Module H:
Carbon Dioxide Transport

Beachey – Ch 9 & 10

Egan – pp. 244-246, 281-284

Carbon Dioxide Transport

At the end of today's session you will be able to :

- Describe the relationship free hydrogen ions have with hemoglobin inside the RBC.
- Describe the Chloride Shift.
- State the ratio of Bicarbonate ions to Carbonic Acid at a normal pH range.
- Describe how carbon dioxide is eliminated from the body.
- Define the Haldane effect.
- Define key terms associated with acid-base balance.
- List one buffer system present in the plasma.

Carbon Dioxide

- Normal byproduct of metabolism.
- Normal Oxygen Consumption ($\bar{c}\ O_2$) is 250 ml/min.
- Normal Carbon Dioxide Production ($\bar{c}\ CO_2$) is 200 ml/min.
- Note: The ratio of CO_2 production to O_2 consumption is 0.8. This is known as the Respiratory Quotient.
  - 200 ml/min/250 ml/min = 0.8

Carbon Dioxide Transport

- Carbon Dioxide is excreted by the lungs.
- Transport from the tissues to the lungs is required.
- Carbon Dioxide is transported in **<u>SIX</u>** different ways:
  - Three in the Plasma
  - Three in the Erythrocyte

Hydrolysis of Water

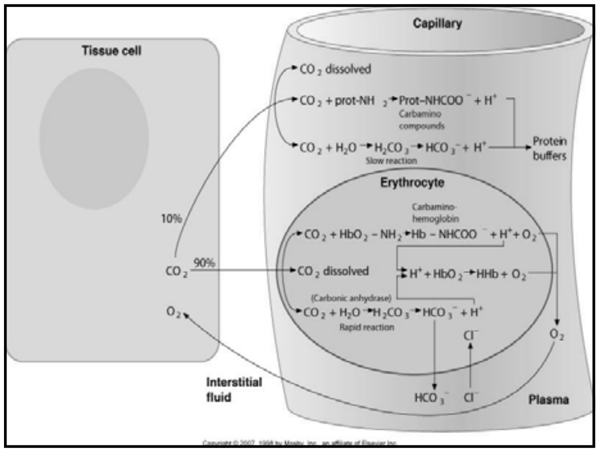
- Carbon Dioxide and water combine in a process called hydrolysis.
- $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
- H_2CO_3 is Carbonic Acid and is a very volatile acid.
- This process is normally very slow but is increased SIGNIFICANTLY in the presence of an enzyme called Carbonic Anhydrase.

Carbon Dioxide Transport - Plasma

- 1% is bound to protein as a Carbamino compound.
- 5% is ionized as plasma bicarbonate (HCO_3^-).
- 5% is dissolved in the plasma and carried as Pa_{CO_2} and $P\dot{v}\ CO_2$.
  - This value is directly proportional to the amount of Carbonic Acid (H_2CO_3) that is formed, and it is in equilibrium. You can convert the Pa_{CO_2} to H_2CO_3 by multiplying the Pa_{CO_2} by 0.03. This will express the Pa_{CO_2} in mEq/L instead of mmHg.

Carbon Dioxide Transport - Erythrocyte

- 5% is dissolved in the intracellular fluid and carried as Pa_{CO_2}.
- 21% is bound to a specific protein: Hemoglobin. It is then carried as a Carbamino-Hb.
- 63% is ionized as plasma bicarbonate (HCO_3^-). This reaction is catalyzed by Carbonic Anhydrase, which is present in great quantities in the erythrocyte, but **<u>not</u>** in the plasma.



Carbon Dioxide Transport – H^+

- Hydrolysis effect
  - $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
    - Free H^+ ions are proton donors and substances that have free H^+ ions to donate are **acids**.
    - Substances that can accept H^+ ions are **bases**.
    - These ions are buffered by reduced (neutralized) by hemoglobin present in the erythrocyte.
    - Free HCO_3^- ions diffuse out into the plasma.
    - These ions combine with Sodium (Na^+) ions to form Sodium Bicarbonate ($NaHCO_3$) and are transported in this form back to the lungs.

Chloride Shift

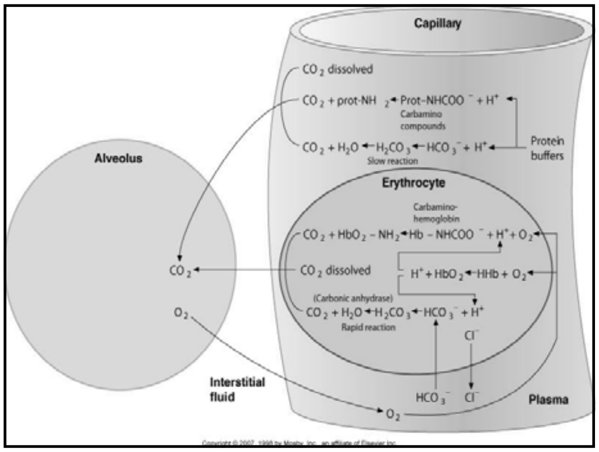
- As Bicarbonate ions move out of the erythrocyte and electrical imbalance exists.
- To maintain electrical neutrality either:
  - A negative ion has to move in to the cell OR
  - A positive ion has to move out with the bicarbonate ion.
- A chloride ion that was freed from its recent union with sodium (NaCl) moves into the cell.
- Known as the Chloride Shift or the Hamburger Phenomenon.

Ratio of HCO_3^- to H_2CO_3

- The ratio of bicarbonate (HCO_3^-) to Carbonic Acid (H_2CO_3) is maintained at a relatively constant level.
- The relationship between the two is at a ratio of **20:1**.
- This ratio keeps the pH in the normal range of **7.35 to 7.45**.
- As the ratio increases, the pH rises and we say the blood becomes more **alkaline**. As the ratio falls, the pH falls, and we say the blood becomes more **acidic.**

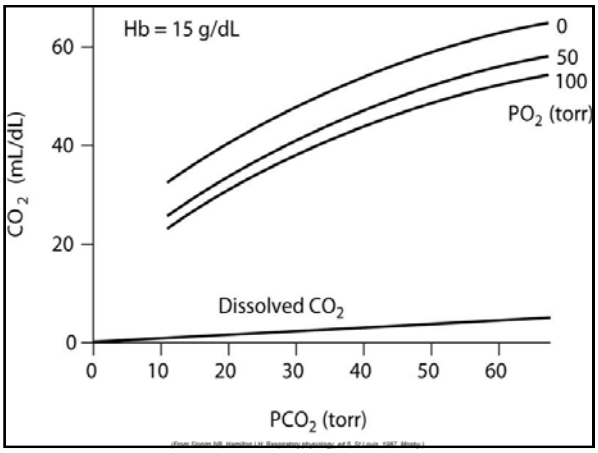
Carbon Dioxide Elimination

- The process of carbon dioxide transport is <u>reversed</u> at the lung.
  - CO_2 is released from the hemoglobin in the erythrocyte.
  - CO_2 is released from protein in the plasma.
  - HCO_3^- is converted back to CO_2 in the plasma.
  - HCO_3^- is transported back into the erythrocyte (Chloride Shift) and is converted back to CO_2 in the presence of Carbonic Anhydrase.
  - The freed sodium ions join back up with chloride ions that have moved out into the plasma.



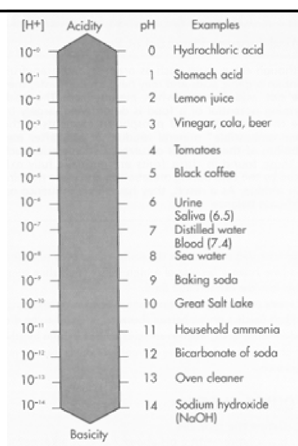
Carbon Dioxide Dissociation Curve

- The relationship between the amount of dissolved carbon dioxide (PCO_2) and the total amount of carbon dioxide carried can be expressed graphically.
  - The result is almost linear.
  - Small changes in PCO_2 between arterial and venous blood.
  - The level of oxygen affects the amount of carbon dioxide that will be transported.
  - This effect is known as the Haldane Effect.



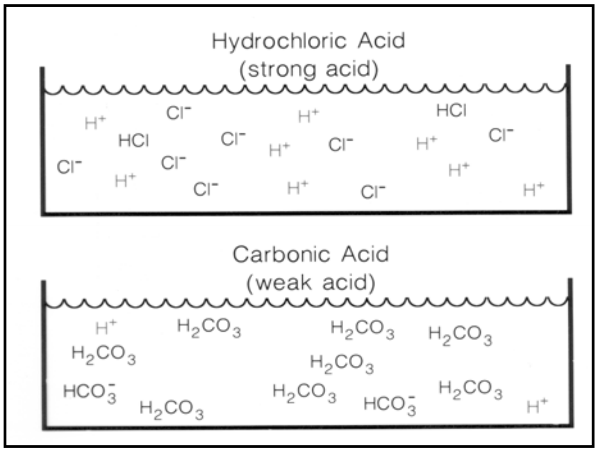
Acid-Base Balance

- Definitions
  - **Electrolyte**: Charged ions that can conduct a current in solution. Example: Na^+, K^+, Cl^-, HCO_3^-
  - **Buffer**: A substance capable of neutralizing both acids and bases without causing an appreciable change in the original pH.
  - **Strong Acid**: An acid that dissociates completely into hydrogen ions and an anion.
  - **Weak Acid**: An acid that dissociates only partially into ions.
  - **Strong Base**: An base that dissociates completely.
  - **Weak Base**: An base that dissociates only partially into Hydroxyl (OH^-) ions.



Dissociation Constants

- At equilibrium, a strong acid (or base) will almost completely dissociate. Conversely, a weak acid will not dissociate as completely and will remain (at least partially) as both the acid and the respective ions.
- The dissociation constant express the degree to which dissociation occurs. A higher number is reflective of greater dissociation.
- The dissociation constant is depicted by K_A.



pH

- The amount of free hydrogen ions present affects metabolic activity and is kept at a relatively constant level through blood buffers.
- Because the actual amount of hydrogen ions are so small (10^{-7} mol/L), the amount of hydrogen ions are expressed on a logarithmic scale.
- The pH scale represents the “negative logarithm of the hydrogen ion concentration”.
  - The negative represents an inverse relationship between pH and $[H^+]$.
    - As the concentration of $[H^+]$ increases, the pH falls.

Control of pH

- pH is normally 7.35 – 7.45 in arterial blood.
- It is maintained at that level by three methods:
  - Blood and tissue buffers
  - The respiratory system’s ability to regulate the elimination of carbon dioxide by altering ventilation.
  - The renal systems ability to regulate the excretion of hydrogen and the reabsorption of bicarbonate ions.

Buffer Systems

- Definition: A buffer system prevents large changes in pH in an acid-base mixture.
- Plasma Buffers
  - Carbonic Acid/Sodium Bicarbonate
  - Sodium Phosphate
  - Plasma Proteins
- Erythrocyte
  - Hemoglobin

Henderson-Hasselbalch Equation

- The Henderson-Hasselbalch equation relates the pH of a system to the concentrations of bicarbonate ions and carbonic acid.
  - $pH = pK + \log ([HCO_3]/[H_2CO_3])$
  - $pH = 6.1 + \log (24/1.2)$
  - $pH = 6.1 + \log (20)$
  - $pH = 6.1 + 1.3010299956639811952137388947245$
  - $pH = 7.4$
- We can simplify Henderson-Hasselbalch to
  - $pH \approx [HCO_3]/Paco_2$
  - pH ≈ Kidney/Lung

Acid-Base Normal Values

- Arterial
  - pH: 7.35 – 7.45
    - Greater than 7.45: Alkaline (Alkalosis is condition)
    - Less than 7.35: Acid (Acidosis is condition)
  - $Paco_2$: 35 – 45 mm Hg
    - Greater than 45 mm Hg: Hypercapnia, Hypoventilation
    - Less than 35 mm Hg: Hypocapnia, Hyperventilation
  - Pao_2: 80 – 100 mm Hg
    - Rough estimate: 110 – Age/2
    - Greater than 100 mm Hg: Hyperoxemia
    - Hypoxemia is staged
      - 60 to 80 mm Hg: Mild
      - 40 to 60 mm Hg: Moderate
      - Less than 40: Severe
  - Sao_2: 97%
  - HCO_3^-: 22 – 26 mEq/L

Acid-Base Balance

- pH is determined by the ratio of $[HCO_3^-]/[H_2CO_3]$
  - As the ratio increases – Alkalosis is present.
    - Can be caused by an INCREASE in $[HCO_3^-]$ OR
    - Can be caused by a DECREASE in $[H_2CO_3]$ (Pa_{CO_2}).
  - As the ratio decreases – Acidosis is present.
    - Can be caused by an DECREASE in $[HCO_3^-]$ OR
    - Can be caused by a INCREASE in $[H_2CO_3]$ (Pa_{CO_2}).

STEP ONE

- **DETERMINE ACID-BASE STATUS**
  - If pH is below 7.35 – An Acidosis is present
  - If pH is above 7.45 – An Alkalosis is present

  LET'S TRY A FEW!!!

STEP TWO

- **DETERMINE SOURCE OF ACID-BASE DISTURBANCE**

Acid-Base Disturbances

- Four primary disturbances exist:
  - Two primary Respiratory disturbances.
    - Respiratory Acidosis
    - Respiratory Alkalosis
  - Two primary Non-Respiratory or Metabolic disturbances.
    - Metabolic Acidosis
    - Metabolic Alkalosis
  - The possibility of a combined or Mixed acidosis or alkalosis can exist.

Respiratory Acidosis

- Increased PA_{CO_2} (CO_2 is not eliminated). Hypoventilation is present.
- Causes include
  - Central Nervous System Depression: Barbiturate overdose, Head Trauma, CVA
  - Neuromuscular Disease: MG, GB, Polio, MD
  - Muscle fatigue secondary to increased resistance: Asthma, COPD, Airway obstruction
  - Muscle fatigue secondary to reduced compliance: Pneumothorax, ARDS, Pleural effusion, Pneumonia
- Compensation
  - Metabolic Alkalosis – Kidney retains HCO_3^- ions. Takes time.
- Treatment
  - Institute mechanical ventilation

Example: Respiratory Acidosis

- pH: 7.10 ⇓
- Pa_{CO_2}: 80 mm Hg ⇑
- HCO_3^-: 24 mEq/L ⇔

STEP THREE

- **DETERMINE IF COMPENSATORY MECHANISM IS PRESENT**
  - **Compensation can be "Partial" or "Full"**
  - **Over-compensation is rare.**

Respiratory Acidosis - Compensation

- The compensatory mechanism is to have the kidney retain HCO_3^- ions. This takes time.
- If the HCO_3^- level has changed from the normal range of 24 $\pm$ 2 mEq/L, we say there is **Compensation** present.
  - If the pH has returned to a normal level (7.35 – 7.45) we say there is **Full Compensation**.
  - If the pH has not returned to a normal level, but the HCO_3^- is outside the normal range, we say there is **Partial Compensation**.

Compensated Respiratory Acidosis

- pH: 7.20 ⇓
- Pa_{CO_2}: 80 mm Hg ⇑
- HCO_3^-: 30 mEq/L ⇑

PARTIALLY COMPENSATED RESPIRATORY ACIDOSIS

- pH: 7.38 ⇔
- Pa_{CO_2}: 80 mm Hg ⇑
- HCO_3^-: 46 mEq/L ⇑

FULLY COMPENSATED RESPIRATORY ACIDOSIS

Respiratory Alkalosis

- Decreased P_{ACO_2} (CO_2 is excessively eliminated). Hyperventilation is present.
- Causes include
  - Pain
  - Anxiety
  - CNS Dysfunction
  - Compensation for hypoxemia or hypoxia.
- Compensation
  - Metabolic Acidosis – Kidney excretes HCO_3^- ions. Takes time.
- Treatment
  - Find Cause and correct it!

Example: Respiratory Alkalosis

- pH: 7.60 ⇑
- Pa_{CO_2}: 25 mm Hg ⇓
- HCO_3^-: 24 mEq/L ⇔

Respiratory Alkalosis - Compensation

- The compensatory mechanism is to have the kidney dump HCO_3^- ions. This, again, takes time.
- If the HCO_3^- level has changed from the normal range of 24 $\pm$ 2 mEq/L, we say there is **Compensation** present.
  - If the pH has returned to a normal level (7.35 – 7.45) we say there is **Full Compensation**.
  - If the pH has not returned to a normal level, but the HCO_3^- is outside the normal range, we say there is **Partial Compensation**.

Compensated Respiratory Alkalosis

- pH: 7.52 ⇑
- Pa_{CO_2}: 25 mm Hg ⇓
- HCO_3^-: 20 mEq/L ⇓

PARTIALLY COMPENSATED RESPIRATORY ALKALOSIS

- pH: 7.43 ⇔
- Pa_{CO_2}: 25 mm Hg ⇓
- HCO_3^-: 16 mEq/L ⇓

FULLY COMPENSATED RESPIRATORY ALKALOSIS

Steps in ABG Classification

- Determine Acid-Base Status
- Determine Cause of Acid-Base Disturbance
- Determine Degree of Compensation

Metabolic Acidosis

- Decreased level of HCO_3^- with a reduced pH.
- Causes include
  - Lactic Acidosis secondary to anaerobic metabolism
  - Ketoacidosis – Diabetic Ketoacidosis (DKA)
    - Kussmaul's breathing
  - Salicylate overdose
  - Renal Failure
- Compensation
  - Respiratory Alkalosis – Hyperventilation (e.g. Kussmaul's breathing)
- Treatment
  - Find Cause and correct it! Sodium Bicarbonate can help in the short term.

Example: Metabolic Acidosis

- pH: 7.30 ⇓
- Pa_{CO_2}: 25 mm Hg ⇓
- HCO_3^-: 12 mEq/L ⇓

Metabolic Acidosis - Compensation

- The compensatory mechanism is to increase ventilation (hyperventilate).
- If the Pa_{CO_2} level has changed from the normal range of 35 – 45 mm Hg, we say there is **Compensation** present.
  - If the pH has returned to a normal level (35 – 45) we say there is **Full Compensation**.
  - If the pH has not returned to a normal level, but the Pa_{CO_2} is outside the normal range, we say there is **Partial Compensation**.

Compensated Metabolic Acidosis

- pH: 7.26 ⇓
- Pa_{CO_2}: 32 mm Hg ⇓
- HCO_3^-: 14 mEq/L ⇓

PARTIALLY COMPENSATED METABOLIC ACIDOSIS

- pH: 7.39 ⇔
- Pa_{CO_2}: 24 mm Hg ⇓
- HCO_3^-: 14 mEq/L ⇓

FULLY COMPENSATED METABOLIC ACIDOSIS

Metabolic Alkalosis

- Increased level of HCO_3^- with a increased pH.
- Causes include
  - Loss of Acid: Vomiting
  - Gain of Base: Excessive $NaHCO_3$ use
- Compensation
  - Respiratory Acidosis – Hypoventilation
  - Treatment: Find Cause and correct it!

Example: Metabolic Alkalosis

- pH: 7.52 ⇑
- Pa_{CO_2}: 40 mm Hg ⇔
- HCO_3^-: 32 mEq/L ⇑

Metabolic Alkalosis - Compensation

- The compensatory mechanism is to decrease ventilation (hypoventilate).
- If the Pa_{CO_2} level has changed from the normal range of 35 – 45 mm Hg, we say there is **Compensation** present.
  - If the pH has returned to a normal level (35 – 45) we say there is **Full Compensation**.
  - If the pH has not returned to a normal level, but the Pa_{CO_2} is outside the normal range, we say there is **Partial Compensation**.

Compensated Metabolic Alkalosis

- pH: 7.56 ⇑
- Pa_{CO_2}: 48 mm Hg ⇑
- HCO_3^-: 42 mEq/L ⇑

PARTIALLY COMPENSATED METABOLIC ALKALOSIS

- pH: 7.44 ⇔
- Pa_{CO_2}: 64 mm Hg ⇑
- HCO_3^-: 42 mEq/L ⇑

FULLY COMPENSATED METABOLIC ALKALOSIS

PRACTICE

- Program in Computer Lab
  - CAUTION! The normal value for HCO_3^- is 22 to 28 mEq/L.
- Random Generator on www.macomb-rspt.com
  - May require an adjustment to MS Excel.
- ..\..\RSPT 2350\pH Tool - RANDOM GENERATOR.xls