Acid-Base Disorders

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Education Gap

To treat critically ill children, a physician must have a clear understanding of acid-base balance.

Objectives   After completing this article, readers should be able to:

1. Describe the mechanisms regulating acid-base physiology and identify blood gas abnormalities associated with an acid-base imbalance.

2. Recognize the differential diagnosis and clinical and laboratory features associated with metabolic acidosis and metabolic alkalosis as well as how to manage each appropriately.

3. Calculate an anion gap and formulate a differential diagnosis associated with various anion gap values.

4. Identify factors contributing to compensatory changes associated with primary metabolic and respiratory acidoses and alkaloses.

INTRODUCTION

The body's ability to maintain acid-base homeostasis is based on a complex set of interactions between the respiratory and metabolic systems. This article reviews normal acid-base physiology and examines disorders of acid-base imbalances, first within a primary metabolic cause and then within a primary respiratory cause.

Covering the complex nuances of acid-base control within a limited-scope review article is impossible. Thus, this article focuses on the traditional model based on the Henderson-Hasselbalch equation rather than the strong ion (or Stewart) model, which explores the difference between all the dissociated cations and anions. Using the traditional model, the authors explore the various metabolic and respiratory disturbances while addressing the implications of the anion gap on metabolic acidoses.

REGULATION OF ACID-BASE

The Henderson-Hasselbalch Equation

Homeostatic control of acid-base balance is critical for all metabolic and physiologic functions of the human body. The Henderson-Hasselbalch equation

describes the relationship between pH and the bicarbonate buffering system (the predominant buffering system in plasma) to establish this homeostasis:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$
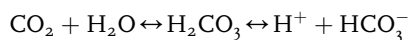
$$pH = pK + \log\left(HCO_3^-/H_2CO_3\right)$$

When accounting for H_2CO_3, the modified equation becomes:

$$pH = pK + \log\left(HCO_3^-/[0.03*PCO_2]\right)$$

Examination of the modified equation reveals the importance of bicarbonate ion (HCO_3^-) and dissolved carbon dioxide (PCO_2) in the determination of pH. The pK is the pH at which the bicarbonate ion (HCO_3^-) and carbon dioxide (CO_2) are equal. This value is approximately 6.35. The 0.03 constant is used to describe the PCO_2 solubility. When changes occur in the pH due to PCO_2 changes, the predominant system involved is the respiratory system. When changes in pH occur due to changes in HCO_3^-, the predominant system involved is the metabolic system. However, the system favors the HCO_3^- at physiologic pH, therefore, the buffering ability of the metabolic system is dependent on the body's ability to eliminate CO_2 through the respiratory system. Thus, it is evident that two complementary systems, respiratory and metabolic, are used to describe changes to the body's pH.

Clinically, the acid-base state is normally determined by a blood gas sample. Although the gold standard remains arterial blood gas measurement, use of the venous or capillary blood gas sample is prevalent within the pediatric population due to the relative ease in obtaining these samples. Although minor differences exist within pH and PCO_2 among the different blood gas sample types, these differences can be accounted for during interpretation by assuming expected slight increases in PCO_2 and decreases in pH for venous samples. As expected due to the location of the blood draw, venous blood gas samples are unreliable for PO_2 measurements. Because capillary blood gradually transitions between arterial and venous states, the PCO_2 and pH normative values often are between the arterial and venous normative values. Of note, a blood gas machine measures the pH and the partial pressure of the gases, but the HCO_3^- ion concentration is a calculated value.

In examining blood gases, acidosis occurs when the pH value is lower than normal. In contrast, alkalosis occurs when the pH value is higher than normal. It is important to characterize pH in context of PCO_2 and HCO_3^- reference ranges and not independently examine any of the variables. For example, a blood gas with a high PCO_2 may reflect a normal pH and should be interpreted as nonacidotic (Table 1).

The Anion Gap

Use of only the Henderson-Hasselbalch equation is insufficient to describe a patient's metabolic acid-base state completely. The anion gap further describes the interactions of the measured positive charges (cations) and negative charges (anions) to the unmeasured charged particles. The anion gap equation is based on the understanding that the cations in the plasma balance the anions in the plasma at equilibrium.

The "measureable" positive and negative charges in the serum refer to those measured with a standard electrolyte panel. To calculate the anion gap, positive charges include sodium (Na^+) and potassium (K^+) while negative charges include bicarbonate (HCO_3^-) and chloride (Cl^-). In normal conditions, the measured cations exceed the measured anions (the normal anion gap), which is predominantly accounted for by the serum proteins. This normal value for the anion gap ranges from 12 to 20 mEq/L (12–20 mmol/L) when the K^+ concentration is included and 8 to 16 mEq/L (8-16 mmol/L) when it is not included.

$$Anion\ Gap = \left(Na^+ + K^+\right) - \left(HCO_3^- + Cl^-\right)$$

In the setting of low serum protein, such as hypoalbuminemia, the normal unmeasured anions are decreased and the anion gap narrows. Thus, with critical illness when protein concentrations are often low, an elevated concentration of unmeasured anions can frequently be masked by an apparently normal (falsely low) anion gap. Consequently, the combination of the modified Henderson-Hasselbalch equation and the anion gap calculation begins to illustrate an individual patient's acid-base balance.

TABLE 1. **General Reference Ranges for Arterial and Venous Blood Gases**

	ARTERIAL	VENOUS
pH	7.38 – 7.42	7.36 – 7.38
PO_2 (mm Hg)	80 – 100	30 – 50
PCO_2 (mm Hg)	38 – 42	43 – 48
HCO_3^- (mmol/L)	22 – 24	25 – 26

HCO_3^-=bicarbonate, PCO_2=partial pressure of carbon dioxide, PO_2= partial pressure of oxygen. Reference normal values are laboratory-dependent and may vary due to differing techniques.

The human body has a natural inclination toward a desired equilibrium, which accounts for the common finding of compensatory changes in the opposite direction. Within settings of respiratory derangement leading to changes in the pH, the compensatory mechanism occurs within the metabolic system. For respiratory acidosis (commonly arising due to an increase of P_{CO_2}), the body compensates by creating metabolic alkalosis (from a retention of HCO_3^-). In contrast, for respiratory alkalosis (commonly arising from a decrease of P_{CO_2}), the body compensates by creating metabolic acidosis (from a loss of HCO_3^-) (Table 2). Metabolic compensation to respiratory derangements often takes hours to days to establish. In comparison, compensatory mechanisms within the respiratory system for primary metabolic derangements generally occur more rapidly, often over minutes to hours.

ASSESSMENT AND DETERMINATION OF ACID-BASE STATE

The first step in the assessment of an acid-base imbalance for a patient is to determine a primary respiratory versus primary metabolic etiology. A detailed history and comprehensive physical examination can offer clues to the presenting cause. Such evaluation may reveal a neurologic (head injury, seizures), respiratory (pneumonia, congenital malformation), cardiovascular (septic shock, myocarditis), gastrointestinal (diarrhea, ingestion), or renal cause (chronic kidney injury, underlying renal disease) of the imbalance.

For example, respiratory compromise from a neurologic cause such as seizures or traumatic brain injury leading to reduced consciousness may result in the body's inability to ventilate properly. This prompts a primary respiratory acidosis. In comparison, gastrointestinal causes can result in primary metabolic alkalosis such as through loss of hydrochloric acid (HCl) by vomiting.

TABLE 2. **Generalized Primary and Compensatory Relationships Between HCO_3^- and P_{CO_2}**

	P_{CO_2}	HCO_3^-
Respiratory Acidosis	↑ (*primary*)	↑ (*compensatory*)
Respiratory Alkalosis	↓ (*primary*)	↓ (*compensatory*)
Metabolic Acidosis	↓ (*compensatory*)	↓ (*primary*)
Metabolic Alkalosis	↑ (*compensatory*)	↑ (*primary*)

HCO_3^-=bicarbonate, P_{CO_2}=partial pressure of carbon dioxide

Extending from this initial assessment, additional clues from results of blood gas analysis and a basic metabolic panel reflecting the anion gap can help discern a primary metabolic versus respiratory cause. Determining the acute or chronic nature of the compensation adds additional diagnostic information.

METABOLIC ACIDOSIS

A combination of the anion gap calculation and knowledge of the pH state within the body is required to describe metabolic acidosis. The regulation of the acid-base state, as noted by the Henderson-Hasselbalch equation, is based on the buffering effect of HCO_3^-. However, from an electroneutrality viewpoint, use of the anion gap calculation can further differentiate causes for the metabolic acidosis. Because reference values in the calculation of unmeasured anions or anion gap vary among laboratories, clinicians must be aware of normal values for the laboratories they use. As noted previously, due to the importance of homeostasis, normal gap versus increased gap acidosis indicate vastly different clinical pictures.

Hyperchloremic (Non-anion Gap) Metabolic Acidosis
Chloride (Cl^-) has an important relationship to HCO_3^- because there are few causes of non-anion gap acidosis. In acidotic states with low HCO_3^- values, a non-anion gap acidosis state (or a normal anion gap) can exist through the buffering effect of Cl^- and is termed hyperchloremic non-anion gap acidosis. In these conditions, the relative ratio of the anions and the cations remains intact, with the anions balanced by an increase of Cl^- equal to the decrease in HCO_3^-.

Non-anion gap acidosis can result from decreased HCO_3^- either through gastrointestinal or renal losses. Both of these types of losses result in a buffering with Cl^- ions. Gastrointestinal (postpyloric) losses include diarrhea and conditions such as short gut syndrome. Renal losses include chronic renal insufficiency and renal tubular acidosis.

A common type of hyperchloremic non-anion gap acidosis occurs in the hospitalized patient who receives infusions of large amounts of normal saline. In these cases, the relative Cl^- load from the exogenous fluid results in a decrease in HCO_3^- to maintain plasma electroneutrality. Often this phenomenon occurs when large amounts of normal saline are delivered to a patient who has metabolic acidosis attributed to dehydration or starvation (presumed due to lactic acidosis from hypoperfusion or ketoacidosis from starvation). These initial metabolic acidosis states generally are high-anion gap acidoses, with an imbalance in the plasma electroneutrality state due to the contribution of lactic acids and ketoacids. Following a large infusion of normal saline, the anion gap resolves, but there may be a

decrease in HCO_3^- values due to the addition of large amounts of Cl^-. Thus, clinicians who do not take into account the anion gap when assessing the acid-base status after fluid resuscitation can be deceived into thinking that the acidosis state has worsened by examining only the HCO_3^- value. Instead, the presence of a normal anion gap (especially if the patient previously exhibited gap acidosis) following hydration with normal saline indicates an improving clinical condition. Although the evidence is unclear regarding whether hyperchloremic non-anion gap acidosis from saline resuscitation worsens outcome, clinicians who understand the physiology may avoid this sequela as much as possible to limit possible adverse effects (eg, increased respiratory work or increased intracranial pressure).

Elevated Anion Gap Acidosis

The presence of an increased gap acidosis (anion gap higher than normal) is due to an increase of unmeasured anions. This can occur following an increase in acid production or an underexcretion of acid. The classic mnemonic for causes of gap acidosis is MUDPILES (**m**ethanol, **u**remia, **d**iabetic ketoacidosis, **p**araldehyde, **i**soniazid, **l**actic acidosis, **e**thylene glycol, **s**alicylates). Although most causes on this list represent exogenous ingestion of acids, physiologically high-anion gap acidosis due to increased production of endogenous acids is more common. The 2 primary sources for such endogenous production are lactic acidosis and ketoacidosis.

Lactic acidosis can be due to a hypoxia event or shock state, among other causes. Cells produce lactic acid when energy creation shifts from aerobic to anaerobic metabolism. Although this most commonly occurs when tissue oxygen delivery falls to a critical level, anaerobic metabolism and increased lactic acid production can also occur in hypermetabolic states. Lactate can be produced from cells in the brain, skeletal muscle, and gastrointestinal tissue exposed to hypoxia. The cause of the hypoxic state can be multifactorial. For example, direct hypoxia such as drowning or respiratory failure may result in lactic acidosis. In addition, the failure of mitochondrial function, as occurs in cyanide poisoning, can lead to anaerobic metabolism and the subsequent creation of lactic acid. Salicylate toxicity similarly causes failure of oxidative phosphorylation that creates subsequent lactic acidosis.

Ketoacidosis occurs in diabetic ketoacidosis or after a prolonged starvation state. In those who have diabetes, the inability to produce insulin results in a state of cellular starvation due to the body's failure to use glucose. Consequently, the body resorts to the breakdown of lipids, producing ketoacids. True starvation states in which a glucose source is limited also move the body toward breakdown of lipids

and creation of ketone bodies. Complicating the diabetic ketoacidosis state is the presence of hyperglycemia (from an inability to transport glucose intracellularly), which leads to high serum osmolality. The resultant osmotic diuresis can progress to hypovolemic shock and lactic acidosis from anaerobic metabolism due to hypoperfusion.

Less commonly, underexcretion of acid leading to gap acidosis can occur from renal failure or impaired clearance of acid (lactate) through the liver due to liver failure. Other causes of gap acidosis include inborn errors of metabolism, and ingestion of toxins, such as those represented in the mnemonic MUDPILES, leading to acid formation.

Respiratory Compensation

When exposed to a low pH from metabolic acidosis, the body responds with an alkalotic respiratory state through hyperventilation. This response can occur over minutes to hours, depending on an intact neurologic response and the ability of the body to maintain hyperventilation. Through hyperventilation, the body reduces the Pco_2 within the system, thereby creating respiratory alkalosis. The respiratory alkalosis combined with the primary metabolic acidosis works to return the body's pH back to (but never past) normal.

The classic example of a respiratory compensation to metabolic acidosis is the diabetic ketoacidosis state. Affected patients often present with deep hyperventilation, called Kussmaul breathing. The deep and fast breathing pattern serves to increase the minute ventilation by increasing both the volume of each breath (tidal volume) and the number of breaths (rate) in a minute. In these cases, neurologic injury can limit the compensatory mechanism for the metabolic derangement. Specifically, with severe diabetic ketoacidosis, cerebral edema is one sequela that may result in an inability to direct an appropriate respiratory compensation. When neurologic injury occurs, the patient may have severe acidosis without an appropriately low Pco_2 as the respiratory system attempts to buffer the metabolic acidosis.

METABOLIC ALKALOSIS

Metabolic alkalosis, as revealed by the Henderson-Hasselbalch equation, is due to an increase in the HCO_3^- content of the serum, resulting in an increase in pH. The causes include gastrointestinal or renal losses of Cl^-. Gastrointestinal losses can occur through profuse amounts of emesis or Cl^--losing diarrhea. Renal tubular losses can occur through the use of diuretics. The subsequent compensation to the Cl^- loss designed to maintain electroneutrality is to increase the amount of HCO_3^- buffer, leading to a higher pH. Similarly, a net gain of cations can also result in metabolic alkalosis. Causes

include large amounts of lactated Ringer solution and the milk-alkali syndrome.

A commonly reviewed cause of metabolic alkalosis in the pediatric setting is hypochloremic alkalosis from pyloric stenosis. In normal physiology, HCl is excreted from the gastric lumen and neutralized by HCO_3^- secreted by the pancreas. In pyloric stenosis, there is a loss of HCl through vomiting and concurrent decrease in secretion of HCO_3^-, resulting in a decrease in serum Cl^- and an increase in serum HCO_3^-. This combination results in the classic hypochloremic alkalosis of pyloric stenosis. Preoperative hydration to correct both the dehydration and hypochloremic alkalosis is important for prevention of postoperative apnea because the respiratory compensation for metabolic alkalosis is hypoventilation (to raise PCO_2).

Another common cause of alkalosis, especially in the pediatric critical care setting, is the contraction alkalosis induced by diuretic use. Contraction alkalosis occurs when there is loss of fluids that contain a proportionately lower amount of HCO_3^- than the serum concentration. With relatively more free fluid lost, the concentration of HCO_3^- remaining in the serum increases. Furthermore, the interplay of the renin-angiotensin system, as triggered by the hypovolemic state sensed by the body, further increases absorption of HCO_3^- through the process of hydrogen ion excretion. Thus, the combination of these factors created by diuretic use results in a higher-than-normal HCO_3^- value and metabolic alkalosis.

Although increased morbidity and mortality are associated with the presence of metabolic alkalosis, most of these events are self-correcting without clinically significant sequelae. One key exception to this rule is from pyloric stenosis. Within the critical care setting, metabolic alkalosis can also be brought on by the use of diuretics before extubation in an attempt to improve respiratory mechanics and pulmonary function in a patient who has had previous fluid overload. In these instances, acetazolamide is often used to waste HCO_3^- through the renal system by inhibiting the carbonic anhydrase enzyme responsible for proximal tubule absorption of HCO_3^-. The rationale for this approach is to prevent acute hypercapnic respiratory failure following extubation. Because the respiratory compensation for metabolic alkalosis is to hypoventilate (and raise PCO_2), this acute rise in PCO_2 can lead to hypercapnic respiratory failure. Thus, acetazolamide is commonly used before extubation if significant contraction alkalosis from diuretics exists.

Respiratory Compensation

Respiratory acidosis through hypoventilation occurs in response to metabolic alkalosis. In response to a high pH, the body's attempt at equilibrium mandates a move toward an acidotic respiratory state through hypoventilation.

By hypoventilating, the body drives up the PCO_2, thereby creating respiratory acidosis. Combined with the primary metabolic alkalosis, the respiratory acidosis works to return the body's pH back to normal.

RESPIRATORY ACIDOSIS

Respiratory acidosis is the result of an increase in PCO_2 leading to a lower pH. This accumulation can be related to increased production or decreased elimination of CO_2 through the respiratory system.

Increased production of CO_2 can be due to multiple causes. The predominant cause within the pediatric population is increasing cellular metabolic activity, which can be seen in infection or fever. Increased production of CO_2 can also be related to the carbohydrate load of the body. This derangement is often due to iatrogenic causes such as parenteral nutrition in which an excess of carbohydrate relative to the body's need is given. With the body's ability to eliminate CO_2 and increase minute ventilation to account for increased production, an overproduction of CO_2 by itself rarely leads to respiratory acidosis unless the body's compensation is limited (such as in a paralyzed patient). Instead, respiratory acidosis more often results from an inability to remove CO_2 from the bloodstream.

Decreased elimination of CO_2 can have several causes. Elimination of CO_2 is based on 3 components of the body working in synchrony: the neurologic component (in recognizing the need to eliminate CO_2), the musculoskeletal component (in physically moving the chest to create appropriate minute ventilation), and the alveolar component (in allowing for diffusion of CO_2 out of the bloodstream). Failure of any of these components can result in respiratory acidosis. Neurologic causes include injuries (eg, traumatic or stroke), seizures, narcotics, and other pharmacologic agents causing neurologic depression. Musculoskeletal failure can result from acute causes such as flail chest or chest wall edema or underlying musculoskeletal disorders such as myasthenia gravis or muscular dystrophy. However, most commonly, respiratory acidosis occurs from the decreased ability to eliminate CO_2 through the alveoli, such as associated with pneumonia, pulmonary edema, and acute respiratory distress syndrome.

Treatment for respiratory acidosis involves enhancing CO_2 elimination and treating the underlying cause. For causes such as pneumonia, treatment with appropriate antibiotics in addition to the short-term use of positive pressure or mechanical ventilation can improve CO_2 elimination. However, there are instances when, despite maximal mechanical ventilation, CO_2 elimination cannot balance CO_2

production. Although not frequent, these instances may require permissive hypercapnia (high P_{CO_2} with low pH) to limit further pulmonary injury from aggressive mechanical ventilation. Similarly, permissive hypercapnia is a recommended approach to a neonatal and pediatric ventilation strategy to limit injury from mechanical ventilation. Studies have shown that permissive hypercapnia is well tolerated, with limited morbidity and mortality in an otherwise healthy patient (without underlying neurologic pathology or pulmonary hypertension), as long as hypoxia is avoided and hemodynamics are normal.

Metabolic Compensation

In response to a low pH from primary respiratory acidosis, the body attempts to achieve equilibrium by moving toward an alkalotic metabolic state through retention of HCO_3^- within the metabolic system. By retaining HCO_3^- through the renal system, the body can drive up the HCO_3^-, thereby creating metabolic alkalosis based on the Henderson-Hasselbalch equation. The primary respiratory acidosis combined with the metabolic alkalosis works to return the body's pH back to normal.

Of note, compensation of the metabolic system to a primary respiratory acid-base disorder is much slower than compensation of the respiratory system to a primary metabolic acid-base disorder. Therefore, in acute respiratory acidosis, the pH is often well below the normal range.

In chronic respiratory disease, such as chronic lung disease, the clinician may notice a chronically compensated state. In these cases, the patient maintains a pH within normal ranges but has a persistently elevated P_{CO_2} due to the underlying chronic condition. Over time, the body maintains homeostasis and the need for a normal pH by chronically retaining HCO_3^-. On blood gas examination, such patients often have a P_{CO_2} in the range of 50 to 60 mm Hg with HCO_3^- in the range of 30 to 40 mEq/L (30–40 mmol/L) at baseline.

RESPIRATORY ALKALOSIS

Respiratory alkalosis is the result of an excessive elimination of P_{CO_2} leading to a higher pH ("hyperventilation"). This inappropriate elimination is much less common than any other acid-base derangements. Causes for primary respiratory alkalosis typically involve an increased respiratory drive due to toxins or primary central nervous system events. Salicylate intoxication and hyperammonemia can promote hyperventilation. Anxiety and stress can also lead to hyperventilation and are typical causes related to the distress a blood draw can induce in a pediatric patient. In addition, some neurologic injuries (including meningitis or some traumatic brain injury or tumors) can cause hyperventilation, depending on the location and severity of the insult. Mild respiratory alkalosis frequently occurs in disease with increased lung water (eg, pneumonia, pulmonary edema) due to alveolar stretch receptors enhancing the respiratory drive.

Metabolic Compensation

In response to a high pH from a primary respiratory alkalosis, the body's attempt to equilibrate mandates a move toward an acidotic metabolic state through elimination of HCO_3^-. The primary respiratory alkalosis combined with the metabolic acidosis works to return the body's pH to normal. Again, such metabolic compensation occurs over days compared to the minutes to hours needed in respiratory compensation.

CONCLUSION

Understanding the acid-base status of a patient is important both for those who are critically ill and those who have general metabolic derangements. Although seemingly complex, an understanding of 2 principles, the Henderson-Hasselbalch equation and the anion gap calculation, can offer clinicians a view into possible causes of the acid-base imbalance. Just as important is a firm grasp of the interdependence of the metabolic and respiratory systems.

Summary

- A fundamental understanding of acid-base balance is vital to caring for pediatric patients with critical illnesses as well as for managing electrolyte disturbances in those who are not critically ill. (1)(2)

- On the basis of strong research evidence, expert opinion, and consensus, acidosis occurs when the pH value is lower than normal when examining blood gases. In contrast, alkalosis occurs when the pH value is higher than normal. It is important to characterize pH as a combination of partial pressure of carbon dioxide (P_{CO_2}) and bicarbonate (HCO_3^-). (1)(2)

- On the basis of strong research evidence, expert opinion, and consensus, the Henderson-Hasselbalch equation by itself is insufficient to completely describe a patient's metabolic acid-base state. The anion gap further describes the interactions of the measured positive charges (cations) and negative charges (anions) to the unmeasured charged particles. (1)(2)

- On the basis of expert opinion and consensus, the first step in the assessment of an acid-base imbalance is to determine a primary respiratory versus primary metabolic cause. A detailed history and comprehensive physical examination can offer clues to suggest the presenting cause. (1)(2)

- On the basis of expert opinion and consensus, understanding of metabolic acidosis requires the use of the anion gap in addition to knowing the pH state. (1)(2)
  - A common type of hyperchloremic non-anion gap acidosis occurs in the hospitalized patient with infusion of large amounts of normal saline. In these cases, the relative chloride load from the exogenous fluid results in a decrease in HCO_3^- to maintain plasma electroneutrality.
  - The presence of an increased gap metabolic acidosis (anion gap higher than normal) is due to an increase of unmeasured anions. This can occur following an increase in acid production or underexcretion of acid. The classic mnemonic for causes of gap acidosis is MUDPILES (**m**ethanol, **u**remia, **d**iabetic ketoacidosis, **p**araldehyde, **i**soniazid, **l**actic acidosis, **e**thylene glycol, **s**alicylates). Although most causes on this list represent exogenous ingestion of acids, physiologically high-anion gap acidosis due to increased production of endogenous acids is more common. The 2 primary sources of such endogenous production are lactic acidosis and ketoacidosis.
  - In response to a low pH from metabolic acidosis, the body's attempt to reach equilibrium mandates a move toward an alkalotic respiratory state through hyperventilation. This response can occur over minutes to hours, depending on an intact neurologic response and the ability of the body to maintain hyperventilation.
- On the basis of strong research evidence, expert opinion, and consensus, metabolic alkalosis, as revealed by the Henderson-Hasselbalch equation, points to an increase in the HCO_3^- content of the serum, resulting in an increase in pH. Two common causes include hypochloremic alkalosis from pyloric stenosis and contraction alkalosis induced by diuretics use. Compensation for the metabolic alkalosis comes from the respiratory system. In response to a high pH, the body's attempt to equilibrate mandates a move toward an acidotic respiratory state through hypoventilation. (1)(2)

- On the basis of strong research evidence, expert opinion, and consensus, respiratory acidosis is the result of an increase in Pco_2 leading to a lower pH. This accumulation can be due to increased production (such as a higher metabolic state) or decreased elimination of CO_2 through the respiratory system. Compensation for primary respiratory acidosis comes from the metabolic system. In response to a low pH, the body's attempt to reach equilibrium mandates a move toward an alkalotic metabolic state through retention of HCO_3^-. Compensation of the metabolic system to a primary respiratory acid-base disorder is much slower than the compensation of the respiratory system to a primary metabolic acid-base disorder. Therefore, in acute respiratory acidosis, the pH is often well below the normal range. (1)(2)
- On the basis of strong research evidence, expert opinion, and consensus, respiratory alkalosis is the result of an excessive elimination of Pco_2 leading to a higher pH ("hyperventilation"). This inappropriate elimination is much less common but can occur through an increased respiratory drive due to toxins or primary central nervous system events. Compensation for a primary respiratory alkalosis comes from the metabolic system. In response to a high pH, the body's attempt to equilibrate mandates a move toward an acidotic metabolic state through elimination of HCO_3^-. (1)(2)

PIR Quiz

1. A 6-year-old girl is evaluated in the emergency department after 2 days of vomiting and diarrhea. She has had low oral intake and scant urine output for the past 16 hours. An electrolyte panel is ordered. The results are as follows:
   Sodium 135 mEq/L (135 mmol/L)
   Potassium 4.8 mEq/L (4.8 mmol/L)
   Chloride 110 mEq/L (110 mmol/L)
   Bicarbonate 8 mEq/L (8 mmol/L)
   Blood urea nitrogen 29 mg/dL (10.4 mmol/L)
   Creatinine 1.0 mg/dL (88.4 μmol/L)
   Calcium 8.5 mg/dL (2.1 mmol/L)
   Albumin 4.5 g/dL (45 g/L)
   The anion gap in this patient equals:

   A. 21.8 mEq/L (21.8 mmol/L).
   B. 25 mEq/L (25 mmol/L).
   C. 25.5 mEq/L (25.5 mmol/L).
   D. 26.3 mEq/L (26.3 mmol/L).
   E. 30.3 mEq/L (30.3 mmol/L).

2. A 4-year-old boy is admitted to the pediatric intensive care unit with overwhelming sepsis due to *Streptococcus pneumoniae.* The anion gap is normal despite a definite metabolic acidosis. Your colleague states that this is likely a falsely low anion gap. Which of the following is the most likely explanation for the low anion gap?

   A. Conservation of bicarbonate due to decreased urine output.
   B. Decrease in unmeasured anions due to hypoalbuminemia.
   C. Increase in carbon dioxide due to respiratory depression.
   D. Increase in lactate concentration due to decreased perfusion of vital organs.
   E. Increase in serum protein concentrations due to inflammation.

3. A previously healthy 3-year-old girl is admitted to the hospital for dehydration. Her initial bicarbonate measures 9 mEq/L (9 mmol/L) with an anion gap of 24 mEq/L (24 mmol/L). After vigorous resuscitation with 2 bolus infusions of 20 mL/kg normal saline, her bicarbonate is 7 mEq/L (7 mmol/L) and the anion gap is 16 mEq/L (16 mmol/L). What is the most likely explanation for her second set of laboratory results?

   A. An increase in her circulatory volume has diluted her chemistry values.
   B. An increased lactate concentration has displaced bicarbonate.
   C. She is becoming more acidotic due to deterioration in her overall status.
   D. She is continuing to lose bicarbonate due to persistent diarrhea.
   E. The relative chloride load caused a decrease in bicarbonate to maintain electroneutrality.

4. An 18-month-old male toddler is brought to the emergency department by his grandparents, who found him in their bathroom after he opened a bottle of "muscle pain relief" wintergreen oil (containing methyl salicylate) and ingested some of its contents. The boy is sleepy and irritable when aroused. Laboratory studies reveal a metabolic acidosis with an elevated anion gap. Keeping in mind the "MUDPILES" mnemonic for causes of an elevated anion gap acidosis, which of the following causes for this child's metabolic condition is most likely?

   A. Ethylene glycol.
   B. Ketoacidosis.
   C. Lactic acidosis.
   D. Methanol.
   E. Uremia.

5. A 6-week-old male infant presents with vomiting that began insidiously but progressed to projectile vomiting of all feedings. Ultrasonography confirms the diagnosis of hypertrophic pyloric stenosis. Which of the following is the expected primary finding in this disorder?

   A. Hyperchloremic metabolic acidosis.
   B. Hypochloremic metabolic alkalosis.
   C. Hypercapneic respiratory acidosis.
   D. Hypocapneic respiratory alkalosis.
   E. Metabolic contraction alkalosis.