Acid-Base Homeostasis

Module G
Malley, Chapter 8 (pp.196-218)

Objectives
At the end of this module you will be able to:
• State the normal range for pH and describe how it is derived.
• List the two major organs responsible for pH regulation.
• Describe the relationship between the partial pressure of carbon dioxide, carbon dioxide production and minute ventilation.
• State four ways carbon dioxide is transported in the blood.
• Differentiate between non-volatile (fixed) and volatile acids and state how both are excreted.

Objectives
• Define buffer system.
• List the primary extracellular and intracellular fluid buffers.
• State the Henderson-Hasselbalch equation.
• Describe how the Henderson-Hasselbalch equation can be used clinically to classify acid-base disorders.

Acid-Base and the Web
• ABG Random Generator
  • pH Tool - RANDOM GENERATOR.xls

pH
• \([H^+]\) is 0.00000004 Eq/L in the blood.
• pH is the negative logarithm of this concentration.
  • "negative" – Inverse relationship
  • "logarithm" – Large changes in \([H^+]\) yield only a small proportional change in pH
    • Doubling \([H^+]\) raised pH by 0.3 units.
• Normal 7.35 – 7.45

<table>
<thead>
<tr>
<th>pH</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.80</td>
<td>Death</td>
</tr>
<tr>
<td>7.40</td>
<td>Convulsions</td>
</tr>
<tr>
<td>7.40</td>
<td>Arrhythmias</td>
</tr>
<tr>
<td>7.40</td>
<td>Irritability</td>
</tr>
<tr>
<td>6.80</td>
<td>Normal</td>
</tr>
<tr>
<td>6.80</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>6.80</td>
<td>Lethargy</td>
</tr>
<tr>
<td>6.80</td>
<td>Coma</td>
</tr>
<tr>
<td>6.80</td>
<td>Death</td>
</tr>
</tbody>
</table>
Acid Base Balance

- Acid: A chemical substance capable of releasing a hydrogen ion.
- Base: Any substance capable of combining with or accepting a hydrogen ion.
- Homeostasis: Maintenance of a constant internal environment.
- pH homeostasis maintained by the lungs, kidneys, and the blood buffers.

Acid Excretion

- Lungs and Kidneys
  - Lungs: 13,000 mEq/day of carbonic acid.
  - Kidneys: 40-80 mEq/day of acid.
- Volatile acids: Those that can be converted from a liquid form to a gaseous form to facilitate excretion (i.e. by the lungs).
- Non-Volatile (Fixed) acids: Those that cannot be converted to a gas and must be excreted in a fixed (liquid) state in the urine (i.e. by the kidneys).

Lung Regulation of Volatile Acids

- Excretion must be done in proportion to production or homeostasis cannot be maintained.
- \( \text{CO}_2 + \text{H}_2\text{O} = \text{H}_2\text{CO}_3 = \text{HCO}_3^- + \text{H}^+ \)
  - This reaction takes place in a closed system.
  - This reaction is in equilibrium.
  - Therefore, blood CO\(_2\) can be used as a marker of Carbonic Acid levels.

Plasma Bicarbonate and Buffering for Respiratory Acidosis

- Hydrolysis Effect: Some rise in HCO\(_3^-\) will occur because of excess PaCO\(_2\) in the system.
  - A 10 mmHg \(\uparrow\) in PaCO\(_2\) will yield a 1 mEq/L \(\uparrow\) in plasma [HCO\(_3^-\)].
  - A 5 mmHg \(\downarrow\) in PaCO\(_2\) will yield a 1 mEq/L \(\downarrow\) in plasma [HCO\(_3^-\)].
Carbonic Acid Production/Excretion

- Carbonic Acid is produced at the tissue level by the combination of carbon dioxide and water (left half).
- Hydrogen ion concentration increases and pH falls.
- Carbonic Acid is released at the lungs.
- Hydrogen ion concentration reduces and pH rises.

Carbonic Acid

H₂O + CO₂ → H₂CO₃ → HCO₃⁻ + H⁺

Carbon Dioxide Homeostasis

- Instantaneous PaCO₂ depends on the quantity of carbon dioxide entering the system (c CO₂) and the quantity of carbon dioxide leaving the system through the lungs.
- c CO₂ is dependent on the metabolic rate and the substrate being metabolized.
- Carbon Dioxide excretion is dependent on alveolar minute ventilation.

Regulation of PaCO₂

PaCO₂ = \( \frac{\text{CO₂ Production} \times (\text{VCO₂})}{\text{Alveolar Ventilation (VA)}} \times 0.863 \)

Relationship between PaCO₂ and VA is inverse.

- \( VA = (V_t - V_d) \times f \)
- \( VA = V_e - V_d \)
- \( V_e = V_i \times f \)

| Table 6-1. MINUTE VENTILATION VERSUS ALVEOLAR VENTILATION |
|---|---|---|---|---|
| Vt (mL) | RR (bpm) | Vd (mL) | vt (mL/min) | Ve (mL/min) | PaCO₂ (mm Hg) |
| 500 | 12 | 150 | 6,000 | 4,200 | 40 |
| 250 | 24 | 150 | 6,000 | 2,600 | 80 |
| 1,000 | 6 | 150 | 6,000 | 5,100 | 30 |

What causes a rise in PaCO₂?

- Inadequate Ventilation
- CNS depression
- Respiratory muscle weakness or paralysis.
- Increased Deadspace
- Increased CO₂ production
- Combination of all of them
Increased Deadspace

- Widening of CO₂ gradient
  - PaCO₂ - PETCO₂
- High c_e with normal or high PaCO₂ levels
- Treatment
  - Treat the underlying cause
  - Tracheostomy

Increases in CO₂ Production

- Metabolism of carbohydrates, fats & proteins determine CO₂ levels
  - ↑ carbohydrates, ↑ CO₂ production
- Body temperature
  - ↑ temperature, ↑ metabolism
- Exercise, TPN therapy, sepsis
- Burns
- Seizures

PaCO₂ Relationship to other ABG Parameters

- ↑ PaCO₂ will result in a ↓ PAO₂ & PaO₂ unless the patient is receiving supplemental O₂
- ↑ PaCO₂ will ↓ pH in an acute situation
  - Henderson Hasselbalch Equation
  - \[ pH = \frac{\text{HCO}_3^-}{\text{PaCO}_2} \]

CO₂ Transport

- 200 mL of CO₂ is produced each minute by the tissues.
- Carbon Dioxide is transported by six different mechanisms
  - Three in the plasma
  - Three in the RBC

CO₂ Transport in the Plasma

- 1% forms Carbamino Compounds
- CO₂ combined with protein
- 5% of CO₂ reacts with H₂O & forms HCO₃⁻
- 5% dissolves in the plasma
  - This is measured by the PaCO₂
  - To change CO₂ from partial pressure to mEq/L multiple by 0.03.
  - \( 40 \text{ mm Hg} \times 0.03 = 1.2 \text{ mEq/L} \).

CO₂ Transport in the RBC

- 5% of CO₂ dissolves in the intracellular fluid
- 21% of CO₂ combines with Hb to from carbamino Hb
- 63% of CO₂ reacts with H₂O to from H₂CO₃
  - H₂CO₃ is a volatile acid.
  - This reaction is accelerated by an enzyme carbonic anhydrase.
**Chloride Shift**

- The presence of carbonic anhydrase speeds up the hydrolysis reaction (conversion of carbon dioxide and water into carbonic acid).
- The dissociation of carbonic acid into hydrogen ions and bicarbonate ions results in a large excess of hydrogen ions, which are buffered by the desaturated hemoglobin, thereby maintaining a constant intracellular RBC pH.
- Bicarbonate ions are transported to the plasma.
- To maintain electrical neutrality, chloride ions enter the cell.
- This swap of negative ions (bicarbonate for chloride) is known as the Chloride Shift or the Hamburger Phenomenon (named for Hartog Jakob Hamburger; discovered in 1892).
- Bicarbonate is then transported in the plasma.

**Haldane Effect**

- Carbon Dioxide reacts with proteins on the hemoglobin molecule (NOT the heme site) to form carbamino-compounds.
- The affinity for carbon dioxide by the hemoglobin molecule depends on how much oxygen is present on the hemoglobin (inverse relationship).
- This inverse relationship (more oxygen, less carbon dioxide carried) is known as the Haldane Effect.
- Carbon Dioxide’s presence on the hemoglobin molecule has an effect on the oxyhemoglobin curve that is known as the Bohr Effect.

**Ratio of $\text{HCO}_3^-/\text{PaCO}_2$**

- $\text{HCO}_3^-$ is 24 mEq/L
- $\text{PaCO}_2$ is 40 mm Hg
- Ratio = $\frac{24 	ext{ mEq/L}}{1.2 	ext{ mEq/L}}$ (40 mm Hg x 0.03)

- Ratio = 20 AT A NORMAL pH.

  - A high ratio, indicates the pH is alkaline
    - $\text{HCO}_3^-/\text{PaCO}_2$ is 30:1 $\Rightarrow$ Alkalosis
  - A low ratio, indicates the pH is acidic
    - $\text{HCO}_3^-/\text{PaCO}_2$ is 10:1 $\Rightarrow$ Acidosis

- Total CO$_2$ = $\text{HCO}_3^- + (\text{PaCO}_2 \times 0.3)$
  - = 24 mEq/L + 1.2 mEq/L
  - = 25.2 mEq/L
The Kidneys and Acid-Base Balance

- 2 major functions in acid-base homeostasis:
  - Fixed Acid Excretion
  - Normal Regulation of Bicarbonate in the blood.

Fixed Acids

- Fixed acids are produced through normal body metabolism (50 to 60 mEq/day).
- They cannot be converted to a gas and excreted through the lungs; they must be excreted in the urine by the kidney.
- Several conditions can result in an abnormal increase in fixed acid production (2,000 mEq/day).
- It is the kidney’s role to excrete these acids and maintain homeostasis.

Metabolism and Fixed Acids

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>FIXED ACIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein catabolism</td>
<td>Sulfuric Acid ($H_2SO_4$)</td>
</tr>
<tr>
<td></td>
<td>Phosphoric Acid ($H_3PO_4$)</td>
</tr>
<tr>
<td>Incomplete lipid metabolism</td>
<td>Ketoacids: Acetoacetic acid and Beta-Hydroxybutyric acid</td>
</tr>
<tr>
<td>Carbohydrate metabolism (anaerobic)</td>
<td>Lactic acid</td>
</tr>
</tbody>
</table>

Excretion of Fixed Acids

- With normal production of fixed acids small, homeostasis normally is not a problem.
- When fixed acid levels are elevated, especially acutely, the kidneys may become overwhelmed and result in a metabolic acidosis.
- The kidneys can excrete or create bicarbonate ions as needed.
- More on this later!

Buffer Systems

- Besides the lungs and kidneys, the buffering of blood is the third major way homeostasis is maintained.
- Every acid has a related base that will be present with dissociation of the $H^+$ ion.
  - Together they are called a conjugate pair.
  - $HCl \rightarrow H^+ + Cl^-$
- Different acids have different degrees of dissociation. (Strong acids have a strong degree of dissociation [lots of $H^+$ free in solution]. Weak acids are weak!)
  - Note size of arrows.

Buffer Solution

- Solution where the pH tends to be stable.
- When an acid or base is added to a buffer solution, the pH changes, but not as significantly as if the buffered solution was not present.
- Buffer solutions accomplish this by converting strong acids to weak acids (and strong bases to weak bases).
- Buffer solutions are composed of a weak acid and the salt of its conjugate base.
Buffer Solution Example

- Weak acid: Carbonic acid ($H_2CO_3$)
- Conjugate base of carbonic acid is the bicarbonate ion ($HCO_3^-$).
- The salt of the conjugate base (bicarbonate ion) is NaHCO₃.
- When a strong acid is added to the buffer solution, the strong acid is converted to a weak acid and a salt.
- $HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$

Blood Buffers

- Multiple buffer system in the blood.
  - Extracellular Fluid Buffers
    - Plasma Bicarbonate
    - Plasma Proteins (albumin, globulin)
    - Inorganic Phosphates
  - Intracellular Fluid Buffers
    - Bicarbonate
    - Hemoglobin
    - Oxyhemoglobin
    - Inorganic Phosphates
    - Organic Phosphates

Buffer Effectiveness

- The effectiveness of a buffer system depends on:
  - The quantity of buffer available.
    - Hemoglobin is abundant in intracellular fluid.
  - pK of the buffer system
    - Buffers function best within 1 pH unit of their pK.
    - Bicarbonate (pK of 6.1) works well between 5.1 and 7.1.
  - Open vs. Closed Systems
    - Buffer systems less effective in closed system.
      - Open: Bicarbonate-Carbonic Acid due to lungs.
      - Closed: Hemoglobin intracellularly.

Henderson-Hasselbalch

- Henderson’s Equation rearranged the formula for finding the dissociation constant for the hydrogen ion concentration.
- Hasselbalch modified Henderson’s equation by using the negative logarithm of the hydrogen ion concentration and the ratio of bicarbonate ions to carbonic acid.
  - $p$ is the negative logarithm.
  - $pH = pK + \log ([HCO_3^-]/[H_2CO_3])$
  - $pH = 6.1 + \log (24/1.2)$
  - $pH = 6.1 + \log (20)$
  - $pH = 6.1 + \log (20)$
  - $pH = 7.4$
- We can simplify Henderson-Hasselbalch to
  - $pH = (HCO_3^-)/Paco_2$
  - $pH = \text{Kidney/Lung}$

Given a fixed alveolar ventilation of 4 L/min, calculate the $PaCO_2$ when the $CO_2$ production is 300 mL/min.
Given a $V_t$ of 400 mL, physiologic $V_d$ of 200 mL and a $f$ of 16/min, calculate the alveolar minute ventilation ($\dot{V}_A$).

A patient with respiratory acidosis on mechanical ventilatory support is 6'2" and weighs 190 lbs. The Exhaled $V_t$ is 400 mL, and the $f$ is 10/min. The patient is on controlled volume ventilation. The $\text{PaCO}_2$ is 60 mm Hg, pH 7.33. The patient's desired $\text{PaCO}_2$ is 40 mm Hg. What ventilator change must be made to decrease the $\text{PaCO}_2$? The doctor asks you to increase the $V_t$ to correct the $\text{PaCO}_2$ to 40 mm Hg.

A patient has a pH of 7.66, $\text{PaCO}_2$ 20 mm Hg, $\text{HCO}_3^-$ 22 mEq/L, $\text{PaO}_2$ 89 mm Hg on $\text{FlO}_2$ of 40% is being ventilated in the control mode with no spontaneous breaths and a $V_t$ of 700 mL, $f$ of 18/min. The doctor asks you to correct the pH and $\text{PaCO}_2$.

You are ventilating a patient in A/C mode with a $V_t$ of 600 mL, $f$ 12/min, $\text{FlO}_2$ 50%, Peak flowrate 60 L/min. The $\text{PaCO}_2$ is 60 mm Hg, $\text{HCO}_3^-$ 35, pH 7.39, $\text{PaO}_2$ 88 mm Hg. What ventilator change would you recommend?

A woman who is 5'2" is on controlled ventilation. She has a $\text{PaCO}_2$ of 58 mm Hg; pH is 7.28, $V_t$ 625 mL, and a $f$ of 7/min. Plateau pressure is measured as 30 cm H$_2$O. How can a desired $\text{PaCO}_2$ of 40 mm Hg be achieved? (IBW is 52 kg)

You are ventilating a patient on the Servo with a minute ventilation of 12 L/min. ABGs show $\text{PaCO}_2$ 24, $\text{HCO}_3^-$ 18, pH 7.50. How would you change the ventilator (change only the $\text{PaCO}_2$) to restore a normal pH?
You are called to the Emergency Department to care for a closed head injured patient who is being intubated. He is placed on mechanical ventilation with the following settings: 

- Vt: 600 mL
- Mode: A/C
- f: 12/min
- FIO₂: .60
- PEEP: 5 cm H₂O

An arterial blood gas shows the following results:

- pH: 7.38
- PaCO₂: 42 torr
- PaO₂: 80 torr
- HCO₃⁻: 24 mEq/L

ICP is elevated and the physician wishes to hyperventilate the patient to a PaCO₂ of 30 torr to decrease the ICP. What changes would you make to accomplish this goal?

You are ventilating a patient on the Servo ventilator with a minute ventilation of 10 L/min. The pH is 7.26, PaCO₂ 70 mm Hg, HCO₃⁻ 30 mEq/L, PaO₂ 62 mm Hg. The doctor asks you to correct the pH. What is the desired level of PaCO₂? How would you change the ventilator settings to correct to the new PaCO₂ level?