Acid-Base Balance

Jacqueline M. Powell, Ph.D.
Learning Objectives

1. Define acidosis and alkalosis
2. Discuss how chemical buffers regulate pH
3. Discuss how the pulmonary system regulates pH
4. Discuss how the kidney regulates pH
5. Identify metabolic and respiratory acid-base disturbances
6. Describe processes that lead to acid-base disturbances and list common causes
**Acid-Base Balance**

Acid-base balance: To maintain normal \([H^+]\) in the body fluids

\[ \text{ECF} = 4.0 \times 10^{-8} \text{ Eq/L or } 0.00004 \text{ mEq/L} \]

\[ \text{pH} = - \log [H^+] = - \log_{10} [4.0 \times 10^{-8} \text{ Eq/L}] = 7.4 \]  
(Logarithmic - inverse relationship)

**Acidemia** - Low arterial pH (<7.35)

**Acidosis**: Process leading to a reduced pH

**Alkalemia** - High arterial pH (>7.45)

**Alkalosis**: Process leading to an increased pH
Acid-Base Regulation

- $[H^+] = 0.00004 \text{ mEq/L}$ but 70-80 mEq of $H^+$ is ingested/produced daily by metabolism therefore...need regulation

- **Volatile acid**: 13,000-20,000 mM CO$_2$/day metabolized from carbohydrates & fats--EXPIRED BY LUNGS

- **Non-volatile (fixed) acid**: 40-60 mM/day lactate, $\beta$-hydroxybutyric acid, acetoacetate, phosphoric and sulphuric acid – form $H^+$-- RENALLY EXCRETED
Defenses against Changes in $[H^+]$

3 primary systems to regulate $H^+$:

1. **Buffering systems of body fluids:**
   IMMEDIATELY combines with acid/base to prevent large changes in $[H^+]$

2. **Respiratory Response:**
   Within minutes to eliminate CO$_2$ (H$_2$CO$_3$) from body

3. **Renal Response:**
   Slowest - hours/days to eliminate excess acid/base
   MOST POWERFUL REGULATORY SYSTEM
I. Buffering Systems

**Buffer:** Any substance that can reversibly bind H⁺

\[\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-\]

(Mixture of a weak acid and its conjugate base OR a weak base and its conjugate acid)

i.e. \(\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-\)

- FIRST line of defense against pH changes
- Buffered solution MINIMIZES A CHANGE IN pH but does not prevent it
- Several buffering systems (ECF and ICF) and the sum = 7.4

**Henderson-Hasselbalch Equation:** To calculate the pH of a buffered solution

\[\text{pH} = \text{pK} + \log \left(\frac{[\text{HCO}_3^-]}{\alpha \text{PCO}_2}\right)\]

\[\text{pH} = \frac{[\text{HCO}_3^-]}{\text{PCO}_2}\]
HCO$_3^-$/$H_2$CO$_3$ Buffer System

($H_2$CO$_3$) CO$_2$ controlled by lungs (respiration rate)

HCO$_3^-$ controlled by kidneys

MOST IMPORTANT ECF BUFFER

1. [HCO$_3^-$] is higher (24 mEq) than HPO$_4^{2-}$ (1-2 mM/L) and can be adjusted by kidney

2. CO$_2$, acid form of buffer is volatile and can be expired by lungs

3. pK is 6.1..close to ECF pH

Extracellular Buffers:
Blood proteins
Inorganic phosphates ($H_2$PO$_4$/HPO$_4^{2-}$)

Intracellular Buffers:
Hemoglobin
ATP
ADP
glucose-phosphates
II. Respiratory Compensation

Acts rapidly to prevent large changes in [H+] until kidney response

Doesn’t return [H+] all the way to normal: effectively gains 1-3 pH units within 3-12 minutes…but 1-2x greater buffering power than ECF buffers combined

With abnormalities: Compensates for changes in [HCO₃⁻]

\[ P_{\alpha CO_2} = 40 \text{mmHg with normal [HCO}_3^-]; \text{pH}= 7.4 \]

if decrease [HCO₃⁻] will compensate by decreasing \( P_{\alpha CO_2} \) (hyperventilating) which returns pH to normal

Compensation…same direction but never completely returns pH to normal
III. Renal Compensation

- Kidney compensates for changes in $P_{\text{a}CO_2}$ by adjusting $[\text{HCO}_3^-]$ reabsorption

- Non-respiratory compensation done by $\text{H}^+$ secretion or titratable acid/ammonia excretion

Regulate ECF $\text{H}^+$ concentration through 3 mechanisms:

A. Secretion of $\text{H}^+$

B. Reabsorption of filtered $\text{HCO}_3^-$

C. Production of new $\text{HCO}_3^-$ (via ammonia/titratable acid excretion)
A.B. Renal HCO₃⁻ Reabsorption & H⁺ Secretion

1. Filtered HCO₃⁻ Reabsorption

- ~ 80-90% HCO₃⁻ reabsorbed (H⁺ secretion) in proximal tubule
B. H⁺ secretion (4400 mEq/day)

- Adding 1 new HCO₃⁻ to blood and secreting 1 H⁺ into lumen until pH 4.5

α-intercalated cells (1° active secretion site)

![Diagram showing the process of H⁺ secretion in the renal tubules.](image)
H⁺ can be buffered in the lumen by urinary buffers

i. Ammonia Buffering (20 - 40 mEq/day)

ii. Titratable buffering systems (i.e. phosphate) (40 mEq/day)

i. Ammonia Buffering

- Excretion of H⁺ as NH₄⁺ in the proximal tubule & collecting duct

- Metabolic processes that allow NH₃ to pick up H⁺ and become NH₄⁺ to be excreted

- POWERFUL FOR INCREASING H⁺ EXCRETION
ii. Titratable Acid

- **Titratable acid**: H⁺ excreted with urinary buffers (phosphate)

- Minimum urine pH is 4.4-4.5. if urine pH < 4.4 H⁺ secretion stops/ NH₄⁺ excretion increases (greater the amount of NH₃ diffusion and the greater the amount of H⁺ excreted as NH₄⁺)

- PHOSPHATE is most important buffering system in this category b/c concentrated in tubules

- **AMOUNT EXCRETED AS TITRATABLE ACID DEPENDS ON THE AMOUNT OF AVAILABLE PHOSPHATE**

- [HPO₄⁻²] is 4x greater than [H₂PO₄⁻]

- HPO₄⁻² + H⁺ ➔ H₂PO₄⁻ which is excreted

- 85% of HPO₄⁻² filtered is reabsorbed leaving 15% to be excreted as titratable acid in H₂PO₄ form
1. In cells, CO₂ + H₂O form H₂CO₃ which dissociates into H⁺ + HCO₃⁻.
2. Luminal membrane has H⁺-ATPase which secretes H⁺ from the cell.
3. Secreted H⁺ joins with HPO₄²⁻ to produce weak acid, H₂PO₄⁻ (the titratable acid that is excreted).
4. For each H⁺ excreted as titratable acid; 1 NEW HCO₃⁻ is made and reabsorbed.

This new HCO₃⁻ replenishes extracellular stores depleted from buffering fixed [H⁺] (amount of new HCO₃⁻ = amount of H⁺ secreted & buffered).
Mechanisms of Renal Regulation

Ammonia Buffering

Titratble Acid

HCO₃⁻ Reabsorption
Test Question

The bicarbonate-carbonic acid system is an important buffer in the body because:

1. It has an ideal $pK$ value that makes it an effective chemical buffer
2. The weak acid form of the buffer can be adjusted by the respiratory system
3. The conjugate base of the buffer system is regulated by respiration
4. It is an important buffer anion that is normally excreted by the kidneys
5. The acid form of the buffer is regulated by renal mechanisms
During titratable acid and ammonia buffering there is reabsorption of newly formed:

1. $H^+$
2. $\text{HCO}_3^-$ (Correct)
3. $\text{NH}_4^+$
4. $\text{HP}_2\text{O}_4^-$
5. $K^+$
Summary

• \( [H^+] = 0.00004 \text{ mEq/L} \) but 70-80 mEq of \( H^+ \) is ingested/produced daily by metabolism therefore…need regulation

• 3 primary systems to regulate \( H^+ \)

1. **Buffering systems of body fluids:**
   - Instantaneous

2. **Respiratory Response:**
   - Within minutes
   - Control centers respond by increasing/decreasing ventilation to keep \( P_{CO_2} \) near 40 mmHg

3. **Renal Response:**
   - Hours/days
   - Regulate ECF \([H^+]\) by 3 mechanisms:
     1. Secretion of \( H^+ \)
     2. Reabsorption of filtered \( HCO_3^- \)
     3. Production of new \( HCO_3^- \) (ammonia/titratable acid excretion)

New \( HCO_3^- \) replenishes extracellular stores depleted from buffering fixed \([H^+]\)
Acid-Base Disorders

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Acid-Base Disorders

Acidemia: $\uparrow$ [H$^+$] in blood or $\downarrow$ [HCO$_3^-$] & pH

Alkalemia: $\downarrow$ [H$^+$] in blood or $\uparrow$ [HCO$_3^-$] & pH

pH = $\frac{[\text{HCO}_3^-]}{P_{\text{CO}_2}}$

Simple acid-base disorders: one disorder present
Mixed acid base disorder: more than one disorder is present

METABOLIC DISTURBANCES: primary disorder with [HCO$_3^-$]
1. Metabolic acidosis: $\uparrow$ [H$^+$] and $\downarrow$ [HCO$_3^-$] – more buffering
2. Metabolic alkalosis: $\downarrow$ [H$^+$] and $\uparrow$ [HCO$_3^-$] – loss of H$^+$ /gain of HCO$_3^-$

RESPIRATORY DISTURBANCES: primary disorder of CO$_2$
3. Respiratory acidosis: hypoventilation/ $\uparrow$ P$_{\text{CO}_2}$
4. Respiratory alkalosis: hyperventilation/ $\downarrow$ P$_{\text{CO}_2}$
Compensation

1st line of defense: ECF/ICF buffering

2 types of compensatory responses:
1. Respiratory compensation
2. Renal compensation

** HELPFUL RULES**
1. If the acid-base disturbance is metabolic (HCO$_3^-$) the primary compensation response is respiratory to alter P$_{CO_2}$ (some renal days later)

2. If the acid-base disturbance is respiratory (P$_{CO_2}$) then compensation response is ONLY metabolic (renal) to alter [HCO$_3^-$]

3. Compensatory response is always in the same direction as the original disturbance

pH = $\frac{[HCO_3^-]}{P_{CO_2}}$
# Metabolic Acidosis

1° Disturbance: Decreased \([HCO_3^-]\) in blood

## Table 7-4 Causes of Metabolic Acidosis

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Excessive production or ingestion of fixed \(H^+\) | Diabetic ketoacidosis | Accumulation of \(\beta\)-OH butyric acid and acetoacetic acid  
↑ Anion gap |
| | Lactic acidosis | Accumulation of lactic acid during hypoxia  
↑ Anion gap |
| | Salicylate poisoning | Also causes respiratory alkalosis  
↑ Anion gap |
| | Methanol/formaldehyde poisoning | Converted to formic acid  
↑ Anion gap |
| | Ethylene glycol poisoning | Converted to glycolic and oxalic acids  
↑ Anion gap |
| Loss of \(HCO_3^-\) | Diarrhea | Gastrointestinal loss of \(HCO_3^-\)  
Hyperchloremia |
| | Type 2 renal tubular acidosis (type 2 RTA) (Proximal) | Renal loss of \(HCO_3^-\) (failure to reabsorb filtered \(HCO_3^-\))  
Normal anion gap  
Hyperchloremia |
| Inability to excrete fixed \(H^+\) | Chronic renal failure | ↓ Excretion of \(H^+\) as \(NH_4^+\)  
↑ Anion gap  
Hyperkalemia |
| | Type 1 renal tubular acidosis (type 1 RTA) (Distal) | ↓ Excretion of \(H^+\) as titratable acid and \(NH_4^+\)  
↓ Ability to acidify urine  
Normal anion gap |
| | Type 4 renal tubular acidosis (type 4 RTA) | Hypoaldosteronism  
↓ Excretion of \(NH_4^+\)  
Hyperkalemia inhibits \(NH_3\) synthesis  
Normal anion gap |
# Metabolic Alkalosis

1° Disturbance: Increased [HCO₃⁻] in blood

| Table 7-5  Causes of Metabolic Alkalosis |
|-----------------|--------------------------------------|
| **Cause**       | **Examples**                          | **Comments**                                      |
| Loss of H⁺       | Vomiting                              | Loss of gastric H⁺                                 |
|                  |                                      | HCO₃⁻ remains in the blood                         |
|                  |                                      | Maintained by volume contraction                   |
|                  |                                      | Hypokalemia                                        |
|                  |                                      |                                                    |
| Gain of HCO₃⁻    | Ingestion of NaHCO₃                   | Ingestion of large amounts of HCO₃⁻                |
|                  | Milk-alkali syndrome                  | in conjunction with renal failure                  |
|                  |                                      |                                                    |
| Volume contraction alkalosis | Loop or thiazide diuretics             | ↑ HCO₃⁻ reabsorption due to ↑ angiotensin II and aldosterone |
Respiratory Acidosis

1° Disturbance: Increased CO₂ retention due to hypoventilation

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition of the medullary respiratory center</td>
<td>Opiates, barbiturates, anesthetics</td>
<td>Inhibition of peripheral chemoreceptors</td>
</tr>
<tr>
<td></td>
<td>Lesions of the central nervous system</td>
<td></td>
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<tr>
<td></td>
<td>Central sleep apnea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oxygen therapy</td>
<td></td>
</tr>
<tr>
<td>Disorders of respiratory muscles</td>
<td>Guillain-Barré syndrome, polio, amyotrophic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>lateral sclerosis (ALS), multiple sclerosis</td>
<td></td>
</tr>
<tr>
<td>Airway obstruction</td>
<td>Aspiration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obstructive sleep apnea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Laryngospasm</td>
<td></td>
</tr>
<tr>
<td>Disorders of gas exchange</td>
<td>Acute respiratory distress syndrome (ARDS)</td>
<td>↓ Exchange of CO₂ between pulmonary capillary blood and alveolar gas</td>
</tr>
<tr>
<td></td>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td></td>
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<tr>
<td></td>
<td>Pneumonia</td>
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<tr>
<td></td>
<td>Pulmonary edema</td>
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</tr>
</tbody>
</table>
Respiratory Alkalosis

1° Disturbance: Decreased CO\textsubscript{2} due to hyperventilation

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<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Stimulation of the medullary</td>
<td>Hysterical hyperventilation</td>
<td>Also causes metabolic acidosis</td>
</tr>
<tr>
<td>respiratory center</td>
<td>Gram-negative septicemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Salicylate poisoning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurologic disorders (tumor; stroke)</td>
<td></td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>High altitude</td>
<td>Hypoxemia stimulates peripheral</td>
</tr>
<tr>
<td></td>
<td>Pneumonia; pulmonary embolism</td>
<td>chemoreceptors</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Severe anemia</td>
<td></td>
</tr>
</tbody>
</table>
Test Questions

1. Which one of the following acid-base disturbances will a mountain climber most likely develop while climbing Mt. Everest?

A. Metabolic Acidosis  
B. Metabolic Alkalosis  
C. Respiratory Acidosis  
D. Respiratory Alkalosis

2. This disturbance is primarily caused by which one of the following problems?

A. Decreased CO₂ due to hyperventilation  
B. Increased CO₂ retention due to hypoventilation  
C. Increased [HCO₃⁻] in blood  
D. Decreased [HCO₃⁻] in blood

COMPENSATION??????  
\[ \text{pH} = \frac{[\text{HCO}_3^-]}{P_{\text{CO}_2}} \]  

Acetazolamide: weak diuretic
RESPIRATORY ACIDOSIS

Cause: hypoventilation
Comp: increase \([\text{HCO}_3^-]\) reabsorption

METABOLIC ACIDOSIS

Cause: increased \([\text{H}^+]\)
Comp: decrease \(P_{\text{CO}_2}\) (hyperventilate) OR make \(\text{HCO}_3^-\) via titratable acid excretion

RESPIRATORY ALKALOSIS

Cause: hyperventilation
Comp: decrease \(\text{HCO}_3^-\) reabsorption

METABOLIC ALKALOSIS

Cause: decreased \([\text{H}^+]\)
Comp: Increase \(P_{\text{CO}_2}\) (hypoventilate) OR excrete \(\text{HCO}_3^-\)

Summary

\[ \text{pH} = \frac{[\text{HCO}_3^-]}{P_{\text{CO}_2}} \]

FOR SIMPLE DISORDERS: COMPENSATION GOES IN THE SAME DIRECTION AS THE DISTURBANCE
# Overview: Acid-Base Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>CO₂ + H₂O</th>
<th>emony</th>
<th>H⁺ + HCO₃⁻</th>
<th>Respiratory Compensation</th>
<th>Renal Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>Hyperventilation</td>
<td>↑ H⁺ excretion</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>Hypoventilation</td>
<td>↑ HCO₃⁻ excretion</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>None</td>
<td>↑ H⁺ excretion</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>None</td>
<td>↓ H⁺ excretion</td>
</tr>
</tbody>
</table>

Heavy arrows indicate initial disturbance.