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Please Use the Subject Line – Renal Physiology Question

Posted on Medical Physiology
Schedule of Classes:
Learning Objectives, Reading Assignments, Handouts, Problems Sets, Tutorials, Review Article
Renal Physiology - Lectures

1. Physiology of Body Fluids – Problem Set Posted – 4/19/11
2. Structure & Function of the Kidneys
3. Renal Clearance & Glomerular Filtration – Problem Set Posted
4. Regulation of Renal Blood Flow – Review Article Posted
5. Transport of Sodium & Chloride – Posting of Tutorials A & B

Renal Physiology - Lectures

6. Transport of Urea, Glucose, Phosphate, Calcium & Organic Solutes
7. Regulation of Potassium Balance
8. Regulation of Water Balance
9. Transport of Acids & Bases
10. Integration of Salt & Water Balance
Renal Physiology Lecture 1

Physiology of Body Fluids
Chapter 1 - Koeppen & Stanton Renal Physiology

1. Terminology
2. Body Fluid Compartments
3. Indicator Dilution Principle
4. Clinical Examples
Three Emergency Room Patients

- 80 yo - over medicated - no drinking 3 d
- 3 wk infant – vomiting & diarrhea 2 d
- Gunshot wound – 2 L blood loss

Terminology

Molarity – number of moles of solute / Liter of solution

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

**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*

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Terminology

**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
Terminology

**Osmolality** - osmoles/kg H₂O

- dependent on number molecules in solution, not size, nature or charge
- body fluid shifts between compartments
- Normal value - 290 mOsmoles/kg of solution

**Osmolarity** - concentration of osmotically active particles in solution –

- osmoles/Liter (Osm/L)
- mosmoles/Liter (mOsm/L)

Dilute solutions: **osmolality ~ osmolarity**
Terminology

**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.
# Solute Composition of Body Fluid Compartments

<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 - 145</td>
<td>142</td>
<td>15</td>
</tr>
<tr>
<td>K⁺</td>
<td>mmol/L</td>
<td>3.5 - 5.0</td>
<td>4.4</td>
<td>140</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>mmol/L</td>
<td>1.14 - 1.3</td>
<td>1.2</td>
<td>100 nM</td>
</tr>
<tr>
<td>H⁺</td>
<td>pH</td>
<td>7.38 - 7.42</td>
<td>7.4</td>
<td>~7.2</td>
</tr>
</tbody>
</table>

<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>Cl⁻</td>
<td>mmol/L</td>
<td>100 - 108</td>
<td>102</td>
<td>10</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>mmol/L</td>
<td>22 - 26</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Protein</td>
<td>g/dl</td>
<td>22 - 26</td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Glucose</td>
<td>mg/dl</td>
<td>70 - 110</td>
<td>100</td>
<td>---</td>
</tr>
<tr>
<td>Osmolality</td>
<td>mosmol/kg H₂O</td>
<td>285 - 295</td>
<td>290</td>
<td>290</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>

**ECFV** determined mainly by amount Na⁺ in ECF  
**ICFV** determined mainly by total body K⁺ content

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**Renal Physiology Lecture 1**  
**Physiology of Body Fluids**  
Chapter 1 - Koeppen & Stanton Renal Physiology

1. Terminology  
2. **Body Fluid Compartments**  
3. Indicator Dilution Principle  
4. Clinical Examples
Ionic Properties of ICF & ECF Different?

- Semi-permeable cell membrane
- Inside-negative membrane potential
- Active transport
- Intracellular localization of multivalent proteins

Serum

- Sodium, potassium, chloride, bicarbonate, urea, glucose = 95% total osmolality
- Albumin (most abundant serum protein) ~ 1 mOsm
Water in Body

**Water** - most abundant substance in body

Solvent for all dissolved constituents in body

**Intracellular** volume – volume of fluid within *all cells* of body

**Extracellular** volume – “NON-intracellular” fluid (interstitial space, intravascular compartment, transcellular)

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Osmotic EQ Across Membrane

**Solutes** (don’t move)  
**H₂O** (moves)  
**Solutes** (don’t move)  
**H₂O** (moves)

Water diffuses across *semipermeable* cell membranes = water channels = **Aquaporins**

Net movement **water** = osmotic EQ
### Osmotic Driven Water Flow

#### INITIAL CONDITIONS

<table>
<thead>
<tr>
<th></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 (mosmoles/L)</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>

\[
\text{Total Solute} \ (\text{mosmoles}) = \text{Conc} \ (\text{mosmoles/L}) \times \text{Volume} \ (\text{L})
\]

\[
\text{Conc} = \frac{1,800 \text{ mosmoles}}{6 \text{ L}} = 300 \text{ mosmoles/L}
\]

---

#### EQUILIBRATION CONDITIONS

<table>
<thead>
<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 (mosmoles/L)</td>
<td>300</td>
<td>300</td>
<td>---</td>
</tr>
<tr>
<td>Amount Solute (mosmoles)</td>
<td>1,200</td>
<td>600</td>
<td>1,800</td>
</tr>
</tbody>
</table>
Total Body Water (TBW) = 0.6 X Body Weight = 42 L

- Extracellular Fluid (ECF) 1/3 of TBW
- Intracellular Fluid (ICF) 2/3 of TBW

Cell membrane

- Plasma ¼ of ECF

- Interstitial Fluid 3/4 of ECF

Capillary membrane

Size of Body Fluid Compartments
Size of Body Fluid Compartments

- Extracellular = 17 L
- Intracellular = 25 L
- Blood Plasma = 3 L
- Interstitial Fluid = 13 L
- Extracellular Fluid (ECF) = 17 L
- Intracellular Fluid (ICF) = 25 L
- Total Body Water (TBW) = 42 L

Approximate Water Distribution
70Kg Adult Human

- Total Body Water (TBW)
  ~ 60% Body Weight (BW) = ~ 42 L
- Intracellular Fluid (ICF)
  ~ 40% BW = ~ 25 L
- Extracellular Fluid (ECF)
  ~ 20% BW = ~ 17 L

“20, 40, 60” rule of thumb
Approximate Water Distribution
70Kg Adult Human

- Total Body Water (TBW)
  \[ \sim 60\% \text{ Body Weight (BW)} = \sim 42 \ L \]
  - Adult Males: 55-60\% of BW
  - Adult Females: 50-55\% of BW
  - Infant: 65-75\% of BW
  - H_2O content adipocytes (10\%)
  < other cell types (muscle 76\%)

Approximate Water Distribution
70Kg Adult Human

- Total Body Water (TBW)
  - 60\% BW = \sim 42 \ L
- Intracellular Fluid (ICF)
  - 60\% TBW = \sim 25 \ L
- Extracellular Fluid (ECF)
  - 40\% TBW = \sim 17 \ L
ECF ~ 17 L

- Interstitial Fluid (ISF)
  - 75% ECF ~ 13 L

- Plasma Volume (PV)
  - 20% ECF ~ 3 L

- Blood Volume (BV)
  \[ \text{PV} / (1 - \text{Hct}) \approx 5.5 \text{ L} \]

- Transcellular Fluid (synovial & cerebrospinal, intraocular, renal tubular)
  - 5% ECF ~ 1 L

Calculating Changes in Body Fluid Volumes

\[
\text{Osmoles} = \frac{\text{Osmolality (milliosmoles/kg H}_2\text{O)}}{\text{Body Water (L)}} 
\]

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

ICF
7,250 milliosmoles = 290 mosmoles/L \times 25 L

ECF
4,930 milliosmoles = 290 mosmoles/L \times 17 L
Body Fluid Compartments

A INITIAL CONDITION

<table>
<thead>
<tr>
<th>Extracellular fluid (ECF)</th>
<th>Intracellular fluid (ICF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 liters</td>
<td>25 liters</td>
</tr>
<tr>
<td>× 290 mOsm</td>
<td>× 290 mOsm</td>
</tr>
<tr>
<td>4930 milliosmoles</td>
<td>7250 milliosmoles</td>
</tr>
</tbody>
</table>

INFUSE 1.5 L Isotonic Saline (145 mM NaCl)

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

Expand ECFV + 1.5 L  ICFV Stays Same
Infuse 1.5 L Pure Water (Isotonic Glucose)

**EARLY**

↑ ECF 1.5 L

**FINAL**

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

Add 217.5 mmoles NaCl to ECF (No Volume)

**INITIAL CONDITION**

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<tbody>
<tr>
<td>× 290 mOsm</td>
<td>× 290 mOsm</td>
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</table>

ECF expands by 0.9 L

ICF shrinks by 0.9 L
Sweat 2 L + Drink 2 L H₂O
↔ TBW Volume
↓ TBW Osmolality
↓ ECF Osmolality
Water Shifts ECF → ICF
↓ ECFV
↑ ICFV
↓ ECF Osmolality
↓ ICF Osmolality

Food for Thought… Eat BIG Bag Chips NO Drinking

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Physiology of Body Fluids
Chapter 1 - Koeppen & Stanton Renal Physiology

1. Terminology
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Measuring Compartment Volumes

- Principle of dilution
- Substance measured
  - colorimetrically
  - radioactive labeled compound

Determination Body Fluid Volumes - Indicators

<table>
<thead>
<tr>
<th>TBW</th>
<th>ECV</th>
<th>BV</th>
<th>PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>D₂O</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deuterium-heavy water</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tritium, tritiated water</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Determination Body Fluid Volumes - Indicators

<table>
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<th>BV</th>
<th>PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{D}_2\text{O}$, deterium-heavy water</td>
<td>Inulin</td>
<td>Radio-active Iron</td>
<td></td>
</tr>
<tr>
<td>HTO, tritium, tritiated water</td>
<td>Mannitol, Sucrose</td>
<td>Cr$^{51}$, RBC</td>
<td>Radioactive Sodium $^{22}\text{Na}$</td>
</tr>
</tbody>
</table>
Determination Body Fluid Volumes - Indicators

<table>
<thead>
<tr>
<th>TBW</th>
<th>ECV</th>
<th>BV</th>
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</tr>
</thead>
<tbody>
<tr>
<td>D$_2$O</td>
<td>Inulin</td>
<td>Radioactive Iron</td>
<td>RISA $^{131}$I-Albumin</td>
</tr>
<tr>
<td>deterium-heavy water</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTO</td>
<td>Mannitol</td>
<td>Cr$^{51}$ RBC</td>
<td>T-1824 Evan’s Blue dye, bound to albumin</td>
</tr>
<tr>
<td>tritium, tritiated water</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radioactive Sodium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{22}$Na</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Measuring Size of Compartments: INDIRECTLY

- Interstitial Fluid – *no indicator*
  
  = ECF volume minus Plasma volume

- ICF - *no indicator*
  
  = TBW volume minus ECF volume
**Indicator Dilution Principle**

![Diagram of indicator dilution principle](image)

**Conc of Indicator** = **Amount of Indicator** / **Volume of Distribution**

**Amount** = **Volume** × **Conc**

\[ V = \frac{\text{Amount}}{\text{Conc of Indicator}} \]

**Body Fluid Problem**

Inject 10 g indicator. Wait 2 hr.

\[ P \ [\text{Indicator}] = 0.2 \text{ g/L} \]

\[ V = \frac{10 \text{ g}}{0.2 \text{ g/L}} \]

\[ V = 50 \text{ L} \]
**Body Fluid Problem**
Inject 60 μCi labeled albumin. Wait 2 hr.
P [Albumin] = 0.02 μCi/ml

What is the body fluid volume to be determined?

\[ V = \frac{\text{Amount}}{\text{Conc of Indicator}} \]
\[ V = \frac{60 \ \mu\text{Ci}}{0.02 \ \mu\text{Ci/ml}} \]
\[ V = 3,000 \ \text{ml} = 3 \ \text{L} \]

Indicator diluted 3,000 times in volume of distribution
**Body Fluid Problem**

Inject 0.5 mg Evans Blue Dye iv

Plasma [EBD] = 0.4 mg/ml

? V ?

Known Indicator 0.5 mg

Plasma [EBD] 0.4 mg/ml

\[
V = \text{amount} / \text{conc} \\
V = 0.5 \text{ mg} / 0.4 \text{ mg/ml} \\
V = 1.25 \text{ ml}
\]

**Renal Physiology Lecture 1**

Physiology of Body Fluids
Chapter 1 - Koeppen & Stanton Renal Physiology

1. Terminology
2. Body Fluid Compartments
3. Indicator Dilution Principle
4. Clinical Examples
3 Stages of Dehydration

1. MILD
   - Thirst
   - Dry lips & mouth
   - Flushed skin
   - Fatigue & Irritability
   - Headache
   - Dark urine
   - Decrease urine output

2. MODERATE (mild +)
   - Very dry mouth & tongue
   - Skin doesn’t bounce when pressed
   - Sunken eyes
   - Limited urine output – dark yellow
   - Cramps, stiff, painful joints
   - Severe irritability & headache
   - Fatigue
3 Stages of Dehydration

3. SEVERE (mild + moderate +)
- Blue lips, cold hands & feet
- Inability to urinate or cry tears
- Rapid breathing
- Rapid & weak pulse
- Low blood pressure
- Dizziness, fainting
- Confusion, convulsions
- Lethargy
- High fever

Disorders of Water Balance

- Hypo-osmolality (Hyponatremia)
  - ↑ cell volume, brain swelling = brain edema
  - ↑ intracranial pressure
  - Confusion, seizures, coma
  - Convulsions
  - Muscle weakness, spasms
  - DEATH
Disorders of Water Balance

- Hyperosmolality (*Hypematremia*)
  - Thirst - may be associated with dehydration
  - CNS dysfunction – brain cell *shrinkage*
  - Confusion
  - Neuromuscular excitability
  - Seizures, COMA

**Learning Objectives**

1. Determine body fluid volumes based on BW
2. Predict changes in fluid volume and osmolality
   - salt & fluid loss & gains
3. Use indicator dilution principle to determine fluid volumes
THE END