Regulation of Acid Base Balance

- Normal serum pH is 7.35-7.45
- Seriously bad things start happening when pH falls to 7.2 or rises to 7.55
- Three physiologic systems act interdependently to maintain a normal serum pH
  - Chemical buffering of excess acid or base by buffer systems in blood plasma and cells
  - Excretion of acid by lungs
  - Excretion of acid or regeneration of base by the kidneys
- Important blood buffers = proteins such as hemoglobin in RBCs and albumin in the plasma
- Important intracellular buffers = negatively charged ions such as phosphate and carbonate
- The status of the bicarbonate buffer is representative of acid-base homeostasis within the body as a whole
- Lungs and kidneys eliminate acid/base...buffers do not eliminate!

Regulation of Volatile Acids by the Lungs

- Volatile acids are those that can be converted to gases (like CO2)
- Recall the hydrolysis reaction we went over in respiratory physiology:
  - In the tissues, the addition of CO2 to the blood drives hydrolysis to the RIGHT forming H+ and HCO3-.
    - The H+ is buffered by hemoglobin
    - The HCO3- diffuses into plasma
    - Chloride moves in to maintain electroneutrality (the chloride shift)
  - In the lungs, CO2 diffuses into alveoli and is exhaled.
    - This drives hydrolysis reaction in reverse
    - In a reversal of the chloride shift, HCO3- reenters the RBCs, and chloride exits. HCO3- combines with H+ (which has been released from its buffers), regenerating CO2 and H2O. Isn’t this exciting?

Regulation of Fixed Acids and Bicarbonate by the Kidneys

- Acids that cannot be converted to gases must be eliminated by the kidneys (fixed acids)
  - Sulfuric, phosphoric and other acids produced by protein metabolism
  - Ketones produced by lipid metabolism and in diabetic ketoacidosis
  - Lactic acid produced by CHO metabolism and in conditions which cause the accumulation of increased metabolic rates and accelerated anaerobic glycolysis (such as in shock and hypoxemia)
  - Occasionally things like ingested toxins (salicylate, drugs and methanol)
- The kidneys regulate serum pH by secreting H+ into urine and be regenerating HCO3- for reabsorption into blood.
- Three buffer systems in the renal tubules:
  - Bicarbonate buffer: for every molecule of H+ secreted, a molecule of HCO3- is returned to the blood to restore components of the plasma bicarbonate buffer system
  - Ammonia buffer: NH3 diffuses into tubular lumen where it binds with H+ to form NH4+ which is large and cannot be reabsorbed. This means the H+ is now trapped in the tubule where it is excreted in urine as ammonium.
  - Phosphate buffer: operates similarly to the ammonia one. The result is the formation of weak acids that are excreted in urine...sodium and bicarb are reabsorbed.

Electroneutrality

- Potassium and Hydrogen
  - When serum K+ is elevated, renal tubular cells secrete more K+ but retain H+ to maintain electroneutrality, leading to acidosis.
  - Low serum K+ promotes renal secretion of H+ (leading to alkalosis)
  - When serum H+ is high, renal tubular cells will secrete more H+, but retain K+...leading to hyperkalemia
  - At tissue level, H+ moves into cells to be buffered by intracellular proteins and K+ moves out...contributes to clinical manifestations of hyperkalemia (though it does not indicate a "true" excess of K+)
  - When serum H+ is low, renal cells retain H+ and secrete more K+, and cellular proteins release H+ to extracellular fluid while K+ shifts intracellularly.

- Sodium and Chloride
  - Active reabsorption of Na+ from the renal tubules drives secretion of H+ and reabsorption of anions such as chloride and HCO3-.
  - JG cells sense low extracellular volume, triggering renin-angiotensin-aldosterone system...aldosterone stimulates...
renal reabsorption of Na+. H+ and K+ are excreted to maintain electroneutrality, and HCO3- is reabsorbed.

Clinical conditions that cause low serum Na+ almost invariably result in low chloride. When chloride is low, the kidneys reabsorb more HCO3- to maintain electroneutrality. The converse is also true (excess loss of HCO3-causes more chloride to be retained...is this the hyperchloremic acidosis I've heard so much about?)

**Proteins**
- Serum proteins such as albumin are also important buffers!
- When H+ is high, serum proteins bind to the H+ displacing other cations such as calcium. This causes the level of free (ionized) calcium to rise, promoting clinical manifestations of hypercalcemia!
- When H+ is low, a greater fraction of serum calcium is bound, decreasing the levels of serum calcium.
- H+ excess creates need for more buffers, including ammonia (which comes from protein)...so increased buffering of acid promotes depletion of protein.
- Low serum albumin caused by renal disease or other disorders may promote H+ excess (not enough proteins there to buffer...so acidotic!)

**Acid-Base Compensation**
- When the cause of the imbalance is due to problems with the kidneys, the respiratory system kicks in to increase ventilation to “blow off” excess acid. Conversely, I suppose the lungs slow down breathing to retain more CO2 if the problem is alkalosis.
- In respiratory failure, the kidneys can compensate for retention of acid by secreting H+ and regenerating HCO3-.
- Lungs and kidneys can compensate, but it takes up to 24 hours for full compensation!...kidneys may require up to 72 hours for optimal compensation!
- Except in mild, chronic respiratory alkalosis, compensation does not FULLY restore normal pH.
  - Respiratory compensation is limited in response to a renal deficit of H+ b/c the reduction in ventilation would eventually lead to hypoxemia...no bueno!
  - Renal compensation for respiratory disorders is potentially limited by many factors including: renal blood flow, tubular flow rates and saturability of tubular transport processes.

**Analysis of Arterial Blood Gases**

**Determination of oxygenation:**
- PaO2 (partial pressure of oxygen)
- SaO2 (percentage of hgb saturated with oxygen or the oxygen saturation)
- PaCO2 (partial pressure of CO2)

**Determination of acid-base status**
- pH
- PaCO2 (the respiratory component of the ABG)
- HCO3- (the metabolic component of the ABG)

**Analysis steps**

**Step 1: Classify the pH**
- Normal = 7.35 - 7.45
- Acidemia = < 7.35
- Alkalemia = > 7.45

**Step 2: Assess PaCO2**
- Normal = 35-45 mm Hg
- Respiratory acidosis = > 45 mm Hg
- Respiratory alkalosis = < 35 mm Hg

**Step 3: Assess HCO3-**
- Normal = 22-26 mEq/L
- Metabolic acidosis = < 22 mEq/L
- Metabolic alkalosis = > 26 mEq/L

**Step 4: Determine presence of compensation (this is where it gets tricky!)**
- Are PaCO2 and HCO3- abnormal (or almost so?) in opposite directions (one acidic, the other alkalotic)? If yes, then compensation is PRESENT
- Is one component normal and the other abnormal? If yes, compensation is ABSENT and the problem is likely acute.

**Step 5: Identify the primary disorder, if possible**
- If pH is clearly abnormal, then the acid-base component most consistent with the pH disturbance is the primary disorder
- If pH is normal or near-normal, the more deviant component is the probable primary (also...note whehter pH is on the acidic or alkalotic side of 7.4. the more deviant component should be consistent with this pH.)

**Step 6: Classify degree of compensation, if present**
Metabolic acidosis: the decrease in PaCO2 is approximately equal to the last two digits of the pH.
Metabolic alkalosis: The PaCO2 is approximately equal to 0.6 x the increase in HCO3- level.
Respiratory acidosis: For every 10 mm Hg increase in PaCO2, the HCO3- level is increased by 1 mEq/L (in acute acidosis) or 4 mEq/L (in chronic acidosis)
Respiratory alkalosis: For every 10 mm Hg decrease in PaCO2, the HCO3- level is decreased by 2 mEq/L (in acute alkalosis) or 5 mEq/L (in chronic alkalosis)
COMPENSATION BEYOND THESE LIMITS SUGGESTS THE PRESENCE OF A COMPLEX DISORDER!!!

Respiratory Alkalosis (some quick facts...not everything!)
- **Etiology:** Most common cause of respiratory alkalosis is hypoxemia (disorders that lead to SOB)
- **Patho**
  - The buffering response results from:
    - shifting of acid from intraceullar fluid into the blood
    - movement of HCO3- into cells in exchange for chloride
  - Renal compensation involves decreased H+ secretion and excretion of excess filtered HCO3-
- **Notable Clinical Manifestations**
  - Abnormal ABGs
  - Hyperventilation (the underlying cause!)
  - CNS manifestations of altered blood flow and neurotransmission: paresthesias, lightheadedness, confusion
  - Musculoskeletal and cardiac probs associated with hypokalemia and hypocalcemia
  - Acute alkalosis may cause GI probs such as N/V, diarrhea (all attributed to SNS effects)
  - Acute lasts 24 hours or less; chronic lasts longer!
- **Outcome Management**
  - Treat the underlying disorder (this is true for all acid-base problems!) Electrolyte imbalances will usually resolve when the underlying problem is fixed. Mild & chronic is not usually treated.
  - Respiratory support...oxygen therapy in the form of rebreathing CO2 provides prompt and short-term relief in anxiety-related respiratory alkalosis (someone freaking out and hyperventilating).

Respiratory Acidosis (the highlights)
- **Etiology:** Results from retention or excessive production of acid production of CO2
  - Acute develops and resolves within 3 days or less (chronic persists longer)
  - Almost always results from hypoventilation
    - Most common cause is COPD d/t airway collapse, air trapping, V/Q disturbances
    - Can also be caused respiratory infection and cardiac disease that increase WOB
    - Hypoventilation occurs when diaphragm movement is impaired (as in Guillain-Barre), or when the medulla is damaged by drugs or lesions.
    - Other causes: obesity hypoventilation syndrome, excessive fatigue/weakness, severe deformities of spine and/or rib cage muscles.
  - Can occur as a result of inadequate mechanical ventilation OR from excessive oxygenation of a pt with COPD.
  - Excessive CO2 production is much less common...this would be a result of hypermetabolism or from excessive metabolism of CHO fuels for energy.
    - enteral feedings or parenteral nutrition formulas that are high in CHOs can lead to elevated PaCO2 levels (esp pts with impaired ventilation)
- **Patho**
  - CO2 accumulates in blood and diffues into all body compartments (hypercapnia)...this drives the hydolysis rxn forward resulting in H+ and HCO3-.
  - Renal compensation proceeds over 3-5 days, with greater secretion of H+ and regeneration of bicarb (HCO3-)
  - Renal ammonia production increases (which depletes protein stores)...ammonia urinary buffer is enhanced
  - As HCO3- rises with compensation, chloride is excreted in greater amounts...can lead to hypochloremia.
  - Renal retention of K+ (remember that the H+ is leaving, so we gotta keep electroneutrality) can lead to hyperkalemia
  - Displacement of calcium from albumin may result in hypercalcemia.
  - The rapid rise of PCO2 results in hypoxemia in pts who are breathing room air (CO2 displaces O2 in the alveoli)
- **Notable Clinical Manifestations**
  - Abnormal ABGs (low pH and high PaCO2)
  - Probably hypoventilation (the usual underlying cause!)
  - Manifestations of hypoxemia (confusion, irritability, lethargy)
  - Compensation will be present to a greater extent in chronic cases
  - Organ system dysfunction: hypotension, cardiac dysrhythmias
  - CNS: tremors, seizures, lethargy, stupor, compa
Outcome Management

- Treat the underlying disorder! Electrolyte issues usually resolve themselves, but hyperkalemia may require emergency treatment with dialysis or cation-exchange resins.
- Respiratory support...mechanical ventilation and supplemental O2. Current trend is to use lower tidal volumes than what would be required to restore PaCO2 to normal levels (fewer airway injuries). However, sedation is usually required. O2 therapy must be administered cautiously to chronic CO2 retainers!
- Exogenous alkali are given only if pt has severe bronchospasm...the alkalization may restore the responsiveness of the airway to beta-agonist drugs.

Metabolic Alkalosis

Excess base or H+ deficit in body fluids...usually d/t gain of bicarb or loss of fixed acids.

Etiology

- Develops through a two-phase mechanism
  1) Generation phase. The imbalance is first created by a loss of acid or gain of base OR a loss of fluids containing more chloride than bicarb (this can happen when loop or thiazide diuretics are overused).
  - Contracted alkalosis = fluid volume loss
  - Posthypercapnic metabolic alkalosis = results from too-rapid correction of chronic respiratory acidosis
  2) Maintenance phase. Alkalosis persists b/c renal excretion of bicarb is impaired. May result from hypovolemia or aldosterone excess (the latter is not very common).
- Metabolic alkalosis from fluid loss is referred to as saline sensitive b/c restoration of volume with fluid containing NaCl permits the kidneys to restore acid-base homeostasis.
- Alkalosis d/t aldosteronism is not fixable with saline, so it is saline resistant.

Pathophysiology

- Respiratory compensation is limited by the hypoxemia that develops d/t hypoventilation.
- Most buffering occurs in extracellular fluid
- Severe alkalemia leads to widespread organ dysfunction....mainly neuro and cardio are affected
- Hypokalemia is more prominent in metabolic alkalosis than respiratory alkalosis

Notable Clinical Manifestations

- Abnormal ABGs (high pH and high HCO3-)
- PaCO2 rises with compensation.
- Hypokalemia & hypomagnesemia may show as cardiac dysrhythmias
- CNS: lethargy, confusion, seizures
- Adaptive hypoventilation (may induce hypoxemia)

Outcome Management

- Treat the underlying disorder
  - replacement of fluids, electrolytes (K+ and Mg+) and support renal function
  - Administration of acetazolamide (a diuretic); promotes loss of bicarb in urine. Can lead to electrolyte imbalance
  - Administration of exogenous acid in SEVERE cases. Risks are substantial

Metabolic Acidosis

- A state of acid excess (gain of fixed acids) or a base deficit (loss of bicarb)

Etiology: the presence or absence of a high anion gap tells you if it’s acid excess or base deficit.

- Anion gap is usually 12 ± 4 mEq/L (but I’ve seen just 8-12 or so).
- The "gap" is serum anions OTHER THAN bicarb and chloride...this could be lactate, phosphate, sulfate, proteins, ions.

Common causes of high anion gap acidosis:

- Lactic acidosis (d/t anaerobic metabolism)
- Diabetic ketoacidosis
- Azotemic renal failure (acid end products of protein metabolism cannot be excreted effectively)
- Ingestion of toxins with acid metabolites (less common)

Non-anion gap acidosis caused by loss of base is also called hyperchloremic metabolic acidosis.

- Kidneys retain chloride when excess bicarb is lost (anion gap remains normal)
- Bicarb can be lost through kidneys (inability to reabsorb) or intestinal tract (drainage tubes, diarrhea, NG sxn).
- Critically ill pts who receive aggressive fluid volume replacement with NS or other bicarb-free solution may develop a bicarb deficiency.

Patho

- Metabolic acidosis is accompanied by a compensatory increase in ventilation.
- Severe acidemia induces insulin resistance and depresses glycolytic enzymes (energy metabolism is impaired!)
- Fxn of regulatory and structural proteins is impaired (leads to organ dysfunction)
- Increased protein catabolism occurs
Hyperkalemia occurs b/c K+ shifts OUT of cells as excess H+ enters

**Notable Clinical Manifestations**
- Abnormal ABGs (low pH and low HCO3-)
- PaCO2 levels drop as respiratory compensation occurs
- Compensatory hyperventilation
- Systemic manifestations are similar to those of resp. acidosis
- Inability to correct the problem with hyperventilation is r/t an increased occurrence of respiratory failure and the need for mechanical ventilation.

**Outcome Management**
- Treat the underlying disorder! Usually involves restoring normal tissue oxygenation and perfusion. Electrolyte imbalance is only treated if it is life-threatening (will otherwise resolve on its own)
- Respiratory support: Assisted mechanical ventilation may be needed for pts who can’t hyperventilate enough
- Administration of exogenous alkali: controversial

**Complex Acid-Base Disorders**
- Mixed acid-base disorders = two primary acid-base imbalances coexist
  - ex: in cardiac arrest, lactic acid accumulates as a result of anaerobic metabolism and carbonic level is elevated d/t respiratory arrest.

- Triple acid-base disorder = present when metabolic acidosis and metabolic alkalosis co-exist with either resp. acidosis or resp. alkalosis. (the two respiratory disorders cannot coexist b/c of effects on ventilation)
  - ex: ingestion of methanol causes metabolic acidosis, vomiting causes metabolic alkalosis, and respiratory arrest from aspiration causing respiratory acidosis. CAN OCCUR SIMULTANEOUSLY!!!

- You should suspect a complex disorder when a PaCO2 value and HCO3- level DO NOT correlate with pH, or when ABG evidence of compensation exceeds predicted levels!

Nursing management I will leave to the ATI book...so that’s that on Acid-Base!