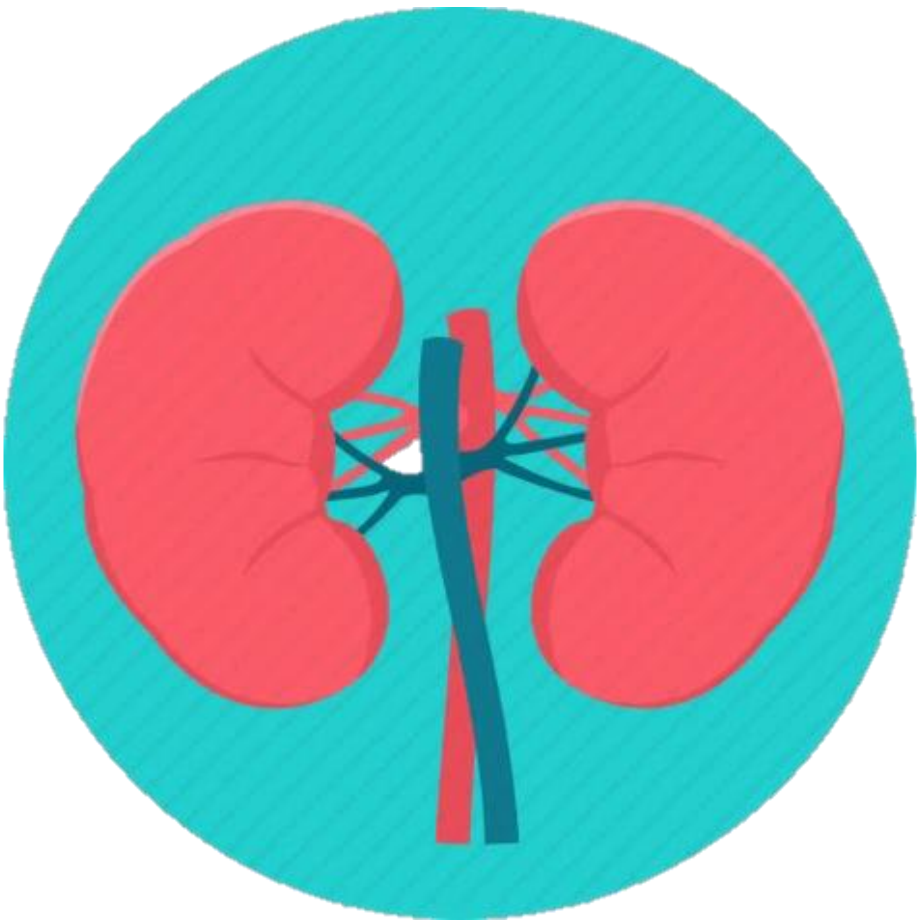
جامعة الملك سعود
King Saud University

MED438
KING SAUD UNIVERSITY

Lecture (7)

Regulation of Fluids



Index:

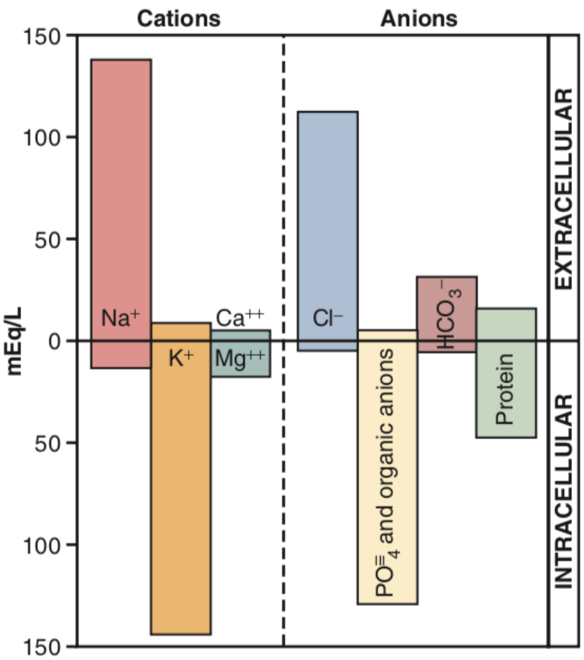
- Text
- Important
- Extra
- Editing file

Physiology

MED438

Osmolarity

- Maintaining normal ECF **volume** and **osmolarity** is crucial
- Normal ECF **volume** is important in maintaining ABP and tissue perfusion
- Normal ECF **volume** is controlled by adjusting NaCl content
- Normal ECF **osmolarity** is important in maintaining cellular volume & function
- Normal ECF **osmolarity** is controlled by adjusting water content
- Two separate yet interrelated control systems regulate ECF volume & osmolarity.



In the ECF

Most abundant cation

Na^+

Most abundant anion

Cl^- and **HCO^{3-}**

Why is Na+ Content the Main Determinant of ECF Volume?

- Sodium and its associated anions are the main constituents of the ECF
- When Na^+ salts move, water must follow

⇑ Na^+ → ⇑ ECF osmolarity → ⇑ H_2O reabsorption → ⇑ ECF volume

- This increase in ECF volume will increase MAP which has a harmful consequence on the body, so Na^+ levels must be regulated

⇑ ECF volume → ⇑ CO → ⇑ MAP

A rough estimate of ECF osmolality can be obtained by doubling Na^+ conc.

ECF Osm = Na^+ Osm x <u>2.1</u> = 142 x 2.1 = 298 mOsm ≈ 300 mOsm

- In clinical situations glucose (diabetes) & urea (chronic renal disease) concentrations must be taken into account. (more in Guyton p.381)

Regulation of Osmolality

- If ⇑ water intake → hypoosmotic urine
  - **Diluted** ≈ 50 mOsm
  - **Large volume** ≈ up to 18 L/day
- If ⇓ water intake → hyperosmotic urine
  - **Concentrated** ≈ 1200 mOsm
  - **Small volume** ≈ as low as 0.5 L/day
- Renal water excretion mechanism is independent of solutes.
- It can allow water to be excreted without damaging solutes homeostasis

Sodium Balance & Regulation

- The body regulates ECF volume by monitoring and adjusting total body content of Na+
- ECF volume is closely linked to Na+ balance.
- Sodium intake is usually 1.5-2.3 g/day (healthy diet)
- Sodium is mainly excreted by the **kidney**
- GI and sweat are <u>minor</u> sodium excretory pathways

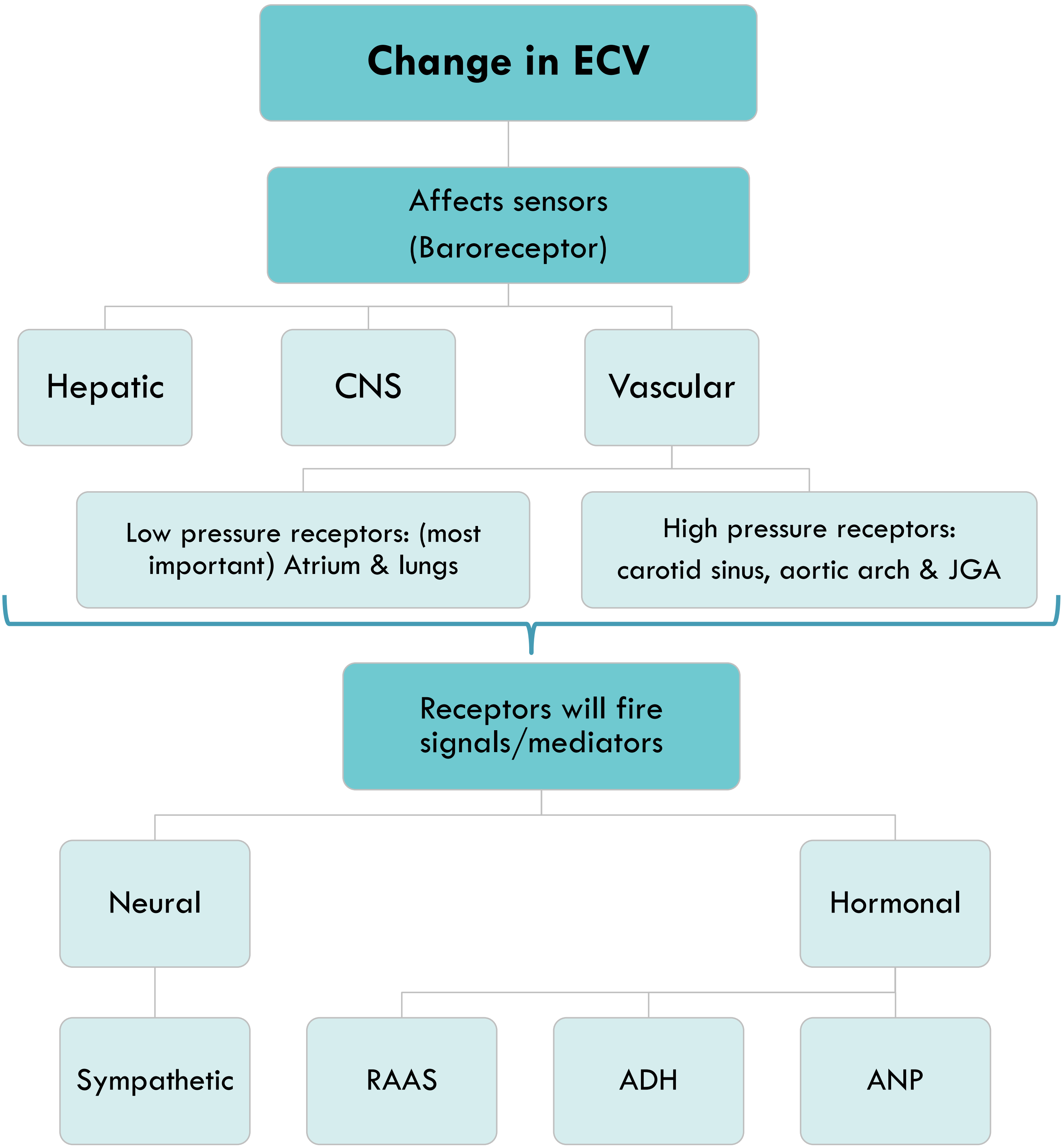
Sodium Distribution in the Body		
Exchangeable		Non-exchangeable
ECF (65%)	ICF (5-10%)	Bones (25-30%)

- The signal that triggers sodium excretion is the ECF volume specifically the effective circulating volume (ECV)
- **Effective circulating volume** is a blood volume that reflects the extent of tissue perfusion is specific region (volume of blood effectively perfusing the tissue)
- Usually any change in ECV changes the ECF

⇑ ECV → trigger Na^+ excretion → ⇓ ECF

⇓ ECV → trigger Na^+ retention → ⇑ ECF

ECV Regulation



Sympathetic Nervous System

- It has a very important role in ECV regulation especially during **stressful** situation such as hemorrhage
- It has direct/indirect effects on the ECV:

  1) **Direct:**

     ➔ Afferent & Efferent arteriole constriction (⇑ renal vascular resistance)

     ➔ ⇓ GFR → ⇓ Na^+ filtration

     ➔ ⇑ Na^+ reabsorption in PCT

  2) **Indirect:**

     ➔ Renin release (⇑ Ang II & ⇑ Aldosterone)

⇓ ECV → Arteriole constriction → ⇓ GFR → ⇓ Na^+ & water excretion

⇑ ECV → Arteriole dilation → ⇑ GFR → ⇑ Na^+ & water excretion

Atrial Natriuretic Peptide (ANP)

- Released from atrial myocytes in response to stretch
- ANP promotes natriuresis (Na^+ excretion)
- Increase in blood volume will stretch the atrium which will release ANP

⇑ ECV → ⇑ ANP release → ⇑ Na^+ & water excretion

⇓ ECV → ⇓ ANP release →⇓ Na^+ & water excretion

It is an antagonist of renin-angiotensin:

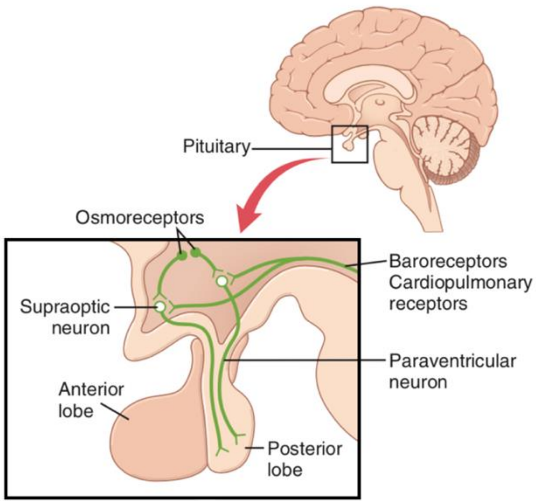
1- ⇓ renin release
2- ⇓ aldosterone release
3- ⇓ Na^+ reabsorption in CD
4- ⇓ ADH release

Antidiuretic Hormone (ADH)

- ADH or vasopressin is a small protein hormone that has a fast-acting short half-life action. It has two main functions:
  1) Water & urea reabsorption **2) Stimulate thirst centers**

ADH is synthesized in the neuroendocrine cells located within the supraoptic and paraventricular nuclei of the **hypothalamus**

- The hormone is packaged in vesicles and stored in the neurohypophysis or the **posterior pituitary gland**

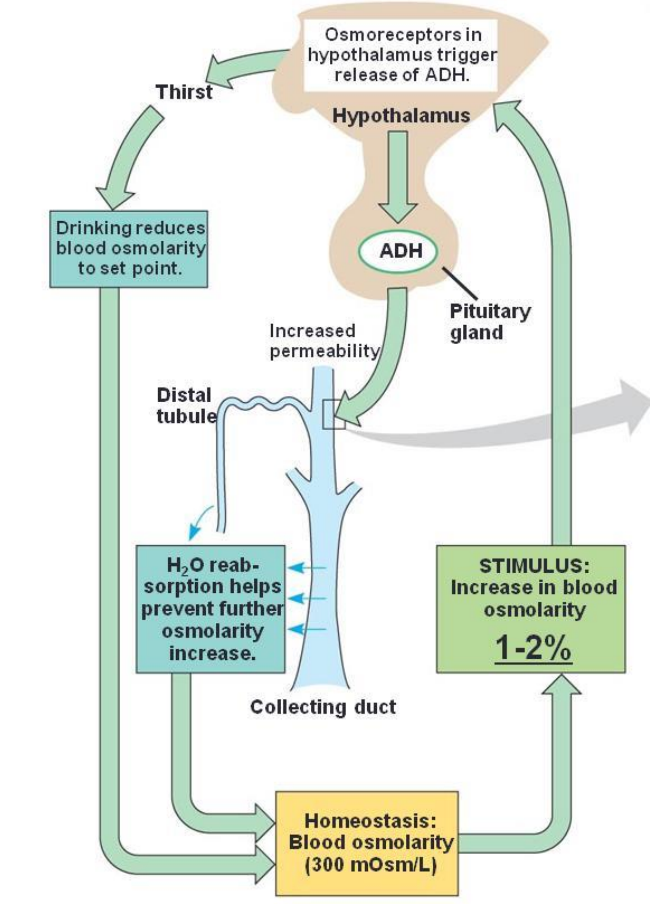


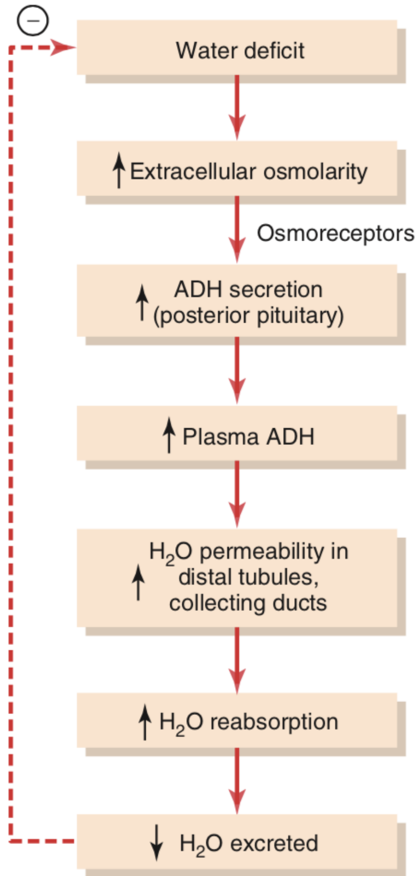
- ADH release and thirst centers are influenced by the following:
  1) Osmolality: 1% increase → ⇑ ADH release
  2) Hemodynamic factors: 5-10% decrease in BP/BV → ⇑ ADH release
  3) Other minor factors

Stimulate ADH	Inhibit ADH
Nausea, hypoxia, Ang II Drugs: morphine, nicotine	ANP Drugs: alcohol

- Thirst is quenched as we drink water by 2 negative feedbacks
  1) Moistening of mouth mucosa
  2) Stretch of stomach and intestines

ADH Action

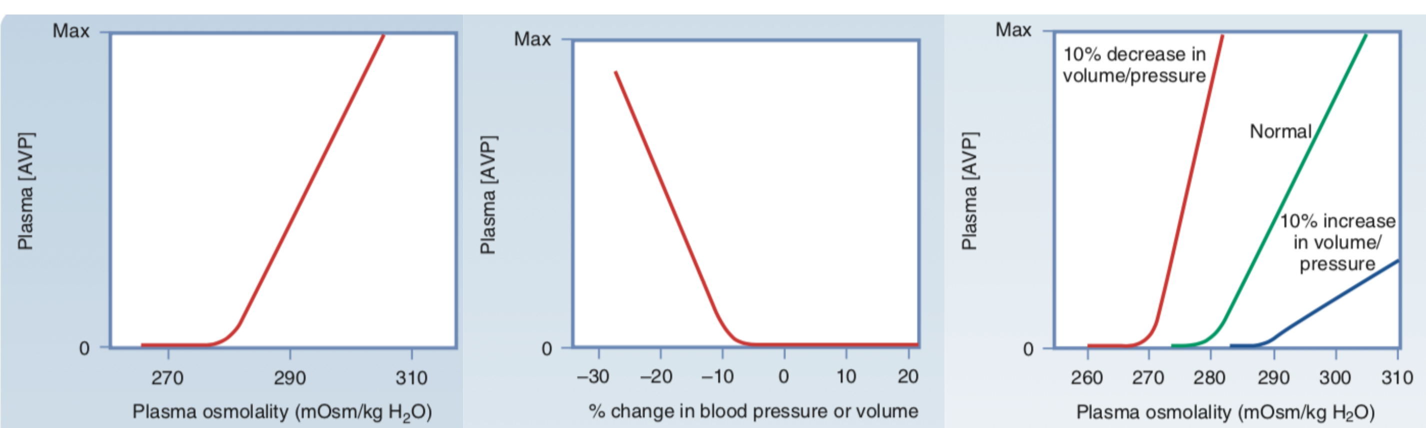




ADH Set Point

- As we said osmolality and hemodynamic factors (blood volume) are the most important triggers for ADH release, each have a setpoint (were its effect starts)

Osmolality setpoint = 280-285 mOsm   BV setpoint = 5-10% decrease

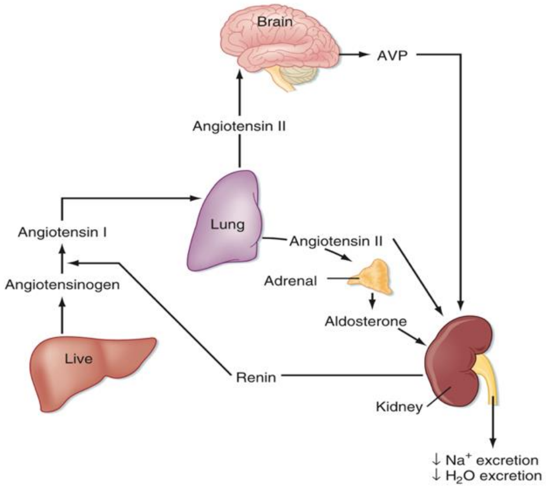


RAAS: Renin-Angiotensin-Aldosterone System

- RAAS system is mainly stimulated by the decrease in ABP (ECF volume)

  ⇓ ABP → ⇓ NaCl delivery to macula densa → Release of renin by JG cells

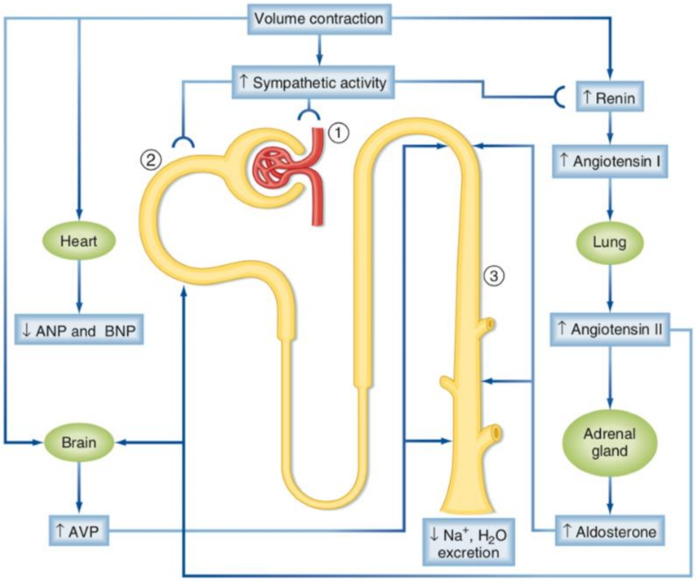
- Renin Secretion is stimulated by:
  1) Sympathetic stimulation
  2) ⇓ in perfusion pressure (MAP)
  3) ⇓ NaCl reaching the macula densa

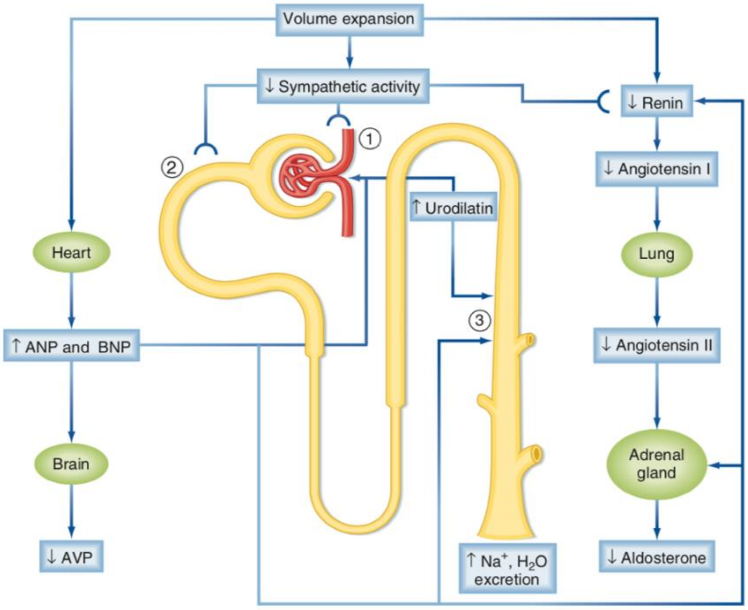


- Angiotensin II is the final product in the RAAS system

- **Angiotensin II has 4 main functions:**
  1) Release aldosterone → increase Na^+ absorption in TAL, DT, and CD
     → the receptor is found in the zona glomerulosa of the adrenal cortex
  2) Vasoconstriction → ⇑ ABP
  3) ADH release → water and urea reabsorption in CD
  4) ⇑ Na^+ reabsorption in PCT

Summary





Increase ADH	Decrease ADH
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
Nausea	
Hypoxia	
Drugs:	Drugs:
Morphine	Alcohol

Increase Thirst	Decrease Thirst
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin II	↓ Angiotensin II
Dry mouth	Gastric distention

Quiz

1. **Which of the following structures stores ADH?**

   A. Neurohypophysis
   B. Hypothalamus
   C. Anterior pituitary gland
   D. Supraoptic neural nuclei

2. **Which of the following is the MAIN trigger of ADH release?**

   A. Nausea
   B. Hypoxia
   C. Osmolality
   D. Blood pressure

3. **Which of the following is an action of Angiotensin II?**

   A. Decrease water reabsorption
   B. Increase K^+ reabsorption
   C. Afferent constriction
   D. Increase BP

4. **Which of the following is an indirect neural effect to regulate ECV?**

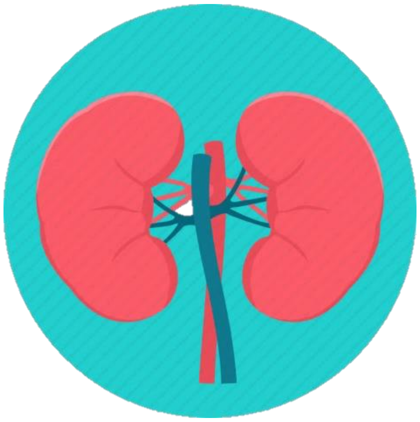
   A. Release renin
   B. Decrease Na^+ reabsorption
   C. Increase renal vascular resistance
   D. Increase Na^+ reabsorption

5. **What is the plasma Osm in a normal person with Na Osm of 135 mOsm?**

   A. 250 mOsm
   B. 270 mOsm
   C. 290 mOsm
   D. 300 mOsm

Answers: A, C, D, A, B

Thank You



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