REGULATION OF EXTRACELLULAR FLUID VOLUME AND OSMOLALITY

Blood Osmolality (mOsm/L) equals:

\[ 2[Na^+] \text{ (mEq/L)} + 0.055[\text{Glucose}] \text{ (mg/dL)} + 0.36[\text{BUN}] \text{ (mg/dL)} \]
OBJECTIVES

At the end of this lecture you should 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.
Renal regulation of ECF Volume & Osmolality

Is a reflex mechanism in which variables reflecting total body sodium and ECV are monitored by appropriate sensors.

Regulation of ECF volume =
Regulation of body Na\(^+\) =
Regulation BP

Thus, regulation of Na\(^+\) is also dependent upon baroreceptors.
Renal Regulation of ECV

- **Sensor**
  - Carotid sinus
  - Volume receptors (large vein, atria, intrarenal artery)

- **Effectors**
  - Rennin/angiotensin, aldosterone
  - Renal sympathetic nerve
  - ANF
  - ADH

- **Affecting**
  - Urinary Na excretion
Renal regulation of blood osmolality

– **Sensors**
  - Hypothalamic osmoreceptors

– **Effectors**
  - ADH
  - Thirst

– **Affecting**
  - Urine osmolality
  - Water intake
Osmoreceptor ADH Feedback System

1. INCREASED OSMOLALITY
2. DECREASED ARTERIAL PRESSURE
3. DECREASED BLOOD VOLUME
### FACTORS AFFECTING ADH

<table>
<thead>
<tr>
<th>Increase ADH</th>
<th>Decrease ADH</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Osmolarity</td>
<td>↓ Osmolarity</td>
</tr>
<tr>
<td>↓ Blood volume</td>
<td>↑ Blood volume</td>
</tr>
<tr>
<td>↓ Blood pressure</td>
<td>↑ Blood pressure</td>
</tr>
</tbody>
</table>

**Renal Sympathetic**

↓ ECV → ↑ renal sympathetic activity → stimulate Na absorption by direct tubular effect mediated through α-receptors on renal tubules (mainly PCT) to correct for low ECV
High Osmolality
Low ECF Volume
decreases 15 to 25 percent or more

Osmoreceptors
Lat Hypothalamus
(Stimulate Thirst)

Low Pressure Receptors
Atria  Aortic Carotid Pulmonary

↑ ADH

Aquaporins 2
P Cell
H2O  H2O  H2O  H2O
Factors affecting the thirst sensation. A plus sign indicates stimulation of thirst, the minus sign indicates an inhibitory influence.
Role of Thirst in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

<table>
<thead>
<tr>
<th>Increase Thirst</th>
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<tbody>
<tr>
<td>↑ Osmolarity</td>
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</tr>
<tr>
<td>↓ Blood pressure</td>
<td>↑ Blood pressure</td>
</tr>
<tr>
<td>↑ Angiotensin</td>
<td>↓ Angiotensin II</td>
</tr>
<tr>
<td>Dryness of mouth</td>
<td>Gastric distention</td>
</tr>
</tbody>
</table>
INCREASE IN WATER INTAKE

Graph showing the effects of drinking 1.0 L of H₂O on urinary osmolarity, urine flow rate, and urinary solute excretion over time.
INCREASE IN SODIUM INTAKE
ATRIAL NATRIURETIC PEPTIDE (ANP)

• INCREASE GLOMERULAR FILTRATION
• INHIBIT Na\(^+\) REABSORPTION.
• INCREASE IN CAPILLARY PERMEABILITY LEADING TO EXTRAVASATION OF FLUID AND A DECLINE IN BLOOD PRESSURE.
• RELAX VASCULAR SMOOTH MUSCLE IN ARTERIOLES AND VENULES
• INHIBIT RENIN SECRETION & ALDOSTERONE
Figure 24.10  Atrial natriuretic peptide and its actions. ANP release from the cardiac atria is stimulated by blood volume expansion, which stretches the atria. ANP produces effects that bring blood volume back toward normal, such as increased Na⁺ excretion.
TUBULOGLomerULAR FEEDBACK
75-160 MMHG

↓Arterial Pressure

↓Glomerular Hydrostatic Pressure

↓GFR

↓Macula Densa
NaCl
send 2 Signals

↑Proximal NaCl
Reabsorption
In ascending LOH

↑Renin

↑Angiotensin II

↑Efferent Arteriolar resistance

↓Afferent Arteriolar resistance

↓TUBULOGLomerULAR FEEDBACK
75-160 MMHG
GLOMERULOTUBULAR BALANCE

An increase in GFR causes an increase in the reabsorption of solutes to keep the percentage of the solute reabsorbed constant.

When the GFR is high, there is a relatively large increase in the oncotic pressure of the plasma leaving the glomeruli via the efferent arterioles and hence in their capillary branches. This increases the reabsorption of Na+ from the tubule.
# SODIUM HANDLING

<table>
<thead>
<tr>
<th>SITE</th>
<th>APICAL TRANSPORTER</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal Tubule</td>
<td>• Na/Gluc CT</td>
<td>• Na &amp; Gluc Uptake</td>
</tr>
<tr>
<td></td>
<td>• Na/Pi CT</td>
<td>• Na &amp; Pi Uptake</td>
</tr>
<tr>
<td></td>
<td>• Na/Amino Acid</td>
<td>• Na &amp; AA Uptake</td>
</tr>
<tr>
<td></td>
<td>• Na/Lactate</td>
<td>• Na &amp; Lactate Uptake</td>
</tr>
<tr>
<td></td>
<td>• Na/H Exchanger</td>
<td>• Na Uptake and H Extrusion</td>
</tr>
<tr>
<td></td>
<td>• Cl/Base Exchanger</td>
<td>• Cl Uptake</td>
</tr>
<tr>
<td>Thick Ascending Limb</td>
<td>• Na, 2 Cl,, K CT</td>
<td>• Na, 2 Cl,, K Uptake</td>
</tr>
<tr>
<td></td>
<td>• Na/H Exchanger</td>
<td>• Na Uptake and H Extrusion</td>
</tr>
<tr>
<td></td>
<td>• K Channels</td>
<td>• K Extrusion</td>
</tr>
<tr>
<td>EarlyDCT</td>
<td>NaCl CT</td>
<td>Na &amp; Cl Uptake</td>
</tr>
<tr>
<td>Late DCTCollecting Duct</td>
<td>Na Channel (ENaC)</td>
<td>Na Uptake</td>
</tr>
</tbody>
</table>
(1) increase the Na permeability of the luminal plasma membrane
(2) increase the number and activity of basolateral plasma membrane Na/K-ATPase pumps
(3) increase the luminal plasma membrane K permeability,
(4) increase cell metabolism.
All of these changes result in increased K secretion.
Effect Of Aldosterone On Cortical Collecting Duct

Renin (from kidneys) → Angiotensinogen $\xrightarrow{\text{Angiotensin converting enzyme}}$ Angiotensin I $\xrightarrow{\text{Angiotensin II converting enzyme}}$ Angiotensin II → Increased K$^+$ ions → Adrenal cortex → Increased aldosterone secretion → Basal membrane → Aldosterone receptor → Apical membrane → Synthesis of transport proteins → Lumen of nephron

Na Channel (ENaC)
Factors Affecting Aldosterone Secretion

- **Stimulatory agents**
  - Angiotensin II
  - Adrenocorticotrophic hormone
  - High potassium
  - Sodium deficiency

- **Inhibitory agents**
  - Atrial natriuretic hormone
  - High sodium concentration
  - Potassium deficiency
Regulation of Aldosterone Secretion

1. Dehydration, Na⁺ deficiency, or hemorrhage
2. Decrease in blood volume
3. Decrease in blood pressure
4. Juxtaglomerular cells of kidneys
5. Increased renin
6. Liver
7. Increased angiotensin I
8. Lungs (ACE = Angiotensin Converting Enzyme)
9. Increased angiotensin II
10. Adrenal cortex
11. Increased aldosterone
12. In kidneys, increased Na⁺ and water reabsorption
13. Increased blood volume
14. Blood pressure increases until it returns to normal
15. Vasoconstriction of arterioles
16. Increased K⁺ in extracellular fluid