Chapter 73: Acid–Base Disorders

INTRODUCTION

- *Acid–base disorders* are caused by disturbances in hydrogen ion (H^+) homeostasis, which is ordinarily maintained by extracellular buffering, renal regulation of hydrogen ion and bicarbonate excretion, and ventilatory regulation of carbon dioxide (CO_2) elimination.

GENERAL PRINCIPLES

- Buffering refers to the ability of a solution to resist change in pH after the addition of a strong acid or base. The body's principal extracellular buffer system is the carbonic acid/bicarbonate (H_2CO_3/HCO_3^-) system.
- Most of the body's acid production is in the form of CO_2 and is produced from catabolism of carbohydrates, proteins, and lipids.
- There are four primary types of acid–base disturbances, which can occur independently or together as a compensatory response.
- Metabolic acid–base disorders are caused by changes in plasma bicarbonate concentration (HCO_3^-). Metabolic acidosis is characterized by decreased HCO_3^-, and metabolic alkalosis is characterized by increased HCO_3^-.
- Respiratory acid–base disorders are caused by altered alveolar ventilation, producing changes in arterial carbon dioxide tension ($PaCO_2$). Respiratory acidosis is characterized by increased $PaCO_2$, whereas respiratory alkalosis is characterized by decreased $PaCO_2$.

DIAGNOSIS

- Blood gases (**Table 73-1**), serum electrolytes, medical history, and clinical condition are the primary tools for determining the cause of acid–base disorders and for designing therapy.
- Arterial blood gases (ABGs) are measured to determine oxygenation and acid–base status (**Figure 73-1**). Low pH values (<7.35) indicate acidemia, whereas high values (>7.45) indicate alkalemia. The $PaCO_2$ value helps determine whether there is a primary respiratory abnormality, whereas the HCO_3^- concentration helps determine whether there is a primary metabolic abnormality. Steps in acid–base diagnosis and interpretation based on observed compensatory responses are described in **Tables 73-2** and **73-3**, respectively.

FIGURE 73-1

Analysis of arterial blood gases.

(HCO_3-, bicarbonate; PaCO2, partial pressure of carbon dioxide.)

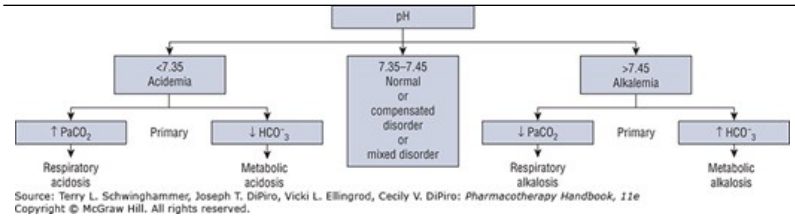


TABLE 73-1

Normal Blood Gas Values

	Arterial Blood	Mixed Venous Blood
pH	7.40 (7.35–7.45)	7.38 (7.33–7.43)
PO_2	80–100 mm Hg (10.6–13.3 kPa)	35–40 mm Hg (4.7–5.3 kPa)
SaO_2	95% (0.95)	70–75% (0.70–0.75)
PCO_2	35–45 mm Hg (4.7–6.0 kPa)	45–51 mm Hg (6.0–6.8 kPa)
HCO_3^-	22–26 mEq/L (mmol/L)	24–28 mEq/L (mmol/L)

HCO_3^-, bicarbonate; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; SaO_2, saturation of arterial oxygen.

TABLE 73-2

Steps in Acid–Base Diagnosis

1. Obtain ABGs and electrolytes simultaneously
2. Compare [HCO_3^-] on ABG and electrolytes to verify accuracy
3. Calculate SAG
4. Is acidemia (pH <7.35) or alkalemia (pH >7.45) present?
5. Is the primary abnormality respiratory (alteration in $PaCO_2$) or metabolic (alteration in HCO_3)?
6. Estimate compensatory response (Table 73-3)
7. Compare change in [Cl^-] with change in [Na^+]

ABG, arterial blood gases; [Cl^-], chloride ion concentration; [HCO_3^-], bicarbonate concentration; [Na^+], sodium ion concentration; $PaCO_2$, partial pressure of carbon dioxide from arterial blood; SAG, serum anion gap.

TABLE 73-3

Guidelines for Interpretation of Acid–Base Disorders Based on Compensatory Responses

Acidosis	**Compensation**
Metabolic	$PaCO_2$ (in mm Hg) should decrease by 1.3 times the fall in plasma [HCO_3^-] (in mEq/L or mmol/L)
Acute respiratory	The plasma [HCO_3^-] should increase by 0.1 times the increase in $PaCO_2 \pm 3$ (in mm Hg)
Chronic respiratory	The plasma [HCO_3^-] should increase by 0.35 times the increase in $PaCO_2 \pm 4$ (in mm Hg)
Alkalosis	**Compensation**
Metabolic	$PaCO_2$ (in mm Hg) should increase by 0.4–0.6 times the rise in plasma [HCO_3^-] (in mEq/L or mmol/L)
Acute respiratory	The plasma [HCO_3^-] should decrease by 0.2 times the decrease in $PaCO_2$ (in mm Hg), but usually not to <18 mEq/L (mmol/L)
Chronic respiratory	The plasma [HCO_3^-] should fall by 0.35 times the decrease in $PaCO_2$ (in mm Hg), but usually not to <14 mEq/L (mmol/L)

[HCO_3^-], bicarbonate concentration; $PaCO_2$, partial pressure of carbon dioxide from arterial blood; multiply values expressed in kPa by 7.519 to convert to mm Hg.

METABOLIC ACIDOSIS: PATHOPHYSIOLOGY

- Metabolic acidosis is characterized by a decrease in pH as a result of a primary decrease in serum HCO_3^- concentration, which can result from the buffering of an exogenous acid (consumption of HCO_3^-), accumulation of an organic acid because of a metabolic disturbance (eg, lactic acid and ketoacids), loss of bicarbonate-rich body fluids (eg, diarrhea, biliary drainage, or pancreatic fistula), or progressive accumulation of endogenous acids secondary to impaired kidney function (eg, phosphates and sulfates). Rapid administration of non–alkali-containing IV fluids can cause dilutional acidosis.
- Serum anion gap (SAG) can be used to infer whether an organic or mineral acidosis is present. SAG is calculated as follows:

  $$SAG = [Na^+] - [Cl^-] - [HCO_3^-]$$ SAG=[Na+]−[Cl−]−[HCO3−]

  The normal anion gap is approximately 9 mEq/L (mmol/L), with a range of 3–11 mEq/L (mmol/L). SAG is a relative rather than an absolute indication of the cause of metabolic acidosis.

CLINICAL PRESENTATION

- Chronic metabolic acidosis is relatively asymptomatic; major manifestations are bone demineralization with the development of rickets in children and osteomalacia and osteopenia in adults.
- Acute severe metabolic acidemia (pH <7.2) involves the cardiovascular, respiratory, and central nervous systems. Hyperventilation is often the first sign of metabolic acidosis. Respiratory compensation may occur as Kussmaul respirations (ie, deep, rapid respirations characteristic of diabetic ketoacidosis).
- The compensatory response for metabolic acidosis is to increase CO_2 excretion by increasing the respiratory rate.

TREATMENT

- The primary treatment is to correct the underlying disorder. Additional treatment depends on the severity and onset of acidosis.
- Manage asymptomatic patients with mild to moderate acidemia (HCO_3^- 12–20 mEq/L [mmol/L]; pH 7.2–7.4) with gradual correction of the acidemia over days to weeks using oral **sodium bicarbonate** or other alkali preparations (**Table 73-4**).
- The dose of bicarbonate can be calculated as follows:

$$\text{Loading dose (mEq or mmol/L)} = (V_d\ HCO_3^- \times \text{body weight}) \times (\text{desired } [HCO_3^-] - \text{current } [HCO_3^-]),$$

Loading dose (mEq or mmol/L)=(Vd HCO3−×body weight)×(desired [HCO3−]−current [HCO3−]),

where $V_d\ HCO_3^-$ is the volume of distribution of HCO_3^- (0.5 L/kg).

- Intravenous alkali therapy can be used to treat patients with acute severe metabolic acidosis due to hyperchloremic acidosis, but its role is controversial in patients with lactic acidosis. Therapeutic options include **sodium bicarbonate** and historically, tromethamine, which is no longer available in the United States.
- Sodium bicarbonate is recommended to raise arterial pH to 7.2. However, an open-label, multicenter, controlled trial found that sodium bicarbonate administration did not reduce mortality at 28 days compared with no sodium bicarbonate administration. If IV sodium bicarbonate is administered, the goal is to increase, not normalize, pH to 7.2 and HCO_3^- to 8–10 mEq/L (mmol/L).

TABLE 73-4

Therapeutic Alternatives for Oral Alkali Replacement

Generic Name	Trade Name(s)	Milliequivalents of Alkali	Dosage Form(s)	Comment
Shohl's solution (sodium citrate/citric acid)	Bicitra (Willen)	1 mEq Na/mL; equivalent to 1 mEq bicarbonate	Solution (500 mg Na citrate, 334 mg citric acid/5 mL)	Citrate preparations increase absorption of aluminum
Sodium bicarbonate	Various (eg, Sodamint)	3.9 mEq bicarbonate/tablet (325 mg)	325 mg tablet	Bicarbonate preparations can cause bloating because of CO_2 production
		7.8 mEq bicarbonate/tablet (650 mg)	650 mg tablet	
	Baking soda (various)	60 mEq bicarbonate/tsp (5 g/tsp)	Powder	
Potassium citrate	Urocit-K (Mission)	5 mEq citrate/tablet	5 mEq tablet	Citrate preparations increase absorption of aluminum
Potassium bicarbonate/potassium citrate	K-Lyte (Bristol)	25 mEq bicarbonate/tablet	25 mEq tablet (effervescent)	Citrate preparations increase absorption of aluminum, while bicarbonate preparations can cause bloating
	K-Lyte DS (Bristol)	50 mEq bicarbonate/tablet (double strength)	50 mEq tablet (effervescent)	
Potassium citrate/citric acid	Polycitra-K (Willen)	2 mEq K/mL; equivalent to 2 mEq bicarbonate	Solution (1,100 mg K citrate, 334 mg citric acid/5 mL)	Citrate preparations increase absorption of aluminum
		30 mEq bicarbonate/unit dose packet	Crystals for reconstitution (3,300 mg K citrate, 1,002 mg citric acid/unit dose packet)	
Sodium citrate/potassium citrate/citric acid	Polycitra (Willen) Polycitra-LC (Willen)	1 mEq K, 1 mEq Na/mL; equivalent to 2 mEq bicarbonate	Syrup (Polycitra); solution (Polycitra-LC) (both contain 550 mg K citrate, 500 mg Na citrate, 334 mg citric acid/5 mL)	Citrate preparations increase absorption of aluminum

METABOLIC ALKALOSIS: PATHOPHYSIOLOGY

- Metabolic alkalosis is *initiated* by increased pH and HCO_3^-, which can result from loss of hydrogen ions via the gastrointestinal (GI) tract (eg,

nasogastric suctioning, vomiting) or kidneys (eg, diuretics, Cushing syndrome) or from gain of bicarbonate (eg, administration of bicarbonate, acetate, lactate, or citrate).

- Metabolic alkalosis is *maintained* by abnormal renal function that prevents the kidneys from excreting excess bicarbonate.

CLINICAL PRESENTATION

- No unique signs or symptoms are associated with mild to moderate metabolic alkalosis. Some patients complain of symptoms related to the underlying disorder (eg, muscle weakness with hypokalemia or postural dizziness with volume depletion) or have a history of vomiting, gastric drainage, or diuretic use.
- Severe alkalemia (pH >7.60) can be associated with cardiac arrhythmias and neuromuscular irritability.
- The compensatory response to metabolic alkalosis is respiratory, manifested as hypoventilation which increases $PaCO_2$.

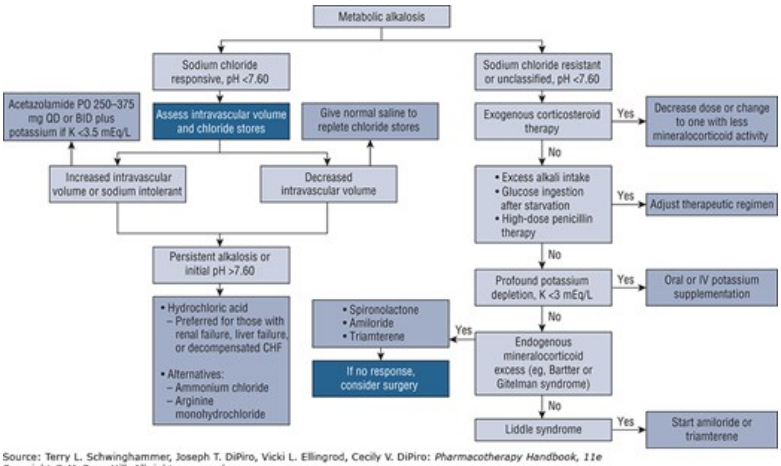
TREATMENT

- Treatment is aimed at correcting the factor(s) responsible for maintaining the alkalosis and depends on whether the disorder is sodium chloride responsive or resistant (**Figure 73-2**).

FIGURE 73-2

Treatment algorithm for patients with primary metabolic alkalosis.

(BID, twice daily; CHF, congestive heart failure; K, potassium [serum potassium in mEq/L is numerically equal to mmol/L]; PO, orally; QD, every day.)



RESPIRATORY ALKALOSIS: PATHOPHYSIOLOGY

- Respiratory alkalosis is characterized by a decrease in $PaCO_2$ that leads to an increase in pH.
- $PaCO_2$ decreases when ventilatory CO_2 excretion exceeds metabolic CO_2 production, usually because of hyperventilation.
- Causes include increases in neurochemical stimulation via central or peripheral mechanisms, or physical increases in ventilation via voluntary or artificial means (eg, mechanical ventilation).

CLINICAL PRESENTATION

- Although usually asymptomatic, respiratory alkalosis can cause adverse neuromuscular, cardiovascular, and GI effects.
- Light-headedness, confusion, decreased intellectual functioning, syncope, and seizures can be caused by decreased cerebral blood flow.
- Nausea and vomiting can occur, probably due to cerebral hypoxia.
- Cardiac arrhythmias can occur in severe respiratory alkalosis.
- Serum electrolytes can be altered; serum chloride is usually increased; serum potassium, phosphorus, and ionized calcium are usually decreased.
- The initial compensatory response is to chemically buffer excess bicarbonate by releasing hydrogen ions from intracellular proteins, phosphates, and hemoglobin. If prolonged (>6 hours), the kidneys attempt to further compensate by increasing bicarbonate elimination.

TREATMENT

- Treatment is often unnecessary because most patients have few symptoms and only mild pH alterations (ie, pH not exceeding 7.50).
- Direct measures (eg, treatment of pain, hypovolemia, fever, infection, or salicylate overdose) can be effective. A rebreathing device (eg, paper bag) can help control hyperventilation in patients with anxiety/hyperventilation syndrome.
- Correct respiratory alkalosis associated with mechanical ventilation by decreasing the number of mechanical breaths per minute, using a capnograph and spirometer to adjust ventilator settings more precisely, or increasing dead space in the ventilator circuit.

RESPIRATORY ACIDOSIS: PATHOPHYSIOLOGY

- Respiratory acidosis is characterized by an increase in $PaCO_2$ and a decrease in pH.
- Respiratory acidosis results from disorders that restrict ventilation or increase CO_2 production, airway and pulmonary abnormalities, neuromuscular abnormalities, or mechanical ventilator problems.

CLINICAL PRESENTATION

- Neuromuscular symptoms include altered mental status, abnormal behavior, seizures, stupor, and coma. Hypercapnia can mimic a stroke or CNS tumor by producing headache, papilledema, focal paresis, and abnormal reflexes. CNS symptoms are caused by increased cerebral blood flow and are variable, depending in part on the acuity of onset.
- Initial compensatory response to acute respiratory acidosis is chemical buffering. If prolonged (>12–24 hours), proximal tubular HCO_3^- reabsorption, ammoniagenesis, and distal tubular H^+ secretion are enhanced, resulting in an increase in serum HCO_3^- concentration that raises pH to normal.

TREATMENT

- Provide adequate ventilation if CO_2 excretion is acutely and severely impaired ($PaCO_2$ >80 mm Hg [>10.6 kPa]) or if life-threatening hypoxia is present (arterial oxygen tension [PaO_2] <40 mm Hg [<5.3 kPa]). Ventilation can include maintaining a patent airway (eg, emergency tracheostomy, bronchoscopy, or intubation), clearing excessive secretions, administering oxygen, and providing mechanical ventilation.
- Treat underlying cause aggressively (eg, administration of bronchodilators for bronchospasm; narcotic or benzodiazepine antagonists to reverse effect of these agents on the respiratory center). Bicarbonate administration is rarely necessary and is potentially harmful.
- Chronic respiratory acidosis (eg, chronic obstructive pulmonary disease [COPD]) is treated essentially the same as acute respiratory acidosis with a few important exceptions. Oxygen therapy should be initiated carefully and only if the PaO_2 is less than 50 mm Hg (6.7 kPa) because the drive to

breathe depends on hypoxemia rather than hypercarbia.

- For information on chronic respiratory acidosis, see Chapter 79.

MIXED ACID–BASE DISORDERS: PATHOPHYSIOLOGY

- Failure of compensation is responsible for mixed acid–base disorders such as respiratory acidosis and metabolic acidosis, or respiratory alkalosis and metabolic alkalosis. In contrast, excess compensation is responsible for metabolic acidosis and respiratory alkalosis, or metabolic alkalosis and respiratory acidosis.
- Respiratory and metabolic acidosis can develop in patients with cardiorespiratory arrest, with chronic lung disease and shock, and with metabolic acidosis and respiratory failure.
- The most common mixed acid–base disorder is respiratory and metabolic alkalosis, which occurs in critically ill surgical patients with respiratory alkalosis caused by mechanical ventilation, hypoxia, sepsis, hypotension, neurologic damage, pain, or drugs; and with metabolic alkalosis caused by vomiting or nasogastric suctioning and massive blood transfusions.
- Mixed metabolic acidosis and respiratory alkalosis occur in patients with advanced liver disease, salicylate intoxication, and pulmonary–renal syndromes.
- Metabolic alkalosis and respiratory acidosis can occur in patients with COPD and respiratory acidosis who are treated with salt restriction, diuretics, and possibly glucocorticoids.

TREATMENT

- Treat mixed respiratory and metabolic acidosis by initiating oxygen delivery to improve hypercarbia and hypoxia. Mechanical ventilation can be needed to reduce $PaCO_2$. During initial therapy, give appropriate amounts of alkali to reverse the metabolic acidosis.
- Correct the metabolic component of mixed respiratory and metabolic alkalosis by administering **sodium and potassium chloride solutions**. Readjust the ventilator or treat the underlying disorder causing hyperventilation to treat the respiratory component.
- Treatment of mixed metabolic acidosis and respiratory alkalosis should be directed at the underlying cause.
- In metabolic alkalosis and respiratory acidosis, pH does not usually deviate significantly from normal, but treatment can be required to maintain PaO_2 and $PaCO_2$ at acceptable levels. Aim treatment at decreasing plasma bicarbonate with sodium and potassium chloride therapy, allowing renal excretion of retained bicarbonate from diuretic-induced metabolic alkalosis.

EVALUATION OF THERAPEUTIC OUTCOMES

- Monitor patients closely because acid–base disorders can be serious and even life-threatening.
- ABGs are the primary tools for evaluation of therapeutic outcome.

See Chapter 69, Acid–Base Disorders, authored by John W. Devlin and Thomas D. Nolin, for a more detailed discussion of this topic.