Body Fluid Compartments

Chapters 1 & 3 in Koeppen & Stanton Renal Physiology

a) Terminology

b) Body Fluid Compartments

Terminology

Molarity – number of moles of solute / Liter of solution

- Molar (M) = moles/L
- millimolar (mM) = mmol/L

Osmole – amount of substance that dissociates in solution to form 1 mole of osmotically active particles

- 1 mole glucose = 1 osmole of solute
- 1 mole NaCl = 2 osmoles of solute

Tonicity – of solution related to effect on cell volume – ability of solute to cross cell membrane

- Isotonic solution: no change in cell volume
- Hypotonic solution: causes cell to swell
- Hypertonic solution: causes cell to shrink
Osmolality - osmoles/kg H₂O
- dependent on number molecules in solution, not size, nature, charge
- body fluid shifts between compartments
- Normal value - 290 mOsmoles/kg solution

Terminology

Osmolality - concentration of osmotically active particles in solution –
- osmoles/Liter (Osm/L)
- mosmoles/Liter (mOsm/L)

Dilute solutions: osmolality ~ osmolarity

Isosmotic - same osmolarity as plasma
- hypoosmotic - below
- hyperosmotic - above

Role of Kidneys

Maintain the volume and composition of body fluids constant despite wide variation in daily intake of water & solute.

Osmotic EQ Across Membrane

Water diffuses across semipermeable cell membranes through water channels, AQUAPORINS. Net movement of water to achieve osmotic EQ.

Osmotic Driven Water Flow

<table>
<thead>
<tr>
<th>INITIAL CONDITIONS</th>
<th>A</th>
<th>B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (L)</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Conc (mOsm)</td>
<td>400</td>
<td>200</td>
<td>---</td>
</tr>
<tr>
<td>Total Solute (mosmoles)</td>
<td>1,200</td>
<td>600</td>
<td>1,800</td>
</tr>
</tbody>
</table>

Total Solute (mosmoles) = Conc (mosmoles/L) X Volume (L)
Conc (mOsm) = 1,800 mosmoles / 6 L
= 300 mOsm
Osmotic Driven Water Flow

**INITIAL CONDITIONS**

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**EQ CONDITIONS**

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<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Volume (L)</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Conc (mOsm)</td>
<td>300</td>
<td>300</td>
<td>...</td>
</tr>
<tr>
<td>Amount Solute (mosmoles)</td>
<td>1,200</td>
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</tbody>
</table>

Solute Composition of Body Fluid Compartments

**Appendix B**

<table>
<thead>
<tr>
<th>Solute</th>
<th>Units</th>
<th>Normal Plasma Range</th>
<th>PLASMA Conc</th>
<th>Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>mmol/L</td>
<td>135 - 147</td>
<td>* 145</td>
<td>10-15</td>
</tr>
<tr>
<td>K⁺</td>
<td>mmol/L</td>
<td>3.5 - 5.0</td>
<td>4.4</td>
<td>*150</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>(ionized) mmol/L</td>
<td>1.14 - 1.3</td>
<td>1.2</td>
<td>100nM</td>
</tr>
<tr>
<td>H⁺</td>
<td>pH</td>
<td>7.35 - 7.45</td>
<td>7.4</td>
<td>~7.2</td>
</tr>
</tbody>
</table>

Major Cations and Anions

<table>
<thead>
<tr>
<th></th>
<th>Cation</th>
<th>Anion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracellular</td>
<td>Na⁺</td>
<td>Cl⁻, HCO₃⁻</td>
</tr>
<tr>
<td>Intracellular</td>
<td>K⁺</td>
<td>Organic Phosphates, Proteins</td>
</tr>
</tbody>
</table>

Water in Body

**Water** - most abundant substance in body

Solvent for all dissolved constituents

- **Intracellular** volume – volume of fluid in all cells
- **Extracellular** volume – fluid throughout compartment
  - interstitial space, vascular compartment

Size of Body Fluid Compartments
Approximate Water Distribution
70Kg Adult Human

• Total Body Water (TBW)
  ~ 60% Body Weight (BW) = ~ 42L

• Intracellular Fluid (ICF)
  ~ 60% TBW = ~ 25L

• Extracellular Fluid (ECF)
  ~ 40% BW = ~ 17L

“20, 40, 60” rule of thumb

Approximate Water Distribution

70Kg Adult Human

• TBW
  ~ 60% BW = ~ 42L

• Intracellular Fluid (ICF)
  ~ 40% TBW = ~ 25L

• Extracellular Fluid (ECF)
  ~ 20% BW = ~ 17L

ECF = 17L

• Interstitial Fluid (ISF)
  ~ 75% ECF = 13L

• Plasma Volume (PV)
  ~ 20% ECF = 3L

• Blood Volume (BV)
  ~ PV/(1-Hct) = 5.5L

• Transcellular Fluid (synovial & cerebrospinal fluid)
  ~ 5% ECF = 1L

Calculating Changes in Body Fluid Volumes

Osmoles = Osmolarity (milliosmoles/L) × Body Water (L)

Total Body
12,180 milliosmoles = 290 mosmoles/L × 42 L

ICF
7,250 milliosmoles = 290 mosmoles/L × 25 L

ECF
4,930 milliosmoles = 290 mosmoles/L × 17 L

Body Fluid Compartments

<table>
<thead>
<tr>
<th>Extracellular fluid (ECF)</th>
<th>Intracellular fluid (ICF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 liters × 290 mOsm</td>
<td>25 liters × 290 mOsm</td>
</tr>
<tr>
<td>4930 milliosmoles</td>
<td>7250 milliosmoles</td>
</tr>
</tbody>
</table>
INFUSE 1.5L Isotonic Saline (145 mM NaCl)

<table>
<thead>
<tr>
<th>ECF</th>
<th>ICF</th>
</tr>
</thead>
<tbody>
<tr>
<td>(17 + 1.5) 18.5 liters × 290 mOsm 5365 milliosmoles</td>
<td>25 liters × 290 mOsm 7250 milliosmoles</td>
</tr>
</tbody>
</table>

Expand ECFV + 1.5L
ICFV Stays Same

Infuse 1.5 L Pure Water (Isotonic Glucose)

<table>
<thead>
<tr>
<th>EARLY</th>
<th>FINAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECF (17 + 1.5) 18.5 liters × 290 mOsm 4930 milliosmoles</td>
<td>ECF 17.6 liters × 280 mOsm 4600 milliosmoles</td>
</tr>
<tr>
<td>ICF 25 liters × 290 mOsm 7250 milliosmoles</td>
<td>ICF 35.9 liters × 280 mOsm 7250 milliosmoles</td>
</tr>
</tbody>
</table>

↑ ECF 40% of 1.5L = 0.6L
↑ ICF 60% of 1.5L = 0.9L

Summary I
1. Determine body fluid volumes based on body weight
2. Predict changes in fluid volume and osmolality caused by salt and fluid loss and gains

Renal Clearance
1. Concept of Clearance
2. Clearance of Inulin, Creatinine = Estimates of Glomerular Filtration Rate (GFR)
3. PAH, estimate of Renal Plasma Flow (RPF)

Renal Processes
- **Filtration**
  - Glomerular capillary lumen ⇒ Bowman’s space (bulk flow)
- **Tubular Reabsorption**
  - Tubular lumen ⇒ peritubular capillary plasma
- **Tubular Secretion**
  - Peritubular plasma (capillary lumen) ⇒ interstitial space ⇒ tubular cell ⇒ tubular lumen (tubular cell interior to tubular lumen)
Renal Plasma Clearance

- Renal CLEARANCE of any substance

**volume of plasma from which a substance is completely removed (cleared) by kidneys per unit time**

Units = Volume plasma per time

ml/min

- QUANTITATIVE evaluation of how kidney handles a specific substance

\[
\text{Clearance } X = \frac{\text{Mass excreted}}{\text{time}}
\]

Plasma \([X]\)

\[
\text{Cl}_X \cdot P_X = \frac{U_X \cdot \dot{V}}{P_X}
\]

**Inulin**

\[
\text{Cl}_{IN} = \text{GFR}
\]

**Inulin Measurements of GFR**

\[
\text{Amount Filtered} = \text{Amount Excreted}
\]

\[
\text{GFR} \cdot P_{IN} = U_{IN} \cdot \dot{V}
\]

\[
\text{GFR} = \frac{U_{IN} \cdot \dot{V}}{P_{IN}} = \text{Cl}_{IN}
\]

<table>
<thead>
<tr>
<th>Substance</th>
<th>CLEARANCE (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>0</td>
</tr>
<tr>
<td>Na(^+)</td>
<td>0.9</td>
</tr>
<tr>
<td>K(^+)</td>
<td>12</td>
</tr>
<tr>
<td>Inulin</td>
<td>125</td>
</tr>
<tr>
<td>Creatinine</td>
<td>140</td>
</tr>
<tr>
<td>PAH</td>
<td>560</td>
</tr>
</tbody>
</table>
Creatinine

ClCr ~ GFR

Creatinine Fig 3-2
- Metabolism of creatine phosphate in muscle
- Produced continuously
- Freely filtered
- NOT reabsorbed
- Small amount secreted PT
- NO infusion required
- Stable P[Cr]
- P[Cr] & U[Cr] ~ colorimetric method

Plasma Creatinine Concentrations

\[ P_{Cr} = 0.8 - 1.2 \text{ mg/dl (1.0 mg/dl)} \]

normal range for adult

Plasma\(_{Cr}\), inversely related to GFR

<table>
<thead>
<tr>
<th>GFR ml/min</th>
<th>P(_{Cr}) mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>1</td>
</tr>
<tr>
<td>60</td>
<td>2</td>
</tr>
<tr>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>15</td>
<td>8</td>
</tr>
</tbody>
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PAH
Para-amino hippuric acid

Cl\(_{PAH}\) ~ RPF
Para-amino hippuric acid (PAH)

• Organic anion
• Freely filtered
• Vigorously secreted
• ≥ 90% removed in single circuit
• ~ 10% remains RV
• NOT produced
• Infusion required

Para-amino hippuric acid (PAH)

**PAH Clearance ~ Renal Plasma Flow**

\[ \text{RPF} \times P_{\text{PAH}} = \dot{U}_{\text{PAH}} \times \dot{V} \]

Rearrange

\[ Cl_{\text{PAH}} = \frac{\dot{U}_{\text{PAH}} \times \dot{V}}{P_{\text{PAH}}} \]

**Filtered Load of Substance A**

GFR \times Plasma [A]

GFR \times P_A

**Excretion Rate**

Urine [A] \times Urine flow

\[ \dot{U}_A \times \dot{V} \]

**Clearance**

- \( Cl_X < GFR \) \text{ net reabsorption X }
- \( Cl_X > GFR \) \text{ net secretion X }
- \( C_X < C_{IN} \) reabsorbed, i.e. glucose
- \( C_X > C_{IN} \) secreted, i.e. PAH
- Protein bound drug is not filtered
- filtered load > rate of excretion = reabsorption X

**Summary II**

1. Clearance of certain substances – index of renal function
2. Plasma creatinine - tool for diagnosing and following renal function

**Problem Set Posted on Schedule**

1. Body Fluid Problems
2. Renal Clearance

**Time for Questions**