Ch 34: Control of Body Fluid Osmolality and Volume
Ch 2 : Homeostasis of Body Fluids

Fluid and Electrolyte Balance

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Fluid and Electrolyte Balance

1. Distribution and measurement of body fluid compartments
2. Compartmental fluid balance and compositions
3. Systemic fluid balance: water intake & output
4. Regulation mechanism of extracellular fluid volume
5. Electrolytes balance
Body Fluid

Young men

60% of body weight

cf. water content; fat tissue (10%), other tissues (70-75%)

Young Women

50% of body weight
Body Fluid Compartments

70 kg man

Intracellular fluid (ICF)
- 40%, 28L

Extracellular Fluid (ECF)
- 15%
  - 10.5L  (ISF)
- 5%
  - 3.5L  (Plasma)
- 1-3%
  - transcellular fluid

Total Body Water (42L)
- 60%
Measurement of body fluid compartments

\[ V = \frac{\text{amount}}{\text{concentration}} \]

<table>
<thead>
<tr>
<th>Substance</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBW</td>
<td>Tritiated water and D(_2)O</td>
</tr>
<tr>
<td>ECF</td>
<td>sulfate, inulin, manitol</td>
</tr>
<tr>
<td>Plasma</td>
<td>radioiodinated serum albumin, Evans blue</td>
</tr>
<tr>
<td>Interstitial</td>
<td>ECF vol – plasma vol</td>
</tr>
<tr>
<td>ICF</td>
<td>TBW – ECF vol</td>
</tr>
</tbody>
</table>
Electrolyte Composition of the Body Fluids

1. Key ions determine fluid volumes
2. Osmolarity determines fluid volumes

<table>
<thead>
<tr>
<th>Electrolytes</th>
<th>(1) Plasma (mEq/L)</th>
<th>(2) Plasma Water (mEq/kg H₂O)</th>
<th>(3) Interstitial Fluid (mEq/kg H₂O)</th>
<th>(4) Intracellular Fluid (Skeletal Muscle) (mEq/kg H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>142</td>
<td>153</td>
<td>145</td>
<td>10</td>
</tr>
<tr>
<td>K⁺</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>159</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>5</td>
<td>5.4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>2</td>
<td>2.2</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>165</td>
<td>154</td>
<td>210</td>
</tr>
<tr>
<td>Anions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cl⁻</td>
<td>103</td>
<td>111</td>
<td>117</td>
<td>3</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>25</td>
<td>27</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Protein</td>
<td>17</td>
<td>18</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td>155</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>165</td>
<td>154</td>
<td>210</td>
</tr>
</tbody>
</table>

Electrolyte composition between ICF and ECF is different, but the osmolarity is the same

\[ \text{Osm}_{\text{ECF}} = \text{Osm}_{\text{ICF}} \]
Osmotic Pressure determines Cell Volumes (ICF)

<table>
<thead>
<tr>
<th>Solution</th>
<th>glucose(g/dL)</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca²⁺(mEq/L)</th>
<th>Cl⁻</th>
<th>lactate</th>
<th>osmolarity(mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% dextrose</td>
<td>5.0</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>Isotonic (278)</td>
</tr>
<tr>
<td>10% dextrose</td>
<td>10.0</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>hypertonic (556)</td>
</tr>
<tr>
<td>5% dextrose in 0.9% saline half strength saline(0.45%)</td>
<td>−</td>
<td>77</td>
<td>−</td>
<td>−</td>
<td>77</td>
<td>−</td>
<td>hypotonic (154)</td>
</tr>
<tr>
<td>normal saline (0.9%)</td>
<td>−</td>
<td>154</td>
<td>−</td>
<td>−</td>
<td>154</td>
<td>−</td>
<td>isotonic (308)</td>
</tr>
<tr>
<td>Lactated Ringer's solution</td>
<td>−</td>
<td>130</td>
<td>4</td>
<td>3</td>
<td>109</td>
<td>28</td>
<td>isotonic (274)</td>
</tr>
</tbody>
</table>
Importance of ECF volume

ISF is a diffusion medium between plasma and ICF.

Maintenance of ECF volume is essential for the adequacy of the circulation.

ECF volume is determined by mainly Na⁺ concentration

\[ \text{[Na}^+\text{]} \rightarrow \text{ECF vol.} \]

cf. cell memb. permeability
Evolutionary changes

sponges

ejellyfish

earthworm
**Cariovascular system**

*separated from ECF*

<table>
<thead>
<tr>
<th>Pump</th>
<th>Tubes</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Radiation Symbol]</td>
<td>![Tube]</td>
</tr>
</tbody>
</table>

**concentrated and packed**

- Hemoglobin
- **RBC**

**Systemic circulation - High Pr, High Resis**

**Pulmonary circulation - Low Pr, Low Resis**
Two Important Factors

**Fluid Volume**
- hyper-volemia
- hypo-volemia
- 42 L

**Osmolarity**
- hyper-osmolarity
- hypo-osmolarity
- 290 mOsm

**Symptoms**
- hypertension
- edema
- hypotension
- shock
- swelling of brain cells
- nausea, malaise, headache, confusion, lethargy, seizures, and coma

70 Kg man
Shifts of water between compartments

ICF

2/3 (28L)

ECF

1/3 (14L)

Darrow-Yannet Diagram
Addition of Pure Water

SIADH (ADH↑)
hyposmotic vol expansion
↓ Prot conc.
⇔ HCT

300 mOsm

osmolality

ICF

ECF

volume

0

28

42 L
Shifts of water between compartments

(a) Normal

(b) Add pure water

(c) Add isotonic saline (0.9%NaCl)

(d) Add pure NaCl

0.9% saline IV

isomotic vol expansion

Prot conc.

Hct

BP

Diarrhea

Hemorrhage

Sweating (hypotonic)

Hyperosmotic vol expansion

Prot conc.

Hct

BP

Prot conc.

Hct

BP

BP

BP

SIADH (ADH↑)

Hypomsotic vol expansion

Prot conc.

Hct

BP

Prot conc.

Hct

BP

Prot conc.

Hct

BP

Prot conc.
Fluid balance between ISF and Plasma: Starling's law

Oncotic proteins – albumin, globulin, fibrinogen
Disorders of Fluid Balance

- **Etiology**: liver, cardiovascular or renal disease, hormonal imbalance, or accidents

  - plasma-to-interstitial shift / plasma-to-transcellular space shift

    - Accumulation of fluid in interstices or connective tissues or transcellular spaces due to increased hydrostatic pressure or decreased osmotic pressure (third space)

- **Edema, hydrothorax (pleural effusion), hydropericardium (pericardial effusion), hydroperitoneum (ascites)**

- **Edema**:
  - Increased hydrostatic pressure
    - CHF, liver cirrhosis, constrictive pericarditis, venous obstruction, heat
  - Reduced plasm osmotic pressure
    - nephrotic syndrome, Liver cirrhosis
  - Lymphatic obstruction
    - inflammatory, neoplastic, postsurgical
  - Sodium Retention – pitting edema
    - Excessive salt intake, Increased RAA system
  - Inflammation
Fluid and Electrolyte Balance

- **Water gain**
  - Food and drink: 2.2 L/day
  - Metabolism: 0.3 L/day
  - Glucose + O₂ → CO₂ + H₂O + ATP

- **Water loss**
  - Skin: Insensible water loss 0.9 L/day
  - Lungs: 1.5 L/day
  - Feces: 0.1 L/day

Intake: 2.2 L/day + Metabolic production: 0.3 L/day = Output: (0.9 + 1.5 + 0.1)L/day

Maximum 4L/h
Water Balance

habit (at rest)

Water intake  Water output

constant

Thirst (emergency)

Water intake

Osm$_{ICF}$

effective circ. bl vol.

Kidney

Cortex

hypothalamus

renin

baroreceptors in CV sys.

Cell vol. change in ant HT osmoreceptor

ADH

cf. CHF – thirst feeling

Cirrhosis
Thirst: control mechanism for fluid intake

- emergency mechanism
- controlled by hypothalamus
- conscious sensation

**Diagram: Thirst Control Mechanism**

- **Osmoreceptor cells**
  - High threshold
  - Low threshold

- **Hypothalamus**
  - Supraoptic nucleus
  - Paraventricular nucleus

- **Posterior pituitary**
  - Release of ADH into capillaries

- **Peripheral Volume receptors**

**ADH**
Regulation of ECF Volume

**Effective circ. bl vol.**

5-10% change

**High pressure baroreceptors**
- carotid sinus & body
- aortic arch & body
- juxtaglomerular apparatus (afferent arteriole)

**Low pressure baroreceptors**
- atrial receptors – ANP
- artium, ventricle, pulmonary vein

**Circumventricular organs**
- organum vasculosum of the lamina terminalis
- subfornical organ

**Hypothalamus**
- supraoptic nucleus
- paraventricular nucleus

$Osm_{ICF}$
Response to decreased blood pressure and volume

\[ \downarrow \text{Blood volume} \]
\[ \downarrow \text{Blood pressure} \]

Volume receptors in atria and carotid and aortic baroreceptors

trigger homeostatic reflexes

Cardiovascular system

\[ \uparrow \text{Cardiac output, vasoconstriction} \]

\[ \uparrow \text{Behavior} \]

\[ \uparrow \text{Thirst causes water intake} \]

\[ \uparrow \text{ECF and ICF volume} \]

Kidneys

\[ \uparrow \text{Blood pressure} \]

Conserve H₂O to minimize further volume loss

Volume contraction

\[ \uparrow \text{Sympathetic activity} \]

\[ \uparrow \text{Renin} \]

\[ \uparrow \text{Angiotensin I} \]

Lung

\[ \uparrow \text{Angiotensin II} \]

Adrenal gland

\[ \downarrow \text{Na⁺, H₂O excretion} \]

\[ \uparrow \text{Aldosterone} \]

\[ \downarrow \text{ANP and BNP} \]

Heart

Brain

\[ \uparrow \text{ADH} \]

\[ U_{Na^+} \dot{V} = \downarrow \text{GFR} \times P_{Na^+} + \uparrow R \]
Response to elevated blood pressure and volume

↑ Blood volume → ↑ Blood pressure

Volume receptors in atria, endocrine cells in atria, and carotid and aortic baroreceptors

trigger homeostatic reflexes

Cardiovascular system → ↑ Cardiac output, vasodilation

Kidneys → Excrete salts and H₂O in urine

↓ ECF and ICF volume

↓ Blood pressure

↓ Sympathetic activity

↓ Renin

↓ Angiotensin I

↓ Angiotensin II

↑ Urodilatin

↑ ANP and BNP

Heart

Brain

↓ ADH

↑ Na⁺, H₂O excretion

↓ Angiotensin II

Adrenal gland

↓ Aldosterone

"\[ U_{Na}\hat{\nu} = \hat{\upsilon}GFR \times P_{Na} - \downarrow R \]"
Four Regulatory Pathways controlling ECF volume

1. Renin-Angiotensin-Aldosterone Axis
2. Renal Sympathetic activation
3. Arginine Vasopressin (ADH)
4. Arterial Natriuretic Peptide (ANP)
1. Renin-Angiotensin-Aldosterone Axis

- Liver constantly produces Angiotensinogen in the plasma.
- JG cells (kidney) produce Renin, which increases blood pressure and effectively reduces blood volume.
- Blood vessel endothelium (Lung) contains ACE (enzyme) to convert Ang I into Ang II in plasma.
- Ang II in plasma affects arterioles, cardiovascular control center in medulla oblongata, hypothalamus, adrenal cortex, and Na+ reabsorption to maintain blood pressure, volume, and osmolarity.
1. Renin-Angiotensin-Aldosterone Axis

Aldosterone

**Diagram:**
- **Lumen of distal nephron**
- **P cell of distal nephron**
- **Intersitial fluid**
- **Blood**
- **Aldosterone**
- **Aldosterone receptor**
- **Translation and protein synthesis**
- **K⁺ secreted**
- **Na⁺ reabsorbed**
- **New channels**
- **New pumps**
- **Proteins modulate existing channels and pumps**
- **ATP**
- **K⁺**
- **Na⁺**
2. Renal Sympathetic activation

Enhanced activity of the renal sympathetic nerves

1. increases renal vascular resistance
2. enhances renin release from granule cells
3. increases tubule reabsorption of Na⁺

H₂O and Na⁺ retention
3. Arginine Vasopressin (ADH)

**Antidiuretic Hormone (ADH)**

**Factors to release ADH**

1. stretch receptors in heart LA and Pul Vein
2. Pr. in carotid sinus and aortic arch
3. kidney-granular cells – renin - angiotensin II

Vasopressin – high conc of ADH by more than 10% loss of blood volume

- **Raise plasma osmolality → shrink hypothal. osmoreceptors → ADH cells → ADH release**

- **Factors to release ADH**
  1. stretch receptors in heart LA and Pul Vein
  2. PR in carotid sinus and aortic arch
  3. kidney-granular cells – renin - angiotensin II
Control of Secretion of Antidiuretic Hormone (ADH)

- Continuous control of ADH level over the set point (278mOsm) and under the -10% change in circulating blood volume
- Osmolarity and effective circulating blood volume work together and reinforce each other
Cellular mechanisms of ADH action

1. Insertion
2. Expression

AQP2

- Insertion
- Expression
Water Absorption

ADH
Vasopressin present

Diabetes insipidus – ADH deficiency (nephrogenic or neurogenic)
20 L/day urine
Systemic responses to changes in blood osmolarity and volume

- Osmolarity greater than 280 mOsM
  - Hypothalamic osmoreceptors
    - Interneurons to hypothalamus

- Decreased atrial stretch due to low blood volume
  - Atrial stretch receptor
    - Sensory neuron to hypothalamus

- Decreased blood pressure
  - Carotid and aortic baroreceptors
    - Sensory neuron to hypothalamus

- Hypothalamic neurons that synthesize vasopressin
  - Vasopressin (released from posterior pituitary)
    - Collecting duct epithelium
      - Insertion of water pores in apical membrane
        - Increased water reabsorption to conserve water

Key:
- Yellow: Stimulus
- Orange: Receptor
- Yellow: Afferent pathway
- Red: Integrating center
- Purple: Efferent pathway
- Blue: Effector
- Green: Tissue response
- Dark Green: Systemic response
4. Atrial Natriuretic Peptide (ANP)

- ANP - atrium
- BNP - ventricle
- Urodilantin - kidney

Increased blood volume causes increased atrial stretch

Atrial myocardial cells stretch and release

Atrial natriuretic peptide (ANP)

Key:
- Stimulus
- Integrating center
- Efferent pathway
- Effector
- Tissue response
- Systemic response

Hypothalamus

- Inhibits vasopressin

Kidney

- $\uparrow$ GFR
- $\downarrow$ Renin

Adrenal cortex

- Inhibits aldosterone

Medulla oblongata

- Decreases blood pressure

$\uparrow$ NaCl and H2O excretion
Increased renal Na⁺ retention counteracts decreased effective circulating volume.

Feedback Control of Effective Circulating Volume

- Renal baroreceptor → GFR
- Juxtaglomerular apparatus (JGA)
- Renin
- Angiotensin II (ANG II)
- Aldosterone
- Atrial low-pressure receptor
- Pulmonary low-pressure receptor
- Carotid sinus
- Central nervous system
- Atrial myocytes
- Atrial natriuretic peptide (ANP)
- Changes in hemodynamics and tubule transport
- Na⁺ excretion

1. Renin
2. Sympathetic division of ANS
3. Posterior pituitary
4. Atrial natriuretic peptide (ANP)
Na\(^+\) ion

• determines ECF volume

• generates electrical activities

• supplies energy for cellular transport
GFR = 180 L/day, PNa+ = 142 mM
Filtered Load = 25,500 mmole/day (1.5kg)
Diet 120 mmole/day

Na+ Transport

67% Na cotransporter
Na/H exchanger
Solvent drag

100 Na-Cl transporter

5% Na channels

8 Na/K/2Cl transporter paracellular

33 cortex medulla

3% ADH

25% Na channels

3 % Urine = 1.5 L/day
Filtered = 100 mmole/day

Transcellular pathway
Paracellular pathway
Regulation of Na\textsuperscript{+} Transport

1. **Glomerulotubular balance**
2. **Aldosterone**
3. **Sympathetic nerves**
   1. Decrease RBF & GFR
   2. Release renin
   3. Stimulate tubular Na\textsuperscript{+} reabsorption (activates NHE3 & Na pump)
4. **Arginine vasopression – ADH**
5. **Atrial Natriuertic Hormone**
   1. Increase RBF & GFR
   2. Inhibit Na reabsorption in the medulla
6. **PG, bradykinin, & dopamine inhibit Na\textsuperscript{+} reabsorption**
Sodium Balance

**INPUT**
- Sodium in diet: 100 - 300 mEq/day

**OUTPUT**
- Extracellular fluid
  - Skin (sweat, burns, hemorrhage)
  - Gastrointestinal losses (diarrhea, vomiting)
  - Kidneys

- Positive Na⁺ balance → ECF vol.↑ → generalized edema

High intake → hypertension
Renal Responses to Na\(^+\) intake

water intake $\rightarrow$ ECF $\uparrow$ $\rightarrow$ Wt gain

Higher Na\(^+\) intake $\rightarrow$ pos. sodium balance $\rightarrow$ increase excretion $\rightarrow$ restore equal balance

(Walser, 1985, Kidney Int)
• **Hypernatremia** > 148 mEq/L
  - hyperaldosteronism, sweating burns, diabetes insipidus, diarrhea
• **Hyponatremia** < 135 mEq/L
  - diuretics, hypoaldosteronism
  - SIADH, CHF, RF
Kidney Failure

Uremia (urine in blood)

- Lack of erythropoietin → anemia
- Plasma urea creatinine and uric acid → azotemia
- Lack of vitamin D activation → bone disease
- Increased ECF → hypertension
- Decreased H⁺ secretion → metabolic acidosis
- Decreased GFR → hyperkalemia

ERDS: End State Renal Disease, GFR <10% of Normal
Hemodialysis: pump blood through dialyzer; more efficient than peritoneal dialysis