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

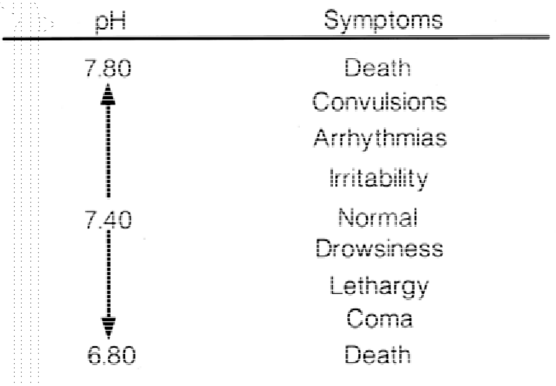
- Define buffer system.
- List the primary extracellular and intracellular fluid buffers.
- State the Henderson-Hasselbalch equation.
- Describe how the Henderson-Hasselbalch equation can be used clinically to classify acid-base disorders.

Acid-Base and the Web

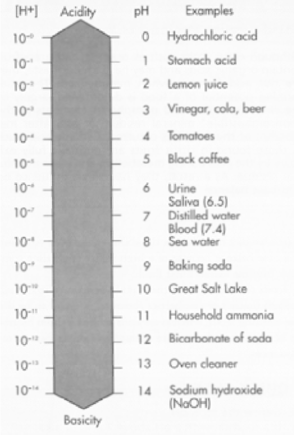
- ABG Random Generator
- ..\pH Tool - RANDOM GENERATOR.xls

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



pH	Symptoms
7.80	Death
↑	Convulsions
	Arrhythmias
	Irritability
7.40	Normal
	Drowsiness
	Lethargy
↓	Coma
6.80	Death

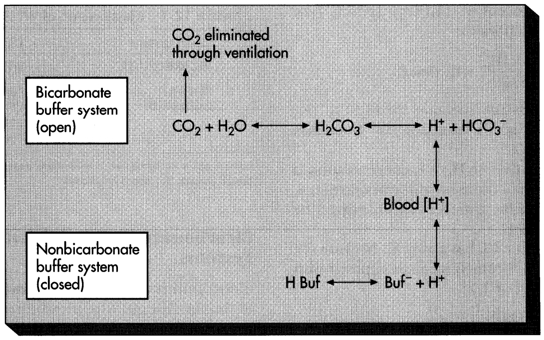


Acid Base Balance

- 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).



CO_2 eliminated through ventilation

Bicarbonate buffer system (open)

$CO_2 + H_2O \longleftrightarrow H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$

Blood $[H^+]$

Nonbicarbonate buffer system (closed)

$H\,Buf \longleftrightarrow Buf^- + H^+$

Lung Regulation of Volatile Acids

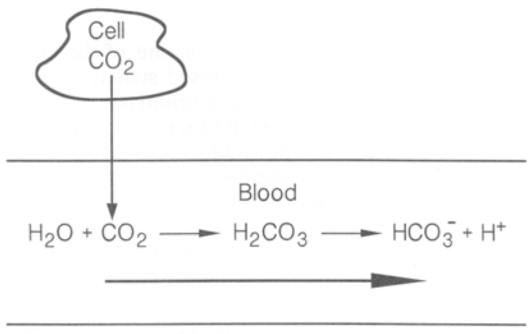
- Excretion must be done in proportion to production or homeostasis cannot be maintained.
- $CO_2 + H_2O = H_2CO_3 = HCO_3^- + H^+$
  - This reaction takes place in a closed system.
  - This reaction is in equilibrium.
  - Therefore, blood CO_2 can be used as a marker of Carbonic Acid levels.

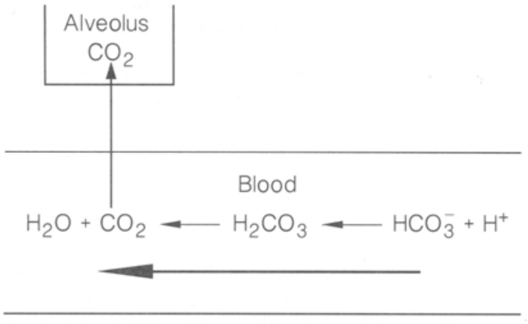
Plasma Bicarbonate and Buffering for Respiratory Acidosis

- Hydrolysis Effect: Some rise in HCO_3^- will occur because of excess Pa_{CO_2} in the system.
  - A 10 mmHg ↑ in Pa_{CO_2} will yield a 1 mEq/L ↑ in plasma $[HCO_3^-]$.
  - A 5 mmHg ↓ in Pa_{CO_2} will yield a 1 mEq/L ↓ 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.





Carbon Dioxide Homeostasis

- Instantaneous P_{aCO_2} depends on the quantity of carbon dioxide entering the system ($\bar{c}$ CO_2) and the quantity of carbon dioxide leaving the system through the lungs.
  - $\bar{c}$ CO_2 is dependent on the metabolic rate and the substrate being metabolized.
  - Carbon Dioxide excretion is dependent on alveolar minute ventilation.

Regulation of P_{aCO_2}

$$\mathbf{PaCO_2} = \frac{\mathbf{CO_2\ Production\left(\dot{V}CO_2\right) \times .863}}{\boldsymbol{\mathit{Alveolar}}\ \mathbf{Ventilation\ (\dot{V}_A)}}$$

Relationship between $PaCO_2$ and V_A is inverse.

$$\mathbf{\dot{V}_A = (V_t - V_d) \times f}$$

$$\dot{V}_A = \dot{V}_E - \dot{V}_D$$

$$\dot{V}_E = V_t \times f$$

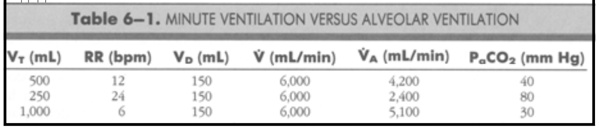


Table 6–1. MINUTE VENTILATION VERSUS ALVEOLAR VENTILATION

V_T (mL)	RR (bpm)	V_D (mL)	$\dot{V}$ (mL/min)	$\dot{V}_A$ (mL/min)	P_aCO_2 (mm Hg)
500	12	150	6,000	4,200	40
250	24	150	6,000	2,400	80
1,000	6	150	6,000	5,100	30

What causes a rise in P_{aCO_2}?

- Inadequate Ventilation
  - CNS depression
  - Respiratory muscle weakness or paralysis.
- Increased Deadspace

$$\mathbf{\dot{V}_A = (V_t - V_d) \times f}$$

- Increased CO_2 production
- Combination of all of them

Increased Deadspace

- Widening of CO_2 gradient
  - Pa_{CO_2} - P_{ETCO_2}
- High $\bar{C}_E$ with normal or high Pa_{CO_2} levels
- Treatment
  - Treat the underlying cause
  - Tracheostomy

Increases in CO_2 Production

- Metabolism of carbohydrates, fats & proteins determine CO_2 levels
  - ↑ carbohydrates, ↑ CO_2 production
- Body temperature
  - ↑ temperature, ↑ metabolism
- Exercise, TPN therapy, sepsis
- Burns
- Seizures

Pa_{CO_2} Relationship to other ABG Parameters

- ↑ Pa_{CO_2} will result in a ↓ P_{AO_2} & Pa_{O_2} unless the patient is receiving supplemental O_2
- ↑ Pa_{CO_2} will ↓ pH in an acute situation
  - Henderson Hasselbalch Equation
  - $\text{pH} = \dfrac{HCO_3}{Pa_{CO_2}}$

CO_2 Transport

- 200 mL of CO_2 is produced each minute by the tissues.
- Carbon Dioxide is transported by six different mechanisms
  - Three in the plasma
  - Three in the RBC

CO_2 Transport in the Plasma

- 1% forms Carbamino Compounds
  - CO_2 combined with protein
- 5% of CO_2 reacts with H_2O & forms HCO_3
- 5% **dissolves** in the plasma
  - This is measured by the **Pa_{CO_2}**.
  - To change CO_2 from partial pressure to mEq/L multiple by 0.03.
    40 mm Hg x 0.03 = 1.2 mEq/L.

CO_2 Transport in the RBC

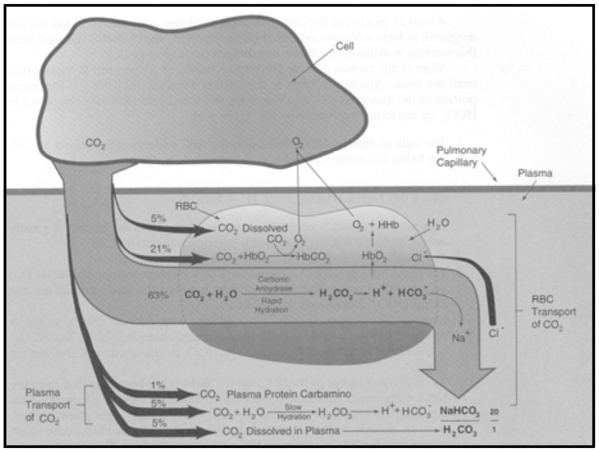
- 5% of CO_2 dissolves in the intracellular fluid
- 21% of CO_2 combines with Hb to from carbamino Hb
- 63% of CO_2 reacts with H_2O to from H_2CO_3
  - H_2CO_3 is a volatile acid.
  - This reaction is accelerated by an enzyme carbonic anhydrase.

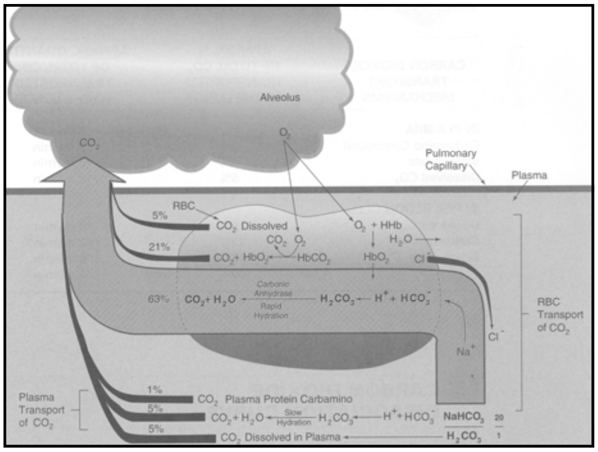
Chloride Shift

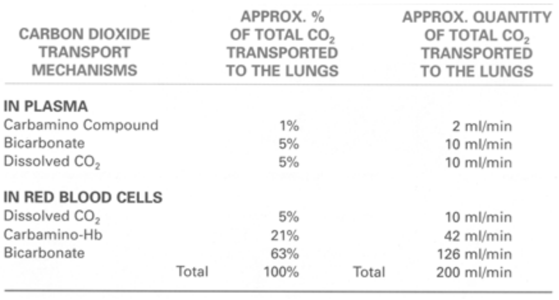
- The presence of carbonic anhydrase speeds up the hydrolysis reaction (conversion of carbon dioxide and water into carbonic acid).
- The dissociation of carbonic acid into hydrogen ions and bicarbonate ions results in a large excess of hydrogen ions, which are buffered by the desaturated hemoglobin, 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.







CARBON DIOXIDE TRANSPORT MECHANISMS		APPROX. % OF TOTAL CO_2 TRANSPORTED TO THE LUNGS		APPROX. QUANTITY OF TOTAL CO_2 TRANSPORTED TO THE LUNGS
IN PLASMA				
Carbamino Compound		1%		2 ml/min
Bicarbonate		5%		10 ml/min
Dissolved CO_2		5%		10 ml/min
IN RED BLOOD CELLS				
Dissolved CO_2		5%		10 ml/min
Carbamino-Hb		21%		42 ml/min
Bicarbonate		63%		126 ml/min
	Total	100%	Total	200 ml/min

Ratio of $HCO_3^-/PaCO_2$

- HCO_3^- is 24 mEq/L
- $PaCO_2$ is 40 mm Hg
- Ratio = 24 mEq/L
  1.2 mEq/L (40 mm Hg x 0.03)
- Ratio = 20 AT A NORMAL pH.
  1
  - A high ratio, indicates the pH is alkaline
    - $HCO_3/PaCO_2$ is 30:1 → Alkalosis
  - A low ratio, indicates the pH is acidic
    - $HCO_3/PaCO_2$ is 10:1 → Acidosis
- Total CO_2 = HCO_3^- + ($PaCO_2$ x .03)
  = 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

SUBSTANCE	**FIXED ACIDS**
Protein catabolism	Sulfuric Acid (H_2SO_4) Phosphoric Acid (H_3PO_4)
Incomplete lipid metabolism	Ketoacids: Acetoacetic acid and Beta-Hydroxybutyric acid
Carbohydrate metabolism (anaerobic)	Lactic acid

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.
    - $HCl \rightleftharpoons H^+ + Cl^-$
- 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

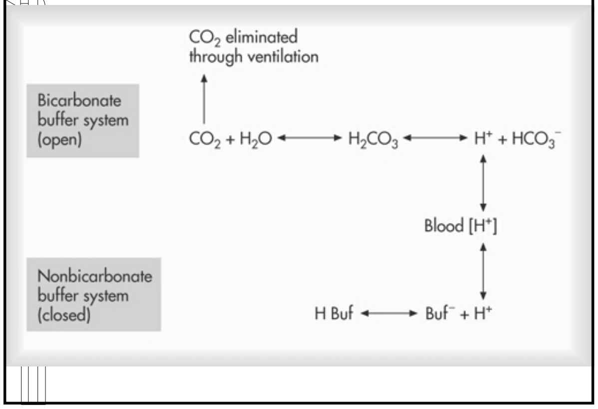
- Weak acid: Carbonic acid (H_2CO_3)
- Conjugate base of carbonic acid is the bicarbonate ion (HCO_3^-).
- The salt of the conjugate base (bicarbonate ion) is $NaHCO_3$.
- When a strong acid is added to the buffer solution, the strong acid is converted to a weak acid and a salt.
- $HCl + NaHCO_3 \rightarrow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

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.
  - $pH = pK + \log ([HCO_3^-]/[H_2CO_3])$
  - $pH = 6.1 + \log (24/1.2)$
  - $pH = 6.1 + \log (20)$
  - $pH = 6.1 + 1.3010299956639811952137388947245$
  - $pH = 7.4$
- We can simplify Henderson-Hasselbalch to
  - $pH \approx [HCO_3^-]/Pa_{CO_2}$
  - pH ≈ Kidney/Lung

Given a fixed alveolar ventilation of 4 L/min, calculate the Pa_{CO_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 ($\dot{V}_A$).

You are ventilating a patient in A/C mode with a V_t of 600 mL, f 12/min, F_{IO_2} 50%, Peak flowrate 60 L/min. The P_{aCO_2} is 60 mm Hg, HCO_3^- 35, pH 7.39, P_{aO_2} 88 mm Hg. What ventilator change would you recommend?

A. Increase the Vt to 800 mL
B. Increase the f to 16/min
C. Decrease the f to 8/min
D. Increase the FIO2 to 60%
E. Maintain current settings

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 P_{aCO_2} is 60 mm Hg, pH 7.33. The patient’s desired P_{aCO_2} is 40 mm Hg. What ventilator change must be made to decrease the P_{aCO_2}? The doctor asks you to increase the V_t to correct the P_{aCO_2} to 40 mm Hg.

A woman who is 5’2” is on controlled ventilation. She has a P_{aCO_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_2O. How can a desired P_{aCO_2} of 40 mm Hg be achieved? (IBW is 52 kg)

A patient has a pH of 7.66, P_{aCO_2} 20 mm Hg, HCO_3^- 22 mEq/L, P_{aO_2} 89 mm Hg on F_{IO_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 P_{aCO_2}.

You are ventilating a patient on the Servo with a minute ventilation of 12 L/min. ABGs show P_{aCO_2} 24, HCO_3^- 18, pH 7.50. How would you change the ventilator (change only the P_{aCO_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:
V_t: 600 mL, Mode: A/C, f: 12/min, F_{IO_2}: .60,
PEEP: 5 cm H_2O.

An arterial blood gas shows the following results: pH: 7.38, P_{aCO_2}: 42 torr, P_{aO_2}: 80 torr, and HCO_3^-: 24 mEq/L. ICP is elevated and the physician wishes to hyperventilate the patient to a P_{aCO_2} 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, P_{aCO_2} 70 mm Hg, HCO_3^- 30 mEq/L, P_{aO_2} 62 mm Hg. The doctor asks you to correct the pH. What is the desired level of P_{aCO_2}? How would you change the ventilator settings to correct to the new P_{aCO_2} level?