Sodium Handling

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Learning Objectives

1. Describe the normal whole-body daily sodium balance

2. Describe the contribution of the major nephron segments to the reabsorption of filtered salt and water

3. Outline the effects on renal blood flow and glomerular filtration if the renin-angiotensin system is activated

4. Discuss the various hormones and their effects in regulating Na⁺ levels with either an increase or decrease in blood volume/blood pressure
### Sodium Balance

<table>
<thead>
<tr>
<th>Substance and Units</th>
<th>Extracellular Fluid (ECF)</th>
<th>Intracellular Fluid (ICF)</th>
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<tbody>
<tr>
<td>Na⁺ (mEq/L)</td>
<td>140</td>
<td>14</td>
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</table>

- **Na⁺** - major cation of ECF compartment (plasma and interstitial fluid) – determines ECF volume → plasma volume → blood volume → blood pressure

- Kidneys maintain normal body Na⁺ content so **Na⁺ balance**: daily Na⁺ intake = daily Na⁺ excretion

- **+ ve Na⁺ balance**: Na⁺ excretion < Na⁺ intake
  - Na⁺ retained in ECF → ECF volume expansion → increase blood volume and blood pressure

- **-ve Na⁺ balance**: Na⁺ excretion > Na⁺ intake
  - Na⁺ lost from ECF → ECF volume contraction → decrease blood volume and blood pressure
**Na⁺ Transport in Early Proximal Tubule**

Most essential solutes are reabsorbed with Na⁺: Glucose, amino acids and HCO₃⁻

**Cotransport mechanisms:**
Na⁺ reabsorption is coupled with uncharged molecules (glucose; amino acids, phosphates, lactate, citrate) – accounts for 10% Na⁺ reabsorption; H₂O follows

**Countertransport/Exchanger:**
Na⁺/H⁺ antiport allows H⁺ secretion for HCO₃⁻ reabsorption; HCO₃⁻ is the anion reabsorbed with Na⁺; accounts for 20-25% Na⁺ reabsorption

**EARLY PROXIMAL TUBULE = NaHCO₃ REABSORPTION**
Late Proximal Tubule

Cellular component: Na\(^+\)/H\(^+\) antiporter coupled to Cl\(^-\) reabsorption and formate secretion; accounts for ~35% Na\(^+\) reabsorption

Paracellular component: Passive reabsorption of Na\(^+\) and Cl\(^-\)

LATE PROXIMAL TUBULE = NaCl REABSORPTION
**Thick Ascending Limb**

**Cellular mechanism:**
Na\(^+\)/K\(^+\)/2Cl\(^-\) cotransporter

Energy is derived from Na\(^+\) gradient with reabsorption of Na\(^+\) K\(^+\) 2Cl\(^-\)

Na\(^+\)/H\(^+\) antiporter to allow for HCO\(_3^−\) reabsorption

Accounts for 25% Na\(^+\) reabsorption
Early Distal Tubule

Cellular Mechanism: 
Na\(^+\)- Cl\(^-\) cotransporter 
Energy is derived from Na\(^+\) gradient with reabsorption of Na\(^+\) and Cl\(^-\)

Accounts for 5% Na\(^+\) reabsorption
Late Distal Tubule & Collecting Duct

2 cell types interspersed

1. Principal: Involved in Na\(^{+}\) reabsorption and K\(^{+}\) secretion
2. \(\alpha\)-Intercalated: Involved in K\(^{+}\) reabsorption and H\(^{+}\) secretion

Mechanism: Na\(^{+}\) Channels
Na\(^{+}\) diffuses through the channels down its electrochemical gradient

Accounts for 3% Na\(^{+}\) reabsorption

Fine adjustments to Na\(^{+}\) excretion
Hormonally regulated by aldosterone – synthesizes Na\(^{+}\) channels to increase Na\(^{+}\) reabsorption
In which portion of the nephron does over 60% of sodium reabsorption occur?

A. Bowman’s capsule
B. Proximal tubule
C. Descending loop of Henle
D. Ascending loop of Henle
E. Distal tubule
Overall Na\textsuperscript{+} Handling in the Nephron

PCT: Bulk

LD/CD: Fine Tuning
Regulation of Na\(^+\) Balance

**Tubuloglomerular Feedback:** Macula densa cells part of juxtaglomerular apparatus that sense tubular flow and GFR and send feedback signals to afferent or efferent arteriole to constrict/dilate to keep GFR at normal levels.
Pathways Involved in Tubuloglomerular Feedback

- Arterial Pressure
- Glomerular Hydrostatic Pressure
- GFR
- Macula Densa NaCl
- Proximal NaCl Reabsorption
- Renin
- Angiotensin II
- Efferent Arteriolar Resistance
- Afferent Arteriolar Resistance

1. GFR increases.
2. Flow through tubule increases.
3. Flow past macula densa increases.
4. Paracrine diffuses from macula densa to afferent arteriole.
5. Afferent arteriole constricts.

Resistance in afferent arteriole increases.
Hydrostatic pressure in glomerulus decreases.
GFR decreases.
Decreased Na\(^+\) Intake

Volume contraction

↑ Sympathetic activity

↑ Renin

↑ Angiotensin I

Lung

↑ Angiotensin II

Adrenal gland

↑ Aldosterone

↓ Na\(^+\), H\(_2\)O excretion

1. Heart

↓ ANP and BNP

Brain

↑ ADH

2. Brain

3. Adrenal gland

↑ ADH
Low blood pressure (BP) stimulates renin secretion from the kidney. Renin stimulates the production of angiotensin I, which is converted to angiotensin II, which in turn stimulates aldosterone secretion from the adrenal cortex. Aldosterone increases Na+ and water reabsorption in the kidney.
**Renin-Angiotensin-Aldosterone System**

Activated by decreased arterial & renal perfusion pressure

**Renin**: Secreted by the *juxtaglomerular cells* (JG) of the afferent arterioles in response to low renal arteriole pressure; catalyzes conversion of plasma protein, angiotensinogen, to Angiotensin I eventually giving Angiotensin II; The macula densa cells located in the distal tubules stimulate the JG cells to release renin in response to decreased NaCl concentration in the tubules.

**Angiotensin II**: Potent arteriole vasoconstrictor, increases Na\(^+\) reabsorption in proximal tubule, stimulates thirst, stimulates aldosterone secretion from adrenal cortex.

**Aldosterone**: Increases Na\(^+\) reabsorption and K\(^+\) secretion by principal cell in late distal tubule and collecting duct; secreted in response to Angiotensin II, hyperkalemia (high blood [K\(^+\)]), hyponatremia (low plasma [Na\(^+\)])
Sympathetic Stimulation

Activated in response to decreased arterial pressure

Nerves decreases Na\(^+\) excretion in 3 ways:

1. Decreases GFR and RBF \(\rightarrow\) decreased filtered Na\(^+\) load for excretion

2. Direct stimulatory effect on Na\(^+\) reabsorption by renal tubules

3. Causes renin release \(\rightarrow\) increases angiotensin II and aldosterone levels for reabsorption
Atrial Natriuretic Peptide (ANP):

Secreted by atria in response to increase in ECF volume

• Increases GFR (dilate afferent / constrict efferent arterioles)
• Inhibits reabsorptive mechanisms along tubule
  – Inhibits Na\(^+\) reabsorption at collecting duct
  – Inhibits renin secretion by juxtaglomerular cells in kidney → inhibits RAA system
  – Inhibits aldosterone secretion by adrenal gland
  – Inhibits ADH secretion
  – Inhibits adenylate cyclase in target tissues
• Increases Na\(^+\) and H\(_2\)O excretion
Test Question

An decrease in which of the following occurs with a decreased intake of Na⁺?

1. Sympathetic activity
2. Renin-angiotensin-aldosterone
3. Na⁺ reabsorption
4. Antidiuretic hormone
5. **Atrial naturietic peptide**
Summary: Na⁺ Handling in the Nephron

PCT: Bulk

LD/CD: Fine Tuning