Acid-Base Disorders

Acid-base disorders are common in patients who present to the emergency department and in hospitalized patients. Your ability to diagnose and treat acid-base disorders depends on knowing patients' underlying medical condition and understanding acid-base pathophysiology.

Acid-base balance hinges on the normal excretion of carbon dioxide by the lung and acid by the kidney. To determine a patient's acid-base status, you need to measure pH, Pco_2, and plasma bicarbonate (HCO_3).

The diagnosis of an acid-base disorder requires several steps. First, you need to determine whether the patient is acidemic or alkalemic and then whether the disorder is respiratory (a primary change in Pco_2) or metabolic (a primary change in HCO_3).

You then need to determine whether there is a simple or mixed (respiratory and metabolic) disorder. The following discussion of acid-base disorders consists of a systematic approach to acid-base problem solving to figure out causes and treatment of the various simple and mixed disorders.

Acid-base problem solving

A systematic approach to acid-base problem solving involves asking four questions:

- What is the primary disturbance?
- Is compensation appropriate?
- What is the anion gap?
- Does the change in the anion gap equal the change in the serum bicarbonate concentration (a value called the "delta-delta")?

Case 1

A 47-year-old man with a three-day history of severe diarrhea presents to the emergency department with weakness, dyspnea, and dizziness.

On physical examination, his supine blood pressure is 100/70 mm Hg and his supine heart rate is 110/min. When the patient sits, his systolic blood pressure decreases to 80 mm Hg and his heart rate increases to 130/min.

Laboratory studies show the following:

- blood urea nitrogen, 30 mg/dL
- serum creatinine, 1.7 mg/dL
- serum sodium, 130 meq/L
- serum potassium, 3.2 meq/L
- serum chloride, 100 meq/L
- serum bicarbonate, 10 meq/L

Arterial blood gas studies on room air reveal pH 7.24, Pco_2 23 mm Hg, Po_2 105 mm Hg, and bicarbonate concentration 9 meq/L.

Commentary

The pH indicates the primary disturbance. A low pH, as in this case, means that an acidosis is present. A low HCO_3 concentration further narrows the diagnosis to primary metabolic acidosis, while a high Pco_2 indicates a primary respiratory acidosis. (In contrast, a high pH indicates an alkalosis. A high bicarbonate concentration means that a metabolic alkalosis is present, whereas a low Pco_2 indicates respiratory alkalosis.)

The compensatory response to a primary disturbance is predictable (see **Table 1**, page 4) and brings the pH toward normal. Compensation may be appropriate even if the pH is abnormal. In this case, increased alveolar ventilation would be expected to decrease the Pco_2 to between 19.5 and 23.5 mm Hg [$Pco_2 = 1.5(9) + 8 \pm 2$]. Because the Pco_2 is 23 mm Hg and therefore within the predicted range, respiratory compensation in this patient is appropriate.

The **anion gap** should be calculated regardless of the primary disturbance. The sum of all anions and all cations in serum (as measured in meq/L) must be equal. On the basis of sodium, chloride, and bicarbonate measurements, healthy persons have an anion gap of 8 to 12 meq/L.

The charges on cations not included in the calculation, such as potassium and magnesium, are balanced by the unmeasured anions, such as phosphates and sulfates. The presence of either a low

Table 1. Acid-Base Disorders and Compensatory Responses

Disorder	H^+	pH	HCO_3	Arterial Blood Pco_2	Adaptive Response	Time for Adaptation
Metabolic acidosis	↑	↓	↓↓	↓	$\Delta Pco_2 = (1.5) HCO_3 + 8 \pm 2$ $\Delta Pco_2 = HCO_3 + 15$	12 to 24 h
Metabolic alkalosis	↓	↑	↑↑	↑	Pco_2 increases 0.7 mm Hg for every 1.0-meq/L increase in HCO_3	24 to 36 h
Respiratory acidosis						
Acute	↑	↓	↑	↑↑	1-meq/L increase in HCO_3 for every 10-mm Hg increase in Pco_2	Minutes to hours
Chronic	↑	↓	↑	↑↑	3.5-meq/L increase in HCO_3 for every 10 mmHg rise in Pco_2	Days
Respiratory alkalosis						
Acute	↓	↑	↓	↓↓	2-meq/L reduction in HCO_3 for every 10-mm Hg decrease in Pco_2	Minutes to hours
Chronic	↓	↑	↓	↓↓	4-meq/L decrease in HCO_3 for every 10-mm Hg fall in Pco_2	Days

Double arrows indicate the primary disturbance.

level of albumin (an anion) or an unmeasured cationic light chain may result in a low anion gap. When the primary disturbance is a metabolic acidosis, the anion gap helps narrow the diagnostic possibilities to an anion gap acidosis or a non-anion gap acidosis. (See **Reference 1**.)

If the primary disturbance is a condition other than metabolic acidosis, calculation of the anion gap helps reveal a "hidden" anion gap metabolic acidosis. In this particular case, the anion gap is 20 (130 - [100 + 10] = 20), indicating an anion gap metabolic acidosis.

The ratio—known as "**delta-delta**"—between the change in anion gap and the change in plasma HCO_3 concentration in an uncomplicated anion gap metabolic acidosis is usually 1 to 2 (Δ anion gap - Δ bicarbonate concentration). This patient has an anion gap of 20.

If a normal anion gap is assumed to be 12, the change in the anion gap is 8. The change in the serum bicarbonate concentration is 14 (24 - 10). The change in the anion gap (8) divided by the change in the bicarbonate (14) yields a ratio of less than 1. This finding suggests the presence of a concurrent non-anion gap metabolic acidosis.

Key points

- Determination of the plasma pH reveals the primary acid-base disturbance.
- The expected change in bicarbonate concentration or Pco_2 compared to the actual change indicates whether compensation is appropriate.
- The anion gap should be calculated regardless of the primary disturbance.

Metabolic acidosis

Metabolic acidosis is discussed here in the context of non-anion gap metabolic acidosis, anion gap acidosis, lactic acidosis, and ketoacidosis. In anion gap metabolic acidosis, the ratio between the change in anion gap and the change in bicarbonate concentration should be 1 to 2.

- **Non-anion gap metabolic acidosis.** When metabolic acidosis reduces the bicarbonate concentration and the anion gap remains normal, hyperchloremic metabolic acidosis is present. That means the chloride concentration is high relative to the sodium concentration.

Hyperchloremic metabolic acidosis develops in one of two ways: Fluids containing high concentrations of sodium bicarbonate or potential sodium bicarbonate are lost from the extracellular fluid, or hydrogen chloride or potential hydrogen chloride is added to the extracellular fluid.

Either condition will cause an increase in chloride concentration and a decrease in bicarbonate concentration. The ensuing hyperchloremic metabolic acidosis will not change the anion gap

because the reduction in the bicarbonate concentration is offset by the increase in chloride.

Diarrhea is the most common cause of non-anion gap metabolic acidosis. Diarrhea leads to loss of sodium bicarbonate, as the intestinal fluid below the stomach is relatively alkaline. In this case, diarrhea accounts for the non-anion gap portion of the metabolic acidosis. Administering sodium bicarbonate and sodium chloride corrects the metabolic acidosis and volume depletion produced by diarrhea.

All types of renal tubular acidosis cause hyperchloremic metabolic acidosis.

Proximal renal tubular acidosis is caused by a reduced capacity of the kidney to reabsorb sodium bicarbonate, causing the serum bicarbonate concentration to decrease to 14 to 20 meq/L.

Distal renal tubular acidosis results from an inability of the renal tubules to generate or maintain a normal pH gradient (normal minimal urinary pH is less than 5.5). Patients with distal renal tubular acidosis excrete inappropriately alkaline urine. Distal renal tubular acidosis frequently leads to medullary calcifications and calcium kidney stones, due to hypercalciuria and deficient excretion of urinary citrate. The presence of hyperchloremic metabolic acidosis and an alkaline urinary pH suggests the diagnosis of renal tubular acidosis.

Key point

- In anion gap metabolic acidosis, the ratio between the change in anion gap and the change in bicarbonate concentration should be 1 to 2.

However, urinary tract infections can also alkalinize the urine because certain bacteria metabolize urea to ammonium and carbon dioxide. Distal renal tubular acidosis can generally be treated with between 60 and 100 meq of sodium bicarbonate daily.

Type 4 renal tubular acidosis is a hyperkalemic hyperchloremic metabolic acidosis usually due to hypoaldosteronism or an inadequate renal tubular response to aldosterone. This state leads to a reduction in urinary excretion of potassium and a resultant hyperkalemia, which leads to development of metabolic acidosis.

Some patients with type 4 renal tubular acidosis require administration of exogenous mineralocorticoids, while others respond well to diuretics and still others require treatment with exogenous sodium bicarbonate. The underlying pathology—such as obstructive uropathy—can sometimes also be corrected.

- **Anion gap metabolic acidosis.** Anion gap metabolic acidosis results when hydrogen ions accumulate with an anion other than chloride. The accompanying unmeasured anion elevates the anion gap.
- **Lactic acidosis.** In the process of gluconeogenesis, lactic acid is generated from metabolism of pyruvate. Lactic acid is transiently buffered by the bicarbonate buffer system and is then converted back to pyruvate, primarily in the liver. In this case, the anion gap portion of the metabolic acidosis is most likely due to lactic acidosis from tissue hypoperfusion.

Use of bicarbonate to treat lactic acidosis caused by tissue hypoxia is controversial. Correction of the underlying disorder allows the accumulated lactate to be regenerated back to bicarbonate. If the bicarbonate concentration is very low and the pH is less than 7.1, administration of sodium bicarbonate may be helpful. (See **Reference 2.**)

- **Ketoacidosis.** When glucose is in short supply or cannot be utilized, the liver converts free fatty acids into ketones to be used as an alternative energy source. Decreased insulin activity and increased glucagon activity lead to formation of acetoacetic acid and beta-hydroxybutyric acid. The presence of these ketoacids decreases the serum bicarbonate concentration and increases the anion gap.

As in lactic acidosis, alkali therapy in ketoacidosis is controversial. Enhancement of glucose utilization will allow regeneration of bicarbonate from ketoacid anions and correction of the acidosis. Occasionally, excretion of the ketoacid anions in the urine will limit the amount of bicarbonate that can be generated through therapy with glucose or insulin. In this case, the patient will have a normal anion gap and may benefit from exogenous alkali therapy.

Metabolic alkalosis

Case 2

A 36-year-old woman presents to the emergency department with generalized weakness. She takes no prescribed medications or any other drugs.

On physical examination, her blood pressure is 105/75 mm Hg. Laboratory studies show the following:

- blood urea nitrogen, 40 mg/dL
- serum creatinine, 1.9 mg/dL
- serum sodium, 130 meq/L
- serum potassium, 3.0 meq/L
- serum chloride, 85 meq/L
- serum bicarbonate, 35 meq/L

Arterial blood gas studies on room air reveal pH 7.49 and Pco_2 48 mm Hg. The urinary sodium concentration is 50 meq/L, potassium concentration is 30 meq/L, and chloride concentration is 2 meq/L.

Commentary

A primary increase in the bicarbonate concentration can result from loss of hydrogen chloride or, less commonly, addition of bicarbonate. Once generated, the metabolic alkalosis is corrected through urinary excretion of the excess bicarbonate. Alkalosis is maintained only when renal bicarbonate excretion is limited owing to a reduction in renal function or stimulation of renal tubule bicarbonate reabsorption. Increased reabsorption is caused by extracellular fluid volume contraction, chloride depletion, hypokalemia, or elevated mineralocorticoid activity.

The most common causes of metabolic alkalosis are vomiting, nasogastric suction, and diuretic therapy. In these cases, which are classified as chloride responsive, administration of sodium chloride reverses the alkalosis by expanding the intravascular volume.

Thiazide and loop diuretics increase renal excretion of sodium chloride and water and thereby contract the extracellular fluid and activate the renin-angiotensin-aldosterone axis.

Key points

- Metabolic alkalosis is often caused by upper gastrointestinal loss of hydrogen chloride or by renal loss of hydrogen chloride with diuretic therapy.
- Metabolic alkalosis is maintained by extracellular fluid volume contraction, chloride depletion, hypokalemia, or elevated mineral corticoid activity.

Persistent distal delivery of sodium chloride in the presence of aldosterone results in urinary loss of potassium and hydrogen. This process generates hypokalemia and metabolic alkalosis. The combination of hypokalemia and extracellular fluid contraction maintain the metabolic alkalosis. Thus, the kidney is the site of both bicarbonate generation and maintenance in patients with diuretic-induced metabolic alkalosis.

The very low urinary chloride concentration in this case suggests vomiting or remote diuretic ingestion. It also suggests that sodium chloride volume expansion will correct the alkalosis.

Less commonly, a generated metabolic alkalosis is maintained in the absence of volume depletion. Patients with metabolic alkalosis and a high urinary chloride level (greater than 20 meq/L) have maintenance mechanisms related to persistent mineralocorticoid effect in the absence of extracellular fluid contraction or hypokalemia. Examples are primary hyperaldosteronism and Cushing's syndrome.

- **Respiratory acidosis.** Respiratory acidosis is due to a primary increase in arterial Pco_2, which accumulates when ventilation is inadequate. Hypoventilation can result from disorders or medications that affect the central nervous system respiratory center, respiratory muscles, and chest wall; obstruction of the airway; or ventilation-perfusion mismatch. **Table 2** (page 7) shows the most common causes of respiratory acidosis.
- **Respiratory alkalosis.** Hyperventilation reduces the arterial Pco_2, which increases the pH. **Table 3** (page 7) shows the causes of respiratory alkalosis.

Mixed acid-base disorders

Case 3

A 38-year-old man with diabetes presents with a four-day history of persistent vomiting. His body temperature is 39 °C (102 °F), heart rate 88/min, and blood pressure 98/56 mm Hg. Laboratory studies show the following:

- serum sodium, 138 meq/L
- serum potassium, 3.0 meq/L
- serum chloride, 80 meq/L
- serum bicarbonate, 34 meq/L
- serum glucose, 510 mg/dL

Arterial blood gas studies on room air reveal pH 7.5, Pco_2 42 mm Hg, and Pco_2 80 mm Hg.

Commentary

Often, more than one acid-base disturbance is present simultaneously. Diagnosis of mixed disturbances requires calculation of renal and respiratory compensation. Calculation of the anion gap and the ratio of the change in anion gap to change in bicarbonate concentration ("delta-delta") may also be helpful.

Mixed metabolic and respiratory acidosis frequently occurs during cardiopulmonary arrest. If a patient with metabolic acidosis has an inappropriately low arterial Pco_2, respiratory alkalosis may coexist. This mixed disorder will tend to normalize the pH. Other frequent causes of this particular mixed disorder are sepsis and salicylate poisoning.

One of the most challenging diagnostic problems is a patient with an elevated Pco_2. The difficulty lies in the different compensatory responses in acute and chronic respiratory acidosis.

For example, in a patient with a Pco_2 of 60 mm Hg, the expected compensatory response in acute respiratory acidosis would be an increase in bicarbonate concentration to 26 meq/L. The expected response in chronic respiratory acidosis is an increase in bicarbonate concentration to 32 meq/L.

Intermediate bicarbonate values, such as 29 meq/L, may mean that a metabolic alkalosis is present with an acute respiratory acidosis or that a metabolic acidosis is complicating a chronic respiratory acidosis. In this case, history and physical examination allow the clinician to distinguish between these possibilities.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

References

1. Ishihara, K, Szerlip HM. Anion gap acidosis. Semin Nephrol. 1998;18:83-97. PMID: 9459291

2. Adrogue HJ, Madias NE. Medical progress: management of life-threatening acid-base disorders. First of two parts. N Engl J Med. 1998;338:26-34. PMID: 9414329; Second of two parts. N Engl J Med. 1998;338:107-11. PMID: 9420343

Adapted from MKSAP 13, "Nephrology and Hypertenson," 2003.

Table 2 Causes of Respiratory Acidosis

Central nervous system depression
- Sedatives
- Central nervous system lesions

Neuromuscular disorders
- Myopathies
- Neuropathies

Thoracic cage restriction
- Kyphoscoliosis
- Scleroderma

Impaired lung motion
- Pleural effusion
- Pneumothorax

Acute obstructive pulmonary disease
- Aspiration
- Tumor
- Bronchospasm

Chronic obstructive pulmonary disease

Miscellaneous
- Ventilator malfunction
- Cardiopulmonary resuscitation

Table 3 Causes of Respiratory Alkalosis

Anxiety

Central nervous system disorders
- Cerebrovascular accident
- Tumor
- Infection

Hormones
- Progesterone
- Catecholamines

Drugs
- Salicylates
- Analeptics

Sepsis and endotoxemia

Hyperthyroidism

Hypoxia

Pregnancy

Cirrhosis

Pulmonary edema

Lung diseases
- Pulmonary emboli
- Restrictive lung disorders

Pneumonia

Ventilator-induced

Hospital medicine fast facts: HIV hospital admissions

The number of U.S. hospital admissions for HIV infection has fallen by half since 1995, just before life-prolonging protease inhibitor drugs known as the "AIDS cocktail" were approved. While the number of admissions fell between 1995 and 2003, more of the costs of those hospitalizations had shifted to Medicare.

Here is a breakdown of HIV admission statistics between 1995 and 2003:

AIDS inpatient deaths
The percentage of AIDS patients who died in the hospital fell

32%

from 12.5% in 1995 to 8.5% in 2003.

Female HIV patients
The percentage of hospitalized HIV patients who were women rose to nearly

34%

in 2003, up from 26% in 1995.

Medicare coverage
Medicare paid for nearly

17%

of all HIV hospital stays in 2003, up from 11% in 1995.

Medicaid, private coverage
The percentage of HIV admissions paid for by Medicaid dropped to

49%

in 2003, down from 53% in 1995. The share paid for by commerical insurers declined in 2003 to

17%

from 22% in 1995.

Uninsured patients
The percentage of HIV hospital stays from uninsured patients rose to nearly

11%

in 2003, up from 8% in 1995.

Source: Agency for Healthcare Research and Quality, Dec. 1, 2005