Conferences and Reviews

A Practical Approach to Acid-Base Disorders

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This discussion was selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from a transcription, it has been edited by Homer A. Boushey, MD, Professor of Medicine, and Nathan M. Bass, MD, PhD, Associate Professor of Medicine, under the direction of Lloyd H. Smith, Jr, MD, Professor of Medicine and Associate Dean in the School of Medicine.

EDITOR'S NOTE: *This discussion of acid-base disorders was presented at Medical Grand Rounds at San Francisco General Hospital Medical Center and impressed the editors as outlining a clinically useful approach to a sometimes complicated subject.*

MERLE A. SANDE, MD*: *Acid-base disturbances are common in patients admitted to our service and are sometimes confusing when three partially offsetting disorders are coincident in the same patient. Recognizing important underlying clinical problems and initiating the proper therapy will be ensured if one combines a simple, disciplined approach to analyzing changes in arterial blood gases and electrolytes with focused correlation with the clinical setting. Richard J. Haber, MD, Chief of the Division of General Internal Medicine at San Francisco General Hospital, reviews his approach to this important topic.*

RICHARD J. HABER, MD†: Because of its reputation for complexity, acid-base analysis intimidates many physicians. In reality, acid-base disturbances obey well-defined biochemical and physiologic rules and are easily recognized and interpreted. In this review I present a practical, stepwise approach to interpreting disturbances in blood gas and electrolyte values. The method is simple and does not require a nomogram or complicated mathematical formulas, yet it will identify clinically important acid-base disorders. I start with simple problems and proceed to more complex abnormalities.

Data Base

Assessing a patient's acid-base status begins with the measurement of the arterial pH, partial pressure of carbon dioxide, and bicarbonate. Blood gas analyzers directly measure the pH and P_{CO_2}. The bicarbonate value is calculated from the Henderson-Hasselbalch equation. A more direct measurement of bicarbonate is obtained from determining the total venous carbon dioxide. Because of the dissociation characteristics of carbonic acid at body pH, dissolved carbon dioxide is almost exclusively in the form of bicarbonate, and, for practical purposes, the total carbon dioxide content is equivalent (± 3 mmol per liter) to the bicarbonate concentration. If a simultaneously determined blood gas bicarbonate value and total venous carbon dioxide content are substantially different, a second measurement is required before analysis can proceed.

Terms and Definitions

Normal values for arterial pH, P_{CO_2}, and bicarbonate and values that define primary acid-base disorders are given in Table 1. If the pH is less than normal (<7.35), the patient is said to be acidemic. If the pH is greater than normal (>7.45), the patient is alkalemic. Note the separate terms for pH to allow for describing the net effect of multiple respiratory or metabolic abnormalities.

If the P_{CO_2} is lower than normal (<35 mm of mercury) and this is a primary process, then a respiratory alkalosis is present. If the P_{CO_2} is higher than normal (>45 mm of mercury) and this is a primary process, then a respiratory acidosis is present. If the P_{CO_2} is abnormal in compensation for a primary metabolic process, the disturbance is described as respiratory compensation—"metabolic acidosis with respiratory compensation," for example.

If the arterial bicarbonate level is less than normal (<22 mmol per liter) and this is a primary abnormality, a metabolic acidosis is present. If the bicarbonate level is higher than normal (>26 mmol per liter) and this is a primary process, a metabolic alkalosis is present. If bicarbonate levels are abnormal in compensation for a primary respiratory abnormality, the disturbance is called metabolic compensation.

Respiratory compensation for metabolic disorders is rapid. Full metabolic compensation for respiratory disturbances requires renal adjustment and takes three to five days.

Simple Acid-Base Disorders

The first step in acid-base analysis is to identify all abnormalities in pH, P_{CO_2}, and bicarbonate. The next is to decide which abnormalities are primary and which are compensatory. Table 2 lists three rules of thumb to help in making this determination.

The first rule directs us to look at the pH. Whichever side of 7.40 the pH is on, the process or processes that caused it to shift to that side are the primary abnormalities. If the pH is lower than 7.40, then an elevated P_{CO_2} (respiratory acidosis) or a lowered bicarbonate (metabolic acidosis) would be pri-

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TABLE 1.—*Primary Acid-Base Disorders*

Variable	*Primary Disorder*	*Normal Range, Arterial Gas*	*Primary Disorder*
pH	Acidemia	←7.35-7.45→	Alkalemia
Pco_2, mm of mercury	Respiratory alkalosis	←35-45→	Respiratory acidosis
Bicarbonate, mmol/liter	Metabolic acidosis	←22-26→	Metabolic alkalosis

TABLE 2.—*Rules of Thumb for Recognizing Primary Acid-Base Disorders Without Using a Nomogram*

Rule 1
Look at the pH. Whichever side of 7.40 the pH is on, the process that caused it to shift to that side is the primary abnormality
Principle: The body does not fully compensate for primary acid-base disorders

Rule 2
Calculate the anion gap. If the anion gap is ≥ 20 mmol per liter, there is a primary metabolic acidosis regardless of pH or serum bicarbonate concentration
Principle: The body does not generate a large anion gap to compensate for a primary disorder

Rule 3
Calculate the excess anion gap (the total anion gap minus the normal anion gap [12 mmol per liter]) and add this value to the measured bicarbonate concentration; if the sum is greater than a normal serum bicarbonate (>30 mmol per liter), there is an underlying metabolic alkalosis; if the sum is less than a normal bicarbonate (<23 mmol per liter), there is an underlying nonanion gap metabolic acidosis
Principle: 1 mmol of unmeasured acid titrates 1 mmol of bicarbonate ($+ \Delta$ anion gap $= - \Delta [HCO_3^-]$)

mary abnormalities. If the pH is higher than 7.40, then a lowered Pco_2 (respiratory alkalosis) or a raised bicarbonate (metabolic alkalosis) would be primary.

The pathophysiologic principle behind this rule is that the body does not fully compensate even for chronic acid-base disorders. Over time the pH approaches but does not completely return to normal. This observation allows us to use the direction of pH change to identify the primary disorder.

Respiratory Alkalosis

Consider a patient with a pH of 7.50, a Pco_2 of 29 mm of mercury, and a bicarbonate concentration of 22 mmol per liter. Because the patient is alkalemic, the low Pco_2 is a primary disturbance and a respiratory alkalosis is present. The lack of metabolic compensation—that is, the normal bicarbonate—indicates that the disorder is acute. The causes of acute respiratory alkalosis are listed in Table 3. Why make such a list?

Acid-base disturbances are manifestations of underlying clinical disorders. Identifying a primary acid-base abnormality—in this case, respiratory alkalosis—identifies a disorder caused by only a limited number of disease processes. Establishing a specific diagnosis is clinically important because treatment is best aimed at correcting the underlying cause of the acid-base abnormality rather than at correcting the abnormality per se.

Respiratory Acidosis

What about a patient with a pH of 7.25, a Pco_2 of 60 mm of mercury, and a bicarbonate of 26 mmol per liter? This person is acidemic with an increased Pco_2 and a normal bicarbonate: a respiratory acidosis with no evidence of metabolic compensation. The causes of acute respiratory acidosis are listed in Table 4.

What if the next patient presented with a pH of 7.34, a Pco_2 of 60 mm of mercury, and a bicarbonate of 31 mmol per liter (Table 5)? In this person, both the Pco_2 and the bicarbonate levels are elevated, two abnormalities with opposite effects on pH. Which one is primary and which compensatory? Because the pH is lower than 7.40, the primary disorder is still a respiratory acidosis. The elevated bicarbonate (and near-normal pH) indicates that metabolic compensation has occurred and that the acidosis is chronic.

Differentiating acute from chronic respiratory acidosis has important clinical implications. Acute respiratory acidosis is a medical emergency that may require emergent intubation and mechanical ventilation, whereas chronic respiratory acidosis is often a clinically stable condition. Attention to the pH and bicarbonate values will differentiate acute from chronic hypoventilation.

Metabolic Alkalosis

Assess the following blood gas combination: pH 7.50, Pco_2 48 mm of mercury, and bicarbonate level 36 mmol per liter. Because the patient is alkalemic, the elevated bicarbonate level is the primary abnormality and the patient has a metabolic alkalosis with respiratory compensation. Although the partial carbon dioxide pressure is a powerful respiratory stimulus, it may rise modestly in compensation for a metabolic alkalosis. A Pco_2 in excess of 55 mm of mercury is unlikely to be solely compensatory, however, and an additional primary respiratory abnormality should be sought.[1,2]

TABLE 3.—*Acute Respiratory Alkalosis*

Arterial Gas Value		*Interpretation*
pH	7.50	Alkalemia
Pco_2*	29 mm of mercury	Respiratory alkalosis
HCO_3^-	22 mmol/liter	Normal HCO_3^-
Causes		
Anxiety		
Hypoxia		
Lung disease with or without hypoxia		
Central nervous system disease		
Drug use—salicylates, catecholamines, progesterone		
Pregnancy		
Sepsis		
Hepatic encephalopathy		
Mechanical ventilation		

*This is the primary abnormality.

TABLE 4.—*Acute Respiratory Acidosis*

Arterial Gas Value		*Interpretation*
pH	7.25	Acidemia
Pco_2*	60 mm of mercury	Respiratory acidosis
HCO_3^-	26 mmol/liter	Normal HCO_3^-

Causes
- Central nervous system (CNS) depression—drugs, CNS event
- Neuromuscular disorders—myopathies, neuropathies
- Acute airway obstruction—upper airway, laryngospasm, bronchospasm
- Severe pneumonia or pulmonary edema
- Impaired lung motion—hemothorax, pneumothorax
- Thoracic cage injury—flail chest
- Ventilator dysfunction

*This is the primary abnormality.

The causes of metabolic alkalosis can be divided into those associated with a decreased extracellular volume, or the posthypercapnic state (low urinary chloride level), and those associated with a normal or increased extracellular volume or recent diuretic use (normal or high urinary chloride level), as listed in Table 6. Measuring the urinary chloride level is the preferred method for assessing the renal response to circulating volume in patients with metabolic alkalosis; the urinary sodium concentration is less reliable as a guide, for the renal threshold for bicarbonate may be exceeded and sodium spilled as the bicarbonate cation even in a patient who is volume depleted.

Metabolic Acidosis

Next consider a patient with a pH of 7.20, a Pco_2 of 21 mm of mercury, and a bicarbonate level of 8 mmol per liter. The patient is acidemic; therefore, the low bicarbonate is the primary abnormality and a metabolic acidosis with respiratory compensation is present. To help in distinguishing the cause, metabolic acidoses are commonly divided into those with and those without an anion gap. Because the serum potassium contributes little to the total extracellular electrolyte pool, the anion gap is traditionally calculated by excluding the potassium value and subtracting the sum of the chloride and bicarbonate (total carbon dioxide) levels from the sodium concentration. In the literature, the normal anion gap is reported as 12 ± 2 (mean ± SD) mmol per liter,[3,4] although the normal range may be lower when measured on the newest generation of autoanalyzers.[4] The causes of anion gap and nongap acidosis are listed in Table 7.

Mixed Acid-Base Disorders

In each of the previous examples, we have assumed that only one primary abnormality is present. In real life, however, patients often have more than one disorder.

TABLE 5.—*Chronic Respiratory Acidosis With Metabolic Compensation*

Arterial Gas Value		*Interpretation*
pH	7.34	
Pco_2*	60 mm of mercury	Respiratory acidosis
HCO_3^-	31 mmol/liter	Metabolic compensation

Causes
- Chronic lung disease—obstructive or restrictive
- Chronic neuromuscular disorders
- Chronic respiratory center depression—central hypoventilation

*This is the primary abnormality.

Mixed acid-base disorders can be identified by determining the expected compensatory response to a given change in the primary abnormality and assuming that any value that falls outside this range represents an additional primary disorder. Such 95% confidence bands are the basis for commonly used nomograms[5] and for the mathematical formulas popularized by Narins and Emmett.[3] Unfortunately, mathematical equations, especially ones that are different for acute and chronic disorders, can be difficult to memorize. Nomograms are simple to use but can further mystify acid-base analysis by providing answers without necessarily requiring an understanding of the relevant pathophysiology. A simpler alternative, which will identify most clinically important disorders, is outlined in Table 2.

We have already discussed the first rule of thumb that directs us to look at the pH to determine which abnormality is primary if more than one abnormality is present. The second rule instructs us to determine the serum electrolyte values—sodium, chloride, and total carbon dioxide—and to calculate the anion gap. If the anion gap is 20 mmol per liter or greater, then a metabolic acidosis is present regardless of the pH or serum bicarbonate concentration.

The physiologic principle behind this assertion is that the body does not generate a large anion gap to compensate even for a chronic alkalosis. Therefore, a substantial increase in unmeasured anions indicates a primary disorder, a metabolic acidosis, regardless of the pH or the bicarbonate concentration. Three lines of evidence support this statement. First, an anion gap of greater than 20 mmol per liter is more than 4 standard deviations from the mean and therefore is unlikely to be due to chance.[3,4] Second, although a modest increase in the anion gap occurs in patients with metabolic or respiratory alkalosis due primarily to an increase in the negative charge of serum proteins, even in severe alkalosis this increase is almost never greater than 20 mmol per liter.[1,6-8] Last, a specific cause for an increased anion gap can be found in fewer than 30% of patients with a gap greater than 12 mmol per liter but less than 20 mmol per liter, as compared with 77% of those with a gap of 20 mmol per liter or greater and all of those with a gap of more than 30 mmol per liter (Table 8).[9] Thus, an anion gap of greater than 20 mmol per liter is highly predictive of the presence of an identifiable metabolic acidosis. The greater the anion gap, the more likely it is that a specific metabolic acidosis will be found.

TABLE 6.—*Metabolic Alkalosis With Respiratory Compensation*

Arterial Gas Value		*Interpretation*
pH	7.50	Alkalemia
Pco_2	48 mm of mercury	Respiratory compensation
HCO_3^-*	36 mmol/liter	Metabolic alkalosis

Causes	
Urinary Chloride Level Low	*Urinary Chloride Level Normal or High*
Vomiting, nasogastric suction	Excess mineralocorticoid activity—Cushing's syndrome, Conn's syndrome, exogenous steroids, licorice ingestion, increased renin states, Bartter's syndrome
Diuretic use in past	Current or recent diuretic use
Posthypercapnia	Excess alkali administration
	Refeeding alkalosis

*This is the primary abnormality.

TABLE 7.—*Metabolic Acidosis With Respiratory Compensation*

Arterial Gas Value		*Interpretation*
pH	7.20	Acidemia
Pco_2	21 mm of mercury	Respiratory compensation
HCO_3^-*	8 mmol/liter	Metabolic acidosis
		Anion gap = sodium − chloride + bicarbonate
		Normal = 12 ± 2 (SD) mmol/liter

Causes	
Nonanion Gap	*Anion Gap*
GI bicarbonate loss	Ketoacidosis
Diarrhea	Diabetic
Ureteral diversions	Alcoholic
Renal bicarbonate loss	Renal failure
Renal tubular acidosis	Lactic acidosis
Early renal failure	Rhabdomyolysis
Carbonic anhydrase inhibitors	Toxins
Aldosterone inhibitors	Methanol
Hydrochloric acid administration	Ethylene glycol
Posthypocapnia	Paraldehyde
	Salicylates

GI = gastrointestinal

*This is the primary abnormality.

If the anion gap is increased, then the third rule instructs us to calculate the excess anion gap—the total anion gap minus the normal anion gap (12 mmol per liter)—and add this value to the measured bicarbonate concentration (total venous carbon dioxide content). If the sum of the excess anion gap and the measured bicarbonate is greater than a normal serum bicarbonate concentration (normal range, 23 to 30 mmol per liter), then an underlying metabolic alkalosis is present regardless of the pH or measured bicarbonate value. If the sum is less than a normal bicarbonate concentration, then an underlying nongap metabolic acidosis is present.

The physiologic basis for this statement is that for each millimole of acid titrated by the carbonic acid buffer system, 1 mmol of bicarbonate is lost through conversion to carbon dioxide and water and 1 mmol of the sodium salt of the unmeasured acid is formed. Because each millimolar decrease in bicarbonate is accompanied by a millimolar increase in the anion gap, the sum of the new (excess) anion gap and the remaining (measured) bicarbonate value should be equal to a normal bicarbonate concentration. These relationships are schematically presented in Figure 1. If the sum of the excess anion gap and the measured bicarbonate value exceeds the normal bicarbonate concentration, then an additional disorder (a metabolic alkalosis) has added bicarbonate to the extracellular space. If the sum is less than normal, then an additional process (a nonanion gap metabolic acidosis) has caused gastrointestinal or renal loss of bicarbonate. Published reports indicate that this reciprocal relationship between the increase in anion gap (and organic acid salt) and the decrease in serum bicarbonate concentration is actually observed in uncomplicated organic acidoses[10-18] but that the one-for-one relationship is altered if there is superimposed vomiting[10,19,20] or renal loss of bicarbonate.[15-17] These data suggest that although the body's titration of acid represents a complex interplay of multiple buffering systems, because bicarbonate remains the major extracellular buffer over a wide range of pH,[21] our rule is empirically correct and clinically useful.

TABLE 8.—*The Relation Between Level of Anion Gap and Biochemical Diagnoses in 51 Patients Without Renal Failure**

Anion Gap, mmol/liter	*Patients, No.*	*Biochemically Confirmed Organic Acidosis Present, No.*	*%*
17 - 19	7	2	29
20 - 24	20	13	65
25 - 29	15	12	80
30 - 45	9	9	100
≥20	44	34	77

*Adapted from Gabow et al.9

Respiratory Alkalosis and Metabolic Acidosis

Consider a patient with a pH of 7.50, a Pco_2 of 20 mm of mercury, a bicarbonate concentration of 15 mmol per liter, a sodium concentration of 140 mmol per liter, and a chloride level of 103 mmol per liter. This person is alkalemic with a low Pco_2 and a low bicarbonate concentration. Because the pH is high, the low Pco_2 represents a primary disorder, and a respiratory alkalosis is present. At first inspection, the low bicarbonate level appears to be in metabolic compensation for a chronic alkalosis. Follow the second rule, however, and calculate the anion gap: 140 − (103 + 15) = 22 mmol per liter. A gap of 22 mmol per liter is greater than would be expected solely in compensation for a chronic alkalosis and suggests that a second primary disorder, an anion gap metabolic acidosis, is also present. If the anion gap had not been calculated, the underlying metabolic acidosis would have been missed. Now, proceed to the third rule and calculate the excess anion gap: 22 − 12 = 10 mmol per liter, and add it to the measured bicarbonate level: 15 mmol per liter. The sum, 25 mmol per liter, is normal, indicating that no further pri-

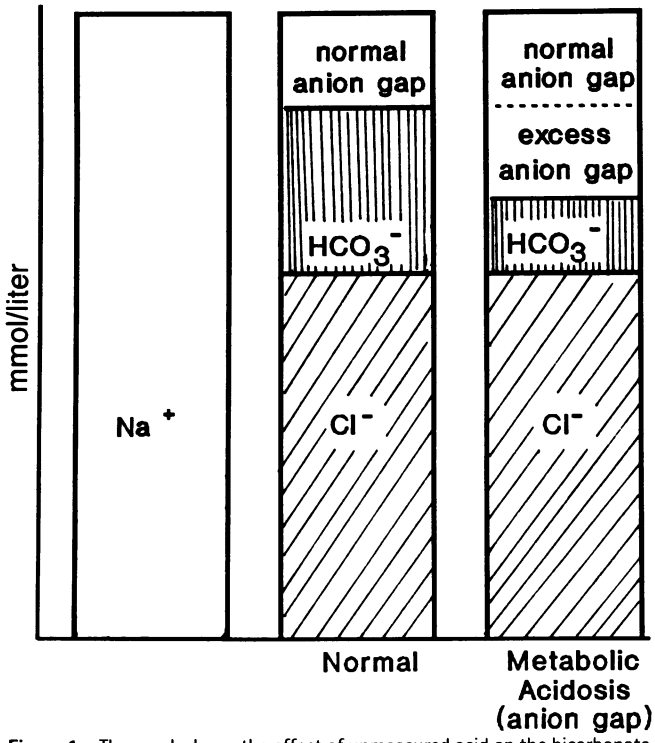

Figure 1.—The graph shows the effect of unmeasured acid on the bicarbonate concentration, anion gap, and excess anion gap. Anion gap = $[Na^+] - ([Cl^-] + [HCO_3^-])$; excess anion gap = total anion gap − normal anion gap (12 mmol/liter).

mary abnormalities are present. This patient had ingested a large quantity of aspirin and displayed the centrally mediated respiratory alkalosis and the anion gap metabolic acidosis associated with salicylate overdose.[22] Respiratory alkalosis and metabolic acidosis, however, can occur together in a variety of related and unrelated clinical conditions (Tables 3 and 7).

Metabolic Acidosis and Metabolic Alkalosis

The following example is adapted from a lecture by Robert Narins, MD: pH 7.40, Pco_2 40 mm of mercury, bicarbonate 24 mmol per liter, sodium 145 mmol per liter, and chloride 100 mmol per liter. This is a seemingly normal set of values until the anion gap is calculated: 145 − (100 + 24) = 21 mmol per liter. The increased gap defines a metabolic acidosis even though the pH is normal. Now calculate the excess anion gap: 21 − 12 = 9 mmol per liter, and add it to the measured bicarbonate: 24 mmol per liter. The sum, 33 mmol per liter, is higher than a normal bicarbonate concentration, indicating a metabolic alkalosis is also present. These laboratory values are from a patient with chronic renal failure (causing the metabolic acidosis) who began vomiting (hence the metabolic alkalosis) as his uremia worsened. The acute alkalosis of vomiting offset the chronic acidosis of renal failure, resulting in a normal pH. Without a systematic approach to acid-base disorders, including calculation of the anion gap and of the excess anion gap, these mixed acid-base disorders could easily have been overlooked.

Respiratory Alkalosis, Metabolic Acidosis, and Metabolic Alkalosis

Analyze the following blood gas and electrolyte values: pH 7.50, Pco_2 20 mm of mercury, bicarbonate 15 mmol per liter, sodium 145 mmol per liter, and chloride 100 mmol per liter. The pH is high, the Pco_2 and bicarbonate values are low, and there is an increased anion gap. Because the pH is above 7.40, the low Pco_2 is a primary abnormality, and the patient has a respiratory alkalosis. Because the anion gap is elevated (30 mmol per liter), a metabolic acidosis is also present. Because the sum of the excess anion gap (18 mmol per liter) and the measured bicarbonate (15 mmol per liter) is greater than a normal bicarbonate concentration, the patient also has a metabolic alkalosis. The near-normal pH reflects the competing effects of these three primary disorders. This person had a history of vomiting (the metabolic alkalosis), evidence of alcoholic ketoacidosis (causing metabolic acidosis), and findings compatible with a bacterial pneumonia (hence the respiratory alkalosis). These three independent disorders can occur concurrently in other clinical settings (Tables 3, 6, and 7). Four primary acid-base disorders cannot coexist, as a patient cannot hypoventilate and hyperventilate at the same time.

Respiratory Acidosis, Metabolic Acidosis, and Metabolic Alkalosis

What if a patient presents with a pH of 7.10, a Pco_2 of 50 mm of mercury, a bicarbonate level of 15 mmol per liter, a sodium level of 145 mmol per liter, and a chloride level of 100 mmol per liter? The person is acidemic with an elevated Pco_2, a lowered bicarbonate, and an increased anion gap (30 mmol per liter). Because the pH is low, the increased Pco_2 (respiratory acidosis) and decreased bicarbonate (metabolic acidosis) are both primary disorders. The anion gap is increased; therefore, the metabolic acidosis is of the anion gap variety. Because the sum of the excess anion gap (18 mmol per liter) and the measured bicarbonate (15 mmol per liter) is greater than the normal bicarbonate concentration, a metabolic alkalosis is also present: three primary disorders. This patient presented in an obtunded state (respiratory acidosis), with a history of vomiting (metabolic alkalosis) and laboratory findings consistent with diabetic ketoacidosis (metabolic acidosis).

Interestingly, identical blood gas values could occur in a patient with chronic respiratory acidosis and metabolic compensation in whom an acute anion gap metabolic acidosis developed. Although the pH, Pco_2, and bicarbonate values would be the same in both these patients, clinical correlation would readily differentiate between the two. As is the case for other diagnostic tests, acid-base abnormalities cannot be properly interpreted without knowledge of the clinical context.

Anion Gap and Nonanion Gap Metabolic Acidoses

Consider a patient with the following values: pH 7.15, Pco_2 15 mm of mercury, bicarbonate level 5 mmol per liter, sodium level 140 mmol per liter, and chloride value 110 mmol per liter. The patient is acidemic with a low Pco_2, a low bicarbonate, and an increased anion gap (25 mmol per liter). At first glance, this patient has a simple anion gap metabolic acidosis with respiratory compensation. The sum, however, of the excess anion gap (13 mmol per liter), and the measured bicarbonate (5 mmol per liter) is lower than the normal bicarbonate concentration, suggesting that additional gastrointestinal or renal loss of bicarbonate has occurred and that both an anion gap and a nonanion gap metabolic acidosis are present. Diabetic ketoacidosis was responsible for the anion gap acidosis in this patient. The nonanion gap (hyperchloremic) acidosis is that phenomenon observed in the recovery phase of diabetic ketoacidosis due to failure to regenerate bicarbonate from ketoacids lost in the urine.[15-17] If the sum of the excess anion gap and the measured bicarbonate had not been calculated, the underlying nongap acidosis would not have been appreciated.

Conclusions

Acid-base disturbances are not difficult to analyze if approached in a systematic manner. First, assess the patient's clinical status. A proper interpretation of laboratory results requires knowledge of the clinical setting. Second, determine blood gas values and identify all abnormalities in pH, Pco_2, and bicarbonate level. Third, determine which abnormalities are primary and which are compensatory based on the pH. If the pH is less than 7.40, then a respiratory or metabolic acidosis is primary. If the pH is greater than 7.40, then a respiratory or metabolic alkalosis is primary. Next, measure the serum electrolytes—sodium, chloride, and total carbon dioxide concentrations—and calculate the anion gap. If the anion gap is 20 mmol per liter or greater, then a metabolic acidosis is present regardless of the pH or serum bicarbonate concentration. If the anion gap is increased, then calculate the excess anion gap (the total anion gap minus the normal anion gap [12 mmol per liter]) and add this value to the measured bicarbonate. If the sum is greater than a normal serum bicarbonate (>30 mmol per liter), then an underlying metabolic alkalosis is present. If the sum is less than a normal bicarbonate (<23 mmol per liter), then an underlying non-

anion gap acidosis is present. Last, determine the cause of each primary disorder that has been identified and begin cause-specific therapy. This approach will allow even complex acid-base disorders to be recognized and will provide a clinically relevant framework for understanding acid-base homeostasis.

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