acid-base metabolism

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An acid is a substance that will relinquish its hydrogen ion (H^+). Strong acids are those which relinquish a large percentage of their hydrogen ion, and weak acids, a small percentage of their hydrogen ion. Then the strength of an acid is characterized by its tendency to dissociate, which is expressed as a dissociation constant.

Ion Measurement

A concentration of hydrogen ion can be measured in a number of ways. We may elect to measure it in terms of grams or milligrams, or, as is more often the convention, in terms of moles. Water is seen to contain .0000001 mole/liter. The problems inherent in working with such a small number may be obviated by moving the decimal 9 places to the right. The new quantity is referred to as a nanomole. Water is seen to contain 100 nanomoles of hydrogen ion per liter of water.

However, we may also arbitrarily elect to use the logarithm of hydrogen ion concentration, and for water this is seen to be —7. By convention, the negative logarithm of the hydrogen ion concentration is selected, and it is this quantity that is called pH. The pH of water, then, is 7.0. Note that —6 is a larger number than —7; consequently, a pH of 6.0 is a more acidic solution than a pH of 7.0. The normal extracellular pH is between 7.38 and 7.42, in arterial blood, and in venous blood, approximately 7.35 to 7.40.

Carbon Dioxide

Every minute, the adult human organism, while at rest, produces between 200 to 300 cc of carbon dioxide per minute. This immediately diffuses into red blood cells, where in the presence of water and carbonic anhydrase carbonic acid is produced. This, in turn, relinquishes a hydrogen ion and a bicarbonate ion ($H^2CO_3 \rightarrow H^+ + HCO_3^+$). Note, then, that increased production of carbon dioxide, or a decreased elimination of carbon dioxide, will result in an increase in carbon dioxide content, which will then result both in increase in hydrogen ion and in increase in bicarbonate ion.

Conversely, a decrease in carbon dioxide production, or increased elimination by the lungs, results in a decrease in carbon dioxide content in the blood, with a resultant decrease in both hydrogen ion and bicarbonate ion. It is often not appreciated that some of the change in bicarbonate ion is related to alteration in lung function. The kidney and the gastrointestinal tract are the other organs that play a role in determining bicarbonate ion concentration. The relative contribution of the lung in bicarbonate ion alteration in disease states has been a subject of interest for many years, and the nomograms of Singer and Hastings [1] and Siggaard-Andersen and Astrup [2] are testimony to this fact. More will be said about this later.

Hydrogen Ion

It is the hydrogen ion concentration with which we are primarily concerned in an evaluation of the acid-base status of the patient. Let us examine further the chemical reaction, $CO_2 + H_2O \rightarrow H_2CO_3$, which, in turn, $\rightarrow H + HCO_3$. The law of mass action states that an increase in the reactants will result in an increase in the products. Therefore, an increase in carbon dioxide concentration will result in an increase in hydrogen ion concentration, and also a decrease in bicarbonate ion will result in an increase in hydrogen ion concentration.

The hydrogen ion concentration will be decreased by either a decrease in carbon dioxide concentration or an increase in bicarbonate concentration.

When the primary disturbance resulting in an alteration in hydrogen ion concentration relates to the pCO_2, the disturbance is said to be respiratory.

A disturbance in hydrogen ion concentration resulting primarily from an increase or a decrease in bicarbonate concentration is said to be metabolic.

Since the concentration of hydrogen ion can be influenced by changes on either side of the equation, it should be apparent that for any alteration on one side of the equation that results in an abnormality in hydrogen ion concentration, the change in pH may be minimized or compensated for by appropriate adjustments on the side of the equation away from the primary disturbance.

Primary Disturbance	Result	Disorder	Compensatory Mechanism
$\uparrow pCO_2$	$\uparrow H^+$ and $\uparrow HCO_3$	Respiratory acidosis	$\uparrow HCO_3$ (renal)
$\downarrow pCO_2$	$\downarrow H^+$ and $\downarrow HCO_3$	Respiratory alkalosis	$\downarrow HCO_3$ (renal)
$\downarrow HCO_3$	$\uparrow H^+$ and $\downarrow HCO_3$	Metabolic acidosis	$\downarrow pCO_2$ (hyperventilation)
$\uparrow HCO_3$	$\downarrow H^+$ and $\uparrow HCO_3$	Metabolic alkalosis	$\uparrow pCO_2$ (hypoventilation)*

Bicarbonate

Alterations in bicarbonate resulting from renal compensatory mechanisms should not be confused with those changes in bicarbonate resulting from an increase or a decrease in pCO_2. The nomograms of Singer and Hastings and of Siggaard-Andersen and Astrup are estimates of the amount of change in bicarbonate related solely to changes in pCO_2. The recent work of Schwartz et al.[3, 4, 5] should also be consulted relative to this subject.

Renal compensatory mechanisms for disturbances in acid-base balance are relatively slow, and the organisms requires a more rapid means of insuring acid-base homeostasis. Buffers constitute such a line of defense. The role of a buffer is exemplified by the action of sodium bicarbonate during acute lactic acidosis.

$$\left.\begin{array}{l} NaHCO_3 \rightarrow Na^+ + HCO_3^- \\ \qquad\qquad + \\ H\ lactate \rightarrow H^+ + lactate^- \end{array}\right\} \begin{array}{c} Na\ lactate + H_2CO_3 \\ \downarrow \\ H + HCO_3 \end{array}$$

Note that H lactate is a strong acid, that is, it yields a large percentage of its hydrogen ions. Carbonic acid is a weaker acid, that is, it yields a smaller percentage of its hydrogen atoms. Also, in the case of this particular buffer, we have the added advantage that carbonic acid can be rapidly excreted by the lungs as carbon dioxide.

Another example of a buffer is the substance, tris hydroxyaminomethane, better known as THAM. For discussion of the pharmacology of this substance. the reader is referred to the review by Nahas,[6] and also the discussion by Schwartz et al.[7]

Hemoglobin

We have seen that the most common source of acid in the body is the production of carbon dioxide, with the resultant production of carbonic acid. Available for the buffering of carbonic acid is hemoglobin, which exists in the red blood clell as KHb and HHb. The reaction that takes place is as follows:

$$\left.\begin{array}{l} H_2CO_3 \rightarrow H + HCO_3 \\ \qquad\qquad + \\ KHb \rightarrow K + Hb \end{array}\right\} \rightarrow \left\{\begin{array}{c} HHb + KHCO_3 \\ \downarrow \\ H + Hb \end{array}\right.$$

The resultant in this reaction, HHb, is a weaker acid than H_2CO_3, and so the desired result is achieved. There is an additional bonus which is realized because HHb combines less tenaciously with oxygen than does KHb, and, therefore, in the more acid milieu of the tissues oxygen becomes more available to the tissues. Contrariwise, in the lung, where carbon dioxide is eliminated, HHb reverts to KHb, which, in turn, is more receptive to the uptake of oxygen from the alveoli than is HHb.

The lung, by virtue of its role in CO_2 elimination, becomes the single most important organ in acid-base balance. Blood through its buffering of carbonic acid and the kidney are the other organs responsible for this narrow and jealously defended range of hydrogen ion concentration witnessed in the normal human organism.

* Not usually seen because of resulting hypoxemia, but may occur in infants if given oxygen when they are alkalotic, e.g., in pyloric stenosis.

References

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