Physiology of the body fluids, Homeostasis

A - BODY FLUIDS
B - BLOOD
  1- Function
  2- Composition
  3- Hemostasis
  4- Blood group
The Body as an open system

1. Open system: The body exchanges material and energy with its environment
2. Homeostasis: The process through which bodily equilibrium (*internal milieu*) is maintained.
   a. Fluid composition
   b. Temperature
   c. pH
   d. ....

Daily intake and output of water (water steady state)

- Daily intake: 2300 ml
- Total output: 2300 ml

Pathologic losses:
- bleeding
- vomiting
- diarrhea......etc.
Expressing fluid composition

1. Molality: Moles solute per kg of solvent
3. Electrochemical Equivalence (Eq): Salts such as NaCl and CaCl₂ dissociate into positive ions (cations) and negative ions (anions). An “equivalent” is the weight in grams of an ionic substance that replaces or combines with one gram (mole) of monovalent H⁺ ions.

Complications in determining plasma concentrations:
- Not all substances in plasma are freely dissociated, many of them bind to proteins or other substances (Ca²⁺, bilirubin…etc)

The indicator dilution principle

\[
\text{Volume A} = \frac{(\text{Volume B} \times \text{Concentration B})}{\text{Concentration A}}
\]

If Volume A >> Volume B
Indicator dilution method with one compartment

Indicator dilution method with two compartments
Distribution of water in body fluid compartments

Total body water

Cell water: 25 L
Interstitial fluid: 8 L
Dense connective: 3 L
Plasma: 3 L
Bone: 2 L
Transcellular: 1 L
### Measurement of Body Fluid Volumes

<table>
<thead>
<tr>
<th>Volume</th>
<th>Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Water</td>
<td>$^3\text{H}_2\text{O}$, $^2\text{H}_2\text{O}$, antipyrene</td>
</tr>
<tr>
<td>Extracellular fluid</td>
<td>$^{22}\text{Na}$, $^{125}$-iothalamat, thisulphate, inulin</td>
</tr>
<tr>
<td>Intracellular fluid</td>
<td>Calculated: TBW – ECF</td>
</tr>
<tr>
<td>Plasma volume</td>
<td>$^{125}$-albumin, <strong>Evans blue</strong></td>
</tr>
<tr>
<td>Blood volume</td>
<td>$^{51}$Cr-labeled red blood cells</td>
</tr>
<tr>
<td>Interstitial fluid</td>
<td>Calculated: ECF - PV</td>
</tr>
</tbody>
</table>

### Compartments of body fluid

1. **Intracellular fluid (cell water):** Approximately 40% of body weight
2. **Extracellular fluid:** Approximately 20% of body weight with many subcompartments
   - Plasma: 3 L ~ 5% of body weight. This is the primary accessible compartment.
   - Interstitial space: 8 L ~ 12% of body weight. This is the environment of cells.
   - The remaining 6 L of extracellular fluid is distributed in minor compartments like bone, transcellular fluid (liquor, etc.)
3. **Pathologic fluid compartments (fluid production)**
   - Transsudatum: increased local blood pressure
   - Exsudatum: increased permeability of barriers
Osmotic concept

Semipermeable membrane

C1 < C2

Osmosis: Movement of water caused by concentration difference.

Osmotic concentration

- osmolarity: concentration of a solution in term of numbers of particles per liter of solution (Osmol/l)

Physiologic value of plasma osmolarity: 286 mOsmol/L (280-290)

- Isotonic (isosmotic) fluid: 280 < π < 290

Non-physiologic osmolarity

- Hypotonic (hyposmotic): π < 280
- Hypertonic (hyperosmotic): π > 280

s.c., i.m. (but not i.v.) injection of non isotonic solution is painful

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Body Fluid Compartments

Table 27.2 Approximate Concentration of Major Solutes in Body Fluid Compartments*

<table>
<thead>
<tr>
<th>Solute</th>
<th>Plasma 153.2</th>
<th>Intersitial Fluid 145.1</th>
<th>Intracellular Fluid 12.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium (Na⁺)</td>
<td>153.2</td>
<td>145.1</td>
<td>12.0</td>
</tr>
<tr>
<td>Potassium (K⁺)</td>
<td>6.3</td>
<td>4.1</td>
<td>150.0</td>
</tr>
<tr>
<td>Calcium (Ca²⁺)</td>
<td>3.8</td>
<td>3.4</td>
<td>4.6</td>
</tr>
<tr>
<td>Magnesium (Mg²⁺)</td>
<td>1.4</td>
<td>1.3</td>
<td>34.0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>162.7</td>
<td>153.0</td>
<td>200.0</td>
</tr>
<tr>
<td>Anions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride (Cl⁻)</td>
<td>118.0</td>
<td>118.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Bicarbonate (HCO₃⁻)</td>
<td>25.7</td>
<td>27.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Phosphate (HPO₄²⁻ plus H₂PO₄⁻)</td>
<td>2.2</td>
<td>2.2</td>
<td>40.0</td>
</tr>
<tr>
<td>Protein</td>
<td>17.0</td>
<td>0.0</td>
<td>54.0</td>
</tr>
<tr>
<td>Other</td>
<td>6.3</td>
<td>6.6</td>
<td>90.0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>162.7</td>
<td>153.0</td>
<td>300.0</td>
</tr>
</tbody>
</table>

*Expressed as milliequivalents per liter (meq/l).
*Data are from several tissues.
Clinical terminology

Hypernatremia (plasma Na⁺ concentration is above the normal)  
- → reduced E.C. → I.C. fluid (shrinkage of cells).

Hyponatremia (plasma Na⁺ concentration is above the normal)  
- → increased E.C. → I.C. fluid (sweling of cells).

Hypervolemia: circulating blood volume is increased

Hypovolemia: circulating blood volume is decreased

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Blood – Physical Characteristics

- Adult ♂ contains 5-6L
- Adult ♀ contains 4-5L
- 5 times as viscous as water
- pH ranges from 7.35 – 7.45 (slightly alkaline)
- Color ranges from scarlet (oxygenated blood) to a deep red (deoxygenated blood).

Blood: Functions:

1 - Transportation - oxygen & carbon dioxide nutrients waste products (metabolic wastes, excessive water, & ions)
2 - Regulation - hormones & heat (to regulate body temperature)
3 - Protection - clotting mechanism protects against blood loss & leucocytes provide immunity against many disease-causing agents
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Components of Whole Blood

- Hematocrit
  - Males: 47% ± 5%
  - Females: 42% ± 5%
Function of plasma proteins
(albumins, globulins, fibrinogen)

1. Maintaining colloid osmotic balance (albumins)
2. Buffering pH changes
3. Transport of materials through blood
(such as water insoluble hormones)
4. Antibodies
   (e.g. gamma globulins, immunoglobulins)
5. Clotting factors (e.g. fibrinogen)

3 Cellular Elements of Blood

1. Red Blood Cells
2. White Blood Cells
3. Platelets
Red blood cells (Erythrocytes)

- biconcave discs
- 2. lack a nucleus & cannot reproduce (average lifespan = about 120 days)
- 3. transport hemoglobin (each RBC has about 280 million hemoglobin molecules)
- 4. typical concentration is 4-6 million per cubic mm (or hematocrit [packed cell volume] of about 42% for females & 45% for males)

**Primary Function** = Transport oxygen from the lungs to the cells of the body & assist with CO₂ removal

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Erythropoiesis

rate is regulated by oxygen levels:

1. hypoxia (lower than normal oxygen levels) is detected by cells in the kidneys

2. kidney cells release the hormone erythropoietin into the blood

3. erythropoietin stimulates erythropoiesis by the bone marrow
2. White Blood Cells (Leukocytes)

- A typical TL of blood contains 6000-9000 WBCs.
- Most of the WBCs in the body at a given moment are located in the connective tissue or in organs of the lymphatic system.
- Circulating WBCs are just a fraction of the total #

WBC functions
- “Seek and Destroy” Functions:
  1. Destroy invading microorganisms
  2. Destroy abnormal cells (ie: cancer)
- Clean up cellular debris (phagocytosis)
  3. Assist in injury repair

Types of WBC’s

Can be classified based on the appearance of granules when viewed under the light microscope.

Agranulocytes
- Do not contain visible granules.

Granulocytes
- Contain visible granules.
3. Platelets (thrombocytes)

• Flattened disk-like cell fragments that are about 4µm.
• Act as a participant in the vascular clotting system. Platelets are sometimes referred to as thrombocytes (thrombus=clot)
• Continuously being replaced. Each platelet circulates for 9-12 days before being removed by splenic phagocytes.
• On average there are 350,000 platelets/µL of blood.
• Produced in the bone marrow. Large cells called megakaryocytes release fragments (platelets) into the circulation.

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   – Anemia
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Anemia

Decreased number of RBCs and reduced hemoglobin content of blood

- blood has abnormally low oxygen-carrying capacity
  - Signs/symptoms: fatigue, paleness, shortness of breath, chills

1. Decreased erythropoiesis
   a. iron deficit (reduced iron intake...)
   b. Vitamin B12 deficit
   c. problem with bone marrow

2. Increased erythroylysis
   (it may cause jaundice)
   d. haemolysis
   e. hepatosplenomegialia

3. Bleeding
   e. acute (e.g. car accident)
   f. chronic (e.g. gastric erosion)
   g. menstruation
   h. pregnancy and delivery

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Hemostasis

- Prevents blood loss thru the walls of damaged blood vessels
- Also establishes a framework for further tissue repairs
- Main phases of hemostasis:
  - Vascular Phase
  - Platelet Phase
  - Coagulation Phase

Vascular Phase

Blood Vessel Damage

Smooth muscle in blood vessel wall contracts

BV diameter decreases

Blood loss slows
Platelet Phase

Occurs within 15sec of the injury

• Platelets begin to attach to sticky endothelial cells

• The aggregation of platelets eventually results in a platelet plug, a temporary mass of platelets that stops blood loss and forms a framework for the clot.

Coagulation Phase

• Begins 30sec or more after vessel damage occurs

• Involves a sequence of steps leading to the conversion of fibrinogen (a circulating plasma protein) to the insoluble protein fibrin.

Extrinsic pathway  Intrinsic pathway

<table>
<thead>
<tr>
<th>Damaged Endothelial Cells</th>
<th>Collagen Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Release Tissue Factor</td>
<td>Platelet Factor</td>
</tr>
</tbody>
</table>

Ca²⁺ Prothrombin Thrombin Fibrinogen Fibrin

Cross-linked fibrin CLOT combines with the platelet plug, RBCs
Fibrinolysis

• As repairs proceed, the clot gradually dissolves (fibrinolysis)
• This process begins with the coagulation process
• Plasmin digests the fibrin strands and erodes the foundation of the clot

Manipulating Hemostasis

Important anticoagulant drugs include:

– Heparin inactivates thrombin
– Coumarin blocks the action of Vitamin K
– Streptokinase
– Aspirin inhibits platelet aggregation
Clotting disorders

• Too much:
  – Inappropriate clot formation is a thrombus (free-floating clots are emboli)
  – An enlarging thrombus narrows and can occlude vessels

• Too little:
  – Hemophilia - too little clotting can lead to life-threatening hemorrhage (caused from lack of one of the clotting factors)
  – Thrombocyte deficiency (low platelets) can also lead to diffuse hemorrhages

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## Blood Types

- A classification of blood based on the presence or absence of inherited antigenic substances on the surface of red blood cells.
- In some case, presence of antibodies in the plasma
- Examples:
  - ABO,
  - Rh,
  - MNS (M+ & N+),
  - Kell (K+ & K-),
  - Lewis (Le^a & Le^b)

## Terminology

- **Agglutination**: clumping red blood cells as a result of mixing of samples from incompatible blood groups (precipitation, coagulation)
- **Agglutinin**: a substance that causes particles to coagulate to form a thickened mass (antibody)
- **Agglutinogen**: a substance that, acting as an antigen, stimulates the production of agglutinin
- **Transfusion**: It is the most frequent type of organ transplantation
Rh blood type

**Rh +:**
- carries D antigen on the RBCs
- no antibody ever present in the plasma

**Rh -:**
- no D antigen on the RBCs.
- no antibody anti-RhD in the plasma
  BUT the person can manufacture them if they are exposed to D antigen (unproper blood transfusion)

RH+: more common (85%)