Introductions

- Abnormal acid-base changes are a result of a disease process. They are not the disease.
- Abnormal acid base disorder predicts the outcome of the case but often is not a direct cause of the mortality, but rather is an epiphenomenon.
- Disorders of acid base balance result from disorders of primary regulating organs (lungs or kidneys etc), exogenous drugs or fluids that change the ability to maintain normal acid base balance.
- An acid is a hydrogen ion or proton donor, and a substance which causes a rise in H^+ concentration on being added to water.
- A base is a hydrogen ion or proton acceptor, and a substance which causes a rise in OH^- concentration when added to water.
- Strength of acids or bases refers to their ability to donate and accept H^+ ions respectively.
- When hydrochloric acid is dissolved in water all or almost all of the H in the acid is released as H^+.
- When lactic acid is dissolved in water a considerable quantity remains as lactic acid molecules.
- Lactic acid is, therefore, said to be a weaker acid than hydrochloric acid, but the lactate ion possess a stronger conjugate base than hydrochlorate.
- The stronger the acid, the weaker its conjugate base, that is, the less ability of the base to accept H^+.
- Carbonic acid ionizes less than lactic acid and so is weaker than lactic acid, therefore termed, ‘weak acid’.
- Thus lactic acid might be referred to as weak when considered in relation to hydrochloric acid but strong when compared to carbonic acid.
- Weak and strong in relation to acids and bases are thus relative terms.
- A buffer solution is one in which the pH changes less when an acid or base is added than would have occurred in a non-buffer solution.

Importance of acid-base balance

- The hydrogen ion (H^+) concentration must be precisely maintained within a narrow physiological range.
- Hydrogen ion concentration is most commonly expressed as pH (= negative logarithm of the H^+ concentration).
- Small changes of pH from normal can produce marked changes in enzyme activity & chemical reactions within the body.
- Acidosis - CNS depression, coma (if severely acidotic, i.e., pH <7.0)
- Alkalosis - CNS excitability, tetany, seizures
• The table on the right doesn’t allow you to mentally calculate every pH and $[H^+]$ value but the 4 basic pairs which are useful and easy to memorize are:

<table>
<thead>
<tr>
<th>$[H^+]$ (nmol/l)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>7</td>
</tr>
<tr>
<td>80</td>
<td>7.1</td>
</tr>
<tr>
<td>63</td>
<td>7.2</td>
</tr>
<tr>
<td>50</td>
<td>7.3</td>
</tr>
<tr>
<td>44</td>
<td>7.36</td>
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<tr>
<td>40</td>
<td>7.4</td>
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<tr>
<td>36</td>
<td>7.44</td>
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<tr>
<td>32</td>
<td>7.5</td>
</tr>
<tr>
<td>25</td>
<td>7.6</td>
</tr>
<tr>
<td>20</td>
<td>7.7</td>
</tr>
</tbody>
</table>

- pH 7.4 is 40 nM
- pH 7.1 is 80 nM
- pH 7.36 is 44 nM
- pH 7.44 is 36 nM

• The last two values above are the normal range of pH values which is easy to remember because the relationship between the $[H^+]$ and the decimal part of the pH (ie the normal range of 7.36 to 7.44 is a $[H^+]$ range of 44 to 36 nmol.
• Now you can work out that a pH of 7.06 has a $[H^+]$ value of 88nm as this is double that at 7.36 (i.e. 44nM) - and so on.

• Normal pH:
  - arterial blood: 7.35 - 7.45
  - venous blood, interstitial fluid: 7.35
  - intracellular: 6.0-7.4 (average 7.0)

**Henderson-Hesselbach Equation**

• The pH resulting from the solution of CO$_2$ in blood and the consequent dissociation of carbonic acid is given by the Henderson-Hesslebach Equation.

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

• The law of mass conservation gives the dissociation constant of carbonic acid as $K_a$

$$K_a \propto \frac{(H^+) \times (HCO_3^-)}{H_2CO_3}$$

• Now, since the concentration of carbonic acid is proportional to the concentration to the concentration of dissolved carbon dioxide, we can change to

$$K_a = \frac{(H^+) \times (HCO_3^-)}{CO_2}$$

• Take log,

$$\log K_a = \log(H^+) + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

• Whence,

$$-\log(H^+) = -\log(K_a) + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

• Since pH is negative logarithm of $H^+$,

$$pH = pK_a + \log\left(\frac{HCO_3^-}{CO_2}\right)$$

• According to Henry’s law, replace CO$_2$ with PCO$_2$ x 0.03
\[ \text{pH} = \text{pK}_a + \log \left( \frac{\text{HCO}_3^-}{\text{PCO}_2 \times 0.03} \right) \]

- The value of \( \text{pK}_a \) is 6.1, and the normal \( \text{HCO}_3^- \) and \( \text{PCO}_2 \) are 24 mmol/L and 40 mmHg, respectively. Substitute these,

\[ \begin{align*}
\text{pH} &= 6.1 + \log \left( \frac{24}{40 \times 0.03} \right) \\
&= 6.1 + \log 20 \\
&= 6.1 + 1.3 \\
&= 7.4
\end{align*} \]

**Regulation of pH**

- Buffer systems - very rapid (seconds), incomplete
- Respiratory responses - rapid (minutes), incomplete
- Renal responses - slow (hours to days), complete

**Buffer Systems**

- Bicarbonate, phosphate and protein buffering systems are the three major buffering systems.
- The bicarbonate system is primarily extracellular and the fastest to respond to pH imbalance, but it has less total capacity than intracellular system.
- Intracellular buffering occurs through the phosphate and protein systems.
- Intracellular buffering has a very large capacity, about 75% of the body chemical buffering.

**Bicarbonate buffer system**

- Primary extracellular buffer system (>50% of extracellular buffering)
- Accurate assessment - readily calculated from PCO\(_2\) and pH using available blood gas machines
- Consists of carbonic acid (weak acid) and bicarbonate
- Carbonic acid dissociates into carbon dioxide and water
  \[ \text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \]
- CO\(_2\) regulated by the lungs - rapidly
- HCO\(_3^-\) is regulated by the kidneys - slowly
- Not powerful
- pKa = 6.1

**Protein buffer system**

- Most powerful
- 75% of all intracellular buffering
- Hemoglobin
  - important extracellular buffer due to large concentration of hemoglobin in blood
  - buffering capacity varies with oxygenation
  - reduced hemoglobin is a weaker acid than oxyhemoglobin
  - dissociation of oxyhemoglobin results in more base available to combine with H\(^+\)
- Plasma protein
  - acid buffer
important intracellular buffer system

- Phosphate buffer system
  - H$_2$PO$_4^-$ and HPO$_4^{2-}$
  - important renal buffering system
  - extracellular concentration, 1/12 that of bicarbonate
  - pKa = 6.8
  - phosphate is concentrated in the renal tubules

**Respiratory Responses**

- Occurs within minutes of alteration in pH due to stimulation/depression of respiratory centers in the CNS
- H$^+$ acts directly on respiratory center in Medulla Oblongata
- Alveolar ventilation increases/decreases in response to changes in CO2
- Alveolar ventilation is inversely proportional to P$_a$CO$_2$
  - 2 x ventilation: pH 7.4 to 7.63
  - 1/4 ventilation: pH 7.4 to 7.0
- Incomplete response because as the change in alveolar ventilation brings pH back towards normal, the stimulus responsible for the change in ventilation decreases

**Renal Responses**

- The kidneys regulate pH by either acidification or alkalinization of the urine
- Complex response that occurs primarily in the proximal renal tubules
- With acidosis, rate of H$^+$ secretion exceeds HCO$_3^-$ filtration
- With alkalosis, rate of HCO$_3^-$ filtration exceeds H$^+$ secretion
- Occurs over hours/days, and is capable of nearly complete restoration of acid/base balance

**Anion Gap (AG)**

- A useful tool to assess mixed acid-base disorders
- Traditionally it has been used to detect lactic acidosis, ketoacidosis and the presence of certain poisons (ethylene glycol etc.)
- The derivation of the anion gap is usually comes from the relationship of preservation of charges of anions and cations.
- The plasma is actually electrically neutral, and total cations equal total anions.
- [Na$^+$] + [K$^+$] + [UC$^+$] = [Cl$^-$] + [HCO$_3^-$] + [UA$^-$] (as body maintains electroneutrality)
- Rearranged, [UA$^-$] – [UC$^+$] = ([Na$^+$] + [K$^+$]) – ([Cl$^-$] + [HCO$_3^-$])
- Since, in clinical sense, [UC$^+$] are negligible the anion gap is basically [UA$^-$], unmeasured anions
- AG = [UA$^-$] = ([Na$^+$] + [K$^+$]) – ([Cl$^-$] + [HCO$_3^-$])
- [UA$^-$] consist of [protein$^-$], phosphates, sulfates, beta hydroxybutyrate, acetoacetate, and citrate
- Therefore, from the above equation, the gap is calculated difference between the sum of serum sodium and potassium and the sum of serum chloride and bicarbonate.
- Anion gap is usually measured in venous blood with HCO$_3^-$ estimated as total CO$_2$.
- Usually an increase in AG implies accumulation of organic acids in the body, and suggest the presence of lactic acidosis, ketosis, sepsis, poisoning or renal failure.
- Normal is approximately 14, and ranges from 12–16 mEq/L
• Commonly, the AG remains normal in an acidosis that is due to simple HCO$_3^-$ loss (as in diarrhea and certain renal diseases) because, as a general principle, [Cl$^-$] increases to meet the drop in HCO$_3^-$ anions, thereby maintaining anionic balance.
• When an acid load is present, HCO$_3^-$ titrates acid and anion gap increases, creating a condition known as ‘anion gap metabolic acidosis’.

**Major Acid Base Disorders and Compensatory Mechanism**

<table>
<thead>
<tr>
<th>Primary Disorder</th>
<th>Primary Disturbance</th>
<th>Primary Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Acidosis</td>
<td>↑ PCO$_2$</td>
<td>↑ HCO$_3^-$</td>
</tr>
<tr>
<td>Respiratory Alkalosis</td>
<td>↓ PCO$_2$</td>
<td>↓ HCO$_3^-$</td>
</tr>
<tr>
<td>Metabolic Acidosis</td>
<td>↓ HCO$_3^-$</td>
<td>↓ PCO$_2$ (hyperventilation)</td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td>↑ HCO$_3^-$</td>
<td>↑ PCO$_2$ (hypoventilation)</td>
</tr>
</tbody>
</table>

• The primary compensation (acute compensation) is generally achieved most rapidly through respiratory control of CO$_2$.
• Ultimately the renal system excretes acid or bicarbonate (chronic compensation) to reach the final response to the disturbance
• Mixed disorders are common

**Blood Gas Evaluation**

What do we get from a blood gas machine?

• pH - measured
• PCO$_2$ - measured
• PO$_2$ - measured
• HCO$_3^-$ - calculated (via Henderson Hesselbalch equation)
• Base excess (deficit) - calculated
• Hemoglobin oxygen saturation - calculated
• Gases (carbon dioxide & oxygen) are reported as partial pressures, commonly in unit of mmHg (US), or KPa (International); 1 KPa = 7.5 mmHg (torr)

**Blood Gas Sampling**

• Arterial vs. venous
• Venous samples are adequate for metabolic function if the respiratory function is near normal
• Venous samples are of limited value in evaluating respiratory components

**Preservation of Sample**

• Heparinize syringe (5 units of heparin/1 ml of blood)
• Eliminate air bubbles from the sample
• Cap the needle with rubber stopper
• If greater than 10 minute delay to the machine, place sample in an ice water bath. Will preserve samples for up to 10 hours
Sites for Arterial Samples

- Dog: dorso pedal, femoral, anterior tibial, lingual
- Cat: femoral, dorso pedal
- Horse: facial, mandibular, lateral metatarsal, posterior auricular, carotid
- Cow: coccygeal, posterior auricular
- Pig: coccygeal, posterior auricular

**Normal Values**

<table>
<thead>
<tr>
<th></th>
<th>Arterial</th>
<th>Venous</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.35-7.45</td>
<td>7.35</td>
</tr>
<tr>
<td>PCO₂</td>
<td>35-45 mmHg</td>
<td>45 mmHg</td>
</tr>
<tr>
<td>PO₂</td>
<td>90-100 mmHg</td>
<td>40 mmHg</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>24 mEq/L</td>
<td>24 mEq/L</td>
</tr>
</tbody>
</table>

**Interpretation**

1st step: What is the pH?
- < 7.35 acidemia
- > 7.45 alkalemia

2nd step: What is the PaCO₂?
- > 45 respiratory acidosis
- < 35 respiratory alkalosis

3rd step: What is the HCO₃⁻?
- < 24* metabolic acidosis
- > 25* metabolic alkalosis

*If PaCO₂ is normal

- When the pH is low (i.e., more acidotic)
  - A low (or normal) PCO₂ points to a primary metabolic acidosis
  - A high PCO₂ points to a primary respiratory acidosis
- When the pH is high (i.e., more alkalotic)
  - A high (or normal) PCO₂ points to a primary metabolic alkalosis
  - A low PCO₂ points to a primary respiratory alkalosis
- Simply stated,
  - If pH and PCO₂ change in the same direction, the primary disorder is metabolic
  - If pH and PCO₂ change in the opposite direction, the primary disorder is respiratory

**Alterations in the HCO₃⁻ due to PₐCO₂**

- Acute change:
  - if PₐCO₂ increases by 10, the HCO₃⁻ is expected to increase by 1 mEq
  - if PₐCO₂ decreases by 10, the HCO₃⁻ is expected to decrease by 2 mEq
- Chronic change:
  - if PₐCO₂ increases by 10, the HCO₃⁻ is expected to increase by 3 - 4 mEq
  - if PₐCO₂ decreases by 10, the HCO₃⁻ is expected to decrease by 4 - 6 mEq
**Bicarbonate Replacement**

- Metabolic acidosis is the most frequent acid base abnormality observed in the critically ill, with the most likely underlying disturbance as ‘lactic acidosis’ (Bihari 1986, Mizock 1987).
- Although sodium bicarbonate has been advocated the drug of choice in treating metabolic acidosis by many critical care clinicians, there is no consensus concerning the use of sodium bicarbonate in the treatment of life-threatening acidosis.
- The American Heart Association removed routine use of sodium bicarbonate as part of Advanced Cardiac Life Support (ACLS) protocol related to the treatment of cardiac arrest in 90’s, indicating little use or potential deterioration of clinical outcome regarding the drug therapy for CPR.
- The use of sodium bicarbonate in the treatment of metabolic acidosis has been very controversial and will probably remain so for a long time.
- The risks of overzealous bicarbonate therapy include
  - paradoxical cerebral acidosis (through increased production of CO₂)
  - hypernatremia
  - hyperosmolality
  - iatrogenic metabolic alkalosis
- If you have a mixed respiratory/metabolic acidosis, important to address the respiratory acidosis first, before treating the metabolic acidosis
- Bicarbonate therapy is not usually recommended unless pH < 7.1 or HCO₃⁻ deficit is greater than 10 meq/L.
- 8.4% NaHCO₃ = 1 meq/ml
- 1 gm of baking soda (e.g. Arm & Hammer) = 12 mEq of NaHCO₃
- Formula for Bicarbonate replacement based on ‘Base deficit’
  - Base deficit = BW (Kg) x 0.3 x (desired – observed bicarbonate, HCO₃⁻)
  - 0.3 assumes 30% of BW is extracellular fluid.
  - It is recommended that 25 % of the calculated dose to be given over 10 to 15 minutes, and the remaining to be given following subsequent evaluation of acid base status to the initial therapy.

**Oxydynamics**

**PₐO₂ vs. O₂ Content**

- PO₂ = partial pressure of oxygen in plasma
- O₂ content = ml of O₂/100 ml of blood
- Hb: 1 gm of saturated Hb carries 1.34 ml of O₂
- Plasma: 0.3 ml of O₂ dissolved/100 mmHg O₂ tension/100 ml blood
- Calculation of O₂ content (O₂CT)

\[
O₂CT = Hb + \text{plasma} = 1.34 \times Hb \times \text{Saturation} + PaO₂ \times 0.003
\]

- Example 1: What is O₂CT if PₐO₂ = 100 and Hb = 10?

\[
(1.34 \times 10 \times 1.0) + (100 \times 0.003) = 13.7 \text{ mg O₂/100 ml blood}
\]

- Example 2: What is the O₂CT if PₐO₂ = 400 and Hb = 10?

\[
(1.34 \times 10 \times 1.0) + (400 \times 0.003) = 14.6 \text{ mg O₂/100 ml blood}
\]
Can you demonstrate the importance of giving 100% oxygen to a very anemic animal (Hb = 4) vs. a normal animal (Hb = 15)? What percentage increase in oxygen content would occur in each if a PaO2 of 500 was achieved from 100?

- **Hb 4**
  
  \[(4 \times 1.34) + (500 \times 0.003) = 6.86 \text{ mg/dl (vs. 5.66 mg/dl at PaO2 100)}\]
  
  \[6.86/5.66 = 21 \% \text{ increase}\]

- **Hb 15**
  
  \[(15 \times 1.34) + (500 \times 0.003) = 21.6 \text{ mg/dl (vs. 20.4 mg/dl at PaO2 100)}\]
  
  \[21.6/20.4 = 6 \% \text{ increase}\]

- It is apparent, even in anemic condition, increasing fraction of oxygen still helps although primary therapeutic goal must be to ‘elevate the Hb concentration’ quickly.

**Examples**

- In each of the following problems, ask the following questions in this order:
  - Is the patient acidotic or alkalotic? Remember, the body never overcompensates!
  - Is there a respiratory component to the blood gas disturbance? (Is the PaCO2 < 35 or > 45?)
  - Is there a metabolic component to the blood gas disturbance? (Is the HCO3- < 24 or > 26?)
  - Remember, HCO3- must be adjusted for PaCO2 changes.

<table>
<thead>
<tr>
<th>PCO2</th>
<th>pH</th>
<th>HCO3-</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mmHg</td>
<td>0.1</td>
<td>6 mEq/L</td>
</tr>
</tbody>
</table>

- **Acute Respiratory Alteration**
  - PCO2 = 52, pH = 7.3.
  - PCO2 = 28, pH = 7.5.

- **Metabolic Alteration**
  - PCO2 = 52, pH = 7.5.
  - PCO2 = 28, pH = 7.3.

- **Mixed**
  - PCO2 = 52, pH = 7.2.
  - PCO2 = 28, pH = 7.6.

**Horse on the surgery table**

- pH = 7.2
- PaCO2 = 76
- HCO3- = 30
- PaO2 = 300

  - What is the acid base status?
    - Acidemia or alkalemia?
    - Is there a respiratory component?
    - Is there a metabolic disturbance?

  - Why is the PaO2 300?

**30 Kg German Shepherd on surgery table with volvulus of intestine**

- pH = 7.1
- PaCO2 = 70
- HCO3- = 21

  - Same as above
    - Same as above
What is the HCO₃⁻ deficit? (expected - actual = deficit)

How much HCO₃⁻ should be given?

500 Kg horse standing, kicking, bouncing in the stocks with colic signs

pH = 7.2
PₐCO₂ = 20
HCO₃⁻ = 15

What is the HCO₃⁻ deficit?

What would happen if we gave this animal 50 gms of NaHCO₃?

Normal cat, awake when sample taken

pH = 7.5
PₐCO₂ = 20
HCO₃⁻ = 20

Why would a cat have this type of blood gas picture?