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 overexcitablilty
    - 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 flucuations

- 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. HCO_3^- buffer
  - 1. Very effective buffer & is most important in body for buffering pH changes caused by anything other than CO_2 generated acid (because HCO_3^- is produced from CO_2 too)
  - 2. $H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_20$
    - 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 CO_2, drives above reaction to right; H^+ ions are absorbed, and CO_2 is produced.
  - 4. When H^+ falls, above reaction is driven to the left, and CO_2 and water combine to produce H^+ and HCO_3^-
- 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 CO_2 diffuses into the blood at the capillaries, it dissociates:
   $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
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 O_2 instead. The H^+ then binds with HCO_3^- to reform CO_2 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 flucuations.
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 CO_2 than usual being expired
D. This leads to a decrease in plasma $[H^+]$ because when you eliminate CO_2, you drive the following reaction to the left and get rid of H^+:
   1. $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
E. Conversely, when $[H^+]$ falls, ventilation is reduced, which causes a build up of CO_2, 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 flucuations
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 HCO_3^-
3. pH almost exactly

C. Do all this by adjusting 3 substances
1. H^+
2. HCO_3^- (bicarbonate)
3. NH_3 (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 HCO_3^- in the tubular system to produce water until all HCO_3^- is used up. Next the H^+ combines with filtered phosphate in the tubules and the $H_2PO_4^-$ so produced is

excreted in the urine. Once all phosphate buffer in urine used up, NH_3 produced from amino acid glutamine combines with H^+& NH_4^+ is excreted in urine

2. HCO_3^- is reabsorbed into the plasma from the tubules.

E. Mechanisms of regulation **during Alkalosis**

1. Rate of H^+ (via CO_2) secretion reduced (note: H^+ can not be reabsorbed)
2. Rate of HCO_3^- filtration increased
    a) plasma levels of HCO_3^- higher than normal under alkalosis because not as much H^+ for HCO_3^- to bind
3. Result: less H^+ in urine, more HCO_3^- in urine, urine becomes alkaline. Continues till acid base balance restored.

V. Acid-base Imbalances

A. Overview

1. Changes in pH are reflected by changes in the ratio of [HCO_3^-] to [CO_2]
    a) When the ratio of [HCO_3^-]/[CO_2] is less than 20/1, acidosis exists
    b) When ratio of [HCO_3^-]/[CO_2] is greater than 20/1, alkalosis exists
2. **The concentration of HCO_3^- in the ECF is 600,000 times the concentration of H^+; hence when CO_2 produces one H^+ and one HCO_3^-, this affects the concentration of H^+ much more than the concentration of HCO_3^-.**

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) CO_2 elevated, HCO_3^- unchanged
        (1) Each CO_2 produces one H^+ and one HCO_3^-, which affects [H^+] much more than the [HCO_3^-].
    b) [HCO_3^-]/[CO_2] 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 CO_2, so too little H^+ in ECF
    b) HCO_3^- stays the same
    c) [HCO_3^-]/[CO_2] 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) HCO_3^- 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) CO_2 (and hence [H^+] remain normal)
b) HCO_3^- reduced (either through loss or through buffering non-CO_2 produced acids)
c) $[HCO_3^-]/[CO_2]$ drops below 20/1
3. Compensation
a) buffers take up extra H^+
b) lungs blow off additional CO_2
c) kidneys excrete more H^+ and conserve more HCO_3^-
(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 HCO_3^-
b) no change in CO_2
c) $[HCO_3^-]/[CO_2]$ 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 HCO_3^-