Endocrine

434 Physiology team
presents to you:

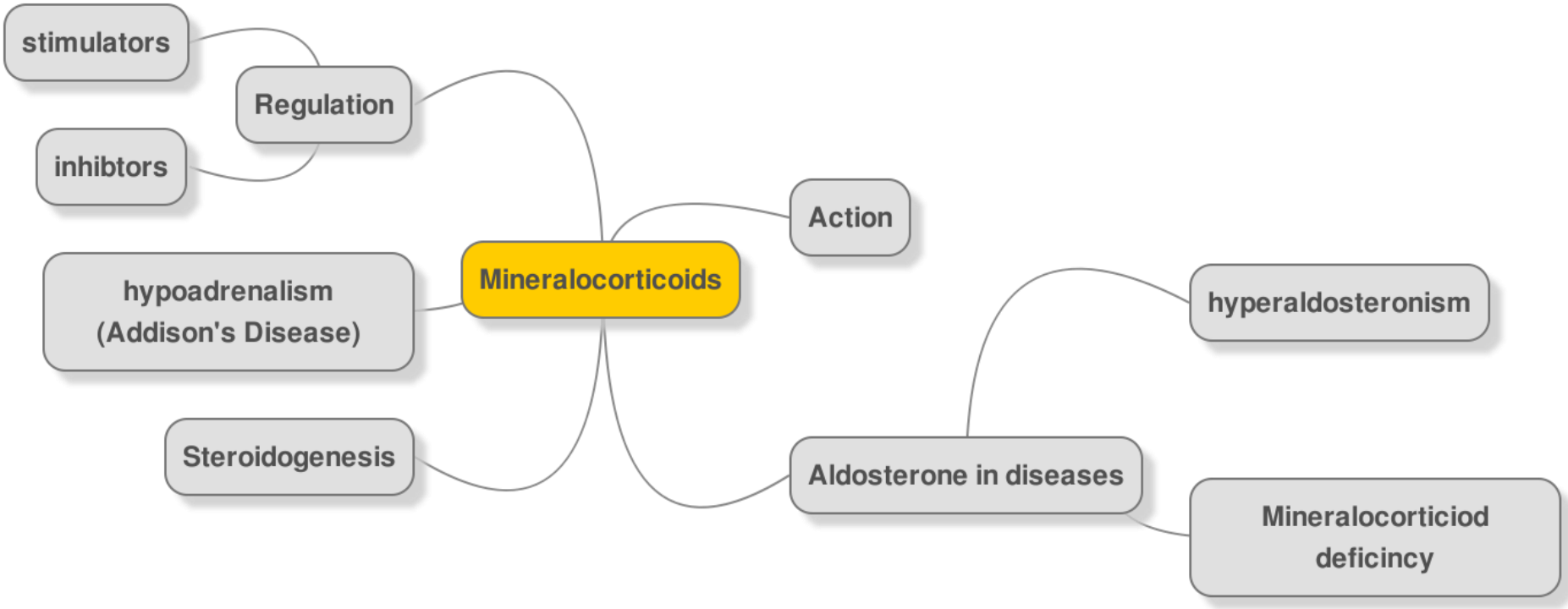
Mineralocorticoids

- Important
- Further explanation
- Based on male slides

Contents

Please check out this link before viewing the file to know if there are any additions/changes or corrections. The same link will be used for all of our work [Physiology Edit]

Mindmap


stimulators
Regulation
inhibtors
hypoadrenalism
(Addison's Disease)
Steroidogenesis
Mineralocorticoids
Action
Aldosterone in diseases
hyperaldosteronism
Mineralocorticiod
deficincy

Mineralocorticoids

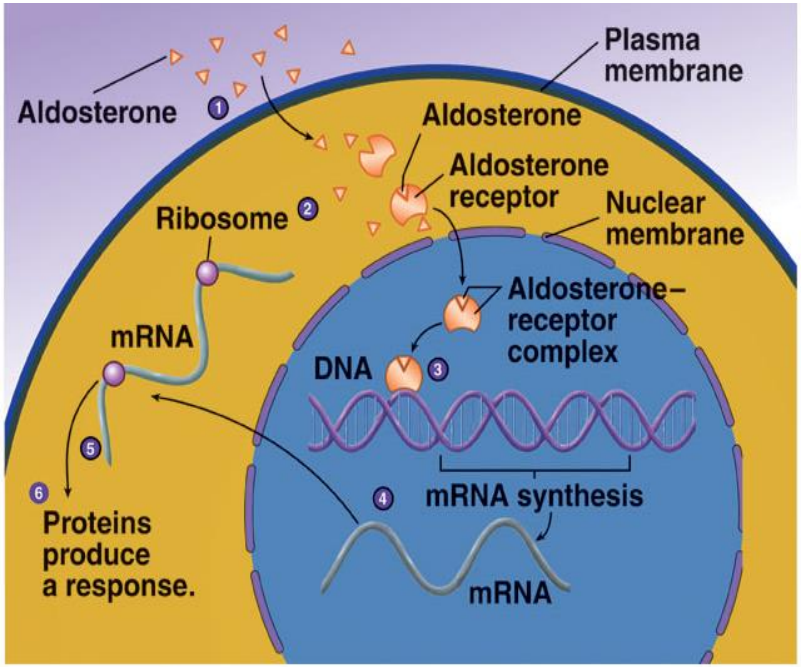
Aldosterone :

- it's an essential steroid hormone secreted from from zona glumerulosa.

- Aldosterone levels are in parallel to cortisol rhythms which are highest during morning (8 AM) and lowest during night (11 PM).

- Aldosterone exerts 90% of the mineralocorticoids activity while cortisol's activity is 10% only (1/400th that of aldosterone), while in plasma cortisol is at 1000 fold higher concentration than aldosterone

Mechanism of Aldosterone action



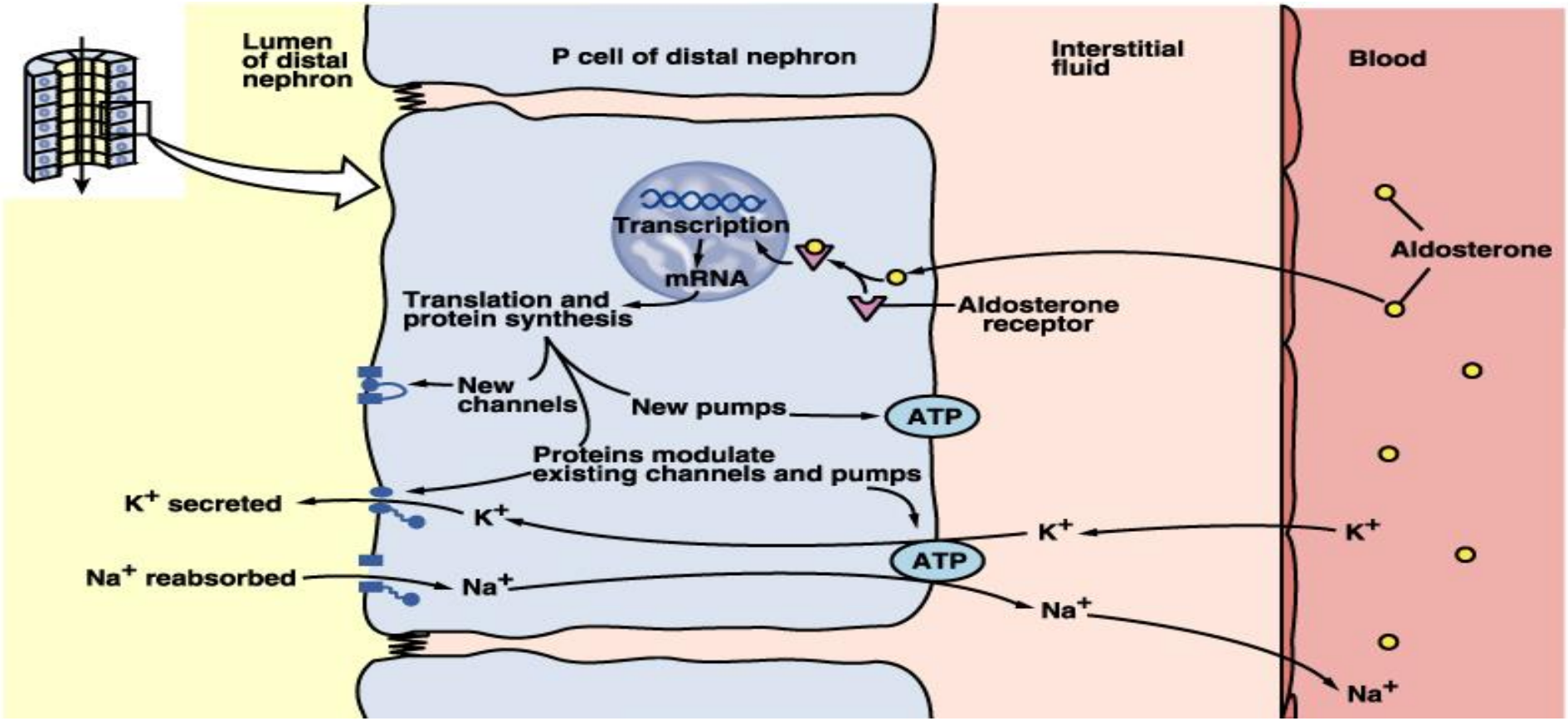
Since Aldosterone is a steroid hormone, it will diffuse easily through the cell membrane and act intracellularly.

It will bind to its receptor on the cytoplasm (aldosterone-receptor complex).

The aldosterone-receptor complex will diffuse into the nucleus and induce the DNA to synthesize mRNA.

mRNA will then produce the protein needed in the cytoplasm with the help of ribosomes

Actions of aldosterone



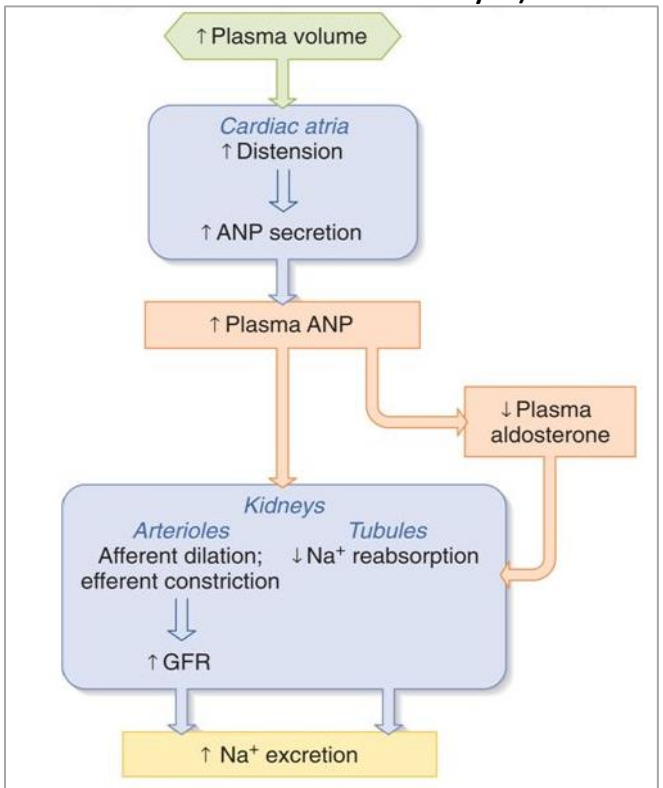
- Aldosterone will increase the reabsorption of sodium in the Principal (P) cells (target cells) of the distal convoluted tubules and the collecting ducts.
- It will also increase the reabsorption of sodium in sweat, salivary and intestinal cells by stimulating the synthesis of more Na/K-ATPase pumps.
- It will stimulate active secretion of potassium and H^+ from distal tubular cells into urine.
- Finally aldosterone will maintain extracellular volume

Regulation of aldosterone

Direct stimulators :

- High plasma potassium level. (less plasma sodium → less H_2O → less blood volume → MORE aldosterone).

- ACTH. (will stimulate the adrenal gland to secrete aldosterone however, ACTH stimulation is more transient than other stimuli & is diminished within several days.)



Indirect stimulators :

- Ang II (RAAS).

RAAS will be activated by renal ischemia.

(will be explained in next slides)

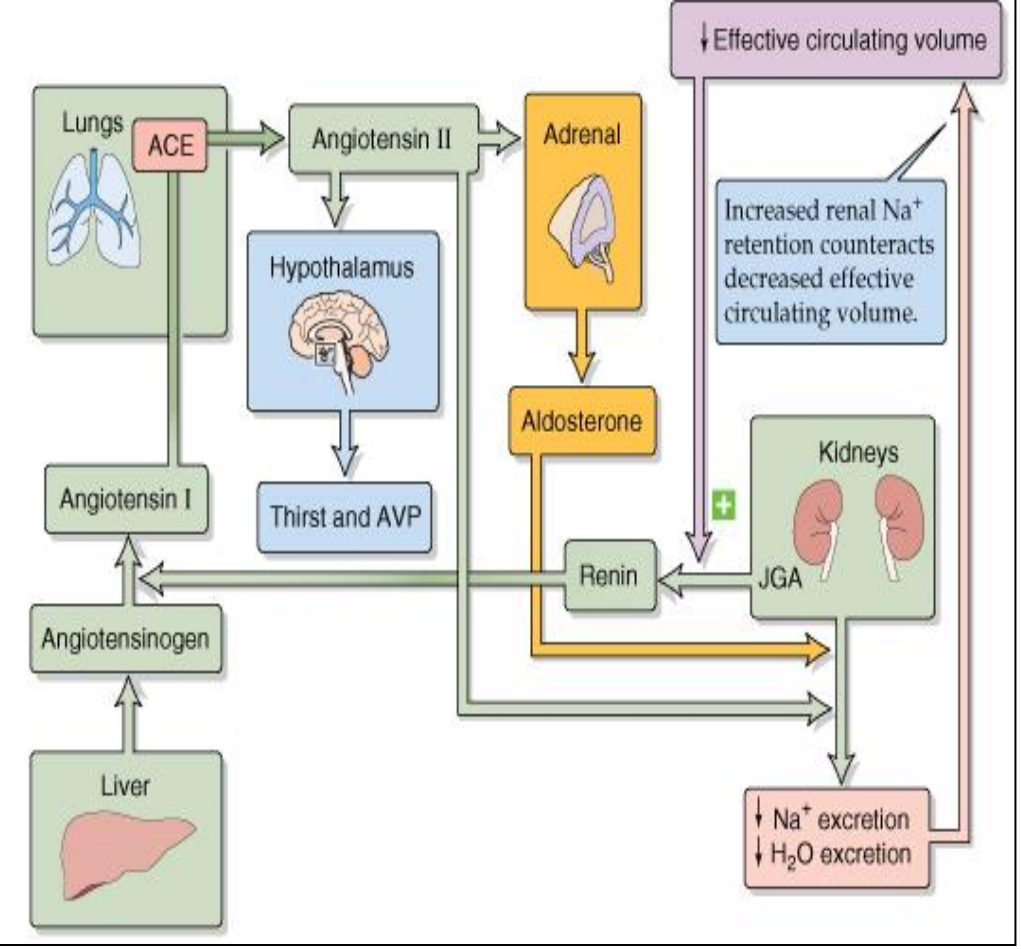
potassium ion concentration and the renin-angiotensin system are by far the most potent in regulating aldosterone secretion.

Inhibitors :

- Atrial natriuretic peptide

Right atrium by its baroreceptors will sense the increase in blood pressure and then release ANP.

ANP will inhibit Renin and Aldosterone→ decreased Na reabsorption



When blood pressure is decreased renin will be released from the Juxtaglomerular cells → it will change angiotensinogen (synthesized by the liver) to Angiotensin I → then ACE will change angI to ang II that will acts on *zona glomerulosa* to stimulate aldosterone synthesis via increased intracellular cAMP which will decrease Na excretion. Dr. Nervana said that ang II can act via cAMP as well as phospholipids mechanisms

Juxtaglomerular apparatus (JGA)

1) Juxtaglomerular Cells

Are smooth muscle cells in the wall of renal arteries act as mechanoreceptors

They respond to decrease in blood pressure of the arteriole → synthesize and secrete renin

2) Macula Densa Cells

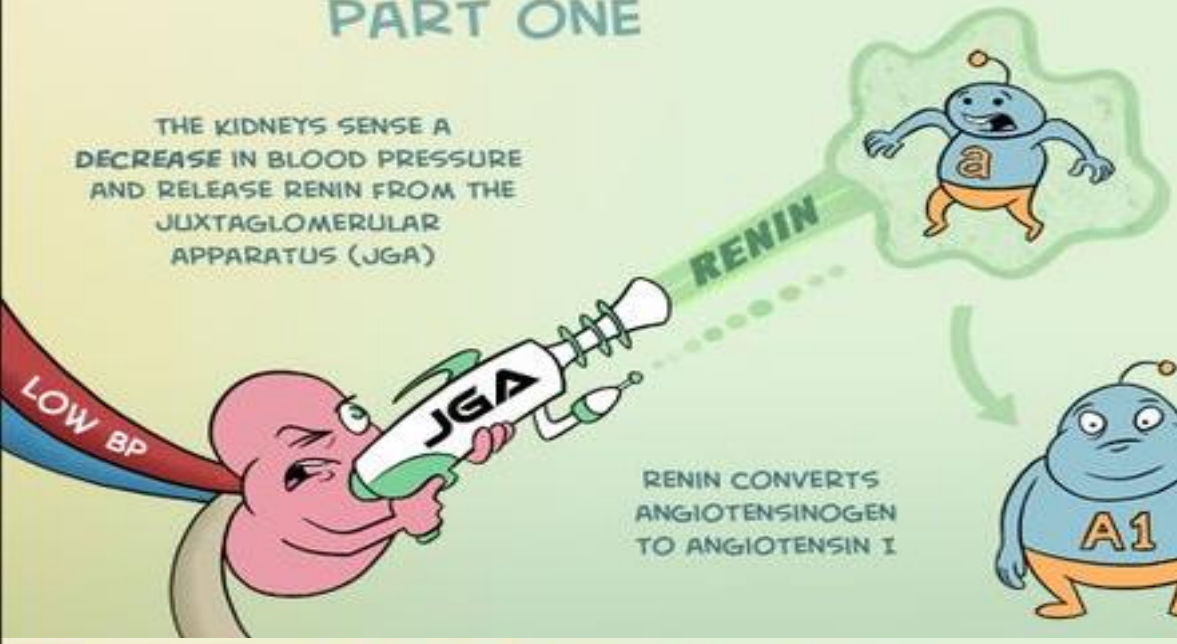
Are chemoreceptors in the distal tubules of the kidneys

Response to changes in Na levels and then send the information to Juxtaglomerular cells to adjust the levels of renin.

RENIN-ANGIOTENSIN SYSTEM

PART ONE

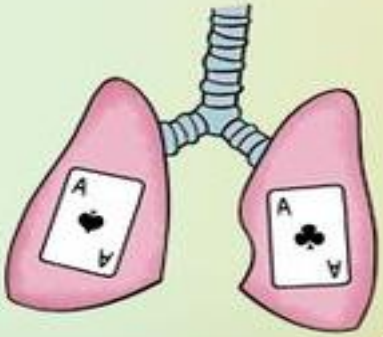
THE KIDNEYS SENSE A **DECREASE** IN BLOOD PRESSURE AND RELEASE RENIN FROM THE JUXTAGLOMERULAR APPARATUS (JGA)



RENIN CONVERTS ANGIOTENSINOGEN TO ANGIOTENSIN I

ACE

IN THE LUNGS, ANGIOTENSIN-CONVERTING ENZYME (**ACE**) CONVERTS ANGIOTENSIN I TO ANGIOTENSIN II



RENIN-ANGIOTENSIN SYSTEM

PART TWO

ANGIOTENSIN II CAUSES VASOCONSTRICTION, RESULTING IN INCREASED BLOOD PRESSURE

ANGIOTENSIN II ALSO STIMULATES THE ADRENAL GLANDS TO RELEASE ALDOSTERONE

WITHIN THE KIDNEYS, ALDOSTERONE PROMOTES THE REABSORPTION OF SODIUM AND WATER

THE CIRCULATING BLOOD VOLUME INCREASES, FURTHER RAISING THE BLOOD PRESSURE

Steroidogenesis

processes by which cholesterol is converted to biologically active steroid hormones

LDLs —> diffuse into the interstitial fluid and attach to **coated pits** on the adrenocortical cell membranes.—> forming vesicles by endocytosis —> fuse with lysosomes and release cholesterol —> cholesterol is delivered to the mitochondria, where it is cleaved by cholesterol desmolase to form **pregnenolone** (The first and rate-limiting step in the synthesis of all steroid hormones) ——> Newly synthesized steroid hormones are **rapidly** secreted from the cell (they are synthesized & secreted on demand -not stored-)

***Steroids are derivatives of cholesterol**

Hypoadrenalism (Adrenal Insufficiency)— **Addison's Disease**

results from an inability of the adrenal cortices to produce sufficient adrenocortical hormones (Glucocorticoid, mineralocorticoid and sex steroids ,, but Aldosterone is the main one), and its most frequently caused by primary atrophy or bilateral destruction of the adrenal cortices.

Causes:

1. Autoimmunity.(causes atrophy in about 80 % of the cases)
2. TB (cause tuberculous destruction of the adrenal glands)
3. Malignancy (lung cancer love to go the Adrenal gland)
4. Radiation.

In some cases, adrenal insufficiency is secondary to impaired function of the pituitary gland, (failure to produce ACTH) → leading to decrease in production of cortisol and aldosterone and atrophy of adrenal (due to lack of ACTH stimulation).

Secondary adrenal insufficiency is much more common than Addison's disease.

Clinical features:

1- bronze pigmintation of skin (in 90% of patients)

(due to ↑ production of POMC by the pituitary , which split to yield **ATCH** + melanocyte stimulating hormone **MSH**)

2-changes of body hair

3-GI disturbances

4-weakness

5-hypoglycemia

6-postural hypotension (due to hypovolaemia and sodium loss, is present in 80–90% of cases)

Might lead to

Addisonian crisis

1. Profound fatigue
2. Dehydration
3. Vascular collapse
4. Renal shut down
5. ↓ serum Na
6. ↑ serum K

Role of Aldosterone in diseases

Complete **failure** to secrete aldosterone

↓

death

↓

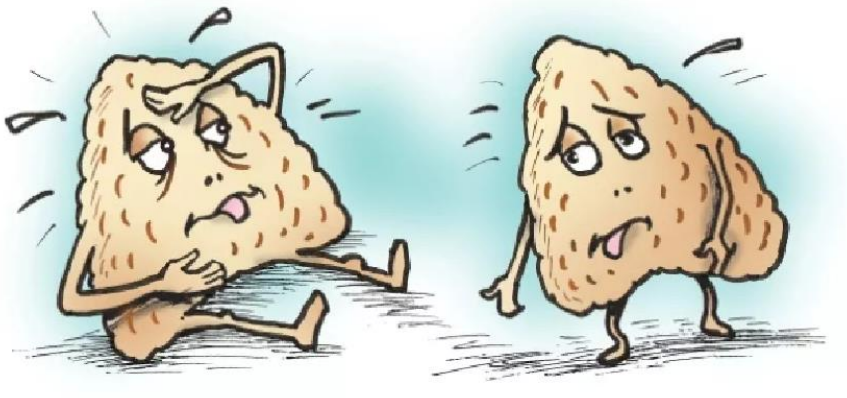
Due to dehydration & low blood volume.

↓

Mineralocorticoid Deficiency

Lack of Aldosterone; leads to:

1. Increased loss of sodium, chloride, water
2. Decrease ECF volume.
3. Hyperkalemia
4. Mild acidosis
5. Plasma sodium decreases and may lead to circulatory collapse, Decrease cardiac output –> shock —> death within 4 days to a 2 weeks if not treated.



Hyperaldosterone states:

↓

Hypertension + ↑ blood volume.

Overproduction of aldosterone

Hyperaldosteronism

Primary

- primay aldosteronism (conn's syndrome)

small tumor of the zona glomerulosa cells
→secretes large amounts of aldosterone.

secondary

- cirrhosis
- ascites
- nephrotic syndrome

Diagnosic tests for Primary Aldosteronism

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

treatment :
1- surgary for adenoma
2-Spironolactone (mineralocorticoid receptor antagonist)

Overproduction of aldosterone

Hyperaldosteronism

The most important effects are:

1-hypokalemia
2-mild alkalosis, due to ↑tubular (intercalated cells) H+ secretion.
3- increase in extracellular fluid volume and blood volume
4-hypernatremia.
5- **almost always hypertension**.
6-heart palpitations
7- intermittent muscle paralysis (due to hypokalemia)
8-headache
9-nocturnal polyuria and polydipsia(small increases in ECF sodium conc. stimulate thirst and increased water intake→ ↑ECF volume → ↑arterial pressure → ↑ kidney excretion of salt and water, called pressure natriuresis and pressure diuresis, despite the excess aldosterone this mechanism is referred to as Aldosterone escape)
10-hand & muscle cramping
11-weakness, paresthesia (tingling of fingers).

Summary

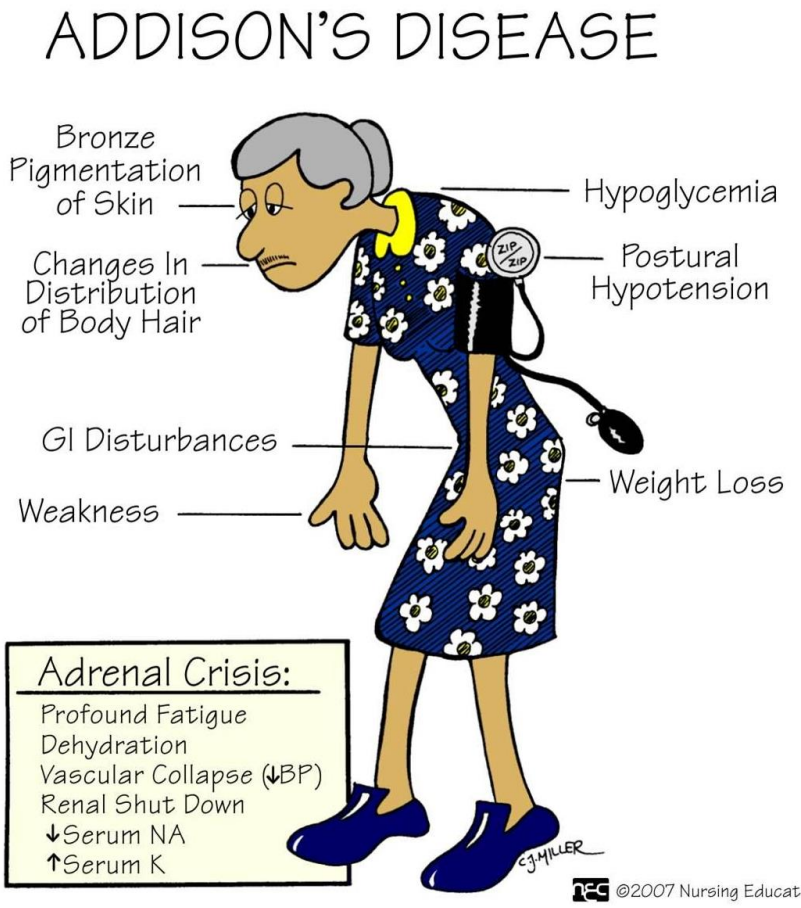
Excess aldosterone

-increase extracellular fluid volume and arterial pressure (hypertension)
-hypernatremia
-hypokalemia and muscle weakness
-alkalosis

aldosterone Deficiency

-decrease extracellular fluid volume, dehydration and low blood volume (↓ CO) —> shock like state —> death (3D - 2W)

-hyperkalemia and cardiac toxicity



Answer key: 1-C, 2-A, 3-B, 4-C, 5-B, 6-A, 7-D, 8-A

MCQs

1- Are modified smooth muscle cells in the wall of afferent arteriole
A.Macula densa cells
B.ACE
C.Juxtaglomerular cells
D.P cells

2-Aldosterone is secreted by
A.Zona glomerulosa
B.Zona reticularis
C.Zone fasciculata
D.Macula densa

3-RAAS system is
A.Direct stimulator
B.Indirect stimulator
C.Direct inhibitor
D.Indirect inhibitor

4-Aldosterone will
A.Increase secretion of Na
B.Increase secretion of H2O
C.Increase excretion of K
D.Decrease excretion of H

5-Mineralocorticoid Deficiency leads to
A. Hypokalemia
B. Decrease ECF volume.
C. Mild Alkalosis
D. Non of the above

6- primay aldosteronism is caused by:
A. small tumor of the zona glomerulosa cells
B. cirrhosis
C. small tumor of the zona fasciculata cells
D. autosomal recessive disease

7- Addison's Disease Is due to:
A. Malignancy
B. Autoimmunity
C. Hyperplasia of the adrenal cortices
D. A & B

8- which one is true about Steroidogenesis?
A. Cholesterol is cleaved by cholesterol desmolase
B. cholesterol is delivered to Golgi apparatus
C. Steroids are derivatives of amino acids
D. New steroids hormones are slowly secreted from cell

SAQs

Q1:Name the 3 layers of the adrenal cortex and their hormones.

Ans: zona fasciculata →Glucocorticoids.
Zona glumerulosa →Mineralocorticoids.
Zona reticularis → Androgens.

Q2:Name 2 Actions of Aldosterone.

Ans:1- Active reabsorption of Na and H2O
2- Active secretion of K and H

Q3:How does ANP work in regulation of Aldosterone secretion ?

Ans:Baroreceptors in atrium will sense the increase in BP and release ANP that will inhibit Renin and Aldosterone.

Q4:whats the role of Aldosterone in diseases ?

Ans: 1-hyperaldestron state →HTN + increase blood volume
2-failure of secretion → dehydration + low blood volume → death

Q5:types of Hyperaldosteronism

Ans: - Primary → conn's syndrome
- Secondry → cirrhosis, ascites, nephrotic syndrome

Q6:what are the tests Confirming Primary Aldosteronism

Ans: 1-Plasma supine aldosterone at 0800h
2-Urinary aldosterone metabolites
3-NaCl infusion/suppression test

Thanks for checking our work

Good Luck

Done by:

Nourah AlShathri

Malak AlKahtani