TOPIC 23: ACID BASE BALANCE
I. Background
A. Why regulate acid-base balance?
   1. Only a narrow pH range is compatible with life
   2. Effects of pH fluctuations
      a) changes in muscle and nerve excitability
         (1) acidosis (too much H⁺) depresses CNS
         (2) alkalosis (too little H⁺) causes overexcitability
      b) change enzyme activities profoundly
   3. influence K⁺ levels (see Topic 22)
B. Acid Chemistry (review)
   1. An acid is a hydrogen containing substance that dissociates in solution to produce
      a) free H⁺
      b) anions (negatively charged ions)
C. Base Chemistry (review)
1. A base is a substance that binds with free H⁺ and removes it from solution
D. pH (review)
   1. pH = log 1/[H⁺]
   2. low pH = high acid
   3. Every unit change in pH = tenfold change in [H⁺] because it is a log scale
E. Buffers (review)
   1. A mixture of several chemical compounds in solution that minimize pH changes when an acid or a base is added or removed from the solution
II. Chemical buffer systems are first line of defense against pH fluctuations
A. Buffers respond within fractions of a second to changes in [H⁺]. Although buffers pick up H⁺ very rapidly, they do not eliminate them from the body, so they are not a solution to long term imbalances.
B. HCO₃⁻ buffer
   1. Very effective buffer & is most important in body for buffering pH changes caused by anything other than CO₂ generated acid (because HCO₃⁻ is produced from CO₂ too)
   2. H⁺ + HCO₃⁻ ↔ H₂CO₃ ↔ CO₂ + H₂O
      a) this is a very important buffering system. The above reaction is almost always catalyzed in the body by carbonic anhydrase; keep that in mind as you read these notes, because I have not explicitly included this enzyme in most of the following discussion.
   3. When H⁺ is added from any source other than CO₂, drives above reaction to right; H⁺ ions are absorbed, and CO₂ is produced.
   4. When H⁺ falls, above reaction is driven to the left, and CO₂ and water combine to produce H⁺ and HCO₃⁻
C. Protein buffers
   1. proteins have both acidic and basic groups that can take up or give up H⁺
   2. Most important in ICF, where most proteins exist
D. Hemoglobin acts as a buffer
1. As CO₂ diffuses into the blood at the capillaries, it dissociates:
   \[ CO₂ + H₂O \leftrightarrow H₂CO₃ \leftrightarrow H^+ + HCO₃^- \]

2. Deoxy-Hb has a great affinity for & binds the free H⁺ at the capillaries; in the lungs, the reaction is reversed and the Hb gives up the H⁺ to bind O₂ instead. The H⁺ then binds with HCO₃⁻ to reform CO₂ and water.

3. Hb very important in buffering the blood.

E. Phosphate buffers
   1. Important buffer in the ICF (secondary to proteins)
   2. Only buffer found in urine
      a) Humans consume excess phosphate which is excreted in urine
      b) The phosphates within the tubular system act as a buffer

III. Pulmonary ventilation is the second line of defense against pH fluctuations.
   A. The respiratory system responds to increases in arterial [H⁺] within a few minutes.
   B. When [H⁺] increases, ventilation rates increase.
   C. Increase in ventilation rates results in more CO₂ than usual being expired
   D. This leads to a decrease in plasma [H⁺] because when you eliminate CO₂, you drive the following reaction to the left and get rid of H⁺:
      \[ CO₂ + H₂O \leftrightarrow H₂CO₃ \leftrightarrow H^+ + HCO₃^- \]
   E. Conversely, when [H⁺] falls, ventilation is reduced, which causes a build up of CO₂, drives the reaction to the right, and causes an increase in [H⁺].
   F. Lungs rid the body fluids of 100 times more H⁺ (derived from carbonic acid) than the kidneys remove from non-carbonic acid sources.
   G. Person can (unless they have a respiratory disease) always alter ventilation rates to change plasma acid-base balance.
   H. Respiratory system usually only returns pH 50% to 75% of normal, because as pH gets closer to normal, the less the ventilation rates are influenced.

IV. Kidneys are third line of defense against pH fluctuations
   A. Slowest but most potent
   B. Can regulate
      1. removal of H⁺ created by any source
         a) All non-carbonic acids must be removed by kidney (lungs can only eliminate carbonic acid)
         b) Carbonic acid also removed by kidneys; very important in cases of respiratory pathologies.
      2. removal of HCO₃⁻
      3. pH almost exactly
   C. Do all this by adjusting 3 substances
      1. H⁺
      2. HCO₃⁻ (bicarbonate)
      3. NH₃ (ammonia)
   D. Mechanism of regulation during acidosis
      1. High secretion of H⁺ into tubules
         a) H⁺ in the tubular system is buffered before it is excreted. First it combines with the filtered HCO₃⁻ in the tubular system to produce water until all HCO₃⁻ is used up. Next the H⁺ combines with filtered phosphate in the tubules and the H₂PO₄⁻ so produced is
excreted in the urine. Once all phosphate buffer in urine used up, NH₃ produced from amino acid glutamine combines with H⁺ & NH₄⁺ is excreted in urine.

2. HCO₃⁻ is reabsorbed into the plasma from the tubules.

E. Mechanisms of regulation during Alkalosis
1. Rate of H⁺ (via CO₂) secretion reduced (note: H⁺ can not be reabsorbed)
2. Rate of HCO₃⁻ filtration increased
   a) plasma levels of HCO₃⁻ higher than normal under alkalosis because not as much H⁺ for HCO₃⁻ to bind

V. Acid-base Imbalances
A. Overview
1. Changes in pH are reflected by changes in the ratio of [HCO₃⁻] to [CO₂]
   a) When the ratio of [HCO₃⁻]/[CO₂] is less than 20/1, acidosis exists
   b) When ratio of [HCO₃⁻]/[CO₂] is greater than 20/1, alkalosis exists
2. The concentration of HCO₃⁻ in the ECF is 600,000 times the concentration of H⁺; hence when CO₂ produces one H⁺ and one HCO₃⁻, this affects the concentration of H⁺ much more than the concentration of HCO₃⁻.

B. Respiratory Acidosis: Hypoventilation
1. Causes
   a) lung disease
   b) depression of respiratory center by drugs or disease, nerve or muscle disorders that reduce respiratory capability, or holding your breath (only a short term event)
2. Results
   a) CO₂ elevated, HCO₃⁻ unchanged
      (1) Each CO₂ produces one H⁺ and one HCO₃⁻, which affects [H⁺] much more than the [HCO₃⁻].
   b) [HCO₃⁻]/[CO₂] drops below 20/1.
3. Compensation
   a) Chemical buffers take up extra H⁺
   b) Lungs can NOT get rid of extra H⁺ since lungs are problem
   c) Kidneys compensate in the long term

C. Respiratory Alkalosis: Hyperventilation
1. Causes
   a) Fever
   b) Anxiety
   c) Aspirin poisoning
   d) Exposure to high altitude
2. Results
   a) Excessive loss of CO₂, so too little H⁺ in ECF
   b) HCO₃⁻ stays the same
   c) [HCO₃⁻]/[CO₂] increases above 20/1
3. Compensation
a) Chemical buffers release H⁺
   (1) This tends to reduce the hyperventilation quickly
b) If alkalosis persists for hours/days, kidneys respond.

D. Metabolic Acidosis
1. Causes
   a) severe diarrhea
      (1) HCO₃⁻ lost from GI tract
   b) diabetes mellitus
      (1) abnormal fat metabolism (in place of glucose) results in production of keto acids
   c) strenuous exercise
      (1) anaerobic metabolism leads to H⁺ production
   d) severe renal failure
2. Results
   a) CO₂ (and hence [H⁺] remain normal)
   b) HCO₃⁻ reduced (either through loss or through buffering non-CO₂ produced acids)
   c) [HCO₃⁻]/[CO₂] drops below 20/1
3. Compensation
   a) buffers take up extra H⁺
   b) lungs blow off additional CO₂
   c) kidneys excrete more H⁺ and conserve more HCO₃⁻
      (1) note: if renal failure is the cause, this can not occur, and complete restoration of acid base balance is not possible

E. Metabolic Alkalosis
1. Causes
   a) vomiting: causes loss of non-carbonic acid H⁺ from GI tract
   b) ingestion of alkaline drugs (e.g., baking soda for upset stomach)
2. Results
   a) Increase in HCO₃⁻
   b) no change in CO₂
   c) [HCO₃⁻]/[CO₂] increases above 20/1
3. Compensation
   a) chemical buffers liberate H⁺
   b) ventilation reduced
   c) after several days, kidneys conserve H⁺ (by secreting less H⁺) and excrete more HCO₃⁻