ADRENAL GLAND: ALDOSTERONE

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OUTLINE

I) ADRENAL GLAND ANATOMY

(1) In the abdominal cavity

- below the diaphragm
  - The liver is on the right side
  - The spleen is on the left side
- Below them are located the two kidneys

(2) The adrenal glands

- sit on top of the kidneys
  - Also called **suprarenal glands**
  - Have a roughly pyramid shape

(3) Parts of the adrenal gland

- Cortex
  - Has three layers
    - **Zona glomerulosa**
      - Most superficial
    - **Zona fasciculata**
      - In the middle
      - The thickest
    - **Zona reticularis**
      - The deepest
  - All layers are mostly **glandular cuboidal epithelial tissue**
- **Medulla**
  - Has only one layer
  - Made up of **neural tissue**

II) STIMULI AND INHIBITORS

(A) LOW BLOOD PRESSURE

(1) The strongest stimulus

- of zona glomerulosa

(2) Low blood pressure causes

- the **juxtaglomerular cells** (JG cells) in the kidneys produce a specific chemical – **renin**
- The liver produces a protein – **angiotensinogen**
  - Renin acts on the angiotensinogen
    - Cuts a specific portion of it
    - Converts it into **angiotensin I**
- In the lungs there is an enzyme - **angiotensin converting enzyme** (ACE)
  - Converts angiotensin I into **angiotensin II** (ATII)

(3) ATII goes

- to zona glomerulosa of the adrenal cortex
- Binds to a G protein-coupled receptor
  - Triggers an intracellular cascade

(4) It activates a G stimulatory protein

- that goes to an effector enzyme on the cell membrane – Adenylate cyclase
  - The effector enzyme has a specific point of attachment for the Gs protein
  - The effector enzyme becomes very active

(5) Adenylate cyclase

- has a specific enzyme – GTPase
  - GTPase cuts the GTP and turns it into GDP
  - Energy is produced and used to convert ATP to cAMP
  - cAMP activates protein kinase A (pkA)

(B) HYPONATREMIA AND HYPERKALEMIA

(1) The second strongest stimulus

- of aldosterone synthesis
  - The condition extremely dangerous

(2) Zona glomerulosa cells

- are very sensitive
  - **Low sodium** levels in the blood
    - Hyponatremia
  - **High potassium** levels in the blood
    - Hyperkalemia
- ↓ Na^+ levels and ↑ K^+ levels exert a specific type of stimulus

(C) ACTH

(1) The weakest stimulus

- of zona glomerulosa

(2) The paraventricular nucleus

- in the hypothalamus secrete **corticotropin-releasing hormone** (CRH)
- CRH goes in the **hypophyseal portal system**
  - ➢ The vascular connection between the hypothalamus and the anterior pituitary (**adenohypophysis**)

(3) CRH stimulates

- specific cells - the **corticotropes** in the adenohypophysis to secrete **adrenocorticotropic hormone** (ACTH) into the bloodstream

(4) ACTH goes

- to the adrenal cortex
- Binds to a g-protein coupled receptor
  - Triggers an intracellular cascade

(5) It activates a G stimulatory protein

- that goes to an effector enzyme on the cell membrane – Adenylate cyclase
  - The effector enzyme has a specific point of attachment for the Gs protein
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(6) Adenylate cyclase

- has a specific enzyme – GTPase
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(D) ATRIAL NATRIURETIC PEPTIDE

(1) An inhibitor for

- the synthesis of aldosterone is
  - Secreted when the blood pressure is high
- Binds to specific receptors
  - Activates a G inhibitory pathway
    - Results in **potassium efflux** out of the cell
      - → **Hyperpolarization** of the cell
        - → Alters the enzymatic activity within the cholesterol pathway
          - → The overall effect is an **inhibitory effect** on aldosterone synthesis

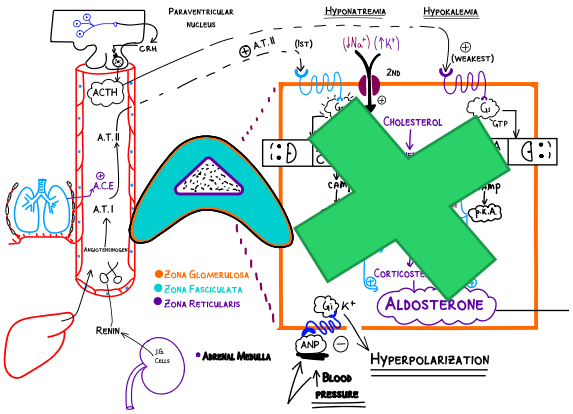

Figure 1 Stimuli and inhibitors of zona glomerulosa.

III) ALDOSTERONE SYNTHESIS

(1) In the adrenal cortex

- steroid hormones are synthesized
  - This synthesis requires cholesterol as a basic unit
- **Cholesterol** is converted to pregnenolone
  - → **Pregnenolone** is converted to progesterone
  - → **Progesterone** is converted to 11-deoxycorticosterone
    - by **21-hydroxylase**
  - → **11-deoxycorticosterone** is converted to corticosterone
  - → **Corticosterone** is converted to **aldosterone**
- Each step in this pathway is regulated by specific enzyme

(2) The activated pkA

- activates by phosphorylation the enzymes catalyzing this pathway
  - On multiple steps

(3) Cortisol is released into the bloodstream

- It is a steroid hormone
  - needs to bind to specific proteins for transportation
    - Mostly it binds to **corticosteroid binding globulin** (CBG)
      - A.k.a. transcortin
    - Sometimes it binds to **albumin**
      - A protein synthesized by the liver

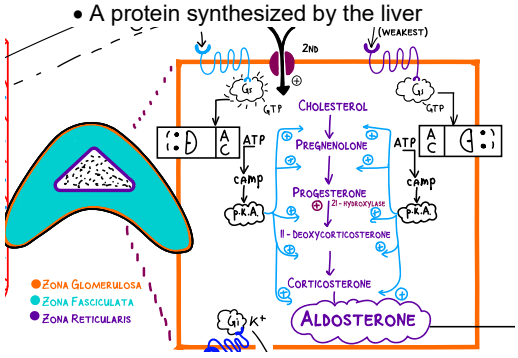

Figure 2 Aldosterone synthesis.

IV) EFFECTS OF ALDOSTERONE

(1) Aldosterone goes

- To the the cells of the **distal convoluted tubule** (DCT)
  - Of the nephron

(2) As a steroid hormone

- cortisol passes through the lipid bilayer of the cell membrane
- Binds to an intracytosolic receptor
  - Activates it

(3) The activated receptor activates

- 3 specific gene sequences expressed in the nucleus
- Those sequences are transcribed
  - Producing three different mRNA
- mRNA goes into the cytoplasm
  - The ribosomes translate it into three different proteins
    - That embed into the cell wall

1) **Sodium-potassium ATPase**
   - Its function is to pumps
     - $3Na^+$ out of the cell
     - $2K^+$ into the cell
   - Utilizes ATP
2) **Protein channels for Na^+** into the luminal membrane
   - Bring Na+ from the filtrate into the cell
   - From the cell it goes into the blood
     - In response to the hyponatremia stimulus
   - It can also take part in the function of the sodium-potassium ATPase
   - "Water follows sodium"
   - → ↑ the blood volume
   - → ↑ the blood pressure
     - In response to the strongest aldosterone synthesis.
3) **Protein channels for K^+** into the luminal membrane
   - Move potassium that comes from the blood from the cell into the filtrate
     - To be lost in the urine.
       - In response to the hyperkaliemia stimulus

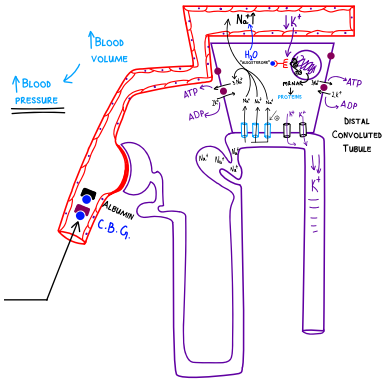

Figure 3 Effects of aldosterone.

V) REVIEW QUESTIONS

1) Which is the outer layer of the adrenal cortex?
a) Zona fasciculata
b) Zona reticularis
c) Zona glomerulosa
d) Zona pellucida

2) Which is the middle layer of the adrenal cortex?
a) Zona reticularis
b) Zona glomerulosa
c) Zona fasciculata
d) Zona pellucida

3) What tissue is the adrenal medulla made of?
a) Epithelial
b) Neural
c) Connective
d) Muscle

4) What do the JG cells produce?
a) ACE
b) Angiotensinogen
c) Renin
d) Angiotensin 2

5) Where does ACE come from?
a) Liver
b) Kidneys
c) Lungs
d) Adrenal gland

6) What is the second strongest stimulus of aldosterone synthesis?
a) Hyperkalemia and hyponatremia
b) Hypernatremia and hypokalemia
c) Hypercalcemia and hypokalemia
d) Hypocalcemia and hyponatremia

7) What are the effects of aldosterone?
a) Rising blood pressure and blood volume
b) Lowering of serum potassium level
c) Increase in serum sodium level
d) Everything of the above is true

8) Which of the following is the weakest stimulus of the Zona glomerulosa?
a) Low blood pressure
b) ACTH
c) Low serum sodium level
d) Low serum renin level

9) What does the atrial natriuretic peptide inhibit?
a) Aldosterone
b) Renin
c) ACE
d) ACTH

10) What is the basic unit that aldosterone requires for its synthesis?
a) Albumin
b) Testosterone
c) Cortisol
d) Cholesterol

CHECK YOUR ANSWERS

VI) REFRENCES