Fundamentals of acid-base balance

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The author presents an overview of acid-base chemistry, discusses the physiological mechanisms employed in the homeostatic maintenance of body fluid pH, and examines some methods for assessing acid base balance. Examples of potential imbalances and compensatory responses are given.

Acid-base chemistry, like other pure physical sciences, is an essentially exact and mathematically predictable discipline. Yet, when placed in the realm of a dynamic, semi-steady state, biological system, acid-base balance becomes an applied science that seems almost whimsical by comparison. Nonetheless, the tenets of acid-base chemistry form the foundation from which acid-base balance in a physiological system must be viewed.\(^1\,^2\)

Acid-base chemistry

In the discussion following, the Brønsted-Lowry concept of acids and bases will be used with the realization that the terminology is sometimes "at odds" with that of classical chemistry.

Hydrogen ion (proton). The hydrogen ion in aqueous solution actually exists as the hydronium ion (H\(_3\)O\(^+\)), but is generally designated simply as H\(^+\), a convention to which this author will adhere.

Acid. An acid is a substance that will, in solution, dissociate (ionize) to form H\(^+\) and a so-called conjugate base (Equation 1).

\[
\begin{align*}
\text{(1) } & \text{HA (acid) } \Leftrightarrow \text{H}^+ \text{ (hydrogen ion) } + \text{A}^- \text{ (conjugate base)} \\
\end{align*}
\]

Acids are categorized in various ways depending upon the characteristics they exhibit when placed in solution.

Strong acid. A strong acid is one whose dissociation is comparatively complete, and a large number of free H\(^+\) are produced (Eq. 2).

\[
\begin{align*}
\text{(2) } & \text{HCl (strong acid) } \rightarrow \text{H}^+ \text{ (hydrogen ion)} + \text{Cl}^- \\
\end{align*}
\]

Weak acid. A weak acid undergoes incomplete dissociation and produces relatively few free H\(^+\) (Eq. 3).

\[
\begin{align*}
\text{(3) } & \text{H}_2\text{CO}_3 \text{ (weak acid) } \rightarrow \text{H}^+ \text{ (hydrogen ion) } + \text{HCO}_3^- \\
\end{align*}
\]

The designation of strong and weak acids should not be confused with the molar strength, or normality, of an acid. The latter terms refer to the chemical concentration of an acid, not to its ability to dissociate.

Another criterion of classification is whether an acid is volatile or fixed, a characteristic with definite physiological implications.

Volatile acid. A volatile acid, or its by-product (that is, carbon dioxide) can exist in the gaseous state (Eq. 4).

\[
\begin{align*}
\text{(4) } & \text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2 \text{ (volatile by-product)} \\
\end{align*}
\]

The reader should note that carbonic acid (\(\text{H}_2\text{CO}_3\)) is classified as both a weak acid (Eq. 3) and a volatile acid (Eq. 4). However, only the former con-
cerns dissociation of the acid, whereas the latter involves dehydration and does not result in production of free H\(^+\).

**Fixed (nonvolatile) acid.** A fixed acid is one which exists in solution only in the dissolved state. Examples of fixed acids are hydrochloric (Eq. 2) and phosphoric acids (Eq. 5) in which none of the components exist in a volatile form.

\[(5) \quad H_2PO_4^- \leftrightarrow H^+ + HPO_4^{2-}\]

The principal physiological ramification of fixed versus volatile forms is that fixed acids must be removed from the body in solution (usually urine) while volatile acids can be removed via the lungs.

**Base.** According to the Bronsted nomenclature, a base is any substance that will, in solution, accept (associate) a H\(^+\) (Eq. 6).

\[(6) \quad A^- \text{ (base)} + H^+ \text{ (hydrogen ion)} \leftrightarrow HA \text{ (conjugate acid)}\]

In the Brønsted system, a strong acid (Eq. 2) contains a weak base (Cl\(^-\)), whereas as weaker acid (Eq. 3) contains a stronger base (HCO\(_7\)).

**Buffer.** The mixture of a weak acid and its conjugate base in solution constitutes a buffer. Such a mixture confers upon a solution the capacity to minimize changes in H\(^+\) concentration in the face of either the addition or the removal of acids or bases. The conjugate base in the buffer mixture acts as a H\(^+\) acceptor when a strong acid is added to the solution (Eq. 7).

\[(7) \quad \text{Conjugate base} + \text{Strong acid} \leftrightarrow \text{Weak acid} + \text{Neutral compound}\]

In contrast, the weak acid in the buffer mixture acts as a H\(^+\) donor when a strong base is added to the solution (Eq. 8).

\[(8) \quad \text{Weak acid} + \text{Strong base} \leftrightarrow \text{Weak base} + \text{Neutral compound}\]

Buffer mixtures perform their function best when the concentration of the weak acid is equal to the concentration of its conjugate base. This situation exists when the [H\(^+\)] (brackets indicate concentration) equals the dissociation constant (K\(_A\)) of the mixture (Eq. 9).

\[(9) \quad K_A = \frac{[H^+][\text{Conjugate base}]}{[\text{Weak acid}]}\]

By rearrangement, it can be noted that when the [H\(^+\)] is equal to the K\(_A\), the members of the buffer mixture exist in equal concentrations and the capacity for donating H\(^+\) is equal to that for accepting H\(^+\) (Eq. 10).

\[(10) \quad [H^+] = \frac{K_A}{[\text{Conjugate base}]} \quad (\text{H}^+ \text{ acceptor})\]

**pH.** The [H\(^+\)] in biological fluids is very low when compared with other ion species (that is, plasma Na\(^+\) = 142 mEq/L as contrasted with plasma H\(^+\) = 0.0000398 or 3.98 \times 10^{-8} mEq/L = 3.98 \times 10^{-8} \text{ Eq/L}). Because of such unwieldy numbers, the term pH is almost universally used for physiological considerations of [H\(^+\)]. The prefix p indicates power (the mathematical exponent) of the [H\(^+\)]. pH is defined as the negative logarithm, to the base 10, of the [H\(^+\)] expressed as Eq/L (Eq. 11).

\[(11) \quad \text{pH} = -\log[H^+] = \log \frac{1}{[H^+]}\]

For example, the normal plasma pH is derived as follows (Eq. 12).

\[(12) \quad \text{pH} = -\log 3.98 \times 10^{-8} \text{ Eq/L} = \log \frac{1}{3.98 \times 10^{-8} \text{ Eq/L}} = 7.40\]

Typical pH values dealt with in physiological systems and their corresponding [H\(^+\)] are given in Table 1.

<table>
<thead>
<tr>
<th>pH</th>
<th>[H(^+)] (Eq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.80</td>
<td>1.58 \times 10^{-7}</td>
</tr>
<tr>
<td>7.00</td>
<td>1.00 \times 10^{-7}</td>
</tr>
<tr>
<td>7.20</td>
<td>6.31 \times 10^{-8}</td>
</tr>
<tr>
<td>7.35</td>
<td>4.46 \times 10^{-8}</td>
</tr>
<tr>
<td>7.45</td>
<td>3.55 \times 10^{-8}</td>
</tr>
<tr>
<td>7.60</td>
<td>2.51 \times 10^{-8}</td>
</tr>
<tr>
<td>7.80</td>
<td>1.58 \times 10^{-8}</td>
</tr>
</tbody>
</table>
The logarithmic nature of the pH scale in Table 1 is borne out by the following considerations: (a) a 1-unit change in pH (that is, 6.80-7.80) represents a 10-fold change in [H+] ; (b) a 0.2-unit change in pH at the lower end of the range (that is, 6.80-7.00) represents a change in [H+] of 5.8 x 10^-8 Eq/L, whereas (c) a 0.2-unit change in pH at the upper end of the scale (that is, 7.60-7.80) represents a change in [H+] of only 9.3 x 10^-9 Eq/L, or approximately one-sixth of that in (b).

The values in Table 1 also show the inverse relationship between pH and [H+]. That is, the greater the [H+] in the solution (acidic), the lower the pH; the lesser the [H+] (basic or alkaline), the higher the pH.

The use of the negative logarithm of [H+] for the expression of pH can be extended to buffer mixtures such that Eq. 10 becomes that shown in Eq. 13.

\begin{align*}
\text{eq}(13) \quad -\log [H^+] & = -\log K_A + \frac{[\text{Weak acid}]}{[\text{Conjugate base}]} \\
\end{align*}

Further restructuring of Eq. 13 results in the expression commonly known as the Henderson-Hasselbalch equation (Eq. 14).

\begin{align*}
\text{eq}(14) \quad \text{pH} & = \text{pK}_A + \log \frac{[\text{Conjugate base}]}{[\text{Weak acid}]} \\
\end{align*}

Extensive use will be made later of the concepts incorporated by Eq. 14.

**Acid-base physiology**

In man and other mammals, the by-products of metabolism are typically acidic; and acid-base homeostasis is maintained by the concerted activity of the following: (1) body fluid buffers, (2) lungs, and (3) kidneys.

**Body fluid buffers.** The various buffer mixtures contained within the body fluids provide for an immediate mitigation of pH changes in the face of potentially hazardous gains or losses of H+. The body fluids contain numerous buffer pairs, the majority of which are accounted for by bicarbonate/carbonic acid, phosphate/phosphoric acid, and proteinate/protein mixtures. In such a buffer system containing several components, each with a distinct dissociation constant (K_A) or pK_A, a change in [H+] or pH in the fluid will affect all the buffer components in a predictable manner. This relationship can be seen through an extension of Eq. 14 to incorporate the specific buffer pairs cited in Eq. 15.

\begin{align*}
\text{eq}(15) \quad \text{pH} & = \text{pK}_A \frac{[\text{HCO}_3^-]}{[H_2CO_3]} + \text{pK}_A \frac{[\text{HPO}_4^{2-}]}{[H_2PO_4^-]} \\
& = \frac{[\text{PF}]}{[\text{HPF}]} \\
\end{align*}

Therefore, since a change in the pH of the system affects the individual ratios of the specific buffer pairs in a proportional, albeit pK_A dependent fashion, one need analyze only the components of a single buffer pair in order to gain an appreciation of the acid-base status.

The bicarbonate/carbonic acid ratio is the one most widely measured because it not only reflects the acid-base status of the body but it also provides an evaluation of the performance levels of the lungs and kidneys.

**Lungs.** Cells performing aerobic metabolic reactions produce CO_2 which diffuses into plasma and then into red blood cells where, aided by the enzyme carbonic anhydrase, it is rapidly hydrated to form H_2CO_3 (Eq. 4) until equilibrium conditions are satisfied. The H_2CO_3 undergoes dissociation (Eq. 3) as equilibrium conditions dictate (Eq. 16).

\begin{align*}
\text{eq}(16) \quad \text{CO}_2 + \text{H}_2\text{O} \xrightarrow{\text{carbonic anhydrase}} \text{H}_2\text{CO}_3 \xrightarrow{\text{anhydrase}} \text{H}^+ + \text{HCO}_3^- \\
\end{align*}

As cells produce CO_2, the reaction in Eq. 16 is driven toward the right, so that the H+ level increases in the blood. When that blood passes through the lungs, CO_2 is removed and the reaction shifts back toward the left, again lowering the [H+]. Thus, during exhalation, the lungs remove gaseous CO_2 (volatile acid) from plasma, which in turn affects the entire bicarbonate/carbonic acid buffer mixture.
In instances of an overabundance of CO₂ and/or H⁺, the respiratory control systems are stimulated, hyperventilation ensues, and the removal of CO₂, and hence H⁺, is augmented. The reverse occurs, that is, hypoventilation, when a CO₂ deficit exists.

These mechanisms performed by the lungs, though not instantaneously responsive like the body fluid buffers, are quite rapid and generally operate within a time frame of minutes.

Kidneys. In contrast to the lungs, the kidneys remove fixed (nonvolatile) acids from the body fluids; however the daily urinary excretion of acid falls far short of that removed by the lungs in the form of CO₂. The primary role of the kidneys in acid-base balance is to conserve bicarbonate (HCO₃⁻) and to replenish depleted HCO₃⁻ reserves when necessary. This role is accomplished by various mechanisms which are closely allied with the excretion of H⁺ in urine.

Both the glomerular filtrate and the peritubular capillary blood supply to the nephron structures contain CO₂ which readily diffuses into the cells of the tubular wall. The CO₂ within those cells proceeds rapidly through the reaction depicted by Eq. 16, whereupon H⁺ and HCO₃⁻ are formed. The tubular cells are so designed that the newly formed H⁺ is actively secreted into the urine and subsequently excreted; the HCO₃⁻ is returned to the blood. Thus, for each H⁺ expelled into the urine, a HCO₃⁻ is retained within the body fluids. The fate of the H⁺ secreted into the urine determines whether the HCO₃⁻ entering the blood represents conservation of existing HCO₃⁻, or the production of additional HCO₃⁻. Examples of the possible fates of secreted H⁺ and the nature of the retained HCO₃⁻ are given in Table 2.

As indicated in Table 2(A), if the secreted H⁺ combines with filtered HCO₃⁻, the removal of H⁺ from the body is effected, but no net gain of HCO₃⁻ is realized. On the other hand, if the secreted H⁺ is incorporated into either titratable acid or ammonium ion, as in Table 2(B) and (C), both a net gain of HCO₃⁻ and a removal of H⁺ are achieved.

Under normal conditions, the kidneys retain virtually all of the filtered HCO₃⁻, while excreting a mildly acidic urine. However, when an acid load (or a base deficiency) is imposed upon the body, normal kidneys can produce a strongly acidic urine to rid the body of H⁺, while manufacturing substantial amounts of HCO₃⁻ to aid in buffering the excess acid. Conversely, kidneys confronted by a base excess (or acid deficiency) allow comparatively large quantities of HCO₃⁻ to "spill" into the urine while secreting relatively few H⁺.

Acid-base regulation by the kidneys is highly precise, but when compared with that of the respiratory system is

<table>
<thead>
<tr>
<th>Substance Secreted</th>
<th>Substance Filtered</th>
<th>Product Formed in Urine &amp; Retained in Body Fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) H⁺ HCO₃⁻</td>
<td></td>
<td>H₂O (and CO₂) HCO₃⁻ (conserved)</td>
</tr>
<tr>
<td>(B) H⁺ HPO₄²⁻</td>
<td></td>
<td>H₂PO₄⁻ (titratable acid) HCO₃⁻ (added)</td>
</tr>
<tr>
<td>(C) H⁺ (and NH₃) NH₄⁺</td>
<td></td>
<td>NH₄⁺ (ammonium ion) HCO₃⁻ (added)</td>
</tr>
</tbody>
</table>
quite slow, requiring hours or even days to offset severe challenges.

**Assessment of the acid-base status**

Arterial blood gas and pH measurements performed routinely in many clinical settings provide the data by which the buffer systems may be evaluated, through the use of Eq. 14 (Henderson-Hasselbalch), as applied specifically to the bicarbonate/carbonic acid ratio as shown in Eq. 17.

\[
\text{pH} = 6.1 + \log \left( \frac{\text{HCO}_3^-}{\text{H}_2\text{CO}_3} \right)
\]

If the ratio of \([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]\) is equal to 20 (\(\log 20 = 1.3\)), the arterial pH is normal (that is, 7.40).

Of the three unknown values (pH, \([\text{HCO}_3^-]\) and \([\text{H}_2\text{CO}_3]\)) in Eq. 17, only two need be measured in order to determine the third. That determination can be performed by calculation or by using a nomogram (discussed later), acid-base “slide-rules”, or other such readily available devices. With the notable exception of pH, the parameters in Eq. 17 may not be measured *per se*, but rather may be derived from other blood gas values. For example, the \([\text{H}_2\text{CO}_3]\) is easily determined from the arterial \(\text{CO}_2\) tension (Eq. 18).

\[
\text{H}_2\text{CO}_3 \text{ (mM/L)} = 0.03 \times \text{PaCO}_2 \quad \text{(torr = formerly mmHg)}
\]

The designation \(\text{H}_2\text{CO}_3\) as derived by Eq. 18 actually includes both carbonic acid (hydrated \(\text{CO}_2\)) and dissolved \(\text{CO}_2\), a fact which does not alter the utility of the expression.

Another commonly measured parameter is that of \([\text{Total CO}_2]\) which is the sum of \([\text{HCO}_3^-]\) and \([\text{H}_2\text{CO}_3]\). Therefore, \([\text{HCO}_3^-]\) may be derived as follows (Eq. 19):

\[
\text{HCO}_3^- \text{ (mM/L)} = \text{Total CO}_2 \text{ (mM/L)} - 0.03 \times \text{PaCO}_2 \text{ (torr)}
\]

It thus becomes possible to rewrite Eq. 17 as shown below (Eq. 20) to broaden its utility without impairing its conceptual accuracy.

\[
\text{pH} = 6.1 + \log \left( \frac{\text{Total CO}_2}{0.03 \times \text{PaCO}_2} \right)
\]

Thus, the blood-gas parameters in Eq. 20 can be used in acid-base evaluations, but for the sake of simplicity, subsequent considerations will hold to the \([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]\) expression incorporated in Eq. 17.

**Normal conditions.** Mean values and normal ranges of the parameters previously discussed are given in Table 3. Also included is the admonition that such tables “chiseled in stone” decrease the buoyancy, so to speak, of those adhering too closely.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{PaCO}_2)</td>
<td>40 (35-48) torr</td>
</tr>
<tr>
<td>(\text{H}_2\text{CO}_3)</td>
<td>1.2 (1.1-1.4) mM/L</td>
</tr>
<tr>
<td>(\text{HCO}_3^-)</td>
<td>24 (23-26) mM/L</td>
</tr>
<tr>
<td>Total (\text{CO}_2)</td>
<td>25.2 (24.1-27.4) mM/L</td>
</tr>
<tr>
<td>pH</td>
<td>7.40 (7.35-7.45)</td>
</tr>
<tr>
<td>([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3])</td>
<td>20 (18-22)</td>
</tr>
</tbody>
</table>

**Abnormal conditions.** The ultimate criterion used for determination of the acid-base status is pH. When the pH of the extracellular fluid is found to be abnormal, the measurement of one or more of the other parameters in Table 3, along with adept clinical observation and judgment, promotes an understanding of the genesis of and the physiological responses to the altered pH. With that understanding, the appropriateness of required therapeutic measures can be determined and, equally important, unnecessary or inappropriate therapy can be avoided.

**Acidosis.** Acidosis is defined as any condition in which the pH of arterial blood is below 7.35. Such a situation exists when the \([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]\) ratio is less than approximately 18:1. Recall that the ratio is 20:1 when the pH = 7.40.

**Alkalosis.** Alkalosis exists when the arterial pH exceeds 7.45 and the \([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]\) ratio is greater than 22:1.
The terms acidemia and alkalemia sometimes supplant the more conventional acidosis and alkalosis, respectively, to indicate pH abnormalities within the blood specifically. However, despite the fact that pH determinations are generally restricted to blood (or plasma), the actual imbalances rarely, if ever, are.

The discussion that follows deals with the nomenclature by which the various disorders of acid-base balance may be classified in accordance with the primary disturbance(s) that exist.

Respiratory imbalances. An abnormal pH due to alterations of those parameters controlled primarily by the lungs, (that is, $[\text{H}_2\text{CO}_3]$ of $\text{PaCO}_2$) is called respiratory acidosis or alkalosis. In the condition of respiratory acidosis, the primary disturbing influence is a carbonic acid excess; in that of respiratory alkalosis, a carbonic acid deficit. It must be understood that a carbonic acid excess (or deficit) does not necessarily mean more (or less) carbonic acid than normal; rather, the terms indicate a divergence from the normal 20:1 ratio of $[\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]$ with the primary disturbance being an altered $[\text{H}_2\text{CO}_3]$.

Metabolic (non-respiratory) imbalances. An abnormal pH due to an alteration in the bicarbonate component of the $[\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]$ buffer system is referred to as metabolic acidosis or alkalosis. The term metabolic acidosis indicates a primary disturbance known as a base deficit (or negative base excess, a needlessly confusing designation in this author's view); metabolic alkalosis connotes a disturbance termed base excess. Once again, a proper understanding of the terminology is essential. A base deficit is indicative of a $[\text{HCO}_3^-]$ this is too low for the existing $[\text{H}_2\text{CO}_3]$, such that the low $[\text{HCO}_3^-]$ is the primary disturbing influence in lowering the pH. The mere finding of a $[\text{HCO}_3^-]$ below the normal range does not, of necessity, reveal a base deficit.

Examples using the foregoing terminology appear in Table 4.

A diagrammatic assessment of acid-base balance

The following pictorial appraisals of normal and abnormal acid-base status may appear at first to be only diabolical machinations, but they allow a visual inspection of both imbalances and compensatory responses. Figure 1 depicts the pH values (6.90-7.80) of extracellular body fluids which are compatible with life, albeit only for brief periods when the pH falls within the so-called “danger zones”. In the danger zones, the pH is such that cellular activity is severely compromised and, even though physiological compensation may be ongoing, the organism may succumb if outside remedial action is not taken.

In Figure 1 and those to follow, the particular pH is indicated by the triangular marker whose position is determined by the relative amounts of $\text{H}_2\text{CO}_3$ (that is, $\text{PaCO}_2 \times 0.03$) and $\text{HCO}_3^-$ as indicated by the arrows along the ver-

<table>
<thead>
<tr>
<th>pH</th>
<th>$\text{HCO}_3^-$ (mM/L)</th>
<th>$\text{H}_2\text{CO}_3$ (mM/L)</th>
<th>$[\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]$</th>
<th>Primary disturbance</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.20</td>
<td>31</td>
<td>2.4</td>
<td>$\swarrow 13$</td>
<td>Carbonic acid excess</td>
<td>Respiratory acidosis</td>
</tr>
<tr>
<td>7.20</td>
<td>12</td>
<td>0.9</td>
<td>$\swarrow 13$</td>
<td>Base deficit</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>7.50</td>
<td>22</td>
<td>0.9</td>
<td>$\swarrow 25$</td>
<td>Carbonic acid deficit</td>
<td>Respiratory alkalosis</td>
</tr>
<tr>
<td>7.50</td>
<td>38</td>
<td>1.5</td>
<td>$\swarrow 25$</td>
<td>Base excess</td>
<td>Metabolic alkalosis</td>
</tr>
</tbody>
</table>
Figure 1

Figure 2
Respiratory acidosis or H₂CO₃ excess (—); partial compensation (—--).

Figures 2-7, the primary acid-base imbalance is designated by the solid pH-indicator triangle and by the solid [H₂CO₃] and [HCO₃⁻] arrows. The superimposed broken lines indicate the effects of compensatory physiological activity and/or appropriate corrective therapy in returning the pH toward normal.

Figure 2 shows a condition in which the pH is below normal and the primary disturbance is one of H₂CO₃ excess (that is, the [H₂CO₃] is farther from the normal range than is the [HCO₃⁻]). Therefore, the condition is classified as respiratory acidosis (such as, hypoventilation), due to the inability of the lungs to rid the body of CO₂. The broken lines show that the pH is returned toward normal by an increased [HCO₃⁻]. Note that with an increased [HCO₃⁻], a further increase in [H₂CO₃] also occurs as dictated by Eq. 16.

However, because of the equilibrium characteristics of Eq. 16, the relative increase in [HCO₃⁻] exceeds that in [H₂CO₃], and the [HCO₃⁻]/[H₂CO₃] ratio approaches 20. The elevated [HCO₃⁻] can be realized either by the kidneys increasing the HCO₃⁻ reserves or by the therapeutic administration of a HCO₃⁻ containing solution. Whatever the actual case, the compensated state in which both the [H₂CO₃] and the [HCO₃⁻] are elevated must be maintained in order to keep the pH at or near normal, pending the correction of the underlying pulmonary CO₂ retention. Many causes of respiratory acidosis

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Figure 3 depicts a H$_2$CO$_3$ deficit as the primary disturbance (such as, hyperventilation), with the resultant condition being respiratory alkalosis. The partial compensation indicated is accomplished via a reduction in [HCO$_3^-$] by urinary excretion, such that the [HCO$_3^-$]/[H$_2$CO$_3$] ratio moves toward 20. A reduction in the [H$_2$CO$_3$] would also occur during compensation per Eq. 16, but the change is slight and largely offset by the reduced stimulus to hyperventilation as a result of the further depression of PaCO$_2$. It should be realized that, in many instances, hyperventilation has an emotional etiology and can be corrected by rebreathing and reassurance before the renal mechanisms are invoked to any large extent. Overzealous use of a respirator can induce an iatrogenic respiratory alkalosis, which is easily corrected, but better prevented.

A primary base [HCO$_3^-$] deficit is illustrated in Figure 4. The physiological compensatory activity is hyperventilation which lowers the [H$_2$CO$_3$] to a level more commensurate with that of the [HCO$_3^-$]. This form of compensation is only partially complete because the lowered PaCO$_2$ removes the respiratory stimulus required for continued hyperventilation. Thus, complete compensation must await either the renal repletion of the HCO$_3^-$ stores or the administration of exogenous HCO$_3^-$. Metabolic acidosis can arise from the direct loss of HCO$_3^-$ (for example, diarrhea with excessive loss of alkaline intestinal fluids in the stool) or from the depletion of the HCO$_3^-$ stores for the buffering of strong acids (for example, the keto-acids of uncontrolled diabetes mellitus).

In Figure 5, a primary base [HCO$_3^-$] excess resulting in metabolic alkalosis is shown along with the compensatory response which will occur if both pulmonary (hypoventilation) and renal (HCO$_3^-$ excretion) mechanisms are invoked. Again, pulmonary compensation is incomplete due to the respiratory drive provided by carbon dioxide; hypoventilation can be maintained only until the increasing PaCO$_2$ begins to stimulate respiration. Metabolic alkalo-
Metabolic alkalosis or base excess (—); partial compensation (---). 

Figure 5

Metabolic alkalosis or base excess (—); partial compensation (---).

Figure 6

Respiratory and metabolic acidosis (—); partial correction (---).

Figure 7

Respiratory and metabolic alkalosis (—); partial correction (---).

sis may be induced directly (such as, by ingestion of too much bicarbonate of soda) or indirectly by excessive loss of acid from the body (such as, prolonged gastric lavage).

In the two examples that follow, the acid-base imbalances portrayed have a primary disturbance in both the respiratory and the metabolic components. Fortunately, such dual, or mixed, imbalances are less common than the more clear-cut examples previously mentioned. Yet, when mixed imbalances do occur, diagnostic aplomb must prevail and especially aggressive therapeutic action may be required.

Figure 6 shows a condition of severe acidosis having a dual etiology of concurrent $H_2CO_3$ excess and base ($HCO_3^-$) deficit. This problem could occur, for example, in an individual who suffers from both chronic obstructive lung disease and acidosis of renal origin. In this somewhat horrifying predicament, both potential compensatory routes are dysfunctional, and corrective measures must be instituted clinically. The illustration shows the effect of the administration of exogenous $HCO_3^-$ in returning the pH to a less ominous level and allowing a somewhat more thought-ful titration of the patient back to normalcy.

Since the correction of the underlying conditions in this example are problematic at best, the treatment of the acid-base imbalance just described is
a stop-gap measure only. Heroic measures, far beyond the purview of this discussion, would be required to obviate repeated recurrences of the acidosis.

Figure 7 represents a mixed alkalois encompassing both a $H_2CO_3$ deficit and a base ($HCO_3^-$) excess. The likelihood of this condition arising is probably more remote than the other examples discussed because of the low probability of causative factors (such as, hyperventilation and excess $HCO_3^-$ ingestion) existing simultaneously. However, such a condition can and does occur.

The compensatory responses shown in Figure 7 are consistent with the effects of simultaneous hypoventilation (or rebreathing) and an increased urinary excretion of $HCO_3^-$. If these routes are unavailable or inadequate under the circumstances, administration of an agent such as an ammonium chloride ($NH_4Cl$) solution will have a similar effect, since the addition of $NH_4Cl$ to the body fluids is tantamount to adding strong acid to the body fluids (Eq. 21).

\[(21) \quad NH_4^+ + Cl^- \rightarrow H^+ + Cl^- + NH_3 \text{ (ammonia)} \quad \text{(in solution)} \quad \text{(metabolized)}\]

The excess $HCO_3^-$ is used for the buffering of the added acid and the $[H_2CO_3]$ is thereby increased (see Eq. 16).

It should be evident, at this point, that corrections of acid-base imbalances—whether they be physiological responses, clinical applications, or both—can be life-preserving occurrences; but, the corrections are lasting only if those factors that initiated the imbalances are rectified.

Other representations of acid-base balance

This section presents two widely-used and well-established representations of the acid-base status both for purposes of comparison with the previous discussion and for further elucidation of the interaction of the parameters with which we have dealt.

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**Figure 8**

The pH-bicarbonate diagram showing acid-base paths *in vivo*. (Reproduced with the permission of Dr. Davenport and The University of Chicago Press.)

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Davenport diagram. Figures 8 and 9 show the diagram devised by Dr. H. W. Davenport\textsuperscript{9,10} incorporating the parameters of arterial pH, plasma $[\text{HCO}_3^-]$ and $P_{\text{CO}_2}$. An attempt by this author to proffer a description of the diagram and its nuances comparable to that given by Davenport\textsuperscript{9} would be fanciful at best, destructive at worst. A brief description will suffice.

The normal point in Figure 9 (point A in Figure 8) indicates a pH of 7.40, $\text{HCO}_3^-$ of 24 mM/L and $P_{\text{CO}_2}$ of 40 mmHg (torr). The slope of the so-called "normal buffer line" passing through the normal point is determined by the buffering capacity of the fluid being studied (such as, blood). Any abnormal pH value for which the corresponding $[\text{HCO}_3^-]$ lies on the normal buffer line is of respiratory origin (Figure 9, points A and D). Any abnormal pH value for which the $[\text{HCO}_3^-]$ lies on the $P_{\text{CO}_2} = 40$ mmHg line, called an "isobar", is of metabolic origin (Figure 9, points G and I).

All the points lying above the normal buffer line represent a base excess; those below, a base deficit. The vertical distance between any abnormal point and the normal buffer line represents the magnitude of the base excess or deficit in mM/L. All the points lying to the left of the $P_{\text{CO}_2} = 40$ mmHg iso-

Table 5

<table>
<thead>
<tr>
<th>Points on Davenport diagram (Figure 9)</th>
<th>Figure number</th>
<th>Primary condition</th>
<th>Compensatory response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Normal point (none)</td>
<td>Normal point</td>
<td>(none)</td>
<td></td>
</tr>
<tr>
<td>2 A</td>
<td>A</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>3 D</td>
<td>D</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>4 G</td>
<td>G</td>
<td>H</td>
<td></td>
</tr>
<tr>
<td>5 I</td>
<td>I</td>
<td>J</td>
<td></td>
</tr>
<tr>
<td>6 K (not shown)</td>
<td>6</td>
<td>K (not shown)</td>
<td></td>
</tr>
<tr>
<td>7 L (not shown)</td>
<td>7</td>
<td>L (not shown)</td>
<td></td>
</tr>
</tbody>
</table>

*Points C and F in Davenport diagram do not appear in the examples.
bar represent a carbonic acid excess; those to the right, a carbonic acid deficit. The actual placement of a point on the diagram determines whether the indicated condition is primary or compensatory.

Table 5 corresponds the examples in the previous section (Figures 1-7) to the points designated by the letters on the Davenport diagram (Figure 9).10

**Siggaard-Andersen alignment nomogram**. The Siggaard-Andersen representation of the acid-base status in Figure 10 is presented without any specific examples, although the reader can apply the values from the examples detailed.
earlier and readily see the utility of the nomogram. The nomogram provides a means for rapidly determining the numerical values of various acid-base parameters following the measurement of any two of those shown in Figure 10.

The mathematical basis for the nomogram is the Henderson-Hasselbalch expression (Eq. 14), but it also incorporates the base excess scale which can be applied if the hemoglobin concentration in the blood is known. That information is necessary because the buffering capacity of the blood is affected by the protein (primarily hemoglobin) component. The idea advanced in Eq. 15 applies in the relative sense, but the magnitude of the base excess requires an absolute value for true quantification. It should be noted that the term “base excess” is used exclusively in Figure 10 and is designated as either positive or negative, the latter being synonymous with the term “base deficit”.

The nomogram has found wide usage in hospital and clinical laboratories because a simple straight-edge applied across two measured values will provide the user with the other pertinent values and no calculations are required. The advantages of the nomogram are strictly utilitarian, and it is presented here for information and not didactic purposes.

Notes on other aspects of acid-base balance

This section touches upon some of the secondary factors that play a role in acid-base problems, but whose detailed considerations exceed the scope of this article.

Potassium. If the buffer systems (such as, proteins) of the intracellular fluid are to operate when the pH of extracellular fluid is altered, the cells must take up or extrude H⁺ which must, in turn, be exchanged for other positively charged ions in order to maintain electroneutrality. Potassium, one of the cations involved in this ionic redistribution, performs highly critical functions in the body and its plasma concentration is zealously regulated. When potassium shifts occur in response to acid-base disturbances, the body readjusts the plasma potassium level by any available means as rapidly as possible.

Thus, plasma potassium measurements may be poor indicators of total body potassium stores during acid-base disturbances. Moreover, a too rapid correction, or overcorrection, of an acid-base problem may induce a dangerous reversal of the compartmental potassium flux that accompanied the initial buffering operation.

Sodium. Sodium, like potassium, undergoes a redistribution for purposes of utilizing the total buffering capacity of the body, but a change of a few milliequivalents in the plasma sodium level does not have the devastating effect that would occur with a comparable change in potassium. However, sodium levels should be monitored closely where acid-base problems are concerned. For example, in the treatment of acidosis, HCO₃⁻ is generally given as a sodium salt, thereby affecting not only acid-base, but also sodium balance.

Diuretic agents. Many diuretics, due to their modes of action, can bring about or aggravate an alkalotic condition. Most of the more potent diuretics increase the loss of sodium chloride, potassium and H⁺ in the urine. That, along with a high level of HCO₃⁻ retention by the kidneys, sets the stage for the development of alkalosis with many types of diuretic therapy.

Summary

The concepts of acid-base chemistry, buffer systems, and the regulation of hydrogen ion concentration in the body are discussed. The metabolic production of acidic substances by cells presents an ongoing challenge to the homeostatic mechanisms of the organism. The lungs and the kidneys serve as the mainstays of pH regulation, but if those routes become dysfunctional or are overwhelmed by inordinate amounts
of acids or bases, the system will fail. The ability to rapidly recognize and to appropriately interpret an impending failure of the system due to an acid-base disturbance is essential to the armamentarium of the well-prepared health professional.

REFERENCES

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