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CHAPTER
SEVENTEEN

**INTRODUCTION TO SIMPLE AND
MIXED ACID-BASE DISORDERS**

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Disturbances of acid-base homeostasis are common clinical problems that will be discussed in detail in Chaps. 18 to 21. This chapter will first review the basic principles of acid-base physiology, the general mechanisms by which abnormalities can occur, and an approach to evaluating patients with simple and mixed acid-base disorders.

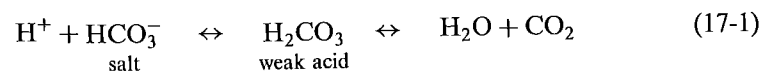
ACID-BASE PHYSIOLOGY

Free H^+ ions are present in the body fluids in extremely low concentrations. The normal H^+ concentration in the extracellular fluid is roughly 40 nanoeq/L, approximately *one-millionth* the milliequivalent-per-liter concentrations of Na^+ , K^+ , Cl^- , and HCO_3^- * However, H^+ ions are small and highly reactive, allowing them to bind more strongly to negatively charged portions of molecules than Na^+ or K^+ . As a result, maintenance of a stable H^+ ion level is required for normal cellular function, since small fluctuations in the H^+ concentration have important

*These concentrations can also be expressed in terms of molarity. Since the valence of H^+ is 1⁺, 40 nanoeq/L equals 40 nanomol/L.

effects on the activity of cellular enzymes (see Fig. 10-1). There is a relatively narrow range of extracellular H^+ concentration that is compatible with life, from 16 to 160 nanoeq/L (pH equals 7.80 to 6.80).

Under normal conditions, the H^+ concentration varies little from the normal value of 40 nanoeq/L. The body buffers play an important role in this regulatory process, as they are able to take up or release H^+ ions to prevent large changes in the H^+ concentration. There are a variety of buffers in the extracellular and intracellular fluids, most of which are weak acids (which can release H^+ ions) and their ionized salts (which can take up H^+ ions) (see Chap. 10). The most important extracellular buffer is HCO_3^- , which combines with H^+ according to the following reaction:



In most circumstances, the concentration of H_2CO_3 is very low in relation to that of HCO_3^- and CO_2 . As a result, the law of mass action for Eq. (17-1) can be expressed solely in terms of the concentrations of H^+ , HCO_3^- , and CO_2 (see page 308):

$$[H^+] = \frac{K'_a \times 0.03P_{CO_2}}{[HCO_3^-]} \quad (17-2)$$

where K'_a is the dissociation constant for this reaction and $0.03P_{CO_2}$ represents the solubility of CO_2 in the plasma. If the H^+ concentration is measured in nanomoles per liter (nanomol/L), the value of K'_a is approximately 800 nanomol/L. If this is substituted in Eq. (17-2), then

$$[H^+] = 24 \times \frac{P_{CO_2}}{[HCO_3^-]} \quad (17-3)$$

Equation (17-2) can also be expressed in logarithmic terms as the Henderson-Hasselbalch equation:

$$pH = 6.10 + \log \frac{[HCO_3^-]}{0.03P_{CO_2}} \quad (17-4)$$

where pH equals $-\log [H^+]$ (the H^+ concentration being measured in moles per liter) and 6.10 equals $-\log pK'_a$ (or $-\log 800 \times 10^{-9}$ mol/L). At the normal H^+ concentration of 40 nanomol/L (or 40×10^{-9} mol/L),

$$\begin{aligned} pH &= -\log (40 \times 10^{-9}) \\ &= -(\log 40 + \log 10^{-9}) \end{aligned}$$

Since $\log 40$ equals 1.6 and $\log 10^{-9}$ equals -9 ,

$$\begin{aligned} pH &= -(1.6 - 9) \\ &= 7.40 \end{aligned}$$

Although the acidity of the extracellular fluid is measured as the pH, it is frequently easier to think in terms of the H^+ concentration and Eq. (17-3). As a result, the following chapters will use both the pH and H^+ concentration to permit the reader to become familiar with these concepts. It is important to recognize the inverse relationship between the pH and the H^+ concentration. An increase in the H^+ concentration reduces the pH, and a decrease in the H^+ concentration raises the pH (Table 17-1).

Measurement of pH

The pH and P_{CO_2} are determined on blood drawn anaerobically (to prevent the loss of CO_2 from the blood into the air) into a heparinized syringe.^{1,2} The pH is measured by an electrode permeable only to H^+ ions (see page 302) and the P_{CO_2} by a CO_2 electrode. The HCO_3^- concentration can then be calculated from the Henderson-Hasselbalch equation or measured directly. The latter procedure involves the addition of a strong acid to the plasma sample and measurement by a colorimetric reaction of the amount of CO_2 generated.¹ The added H^+ ions will combine with plasma HCO_3^- , leading to the formation of H_2CO_3 and then CO_2 as Eq. (17-1) is driven to the right. Thus, this method measures the *total CO_2 content*, since it also includes the dissolved CO_2 (equals to $0.03P_{CO_2}$, which in the physiologic range adds 1 to 2 meq/L to the HCO_3^- concentration). For the sake of simplicity, the following discussion will refer only to the HCO_3^- concentration, since it is this parameter that is directly affected by changes in renal H^+ secretion and by the addition of acid or alkaline loads to the extracellular fluid.

Although the calculated and measured values for the plasma HCO_3^- concentration are generally similar, they may occasionally differ by as much as 7 to 8 meq/L. Some observers have suggested that the measured value is likely to be

Table 17-1 Relationship between the arterial pH and H^+ concentration in the physiologic range

pH	$[H^+]$, nanomol/L
7.80	16
7.70	20
7.60	26
7.50	32
7.40	40
7.30	50
7.20	63
7.10	80
7.00	100
6.90	125
6.80	160

more accurate in this setting, since calculation of the HCO_3^- level assumes, perhaps incorrectly, that the pK_a of 6.10 and the solubility constant for CO_2 of 0.03 are unchanged in acute acid-base disturbances.³ On the other hand, other investigators claim that the calculated value is usually a better estimate, since there may be errors in the automated test used to directly measure the total CO_2 content⁴ and since the pK_a seems to vary little in most clinical conditions.⁵ This issue is at present unresolved. Fortunately, the difference is usually small, and the only clinical problem may occur with calculation of the anion gap, where accurate determination of the plasma bicarbonate concentration is important (see Chap. 19).⁴

The normal values for the major acid-base variables in arterial and venous blood are

	pH	$[\text{H}^+]$, nanoeq/L	P_{CO_2} , mmHg	$[\text{HCO}_3^-]$, meq/L
Arterial	7.37–7.43	37–43	36–44	22–26
Venous	7.32–7.38	42–48	42–50	23–27

The decrease in pH (and increase in H^+ concentration) in venous blood is due to the uptake of metabolically produced CO_2 in the capillary circulation.

In general, arterial rather than venous blood is used to measure the extracellular pH. Arterial blood allows concurrent measurement of arterial oxygenation and is not as influenced by local changes in tissue perfusion. However, venous blood is easier to obtain and just as accurate for pH determination if drawn without a tourniquet from a well-perfused area.

Pitfalls There are several pitfalls that can lead to inaccurate results when the extracellular pH is measured. In addition to preventing CO_2 loss into the air by drawing the blood sample anaerobically,² rapid measurement or cooling to 4°C is required. At room temperature, continued anaerobic glycolysis by red cells and white cells leads to the production of organic acids that can induce small reductions in the pH and the plasma HCO_3^- concentration.¹

If air bubbles occupy more than 1 to 2 percent of the blood volume in the syringe, an artifactually high arterial P_{O_2} and an underestimation of the true arterial P_{CO_2} may result from equilibration of these gases between air bubbles and the specimen.⁶ The magnitude of this error is greatest when the difference in gas tensions between blood and air are high, when the surface area of bubbles is maximized by agitation, and when the time between specimen collection and analysis is prolonged.^{7,8}

Dilution of the blood specimen with heparin is another potential problem. For example, patients in an intensive care unit often have their pH measured using arterial blood drawn from an indwelling intraarterial catheter that is routinely flushed with heparin. To minimize contamination of the blood sample, the first 8 to 10 mL should be discarded. Use of the first 2 mL (which mostly contains

heparin) can lead to erroneous values for pH and P_{CO_2} , as low as 6.50 and 3.5 mmHg, respectively.⁹

A similar error can occur with the use of a heparinized syringe.¹⁰ There should be enough heparin to coat the sides of the syringe, but the volume of anticoagulant solution should be less than 5 percent of the volume of the blood sample.

Lastly, it is not always correct to assume that the arterial pH reflects the pH at the tissue level. This is a particular problem in patients with severe circulatory failure or cardiac arrest, in whom pulmonary blood flow is often substantially reduced. In this setting, blood that is delivered to the lungs may be adequately cleared of CO_2 , resulting in a relatively normal or even diminished arterial P_{CO_2} . However, the low cardiac output slows the return of CO_2 -containing blood from the periphery. As a result, the *mixed venous* P_{CO_2} , which represents blood that has not yet entered the pulmonary circulation, may be markedly higher than the P_{CO_2} in arterial blood.^{11,12} In one study, for example, patients with a mean arterial pH of 7.42 and P_{CO_2} of 32 mmHg during cardiopulmonary resuscitation had respective mixed venous values of 7.14 and 74 mmHg.¹¹ If the latter results more closely reflect the pH at the cellular level, then arterial measurements can lead to the misleading assumption that acid-base balance is being maintained.

In addition to testing of mixed venous blood samples, the presence of diminished pulmonary blood flow may be suggested from measurement of the *end-tidal* CO_2 concentration.¹³ A value above 1.5 percent suggests adequate pulmonary perfusion and the likelihood that arterial and mixed venous blood have a similar pH and P_{CO_2} . A value below 1 percent, however, is often indicative of a significant impairment in venous return.

Regulation of Hydrogen Concentration

The $\text{HCO}_3^-/\text{CO}_2$ system is the principal buffer in the extracellular fluid, because of both the high concentration of HCO_3^- and the ability to control the plasma HCO_3^- concentration and the P_{CO_2} independently (see Chap. 11). The former is regulated by *changes in the rate of H^+ secretion from the renal tubular cell into the tubular lumen*. Most of the secreted H^+ ions combine with filtered HCO_3^- , so that the final urine is virtually HCO_3^- free. Reabsorption of the filtered HCO_3^- is essential if acid-base balance is to be maintained, since loss of HCO_3^- in the urine is equivalent to the retention of H^+ (both H^+ and HCO_3^- being derived from the dissociation of H_2CO_3).

In addition, some secreted H^+ ions combine either with HPO_4^{2-} (to form H_2PO_4^-) or with NH_3 (to form NH_4^+). These processes play a central regulatory role, since they result in the generation of *new HCO_3^- ions* in the extracellular fluid (see Figs. 11-3 and 11-4). Thus, an increase in net H^+ secretion (as H_2PO_4^- and NH_4^+) leads to a rise in the plasma HCO_3^- concentration, whereas a reduction in net H^+ secretion results in H^+ retention and a fall in the plasma HCO_3^- concentration.

CO_2 , on the other hand, is eliminated by the lungs. Thus, the P_{CO_2} is regulated by the *rate of alveolar ventilation*. Hyperventilation enhances CO_2 excretion and

lowers the P_{CO_2} ; hypoventilation reduces CO_2 excretion and raises the P_{CO_2} . Although CO_2 is not an acid, since it contains no H^+ ions, it acts as an acid in the body by combining with water to form H_2CO_3 [Eq. (17-1)].

The kidneys and lungs play a central role in the maintenance of acid-base balance, because they can adjust the rate of acid excretion to meet homeostatic needs. Each day, approximately 15,000 mmol of CO_2 is produced by endogenous metabolism and then excreted by the lungs. Similarly, a normal diet generates 50 to 100 meq of H^+ per day, derived mostly from the metabolism of sulfur-containing amino acids and the subsequent generation of H_2SO_4 .^{14,15} These H^+ ions are initially buffered by HCO_3^- and the cellular and bone buffers to minimize the fall in extracellular pH (see page 315). Acid-base balance is then restored by urinary H^+ excretion, which regenerates the HCO_3^- lost in the original buffering reaction.

When acid-base disturbances do occur, renal and respiratory function change in an attempt to normalize the pH. From the law of mass action,

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

it can be seen that the H^+ concentration is related to the $P_{CO_2}/[HCO_3^-]$ ratio, not to the absolute value of either compound. If the H^+ concentration is increased, regardless of cause, it can be reduced toward normal by a decrease in the P_{CO_2} and/or an elevation in the plasma HCO_3^- concentration. Both of these changes occur, as both alveolar ventilation and urinary H^+ excretion are enhanced in this setting. At least part of the signal for these adaptations appears to be a parallel increase in H^+ concentration (or reduction in pH) in the cerebral interstitium surrounding the central respiratory centers and in the renal tubular cells.¹⁶⁻¹⁸

Conversely, alveolar ventilation and H^+ secretion are diminished when the H^+ concentration is reduced. The resultant increase in the P_{CO_2} and decline in the plasma HCO_3^- concentration raise the H^+ concentration toward normal.

ACID-BASE DISORDERS

Definitions

A change in the extracellular pH may be seen when renal or respiratory function is abnormal or when an acid or base load overwhelms excretory capacity. *Acidemia* is defined as a decrease in the blood pH (or an increase in the H^+ concentration), and *alkalemia* as an elevation in the blood pH (or a reduction in the H^+ concentration).

On the other hand, *acidosis* and *alkalosis* refer to processes that tend to lower and raise the pH, respectively. In most conditions, an acidotic process leads to acidemia and an alkalotic process to alkalemia. However, this may not be true in

patients with mixed acid-base disturbances, in whom the final pH depends upon the balance between the different disorders that are present (see below).

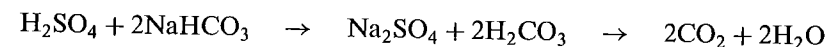
Changes in the plasma H^+ concentration and pH can be induced by alterations in the P_{CO_2} or plasma HCO_3^- concentration [Eqs. (17-3) and (17-4)]. Since the P_{CO_2} is regulated by respiration, primary abnormalities in the P_{CO_2} are called *respiratory acidosis* (high P_{CO_2}) and *respiratory alkalosis* (low P_{CO_2}). In contrast, primary changes in the plasma HCO_3^- concentration are referred to as *metabolic acidosis* (low HCO_3^-) and *metabolic alkalosis* (high HCO_3^-).

In each of these disorders, compensatory renal or respiratory responses act to minimize the change in H^+ concentration by minimizing the alteration in the $P_{CO_2}/[HCO_3^-]$ ratio (Table 17-2). To achieve this, the compensatory response always *changes in the same direction* as the primary disturbance. Thus, a high P_{CO_2} in respiratory acidosis results in enhanced renal H^+ excretion and an appropriate elevation in the plasma HCO_3^- concentration.

Table 17-2 also demonstrates that the diagnosis of an acid-base disorder requires *measurement of the extracellular pH*. Simply looking at the plasma HCO_3^- concentration (which is routinely measured with the plasma Na^+ , K^+ , and Cl^- concentrations) is not sufficient. A high value, for example, can be seen both in metabolic alkalosis (where it is the primary problem) and in respiratory acidosis (where it represents the appropriate renal compensation). These disorders can be differentiated by measurement of the pH.

Metabolic Acidosis

Metabolic acidosis is characterized by a fall in the plasma HCO_3^- concentration and a low pH (or high H^+ concentration). It can be induced either by HCO_3^- loss (as with diarrhea) or by the buffering of a noncarbonic acid, such as lactic acid or retained diet-generated sulfuric acid (as occurs in renal failure):



The reduction in pH stimulates ventilation, resulting in a compensatory decrease in the P_{CO_2} .^{19,20} Ultimate restoration of the pH usually depends upon renal excretion of the excess acid, a process that takes several days.

Table 17-2 Characteristics of the primary acid-base disturbances

Disorder	pH	$[H^+]$	Primary disturbance	Compensatory response
Metabolic acidosis	↓	↑	↓ $[HCO_3^-]$	↓ P_{CO_2}
Metabolic alkalosis	↑	↓	↑ $[HCO_3^-]$	↑ P_{CO_2}
Respiratory acidosis	↓	↑	↑ P_{CO_2}	↑ $[HCO_3^-]$
Respiratory alkalosis	↑	↓	↓ P_{CO_2}	↓ $[HCO_3^-]$

Metabolic Alkalosis

Metabolic alkalosis results from an elevation in the plasma HCO_3^- concentration and is associated with a high pH (or low H^+ concentration). This disorder can be produced by HCO_3^- administration or, more commonly, by H^+ loss, as with vomiting or the use of diuretics. The respiratory compensation consists of hypoventilation and an elevation in the P_{CO_2} .^{21,22}

Renal excretion of the excess HCO_3^- (as NaHCO_3) should rapidly correct the pH. However, this does not occur in patients with metabolic alkalosis because HCO_3^- reabsorptive capacity is enhanced, usually because of concomitant volume depletion and chloride (see Chap. 18).

Respiratory Acidosis

Respiratory acidosis is due to decreased effective alveolar ventilation, resulting in reduced pulmonary excretion of CO_2 and an increase in the extracellular P_{CO_2} (hypercapnia). The renal compensation consists of enhanced H^+ excretion, which raises the plasma HCO_3^- concentration.^{23,24} This response takes 3 to 5 days to reach completion.²³ As a result, two different acid-base disorders may occur: *acute* respiratory acidosis, in which there may be a dramatic fall in pH, and *chronic* respiratory acidosis, in which the pH is relatively well protected as a result of the renal compensation (see Chap. 20). Similar considerations apply to respiratory alkalosis but not to metabolic acidosis or alkalosis, since the respiratory compensation in these disorders is rapid, beginning within minutes and being complete within 12 to 24 h.²⁰

Respiratory Alkalosis

The primary disturbance in respiratory alkalosis is hyperventilation, resulting in a fall in the extracellular P_{CO_2} (hypocapnia) and an increase in pH (or reduction in H^+ concentration). The compensatory response consists of diminished renal H^+ secretion, producing HCO_3^- loss in the urine and an appropriate decrease in the plasma HCO_3^- concentration. As with respiratory acidosis, the renal compensation is time-dependent, so that both acute and chronic respiratory alkalosis can occur.²⁵⁻²⁷

Mixed Acid-Base Disorders

It is not uncommon for more than one of the above primary disorders to be present. Suppose a patient has a low arterial pH and is therefore acidemic. In this setting, a low plasma HCO_3^- concentration indicates metabolic acidosis and a high P_{CO_2} indicates respiratory acidosis. If both are present, then the patient has a *combined* metabolic and respiratory acidosis. Similar reasoning can lead to the diagnosis of a combined metabolic and respiratory alkalosis in a patient with an elevated pH, a high plasma HCO_3^- concentration, and a low P_{CO_2} .

Knowledge of the extent of the renal and respiratory compensations allows more complex disturbances to be diagnosed.* The responses listed in Table 17-3 have been empirically derived from observations in humans with different acid-base disorders.¹⁹⁻²⁶ A simple example can illustrate how this information can be utilized. A patient with a salicylate overdose is found to have the following arterial blood values:

$$\text{pH} = 7.45$$

$$\text{P}_{\text{CO}_2} = 20 \text{ mmHg}$$

$$[\text{HCO}_3^-] = 13 \text{ meq/L}$$

Evaluation of acid-base status begins with the pH. The slightly high pH indicates that the patient is alkalemic. This can be due to a high HCO_3^- concentration or a low P_{CO_2} . Since only the latter is present, the primary diagnosis is respiratory alkalosis, most likely acute given the history. In this disorder, the body buffers will reduce the plasma HCO_3^- concentration by 2 meq/L for every 10 mmHg decrease in the P_{CO_2} (Table 17-3).^{25,26} Thus, the $[\text{HCO}_3^-]$ should fall from 24 to 20 meq/L as the P_{CO_2} drops acutely from 40 to 20 mmHg. The actual $[\text{HCO}_3^-]$ of 13 meq/L is lower than expected, suggesting that the patient has a combined respiratory alkalosis and metabolic acidosis, a common finding with salicylate intoxication.²⁷

Table 17-3 Renal and respiratory compensation to primary acid-base disturbances in humans

Disorder	Primary change	Compensatory response
Metabolic acidosis	↓ $[\text{HCO}_3^-]$	1.2 mmHg decrease in P_{CO_2} for every 1 meq/L fall in $[\text{HCO}_3^-]$
Metabolic alkalosis	↑ $[\text{HCO}_3^-]$	0.7 mmHg elevation in P_{CO_2} for every 1 meq/L rise in $[\text{HCO}_3^-]$
Respiratory acidosis	↑ P_{CO_2}	
Acute		1 meq/L increases in $[\text{HCO}_3^-]$ for every 10 mmHg rise in P_{CO_2}
Chronic		3.5 meq/L elevation in $[\text{HCO}_3^-]$ for every 10 mmHg rise in P_{CO_2}
Respiratory alkalosis	↓ P_{CO_2}	
Acute		2 meq/L reduction in $[\text{HCO}_3^-]$ for every 10 mmHg fall in P_{CO_2}
Chronic		4 meq/L decrease in $[\text{HCO}_3^-]$ for every 10 mmHg reduction in P_{CO_2}

* Calculation of the anion gap and the ratio of the rise in the anion gap to the fall in the plasma HCO_3^- concentration also may be diagnostically important in patients with metabolic acidosis (see Chap. 19).

The renal and respiratory compensations return the pH *toward* but rarely *to* normal. Thus, a normal pH in the presence of changes in the P_{CO_2} and plasma HCO_3^- concentration immediately suggests a mixed disorder. For example, the following arterial blood values:

$$\begin{aligned} \text{pH} &= 7.40 \\ P_{CO_2} &= 60 \text{ mmHg} \\ [HCO_3^-] &= 36 \text{ meq/L} \end{aligned}$$

are due to a combination of respiratory acidosis (elevated P_{CO_2}) and metabolic alkalosis (high plasma HCO_3^- concentration). This disorder is most often due to diuretic therapy in a patient with severe chronic lung disease.

Finally, an arterial P_{CO_2} of 40 mmHg or a plasma HCO_3^- concentration of 24 meq/L is not always normal. A patient with metabolic acidosis should hyperventilate to minimize the reduction in pH. On the average, the P_{CO_2} falls 1.2 mmHg for every 1 meq/L fall in the plasma HCO_3^- concentration.¹⁹ Thus, a 16-meq/L reduction in the plasma HCO_3^- concentration from 24 to 8 meq/L should lower the P_{CO_2} by about 19 mmHg (16×1.2), from 40 to 21 mmHg. In this setting, the new pH will be 7.20. If, however, the P_{CO_2} remains at 40 mmHg, then the degree of acidemia will be more severe,

$$\begin{aligned} \text{pH} &= 6.10 + \frac{8}{0.03 \times 40} \\ &= 6.92 \end{aligned}$$

Since the P_{CO_2} of 40 mmHg is *inappropriately high* by 19 mmHg, this patient has a combined metabolic and respiratory acidosis.

Acid-Base Map

If the relationship between the arterial pH (or H^+ concentration), P_{CO_2} , and HCO_3^- concentration in the different acid-base disorders is plotted, the result is the *acid-base map* in Fig. 17-1. The stippled areas represent the responses of otherwise normal subjects to metabolic and respiratory acidosis and alkalosis, including the appropriate compensations that should be present. Thus, a given increase in the P_{CO_2} is associated with a greater reduction in pH in acute, as compared to chronic, respiratory acidosis. This difference is due to the compensatory elevation in the plasma HCO_3^- concentration seen with chronic hypercapnia.

Values between the stippled areas, on the other hand, represent mixed acid-base disturbances. This can be appreciated by plotting the three mixed disorders described above: Point A lies between respiratory alkalosis and metabolic acidosis, point B between respiratory acidosis and metabolic alkalosis (even though the pH is normal), and point C between metabolic and respiratory acidosis.

As mentioned above, the diagnostic approach used in this and the following four chapters is based upon the observed *in vivo* compensatory responses of

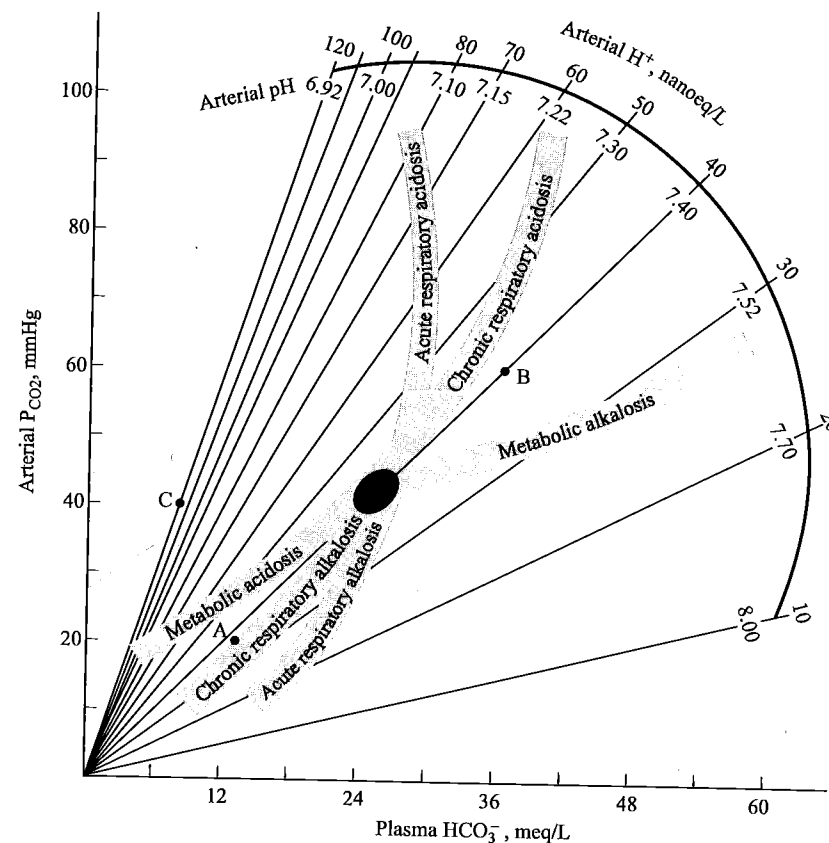


Figure 17-1 Acid-base map describing the relationships between the arterial pH, H^+ concentration, P_{CO_2} , and HCO_3^- concentration. The dark area in the center represents the range of normal values for these parameters; the stippled areas represent the different simple acid-base disturbances. Points A, B, and C indicate the three mixed acid-base disorders discussed in the text. (From Harrington JT, Cohen JJ, Kassirer JP, *Mixed acid-base disturbances*, in Cohen JJ, Kassirer JP (eds): *Acid/Base*. Little, Brown, Boston, 1982, with permission.)

patients with the different acid-base disorders.¹⁹⁻²⁶ *In vitro* measurements such as the base deficit, whole blood buffer base, and standard bicarbonate offer no advantages and frequently are confusing.²⁸ Consequently, they will not be used in this text.

CLINICAL USE OF HYDROGEN CONCENTRATION

Although the acidity of the blood is measured in terms of pH, it is somewhat difficult to use logarithms at the bedside. In contrast, the calculation of the H^+ concentration is much easier. As stated in Eq. (17-3),

$$[\text{H}^+] = 24 \times \frac{\text{P}_{\text{CO}_2}}{[\text{HCO}_3^-]}$$

If the normal arterial P_{CO_2} is 40 mmHg and the HCO_3^- concentration is 24 meq/L, then the normal H^+ concentration is 40 nanoeq/L. To use this formula, one only has to know how to convert the measured pH into H^+ concentration, a process involving a few simple calculations (Table 17-1).²⁹ If one begins at a pH of 7.40 and a H^+ concentration of 40 nanoeq/L, then for every 0.10 increase in pH, the H^+ concentration must be multiplied by 0.8; for every 0.10 decrease in pH, the H^+ concentration must be multiplied by 1.25. For example,

$$\begin{aligned} \text{pH} = 7.30 & \quad [\text{H}^+] = 40 \times 1.25 = 50 \text{ nanoeq/L} \\ \text{pH} = 7.20 & \quad [\text{H}^+] = 40 \times 1.25 \times 1.25 = 63 \text{ nanoeq/L} \\ \text{pH} = 7.50 & \quad [\text{H}^+] = 40 \times 0.8 = 32 \text{ nanoeq/L} \end{aligned}$$

Values at less than 0.10-unit steps can be estimated from interpolation. A pH of 7.27 is three-tenths of the way between 7.30 and 7.20. Since the H^+ concentration increases by 13 nanoeq/L (from 50 to 63 nanoeq/L) as the pH falls from 7.30 to 7.20, the H^+ concentration at a pH of 7.27 can be calculated from

$$[\text{H}^+] = 50 + (0.3 \times 13) = 54 \text{ nanoeq/L}$$

The following example illustrates how this equation can be used in the clinical setting. Suppose a patient with salicylate intoxication is found to have the following arterial values, which are consistent with a mild metabolic acidosis:

$$\begin{aligned} \text{pH} &= 7.32 \\ \text{P}_{\text{CO}_2} &= 30 \text{ mmHg} \\ [\text{HCO}_3^-] &= 15 \text{ meq/L} \end{aligned}$$

An important facet of therapy in this disorder is to alkalinize the blood, which will decrease the concentration of salicylate in the tissues (see Chap. 19). Thus, the initial aim of therapy is to raise the arterial pH to 7.45 (H^+ concentration equal to 36 nanoeq/L). Assuming that the P_{CO_2} remains constant, the level to which the plasma HCO_3^- concentration has to be raised to achieve this goal can be estimated from

$$\begin{aligned} [\text{H}^+] &= 24 \times \frac{\text{P}_{\text{CO}_2}}{[\text{HCO}_3^-]} \\ 36 &= 24 \times \frac{30}{[\text{HCO}_3^-]} \\ [\text{HCO}_3^-] &= 20 \text{ meq/L} \end{aligned}$$

POTASSIUM BALANCE IN ACID-BASE DISORDERS

There are important interactions between potassium and acid-base balance that involve both transcellular cation exchanges and alterations in renal function.

Metabolic Acid-Base Disorders

In metabolic acidosis, more than one-half of the excess hydrogen ions are buffered in the cells. In this setting, electroneutrality is maintained in part by the movement of intracellular potassium into the extracellular fluid. Thus, metabolic acidosis results in a plasma potassium concentration that is elevated in relation to total body stores. The net effect in some cases is overt hyperkalemia; in other patients, who are potassium-depleted due to urinary or gastrointestinal losses, the plasma potassium concentration is normal or even reduced.³⁰ There is still relative hyperkalemia, however, as evidenced by a further fall in the plasma potassium concentration if the acidemia is corrected.

On average, the plasma potassium concentration will rise by 0.6 meq/L (the range is 0.2 to 1.7 meq/L) for every 0.1-unit reduction in extracellular pH.³¹ The wide range, however, means that the degree to which the plasma potassium concentration will fall with treatment of the acidemia cannot be accurately predicted. Thus, careful monitoring is required.

A fall in pH is much less likely to raise the plasma potassium concentration in patients with lactic acidosis or ketoacidosis.^{31,32} The hyperkalemia that is commonly seen in diabetic ketoacidosis, for example, is more closely related to insulin deficiency and hyperosmolality than to the degree of acidemia.^{31,32} Why this occurs is not well understood.

Just as metabolic acidosis can cause hyperkalemia, a rise in the plasma potassium concentration can induce a mild metabolic acidosis. Two factors contribute to this phenomenon. First, a transcellular exchange occurs, as the entry of most of the excess potassium into the cells is balanced in part by intracellular hydrogen ions moving into the extracellular fluid.³³ The net effect is an extracellular acidosis and an intracellular alkalosis. Second, the rise in cell pH within the renal tubular cells reduces ammonium and therefore net acid excretion. In patients with hypoadosteronism, for example, the mild metabolic acidosis is primarily due to the associated hyperkalemia.

The net effect of these changes in cation distribution and renal function is that metabolic acidosis and relative hyperkalemia are often seen together. For similar reasons, when the above ionic changes are reversed, hypokalemia and metabolic alkalosis are also a common combination.^{12,13}

Respiratory Acid-Base Disorders

Respiratory acidosis and alkalosis induce relatively small changes in potassium balance. The reason for this minor effect is not well understood.

Concurrent Disorders of Potassium Balance

The preceding discussion has emphasized the effect of pH on potassium distribution between the cells and extracellular fluid. However, some patients have concurrent disorders of potassium balance that can affect this relationship. In particular, although metabolic acidosis typically produces relative hyperkalemia, patients may be hypokalemic at presentation if there is a source of potassium loss. Examples include diarrhea and renal tubular acidosis. On the other hand, true hyperkalemia (i.e., associated with increased body potassium stores) is present in patients with hypoadosteronism (type 4 renal tubular acidosis) as a result of impaired urinary potassium excretion.

The situation may be more complicated in patients with diabetic ketoacidosis. These patients are often markedly potassium-depleted because of urinary and gastrointestinal losses; however, hyperkalemia is found in approximately one-third of patients at presentation because of the hyperosmolality and insulin deficiency, not, as noted above, the metabolic acidosis. The administration of insulin typically leads to hypokalemia, unmasking the true state of potassium balance (see Chap. 25).

PROBLEMS

17-1 Convert the following values for arterial pH to H^+ concentration:

- (a) 7.60
- (b) 7.15
- (c) 7.24

17-2 What acid-base disorders are represented by the following sets of arterial blood tests:

	pH	P_{CO_2} , mmHg	$[HCO_3^-]$, meq/L
(a)	7.32	28	14
(b)	7.47	20	14
(c)	7.08	49	14
(d)	7.51	49	38

17-3 A patient with severe diarrhea has the following laboratory tests:

Arterial pH = 6.98

P_{CO_2} = 13 mmHg

$[HCO_3^-]$ = 3 meq/L

(a) What is the acid-base disorder?

To get the patient out of danger, the initial aim of therapy is to increase the pH to 7.20 by the administration of $NaHCO_3$. Assuming that the P_{CO_2} remains constant:

(b) To what level must the plasma HCO_3^- concentration be raised to reach a pH of 7.20?

If the P_{CO_2} increased to 18 mmHg with therapy, due to partial removal of the acidemic stimulus to hyperventilation:

(c) To what level must the plasma HCO_3^- concentration now be increased to achieve a pH of 7.20?

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