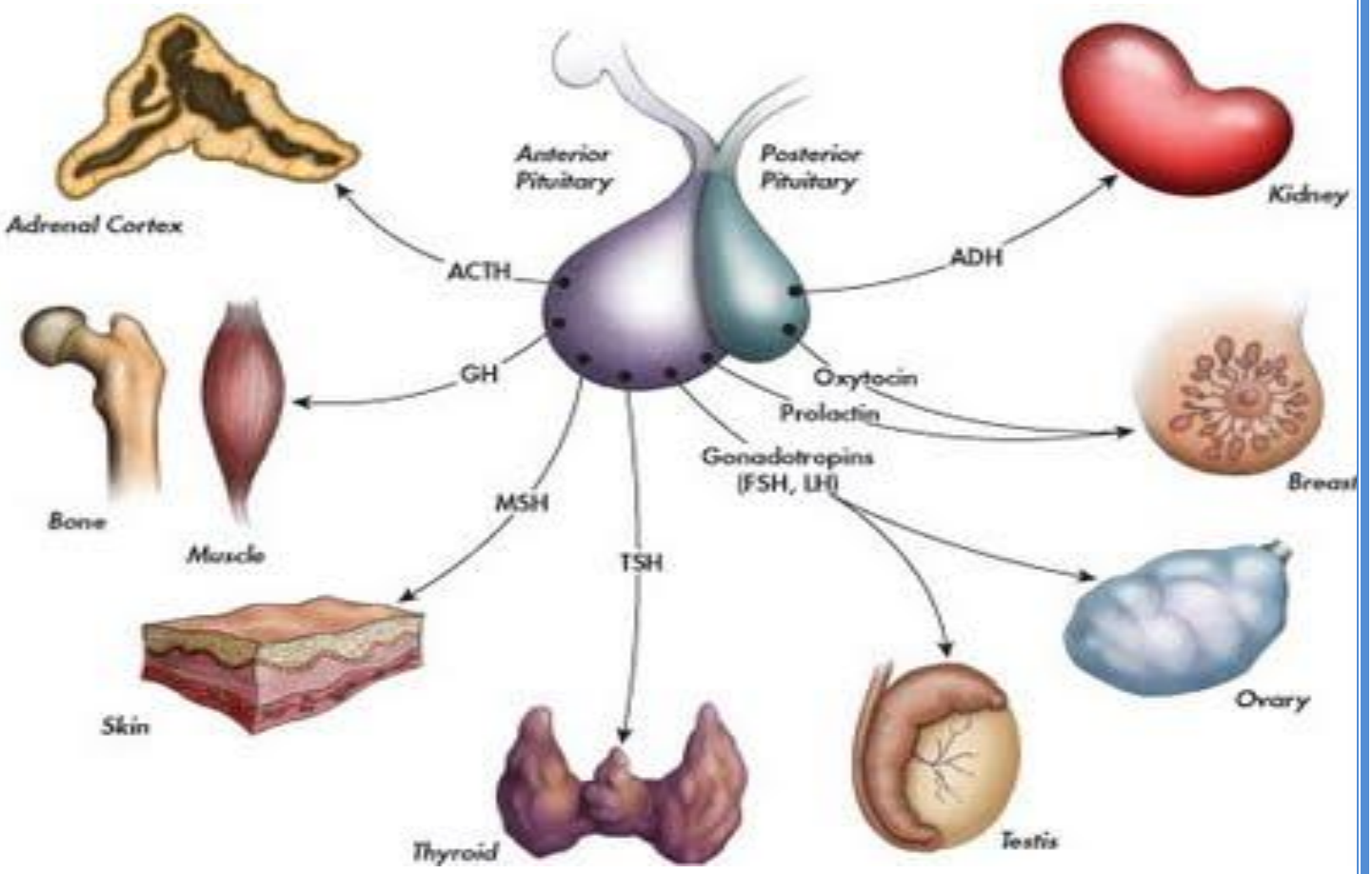
Endocrine Block

10th Lecture

Minralocorticoids



PHYSIOLOGY TEAM – 430

Physiology Team Leaders:

Al-Waleed Al-Johar Layan Akkielah

This Lecture is done by:

Al-Waleed Al-Johar Yara Al-Saif

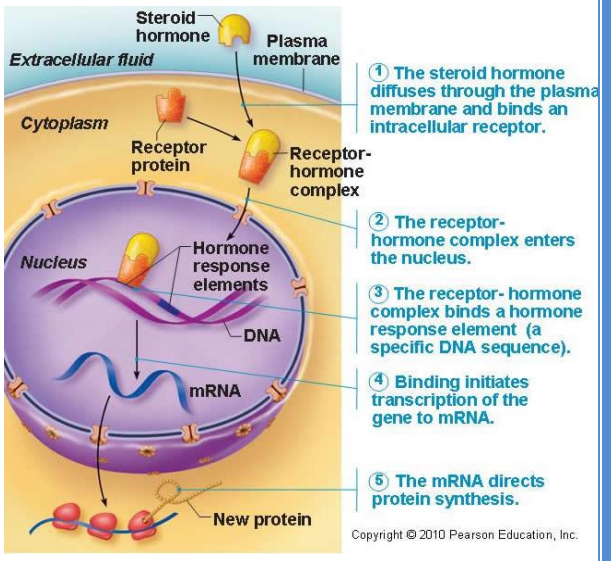
Organized by : Al-Waleed Al-Johar

Mineralocorticoids

- **What is aldosterone?**

- An adrenocortical hormone,synthesised in ZonaGlomerulosa of the cortex of the adrenal gland.

- It is essential for life, for maintaining Na reabsorption, K secretion &maintaining ECF volume.
- Aldosterone levels fluctuate diurnally (24 hours) → highest concentration being at 8 am, lowest at 11 pm, in parallel to cortisol rhythms
- Target cells are called principal cells or P cells.



How does aldosterone cause its actions?

- Aldosterone binds to the mineralocorticoid receptor in renal tubular cells (Principal cells) and, like all steroid hormones, the hormone-receptor complex moves to the nucleus, binds to a DNA element & initiate gene transcription leading to synthesis of new protein.

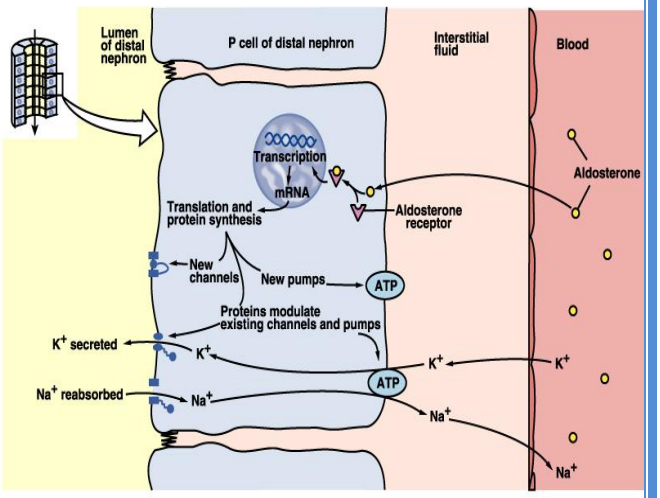
Actions of aldosterone

Na^+-K^+ balance and blood pressure homeostasis. How?

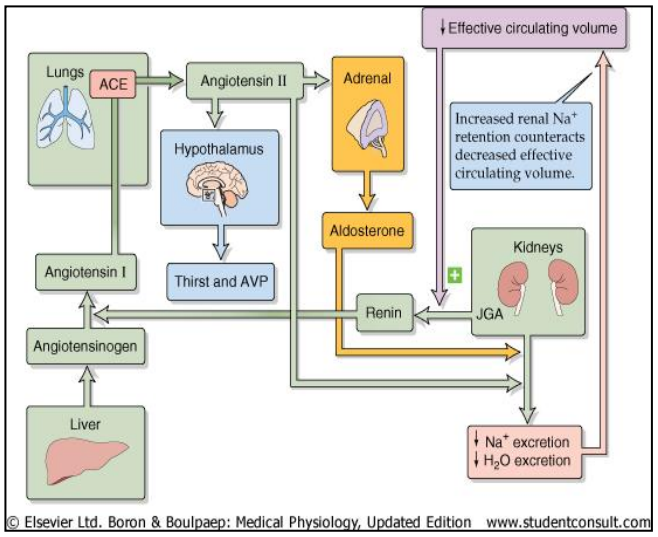
- During formation of urine, at the principal site of action: the **collecting tubules** of the kidney, this is what happens:

✓ 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:**

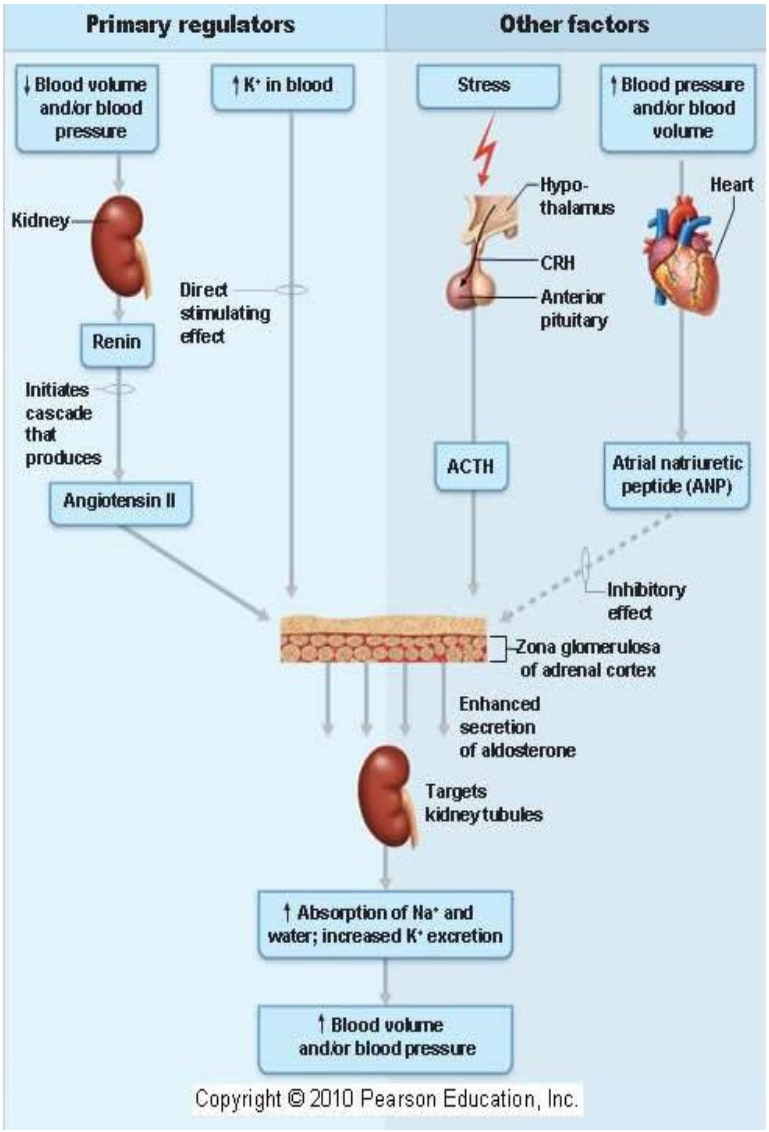


What increases aldosterone secretion?

1) Activation of Renin-Angiotensin-Aldosterone-System (RAAS) by decreased ECF Na^+& decreased ECF volume (hypovolemia)
2) Increased ECF K^+
3) ACTH
   But actually, ACTH primarily promotes the secretion of cortisol, not aldosterone.
   So it is a transient mode & is diminished within several days.

Here's a closer look:

In transient situations of stress it is believed that ACTH provides a tonic control of aldosterone synthesis, and also helps to increase aldosterone secretion



So what would inhibit aldosterone synthesis?

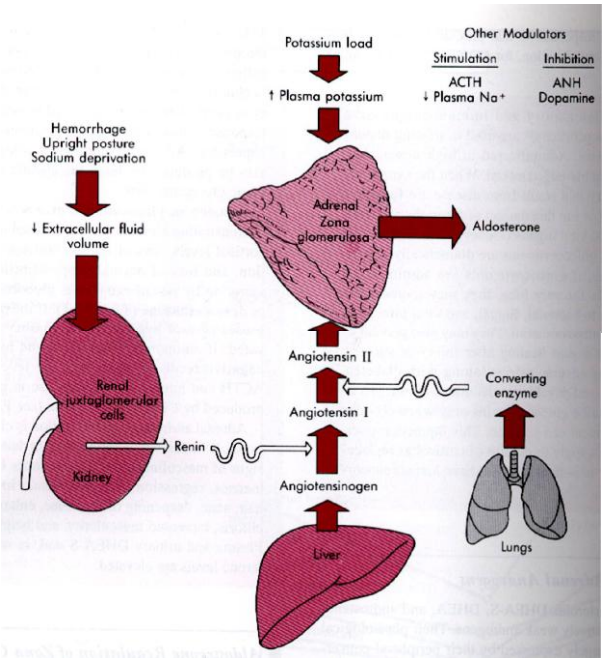
- Overhydration
- Atrial Natriuretic Peptide (ANP)

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

- **Formation of Aldosterone:**

- The juxtaglomerular cells of the kidney respond to hypovolemia by secreting renin
- 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



- **Aldosterone and Electrolytes:**

- Aldosterone stimulates the active reabsorption of Na^+ from the tubular urine back into the nearby capillaries in the distal tubule
- Water is passively reabsorbed with Na^+which maintains Na^+concentrations at a constant level
- Hence extracellular fluid volume expands in a virtually isotonic fashion
- Aldosterone facilitates K^+ Excretion loss from ECF
- Increased ECF K^+stimulates aldosterone synthesis → thus providing a feedback control mechanism to control K^+levels
- Conversely, K^+depletion lowers aldosterone secretion

- **Hypoaldosteronism:**

- Adrenal cortex produces inadequate amounts of hormones- Addison's Disease
- Decreased plasma Na^+ with increased K^+ levels

Causes:

- Autoimmunity against cortices 80%
- Tuberculosis, drugs, cancer/ irradiation

What do we see?

- 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.
- Cardiac toxicity

- **Hyperaldosteronism:**

- Overproduction of aldosterone in conditions such as Conn's syndrome →Na^+& water retention →hypertension
- Conditions of low cardiac output are also known to stimulate synthesis of aldosterone (secondary hyperaldosteronism)
- Both conditions result in Na^+& water retention → sustained hypertension
- The treatment of patients with severe congestive heart failure with spironolactone (mineralocorticoid antagonist) produced significant reduction in mortality and morbidity, despite the very modest diuretic effect of the drug
- The demonstration of local synthesis of aldosterone by cardiac and vascular cells

Clinically:

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

✓ weakness, paresthesia
✓ intermittent paralysis