Acid Base lecture

D. Hammoudi. MD
Adapted from *High-Yield Acid-Base*, by J. Longenecker.
Henderson-Hasselbalch Equation

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

\[ \rightarrow \quad \text{pH} = \text{p}K_a + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \]

\[ \rightarrow \quad \text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{0.03 \times \text{p}\text{CO}_2} \]
MASS ACTION EQUATION \[ H^+ + HCO_3^- = H_2CO_3 = CO_2 + H_2O \]

HENDERSEN-HASSELBACH EQUATION \[ pH = pK + \log \frac{HCO_3^-}{.03pCO_2} \]

KASSIRER-BLEICH MODIFICATION \[ H^+ = 24 \frac{CO_2}{HCO_3^-} \]

<table>
<thead>
<tr>
<th>pH</th>
<th>7.0</th>
<th>7.1</th>
<th>7.2</th>
<th>7.3</th>
<th>7.4</th>
<th>7.5</th>
<th>7.6</th>
<th>7.7</th>
<th>7.8</th>
<th>7.9</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>H^+</td>
<td>100</td>
<td>80</td>
<td>64</td>
<td>51</td>
<td>40</td>
<td>32</td>
<td>26</td>
<td>20</td>
<td>16</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>ARTERIAL</td>
<td>VENOUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>----------</td>
<td>---------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.40</td>
<td>&lt; 7.35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pCO2</td>
<td>40</td>
<td>&gt; 40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCO3</td>
<td>24</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pO2</td>
<td>&gt; 70</td>
<td>&lt; 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
As dictated by the Henderson-Hasselbalch equation, disturbances in either the respiratory component (pCO₂) or metabolic component (HCO₃⁻) can lead to alterations in pH.

- **Metabolic Acidosis**
  - (Too little HCO₃⁻)
- **Metabolic Alkalosis**
  - (Too much HCO₃⁻)
- **Respiratory Acidosis**
  - (Too much CO₂)
- **Respiratory Alkalosis**
  - (Too little CO₂)
When a primary acid-base disorder exists, the body attempts to return the pH to normal via the “other half” of acid base metabolism.

- Primary metabolic disorder → Respiratory compensation
- Primary respiratory disorder → Metabolic compensation
<table>
<thead>
<tr>
<th>Primary Disorder</th>
<th>Compensatory Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>Increased ventilation</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>Decreased ventilation</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>Increased renal reabsorption of $\text{HCO}_3^-$ in the proximal tubule</td>
</tr>
<tr>
<td></td>
<td>Increased renal excretion of $\text{H}^+$ in the distal tubule</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Decreased renal reabsorption of $\text{HCO}_3^-$ in the proximal tubule</td>
</tr>
<tr>
<td></td>
<td>Decreased renal excretion of $\text{H}^+$ in the distal tubule</td>
</tr>
<tr>
<td>Type of Disturbance</td>
<td>Type of Primary Alteration</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Decrease in plasma $[\text{HCO}_3^-]$</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>Increase in plasma $[\text{HCO}_3^-]$</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>Increase in Pa$\text{CO}_3$</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Decrease in Pa $\text{CO}_3$</td>
</tr>
<tr>
<td>Acid-Base Disorder</td>
<td>Rule for PaCO₂ or PsCO₂</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>PaCO₂ should fall by 1.0 to 1.5 X the fall in plasma HCO₃⁻ concentration</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>PsCO₂ should rise by 0.25 to 1.0 X the rise in plasma HCO₃⁻ concentration</td>
</tr>
<tr>
<td>Acute respiratory acidosis</td>
<td>Plasma HCO₃⁻ concentration should rise by about 1 mmmole per liter for each 10 mm Hg increment in PaCO₂ (± 3 mmoles per liter).</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td></td>
</tr>
<tr>
<td>Acute respiratory alkalosis</td>
<td>Plasma HCO₃⁻ concentration should fall by about 1 to 3 mmoles per liter for each 10 mm Hg decrement in the PaCO₂, usually not to less than 18 mmoles per liter.</td>
</tr>
<tr>
<td>Chronic respiratory alkalosis</td>
<td></td>
</tr>
</tbody>
</table>
REGULATION OF CO$_2$ (Read also the separate article in the syllabus)

Plasma CO$_2$ is determined by the rate of metabolic CO$_2$ production and by alveolar ventilation:

\[
pCO_2 = \frac{CO_2 \text{ production}}{alveolar \text{ ventilation}} \times 0.84
\]
• $H_2O \overset{\leftrightarrow}{=} H^+ + OH^-$

• Only 1 in 14 million H2O molecules is ionized to H+ and OH-

• When $[H^+] = [OH^-]$ solution is neutral

\[
K = [H^+][OH^-] = 1 \times 10^{-14}
\]

\[
K = [H^+]^2 = 1 \times 10^{-14}
\]

In a neutral solution $[H^+] = 1 \times 10^{-7}$ M

\[
pH = \log \frac{1}{[H^+]} = -\log[H^+]
\]

pH of a neutral solution = $-\log(1 \times 10^{-7}) = 7$
- If pH of solution is <7, acidic
- If pH of solution is > 7, basic

<table>
<thead>
<tr>
<th>solution</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1M NaOH</td>
<td>14</td>
</tr>
<tr>
<td>Human blood</td>
<td>7.4</td>
</tr>
<tr>
<td>Coffee</td>
<td>5</td>
</tr>
<tr>
<td>Coke</td>
<td>3</td>
</tr>
<tr>
<td>1M HCl</td>
<td>0</td>
</tr>
</tbody>
</table>
Acids are compounds that *donate a H+ to solution*

\[ HCl \rightleftharpoons H^+ + Cl^- \]

Bases are compounds that accept H+ from solution

\[ H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \]
So what’s the big deal with H+?

- H+ is very reactive
- Almost all aspects of cell function can be influenced by H+
- Enzyme reactions are particularly sensitive to [H+]; there is an optimal pH above or below which the enzyme functions poorly
- Normal extracellular pH=7.4
- Acidosis pH<7.4 (death <6.8)
- Alkalosis pH>7.4
The body normally produces some acids:
- Metabolism of proteins
- Lactic acid from muscle

Disturbances of Acid-Base Balance
1. **Respiratory** – changes in CO2

2. **Metabolic** – no change in CO2
Metabolic Acid-Base Disturbance

1. Metabolic Acidosis

A. Causes
• Diarrhea (loss of HCO3-)
• Acid ingestion (aspirin – acetylsalicylic acid)
• Kidney failure to secrete H+

B. Effects
• CNS depression and coma, death

2. Metabolic Alkalosis

A. Causes
• Vomiting (loss of H+)

B. Effects
• CNS excitability, muscle tetanus, death
Acid-Base balance

1. Fluid Buffering systems
2. Kidney
3. Respiratory
• consists of a mixture of a weak acid and its base
• Resists changes in pH when small amounts of H+ or OH- are added

Major physiologically important buffer in blood plasma:
  a) Bicarbonate

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

A buffering system
First line of defense against pH shift
- Chemical buffer system
  - Bicarbonate buffer system
  - Phosphate buffer system
  - Protein buffer system
  - Respiratory mechanism (CO₂ excretion)
  - Renal mechanism (H⁺ excretion)

Second line of defense against pH shift
- Physiological buffers
General strategy

1. Balance the H+ intake and production with H+ excretion

2. Recover HCO3 to preserve buffering capability

Renal regulation of H+ and HCO3
Basic Renal $\text{HCO}_3^-$ handling

Almost all the $\text{HCO}_3^-$ in the plasma is filtered

Filtered $\text{HCO}_3^-$

$\text{HCO}_3^- + \text{H}^+ \rightarrow \text{H}_2\text{CO}_3$

$\text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2$

Carbonic anhydrase

$\text{HCO}_3^- \rightarrow \text{H}_2\text{CO}_3$

$\text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2$
1. CO2 and H2O form H2CO3, which splits into H+ and HCO3

2. HCO3 moves to the interstitial fluid and blood

3. H+ is secreted into tubule, where it reacts with filtered HCO3 to regenerate CO2 and H2O

4. For every HCO3 filtered, an HCO3 is formed within the tubular cell & transported to the interstitial fluid and blood

- “HCO3 reabsorption”

- A second important buffer in the tubular fluid is the **phosphate system**
  - Works in the tubular fluid to buffer H+ and allows for production of new HCO3

A third important buffer in the tubular fluid is the **ammonia system**
- Also, works in the tubular fluid to buffer H+ and allows for production of new HCO3
Renal $\text{HPO}_4^{2-}$ handling and new $\text{HCO}_3^-$

Almost all the $\text{HPO}_4^{2-}$ in the plasma is filtered

Filtered $\text{HPO}_4^{2-}$

$\text{HPO}_4^{2-} + \text{H}^+ \rightarrow \text{H}_2\text{PO}_4^-$

$\text{H}_2\text{PO}_4^- \rightarrow \text{CO}_2 + \text{H}_2\text{O}$

$\text{H}^+ \rightarrow \text{HCO}_3^-$

$\text{H}_2\text{CO}_3 \rightarrow \text{CO}_2 + \text{H}_2\text{O}$

$\text{Na} \rightarrow \text{K}$

Carbonic anhydrase
Renal $\text{NH}_4^+$ handling and new $\text{HCO}_3^-$
Renal Regulation of Acid-Base
Bicarbonate buffers are important in the blood and extracellular fluids.

- **In the kidney:**
  - Bicarbonate allows for excretion of H+ as water and preservation of HCO3
  - **Phosphate and ammonia serve as tubule** fluid specific buffers and they allow for production of ‘new’ HCO3-

Renal Response to Acid-Base Disturbance

1. **Metabolic Acidosis**
   - Increase HCO3 reabsorption
   - Increase H+ secretion
   - Increase new HCO3 production

2. **Metabolic Alkalosis**
   - decrease HCO3 reabsorption
   - decrease H+ secretion

Responses to acid-base imbalance

1. Fast - Fluid buffering systems as outlined above
2. Moderate – Respiratory chemoreceptors sensitive to CO2 and [H+] regulate breathing and CO2 levels
3. Slow (days) Renal - adjust HCO3 and H+ handling and production of new HCO3
1. Check the pH

If the pH < 7.35, acidemia (and at least 1 acidosis) is present.

If the pH > 7.45, alkalemia (and at least 1 alkalosis) is present.
2. Check the $pCO_2$

$\text{pH} < 7.35 \text{ and } pCO_2 < 40 \rightarrow \text{metabolic acidosis}$

$\text{pH} < 7.35 \text{ and } pCO_2 > 40 \rightarrow \text{respiratory acidosis}$

$\text{pH} > 7.45 \text{ and } pCO_2 < 40 \rightarrow \text{respiratory alkalosis}$

$\text{pH} > 7.45 \text{ and } pCO_2 > 40 \rightarrow \text{metabolic acidosis}$
## Practical Approach

<table>
<thead>
<tr>
<th>Most prominent disorder</th>
<th>Compensation formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>( pCO_2 \approx 1.5 \left[HCO_3^-\right] + 8 )</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>( pCO_2 \approx 0.9 \left[HCO_3^-\right] + 16 )</td>
</tr>
</tbody>
</table>
| Respiratory acidosis    | For every 10 Δ in \( pCO_2 \), pH decreases by:  
  0.08 (in acute resp. acidoses)  
  0.03 (in chronic resp. acidoses) |
| Respiratory alkalosis   | For every 10 Δ in \( pCO_2 \), pH increases by:  
  0.08 (in acute resp. alkaloses)  
  0.03 (in chronic resp. alkaloses) |
Anion "Gap"

1. An "artefact" of how we measure blood electrolytes
2. Determined by:

Normal = 10

3. If the anion gap is normal with acidosis then Cl\(^-\) has increased to match HCO\(_3^-\) decline
4. If the anion gap is increased some other anion is involved
Anion Gap (AG)

$$AG = (Na^+ - (Cl^- + HCO_3^-))$$

140

$Na^+$

105

Cl$^-$

25

HCO$_3^-$

proteins - SO$_4^-$ organic acids

$K^+, Mg^{++}, Ca^{++}$

- Normal AG
  10-14

- AG is primarily due to albumin

- Increased AG almost always due to a rise in unmeasured anions

\[ \text{Anion Gap} = 10 \]
Increased anion gap metabolic acidosis

- $\text{Na}^+$
- Cl-
- HCO$_3$-
- Proteins - SO$_4$ - organic acids

Anion Gap = 25
Normal anion gap metabolic acidosis

140

K⁺, Mg²⁺, Ca²⁺

Na⁺

115

Cl⁻

HCO₃⁻

proteins -
SO₄⁻ -
organic acids

15

\text{Anion Gap} = 10
5. Calculate the anion gap

\[
\text{Anion gap} = [\text{Na}^+] - ( [\text{Cl}^-] + [\text{HCO}_3^-] )
\]

If the anion gap is elevated, an elevated gap metabolic acidosis is likely present.
Overview of Biochemical Homeostasis

Produced Internally

Outside World
- Enters via the lungs
- Enters via the GI tract
- Enters via the skin

Blood

Consumed Internally

Outside World
- Leaves via the lungs
- Leaves via the GI tract
- Leaves via the skin
- Leaves via the urine

Internal Reservoir
(Cannot be directly measured)
Differential Diagnosis for Acid-Base Disorders

Produced Internally

Physiologic Acid Production
Aerobic Metabolism (carbohydrates, fats, protein → CO₂; fats, protein → non-volatile acids)

Pathologic Acid Production
Anaerobic Metabolism (carbohydrates → non-volatile acids)
Metabolism of Various Toxins (e.g. methanol, ethylene glycol)

Consumed Internally
Neither H⁺ nor CO₂ is consumed internally

Outside World
HCO₃⁻ and H⁺ enter via the GI tract

Blood
HCO₃⁻ + H⁺ ↔ CO₂ + H₂O

Various Intracellular & Extracellular Buffers

Metabolic Acidosis
(Too much H⁺ / Too little HCO₃⁻)

Increased intake of H⁺
Increased aerobic metabolism
Production of pathologic acids (lactate, ketones)
Increased GI loss of HCO₃⁻
Decreased GI loss of H⁺
Increased urinary loss of HCO₃⁻
Decreased urinary loss of H⁺

Metabolic Alkalosis
(Too little H⁺ / Too much HCO₃⁻)

Decreased intake of H⁺
Increased intake of HCO₃⁻
Decreased aerobic metabolism
Decreased GI loss of HCO₃⁻
Increased GI loss of H⁺
Decreased urinary loss of HCO₃⁻
Increased urinary loss of H⁺

Respiratory Acidosis
(Too much CO₂)

Increased aerobic metabolism
Decreased CO₂ excretion via the lungs (aka hyperventilation)

Respiratory Alkalosis
(Too little CO₂)

Decreased aerobic metabolism
Increased CO₂ excretion via the lungs (aka hypoventilation)
- M ethanol
- U remia
- D iabetic Ketoacidosis, Ketoacidosis
- P araldehyde
- I ron, Isoniazid (INH)
- L actic Acidosis
- E thanol, Ethylene glycol
- S alicylates

Anion gap Acidosis
“MUDPILES”
- Drunk off their ____
- Hx of drug use
- Fruity breath
- Kussmaul’s breathing
- tinnitus
- hypotension
Laboratory Workup

- Chemistries
  - BUN, Cr, glucose
- Lactate level
- Ketones
- Ethanol level
- Salicylate level
- Osmolal gap
- UA
- Uremic Acidosis
- Lactic Acidosis
- Ketoacidosis
- Salicylates

**Osmolar Gap**
Normal (< 25mOsm/kg)
- Ethylene Glycol
  - Look for Oxalate crystals in the Urine

- Methanol Intoxication
  - Visual Changes

**Osmolar Gap**
*Increased (>25mOsm/kg)*
• Treat underlying condition

• Remember:
  ◦ Methanol
  ◦ Ethanol
  ◦ Ethylene Glycol
  ◦ Salicylates

• Can Be Removed via Dialysis
Non gap Acidosis
“HARDUFS”

- Hyperalimentation
- Acetazolamide, amphotericin
- R TA
- Diarrhea
- Uteral Diversions
- Pancreatic fistula
- Saline resuscitation
IF **YES** THINK About

- Ileostomy
- Diarrhea
- Enteric Fistula

**Non Gap Acidosis**

**Is There Intestinal Fluid Loss?**