AN ASSESSMENT OF ACID–BASE BALANCE

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An assessment of the acid–base state of blood and, by inference, that of the body, is important in recognizing the effects of many disorders of respiratory, cardiovascular and metabolic function, in assessing their severity and in determining any necessary therapy. In making an assessment many students may now become confused for two reasons. First, the introduction of the S.I. system of units has changed much familiar terminology. Second, the recent developments in technology (Blackburn, 1978; this issue, p. 51) have led to machines generating a whole series of acid–base “indices” from, essentially, two primary measurements. These indices aim to help assess the metabolic component of any disorder, but their multiplicity might suggest that none is entirely satisfactory.

The assessment presented in this paper looks at the common disorders of acid–base balance to see what pattern will be found using only the two primary measurements made in most systems—the pH and the carbon dioxide tension ($P\text{CO}_2$). If students of acid–base balance understand these then more complex disorders will be more easily assessed. However, initially it is worthwhile emphasizing how the acid–base state of blood is regulated in the body. Knowledge of the regulation is essential for any assessment to be meaningful.

REGULATION OF THE ACID–BASE STATE OF BLOOD

Terminology

An acid is a substance which tends to lose hydrogen ions and a base a substance which tends to gain them (Bronsted, 1923). In aqueous solutions hydrogen ions exist in combinations with water molecules; no harm results from ignoring this and concentrating attention only on hydrogen ions. Strong acids easily lose hydrogen ions giving high concentrations in aqueous solutions: the greater the concentration of hydrogen the greater the acidity of the solution. The acidity of any solution is measured by determining its pH value. pH has no S.I. unit and the pH scale is defined with reference to a number of standard solutions. These can be prepared in any laboratory in terms of S.I. units—weights of substance per volumes of solution. In an ideal (chemical) world the pH of a solution is related to the hydrogen ion concentration in the following way:

$$\text{pH} = -\log [H^+]$$

In the real non-ideal world (especially as seen in biological fluids) this relationship may not hold exactly and it should be remembered that the scale is in pH units. But the transformation from pH to hydrogen ion concentration is easily made; some prefer to work in units of hydrogen ion concentration:

$$[H^+] = 10^{-\text{pH}}$$

This transformation is only a mathematical game. Some numbers relevant to blood are given in table I.

<table>
<thead>
<tr>
<th>pH (units)</th>
<th>$H^+$ (nmol)</th>
</tr>
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<tbody>
<tr>
<td>3</td>
<td>1 000 000</td>
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<tr>
<td>6</td>
<td>1000</td>
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<tr>
<td>7</td>
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<td>7.1</td>
<td>80</td>
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<tr>
<td>7.4</td>
<td>40</td>
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<td>7.7</td>
<td>20</td>
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<tr>
<td>8</td>
<td>10</td>
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<tr>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

The vital number to remember is that a change of pH of 0.3 units represents a twofold change in hydrogen ion concentration.

Regulation of blood acid–base state

In most circumstances in normal health the pH of blood is well regulated and does not vary much from 7.4 units. In 1908 Henderson appreciated exactly how this happened. There are three main defence mechanisms.

Buffers. A buffer is a mixture of a weak acid and its conjugate base such as carbonic acid and bicarbonate ions. The buffers present in blood are the carbonic acid–bicarbonate pair, and the phosphates and the proteins present in plasma and red cells. The presence
of such mixtures acts to minimize any change in pH that would otherwise occur with the addition of strong acids or bases. How does this happen? Imagine a closed flask containing water. Water is a weak acid and has a pH value of 7 at room temperature (and 6.8 at body temperature). Add to the flask sufficient strong acid (such as hydrochloric acid) to give a concentration of 10 mmol. The acid dissociates completely, the resultant hydrogen ion concentration is 10 mmol and the pH 2, that is a change of 100 000-fold in acidity. Now imagine that the closed flask initially had dissolved in the water some 24 mmol litre⁻¹ of sodium bicarbonate and 1.2 mmol of carbonic acid. In such a mixture the following reactions can occur:

\[
\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-
\]

At equilibrium the Law of Mass Action applies and states that the product of the concentrations of hydrogen ions and bicarbonate ions divided by the concentration of carbonic acid will be constant. Henderson (1908) rearranged this equation to allow calculation of the hydrogen ion concentration:

\[
[H^+] = K \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]}
\]

where \(K\) is the dissociation constant and at body temperature has a value of 800 nmol. Hasselbalch (1916) used a transformation to turn Henderson’s equation into one with the pH nomenclature:

\[
\text{pH} = pK + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}
\]

In our example the hydrogen ion concentration is 40 nmol and the pH 7.4. Now imagine the addition of 10 mmol litre⁻¹ of hydrochloric acid and remember the flask is closed and carbon dioxide cannot escape. The ensuing reaction can be summarized:

\[
\text{HCl} + \text{HCO}_3^- \rightarrow \text{H}_2\text{CO}_3 + \text{Cl}^-
\]

and overall

\[
\text{HCl} + \text{H}_2\text{CO}_3 + \text{H}_2\text{CO}_3 \rightarrow \text{Cl}^+ + \text{HCO}_3^- + \text{H}_2\text{CO}_3
\]

10 mmol 24 mmol 1.2 mmol 10 mmol 14 mmol 11.2 mmol

Henderson’s and Hasselbalch’s equation now allows us to calculate the new hydrogen ion concentration and pH. These are 640 nmol litre⁻¹ and 6.20 respectively. The presence of the buffering carbonic acid and bicarbonate ions has reduced the change in acidity considerably; by a factor of 10 000.  

**Carbon dioxide.** The next system in numerical importance by which the body maintains a nearly constant pH value is the maintenance of a nearly constant carbon dioxide tension. Carbonic acid dissociates to give carbon dioxide gas which is removed by ventilation of the lungs. The body is an open system and the gaseous respiratory exchange helps maintain the constancy of pH. Using the example already given, if our flask of bicarbonate ions and carbonic acid maintains a constant \(P_{\text{CO}_2}\) of 5.3 kPa and hence a carbonic acid concentration of 1.2 mmol litre⁻¹ then the addition of the 10 mmol litre⁻¹ of strong acid causes the evolution of 10 mmol of carbon dioxide. The hydrogen ion concentration and pH are given by the ratios of 14 mmol of bicarbonate and 1.2 mmol of carbonic acid; they are 69 nmol and 7.17 respectively. The gain is another 10-fold improvement in the defence of the acidity of the fluid.

**Physiological control.** The presence of buffers and especially of the open carbonic acid–bicarbonate system are the main regulators of the acid–base state of blood. Further fine control is produced by the effects of alterations in blood acidity. Acidity is one stimulus for the respiratory chemoreceptors which reflexly increase alveolar ventilation. The consequent decrease in the carbon dioxide tension moves the blood pH towards normal. Renal mechanisms operate over a longer time but will act to excrete any non-volatile acid or base provided that that does not compromise the more important renal defence of body water and extracellular fluid composition.

The normal transport of carbon dioxide from the tissues to the lungs would produce a more marked change in blood pH but for the interaction between oxygen, carbon dioxide and haemoglobin described by Christiansen, Douglas and Haldane in 1914. These three mechanisms combine to maintain the acidity of blood at its nearly constant value. The importance of the Henderson and Hasselbalch equations does not lie in their use to calculate one of the three main variables from measurements of the other two, although that is useful (fig. 1). There are too many assumptions in the full derivations of the equations (Linden and Norman, 1971). The importance lies in the recognition that changes in the acidity of blood must be produced by changes in the carbonic acid–bicarbonate ion relationship. The change in the hydrogen ion concentration is usually secondary. However, it can of itself produce further changes which usually help restore a more normal pH. Thus, in assessing disorders of the acid–base
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FIG. 1. Alignment nomogram for the Henderson-Hasselbalch equation. A straight line joins simultaneous values of \( \text{Pco}_2 \) (left-hand scale), plasma bicarbonate ion concentration (right-hand scale), and the resultant pH or H\(^+\) concentration (centre scale).

state of blood, causes of such changes in pH should be sought.

CLINICAL PATTERNS OF ACID-BASE DISORDERS

Most modern systems for determining acid-base parameters measure the pH and \( \text{Pco}_2 \) of blood. The pH expresses the overall acidity and the \( \text{Pco}_2 \) one of the main determinants of that pH. If attention is concentrated on these and how they are likely to change in common disorders, the other calculated parameters may not be necessary for the assessment of the patients. These two are interrelated and a diagram (fig. 2) can be used to show the common patterns. Because anaesthetists commonly are involved in changing alveolar ventilation both in anaesthetized patients and in those in need of intensive care, it seems sensible to plot this as the independent variable and the resultant—the pH—as the dependent variable. The logarithmic scale for \( \text{Pco}_2 \) is used deliberately, for it helps turn some patterns from curves into straight lines. The pH scale shows increasing acidity on the ordinate. The diagram can be looked at as one popularized by Astrup and his colleagues (1960) but turned on its side.

Acute respiratory disorders

In anaesthesia the most common change in acid-base balance is seen with changes in alveolar ventilation. These are associated with either respiratory depression and spontaneous ventilation or hyperventilation produced either manually or mechanically. The patterns produced have been described many times (for example, Brown, 1960; Michel, Lloyd and Cunningham, 1966; Prys-Roberts, Kelman and Nunn, 1966; Stoker et al., 1972). If the patient starts in normal balance then, should his carbon dioxide tension either double or decrease to half its normal value, the pH change is approximately 0.27 units. If \( \text{Pco}_2 \) changes from 5.3 to 10.7 kPa, the pH changes from 7.4 to 7.13 units and for the corresponding change on decreasing to \( \text{Pco}_2 \) of 2.67 kPa the pH becomes 7.67. Figure 2 illustrates such changes.

Provided that no gross reductions in cardiac output are also seen, this pattern is remarkably constant. It is detectable within 2–3 min of changing ventilation and persists for some hours.

These changes are therefore clinically predictable. They can be compared with those seen when bicarbonate and carbonic acid are the only buffer system,
as in a Severinghaus carbon dioxide electrode. There, a similar two-fold change in carbon dioxide tension changes pH by 0.3 units at full equilibrium. When blood alone is examined as in the microtonometer system described by Astrup (1959), the change in pH is less—about 0.19 units. The different behaviour seen when blood from patients is examined is the result of carbon dioxide affecting all body fluids and bicarbonate ions being fairly freely diffusable across all membranes. Blood has a higher concentration of buffers, notably haemoglobin, than have other tissue fluids. Thus, with the diffusible bicarbonate ions, the net effect in the body of changing $P_{CO_2}$ on blood pH lies between the behaviour of blood in vitro and the Severinghaus electrode. Van Slyke and Cullen (1917) noted that about one-sixth of the body buffering was in blood which usually only occupies about one-twelfth of the body mass.

The general failure to observe this fact has led to most of the indices of the non-respiratory component of acid–base balance showing an erroneous metabolic component to accompany an acute respiratory acidosis or alkalosis.

**Chronic respiratory acidosis**

In patients with chronic respiratory failure renal mechanisms modify the acid–base picture seen in acute changes. The renal threshold for the elimination of bicarbonate ions increases in a manner dependent on the $P_{CO_2}$. The result is a greater retention of bicarbonate ions with a net result of returning the pH towards normal. Refsum (1966) provided data which allowed the pathway seen in patients to be determined; this is shown in figure 2. On average, only when $P_{CO_2}$ doubles will the pH be found to be less than 7.3 units.

The renal defence of pH takes some 5 days to achieve this compensation when normal man is exposed to increases in the atmospheric carbon dioxide concentration (Brackett et al., 1969). This has a practical corollary: should a patient with mild chronic respiratory acidosis suffer an exacerbation and go into acute failure as well, he will develop a pH change that moves parallel to the normal “acute” respiratory disturbance. Further, artificial ventilation, if used as part of therapy, will also move him along an acute line. Thus, should his $P_{CO_2}$ be suddenly returned to normal values, his pH will be well on the alkaline side of normal!

Further complications in assessment of chronic respiratory disorders occur in that therapy such as diuretics may lead to further chloride loss from the body and a greater bicarbonate ion concentration; hence the pH may even be on the alkaline side of normal even with a high $P_{CO_2}$ as the cause of the initial disturbance. In contrast, drugs of the carbonic acid anhydrase inhibitor group such as diamox produce an additional metabolic acidosis by increasing the excretion of bicarbonate ions in the urine.

In assessing acid–base measurements in chronic respiratory acidosis it becomes essential to review the results in the light of the history of the illness and the various forms of therapy that might have been used.

**Metabolic acidosis**

The original description of disorders of acid–base balance were of patients with a metabolic or non-respiratory acidosis (O'Shaughnessy, 1831; Stadelman, 1883). The acids observed were caused by a loss of bicarbonate ion (cholera), by the failure to excrete normal non-volatile acids (renal failure) or by a disorder of metabolism with an increase in plasma keto-acid concentrations (diabetes). When two of the three measurements of the factors in the Henderson–Hasselbalch equation were made, a common pathway was observed for these differing disorders. Progression of the acidosis led to an increase in ventilation (Kussmaul respiration) and a decrease of $P_{CO_2}$. This reduces the extent of the change in pH. The average pathway plotted in figure 2 is taken from Peters and Van Slyke (1931).

This pathway of disorder is seen in many types of metabolic acidosis and will be seen in normal subjects following severe exercise. However, anaesthetists can see other patterns if they are controlling the patient’s ventilation and thereby maintaining $P_{CO_2}$ at near normal values. It is then not possible for respiratory compensation to occur. Again, following severe hypoxia and cardiac arrest, it may be that there is respiratory failure as well as the metabolic acidosis from anaerobic metabolism. Examination of the results in conjunction with the history should resolve the matters.

**Metabolic alkalosis**

Patients with pyloric stenosis who develop metabolic alkalosis as a result of loss of gastric acid also show some respiratory compensation in that as the pH becomes more alkaline the $P_{CO_2}$ increases (figure 2 shows an average pathway). However, respiratory compensation is rarely as marked as with a metabolic acidosis and few reports show the $P_{CO_2}$ to increase much above 6.5 kPa even with a severe alkalosis. The increase in $P_{CO_2}$ is rarely sufficient to...
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produce a dangerous decrease in Po$_2$. Partly, this is a result of the frequent association of metabolic alkalosis with hypokalaemia. Low serum potassium concentrations may reflect intracellular hypokalaemia in which case hydrogen ions are generated in excess in the cells; there may then be an intracellular acidosis although the blood shows an alkalosis. This intracellular acidosis in the brain may maintain a normal ventilation and Pco$_2$ (Goldring et al., 1968).

Complex patterns

By now it must be apparent that even the simplest type of acid–base disorder may become complicated by secondary physiological responses, by further pathophysiological disorders and by therapy. One additional pattern may help in assessing the progress of patients treated by artificial ventilation. Stoker and his colleagues (1972) determined the pathways of pH change when the Pco$_2$ was altered in patients who presented with a metabolic acidosis. They were then able to calculate how much pH change would be expected on changing ventilation and Pco$_2$ in these conditions. Figure 3 shows their lines in addition to the four fundamental pathways. Although they used them to derive another index of the “metabolic” state of blood—the non-respiratory pH—they are much more useful to the anaesthetist in allowing him to predict what pH will be achieved in the short term on changing the Pco$_2$ and allowing him to consider what other therapy might be needed.

THE INDEX OF THE METABOLIC STATE OF BLOOD

So far I have produced an assessment of the blood acid–base state based solely on the two measurements commonly made—pH and Pco$_2$. These two, if used in conjunction with a diagram such as figure 3 and a knowledge of the history of the patient’s disease and his therapy, should allow most problems to be assessed. Should discrepancies arise between the clinical state and the laboratory results the doctor must then hunt the cause, whether it be laboratory error or some other clinical process.

However, many find it useful to have another number to complete the diagnostic picture. We have two, the pH giving the acidity and the Pco$_2$ the respiratory factor. Which one is used for the metabolic factor depends on personal choice, but all have some limitations and must be interpreted in the light of the clinical history. One of the first to be introduced was the alkali reserve (Van Slyke and Cullen, 1917). It involved separating plasma, re-equilibrating it with a normal Pco$_2$ and determining the carbon dioxide concentration. Any procedure that involves titration of blood outside the body with carbon dioxide or strong acid or alkali will produce similar problems in that the same results are unlikely to be seen with similar in vivo titrations. Thus standard bicarbonate, buffer base and base excess values need interpretation in the light of in vivo events. The discussion of these indices was initiated by Schwartz and Relman (1963) who emphasized the need to study the patient. Severinghaus (1977) has summarized the present alternative approaches. In presenting this assessment of acid–base balance to the reader, my intention is to help those students who find it a difficult topic. I suggest that concentration on those two parameters usually measured, and a consideration of all the relevant history should allow most patients to be assessed. This assessment should lead to questions as to how to institute effective therapy. The answers lie elsewhere but, generally, therapy directed to the causes of the disturbances will be more effective than that aimed solely at correcting the numbers.

REFERENCES


Other suggested reading
