Core Curriculum Lecture Objectives

- Understand the basic concepts in acid-base physiology
  - Henderson-Hasselback equation

- To be able to analyze ABG’s, and identify simple and mixed acid base disorder (5 steps)
  - Metabolic acidosis vs. Metabolic alkalosis
  - Respiratory acidosis vs. Respiratory alkalosis
  - Calculate anion gap and delta gap
Regulation of pH is essential

- Acid base physiology is the regulation of hydrogen ion concentration.
  - What is a normal hydrogen concentration?

- Extreme ranges of pH (<7.2 or > 7.55) are potentially life threatening.
  - What is the pH range compatible with life?

Every change of 0.3 pH units represents a change in H⁺ by a factor of 2.
The disease is more important!

- pH changes have dramatic effects on normal cell function and physiological process.
  - Disruption of protein structure and enzyme function
  - Changing distribution of electrolytes (K+, Na+, and Ca++)
  - Changes in excitability of nerve and muscle cells
  - Decreasing effectiveness of medications

- It is imperative to rapidly assess the cause of an acid-base disturbance.
  - The absolute pH is less important than the etiology.
ABGs

An arterial blood gas (ABG) is a sample of arterial blood that reports: **pH / pO\textsubscript{2} / pCO\textsubscript{2} / HCO\textsubscript{3}**

- **pH**: 7.4 (H ion concentration)
- **PaCO\textsubscript{2}**: 40 mmHg. (dissolved CO\textsubscript{2} in blood or ventilatory effectiveness)
- **HCO\textsubscript{3}**: 24 mEq/L (metabolic effectiveness)
- **PaO\textsubscript{2}**: 80-100 mmHg (O\textsubscript{2} content of blood)
When to order ABG?

- Intubated ICU pt. for ventilator management
- Respiratory distress
- Home O₂ criteria
- Abnormal serum bicarbonate or H&P suggest severe acid base disorders
- Indication for dialysis
- AMS work-up
- Critical and unstable patients
  - Abnormal levels of pH and PCO₂ are best indicators of trouble.
The Henderson-Hasselbalch formula is the mantra of acid-base physiology

- Dissolved CO₂ + H₂O ⇌ H₂CO₃ ⇌ HCO₃⁻ + H⁺

\[ \text{pH} = pK_a + \log \frac{[\text{HCO}_₃^-]}{[\text{CO}_₂]} \]

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

\[ \text{Acidity} = \frac{\text{Bicarbonate}}{\text{Carbon Dioxide}} \]

\[ A = \frac{B}{C \times D} \]
There are 4 primary ways that pH can change

Increase in $\text{HCO}_3^-$, increases pH.

Metabolic alkalosis

$$\text{pH} \propto \frac{[\text{HCO}_3^-]}{[\text{CO}_2^-]}$$
There are 4 primary ways that pH can change

Increase in $\text{HCO}_3^-$, increases pH
→ **Metabolic alkalosis**

Decrease in $\text{HCO}_3^-$, decreases pH.

Metabolic acidosis
There are 4 primary ways that pH can change:

- Increase in $\text{HCO}_3^-$, increases pH
  $\rightarrow$ **Metabolic alkalosis**

- Decrease in $\text{HCO}_3^-$, decreases pH
  $\rightarrow$ **Metabolic acidosis**

- Increase in $\text{pCO}_2$, decreases pH.
  **Respiratory acidosis**

$pH \propto \frac{[\text{HCO}_3^-]}{[\text{CO}_2]}$
There are 4 primary ways that pH can change

Increase in $\text{HCO}_3^-$, increases pH
$\rightarrow$ **Metabolic alkalosis**

Decrease in $\text{HCO}_3^-$, decreases pH.
$\rightarrow$ **Metabolic acidosis**

Increase in $\text{pCO}_2$, decreases pH
$\rightarrow$ **Respiratory acidosis**

Decrease in $\text{pCO}_2$, increases pH.
**Respiratory alkalosis**
Patients with primary acid-base disorders compensate to restore normal pH.

- In primary respiratory disorders, the kidney modifies the serum bicarbonate to return pH toward normal.
- In primary metabolic disorders, breathing is altered to change the pCO$_2$ in order to return pH toward normal.
Compensation minimizes changes in pH

Metabolic alkalosis

*Increased* $\text{HCO}_3^-$, increases pH.

*Increased* $\text{CO}_2$ compensates to reduce the change in pH.
Compensation minimizes changes in pH

Metabolic acidosis

Decreased $\text{HCO}_3^-$, decreases pH.

Decreased $\text{CO}_2$ compensates to reduce the change in pH.
Compensation minimizes changes in pH

**Respiratory acidosis**

**Increased** $\text{CO}_2$, decreases pH.

**Increased** $\text{HCO}_3^-$ compensates to reduce the change in pH.
Compensation minimizes changes in pH

Respiratory alkalosis

Decreased CO₂, increases pH.

Decreased HCO₃ compensates to reduce the change in pH.
Compensation is always in **the same direction** as the primary disorder.

<table>
<thead>
<tr>
<th>Primary Disorder</th>
<th>Primary</th>
<th>Compensation</th>
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<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>$\downarrow \text{HCO}_3$</td>
<td>$\downarrow \text{pCO}_2$</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>$\downarrow \text{pCO}_2$</td>
<td>$\downarrow \text{HCO}_3$</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>$\uparrow \text{pCO}_2$</td>
<td>$\uparrow \text{HCO}_3$</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>$\uparrow \text{HCO}_3$</td>
<td>$\uparrow \text{pCO}_2$</td>
</tr>
</tbody>
</table>
If all three variables move in the same direction → metabolic
if they move in discordant directions → respiratory

<table>
<thead>
<tr>
<th>Condition</th>
<th>Primary</th>
<th>Compensation</th>
<th>pH</th>
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</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>$\downarrow$ HCO$_3$</td>
<td>$\downarrow$ pCO$_2$</td>
<td>$\downarrow$</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>$\downarrow$ pCO$_2$</td>
<td>$\downarrow$ HCO$_3$</td>
<td>$\uparrow$</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>$\uparrow$ pCO$_2$</td>
<td>$\uparrow$ HCO$_3$</td>
<td>$\downarrow$</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>$\uparrow$ HCO$_3$</td>
<td>$\uparrow$ pCO$_2$</td>
<td>$\uparrow$</td>
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**Clinical Pearls in Acid-Base Disorders**

- ABG and BMP should be obtained at the same time.

- Simple metabolic d/o move in the same direction:
  - Acidosis: all values decreased
  - Alkalosis: all values increased

- Simple respiratory d/o has reverse relationship:
  - Increase PaC02 and HC02, Decrease pH
  - Decrease PaC02 and HC02, Increase pH

- Compensation **NEVER** completely normalizes pH from original disorder.
  - If pH is normal, mixed acid-base disorder must be present.
“Rules of Five”

The key to ABG interpretation is following the 5 steps in order.
“Rules of Five” -- #1

- **Identify the acidemia or alkalemia**

  \[ \text{pH} < 7.4 = \text{Acidemia} \]

  \[ \text{pH} > 7.4 = \text{Alkalemia} \]
“Rules of Five” -- #2

- **Determine if it is respiratory or metabolic**

- Compare the directional change of the pH and PaCO$_2$
  - If both change in the same direction (up or down), the primary disorder is metabolic.
  - If both change in opposite direction (up and down), the primary disorder is respiratory.
Check for correct degree of compensation

- Each primary acid base disorder has its own formula for prediction.

- Is the compensation appropriate?

- If the magnitude of the compensation deviates from predicted, it indicates additional primary acid-base disorder.
“Rules of Five” -- #3

METABOLIC ACIDOSIS:  Winter’s Formula
\[ pCO_2 = (HCO_3 \times 1.5) + 8 \pm 2 \]

METABOLIC ALKALOSIS:
Each \textit{rise} in HCO_3 by 1 mEq/L, pCO_2 should \textit{rise} 0.7 mmHg, \pm 2
Case 1

43 y/o male came in to clinic for routine visit. He had labs drawn that morning, and BMP revealed the following:
Na 135, K 3.5, Cl 112, HCO₃ 12, BUN 12, Cr 0.7 Alb 4

ABG was obtained:

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>pH</td>
<td>7.25</td>
</tr>
<tr>
<td>pCO₂</td>
<td>25</td>
</tr>
<tr>
<td>HCO₃</td>
<td>10</td>
</tr>
<tr>
<td>pO₂</td>
<td>90</td>
</tr>
</tbody>
</table>
Case 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.25</td>
<td>low (acidemia)</td>
</tr>
<tr>
<td>$\text{HCO}_3^-$</td>
<td>12</td>
<td>low</td>
</tr>
<tr>
<td>$\text{PaCO}_2$</td>
<td>25</td>
<td>low</td>
</tr>
<tr>
<td>AG</td>
<td>11</td>
<td>nl</td>
</tr>
</tbody>
</table>

- What is the primary process?
  - metabolic acidosis

- Is the primary process appropriately compensated?
  - Expected $\text{PaCO}_2$ based on Winter’s equation:
    \[1.5 \times 12 + 8 = 26 \pm 2\] (same as observed)
  - Compensatory respiratory alkalosis
Case 2

- Now your last pt’s twin brother came in, and he also had diarrhea throughout the night after having eaten the same meal. He had the same BMP, but what happened to his PaCO2?

  - pH: 7.25 low (acidemia)
  - HCO₃⁻: 12 low
  - pCO₂: 30 low (higher than his twin pCO₂ 25)
  - AG: 11 nl

- Additional respiratory acidosis superimposed on acute metabolic acidosis

- Furthermore, the twin brother admitted long standing h/o heavy tobacco use
“Rules of Five” -- #3: Metabolic compensation for Respiratory Disorders is slow!

If primary process is respiratory, is it acute or chronic?

- Compensation is always more pronounced in chronic respiratory disorders (days) than in acute respiratory disorders (min-hrs).

**RESPIRATORY ACIDOSIS**

**ACUTE:** Each rise in pCO2 by 10 mmHg, HCO3 should rise 1 mEq/L

**CHRONIC:** Each rise in pCO2 by 10 mmHg, HCO3 should rise 3 mEq/L

**RESPIRATORY ALKALOSIS**

**ACUTE:** Each fall in pCO2 by 10 mmHg, HCO3 should fall 2 mEq/L

**CHRONIC:** Each fall in pCO2 by 10 mmHg, HCO3 should fall 4 mEq/L
Respiratory Acidosis

- For every increase in pCO₂ of 10 mmHg, bicarbonate should increase:
  - 1 mEq/L in acute
  - 3 mEq/L in chronic

- Example:

  pH / pO₂ / pCO₂ / HCO₃
  7.19 / 78 / 80 / 30

- pCO₂ is 40 above normal, so
  - If the condition is acute, HCO₃ should be 28 ± 2
  - If the condition is chronic, HCO₃ should be 36 ± 2
  - Actual HCO₃ is 30, which is within the predicted range, for acute respiratory acidosis and outside of the range for chronic.
Respiratory Alkalosis

- For every decrease in pCO$_2$ of 10 mmHg, bicarbonate should decrease:
  - 2 mEq/L in acute
  - 4 mEq/L in chronic

- Example: $7.44 / 78 / 25 / 17$
  - pCO$_2$ is 15 below normal, so
  - If the condition is acute, the HCO$_3^-$ should be decreased by 3 or 21 ± 2
  - If the condition is chronic, the HCO$_3^-$ should be decreased by 6 or 18 ± 2
“Rules of Five” -- #4

- **ALWAYS Calculate the Anion Gap**

- If there is an anion gap, there is an anion gap metabolic acidosis!

- Remember to correct for low albumin state
  - For each drop in albumin by 1mg/dl (from 4mg/dl), add 2.5 to your calculated Anion Gap
“Rules of Five” -- #4
LAW OF ELECTRONEUTRALITY → Why We Don’t Spark!

- **ALWAYS Calculate the Anion Gap**
- Anion gap = UA – UC
  = Na⁺ – (Cl⁻ + HCO₃⁻)
- Normal AG: 12
  - **UC**: Ca++, Mg++, IgG
  - **UA**: albumin, PO₄⁻, lactate, ketones, sulfates, IgA

- Increased AG occurs with an increase in anions of organic acids (lactic-acids, keto-acids)
What is the anion?

- Metabolic acidosis is further evaluated by determining the anion associated with the increased $H^+$ cation.
- These can be differentiated by measuring the anion gap.

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

Loss of $\text{HCO}_3^-$ (GI vs. renal) with increased $\text{Cl}^-$ $\Rightarrow$ RTA vs. Diarrhea
Metabolic Acidosis

- Elevated AG: Over production of organic acids (MUD PILES)
  - **M** - Methanol
  - **U** - Uremia (uncleared organic acids)
  - **D** - DKA or starvation ketoacidosis
  - **P** - Propylene Glycol (additive in IV benzo’s)
    *paraldehyde: rarely seen -- previous use for EtOH detox
  - **I** - Ingestions (Isopropyl alcohol/Cocaine/MDMA or Ecstasy)
    *INH: rare, unless seizure present / Iron toxicity rare
  - **L** - Lactate (sepsis or ischemia)
  - **E** - EtOH ketoacidosis / Ethylene Glycol
  - **S** - Salicylates

- Normal AG: Loss of HCO₃⁻ (GI vs. renal)
  - Diarrhea vs. RTA
“Rules of Five” -- #5: delta delta

Step 5: if you have an AGMA, determine what the bicarbonate was before the anion gap

- Are there any other hidden metabolic disturbances?
  - Pre-existing metabolic alkalosis
  - Pre-existing non-anion gap metabolic acidosis
  - No pre-existing acid-base disorders
**ANION GAP**

\[ \text{Na}^+ + \text{X}^- \]

\[ \text{H}^+ + \text{X}^- \]

\[ \text{Na}^+ + \text{HCO}_3^- \]

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

\[ \text{AG} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-) = 12 \pm 2 \text{ mM} \]

**METABOLIC ACIDOSIS**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>AG Acidosis</th>
<th>High AG Acidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Na}^+)</td>
<td>140</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>(\text{Cl}^-)</td>
<td>105</td>
<td>115</td>
<td>105</td>
</tr>
<tr>
<td>(\text{HCO}_3^-)</td>
<td>25</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>AG</td>
<td>10</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>(\Delta\text{HCO}_3^-)</td>
<td>-10</td>
<td>-10</td>
<td>-10</td>
</tr>
<tr>
<td>(\Delta\text{AG})</td>
<td>0</td>
<td>0</td>
<td>+10</td>
</tr>
<tr>
<td>LACT.</td>
<td>1</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>(\Delta\text{LACT.})</td>
<td>0</td>
<td>0</td>
<td>+10</td>
</tr>
</tbody>
</table>

* \(\Delta\): Change from Normal
Calculate Delta Delta:

In a simple anion gap acidosis, the magnitude of increase in anion gap ($\Delta$ gap) should be similar to the fall in serum bicarbonate ($\Delta$ bicarbonate).

$$\Delta \text{ Anion Gap} = \Delta \text{ HCO}_3$$

$$\Delta \text{ Anion Gap} = \text{current AG } - \text{ normal AG } \quad (12)$$

$$\Delta \text{ HCO}_3 = \text{baseline HCO}_3 - \text{measured HCO}_3$$

Baseline $\text{HCO}_3 = \text{measured HCO}_3 + \Delta \text{ Anion Gap}$

$\text{HCO}_3 > 28 = \text{Concurrent “hidden” met alkalosis}$

$\text{HCO}_3 < 24 = \text{Concurrent “hidden” non-gap met acidosis}$
Determine the primary Acid-Base disorder

- Metabolic acidosis
- Metabolic alkalosis
- Respiratory acidosis
- Respiratory alkalosis

Determine if the compensation is appropriate

- Winter’s formula
- $\frac{1}{3}$ the $\Delta$ HCO$_3$ for acute, 3:10 chronic
- 1:10 acute, 2:10 chronic

Determine the anion gap

- Non-Anion gap
- Anion gap

Determine the urinary anion gap

- Positive gap (RTA)
- Negative gap (GI, IVF)

Determine the osmolar gap

- Osmolar gap
- Non-osmolar gap

Determine the bicarbonate before

- Pre-existing met. alkalosis
- Pre-existing NAGMA
- No pre-existing acid-base disorders
Case 3

- 38 yo male c/o lightheadedness and lethargy for 3-4 days. He had ‘stomach flu’ for 1 wk., and reports multiple episodes of vomiting and poor PO intake.
- On exam, he was found to have BP 90/60, P 129, RR 30.
- Labs revealed Na 140, K 6.5, Cl 97, HCO₃ 5 (¿ AG)

<table>
<thead>
<tr>
<th>pH</th>
<th>7.10</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCO₂</td>
<td>15</td>
</tr>
<tr>
<td>HCO₃</td>
<td>5</td>
</tr>
<tr>
<td>pO₂</td>
<td>90</td>
</tr>
</tbody>
</table>
Case 3

- pH: 7.1 (low, acidemia)
- pCO$_2$: 15 low
- HCO$_3$: 5 low

- Primary process: metabolic acidosis (Anion Gap: 38)
- Winter’s equation (expected pCO$_2$): 16 (same as observed)
- Delta change HCO$_3$: (38-12= 26)+ 5 (observed) = 31 (an elevated HCO$_3$)

- Answer:
  - anion gap metabolic acidosis (primary)
  - metabolic alkalosis (second primary)
  - compensatory respiratory alkalosis
Case 4

32 yo hispanic female with a 1 week history of bloody diarrhea. She comes to the ER with SOB, weakness and a feeling of doom.

PE: T 38.7° BP 90/40, P 100
Abd: diffusely tender with hyperactive bowel sounds and OB+ stools
Labs: Na 140, K 3.7, Cl 115, HCO3 5 (? AG)

<table>
<thead>
<tr>
<th>pH</th>
<th>7.11</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCO₂</td>
<td>16</td>
</tr>
<tr>
<td>HCO₃</td>
<td>6</td>
</tr>
</tbody>
</table>
Case 4

- pH: 7.11 (low, acidemia)
- pCO₂: 16 low
- HCO₃: 5 low

- Primary process: metabolic acidosis (Anion Gap 20)
- Winter’s equation (expected pCO₂): 16 (same as observed)
- Delta change HCO₃: (20-12)+5 (observed) = 13 (a low HCO₃)

- Answer:
  - anion gap metabolic acidosis (primary)
  - non-anion gap metabolic acidosis (second primary)
  - compensatory respiratory alkalosis
Case 5

- A 21 y/o female is brought to the ER at ~3am, stuporous and tachypneic. History is remarkable for h/o depression and SI’s. An ABG and electrolytes have been drawn by the nurse.

- Labs: Na 140, K 3, Cl 106, HCO₃ 10 (? AG)
  - pH=7.53
  - PaCO₂=12
Case 5

pH: 7.53 (high, alkalemia)
pCO2: 12 low
HCO3: 10 low

- Primary process: respiratory alkalosis (acute)
- Is metabolic compensation appropriate?
  - PaCO2 ↓ed by ~30 mm Hg; HCO3 should fall by 6 mmole/l; HCO3 ↓ is too great, so superimposed metabolic acidosis
- Anion Gap: 24 (anion gap met. Acidosis)
- Combined primary respiratory alkalosis and metabolic acidosis seen in sepsis, or salicylate intoxication
Thank you!
1. What is the pH? acidemia vs. alkalemia
2. Which is the primary process explaining pH?

3. Is the primary process appropriately compensated?
   - If compensatory responses do not lie within the accepted range, by definition a combined disorder exists.

4. ALWAYS calculate AG regardless, and remember to correct for hypoalbuminemia.

5. Is there an additional metabolic disorder? (Delta Delta)
   - Corrected HCO$_3^-$ = (Pt’s AG – 12 )+ pt’s HCO$_3^-$
     - $>28 =$ Concurrent Met Alkalosis
     - $<24 =$ Non-gap Met Acidosis
References


