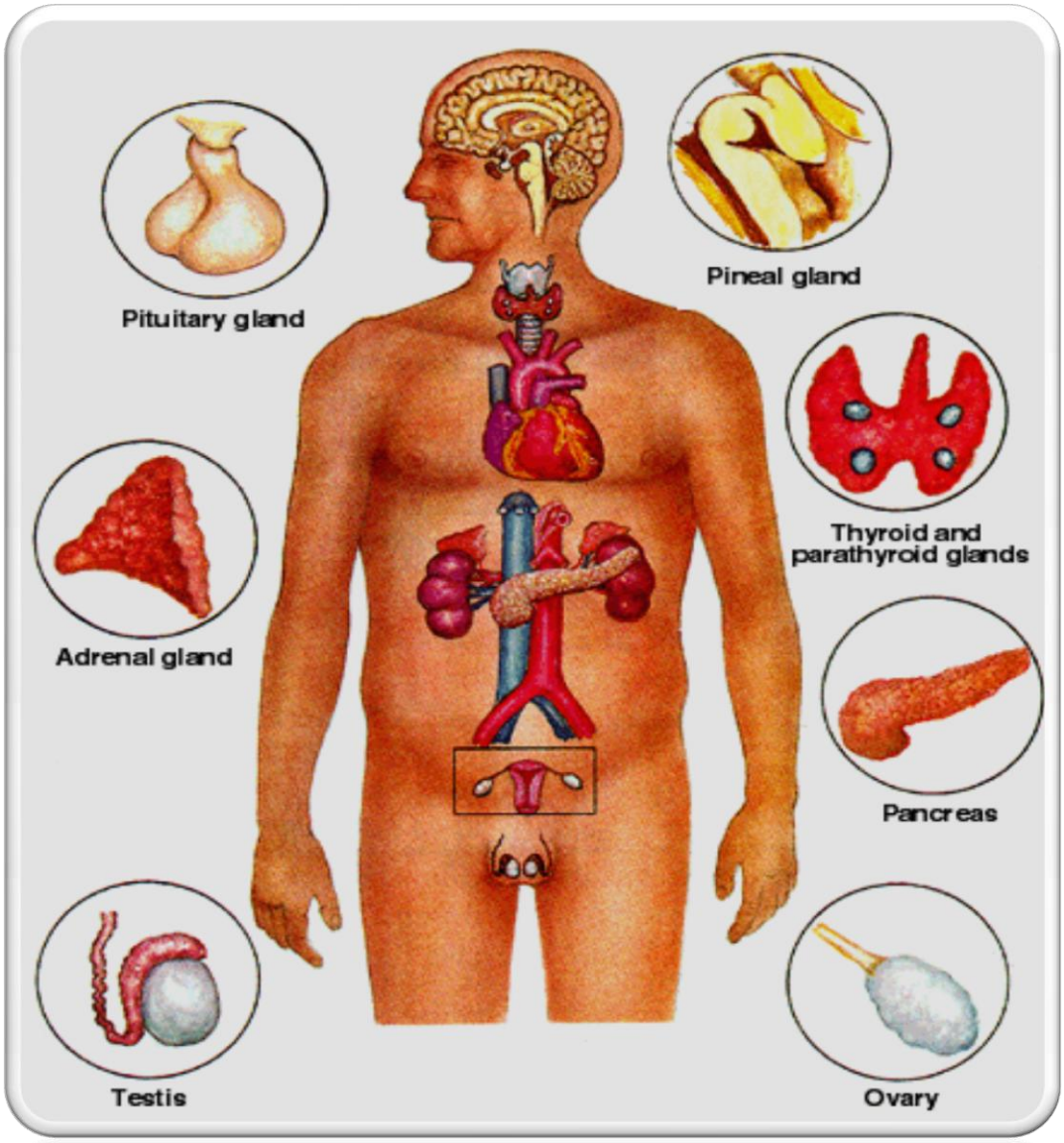
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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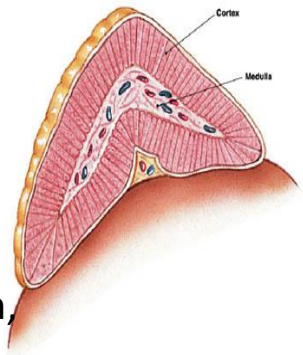
Adrenal Gland :



Small, triangular glands loosely attached to the kidneys;
Divided into two morphologically and distinct regions:

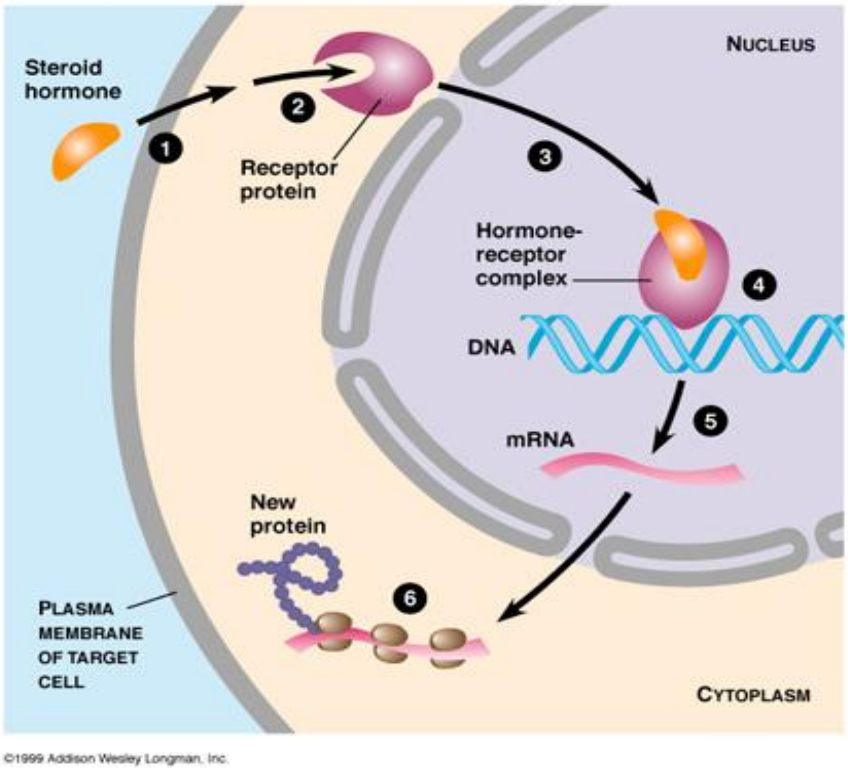
- **Adrenal cortex :** (80-90%)– glandular tissue derived from embryonic mesoderm.
- **Adrenal medulla:** (10-20%)– formed from neural ectoderm, can be considered a **<u>modified sympathetic ganglion.</u>**

Hormones of Adrenal gland :

- **Cortex: (Secretes STEROID hormones) ;**
  - **Mineralocorticoids (mainly aldosterone)**
  - **Glucocorticoids (mainly cortisol and corticosterone)**
  - **Androgens**
- **Medulla (AMINO ACID secretions) ;**
  - **Catecholamines**

Mechanism of action of steroid hormones :

Steroid hormones pass through the cell membrane of the target cell ➔ binds with a specific receptor in the cytoplasm ➔ hormone travels into the nucleus and binds to another specific receptor on the chromatin ➔ The steroid hormone-receptor complex calls for the production of mRNA ➔ production of proteins.



Mineralocorticoids; ALDOSTERONE :

- A steroid hormone, secreted by **Zona glomerulosa**.
- Essential for life.
- Aldosterone exerts the 90% of the mineralocorticoid activity.
- **Cortisol also have mineralocorticoid activity**, but only 1/400th that of aldosterone.
- **Responsible for regulating Na+ reabsorption in the distal tubule and the cortical collecting duct.**
- Target cells are called **"principal (P) cell"**.
- Metabolized in the liver to **Tetrahydroglucuroind** derivative.

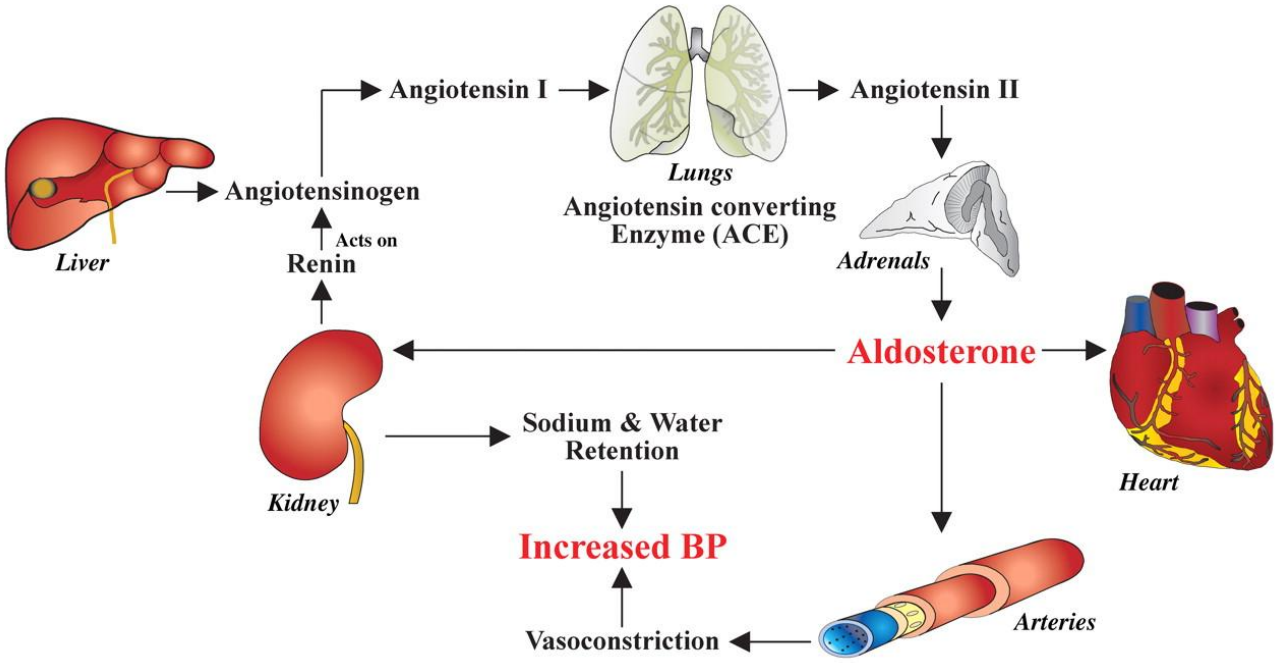
Aldosterone Action :

- Maintains extracellular fluid volume by **conserving body sodium**; by stimulating **sodium reabsorption** by distal tubule and collecting duct of the nephron and promotes **potassium and hydrogen ion excretion** from the tubular cell into the urine.
- Aldosterone stimulates sodium & potassium transport in sweat glands, salivary glands, & intestinal epithelial cells.
- **INCREASE synthesis of Na-K-ATPase in target cells.**
- **Na+-K+ balance and blood pressure homeostasis**. HOW ?!

During formation of urine, at the principal site of action; the collecting tubules of the kidney, this is what happens:

- ***Na+ retention is promoted***
- ***K+ elimination***

- Secondarily to Na+ retention, **osmotic retention of water** is induced which expands the ECF volume, which is important in the long term regulation of blood pressure
- So, Na+/K+-ATPase, and Na+ channels work together to **increase volume and pressure, and decrease K+** .



Regulation of Aldosterone Release :

Serum K^+

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

Angiotensin II

- Angiotensin-II stimulates secretion of aldosterone. Angiotensin-II has an early action on the conversion of cholesterol to pregnenolone, and a late action on the conversion of corticosterone to aldosterone.

ACTH

- ACTH stimulates the output of aldosterone. Its effect on aldosterone is transient -situations of stress- (lasting a day or two) because a rise in aldosterone produces hypervolemia (which inhibits angiotensin-II production) and hypokalemia. Both these factors tend to lower aldosterone secretion.
- In other words, in the presence of stronger controllers of aldosterone secretion (angiotensin-II, hyperkalemia), ATCH does not act as an important controller of aldosterone.

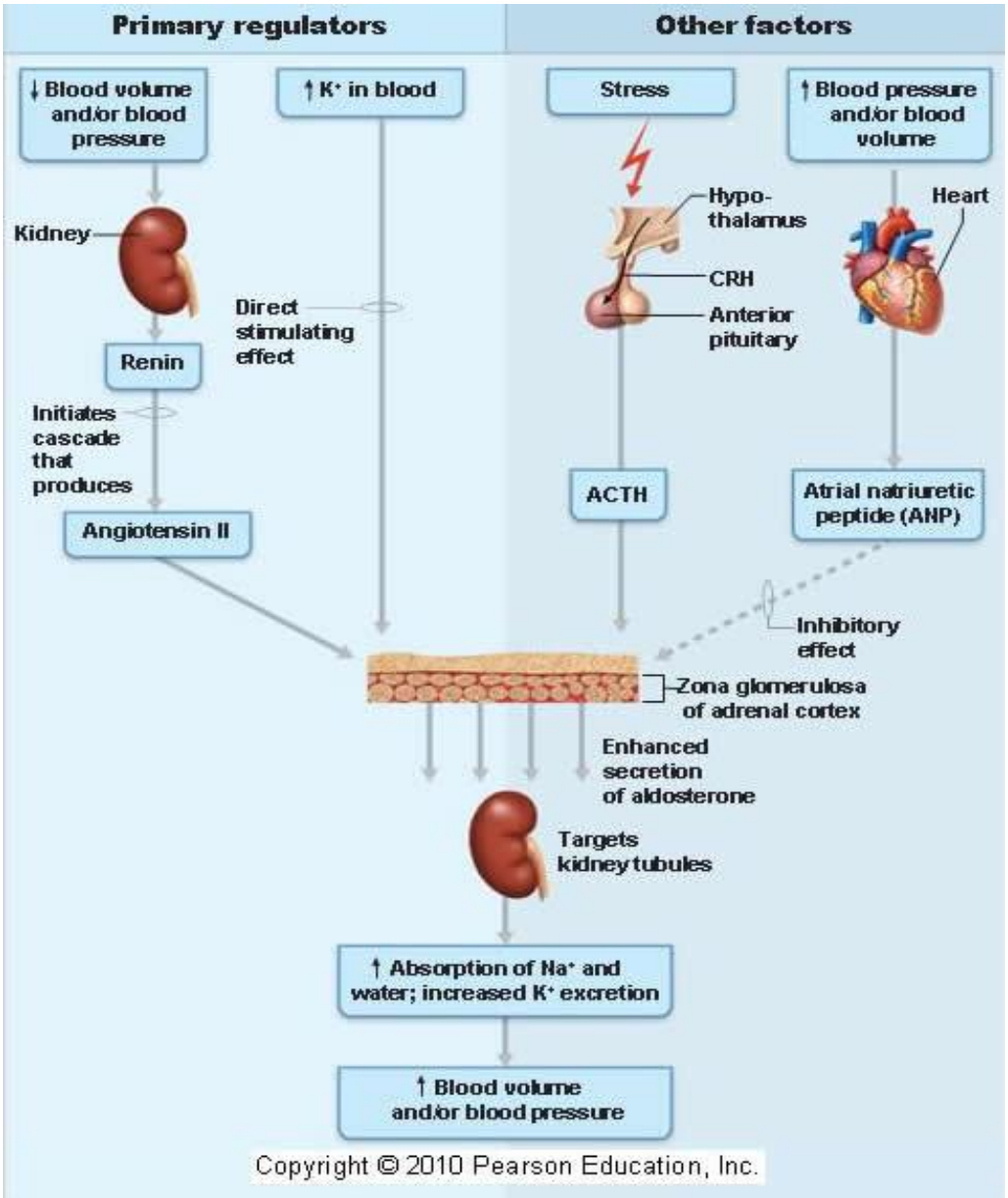
Cont. Regulation of Aldosterone Release :

Aldosterone Stimulators:

- Activation of Renin-Angiotensin-Aldosterone-System (RAAS) ➔HYPOVOLEMIA
- Increased ECF K+
- ACTH

Aldosterone Inhibitors:

- Overhydration.
- Atrial Natriuretic Peptide (ANP)



How does ANP inhibit aldosterone synthesis?

- In response to volume expansion, arterial myocytes secrete ANP which binds to receptors in the zonaglomerulosa to inhibit aldosterone synthesis.
- ANP acts via increased intracellular cGMP which opposes cAMP and inhibits aldosterone synthesis .
- ANP also reduces aldosterone indirectly by inhibiting renin Release.

Aldosterone Synthesis :

The **juxtaglomerular apparatus** of the kidney respond to hypovolemia by secreting renin (via: **- low BP** (effects on JGA), **-low NaCl** at macula densa, **-Low renal perfusion pressure** (renal baroreceptor) ➔ Renin acts on angiotensinogen (which is secreted by the liver) to form angiotensin I ➔ Then angiotensin converting enzyme, ACE
(which is secreted by the lungs) acts on angiotensin I ➔ It cleaves it to angiotensin II ➔ Then Angiotensin II acts, via increased intracellular cAMP in ZonaGlomerulosa, to stimulate aldosterone synthesis.

Juxtaglomerular Apparatus JGA :

A specialized collection of two cell types:

- **Macula densa cells ;**(Specialized **chemoreceptor** cells in the wall of the distal convoluted tubule respond to changes in solute concentration).
- **Juxtaglomerular cells ;** (Specialized smooth muscle cells which act as **mechanoreceptors** which stretch in response to increases in the blood pressure of the afferent arteriole).

Located at the juncture of the afferent and efferent arterioles with a portion of the distal convoluted tubule of the nephron of the kidney

Adrenal Cortex Dysfunctions :

• Hypoadrenalism – Addison's Disease :

- Adrenal cortex produces **inadequate** amounts of hormones.
- **Causes:**
  - Autoimmunity against cortices 80%
  - tuberculosis, drugs, cancer/ irradiation

Cont. Hypoadrenalism :

- **Lack of aldosterone cause:**
  - Increased sodium, chloride, water loss
  - Decrease ECF volume
  - Hyperkalemia
  - Mild acidosis
  - Increase RBC concentration
  - Plasma sodium decreases and may 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.**
- Conditions of low cardiac output are also known to stimulate synthesis of aldosterone.
- Both conditions result in **sustained hypertension.**

Clinically:

- Hypertension.
- Hypokalemia
- Nocturnal polyuria & polydipsia
- Increased tubular (intercalated cells) hydrogen ion secretion, with resultant mild alkalosis.
- Neuromuscular manifestations
  - Weakness, paresthesia.
  - Intermittent paralysis.

Summary

- **Mineralocorticoids (mainly aldosterone) :** A steroid hormone, secreted by **Zona glomerulosa**

Aldosterone responsible for sodium reabsorption and promotes **potassium and hydrogen ion excretion**

Aldosterone Stimulators:

- **Activation of Renin-Angiotensin-Aldosterone-System (RAAS) ➔HYPOVOLEMIA**
- **Increased ECF K+**
- **ACTH**

Aldosterone Inhibitors:

- **Overhydration.**
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Questions :

1- Which one of the following cells release rennin ?

A. Macula densa cells

B. Juxtaglomerular cells

C. principal (P) cell

D. A+B

2- Which one of the following is responsible for aldosterone secretion ?

A. Hypervolemia

B. Increased ECF K+

C. overhydration

D. Atrial Natriuretic Peptide (ANP)

3 - Which one of the following is the action of rennin ?

A. Conversion of angiotensin I to angiotensin 2

B. Conversion of angiotensinogen to angiotensin 2

C. Conversion of angiotensinogen to angiotensin 1

D. Released of angiotensinogen from liver

4 - Which one of the following is the action of ACE ?

A. Conversion of angiotensin I to angiotensin 2

B. Conversion of angiotensinogen to angiotensin 2

C. Conversion of angiotensinogen to angiotensin 1

D. Released of angiotensinogen from liver

5 - which one of the following can be seen in case of hyperaldosteronism ?

A. Increased hydrogen ion secretion

B. mild acidosis

C. Hyperkalemia

D. Decrease ECF volume

Answers : 1(B)-2(B)-3(C)-4(A)-5(A)