The Basic Principles of Acid-Base Regulation*

ORHAN MUREN, M.D.

*Associate Professor of Medicine and Anesthesiology,
Medical College of Virginia, Health Sciences Division of
Virginia Commonwealth University, Richmond, Virginia*

Acid-base homeostasis refers to those chemical and physiological processes which maintain the hydrogen ion (H^+) activity in body fluids at the levels compatible with life and normal functioning. This is an enormous task due to the fact that reactions which produce H^+ and reactions which consume H^+ are continously occurring in human beings.

On one hand there is acid production (fixed and volatile acid) and on the other hand acid elimination (fixed and volatile acid). Normally in a given time, such as in a day, acid elimination is equal to acid production. Whenever there is imbalance between input and output, acid-base disturbances will occur.

Many biochemical processes require optimum H^+ ion concentration. Changes in H^+ concentration markedly affect the catalytic activity of enzymes. Myocardial and muscular contraction, vascular tone, central nervous system, and so forth all require optimum H^+ ion concentrations to function properly. This is why the regulation of hydrogen ion concentration is so important.

The relationship between extra- and intracellular H^+ ion concentrations is still disputed because of differences in opinion concerning the measurements of intracellular pH. Intracellular pH has been found to be 5.9 to 7 depending upon the method used. Another problem in measurement of intracellular pH is the multicompartmental structure of most cells. It is believed that mitochondria, nuclei, and cell sap have different pH. As a result of this, intracellular pH is probably not homogeneous for a given cell. For these reasons extracellular fluid, especially arterial blood, is used to study the acid-base status of the patients.

In normal people, the concentration of H^+ is approximately 40 nanomoles (n moles) per liter of plasma. One nanomole equals 10^{-9} moles. However, it would be more correct to indicate the thermodynamic activities rather than the concentrations, the two being related as follows:

$$\frac{activity}{concentration} = activity\ coefficient$$

At infinite dilution the activity coefficient is equal to one. However, in concentrations in body fluids, it is much less than one. The pH meter electrode responds to hydrogen ion activity and not concentration. However, it is customary to work in concentrations, and values for the different equilibrium constants are adjusted accordingly, as indicated by a prime after a symbol such as K'.

Since concentration of H^+ ions in arterial blood is extremely small, the activity coefficient of H^+ ions may be assumed to be equal to one. Therefore, in this discussion the term H^+ ion concentration will be used interchangeably with H^+ ion activity.

The body maintains H^+ ion concentrations between 44 to 36 nanomoles per liter of plasma which correspond to a pH of 7.36 to 7.44. The most extreme pH that is compatible with life ranges between 6.8 and 7.8 which is equal to a ten-fold change in H^+ ion concentrations.

As can be seen, the body could tolerate four times an increase in H^+ ion concentrations and 2.5 times a decrease in H^+ ion concentrations, indicating better tolerance to acidosis than to alkalosis. These also indicate that H^+ ion regulation is not the most precise regulatory mechanism in the body. A similar change in potassium or sodium concentrations is usually fatal (Table 1).

Since modern chemical formulation of acids

TABLE 1.
SOME USEFUL COMPARISONS OF pH AND NEQ/L

	pH	NEq/L
"Neutral" Solution at 37° C	6.8	160
Severe Acidosis	6.9	125
Neutral Solution at 25° C	7.0	100
Normal Arterial Blood	7.4	40
Severe Alkalosis	7.8	16
	8.0	10
	9.0	1

1) Buffers:

a) Chemical—$\dfrac{HCO_3^-}{H_2CO_3}, \dfrac{HPO_4^-}{H_2PO_4^-}, \dfrac{Pr^-}{HPr}$

b) Physiological—$\dfrac{HCO_3^-}{H_2CO_3}$

2) Pulmonary regulatory mechanism:
   (13,000 − 20,000 m M/day CO_2 of H_2CO_3 eliminated)
3) Renal: 40 − 90 meq [H^+] day secreted.
4) Exchanges of ions between intracellular and extracellular fluid compartments.

and bases by Brønsted, acid-base regulation has been easier to understand. Brønsted defines an acid as any molecule capable of donating H^+ or a proton to a base, and a base as any compound that will accept a H^+. HCl, H_3PO_4, or H_2CO_3 are acids since they form H^+ ions in solution and can donate these protons to a base. HCO_3^- is considered a base, since it accepts H^+ ions and produces H_2CO_3. Almost all protons (H^+) in aqueous solutions are reacted with H_2O to form hydrated ions such as H_3O^+, called hydronium ions. It should be clear that what is meant by the concentration of H^+ in body fluids is hydronium ions or hydrated protons.
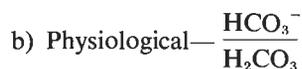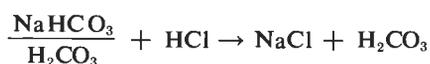
Since concentrations of free H^+ ions in plasma of human beings are very small, in 1909 Sorenson proposed the term of pH which he defined as the negative logarithm to the base 10 of H^+ ion concentration:

$$pH = - \log (H^+)$$
$$H^+ = 40 \times 10^{-9} Eq/L$$
$$pH = - \log (40 \times 10^{-9})$$
$$= - \log 40 - \log 10^{-9}$$
$$= - 1.6 - (-9)$$
$$pH = 7.4$$

Distilled water molecules at 25° C dissociate into very small amounts of H^+ ions and the same number of OH^- ions. The concentration of H^+ and OH^- is 10^{-7} Eq/L. Water is neutral and has a pH of 7.0. In normal plasma, there is a slight predominance of OH^- ions resulting in a pH of 7.40. Since the scale is logarithmic, a reduction of one pH unit indicates 10 times an increase in H^+ ion concentration.

The following are four primary mechanisms which regulate H^+ ion concentration or activity in the blood:

Hydrogen ions are produced from oxidation of sulfur containing amino acids, from oxidation and hydrolysis of phosphoprotein compounds, and from incomplete breakdown of fat and carbohydrate. An average healthy man on a normal meat diet produces 40 − 90 meq H^+ ions per day. The reason that there are so few free H^+ ions in blood is that the body has chemical and physiological means of reducing the concentration of H^+ ions. Chemically, the body has buffers that use up H^+ ions. Physiologically, normal lungs and kidneys excrete the acid end products almost as fast as they are produced. Buffers are substances that resist changes in pH when acids or bases are added to them. A typical example of a buffer is a weak acid (or a weak base) and its salt:

$$\frac{NaHCO_3}{H_2CO_3} + HCl \rightarrow NaCl + H_2CO_3$$

HCl will react with the sodium bicarbonate to form additional carbonic acid. Since carbonic acid is a weak acid, it is only partly ionized, and the above reaction decreases the concentration of free H^+ ions in solution. A bicarbonate buffer system functions as a chemical as well as a physiological buffer system. It is physiological because it works in an open system. The denominator of this buffer pair, CO_2, is constantly being produced in the tissues and eliminated from the lungs almost as fast as it is formed.

The body plays an important role in the regulation of H^+ ions by increasing or decreasing the elimination of CO_2 through the lungs. This is why a bicarbonate buffer system is very important. As a matter of fact, bicarbonate buffer is the most important buffer in the plasma, and approximately

50% of the entire buffering of whole blood resides in the bicarbonate buffer system.

In an open system CO_2 produced during the reaction between HCO_3 and added H^+ ($H + HCO_3 \rightarrow CO_2 + H_2O$) is eliminated by the lungs so, physically, dissolved CO_2 remains unchanged. However, this is not possible in a closed system. Dissolved CO_2 will be increased. Since pH is determined by the ratio between HCO_3 and dissolved CO_2, in a closed system pH will be reduced to a greater extent than in an open system (Table 2).

In the red blood cells, the hemoglobin is the most important buffer. The other buffers of less significance in red blood cells are proteins and phosphate compounds. In the body H_2CO_3 can only be buffered by non-bicarbonate buffer systems which consist of hemoglobin, proteins, and phosphate buffers.

The buffer capacity of hemoglobin is far greater than that of plasma proteins. This is partly due to greater buffer value of hemoglobin and partly to greater quantity of hemoglobin in a given volume of blood as compared with plasma proteins. The conjugate base of non-bicarbonate buffer pairs is represented as Buf^-; during the buffering of H_2CO_3 the following reaction takes place:

$$CO_2 + H_2O$$
$$\downarrow$$
$$H_2CO_3 + Buf^- \rightarrow H\,Buf + HCO_3^-$$
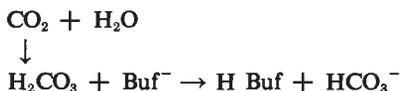
All the buffers in the body are in equilibrium with one another. A change in one buffer pair would immediately change the ratios in the other buffers. Since it is easy to study the bicarbonate system, this is used for the determination of H^+ ion concentration.

The bicarbonate buffer system is described as follows:

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

TABLE 2.
QUANTITATIVE RESPONSE OF CLOSED AND OPEN SYSTEMS TO ADDITION OF 10 MEQ/L OF STRONG ACID

$[HCO_3^-]$ = 24.0 meq/L	
$S \times P_{CO_2}$ = 1.2 m M/L	
+10 meq/L	+10 meq/L
H^+	H^+
$[HCO_3^-]$ = 14.0 meq/L	$[HCO_3^-]$ = 14.0 meq/L
$S \times P_{CO_2}$ = 11.2 m M/L	$S\ P_{CO_2}$ = 1.2 m M/L
Closed System	Open System

If V_1 is the rate of ionization of carbonic acid, it is related to the concentration of H_2CO_3.

$$V_1 = K_1[H_2CO_3]$$

K_1 is the rate constant. The rate of opposite reaction, V_2, is proportional to the product of the molar concentrations of H^+ and HCO_3^-:

$$V_2 = K_2[H^+][HCO_3^-]$$

At equilibrium, $V_1 = V_2$. Hence,

$$K_1[H_2CO_3] = K_2[H^+][HCO_3^-]$$
$$\frac{K_1}{K_2} = \frac{[H^+][HCO_3^-]}{[H_2CO_3]}$$

The ratio of the two rate constants must also be constant, and can be expressed as:

$$K = \frac{[H^+][HCO_3^-]}{[H_2CO_3]}$$

if solved for $[H^+]$:

$$[H^+] = K\frac{[H_2CO_3]}{[HCO_3^-]}$$

obtaining the negative logarithm of both sides:

$$-\log[H^+] = -\log K - \log\frac{[H_2CO_3]}{[HCO_3^-]}$$

since $pH = -\log[H^+]$ and $-\log K = pK$

$$pH = pK - \log\frac{[H_2CO_3]}{[HCO_3^-]} = pK_1' + \log\frac{[HCO_3^-]}{[H_2CO_3]}$$

The pK_1' for this system in blood is 6.1. This is the pH corresponding to half neutralization and the point of most efficient buffering. It represents the negative logarithm of the apparent first ionization constant of H_2CO_3 corrected for the ratio of CO_2 to H_2CO_3. Replacing the human value for pK (6.1) expresses Henderson-Hasselbalch equation.

$$pH = 6.1 + \log\frac{[HCO_3^-]}{[H_2CO_3]}$$

Since the solubility constant of CO_2 is 0.03 total H_2CO_3 pool = 0.03 $\times$ P_{CO_2}, where p is the partial pressure of dissolved CO_2. So final expression of Henderson-Hasselbalch formula would be:

$$pH = 6.1 + \log\frac{[HCO_3^-]}{P_{CO_2} \times 0.03}$$

As can be seen, the ratio between HCO_3^- and dissolved CO_2 determines the pH. Normally,

$$pH = 6.1 + \log\frac{24}{40 \times 0.03}$$

$$pH = 6.1 + \log\frac{24}{1.2}$$

$$pH = 6.1 + \log\frac{20}{1}$$

$$pH = 6.1 + 1.3 = 7.40$$

It should be emphasized that buffers are the first defense lines in any acid-base disturbance. They work within seconds; however, this effect is only temporary. Restoration of normal acid-base status depends upon the elimination of excess acid or base and restoration of buffers to normal levels.

The lungs react to acid-base disturbances within seconds to minutes by increased or decreased elimination of CO_2. Renal compensatory mechanisms are slow; it may take five to seven days before efficient compensation can operate. Exchanges of ions between intracellular (ICC) and extracellular (ECC) fluid compartments also begin to operate fast; however, full equilibrium may take a few hours. For instance, in metabolic acidosis, intracellular K^+ moves into plasma and H^+ ions from plasma move into cells.

The Henderson-Hasselbalch equation:

$$pH = pK_1' + \log \frac{[HCO_3]}{P_{CO_2} \times 0.03}$$

The numerator of this equation, HCO_3^-, is primarily under the influence of the kidneys and is the metabolic component. The denominator of this formula, P_{CO_2}, indicates the level of ventilation and is primarily under the influence of the lungs. This is considered a respiratory component.

$$\text{Blood pH} \propto \frac{[\text{metabolic component}]}{[\text{respiratory component}]}$$

Normally the kidneys reabsorb more than 4,000 meq of bicarbonate daily. Only less than 5 meq of bicarbonate is found in the urine per day. Approximately 85% to 90% of the filtered bicarbonate is reclaimed in the proximal tubule, and the rest is reabsorbed from the distal tubules. HCO_3 is reabsorbed indirectly across the luminal tubular membrane. When $NaHCO_3$ is filtered, Na^+ is actively reabsorbed in exchange for H^+ formed within the tubule cells by the carbonic anhydrase catalyzed hydration of CO_2. $NaHCO_3$ formed within the tubule cells is reabsorbed into peritubular blood. The secreted H^+ reacts with the HCO_3^- in the lumen of the tubule, and the following reaction takes place:

$$HCO_3^- + H^+ \rightarrow H_2CO_3 \xrightarrow{CA} CO_2 + H_2O$$

The CO_2 produced diffuses back into the cell and produces H_2CO_3. The pH of the fluid leaving the proximal tubules is not significantly different from that of the initial glomerular filtrate.

This event conserves filtered HCO_3^-. However, in order to maintain normal H^+ ion concentration, the kidneys must generate about 40 to 90 meq of new HCO_3^- daily. This newly generated HCO_3^- replaces the HCO_3^- consumed daily to buffer fixed acids produced from metabolism. Generation of HCO_3^- is performed by excretion of 40 to 90 meq of H^+ ion by the kidney as ammonium ions (NH_4^+) and titratable acids. The titratable acid represents buffer reaching the tubular urine by glomerular filtration; on the other hand, NH_3 buffer is produced by tubular cells.

The net quantity of acid eliminated in the urine is equal to titratable acid plus NH_4^+, minus any small amount HCO_3^- that escapes into the urine. Normally, NH_4^+ is responsible for about two-thirds of the acid excreted, and titratable acid for the rest of the one-third.

Acid-Base Abnormalities. There are four simple or primary acid-base disturbances: respiratory acidosis and alkalosis, and metabolic acidosis and alkalosis. In addition, there are mixed or combined acid-base disturbances which indicate the presence of two independent acid-base abnormalities going on at the same time.

Respiratory Acidosis. This is characterized by a primary increase in P_{CO_2}, and it results when CO_2 production in the tissues exceeds the rate of its removal by the lungs. In acute hypercapnia, the body's defense mechanisms are very limited. The pH is always acidotic. Blood (H^+) increases linearly as P_{CO_2} increases.

$$[H^+] \text{ nano Eq/L} = 0.76 \ P_{CO_2} \text{ mm Hg} + 9.3$$

When P_{CO_2} increases from 40 mm Hg to 80 mm Hg, plasma HCO_3^- increases only slightly (by < 3 meq/L). This small rise in plasma (HCO_3^-) is almost entirely due to non-bicarbonate buffers of blood, mainly hemoglobin.

In chronic respiratory acidosis, blood (H^+) is also a direct linear function of arterial P_{CO_2}, but the slope is less steep.

$$[H^+] \text{ nano Eq/L} = 0.24 \ P_{CO_2} \text{ mm Hg} + 27.2$$

At any given arterial P_{CO_2}, plasma (HCO_3^-) is higher and blood (H^+) is lower in chronic hypercapnia than during acute hypercapnia. During hypercapnia, renal acid elimination (ammonium + titratable acid) increases, thus generating more new HCO_3^-. Increased generation and absorption of HCO_3 from the kidneys may bring pH towards normal. It may take from 5 to 7 days before pH may come within normal range.

In chronic respiratory acidosis at a P_{CO_2} of

50 mm Hg, 75% of the patients may have pH values in the normal range. At a P_{CO_2} of 60 mm Hg, approximately 15% of the patients may have low normal pH values; at a P_{CO_2} of 70 mm Hg, less than 1% of the patients may have low normal pH values.

In summary, body buffers play a major role against acute hypercapnia; however, this buffering is limited. On the other hand, renal mechanisms play a major part against chronic hypercapnia, and pH may reach within low normal range.

Respiratory Alkalosis. This is characterized by a primary decrease in arterial P_{CO_2}. When CO_2 elimination by the lungs exceeds CO_2 production in the tissues, the result will be a lowering of arterial P_{CO_2}. During acute hypocapnia, blood (H^+) is again a linear function of arterial P_{CO_2}.

$$[H^+] \text{ nano Eq/L} = 0.74 \ P_{CO_2} + 10.4$$

During acute hyperventilation, the tendency for H^+ ion activity in the body fluids to decrease is somewhat opposed by buffers. Approximately one-third of the extracellular fluid HCO_3^- reduction seen *in vivo* with acute hyperventilation is due to blood buffers, mainly hemoglobin; the remaining two-thirds is due to tissue buffering. During acute hyperventilation, there is a slight increase in blood lactate and to a lesser degree, pyruvate; the role played by these organic acids in regard to the buffering is small. When P_{CO_2} falls acutely from 40 to 20 mm Hg plasma HCO_3^- falls, on the average, by 7.5 meq/L.

Chronic hypocapnia causes lowering of the renal HCO_3^- threshold and a retention of the chloride ion by the kidneys. Patients with chronic respiratory alkalosis do not appear to have increased lactate in the plasma. The pH tends to be slightly high but may be normal. In chronic respiratory alkalosis, low plasma HCO_3 is associated with hyperchloremia. The same electrolyte composition is seen in patients with hyperchloremic metabolic acidosis. However, the pH tends to be high in chronic respiratory alkalosis and lowered in hyperchloremic metabolic acidosis.

Metabolic Acidosis. This is characterized by increased H^+ ion activity in the extracellular space due to increased concentration of fixed acids. There is primary reduction in plasma (HCO_3^-) concentration.

Decreased pH stimulates respiration, thus lowering arterial P_{CO_2}. If kidneys are normal, they secrete more H^+ into the final urine. There will be more complete titration of filtered phosphate. As the duration of metabolic acidosis becomes longer, pulmonary compensation is reduced. This is probably due to the fatigue of the respiratory muscles secondary to the excessive work required. Arterial P_{CO_2} would have a tendency to rise toward normal. Kidneys increase renal acid secretion by increasing urinary NH_4^+ content. Provided acid loads are not excessive (>500 meq per day), renal acid secretion may reach acid production, hence increasing plasma HCO_3^- and, for a short time, exceed towards normal.

In simple metabolic acidosis, the ventilatory response is probably the most predictable. Predicted P_{CO_2} can be calculated by the following formula:

$$P_{CO_2} = 1.54 \times [HCO_3^-] + 8.36 \pm 1.1$$

If the P_{CO_2} is markedly lower than that predicted by the above equation, there is probably also a primary respiratory alkalosis. If measured P_{CO_2} is markedly higher than P_{CO_2} predicted by the above equation, then there is a complicated respiratory acidosis.

Metabolic Alkalosis. This is characterized by a primary increase in plasma bicarbonate concentration. This should not be confused with elevation of plasma (HCO_3^-) concentration secondary to chronic hypercapnia, which represents a renal compensatory mechanism for a primary respiratory dysfunction. Hypoventilation is a compensatory mechanism in metabolic alkalosis.

In general, respiratory compensation is poor. In most of the patients arterial P_{CO_2} rises by 5 mm Hg; however, in rare occasions P_{CO_2} may reach 60 or 65 mm Hg. An arterial P_{CO_2} higher than 65 mm Hg virtually always indicates primary respiratory acidosis rather than hypercapnia secondary to primary metabolic alkalosis.

The following are common causes of metabolic alkalosis:

1) Loss of acid (vomiting, gastric suction).
2) Excessive alkali administration.
3) Chloride depletion.
4) Post hypercapnic alkalosis.
5) Mineralocorticoid excess syndrome.
6) Severe potassium depletion.
7) Contraction alkalosis.

In clinical medicine, more than one factor is generally responsible for metabolic alkalosis, for instance in a patient with pyloric stenosis who has been vomiting. He is losing not only acid and potassium but he is also volume depleted.

Chloride depletion is an important and common

cause of metabolic alkalosis. Sodium is actively reabsorbed in renal tubules. Multiple factors influence how much sodium is reabsorbed, such as: effective plasma volume, aldosterone, filtration fraction, and so forth. The amounts of sodium reabsorbed as NaCl and in exchange for H^+ or K^+ depend mainly on the amount of chloride, the only permeant anion present in glomerular filtrate.

In chloride depletion, the amount of sodium reabsorbed in exchange for H^+ and K^+ increases. It should be remembered that for every meq of H^+ secreted into the urine, the same amount of HCO_3^- enters into the blood, either by indirect reabsorption of HCO_3^- or by generation of new HCO_3^- in the renal tubular cells. During this increased cation exchange, some potassium will also be lost. The result will be hypochloremic metabolic alkalosis. The serum potassium level may also be reduced. Diuretic induced metabolic alkalosis is primarily related to the chloride depletion and volume contraction. In these simple acid-base disturbances, the stimulus for compensation is the change in pH brought about by the primary change in P_{CO_2} or HCO_3^-.

Since abnormal pH is the stimulus, normal compensation should not over-correct or overcompensate. It should not even return pH to control levels; however, this does not mean that in simple acid-base abnormalities, normal pH cannot be observed. Since the normal pH range is 7.36–7.44, a slight acid-base disturbance, once compensated, might return pH to the normal limits.

A pH value opposite to that expected by the initial disturbance indicates a mixed acid-base disturbance. And again, if there is a marked disturbance in a primary acid-base disorder, there will be less likelihood of a normal pH. A normal pH in this instance strongly suggests the presence of a mixed acid-base disorder.

A lack of any compensatory response strongly suggests a mixed acid-base disorder. However, there are two exceptions: very little, if any, increase in plasma (HCO_3^-) occurs in acute respiratory acidosis, and only a slight or moderate rise in arterial P_{CO_2} occurs in acute or chronic metabolic alkalosis. It should be pointed out that pulmonary compensation in metabolic acidosis is reduced as metabolic acidosis continues, and renal compensation in hypercapnia becomes more efficient with time. Because of these last two points, the use of 95% confidence bands cannot truly reflect the expected responses in acute and chronic acid-base disturbances.

From serum total CO_2 content alone, one cannot draw any definite conclusion. At least two unknown factors in the Henderson-Hasselbalch equation should be measured. The third can be calculated. For instance, in acute respiratory acidosis the total CO_2 content may be entirely normal. For example, a serum total CO_2 content of 24 meq/L in a patient may suggest normal acid-base status. The pH might be found to be 7.2 which is equal to $[H^+] = 40 + 23 = 63$ nano Eq/L. If one uses a rearranged Henderson's equation,

$$P_{CO_2} = \frac{[H^+][HCO_3]}{0.03 \times K}$$
$$K = 800$$

$[H^+]$ is given in nano Eq/L

$$P_{CO_2} = \frac{[H^+][HCO_3]}{24}$$

In the above example, P_{CO_2} will be:

$$P_{CO_2} = \frac{63 \times 24}{24} = 63$$

For intelligent interpretation of the acid-base status of the patients the following points should be checked:

1. Clinical information should include history and physical examination, medication taken, therapeutic measures undertaken such as assisted mechanical ventilation, limited salt intake, and so forth.
2. Routine serum electrolytes. It should be known that serum CO_2 content in m M/L represents almost entirely HCO_3^-. The total H_2CO_3 pool (H_2CO_3 and physically dissolved CO_2) is equal to $0.03 \times P_{CO_2}$.

P_{CO_2} and pH should be known. Anion gap or undetermined anion fraction should be calculated. This is normally less than $12 - 14$ meq/L which represents phosphates, sulfates, anionic proteins, and organic anions normally present. It is measured by subtracting the sum of the plasma chloride and (HCO_3^-) concentrations from the plasma sodium concentration.

The following are causes of increased anion gap:

1) Azotemic renal failure.
2) Diabetic ketoacidosis.
3) Lactic acidosis.

4) Ingestion or administration of:
   a) methyl alcohol.
   b) salicylate.
   c) ethylene glycol.
   d) paraldehyde.

In chronic azotemic renal failure alone anion gap seldom exceeds 20 meq/L. Undetermined anion fractions above 25 meq/L are usually observed only in salicylate, methanol, ethylene glycol poisoning, and lactic or diabetic ketoacidosis.

Serum potassium levels may be useful in predicting arterial pH. In acidosis, there is a tendency for serum potassium to rise unless there is underlying potassium depletion or acidosis was secondary to loss of $K\ HCO_3$ which occurs in diarrhea, acetazolemide (Diamox®) administration, and renal tubular acidosis.

Other laboratory findings such as blood sugar, BUN, urinalysis, liver function studies, and so forth should be examined for an explanation of acid-base disorder. For instance, in a patient with metabolic alkalosis, in the absence of diuretic administration, lack of urinary chloride is virtually diagnostic of metabolic alkalosis due to chloride depletion.

In summary, arterial gas studies including pH determinations can be vitally important in the diagnosis and management of patients with a variety of serious medical problems. These studies should be interpreted in the light of clinical and other necessary laboratory findings.

BIBLIOGRAPHY

BRACHETT, N. C., JR., WINGO, C. F., MUREN, O., AND SOLONA, J. T. Acid-base response to chronic hypercapnia in man. *New Eng. J. Med.* 280:124, 1969.

EGGLETON, M. G. Some factors affecting the acidity of urine in man. *J. Physiol.* (London) 106:456, 1947.

HUCKABEE, W. E. Abnormal resting blood lactate. II. Lactic acidosis. *Amer. J. Med.* 30:833, 1961.

PITTS, R. F. Renal excretion of acid. *Fed. Proc.* 7:418, 1948.

PITTS, R. F. Renal production and excretion of ammonia. *Amer. J. Med.* 36:720, 1964.

SCHWARTZ, W. B. AND RELMAN, A. S. A critique of the parameters used in the evaluation of acid-base disorders. *New Eng. J. Med.* 268:1382, 1963.

WEGER, E. M. AND NAHAS, G. G. Current concepts of acid-base measurement. *Ann. N. Y. Acad. Sci.* 133:1–274, 1966.