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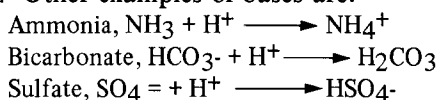
Acid-Base Review

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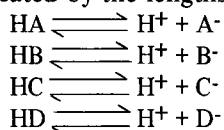
In the normal, healthy individual the acid-base balance within the body is remarkably constant. For example, arterial blood, drawn from healthy individuals at sea level, will show that, in over 95% of the individuals, the pH of the blood is between 7.35 and 7.45. Furthermore, the $p\text{CO}_2$ will be maintained between 35 and 48 mmHg while the bicarbonate concentration will be between 23 and 28 mEq/L. This homeostasis is not accidental but essential to the functioning of most life processes. Any drastic change in pH results in failure of the multiple enzyme systems which require constant conditions in order to mediate life processes. A pH below 7.0 or above 7.8 is not compatible with life for any length of time. The circulatory system, including lungs and kidneys, is the primary homeostatic mechanism. Since it is the aim of extracorporeal technology to substitute for the circulation; in part as in dialysis, or in total as in heart-lung bypass, it is important that we who deliver extracorporeal technology service understand acid-base balance, disturbances in this balance, and corrective actions in the case of disturbances.

In order to discuss acid-base balance, it is essential to agree on definitions. An **acid**, as defined by Bronsted, is any compound capable of donating a proton (or hydrogen ion) to a base. A **base** is any compound capable of accepting a proton. A substance that can neither donate nor accept protons is neither acid or base. An example of an acid is Hydrochloric acid (HCL) which will disassociate when dissolved in water into H^+ and Cl^- . The H^+ or proton is then available for reaction with a base. Other examples are Ammonium, $\text{NH}_4^+ \longrightarrow \text{NH}_3 + \text{H}^+$
Carbonic acid, $\text{H}_2\text{CO}_3 \longrightarrow \text{H}^+ + \text{HCO}_3^-$
Bicarbonate, $\text{HCO}_3^- \longrightarrow \text{H}^+ + \text{CO}_3^-$

An example of a base is the hydroxyl ion (OH^-) which can react with the proton to form water. $\text{H}^+ + \text{OH}^- \longrightarrow \text{HOH}$. Other examples of bases are:



We should note that several of these reactions demonstrate that a substance can act as either an acid or a base. Also, many of the reactions are reversible and the direction of reaction is dependent on the concentration of the reactants and products. By convention, reactants appear on the left and products on the right of the chemical equation. The comparative amounts of the reactants and products under the condition of equilibrium are indicated by the lengths of arrows:



A, B, C and D in the above reactions are the conjugate bases of acids HA, HB, HC and HD respectively. According to our convention, HA tends to exist more in the disassociated condition than HB. HD exists in the completely disassociated condition while HC exists in equal parts, associated and disassociated.

A **strong** acid has a **weak conjugate base**. As an example, chloride (Cl^-) is a weak conjugate base in that it does not hold the H^+ of hydrochloric acid (HCL) in association when dissolved in water. HCL completely disassociates into H^+ and

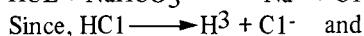
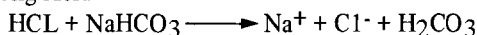
C1⁻. This defines HCL as a **strong acid**. **Weak acids**, on the other hand, have **strong conjugate bases**. An example of a strong conjugate base is bicarbonate (HCO₃⁻) in carbonic acid. When dissolved in water the concentration of H⁺ present is far lower than the concentration of carbonic acid. The bicarbonate conjugate base tends to hold the H⁺ in association making less H⁺ available for reaction with a base. Thus, carbonic acid is a relatively weak acid.

Buffers are substances in solutions that minimize changes in pH when either acids or bases are added to the solution. There are many buffers in blood. Proteins are formed from amino acids. Each amino acid has at least one acidic group, (R-COOH → R-COO⁻ + H⁺) and one basic group, (R-NH₂ + H⁺ → R-NH₃⁺) The numerous -COOH and -NH₂ groups exposed on proteins serve as reaction sites for acids and bases. As a simplified example; imagine a protein with four -NH₂ and four -COOH groups exposed. If four H⁺ ions are added to the solution, three of the H⁺ ions are combined, H⁺ + NH₂ → NH₃⁺ while only one remains free in the solution to alter the pH. Hemoglobin is a special blood protein that has great buffering capability. The imidazole group in the amino acid histidine is an especially potent H⁺ ion receptor at normal blood pH. This, plus the large concentration of hemoglobin in blood makes it an extremely important blood buffer.

A buffer system is the combination of a weak acid and its conjugate base in a solution. The conjugate base is usually more present as the salt of the weak acid since the salt disassociates more completely than the acid. There are many such systems present in blood but one of the most important is the bicarbonate, carbonic acid system.

What happens when a strong acid or base is added to a buffer system? The presence of the buffer moderates the change in pH. As an example, the addition of strong acid and base to the carbonic acid-bicarbonate buffering system is illustrated below:

Strong Acid:



$\text{H}_2\text{CO}_2 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$ the addition of H⁺ from the HCl drives the carbonic acid equation to the left thus removing some of the H⁺ added upon the addition of HCl.

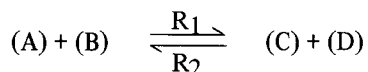
Strong Base:



A strong base will react with the weak acid of buffer system to yield water and the salt of the weak acid.

The Concept of pH

The law of mass action states that the rate of a reaction is proportional to the product of the molar concentrations of the reactants. In the case of a reversible reaction



rate 1 is proportional to (A) x (B) and rate 2 is proportional to (C) x (D). At equilibrium, when two velocities are equal and no further change is occurring, the following relationship exists:

$$\frac{(C)}{(A)} \times \frac{(D)}{(B)} = K$$

This constant is a property of A + B regardless of the concentrations of reactants. In the case of an acid, Ha, the equation is: $(\text{Ha}) \rightleftharpoons (\text{H}^+) + (\text{a}^-)$ and the constant $K_a = \frac{(\text{H}^+) \times (\text{a}^-)}{(\text{Ha})}$ and the constant K_a becomes known as the disassociation

constant. It should be obvious from the above equation that the stronger the acid, the larger the K_a . This is true since the acid exists in the disassociated form to a larger extent than in the case of a weak acid.

If the above equation is solved for the H^+ concentration, one derives Henderson's equation: $(\text{H}^+) = K_a \frac{(\text{Ha})}{(\text{a}^-)}$. Further, if we take the reciprocal of both

side of the equation: $\frac{1}{(\text{H}^+)} = \frac{1}{K_a} = \frac{(\text{a}^-)}{(\text{Ha})}$ and then take the log of both sides, remembering that logs are exponents so that $\log(a \times b) = \log a + \log b$, we arrive at the Henderson-Hasselbach equation: $\log \frac{1}{(\text{H}^+)} = \log \frac{1}{K_a} + \log \frac{(\text{a}^-)}{(\text{Ha})}$. By definition, the right

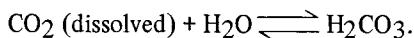
hand term, $\log \frac{1}{(\text{H}^+)}$, is pH. Again, recalling exponent laws, this may be expressed as the

negative log of the H^+ concentration. The log of $\frac{1}{K_a}$ is defined as pK, so the expression

can be rewritten to read; $\text{pH} = \text{pK} + \log \frac{(\text{a}^-)}{(\text{Ha})}$.

For the carbonic acid-bicarbonate system the equation will read: $\text{pH} = \text{pK} + \log \frac{(\text{HCO}_3^-)}{(\text{H}_2\text{CO}_3)}$

Experimentally, the pK for the bicarbonate system has been shown to be 6.10 and the bicarbonate concentration to be 24 m Moles/Liter. The denominator in the equation is a little more complex but extremely important to understand. We are able to substitute into the equation, (CO_2) for H_2CO_3 , since another reaction exists:



As should be noted, this formula indicated that the dissolved CO_2 concentration far exceeds the carbonic acid concentration at equilibrium. The magnitude of this is in the order of 800 times more dissolved CO_2 . Thus the amount of weak acid in the system is dependent upon the amount of CO_2 dissolved which can be calculated if one knows the partial pressure of the CO_2 (pCO_2) and the solubility coefficient of CO_2 which is a constant (S) which is equal to 0.03. The normal pCO_2 of arterial blood has been shown to be 40 mmHg, thus the denominator becomes $0.03 \times 40 = 1.2 \text{ m Moles/Liter}$. Finally, the Henderson-Hasselbach equation appears:

$$\text{pH} = 6.10 + \log \frac{24.0}{1.2}$$

$$\text{pH} = 6.10 + 1.30$$

$$\text{pH} = 7.40$$

Why do we pay so much attention to this carbonic acid-bicarbonate system? The answer is apparent when you consider that CO_2 is directly controllable by the ventilation of either the lungs or the oxygenators of our bypass systems.

Acid-Base Disturbances

When disturbances in acid-base balance occur, the body reacts to keep the pH as close to normal as possible. There are three mechanisms by which the body modifies these disturbances: buffer systems, respiratory compensation and renal compensation. Immediately, upon the introduction of excess acid, or base, the buffer

systems, outlined earlier, modify the change in pH. The second system that comes into play is the respiratory system. An increased hydrogen ion concentration causes hyperventilation which lowers the $p\text{CO}_2$ and thus decreases the carbonic acid concentration. Conversely, if the pH is elevated (decreased hydrogen ion concentration) respiration decreases, retaining CO_2 thus returning the pH toward normal. This compensation usually starts within a few hours of the disturbance. Finally, the kidneys start to modify acid-base changes within 6-12 hours and reach their maximal effect in several days. There are numerous mechanisms available to the kidneys including; acidification of urine by direct hydrogen ion secretion, retention of bicarbonate, secretion of ammonia (NH_3) into the tubules where it reacts with hydrogen ions to form ammonium which is excreted, increased potassium ion secretion which leads to a decreased hydrogen ion excretion, the secretion of titratable acids, etc.

These various mechanisms may act to return the pH to normal (complete compensation) or only toward normal (partial compensation).

Respiratory and Metabolic Disturbances

If we look at the ratio between bicarbonate and carbon dioxide in the Henderson-Hasselbach equation, $\frac{(\text{HCO}_3^-)}{(\text{CO}_2)}$, we can visualize what are considered the respiratory and metabolic components of the acid-base system. Since the denominator of the ratio is a function of respiration, this has become known as the respiratory component. A disturbance is respiration leading to an accumulation of CO_2 , thus in carbonic acid, with a decrease in pH is known as respiratory acidosis. Conversely, hyperventilation will lead to a decreased $p\text{CO}_2$ and respiratory alkalosis.

Changes in the numerator of the fraction can be due to either a direct change in the bicarbonate concentration i.e., renal conservation or to changes in bicarbonate concentration due to its participation in buffering reactions. These changes are labeled metabolic changes and lead to metabolic acidosis (decreased bicarbonate concentration) and metabolic alkalosis (increased bicarbonate concentration). This description of metabolic and respiratory acid-base disturbance would be simple but for the fact that combinations of the disturbance occur.

For examples, we shall only look at disturbances common to heart-lung bypass. We should remain aware though, that there are many other causes for these disturbances.

Pure respiratory acidosis can occur with heart-lung bypass when the oxygenator does not blow off as much CO_2 as the body produces and thus an accumulation occurs increasing the concentration of CO_2 in the blood. Typical arterial blood gas values would be: $\text{pH} = 7.25$, $p\text{CO}_2 = 67$ mmHg, $p\text{O}_2 =$ normal range. This type of disturbance is unusual in the commonly used blood-gas interface oxygenators since CO_2 diffuses through liquids much more rapidly than does oxygen. Thus, if the $p\text{O}_2$ is normal one usually does not observe an over accumulation of CO_2 . As we use more oxygenators that have membranes that may impede CO_2 removal or, as the gas efficiency of the bubble oxygenators improves so that we don't have to use such high volumes of gas flow, CO_2 retention may become more significant.

A far more common respiratory acid-base disturbance is respiratory alkalosis which occurs due to the ease with which CO_2 is removed from blood by the blood-gas interfacial type oxygenators. In order to maintain normal $p\text{CO}_2$ values in arterial blood, it is often necessary to add CO_2 to the gas mixture. If a profound, prolonged respiratory alkalosis is allowed to occur, a number of things can happen. These

include; a shift of the oxyhemoglobin dissociation curve to the left, making less oxygen available to the tissues at a given pO_2 , hypokalemia and vasoconstriction of cerebral blood vessels.

Metabolic disturbances can be due to the addition of acids or bases directly to the patient. An example of metabolic acidosis from oxogenous acid is the introduction of large amounts of citric acid from multiple additions of ACD or CPD blood units as fluid replacement during bypass or as priming solution. Metabolic alkalosis can result from the improper administration of bicarbonate or THAM.

The more subtle but more important cause of metabolic acidosis while on heart-lung bypass is the failure to deliver adequate oxygen to the tissues. At first glance, poor tissue oxygenation sounds like it should be labeled respiratory, and, in fact, the cause may be respiratory insufficiency. However, if we remember that we have reserved the term **respiratory** to disturbances leading to a change in the denominator of our acid-base fraction, the difference should be clear. A decrease in tissue oxygenation leads to the accumulation of many acid metabolic products from anaerobic glycolysis, not to an accumulation of CO_2 which requires oxygen for its production.

Other causes for metabolic acidosis caused by inadequate tissue oxygenation are; low pump output, arterio-venous shunting or localized ischemia and decreased oxygen carrying capacity due to hemodilution.

Typical arterial blood gas values in the case of metabolic acidosis might be: pH 7.25, pCO_2 40, pO_2 -normal.

To sum up the disturbances and to use the concept of respiratory and metabolic component disturbance, the following chart should be useful.

ARTERIAL

Disturbance	PCO_2 (mmHg)	HCO_3^- (mEq/L)	Denominator	Numerator	Ratio
Addition of H	40	16	-----	decrease	decrease
Increase of pCO_2	60	24	increase	-----	decrease
Add OH^-	40	30	-----	increase	increase
Add H and add HCO_3^-	40	30	-----	increase	increase
Add H and decrease CO_2	19	12	decrease	decrease	-----