Fluid, Electrolyte, and Acid-Base Balance

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Body Fluids

- A typical adult body contains about 40 L of body fluids.
- 25 L of fluids (or 63%) are located inside body cells, called **intracellular fluid** (ICF).
- 15 L of fluids (or 37%) are located outside of body cells, called **extracellular fluid** (ECF).
- 80% of ECF is **interstitial fluid** (which includes lymph, synovial fluid, cerebrospinal fluid, GI tract fluids, and fluids in the eyes and ears), and 20% of ECF is **blood plasma**.
- ICF is mostly water and is rich in K⁺, Mg⁺⁺, HPO₄²⁻, SO₄²⁻, and protein anions.
- ECF contains more Na⁺, Cl⁻, HCO₃⁻, and Ca⁺⁺.
Total body water volume = 40 L, 60% body weight

<table>
<thead>
<tr>
<th>Extracellular fluid volume = 15 L, 20% body weight</th>
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</thead>
<tbody>
<tr>
<td>Intracellular fluid volume = 25 L, 40% body weight</td>
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<tr>
<td>Interstitial fluid volume = 12 L, 80% of ECF</td>
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<tr>
<td>Plasma volume = 3 L, 20% of ECF</td>
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</tbody>
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Concentrations of substances dissolved in ICF and ECF are constantly different because the cell membrane is selectively permeable, which maintains a relatively unchanged distribution of substances in different body fluids.

Fluid balance refers to the proper levels of water and electrolytes being in the various body compartments according to their needs.

Osmotic pressure (created by the dissolved electrolytes in body fluids) and hydrostatic pressure (created by the water in body fluids) are the main forces behind any molecular movement between body compartments.
Water balance

- Water is the most abundant constituent in the body, varying from 45% to 75% of body weight. Water balance occurs when water intake equals water output. A normal adult consumes about 2,500 ml of water daily -- 1,500 ml in beverages, 750 ml in food, and 250 ml from cellular respiration and anabolic metabolism. At the same time, this adult is releasing about 2,500 ml of water daily -- 1,500 ml in urine, 700 ml by evaporation (through the skin and lungs), 100 ml in the feces, and 200 ml in sweating.
Water balance in the body

Water gain

- 2.2 L/day Food and drink

Water loss

- Insensible water loss 0.9 L/day
- Lungs
- Urine 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 = 0

Glucose + O₂ → CO₂ + H₂O + ATP

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Regulation of Water intake

1. The body loses as little as 1% of its water.
2. An increase in osmotic pressure of extracellular fluid due to water loss stimulates osmoreceptors in the thirst center (hypothalamus).
3. Activity in the hypothalamus causes the person to be thirsty and to seek H₂O.
   - Drinking and the resulting distension of the stomach by water stimulants nerve impulses that inhibit the thirst center.
   - Water is absorbed through the wall of the stomach, small intestine, and large intestine.
   - The osmotic pressure of extracellular fluid returns to normal.
The Thirst mechanism for regulating water intake

- **Plasma osmolality**
  - **Plasma volume**
    - Blood pressure
      - Granular cells in kidney
        - Renin-angiotensin mechanism
          - Angiotensin II
            - Water moistens mouth, throat; stretches stomach, intestine
          - Water absorbed from GI tract
            - Hypothalamic thirst center
              - Sensation of thirst; person takes a drink
            - Plasma osmolality

(*Minor stimulus*)

**Key:**
- Increases, stimulates
- Reduces, inhibits
- Initial stimulus
- Physiological response
- Result

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Events in regulation of water output

I. Dehydration:

1. Extracellular fluid becomes osmotically more concentrated.

2. Osmoreceptors in the hypothalamus are stimulated by the increase in the osmotic pressure of body fluids.

3. The Hypothalamus signals the posterior pituitary gland to release ADH into the blood.

4. Blood carries ADH to the kidneys.

5. ADH causes the distal convoluted tubules & collecting ducts to increase water reabsorption.

6. Urine output decreases, and further water loss is minimized.
Excess water intake

1. Extracellular fluid becomes osmotically less concentrated.
2. This change stimulates osmoreceptors in the hypothalamus.
3. The posterior Pituitary gland decrease ADH release.
4. Renal tubules decrease water reabsorption.
5. Urine output, increases and excess water is excreted.
Electrolyte balance

Electrolytes are chemical substances that release cations (positively charged ions) and anions (negatively charged ions) when they are dissolved in water. Electrolytes serve 4 primary functions in the body.

- as essential minerals (e.g. iodine, calcium).
- control osmosis between body compartments by establishing proper osmotic pressure (e.g. sodium, chloride).
- help maintain acid-base balance (e.g. hydrogen ion, bicarbonate ion).
- carry electrical current that allows the production of action potentials (e.g. sodium, potassium).

The most important electrolytes include Na\(^+\), K\(^+\), Cl\(^-\), Ca\(^{++}\), and HPO\(_4\)\(^{2-}\).
- **Na**\(^+\) is the most abundant extracellular cation; involved in nerve impulse transmission, muscle contraction, and creation of osmotic pressure.

- **Cl**\(^-\) is a major extracellular anion; involved in regulating osmotic pressure between body compartments, forming HCl in stomach, and involved in the “chloride shift” process in blood.

- **K**\(^+\) is the most abundant cation in ICF; involved in maintaining fluid volume, nerve impulse transmission, muscle contraction, and regulating pH.
- **Ca**^{++} is the most abundant ion in the body, located mainly in ECF; a major structural component of bones and teeth; functions in blood clotting, neurotransmitter release, muscle tone, and excitability of nervous and muscle tissues.

- **HPO_{4}^{2-}** is an important intracellular anion; another major structural component of bones and teeth; required for synthesis of nucleic acids and ATP, and for buffering reactions.

- Level of electrolytes are mainly regulated by hormones:
  - **Aldosterone** (from adrenal cortex) causes an increase in sodium reabsorption and potassium secretion at the kidney tubules.
  - **Parathyroid hormone** (PTH) from the parathyroid glands and **Calcitonin** (CT) from the thyroid gland regulate calcium balance.
Regulation of electrolyte Intake & output

- **Electrolyte intake:**
  - Electrolytes are usually obtained in sufficient quantities in response to hunger and thirst mechanism.
  - In a severe electrolyte deficiency, a person may experience a salt craving.

- **Electrolyte output:**
  - Electrolytes are lost through perspiration, feces and urine. The greatest electrolyte loss occurs as a result of kidney functions.
  - Quantities lost vary with temp. and exercise.
Electrolyte Balance

- 1. Concentrations of Na, K and calcium ions in the body fluid are very important.

- 2. The regulation of Na$^+$ and K$^+$ ions involve the secretion of Aldosterone from adrenal glands.
  
  1. K$^+$ ion concentration increases.
  2. Adrenal cortex is signaled.
  3. Aldosterone is secreted.
  4. Renal tubules increase reabsorption of Na$^+$ ion and increase secretion of K$^+$ ions (excretes K ions).
  5. Na$^+$ ions are conserved and K$^+$ ions are excreted.
3. **Calcitonin** from the thyroid gland and parathyroid hormone from the parathyroid glands regulate \( \text{Ca}^+ \) ion concentration.

- Parathyroid hormone increases activity in bone-resorbing cells (osteocytes & osteoclasts) which increase the conc. of both \( \text{Ca}^+ \) and phosphate ions in extracellular fluids. This hormone also causes increase absorption of \( \text{Ca}^+ \) and increase excretion of phosphate, from the kidney.
- **Acid-base balance**

- Acids are electrolytes that release hydrogen ions (H\(^+\)) when they are dissolved in water.

- Bases are electrolytes that release hydroxide ions (OH\(^-\)) when they are dissolved in water.

- Acid-base balance is primarily regulated by the concentration of H\(^+\) (or the pH level) in body fluids, especially ECF.
Acid-base balance

- Normal pH range of ECF is from 7.35 to 7.45.
- Most H⁺ comes from metabolism -- glycolysis, oxidation of fatty acids and amino acids, and hydrolysis of proteins.
- Homeostasis of pH in body fluids is regulated by acid-base buffer systems (primary control), respiratory centers in brain stem, and by kidney tubule secretion of H⁺.
- Acid-base buffer systems are chemical reactions that consist of a weak acid and a weak base, to prevent rapid, drastic changes in body fluid pH. one of the most carefully regulated conc. in the body is that of H⁺ ion.
one of the most carefully regulated conc. in the body is that of $H^+$ ion.

- When acid ($H^+$) is added to the blood, the pH decreases. Then increased acidity (decreased pH) is minimized by buffers which bind some of the added $H^+$.

- When acid is taken away, blood becomes more alkaline (pH increases). This change is minimized by buffers, which release $H^+$ and replace some of the acid that was lost.
The pair bicarbonate / carbonic acid forms an important buffer system. \( \text{H}_2\text{CO}_3 \) (carbonic acid) is the acid member of the pair because it can release \( \text{H}^+ \). \( \text{HCO}_3^- \) is the base member of the pair because it can accept \( \text{H}^+ \). This system is important because two of its components are rigorously controlled by the body: the lungs control \( \text{CO}_2 \) and the kidney control \( \text{HCO}_3^- \).
1. Bicarbonate buffer system:

- Bicarbonate ion (HCO$_3^-$) – converts a strong acid into a weak acid.
- Carbonic acid (H$_2$CO$_3$) – converts a strong base into a weak base.
- Bicarbonate buffer system produces carbonic acid (H$_2$CO$_3$) and sodium bicarbonate (NaHCO$_3$) to minimize H$^+$ increase, mainly in the blood:

\[
\begin{align*}
(1) \text{HCl} + \text{NaHCO}_3 & \rightarrow \text{H}_2\text{CO}_3 + \text{NaCl} \\
(2) \text{NaOH} + \text{H}_2\text{CO}_3 & \rightarrow \text{NaHCO}_3 + \text{H}_2\text{O}
\end{align*}
\]
• **Phosphate buffer system**: produces sodium hydrogen phosphates (NaH$_2$PO$_4$ and Na$_2$HPO$_4$) to regulate H$^+$ levels, mainly in kidney tubules and erythrocytes:

\[
\begin{align*}
(1) \text{HCl} + \text{Na}_2\text{HPO}_4 & \rightarrow \text{NaH}_2\text{PO}_4 + \text{NaCl} \\
(2) \text{NaOH} + \text{NaH}_2\text{PO}_4 & \rightarrow \text{Na}_2\text{HPO}_4 + \text{H}_2\text{O}
\end{align*}
\]

• **Protein buffer system**: relies on the carboxylic acid group of amino acids to release H$^+$, and the amino group to accept H$^+$, mainly inside body cells and in blood plasma.
Respiratory centers in the pons and medulla oblongata regulate the rate and depth of breathing, which controls the amount of carbon dioxide gas ($CO_2$) remained in the blood and body fluid -- e.g. slower breathing rate $\rightarrow$ an increase in blood $CO_2$ level $\rightarrow$ an increase in carbonic acid ($H_2CO_3$) in blood $\rightarrow$ more $H^+$ is released into body fluids $\rightarrow$ pH of blood and body fluids drops.

Nephrons react to the pH of body fluids and regulate the secretion of $H^+$ into urine -- e.g. a diet high in proteins causes more $H^+$ to be produced in body fluids (which lowers body fluid pH), as a result the nephrons will secrete more $H^+$ into the urine.
Tubule H secretion & reabsorption of filtered HCO3

Key:
- Primary active transport
- Secondary active transport
- Carbonic anhydrase
- Simple diffusion
- Protein carrier

1. Carbonic anhydrase (CA) catalyzes the reaction: HCO3^- + H^+ → H2CO3
2. ATPase uses energy to pump Na^+ and HCO3^- into the cell
3. ATPase pumps H^+ out of the cell
4. ATPase pumps Na^+ and HCO3^- into the cell
5. CA catalyzes the reaction: H2CO3 → H2O + CO2
6. Simple diffusion of CO2 and H2O
**Compensation**

- Compensation is a series of physiological responses that react to acid-base imbalances, by returning blood pH to the normal range (7.35 – 7.45).

- **Respiratory acidosis:** (due to deficiency of CO₂ expiration) and respiratory alkalosis (due to abnormally high CO₂ expiration) are primary disorders of CO₂ pressure in the lungs. These may be compensated by renal mechanisms where nephrons will secrete more H⁺ to correct acidosis and secrete less H⁺ to correct alkalosis.

- It is due to increased CO₂ retention (due to hypoventilation), which can result in the accumulation of carbonic acid and thus a fall in blood pH to below normal.

- **Metabolic Acidosis:** increased production of acids such as lactic acid, fatty acids, and ketone bodies, or loss of blood bicarbonate (such as by diarrhea), resulting in a fall in blood pH to below normal.
Acidosis & Alkalosis

(a) Type A intercalated cell function in acidosis.
H⁺ is excreted; HCO₃⁻ and K⁺ are reabsorbed.

Lumen of collecting duct

- Filtered K⁺
- ATP
- H⁺ excreted in urine

Type A intercalated cell

- H₂O + CO₂ → CO₂ + HCO₃⁻ + H⁺
- CA
- H⁺ + HCO₃⁻ → H₂CO₃
- H₂CO₃ acts as a buffer to ↓ [H⁺]
- High [K⁺]
- K⁺ reabsorbed

Interstitial space

[b] [H⁺] high

(b) Type B intercalated cell function in alkalosis.
HCO₃⁻ and K⁺ are excreted; H⁺ is reabsorbed.

Lumen of collecting duct

- H₂O + CO₂
- CA
- HCO₃⁻
- ATP
- H⁺

Type B intercalated cell

- H⁺

Interstitial space

[b] [H⁺] low

Blood

Excreted in urine

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**Respiratory Alkalosis:**

- A rise in blood pH due loss of CO$_2$ and carbonic acid (through hyperventilation).

**Metabolic Alkalosis:**

- A rise in blood pH produced by loss of acids (such as excessive vomiting) or by excessive accumulation of bicarbonate base.
Respiratory Excretion of CO2

- The respiratory center is located in the brain stem.

- It helps control pH by regulating the rate and depth of breathing.

- Increasing CO$_2$ and H$^+$ ions concentration stimulate chemoreceptors associated with the respiratory center; breathing rate and depth increase, and CO$_2$ concentration decreases.

- If the CO$_2$ and H$^+$ ion concentrations are low, the respiratory center inhibits breathing.
Renal excretion of H⁺

- Nephrons secrete hydrogen ions to regulate pH.
- Phosphate buffer hydrogen ions in urine.
- Ammonia produced by renal cells help transport H⁺ to the outside of the body:
  \[ \text{H}^+ + \text{NH}_3 \rightarrow \text{NH}_4^+ \]
- Chemical buffer system (Bicarbonate buffer system, phosphate buffer, and protein buffer system) act rapidly and are the first line of defense against pH shift.
- Physiological buffer (respiratory mechanism CO₂ excretion), renal mechanism (H⁺ excretion) act slowly and are the 2nd line of defense against pH shift.
Source of H⁺

- a. Aerobic respiration of glucose produces CO₂, which reacts with water to form carbonic acid.
- carbonic acid dissociates to release H⁺ and bicarbonate ions.
- b. Anaerobic respiration of glucose produces lactic acid.
- c. Incomplete oxidation of fatty acids releases acidic ketone bodies.
- d. Oxidation of sulfur-containing amino acids produces sulfuric acid.
- e. Hydrolysis of phosphoproteins and nucleic acids gives rise to phosphoric acid.
Factors Associated with Edema

1. Low plasma protein concentration: cause is liver disease, kidney disease, loss of protein in urine, lack of protein in diet due to starvation.

   Effect: plasma osmotic pressure decreases, less fluid enters venular end of capillaries by osmosis.

2. Obstruction of lymph vessels: causes are surgical removal of portions of lymphatic pathways and parasitic infections.

   Effect: back pressure in lymph vessels, interferes with movement of fluid from interstitial spaces into lymph capillaries.

3. Increased venous pressure: venous obstruction or faulty valves.

   Effect: back pressure in veins increases capillary filtration and interferes with return of fluid from interstitial spaces into venular end of capillaries.
4. Inflammation: cause is tissue damage.

Effect: capillaries become abnormally permeable and fluid leaks from plasma into the interstitial spaces.