ACID-BASE DISORDER

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OBJECTIVES OF PRESENTATION

1. To refresh knowledge of acid-base disorders
2. To evaluate acid-base disorders using stepwise approach
INTRODUCTION

- Changes in arterial PCO2, HCO3−, and serum pH.
  - Acidemia is pH < 7.35.
  - Alkalemia is pH > 7.45.

- Acidosis: physiologic processes that cause acid accumulation or alkali loss.

- Alkalosis: physiologic processes that cause alkali accumulation or acid loss.
Regulation of acid-base

Kidney regulation

Pulmonary regulation
- HCO$_3^-$/$\text{H}_2\text{CO}_3$ buffering system

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

CO2: controlled by alveolar ventilation

H+ and HCO3-: regulated by renal excretion
Relationship pH and acid-base pair:

Henderson-Hasselbalch equation

\[ \text{pH} = \text{pK} + \log \left( \frac{[\text{base}]}{[\text{acid}]} \right) \]

\[ \text{pH} = 6.1 + \log \left( \frac{\text{HCO}_3^-}{0.03 \times \text{PCO}_2} \right) \]
Respiratory regulation

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

\[ k \times \text{CO}_2 \text{ (gas)} \]
Renal regulation

Blood

Renal tubule cell

Tubule lumen

\[ \text{HCO}_3^- + H^+ \leftrightarrow H_2CO_3 \leftrightarrow CO_2 \text{ (dissolved)} + H_2O \]
Type of acid-base disorders

(i) Metabolic acidosis
(ii) Metabolic alkalosis
(iii) Respiratory acidosis
(iv) Respiratory alkalosis
(v) Mixed acid-base disorders
Lab. values in simple acid-base disorders

<table>
<thead>
<tr>
<th>Arterial pH</th>
<th>Primary change</th>
<th>Compensatory change</th>
<th>Disorder</th>
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<td>↓</td>
<td>↓HCO₃⁻</td>
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pH (7.35-7.45);
PCO₂ (35-45mmHg);
HCO₃⁻ (22-26mmol/L)
METABOLIC ACIDOSIS

- Characterized by ↓pH (7.35-7.45) and ↓serum $\text{HCO}_3^-$ (22-26mmol/L), typically with compensatory reduction in $\text{PCO}_2$ (35-45mmHg).

- Categorized as elevated or normal anion gap (AG).
  \[
  \text{AG} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)
  \]

- Normal AG: caused by loss of $\text{HCO}_3^-$ and can be further characterized as hypokalemic or hyperkalemic.

- Elevated AG: caused by overproduction of organic acids or with decreased acid excretion.
Common causes of metabolic acidosis

<table>
<thead>
<tr>
<th>NORMAL AG</th>
<th>ELEVATED AG</th>
</tr>
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<tbody>
<tr>
<td><strong>Hypokalemic</strong></td>
<td></td>
</tr>
</tbody>
</table>
  - Diarrhea  
  - Fistulous disease  
  - Type I RTA  
  - Type II RTA  
  - Carbonic anhydrase inhibitors |
| **Hyperkalemic** | 
  - Hypoaldosteronism  
  - Hydrochloric acid or precursor  
  - Type IV RTA  
  - Potassium-sparing diuretics |
| | 
  - Renal failure  
  - Lactic acidosis  
  - Ketoacidosis  
  - Starvation  
  - Ethanol  
  - Diabetes mellitus  
  - Drug intoxications  
  - Methanol  
  - Salicylates |
Metabolic acidosis: Compensation

- 1.2 mmHg decrease in PCO2 for every 1 mmol/L decrease in HCO3-

\[
\downarrow \text{PCO2 (mmHg)} = 1.0-1.2 \times \text{HCO3- (mmol/L)}
\]

- If PCO2 falls outside the compensatory range, possibilities:
  i) Mixed acid-base disorder
  ii) Inadequate extent of compensation
  iii) Inadequate time for compensation
Metabolic acidosis: Treatment

1) Correct underlying causes if possible

2) Sodium bicarbonate \((\text{NaHCO}_3)\)

- MOA: dissociates to provide \(\text{HCO}_3^-\) which neutralizes \(\text{H}^+\) concentration and raises blood and urinary pH.

- Onset of action:
  - Oral: rapid
  - IV: 15 min √

- Duration of action:
  - Oral: 8-10 min
  - IV: 1-2 hr √
Dose: Infants, children, and adults

\[
\text{HCO}_3^- (\text{mmol}) = 0.3 \times \text{weight (kg)} \times \text{base deficit (mmol/L)}
\]

Preparation:

NaHCO3 8.4% (10mL, 50mL) [1mmol/1mL]

50mL, 8.4% = 4.2g = 50mmol

Administration

½ dose initially, remaining ½ dose infuse over the next 24 H
METABOLIC ALKALOSIS

- Characterized by ↑pH, primarily ↑ in HCO₃⁻ and a compensatory ↑ in PCO₂.
- The major causes in the ICU are vomiting, nasogastric suction, diuretics, corticosteroids, acetate used in TPN.
Metabolic alkalosis: Compensation

- 0.5-0.7 mmHg increase in PCO2 for every 1 mmol/L increase in HCO3-.

\[ \uparrow \text{PCO}_2 = 0.5 - 0.7 \times \uparrow \text{HCO}_3^- \]

- If compensatory value PCO2 falls outside the range, mixed disorder should be suspected.
Metabolic alkalosis: Treatment

- Treatment of metabolic alkalosis depends on removing the cause\(^1\).
  - Replacing diuretic induced potassium losses → amiloride, spironolactone
  - Minimizing nasogastric suction
Infusion of sodium and potassium chloride to correct fluid deficits and replace K+ and Cl-

Fast correction of electrolyte:
adult: 0.6 x BW(kg) (target level-current level)
children: 0.7 x BW (kg)(target level-current level)

Ex: Pt, 55yo/male/malay, 70kg. BUSE, K+ = 2.9mmol/L (3.5-4.5mmol/L)

K+ correction = 0.6 X 70kg x (4.0-2.9)
= 0.6 x 70 x 1.1
= 46.2 mmol

1 vial KCl (10%w/v) = 10mL (1g) = 13.4 mmol

13.4mmol x 3 = 40.2mmol ............30 mL(3g)

→ Infuse 30mL over 2 hours
- Acetazolamide (blocks H+ secretion in the renal tubule), IV 250mg q 6 hr for 4 doses or 500mg single dose → reassess ABG.
RESPIRATORY ACIDOSIS

- Characterized by a primarily ↑PCO2, ↓pH and a compensatory ↑ in HCO3-.

- It occurs as a result of inadequate ventilation by the lungs.

- When the lungs do not excrete CO2 effectively, the PCO2 rises which lead to fall in pH.
Respiratory acidosis: Compensation

- Compensation occurs acutely through cell buffers and chronically through renal compensation.

- Acute: 1 mmol/L increase in serum bicarbonate for every 10 mmHg increase in PCO2.

  \[ \text{\uparrow HCO}_3^- = 0.1 \times \text{\uparrow PCO}_2 \]

- Chronic: 4 mmol/L rise in HCO3- for every 10 mmHg increase in PCO2.

  \[ \text{\uparrow HCO}_3^- = 0.4 \times \text{\uparrow PCO}_2 \]
Common causes of respiratory acidosis

**Airway Obstruction**
- foreign body aspiration
- Asthma
- COPD
- B-adrenergic blockers

**CNS disturbances**
- Cerebral vascular
  - Sleep apnea
  - Accident
  - Tumor
  - CNS depressant drugs

**Cardiopulmonary**
- Cardiac arrest
- Pulmonary edema
- PE
- Pulmonary fibrosis

**Neuromuscular**
- Hypokalemia
- Hypophosphatemia
- Drugs
  - Aminoglycosides
  - Antiarrythmias’
  - Lithium
  - Phenytoin
Respiratory acidosis: Treatment

- Treatment primarily involves correction of the underlying cause of respiratory insufficiency.
- For example: treat with ipratropium or a β-adrenergic agent (inhaled salbutamol); increase ventilation (mechanical ventilator)
RESPIRATORY ALKALOSIS

- Characterized by $\uparrow$ pH, primarily $\downarrow$ PCO2 and a compensatory with $\downarrow$ in HCO3-

- Associated with excessive rate or depth of respiration results in increased excretion of CO2.

- A fall in PCO2 $\Rightarrow$ rise in arterial pH
Respiratory alkalosis: Compensation

- A small acute decrease due to tissue buffers
- Chronic decrement due to a decrease in renal titratable acid excretion and an increase in renal HCO3- excretion.

**Acute:** 2 mmol/L decrease in HCO3− for every 10mm Hg decrease in PCO2

\[ \downarrow \text{HCO3−} = 0.2 \times \downarrow \text{PCO2} \]

**Chronic:** 4 – 5 mmol/L decrease in HCO3− for every 10mm Hg decrease in PCO2

\[ \downarrow \text{HCO3−} = 0.4 – 0.5 \times \downarrow \text{PCO2} \]
Common causes of respiratory alkalosis

CNS disturbances
- Bacterial septicemia
- Cerebrovascular accident
- Fever
- Hepatic cirrhosis
- Hyperventilation
- Meningitis
- Pregnancy
- Trauma
- Drugs
  - Respiratory stimulant
  - Salicylate overdose

Pulmonary
- Pneumonia
- Pulmonary edema
- Pulmonary embolus

Tissue hypoxia
- High altitude
- Hypotension
- CHF

Other
- Excessive mechanical ventilation
Respiratory alkalosis: Treatment

- Usually involves correcting the underlying disorder

- Intubation and muscle relaxation are often required to control hyperventilation and redirect blood flow.
MIXED ACID-BASE DISORDERS

- Are defined as independently coexisting disorders

- The diagnosis of this disorder can be confirm by using compensatory equation.
Ex. of mixed acid-base disorders

<table>
<thead>
<tr>
<th>ABG</th>
<th>Impression</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH: 7.06</td>
<td>severe acidosis</td>
</tr>
<tr>
<td>PCO2: 48mmHg</td>
<td>PCO2 and HCO3- changed in opposite directions</td>
</tr>
<tr>
<td>HCO3-: 13mmol/L</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(\downarrow)PCO2 (mmHg) = 1.0-1.2 x (\downarrow)HCO3- (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\downarrow)PCO2 = 1.0 x 11 – 1.2 x 11</td>
</tr>
<tr>
<td>= 11 – 13.2</td>
</tr>
</tbody>
</table>

If metabolic acidosis, value PCO2 should be within 26.8 to 29mmHg. Thus, PCO2 48mmHg is significantly higher than the predicted.

→ Coexistent **respiratory acidosis**
Ex. of
ABG report

<table>
<thead>
<tr>
<th>Blood Gas Values</th>
<th>pH</th>
<th>7.312</th>
<th>7.350 - 7.450</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCO₂</td>
<td>36.7</td>
<td>mmHg</td>
<td>[35.0 - 45.0]</td>
</tr>
<tr>
<td>pO₂</td>
<td>30.5</td>
<td>mmHg</td>
<td>[75.0 - 100]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oximetry Values</th>
<th>sO₂</th>
<th>53.2%</th>
<th>[95.0 - 100.0]</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRO₂Hₐ, ß</td>
<td>52.8%</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>cH⁺H⁺</td>
<td>46.4%</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Electrolyte Values</th>
<th>cK⁺</th>
<th>3.4 mmol/L</th>
<th>[3.5 - 5.0]</th>
</tr>
</thead>
<tbody>
<tr>
<td>cNa⁺</td>
<td>136 mmol/L</td>
<td>[135 - 148]</td>
<td></td>
</tr>
<tr>
<td>cCa²⁺</td>
<td>1.02 mmol/L</td>
<td>[1.18 - 1.35]</td>
<td></td>
</tr>
<tr>
<td>cCl⁻</td>
<td>106 mmol/L</td>
<td>[98 - 107]</td>
<td></td>
</tr>
</tbody>
</table>

| Metabolite Values | cLac | 6.1 mmol/L | [0.6 - 2.4] |

<table>
<thead>
<tr>
<th>Temperature Corrected Values</th>
<th>pH(T₁)</th>
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<th>7.350 - 7.450</th>
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<tbody>
<tr>
<td>pCO₂(T₁)</td>
<td>36.7 mmHg</td>
<td>[35.0 - 45.0]</td>
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<tr>
<td>pO₂(T₁)</td>
<td>30.5 mmHg</td>
<td>[75.0 - 100]</td>
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<th>Oxygen Status</th>
<th>pS₉</th>
<th>28.87 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>cO₂P₉c</td>
<td>43.0 Vo%</td>
<td></td>
</tr>
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<table>
<thead>
<tr>
<th>Acid Base Status</th>
<th>cBase(Ecf)</th>
<th>-7.0 mmol/L</th>
</tr>
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<tbody>
<tr>
<td>cHCO₃(P,st)</td>
<td>17.9 mmol/L</td>
<td></td>
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</table>
Role of clinical pharmacist..

- Able to interpret ABGs result and assist in dosage calculation
- Follow up the progression of the patient
EVALUATION OF ACID-BASE DISORDER

- **Stepwise approach**
  1. Determine whether the pH is consistent with acidosis or alkalosis
  2. Determine whether the CO$_2$ and HCO$_3^-$ consistent with the pH
  3. Review the history
  4. Determine primary disorder is of respiratory or metabolic origin
  5. Calculate the expected compensatory response
  6. Determine the probable cause
Example of case

LJ, 34 yo, 60 kg man, brought to A&E in a semicomatose state. He has a long history of alcohol abuse.

Lab values
Na+ : 140mmol/L (135-145)
K+  : 5.8mmol/L (3.5-5.0) ↑
Cl- : 103mmol/L (95-105)
pH  : 7.16 (7.35-7.45) ↓
PCO2 : 23mmHg (35-45) ↓
HCO3- : 8mmol/L (22-26mmol/L) ↓
1) **Determine whether the pH is consistent with acidosis or alkalosis**

Pt’s pH: 7.16 ??

→ Acidosis
2) Check the laboratory validity by using Henderson-Hasselbalch equation

\[
\text{pH} = 6.1 + \log \frac{(\text{HCO}_3^-)}{(0.03)(\text{PCO}_2)}
\]

\[
\begin{align*}
pH &: 7.16 \\
\text{PCO}_2 &: 23\text{mmHg} \\
\text{HCO}_3^- &: 8\text{mmol/L}
\end{align*}
\]

\[
\text{pH} = 6.1 + \log \frac{8}{(0.03)(23)} = 7.16 \quad \checkmark
\]
3) Review the history

Alcohol abuse
4) Determine whether the primary disorder is of respiratory or metabolic origin

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pH : 7.16 (7.35-7.45) ↓
PCO₂ : 23mmHg (35-45) ↓
HCO₃⁻ : 8mmol/L (22-26mmol/L) ↓
5) Calculate the expected compensatory response

↓PCO2 : 17mmHg (40-23)
↓HCO3- : 16mmol/L (24-8)

↓PCO2 (mmHg) = 1.0-1.2 x HCO3- (mmol/L)
= 1.0 x 16 – 1.2 x 16
= 16 – 19.2

→ normal respiratory compensation
6) Calculate anion gap to determine the probable cause

Lab values

- Na\(^+\) : 140mmol/L (135-145)
- Cl\(^-\) : 103mmol/L (95-105)
- HCO\(_3\)^- : 8mmol/L (22-26mmol/L)

\[ AG = 140 - (103 + 8) = 29\text{mmol/L (Elevated AG)} \]

→ Alcohol results in formation of formic and lactic acid (organic acids)
Treatment

- Bicarb dose (mmol) = 0.3 x weight (kg) x base deficit (mmol/L)
  
  base deficit = 24 - 8 = 16

To avoid overtreating, base deficit recommended is 4-8mmol/L
  
  = 0.3 x 60kg x (6)
  
  = 108 mmol

Administration: ½ dose initially, remaining ½ over the next 24 H

Effect of HCO3- can be determined 30 min after administration. ABG should be repeated.
THANK YOU!