جامعة الملك سعود
King Saud University

Index:
- Important
- Extra information
- Doctor's notes
- Only in female slides
- Only in male slides

Renal Regulation of Body Fluids

Lecture 7

RENAL BLOCK

PHYSIOLOGY TEAM 437

Editing file

Objectives:

by the end of this lecture you will be able to:

- Identify and describe the role of the Sensors and Effectors in the renal regulation of body fluid volume & osmolality
- Describe the role of the kidney in regulation of body fluid volume & osmolality
- Understand the role of ADH in the reabsorption of water and urea
- Identify the site and describe the influence of aldosterone on reabsorption of Na+ in the late distal tubules.

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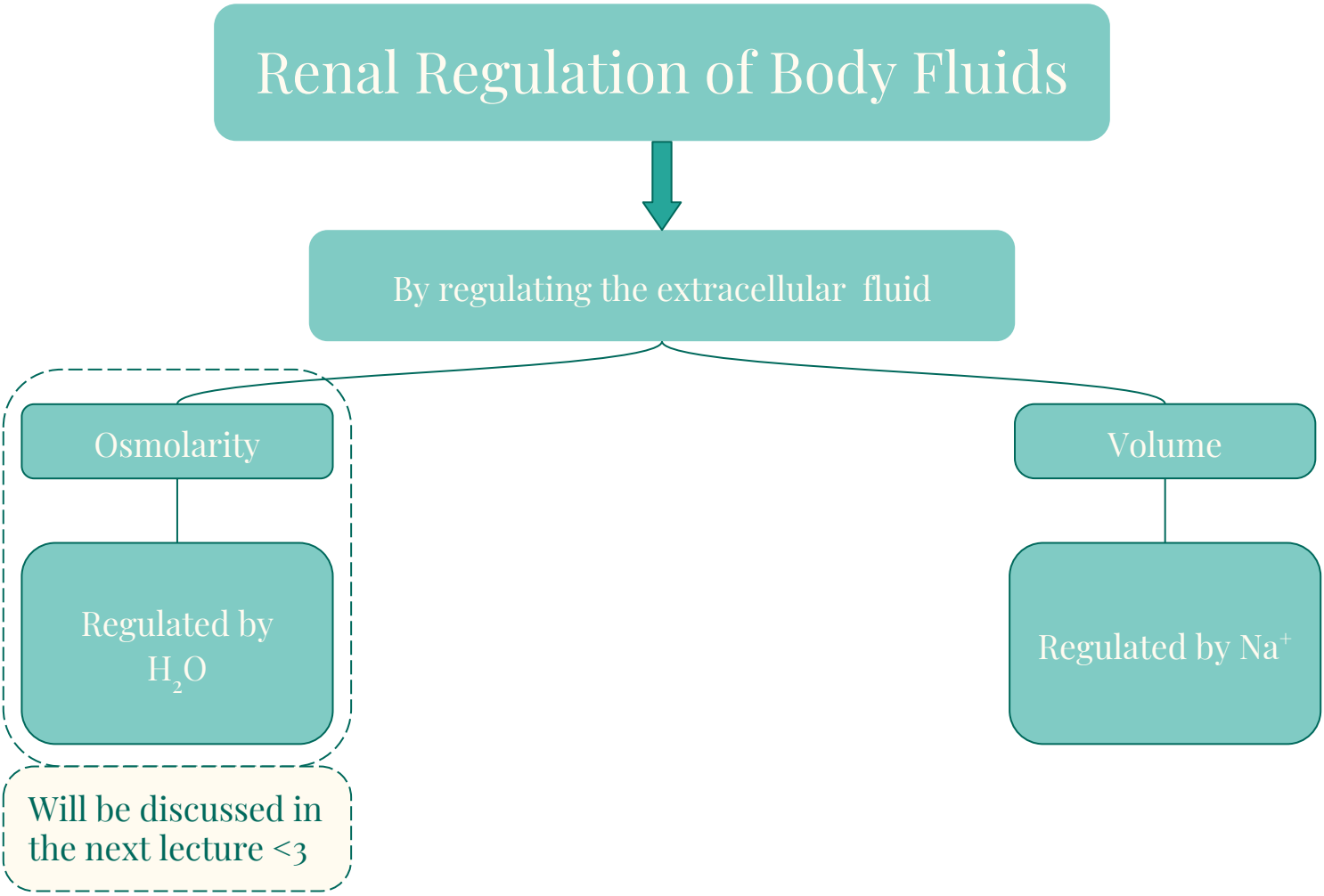
OVERVIEW



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Introduction

- Maintaining normal ECF ***volume*** and ***osmolarity*** is crucial for the well-being of human beings.
- Normal ***ECF volume*** is important for maintenance of normal ABP which ensures adequate tissue perfusion.
- Normal ***ECF osmolarity*** is crucial for maintenance of normal cell volume & function.
- Two separate yet interrelated control systems regulate ECF volume & osmolarity.
- ***ECF volume*** is regulated through adjusting ***body NaCl content***.
- ***ECF osmolarity*** is regulated through adjusting ***body water content***.

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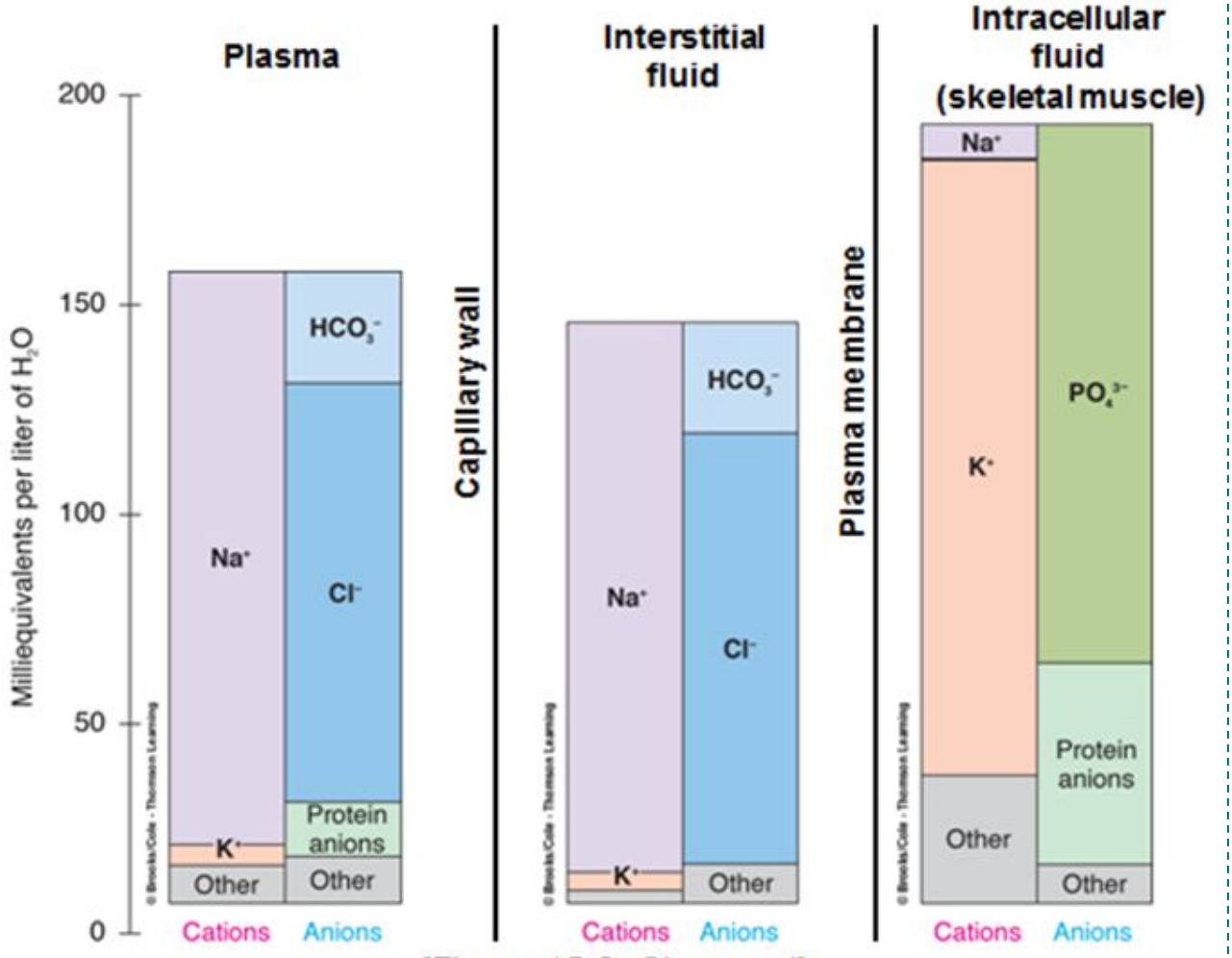
Electrolyte Composition of Body Fluids



[Figure 15-2; Sherwood]

ECF Volume

- The most abundant cation in ECF is **Na^+**
- The most abundant anions in ECF are **Cl^-** and **HCO_3^-**
- The body regulates ECF volume by monitoring and adjusting total body content of **Na^+**
- ECF volume is closely linked to **Na^+** balance.
- To understand ECF volume regulation one must understand **Na^+** regulation.

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

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

↑↑ **[Na^+]** in ECF

↑↑ ECF osmolarity

↑↑ **H_2O** reabsorption by kidney and stimulate thirst

Increases ECF volume

Why is it Important to Regulate ECF Volume?

↑↑ ECF volume

↑↑ Effective circulating volume

↑↑ **CO**

↑↑ **MAP**

This will have detrimental consequences on the body.

Regulation of Volume & Osmolality

If water intake

- Increases → hypoosmotic urine dilute (~ 50 mOsm/kg) large volume (up to 18 L/d)
- Decreases → hyperosmotic urine concentrated (up to 1200 mOsm/kg) small volume (0.5 L/d)

- Renal water excretion mechanism(s) independent of solute excretion mechanism(s).
- Allows water balance maintenance without damaging solute homeostasis (e.g. **Na+**, **K+**).

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- Body water balance must be maintained.
- Kidneys concentrate or dilute urine.
- To remain properly hydrated, water intake must equal water output.
- Increases in plasma osmolality trigger thirst and release of antidiuretic hormone (ADH)

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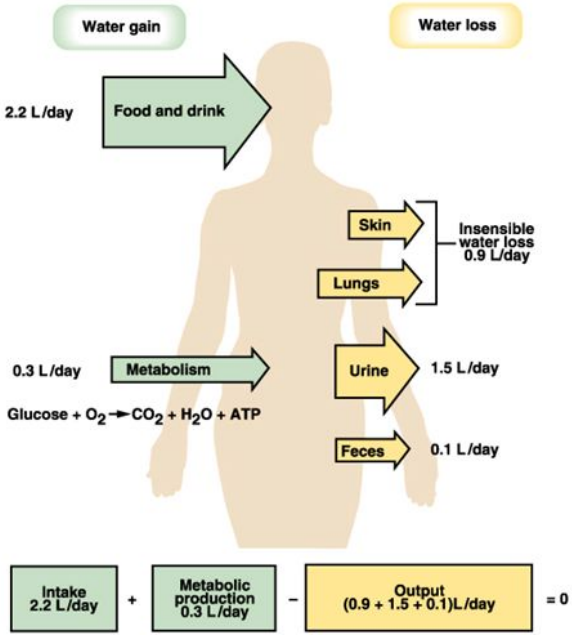
Water Steady State

- Amount ingested = amount eliminated
- Pathological losses:
  - Vascular bleeding.
  - Vomiting.
  - Diarrhea.



Control of Circulating Volume

All down to **Na**+ balance i.e. absorption & excretion.

Volume Sensors
(Effectively pressure receptors)

- Hepatic
- Vascular
- Central Nervous System

High pressure sensors, Carotid Sinus, Aortic Sinus, Juxtaglomerular Apparatus of the Kidney.

Low pressure sensors, Cardiac Atria (ANP), Pulmonary Vasculature.

Volume sensor signals/Mediators:

Neural

If pressure decreases

- Afferent & Efferent arterioles constrict
  - GFR ↓
  - Less **Na**+ filtered
  - More **Na**+ absorbed by PCT
- Renin released*
  - ↑ Angiotensin II
  - ↑ Aldosterone

*By macula densa

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**In the situation of decreased BP, RAAS starts acting, to rise BP back to normal.

Hormonal

1) Renin-angiotensin-aldosterone system, RAAS. (↓ pressure)**:

- Angiotensin II:
  1) Aldosterone release by adrenal cortex
  ↑ Na+ reabsorption in TAL, DT, CD
  2) Vasoconstriction.
  3) ADH release.
  4) ↑ Na+ reabsorption in PCT.
- Renin Secreted by:
  1) Sympathetic stimulation.
  2) ↓ Perfusion pressure.
  3) ↓ Na+ reaching macula densa.

2) ANP:

- From atrial myocytes.
- Released by stretch of atrium ⇒ ↑ NaCl & water excretion.

Antagonist of renin-angiotensin:
1) Vasodilation of afferent arteriole, vasoconstriction of efferent i.e. ↑ GFR.
2) ↓ Renin release.
3) Direct ↓ aldosterone release.
4) ↓ Na+ reabsorption in CD.
5) ↓ ADH release.

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Antidiuretic hormone (ADH)/Vasopressin

- It is synthesized in neuroendocrine cells located within the supraoptic and paraventricular nuclei of the hypothalamus.
- The synthesized hormone is packaged in granules that are transported down the axon of the cell and stored in nerve terminals located in the neurohypophysis (posterior pituitary).
- Prevents water loss
- Small protein hormone (only 9 amino acids)
- Fast acting, short half life in circulation
- ↑ Thirst

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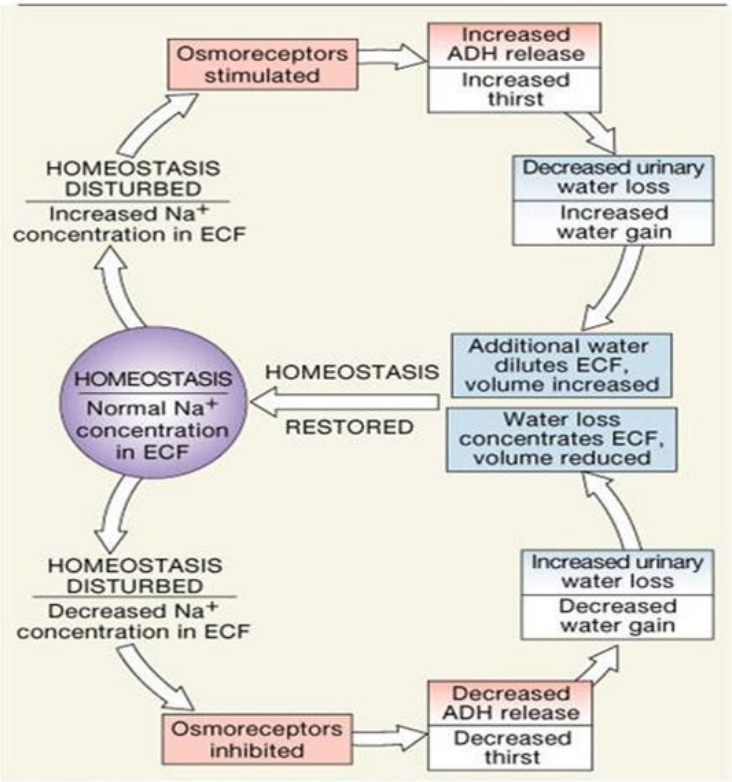
Atrial Natriuretic Peptide (ANP)

- ANP promotes ***natriuresis*** (Na^+ excretion).
- Secreted by atrial myocytes in response to stretch

⇊ ECV → ⇊ ANP release → ⇊ **Na^+** excretion

Antidiuretic Hormone (ADH)



Na is the most important solute in the body.

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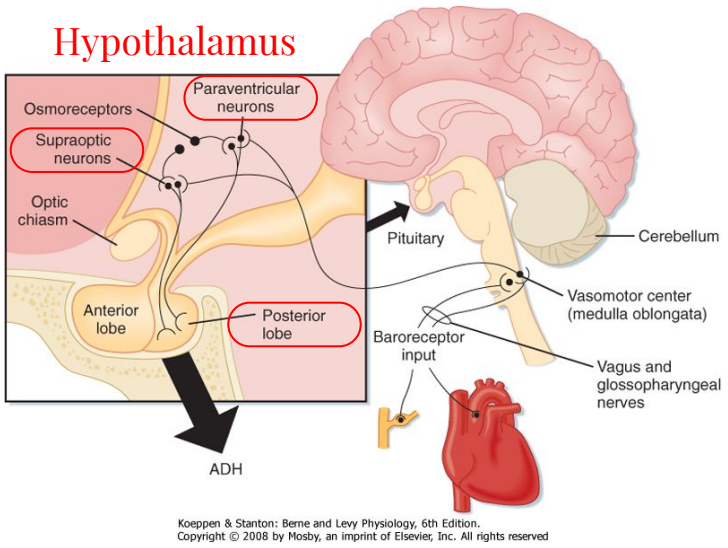
Main physiological factors



- Factors influencing release:

*As the volume increase, Haemodynamic factors will increase and vice versa.

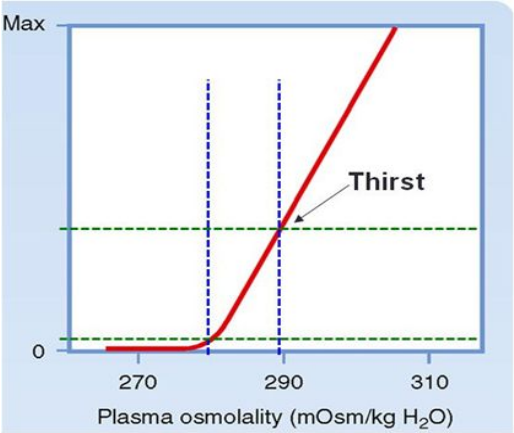
1) Osmolality
2) Haemodynamic factors*
3) Nausea → stimulates
4) Atrial natriuretic peptide (ANP) → inhibits.
5) Angiotensin II → Stimulates.

- A rough estimate of ECF osmolality can be obtained by doubling Plasma sodium concentration.
- 145 mEq/l X 2 = 290 (Normal 285-295 mOsm/kg H2O).
  ∴ Sodium concentration gives best estimate of effective osmolality of ECF.
- In clinical situations glucose & urea concentrations (mmols) are also taken into account, useful in cases of patients with diabetes mellitus or chronic renal failure.
- (non-absorbed glucose in kidney tubule can however prevent fluid absorption generating an osmotic diuresis).

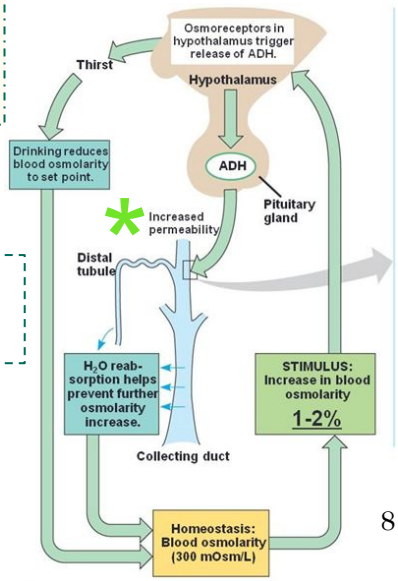
Osmolality

Most important factor

- Osmoreceptors in hypothalamus, outside blood-brain barrier.
- ↑ osmolality → ADH release
- "Set Point" ~ 280 – 285 mOsm/kg H2O

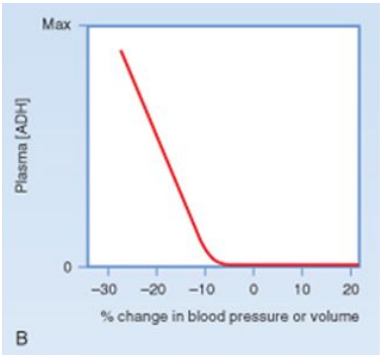


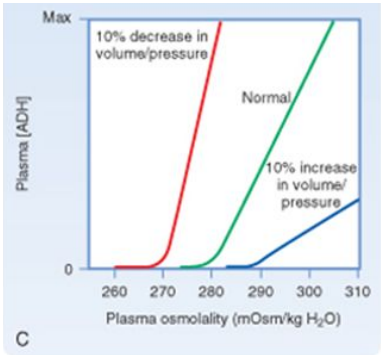
Increase water Reabsorption



Blood volume

- ↓ Blood volume → ADH release
- Less sensitive than osmolality
- Need 5 – 15% ↓ blood volume
- As would be expected changes in blood volume affect osmolality
- ↓ Volume/BP → ↓ set point steeper curve





Control of ADH secretion

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

Regulation of ADH, Duration: 6:21 mins

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

ADH Renal Target

- Collecting duct cells only permeable to water in presence of ADH.
- ADH causes ↑ in urea permeability in inner medullary* CD.
- ADH stimulates reabsorption of NaCl by the thick ascending limb of Henle's loop and by the DCT and cortical segment of CD.

*In cortical area too

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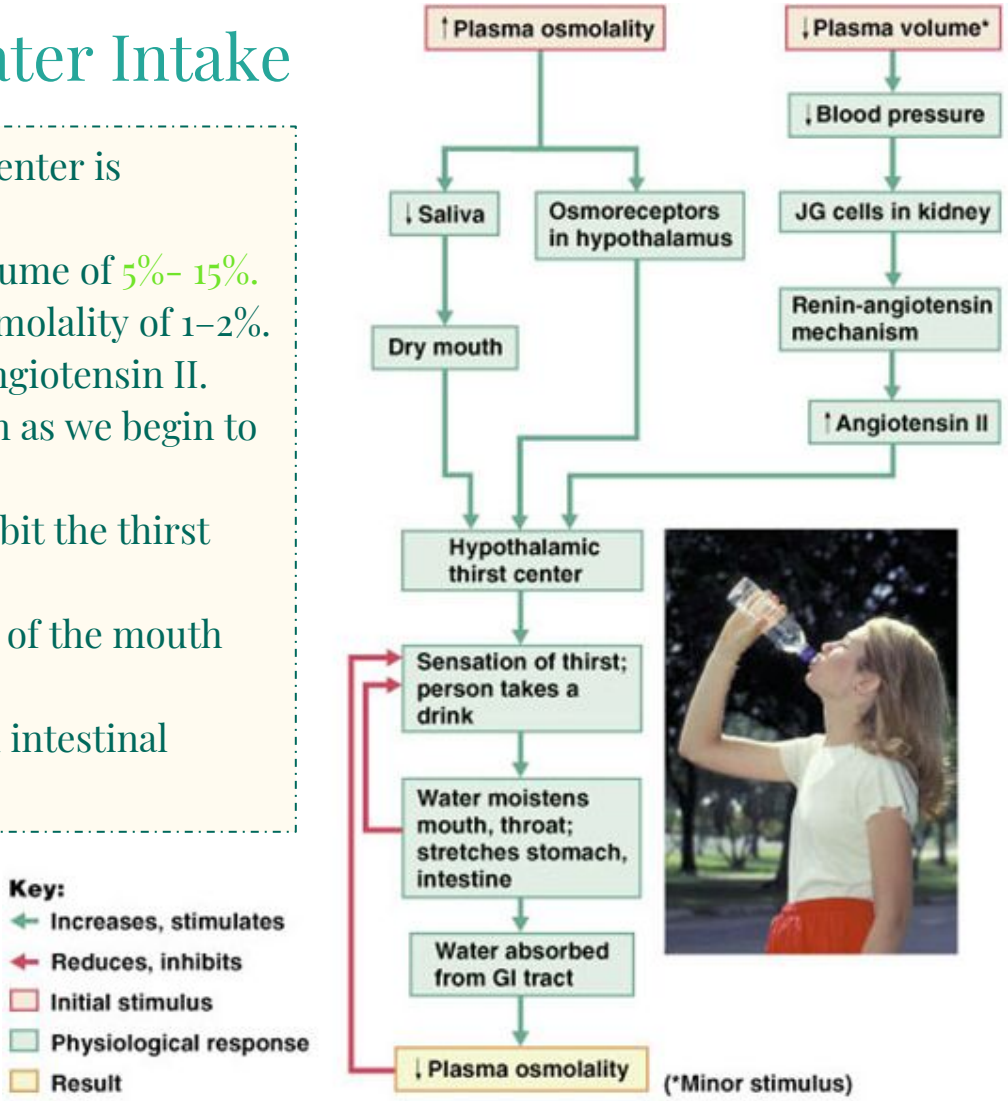
Regulation of Water Intake

- The hypothalamic thirst center is stimulated:
  - By a decline in plasma volume of 5%- 15%.
  - By increases in plasma osmolality of 1–2%.
  - Via baroreceptor input, angiotensin II.
- Thirst is quenched as soon as we begin to drink water
- Feedback signals that inhibit the thirst centers include:
  - Moistening of the mucosa of the mouth and throat.
  - Activation of stomach and intestinal stretch receptors.



Actions of Angiotensin II

1. Angiotensin II receptors are found on the zona glomerulosa cells of the adrenal cortex.
- Activation of these receptors leads to an immediate and rapid increase in aldosterone secretion.
- Aldosterone acts on the distal tubule and collecting duct to cause sodium retention.
- This is likely to be an important mechanism for determining long-term sodium balance.

2. Vascular actions
- Angiotensin II is one of the most potent vasoconstrictors known.
- Constriction of vascular smooth muscle leads to a prompt rise in blood pressure.
- It plays an important role in maintaining vascular tone and blood pressure in volume depleted states, for example haemorrhage and fluid depletion.

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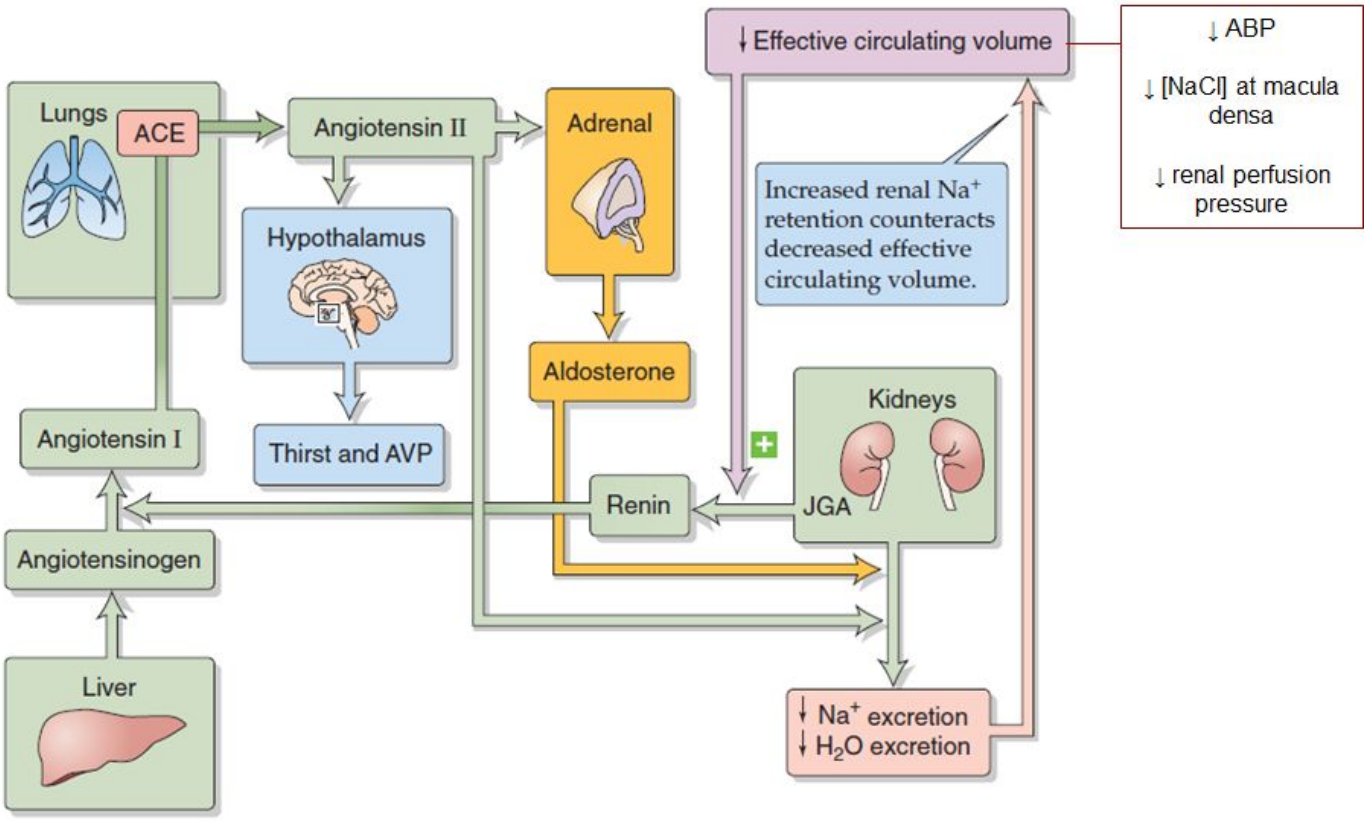
The Renin-Angiotensin-Aldosterone System (RAAS)



Sympathetic Nervous System (SNS)

Its role is thought to be especially important during stressful conditions, e.g. hemorrhage.

Angiotensin II:

Video of RAAS Duration 5:14 mins

- Direct
  - ↑↑ Na^+ Reabsorption
  - ↑↑ Renal Vascular Resistance
- Indirect
  - Stimulate Renin Release

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Sodium Balance

Input

Dietary intake;

- RDA* = 1.5-2.3 g/day
- Actual content in western diet = 7g/day

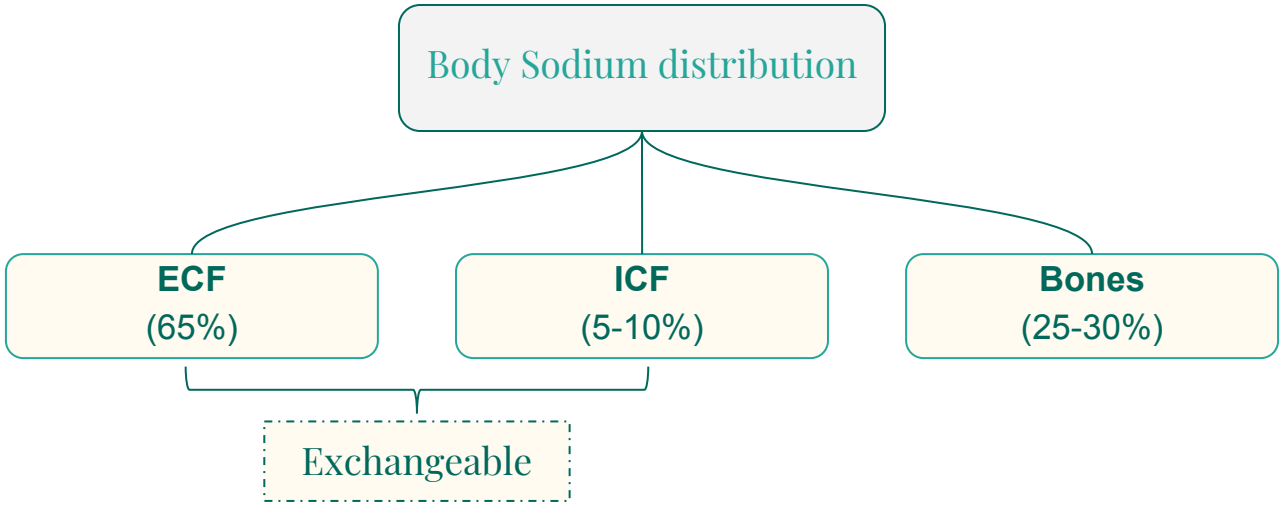
*Recommended dietary allowance

Outpot

Kidney (most important).

GI loss, Sweat } Minor pathways under normal conditions

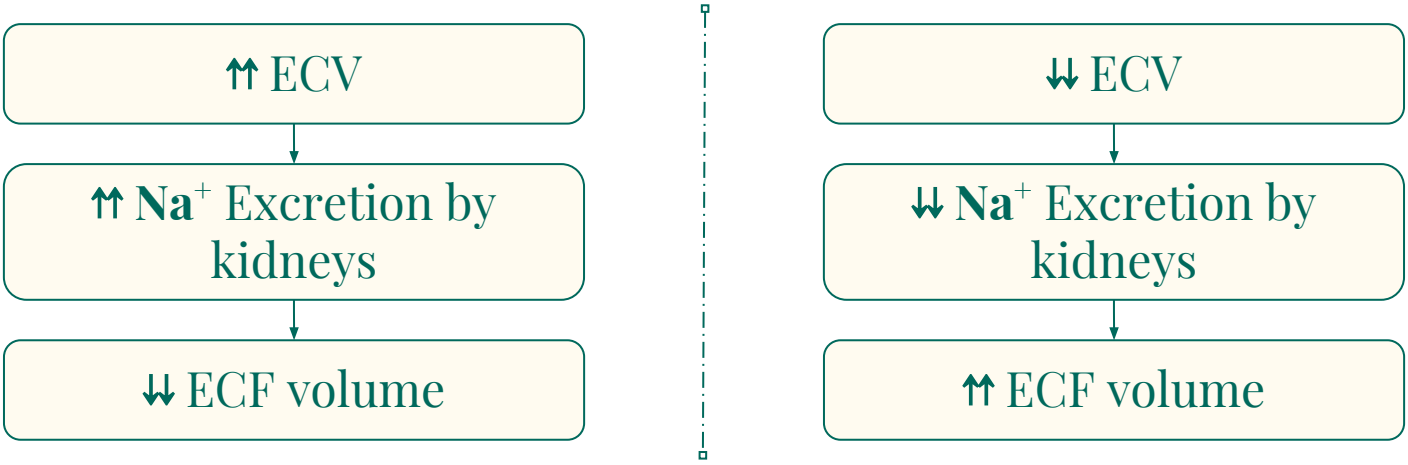
Sodium Distribution in the Body

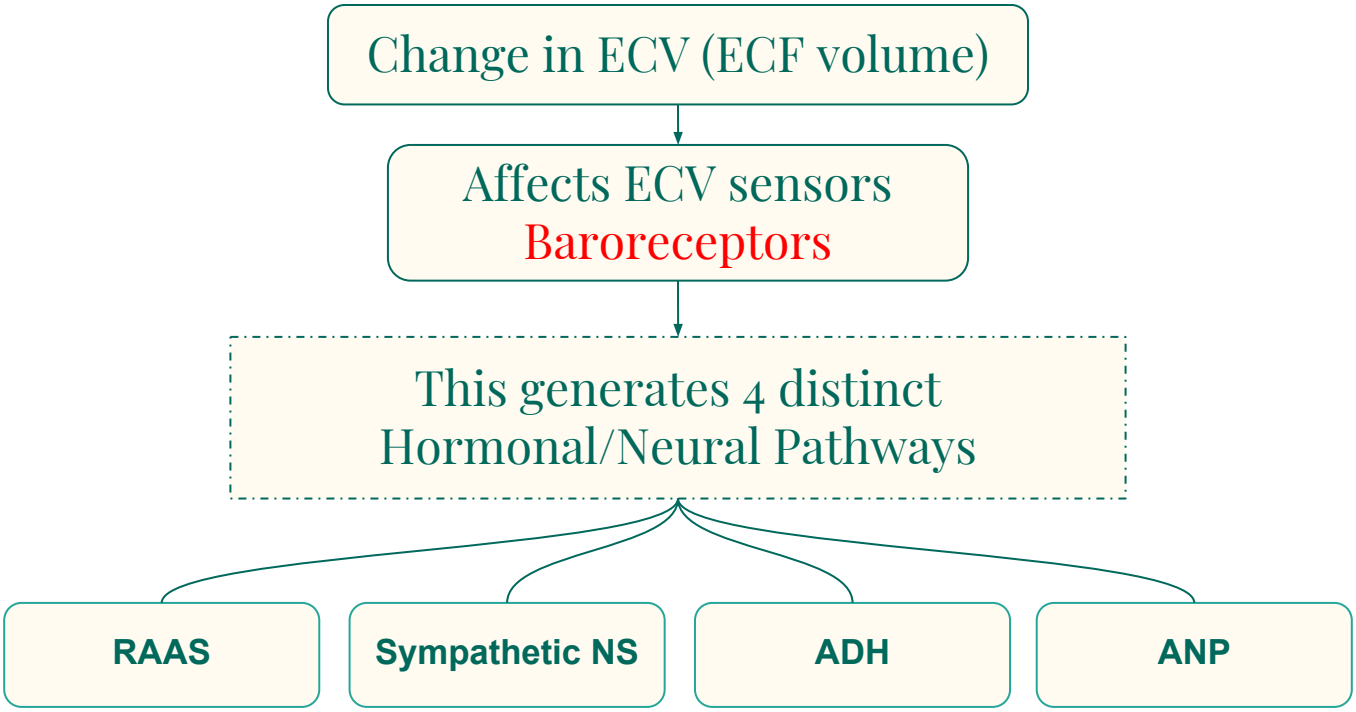


Regulation of Na^+ Excretion by the Kidney

- The kidney is the main route for the body to rid itself of excess **Na^+**
- The signal that triggers enhanced **Na^+** excretion by the kidney is actually the ***ECF volume*** specifically the ***effective circulating volume.***
- **Effective circulating volume (ECV)** = a functional blood volume that reflects the extent of tissue perfusion in specific regions, as evidenced by the pressure in their blood vessels.
- Usually changes in ECV parallels those of ECF volume.

Regulation of ECF Volume (ECV)

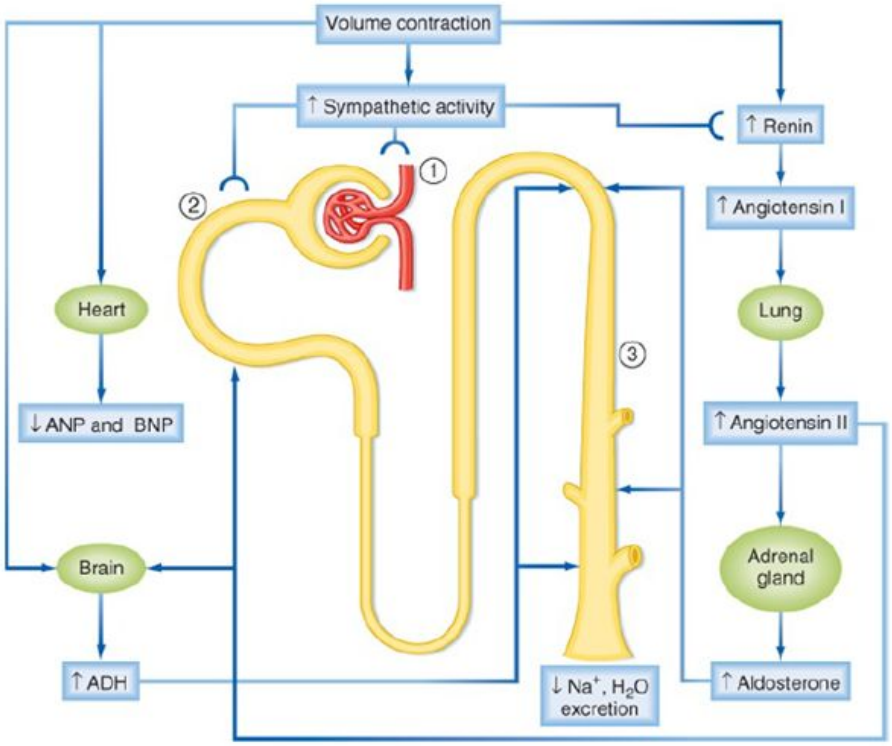




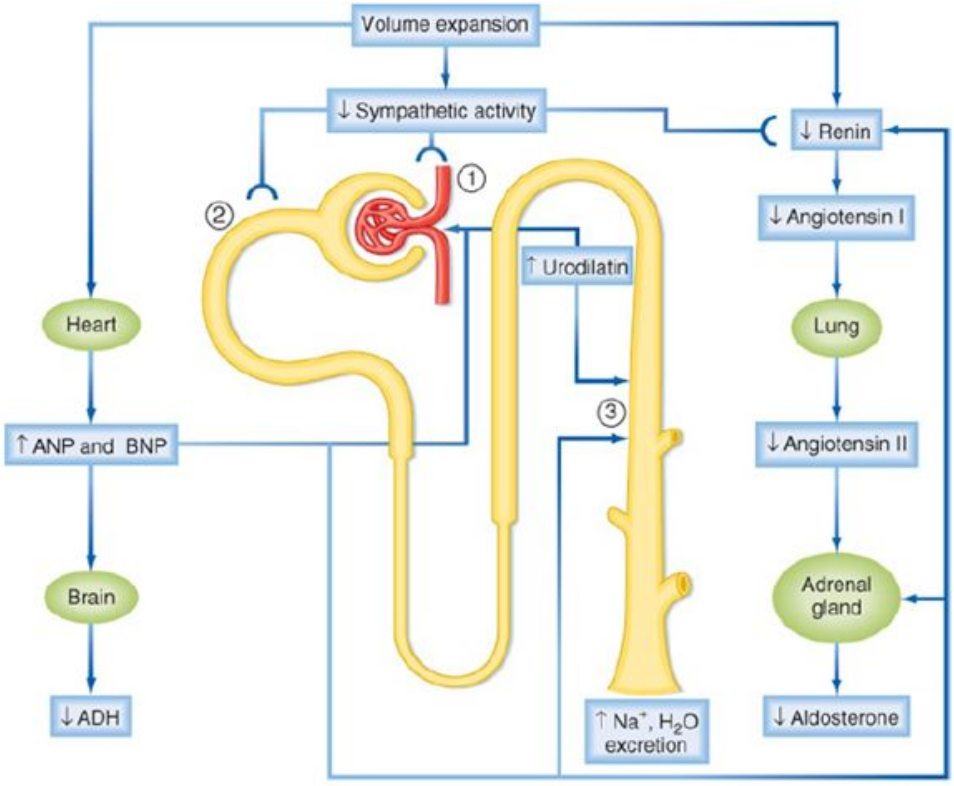
Final Note

- Although, under physiologic conditions, the body regulates plasma volume & plasma osmolarity independently.
- Severe derangements in fluid & electrolyte balance may challenge the system by presenting two conflicting changes in osmolarity and volume.
- In general, ***the body defends volume at the expense of osmolarity***.

Summary



$U_{Na^+}\dot{V} = \downarrow GFR \times P_{Na^+} - \uparrow R$



$U_{Na^+}\dot{V} = \uparrow GFR \times P_{Na^+} - \downarrow R$

Quiz

1- Patient with decreased blood pressure, this will stimulate his renal sympathetic, which lead to?
A. Increase Na filtered.
B. Decrease aldosterone secretion.
C. Decrease Na reabsorption.
D. Decrease GFR.

2- Decreased blood volume will:
A. Stimulate ADH release.
B. Suppress ADH release.
C. Less ADH release.
D. Both A & C

3- When the atrium stretched the atrial natriuretic peptide (ANP) will released from atrial myocytes, which will lead to increase of NaCl & water excretion, what's the expected action to happen?
A. Vasodilation of both afferent and efferent. Arterioles.
B. Vasoconstriction of afferent arteriole, vasoconstriction of efferent.
C. Vasodilation of afferent arteriole, vasoconstriction of efferent.
D. Vasodilation of efferent arteriole, vasoconstriction of afferent.

4- The ADH is synthesized in:
A. Posterior pituitary.
B. Anterior pituitary.
C. Cells located within the supraoptic and paraventricular nuclei of the hypothalamus.
D. Neurohypophysis.

5- increase thirst occurs due to:
A. Decrease plasma osmolarity.
B. Increase plasma osmolarity.
C. Increase blood volume.
D. Increase blood pressure.

Answers:
1D 2A 3C 4C 5B

Thank you for checking our work

Male Team:

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