Cell function depends not only on continuous nutrient supply / waste removal, but also on the physical / chemical homeostasis of surrounding fluids.

1) **Water**: (universal solvent)

- Body water varies based on age, sex, mass, and body composition

\[
\begin{align*}
\text{H}_2\text{O} & \sim 73\% \text{ body weight} \\
\text{Low body fat} & \\
\text{Low bone mass} & \\
\text{H}_2\text{O} (\varnothing) & \sim 60\% \text{ body weight} \\
\text{H}_2\text{O} (\varphi) & \sim 50\% \text{ body weight} \\
\varphi & = \uparrow \text{ body fat} / \downarrow \text{ muscle mass} \\
\text{H}_2\text{O} & \sim 45\% \text{ body weight}
\end{align*}
\]
Body Fluids:

Cell function depends not only on continuous nutrient supply / waste removal, but also on the physical / chemical homeostasis of surrounding fluids

1) Water: (universal solvent)

Total Body Water
Volume = 40 L
(60% body weight)

Intracellular Fluid (ICF)
Volume = 25 L
(40% body weight)

Interstitial Fluid
Volume = 12 L

Extracellular Fluid (ECF)
Volume = 15 L
(20% body weight)

Clinical Application:

The volumes of the body fluid compartments are measured by the dilution method

Step 1: Identify appropriate marker substance
- **Total Body Water:**
  - A marker is placed in the system that is distributed wherever water is found
  - Marker: $D_2O$
- **Extracellular Fluid Volume:**
  - A marker is placed in the system that can not cross cell membranes
  - Marker: Mannitol

Step 2: Inject known volume of marker into individual

Step 3: Let marker equilibrate and measure marker
- Plasma concentration
- Urine concentration

Step 4: Calculate volume of body fluid compartment

\[
\text{Volume} = \frac{\text{Amount}}{\text{Concentration}} (L)
\]

Amount:
- Amount of marker injected (mg) – Amount excreted (mg)

Concentration:
- Concentration in plasma (mg/L)

Note:
- ICF Volume = TBW – ECF Volume
Body Fluids:

Cell function depends not only on continuous nutrient supply / waste removal, but also on the physical / chemical homeostasis of surrounding fluids

2) Solute:

A) Non-electrolytes
   (do not dissociate in solution – neutral)
   • Mostly organic molecules (e.g., glucose, lipids, urea)

B) Electrolytes
   (dissociate into ions in solution – charged)
   • Inorganic salts
   • Inorganic / organic acids
   • Proteins

Although individual [solute] are different between compartments, the osmotic concentrations of the ICF and ECF are usually identical...

Fluid Movement Among Compartments:

The continuous exchange and mixing of body fluids are regulated by osmotic and hydrostatic pressures

In a steady state, intracellular osmolarity is equal to extracellular osmolarity

The shift of fluids between compartments depends on osmolarity of solute present

The volume of a particular compartment depends on amount of solute present

Electrolytes have great osmotic power:

\[
\text{MgCl}_2 \rightarrow \text{Mg}^{2+} + \text{Cl}^{-} + \text{Cl}^{-}
\]
Water Balance:

For proper hydration: \( \text{Water}_{\text{intake}} = \text{Water}_{\text{output}} \)

<table>
<thead>
<tr>
<th>Water Intake</th>
<th>Water Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism (10%)</td>
<td>Feces (2%)</td>
</tr>
<tr>
<td>Solid foods (30%)</td>
<td>Sweat (8%)</td>
</tr>
<tr>
<td>Ingested liquids (60%)</td>
<td>Skin / lungs (30%)</td>
</tr>
<tr>
<td>2500 ml/day</td>
<td>Urine (60%)</td>
</tr>
</tbody>
</table>

Water Output:

\[ > 0 \]
Osmolarity rises:
- Thirst
- ADH release

\[ < 0 \]
Osmolarity lowers:
- Thirst
- ADH release

\[ = 0 \]

ICF functions as a reservoir

Water Balance:

Thirst Mechanism:

\[ \downarrow \text{osmolarity} / \uparrow \text{volume of extracellular fluid} \]

\[ \downarrow \text{volume} / \uparrow \text{osmolarity of extracellular fluid} \]

\[ \downarrow \text{saliva secretion} \]

\[ \downarrow \text{sensation of thirst} \]

\[ \downarrow \text{drinking} \]

\[ \downarrow \text{saliva secretion} \]

\[ \downarrow \text{thirst} \]

\[ \downarrow \text{ADH release} \]
Pathophysiology:

Disturbances that alter solute or water balance in the body can cause a shift of water between fluid compartments.

**Volume Contraction:** A decrease in ECF volume

- **Isomotic Contraction**
  - ECF volume = Decrease
  - ECF osmolality = No change
  - ICF volume = No change
  - ICF osmolality = No change

- **Hyperosmotic Contraction**
  - ECF volume = Decrease
  - ECF osmolality = Increase
  - ICF volume = Decrease
  - ICF osmolality = Increase

- **Hyposmotic Contraction**
  - ECF volume = Decrease
  - ECF osmolality = Decrease
  - ICF volume = Increase
  - ICF osmolality = Decrease

**Volume Expansion:** An increase in ECF volume

- **Isomotic Expansion**
  - ECF volume = Increase
  - ECF osmolality = No change
  - ICF volume = No change
  - ICF osmolality = No change

- **Hyperosmotic Expansion**
  - ECF volume = Increase
  - ECF osmolality = Increase
  - ICF volume = Decrease
  - ICF osmolality = Increase

- **Hyposmotic Expansion**
  - ECF volume = Increase
  - ECF osmolality = Decrease
  - ICF volume = Increase
  - ICF osmolality = Decrease

Water intoxication

Greater than normal water reabsorption

IV bags of varying solutes allow for manipulation of ECF / ICF levels...
Acid-Base Balance:

Acid-base balance is concerned with maintaining a normal hydrogen ion concentration in the body fluids.

\[ \text{pH} = -\log_{10} [\text{H}^+] \]

\[ \text{pH} = -\log_{10} [40 \times 10^{-9}] \]

\[ \text{pH} = 7.4 \]

Note:
1) \([\text{H}^+]\) and pH are inversely related
2) Relationship is logarithmic, not linear

Normal range of arterial pH = 7.37 – 7.42

Problems Encountered:
1) Disruption of cell membrane stability
2) Alteration of protein structure
3) Enzymatic activity change

Costanzo (Physiology, 4th ed.) – Figure 7.1

Fluid / Electrolyte / Acid-Base Balance

Acid production in the human body has two forms: volatile acids and fixed acids.

1) **Volatile Acids:** Acids that leave solution and enter the atmosphere

\[
\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+ \]

End product of aerobic metabolism

(13,000 – 20,000 mmol/day)

Eliminated via the lungs

2) **Fixed Acids:** Acids that do not leave solution (~ 50 mmol/day)

- **Products of normal catabolism:**
  - Sulfuric acid (amino acids)
  - Phosphoric acid (phospholipids)

  Eliminated via the kidneys

- **Products of extreme catabolism:**
  - Acetoacetic acid (ketobodies)
  - B-hydroxybutyric acid
  - Lactic acid (anaerobic respiration)

- **Diabetes mellitus**

- **Ingested (harmful) products:**
  - Salicylic acid (e.g., aspirin)
  - Formic acid (e.g., methanol)
  - Oxalic acids (e.g., ethylene glycol)
Chemical Buffer:
A mixture of a weak acid and its conjugate base or a weak base and its conjugate acid that resist a change in pH

Brønsted-Lowry Nomenclature:
Weak acid:
Acid form = HA = H⁺ donor
Base form = A⁻ = H⁺ acceptor

Weak base:
Acid form = BH⁺ = H⁺ donor
Base form = B = H⁺ acceptor

Robert Pitt:

For the human body, the most effective physiologic buffers will have a pK at 7.4 ± 1.0

The Henderson-Hasselbalch equation is used to calculate the pH of a buffered solution

Henderson-Hasselbalch Equation:

\[ \text{pH} = \text{pK} + \log \frac{[A^-]}{[HA]} \]

\[ \text{pH} = -\log_{10} [H^+] \]
\[ \text{pK} = -\log_{10} K \text{ (equilibrium constant)} \]
\[ [A^-] = \text{Concentration of base form of buffer (mEq / L)} \]
\[ [HA] = \text{Concentration of acid form of buffer (mEq / L)} \]

pK is a characteristic value for a buffer pair (strong acid = ↓ pK; weak acid = ↑ pK)
Acid-Base Balance:

The major buffers of the ECF are bicarbonate and phosphate

1) $\text{HCO}_3^- / \text{CO}_2$ Buffer:

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+ \\
\text{(HA)}
\]

Utilized as first line of defense when $\text{H}^+$ enters / lost from system:

1. Concentration of $\text{HCO}_3^-$ normally high at 24 mEq / L
2. The $\text{pK}$ of $\text{HCO}_3^- / \text{CO}_2$ buffer is 6.1 (near pH of ECF)
3. $\text{CO}_2$ is volatile; it can be expired by the lungs

The pH of arterial blood can be calculated with the Henderson-Hasselbalch equation:

\[
\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{0.03 \times \text{P}_{\text{CO}_2}}
\]

\[
\text{pH} = 6.1 + \log \frac{24}{0.03 \times 40}
\]

\[
\text{pH} = 7.4
\]

Acid-base map:

Shows relationship between the acid and base forms of a buffer and the pH of the solution

Ellipse:

Normal values for arterial blood

Note:

Abnormal combinations of $\text{P}_{\text{CO}_2}$ and $\text{HCO}_3^-$ concentration can yield normal values of pH (compensatory mechanisms)
Acid-Base Balance:

The major buffers of the ECF are bicarbonate and phosphate

2) $\text{H}_2\text{PO}_4^- / \text{HPO}_4^{2-}$ Buffer:

$$
\begin{array}{c}
\text{H}_2\text{PO}_4^- \\
\text{(HA)}
\end{array} \rightleftharpoons
\begin{array}{c}
\text{HPO}_4^{2-} \\
\text{(A)}
\end{array} + \text{H}^+
$$

Why isn't inorganic phosphate the primary ECF buffer?
(1) Lower concentration than bicarbonate (~ 1.5 mmol/L)
(2) Is not volatile; cannot be cleared by lung

---

Acid-Base Balance:

The major buffers of the ICF are organic phosphates and proteins

1) Organic phosphates:
   - ATP / ADP / AMP
   - Glucose-1-phosphate
   - 2,3-diphosphoglycerate
      - $pK$s range from 6.0 to 7.5

   The most significant ICF protein buffer is hemoglobin

2) Proteins:

$$
\begin{array}{c}
\text{R} - \text{COOH} \\
\text{R} - \text{NH}_2 + \text{H}^+
\end{array} \rightleftharpoons
\begin{array}{c}
\text{R} - \text{COO}^- + \text{H}^+ \\
\text{R} - \text{NH}_3^+
\end{array}
$$

If pH falls

Proteins also buffer $\text{H}^+$ in the ECF

A relationship exists between $\text{Ca}^{2+}$, $\text{H}^+$, and plasma proteins

Normal $\text{pH}$

Accidemia

$\text{Ca}^{2+}$ $\text{Ca}^{2+}$ $\text{Ca}^{2+}$ $\text{Ca}^{2+}$

$\text{H}^+$ $\text{H}^+$ $\text{H}^+$ $\text{H}^+$

Hypercalcemia

Hypocalcemia

Normal circulating $\text{Ca}^{2+}$

Alkalemia

$\text{Ca}^{2+}$ $\text{Ca}^{2+}$ $\text{Ca}^{2+}$ $\text{Ca}^{2+}$

$\text{H}^+$ $\text{H}^+$ $\text{H}^+$ $\text{H}^+$

Acidemia

Hypocalcemia

Hypercalcemia
Maintenance of Acid-Base Balance:

Buffers are a short-term fix to the problem; in the long term, $H^+$ must be removed from the system...

1) Respiratory Regulation:

If $H^+$ begins to rise in system, respiratory centers excited

$\uparrow$ CO$_2$ leaves system

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+\quad (\downarrow H; \text{homeostasis restored})
\]

If $H^+$ begins to fall in system, respiratory centers depressed

$\downarrow$ CO$_2$ leaves system

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+\quad (\uparrow H; \text{homeostasis restored})
\]

Buffers are a short-term fix to the problem; in the long term, $H^+$ must be removed from the system...

2) Renal Regulation:

A) $\text{HCO}_3^-$ reabsorption:

Process continues until 99.9% of $\text{HCO}_3^-$ reabsorbed

If $HCO_3^-$ loads reach 40 mEq / L, transport maximized and $HCO_3^-$ excreted.

Kidneys are ultimate acid-base regulatory organs
- Reabsorb $HCO_3^-$
- Secrete fixed $H^+$

Costanzo (Physiology, 4th ed.) – Figure 7.5
Buffers are a short-term fix to the problem; in the long term, $H^+$ must be removed from the system...

(Removes 40% of fixed acids – 20 mEq / day)

2) Renal Regulation:

B) Secretion of fixed $H^+$:

Excretion of $H^+$ as titratable acid

Titratable Acid:

$H^+$ excreted with buffer

Minimum urinary pH is 4.4

(Maximum $H^+$ gradient $H^+$ ATPase can work against)

$H_2PO_4^-$ (titratable acid is excreted)

Costanzo (Physiology, 4th ed.) – Figure 7.6

Buffers are a short-term fix to the problem; in the long term, $H^+$ must be removed from the system...

(Removes 60% of fixed acids – 30 mEq / day)

2) Renal Regulation:

B) Secretion of fixed $H^+$:

Excretion of $H^+$ as $NH_4^+$

Diffusional trapping:

Lipid soluble $NH_3$ is able to diffuse into tubule but once combined with $NH_4^+$ it is unable to leave

Costanzo (Physiology, 4th ed.) – Figure 7.8
Disturbances of Acid-Base Balance:

1) **Respiratory Acid / Base Disorders**:

<table>
<thead>
<tr>
<th>Cause: Hypoventilation (e.g., emphysema) (Most common acid / base disorder)</th>
</tr>
</thead>
</table>

**Respiratory Acidosis:**

↑ CO₂ retained in body

**Causes:**

- Starvation (↑ ketone bodies)
- ↑ Alcohol consumption (↑ acetic acid)
- Excessive HCO₃⁻ loss (e.g., chronic diarrhea)

2) **Metabolic Acid / Base Disorders**:

<table>
<thead>
<tr>
<th>Cause: Hyperventilation (e.g., stress) (Rarely persists long enough to cause clinical emergency)</th>
</tr>
</thead>
</table>

**Respiratory Alkalosis:**

↓ CO₂ retained in body

**Causes:**

- Repeated vomiting (alkaline tide 'amped')
- Antacid overdose (Rare in body)

**A) Metabolic Acidosis:**

↑ fixed acids generated in body

**A) Metabolic alkalosis:**

↑ HCO₃⁻ generated in body

In the short term, respiratory / urinary system will compensate for disorders...