ACID BASE BALANCE

By

Dr. Sumaira Iqbal
Learning objectives

By the end of the session should be able to comprehend:

• Regulation of Hydrogen ion
  – Production
  – Elimination

• Concept of acid and a base

• Defense mechanisms

• Buffer and its types
Acid Base Balance

• Precise regulation of hydrogen ions
• Balance between intake, production and excretion of H+ ions is maintained
• Optimum hydrogen ion balance is maintained for homeostasis
Introduction

- **pH**: Measure of hydrogen ions, Normal pH = 7.35-7.45
- **pCO₂**: Partial Pressure of CO₂: is the concentration of CO₂ in the blood
  - High pCO₂ indicates acidosis and vice versa
- **HCO₃ or Bicarbonate**: Measures the concentration of HCO₃ ions only
  - High values indicate alkalosis and vice versa
Introduction

• Acids: Liberate free $H^+$ ions
  – Strong Acid: Greater tendency to dissociate into free $H^+$ & Anions e.g. HCl
  – Weak Acid: Only less no of molecules dissociate in solution e.g.: $H_2CO_3$
• Base: Accepts free $H^+$ ions
  – Strong Base: is able to bind $H^+$ ions more readily than weak base
• $K$: Dissociation constant
  – Every acid has constant degree of dissociation, when in solution

$$\frac{[H^+][\text{HCO}_2^-]}{[\text{H}_2\text{CO}_3]} = K$$

Undissociated Acid
\[ \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow [\text{H}_2\text{CO}_3] \leftrightarrow \text{H}^+ + \text{HCO}_3^- \]

- \text{CO}_2 \text{ from metabolism (volatile)}
- \text{H}_2\text{O} \text{ always available}
- \text{[H}_2\text{CO}_3] \text{ unstable intermediate}
- \text{H}^+ \text{ the pH term}
- \text{HCO}_3^- \text{ major species in blood}
Introduction

• Normal pH = 7.4
  – pH of Arterial Blood = 7.45
  – pH of Venous Blood = 7.35

• Normal Range = 6.8 – 8.0   Beyond which death occurs in seconds.
  – Acidosis = Blood pH < 7.35
  – Alkalosis = Blood pH > 7.45

• pH of ICF is lower than plasma   i.e.   6.0 - 7.4
• pH of urine ranges between 4.5 – 8.0
• Extreme Acidic pH in body is of gastric Acid = 0.8
Introduction

• As a result of metabolic processes ‘Acids’ are produced
• Daily production of H⁺ ions by metabolism or ingestion with food [e.g. Citric Acid in oranges] = 80 mEq/L
• Types
  i. Respiratory or Volatile acids; CO2
  ii. Metabolic or fixed acids
• To maintain balance ‘acids’ are to be; “Excreted” or “Metabolized”
• Non-volatile acids (fixed acids), not excreted by lungs, but excreted by kidneys
Introduction

• Lungs regulate amount of $\text{CO}_2$ in the blood
• Kidneys regulate the bicarbonate ions
• Both acidosis and alkalosis can be of two different types:
  – Respiratory
  – Metabolic
• Respiratory disturbances caused by various malfunctions of the lungs.
• Metabolic disturbances are caused by metabolic disorders which result in an excessive build up or loss of acids or bases.
Defense Mechanisms

• Hydrogen ions in the body are regulated by Three Defense Mechanisms:-
  1st defense: Chemical buffering
  2nd defense: Respiratory (*alteration in arterial CO2*)
  3rd defense: Renal (*alteration in HCO₃⁻ excretion*)
Buffer

• A substance that can reversibly bind H+ ions

\[ \text{Buffer} + \text{H}^+ \rightleftharpoons \text{H Buffer} \]
  – If excess reaction shifts to the right
  – If deficient reaction shifts to the left

• Normal H+ ions concentration in body = 0.00004mEq/L
  – Can alter from 10nEq/L to 160nEq/L

• Daily intake or by metabolism = 80mEq/L

• Buffering system is needed to maintain the concentration
<table>
<thead>
<tr>
<th></th>
<th>H⁺ Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mEq/L</td>
</tr>
<tr>
<td>Gastric HCl</td>
<td>150</td>
</tr>
<tr>
<td>Maximal urine acidity</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma</td>
<td></td>
</tr>
<tr>
<td>Extreme acidosis</td>
<td>0.00001</td>
</tr>
<tr>
<td>Normal</td>
<td>0.00004</td>
</tr>
<tr>
<td>Extreme alkalosis</td>
<td>0.00002</td>
</tr>
<tr>
<td>Pancreatic juice</td>
<td>0.00001</td>
</tr>
</tbody>
</table>
1. Chemical Buffer system:
   - Responds within seconds
   - Does not eliminate or add $H^+$ from body
   - Operates by binding or to tied up $H^+$ till balance is reestablished.

a. In ECF:
   - Mainly $HCO_3^-/CO_2$ Buffer system
   - Plasma Proteins
   - $HPO_4^{2-}/H_2PO_4^-$ Buffer system

b. In ICF:
   - Proteins Mainly e.g.: Hb in RBCs
   - $HPO_4^{2-}/H_2PO_4^-$ Buffer system
Buffer

- Routes of excretion of acids
  - Lungs
  - Kidneys

2. **Respiratory Mechanisms:**
   - Responds within minutes
   - Takes 6-12 hours to be fully effective
   - Operates by excreting CO2 or \((\text{adding } \text{H}_2\text{CO}_3/\text{HCO}_3^-)\)
3. Renal Mechanisms:

• Responds slowly *(effectively in 3-5 days)*
• Eliminates excess Acids or Bases from body
• The most powerful mechanism
  
ed. i. $\text{HCO}_3^-/\text{CO}_2$ Buffer system
  
  ii. $\text{NH}_3/\text{NH}^+4$ Buffer system
  
  iii. $\text{HPO}^-4/\text{H}_2\text{PO}^-4$ Buffer system
Bicarbonate buffer system

• Consist of
  – A weak acid
  – A bicarbonate salt

  \[
  \text{CO}_2 + \text{H}_2 \text{O} \leftrightarrow \text{H}_2 \text{CO}_3
  \]

• Slow reaction without carbonic anhydrase

• Present in walls of alveoli and renal tubules

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

• Second component

  \[
  \text{NaHCO}_3 \leftrightarrow \text{Na} + \text{HCO}^-_3
  \]
Bicarbonate buffer system

- When strong acids like HCl combine with NaHCO3
  - Forms weak acid
  - CO₂ is exhaled

\[ \text{HCl} + \text{NaHCO}_3 \rightarrow \text{NaCl} + \text{CO}_2 + \text{H}_2\text{O} \]

- When strong bases like NaOH combine with HCO⁻³
  - Forms weak base/salt
  - H₂O is eliminated

\[ \text{NaOH} + \text{H}_2\text{CO}_3 \rightarrow \text{NaHCO}_3 + \text{H}_2\text{O} \]
Buffer Power

- pH=pK
- Most effective when pK is near to pH in the central part of curve
- 1.0 pH unit deviation ---- reasonably effective
- Bicarbonate buffering power 6.1
- Can extend from 5.1 to 7.1
Phosphate Buffer System

• Not important in ECF buffers: $\text{H}_2\text{PO}_4^- / \text{HPO}_4^{2-}$
• Strong **acids** bind with $\text{HPO}_4^{2-}$ (salt) to form salts
  \[ \text{HCl} + \text{Na}_2\text{HPO}_4 \rightarrow \text{NaH}_2\text{PO}_4 + \text{NaCl} \]
• Strong **bases** bind with $\text{H}_2\text{PO}_4^-$ (weak acid) to form weak acid and water
  \[ \text{NaOH} + \text{NaH}_2\text{PO}_4 \rightarrow \text{Na}_2\text{HPO}_4 + \text{H}_2\text{O} \]
• pK 6.8
• About 8% in ECF
• Most efficient in renal tubules
Protein Buffer

• ICF buffer—60-70%
• Most powerful buffer in body
  – Increased conc. of proteins in cells
• Slight diffusion of H+ between ECF & ICF
  – Decreased pH in ECF also decreased pH in ICF
  – Already less pH in ICF
• RBC – Hemoglobin: buffer action
  – H+ + Hb ---→ HHb
Respiratory control

- Second line of defense
- 50% control of pH regulation - by lung
- 50% - 75% effective in reversing H+ conc. to normal (not 100%)
- Response in 3-12 minutes
- Role of lungs - alteration in breathing rate
  - Minimum ventilation = pH drops to 6.95
  - Maximum ventilation = pH rises to 7.63
Respiratory control

- Continually formed during metabolic processes
- From cells reach lungs to be exhaled
- 1.2mol/L of dissolved CO$_2$ impart PCO$_2$ of 40mmHg
- Metabolism increases CO2 formation increases
- If pulmonary ventilation decreases PCO$_2$ decreases
- \[ \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+\text{ions} \rightarrow \downarrow \text{pH} \]
Respiratory control

- Sensitivity – alveolar ventilation doubles with pH drop by 0.23
- As pH drops, sensitivity of respiratory center increases tremendously

<table>
<thead>
<tr>
<th>pH</th>
<th>VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.4</td>
<td>1</td>
</tr>
<tr>
<td>7.3</td>
<td>1.3</td>
</tr>
<tr>
<td>7.2</td>
<td>1.6</td>
</tr>
<tr>
<td>7.1</td>
<td>2.6</td>
</tr>
<tr>
<td>7.0</td>
<td>3</td>
</tr>
</tbody>
</table>

- The respiratory component responds less to alkalosis so at pH 7.4, the alveolar ventilation changes only 1 time
Respiratory control

- Partial compensation in metabolic acidosis & alkalosis
- Resp compensation - More effective in acidosis than in alkalosis
- Not as effective as renal buffer system
- Mechanism
  - < pH, more $\text{H}_2\text{CO}_3$ to $\text{CO}_2$
  - Central chemoreceptors stimulated, increased ventilation
Respiratory Regulation

- ↑ Hydrogen ions → ↑ alveolar ventilation → ↓ CO2
- Decreased CO2 will decrease H ions
- Returns pH back to normal
Respiratory Regulation

- \( \uparrow \) Hydrogen ions \( \rightarrow \) \( \uparrow \) alveolar ventilation \( \rightarrow \) \( \downarrow \) CO2
- Decreased CO2 will decrease H ions
- Returns pH back to normal
Regulation of H+ Ions

• More HCO₃ filtered more H+ ions secreted
• More loss of acid
• 80mEq of non volatile acids are produced
• Elimination of non-volatile acids: (H₂SO₄ H₃PO₄ )
  – Secretion of H +
• Kidney prevent loss of bicarbonate ions
• To preserve body buffer
4320 mEq/day

85%
(3672 mEq/day)

10%
(432 mEq/day)

>4.9%
(215 mEq/day)

(1 mEq/day)
Regulation of H+ Ions

• In alkalosis
  – Less H+ ions are secreted
  – Less HCO3 are filtered and reabsorbed
  – Net loss of HCO3 ions and preservation of H+ ions
  – Decreases ECF pH

• In acidosis
  – More H+ ions are secreted
  – More HCO3 are filtered and reabsorbed
  – Net preservation of HCO3 ions and loss of H+ ions
  – Raises ECF pH
Regulation of H+ Ions

• Normally kidney regulates ECF pH
  – Secretion of H+ ions
  – Reabsorption/Filtration of HCO3 ions
  – Production of new HCO3- ions
Renal buffer systems:

1. Phosphate buffer system
2. Ammonia buffer system
3. Carbonic Acid buffer system

Less important are urates and citrates
Renal buffer systems

• Kidney’s acid-base regulatory potency is that it has ability to return the pH almost exactly to normal by:-
  
  i. Active secretion of H⁺ ions
  
  ii. H⁺ ion buffering within tubular lumen:
      a. Buffering with HCO⁻³;
         Result in reabsorption of filtered HCO⁻³ ions
      b. Buffering with HPO⁻⁴ or NH₃;
         Result in H⁺ ion excretion & generation of new HCO⁻³ ions
  
Outcome: by excreting acidic or basic urine
Phosphate buffers

• pH=6.8
• Renal tubular and intracellular buffer
• Only 8% in ECF
• Consists of
  – $\text{HPO}_{4}^{2-}$ (salt)
  – $\text{H}_{2}\text{PO}_{4}^{-}$ (acid)

(become concentrated in renal tubules by reabsorption of $\text{H}_{2}\text{O}$).
Phosphate buffer

- 75% of filtered \( \text{HPO}_4^- \) is reabsorbed
- Remaining 25% is available for buffering, concentrated in tubules
- Under normal conditions 30-40 mEq/day filtered phosphate is available for buffering \( \text{H}^+ \).
- Operates when secreted \([\text{H}^+]\) is in excess than filtered \([\text{HCO}_3^-]\)
- Renal tubules has relatively less pH than ECF
Ammonia buffer

- 2\textsuperscript{nd} Special Buffer System
- Consists of NH3 & NH\textsuperscript{+4}
- More important \textit{‘quantitatively’} than phosphate buffer system
- 50 \% of H\textsuperscript{+} secreted in kidneys – handled by NH3 buffer
- NH4 ions are synthesized from glutamine in PCT, LOH & DT
- Secreted into tubular fluid by Na\textsuperscript{+}-H\textsuperscript{+} exchange (\textit{counter transport}) mechanism i.e. NH\textsuperscript{+4} is secreted in place of H\textsuperscript{+}. 
Ammonia buffer

- Main buffer system in renal tubules in chronic acidosis
- Production of NH3+ from glutamine in liver mainly
- From 01 glutamine molecule, 02 NH4 & 02 ‘NEW’ HCO3 molecules generated in renal tubules
- PCT, LOH, DCT - permeable to NH4 – Na+-NH4+ counter-transport secreted as NH4Cl
- CD - impermeable to NH4 – NH3 secreted & combine with H+
- For each NH4 secreted one ‘NEW’ HCO3 generated
When there is excess H⁺ ions in ECF:

• Kidneys tackle it by;

1. Reabsorption of all filtered HCO⁻³
2. Generation of new HCO⁻³ (to replenish decreased level of HCO⁻³ in ECF)
Regulation of H+ Ions

- Maximum H+ conc. – 900 folds in DCT & CD
- Reabsorption of all filtered HCO3
- Production of new HCO3 (In PCT, DCT & CD)
  - PO4 buffer (one new HCO3 for each H+ secreted)
  - Ammonia buffer (two new HCO3 for each H+ secreted)
- In chronic acid-base disorder – NH3 buffer most effective
- Partial compensation in respiratory and non-renal metabolic acid base disorders
<table>
<thead>
<tr>
<th>Features</th>
<th>PCT</th>
<th>DCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCO₃ reabsorption</td>
<td>70%</td>
<td>4-5%</td>
</tr>
<tr>
<td>HCO₃ reabsorption</td>
<td>Na⁺-HCO₃ co-tpt Cl⁻-HCO₃ counter-tpt</td>
<td>Na⁺-HCO₃ co-tpt</td>
</tr>
<tr>
<td>Net Gain/loss of HCO₃</td>
<td>Nil (all filtered HCO₃ reabsorbed)</td>
<td>Depend on ECF pH</td>
</tr>
<tr>
<td>H⁺ secreted by</td>
<td>Counter-tpt (Na⁺-H⁺) (Inc by Ang II)</td>
<td>Primary active (H⁺ pump) (Inc by Ang II &amp; aldosterone)</td>
</tr>
<tr>
<td>Rise in Tubular H⁺ conc</td>
<td>3-4 folds</td>
<td>900 folds</td>
</tr>
<tr>
<td>Minimum pH in lumen</td>
<td>6.7</td>
<td>4.5</td>
</tr>
<tr>
<td>H⁺ handling</td>
<td>By NH₃ buffer mainly</td>
<td>By both HPO₄ &amp; NH₃ buffer</td>
</tr>
<tr>
<td>In acid-base disorder</td>
<td>Mainly HCO₃ reabsorption H⁺ secretion (4 folds)</td>
<td>Mainly H⁺ secretion &amp; buffering (900 folds)</td>
</tr>
<tr>
<td>Role in acid-base disorder</td>
<td>Fairly imp</td>
<td>Extremely imp (pH of urine determined by DCT)</td>
</tr>
</tbody>
</table>
Renal buffer systems

- H+ ion secretion in excess of HCO3 ions
- Urine minimal pH 4.5
- H+ ion concentration 0.03mEq/L
- 80mEq/L non-volatile acid require 2667L of urine to be excreted
- Large amount of H+ ions excreted with buffers
Renal Acid Base Excretion

- Bicarbonate excretion is calculated as urine flow rate multiplied by urinary bicarbonate concentration
- Bicarbonate reabsorption = H+ ion secretion or NH4+ ions
- Titrable acids --- non bicarbonate buffers excreted in urine

Net acid excretion = NH4+ excretion + urinary titratable acids – bicarbonate excretion
<table>
<thead>
<tr>
<th>Increase H⁺ Secretion and HCO₃⁻ Reabsorption</th>
<th>Decrease H⁺ Secretion and HCO₃⁻ Reabsorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ PCO₂</td>
<td>↓ PCO₂</td>
</tr>
<tr>
<td>↑ H⁺, ↓ HCO₃⁻</td>
<td>↓ H⁺, ↑ HCO₃⁻</td>
</tr>
<tr>
<td>↓ Extracellular fluid volume</td>
<td>↑ Extracellular fluid volume</td>
</tr>
<tr>
<td>↑ Angiotensin II</td>
<td>↓ Angiotensin II</td>
</tr>
<tr>
<td>↑ Aldosterone</td>
<td>↓ Aldosterone</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Hyperkalemia</td>
</tr>
</tbody>
</table>
Anion gap

- Anion gap derives from the principle of ‘electroneutrality’.
- Routinely some cations & anions are measured and others are not (Na+, HCO-3, Cl-)
- When conc. of Na+ is compared to sum of HCO-3 & Cl-, there is an anion gap i.e. conc. of Na+ is greater than sum of HCO-3 & Cl-.
- To keep electroneutrality, plasma must contain unmeasured anions to make up difference.
- Plasma anion gap = 8-16 mEq/L.
  
  \[\text{Plasma anion gap} = [\text{Na}^+] - ([\text{HCO}-3] + [\text{Cl}^-])\]
  
  \[= 144 - 24 - 108\]
  
  \[= 12 \text{ mEq/L (Normal)}\]
ANION GAP OF PLASMA

Cations

Anions

Na\(^+\)

HCO\(_3^-\)

Cl\(^-\)

Anion gap

Protein, phosphate, citrate, sulfate
Anion gap

- Plasma anion gap is primarily useful in differential diagnosis of metabolic acidosis.
- Increased anion gap: *e.g.* metabolic acidosis, starvation, CRF
- An accumulation of an organic anion; *e.g.* ketoacid, lactate, formate, salicylate.
- [Unmeasured cations include; Ca++, Mg++, & K+]
### Metabolic Acidosis Associated with Normal or Increased Plasma Anion Gap

<table>
<thead>
<tr>
<th>Increased Anion Gap (Normochloremia)</th>
<th>Normal Anion Gap (Hyperchloremia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus (ketoacidosis)</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td>Renal tubular acidosis</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Carbonic anhydrase inhibitors</td>
</tr>
<tr>
<td>Aspirin (acetylsalicylic acid)</td>
<td>Addison’s disease</td>
</tr>
<tr>
<td>poisoning</td>
<td></td>
</tr>
<tr>
<td>Methanol poisoning</td>
<td></td>
</tr>
<tr>
<td>Ethylene glycol poisoning</td>
<td></td>
</tr>
<tr>
<td>Starvation</td>
<td></td>
</tr>
</tbody>
</table>
Anion gap

• No accumulation of an organic anion, but decrease in HCO-3 conc. is offset by an increase in conc. of Cl-

• ‘Hyperchloremic metabolic acidosis’ with normal anion gap (e.g. diarrhea, renal tubular acidosis)--- ‘non anion gap’.
THANK YOU