Sodium Balance

Pedram Fatehi, MD
Division of Nephrology

fatehi@stanford.edu
Learning Objectives

• ECF volume matches total ECF sodium content.

• The kidney matches sodium excretion to sodium intake in order to maintain ECF volume.

• Recognize the volume sensors and effector mechanisms that regulate sodium excretion (i.e. regulate ECF volume).

• Explain why sodium saving mechanisms developed during evolution to prevent ECF volume reduction may be activated in disease, causing an increase in the ECF volume above normal.
Water follows Salt

Salts are ionic compounds of cations and anions.

For our discussion, we’ll use the term “salt” to mean sodium chloride or just sodium.

Semipermeable membrane
Maintaining the Internal Environment

What Goes In = What Comes Out

Intracellular Fluid
- 290 mOsm
- Na+ 10
- K+ 120

Extracellular Fluid
- 290 mOsm
- Na+ 140
- K+ 4
Central mechanisms of osmosensation and systemic osmoregulation

Mammals ECF
~300 mOsm/kg

Non-mammals ECF
(vertebrates and invertebrates)
42 – 1140 mOsm/kg
~range of U Osm

Figure 1: Extracellular fluid osmolality in animals. The plot shows values of extracellular fluid (ECF) osmolality in various animals. The values were obtained by measuring the osmolality of their blood or blood-related fluids. The figure also includes a range of values for different species, with mammals having ECF osmolalities around 300 mOsm/kg and non-mammals ranging from 42 to 1140 mOsm/kg. Although different types of animals may display slightly different values, these general ranges provide a useful comparison for understanding osmoregulatory mechanisms in various species.
Galapagos marine iguana has nasal salt glands to excrete excess salt.
Terrestrial elephant finds salt deposits to replete salt deficiency.
Intake of salty foods will prompt thirst so water (and volume) will follow.

Boy, these pretzels are making me thirsty.
Maintaining the Internal Environment
What Goes In = What Comes Out

Effect of abrupt changes in Na+ intake on body weight and renal Na+ excretion in a normal human. The shaded areas refer to changes in total body Na+ stores due to the difference between intake and excretion. (From Earley LE, Clinical Disorders of Fluid and Electrolyte Metabolism, 1972)
Na⁺ excretion in humans is regulated by the kidney

GFR ≈ 100 mL/min
≈ 150 L/day

[Na] ≈ 150 mEq/L

Na filtered ≈ 150 L/day x 150 mEq/L
≈ 22,500 mEq/day

Na excreted ≈ 1 to 50 mEq/day (less than 1%)
In nature, salt and the water that accompanies it are hard to obtain and easily lost, eg. in fever, sweat, diarrhea, blood loss; thus, evolved responses to **maintain and replete ECF volume** by:

- Increasing sodium intake (‘salt hunger’)
- Restricting sodium loss in the kidneys *
How would you describe a patient with severe diarrhea from cholera? (may choose more than one)

a. Dehydrated
b. Volume depleted
c. Hypervolemic
d. Hypovolemic
e. Edematous
How would you describe a patient with severe diarrhea from cholera? (may choose more than one)

a. Dehydrated  
b. Volume depleted  
c. Hypervolemic  
d. Hypovolemic  
e. Edematous
Patients with very low ECF volume (ie, low salt content or salt deficiency) will have: (may choose more than one)

- Low urine sodium concentration
- Low cardiac output
- High stroke volume
- Fast heart rate
- Low blood pressure
- Poor tissue perfusion
Patients with very low ECF volume (ie, low salt content or salt deficiency) will have:
(may choose more than one)

a. Low urine sodium concentration
b. Low cardiac output
c. High stroke volume
d. Fast heart rate
e. Low blood pressure
f. Poor tissue perfusion

\[ \text{CO} = \text{HR} \times \text{SV} \]

Same for diarrhea or blood loss, both hypovolemic states.
Reasonable options to manage severe diarrhea from cholera include:
(may choose more than one)

a. PO (oral) Water
b. IV D5W (water with 5% dextrose)
c. IV NS (normal saline, Na/Cl, ~290 mOsm)
d. Oral ‘Rehydration’ Therapy (Na/Cl/K/citrate/glucose, ~250 mOsm)
e. IV LR (lactated ringers, Na/Cl/K/Ca/lactate, ~270 mOsm)
Reasonable options to manage severe diarrhea from cholera include:
(may choose more than one)

- a. PO (oral) Water
- b. IV D5W (water with 5% dextrose)
- c. IV NS (normal saline, Na/Cl, ~290 mOsm)
- d. Oral ‘Rehydration’ Therapy (Na/Cl/K/citrate/glucose, ~250 mOsm)
- e. IV LR (lactated ringers, Na/Cl/K/Ca/lactate, ~270 mOsm)
Hypovolemic states are managed with sodium-containing isotonic solutions, because Na+ is the major determinant of ECF volume.
Gatorade provides (per liter):
- sodium 20 mEq
- potassium 3 mEq
Ernest Starling, M.D.
1866 - 1927

Starling Law of the Heart
Starling Forces of capillary filtration
Net filtration pressure = 
Lp S [Δ hydraulic pressure – Δ oncotic pressure]

Lp, permeability of capillary wall; S, surface area available for filtration

**FIGURE 4.1.** Schematic representation of the effect of the hydraulic pressure (P) and the oncotic pressure (σ) in the capillary (cap) and the interstitial (is) on fluid movement between the vascular space and the interstitium. The arrows point in the direction in which that parameter will cause fluid to move. The resistance at the precapillary sphincter is an important regulator of the capillary hydraulic pressure, allowing it to remain relatively constant despite changes in the arterial perfusion pressure.
Extracellular Fluid (ECF) Volume determined by Na+ content

Plasma and interstitium are normally in equilibrium, but edema forms if altered Starling forces favor filtration into the interstitial space.

Total Body Water = 42 L (70kg x 60%)
Kidneys and body will respond to ‘perceived’ plasma volume (not the interstitial fluid).
| Major Sensors and Effectors of the Osmoregulatory and Volume Regulatory Pathways |
|---------------------------------|---------------------------------|
| **What is sensed**              | **Volume Regulation**           |
| Osmoregulation                  |                                 |
| What is sensed                  | Effective tissue perfusion      |
| Plasma osmolality               | Macula densa                    |
| Sensors                         | Afferent arteriole              |
| Hypothalamic osmoreceptors      | Atria                           |
| Effectors                       | Carotid sinus                   |
| Antidiuretic hormone            | Aortic Arch                     |
| Thirst                          |                                 |
| What is affected                |                                 |
| Urine osmolality                | Urinary sodium                  |
| Water intake                    | Thirst                           |
|                                 |                                 |
In altered Starling forces, kidney/body effort to restore plasma volume may improve volume deficit somewhat, but will also worsen interstitial edema.

Figure 16-1 Pathophysiology of edema formation when there is an alteration in capillary hemodynamics, such as an elevated capillary hydraulic pressure, that favors the movement of fluid out of the vascular space into the interstitium. The normal plasma volume is depicted as the full size of the plasma square. The shaded area in the edema square refers to the increase in the interstitial fluid volume as edema. The initial reduction in the plasma volume produced by the loss of fluid into the interstitium (a) stimulates renal Na+ and water retention (b). This appropriately restores the plasma volume toward normal, but, because of the altered capillary hemodynamics, much of the retained fluid enters the interstitium and becomes apparent as edema.
Barger’s Caval Constriction Experiment

- Ring placed at thoracic inferior vena cava
- Dogs fed 75 meq / day sodium
- On Day 1: TIVC constriction
- On Day 2: Increased constriction
- On Day 15: Release constriction
Renal response to low effective circulating volume is sodium (volume) retention

BLOOD PRESSURE
~effective circulating volume
~effective tissue perfusion

RENIN

ALDOSTERONE

URINE SODIUM

PLASMA VOLUME

Figure 8-7 Sequential changes in mean aortic pressure, plasma renin activity, plasma aldosterone concentration, plasma volume, and urinary sodium excretion in a dog with moderate septic shock. A Carr constrictor was placed around the aorta, and a marked reduction in cardiac output. On day 1, however, a new steady state is achieved in which renin and aldosterone levels and Na⁺ excretion have returned to baseline levels. The associated plasma volume expansion is responsible for restoring cardiac output to the heart, thereby allowing systemic hypotension to be maintained. (From Wadee J Jr, Yee GC, Becker LC: Circ Res 39:158, 1976; by copyright permission of the American Heart Association for Clinical Investigation.)
Renal response to high effective circulating volume is sodium (volume) excretion.
Renal response to high effective circulating volume is sodium (volume) excretion.
FIGURE 2.8. Effect of gradually increasing sodium intake in normal subjects from a low value of 10 up to 350 mEq/day. Decreased activity of the renin-angiotensin-aldosterone system and increased atrial natriuretic peptide (ANP) release are required for the excess sodium to be excreted.
65M is in ED with shortness of breath; he is waiting to be seen

PMHx: HTN, DM, lipids, CAD

Extracellular fluid volume and TBW are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M is in ED with shortness of breath; he is waiting to be seen

PMHx: HTN, DM, lipids, CAD

Extracellular fluid volume and TBW are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Extracellular fluid (ECF) volume and TBW are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Extracellular fluid (ECF) volume and TBW are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk

PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Effective circulating volume is:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Effective circulating volume is:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx:  HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Sympathetic nervous system and RAAS activity are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Sympathetic nervous system and RAAS activity are:
A. Decreased
B. Normal
C. Increased
D. Need more information
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk
PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Urine sodium concentration is likely
A. low, < 10 mEq/L
B. high, > 50 mEq/L
65M presents to ED with progressive dyspnea and orthopnea, ran out of diuretics x 1 wk

PMHx: HTN, DM, lipids, CAD

AF 70/palp 120 30 85%RA
Tripod position, 1 word sentences
+JVD, crackles; tachycardic, S3
Cool extremities, 3+ LE edema

Urine sodium concentration is likely

A. low, < 10 mEq/L
B. high, > 50 mEq/L
In altered Starling forces, kidney/body effort to restore plasma volume may improve volume deficit somewhat, but also worsen interstitial edema.

Figure 16-1 Pathophysiology of edema formation when there is an alteration in capillary hemodynamics, such as an elevated capillary hydraulic pressure, that favors the movement of fluid out of the vascular space into the interstitium. The normal plasma volume is depicted as the full size of the plasma square. The shaded area in the edema square refers to the increase in the interstitial fluid volume as edema. The initial reduction in the plasma volume produced by the loss of fluid into the interstitium (a) stimulates renal Na⁺ and water retention (b). This appropriately restores the plasma volume toward normal, but, because of the altered capillary hemodynamics, much of the retained fluid enters the interstitium and becomes apparent as edema.
Learning Objectives

• ECF volume matches total ECF sodium content.

• The kidney matches sodium excretion to sodium intake in order to maintain ECF volume.

• Recognize the volume sensors and effector mechanisms that regulate sodium excretion (i.e. regulate ECF volume).

• Explain why sodium saving mechanisms developed during evolution to prevent ECF volume reduction may be activated in disease, causing an increase in the ECF volume above normal.
Questions

fatehi@stanford.edu
Renin - Angiotensin - Aldosterone System (RAAS)

**FIGURE 2.5.** Regulation of renin release.
Renin - Angiotensin - Aldosterone System (RAAS)

- Renin
- Angiotensinogen
- Angiotensin I
- Angiotensin-converting enzyme
- Angiotensin II

- Vasoconstriction
- Aldosterone
- Norepinephrine
- Renal function
Volume Regulation

- Baro-receptors
- Sympathetic NS
- RAAS
- Natriuretic Peptides
Natriuretic Peptides
Physiologic effects of increased venous return (hypervolemia)
Consequence of low effective circulating volume

If we performed the IVC constriction experiment on an unsuspecting 70 kg medical student, and he ate the recommended daily intake of sodium (2400 mg) for 3 days. Approximately how much would his weight increase?  
(HINT, 2400 mg of Na+ = ~ 100 meq Na+)

a. 2 liters
b. 0.2 liters
c. 20 liters