Acid-Base Disorders

Janice L. Zimmerman, MD, FCCP

Objectives:
1. To define terminology used in describing acid-base disturbances.
2. To diagnose simple and mixed acid-base disorders.
3. To differentiate anion gap and nonanion gap metabolic acidoses.
4. To review appropriate treatment for major causes of acidosis and alkalosis.

Key words: acid; acidemia; acidosis; alkalemia; alkalosis; anion gap; base; strong ion difference

Acid-base disturbances are common and result from a large number of disease processes. These disorders may be secondary to, or a cause of, major organ dysfunction. Appropriate diagnosis and management of acid-base disorders require accurate interpretation of simultaneous measurements of plasma electrolytes and arterial blood gases, as well as knowledge of compensatory physiologic responses.

Acid-Base Physiology

The acidity of body fluids is measured in terms of hydrogen ion concentration, which is expressed as pH (the negative log of the hydrogen ion concentration). Hydrogen ion concentration and pH are inversely related. Changes in acidity can be stabilized though not totally corrected by buffers, molecules that accept or donate hydrogen ions. Important buffers including the following: bicarbonates ($HCO_3^- + H^+ \leftrightarrow H_2CO_3 \leftrightarrow H_2O + CO_2$); proteins (protein$^-$ + $H^+ \leftrightarrow$ H-protein); hemoglobin (hgb$^-$ + $H^+ \leftrightarrow$ H-hgb); and phosphates ($HPO_4^{2-} + H^+ \leftrightarrow H_2PO_4^-$).

The major buffering system in the body is the carbonic acid–bicarbonate pair. The relation of pH to this buffering system is expressed by the Henderson-Hasselbalch equation:

$$pH = pK + \log\frac{[HCO_3^-]}{[H_2CO_3]} = 6.1 + \log\frac{[HCO_3^-]}{0.03\ Pa_{CO_2}}$$

The interrelation of [H+], Pa_{CO_2}, and $[HCO_3^-]$ can also be illustrated by the Henderson equation. This equation is helpful as a bedside tool to predict or evaluate the accuracy of the three acid-base parameters.

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

An estimation of $[H^+]$ can be made from pH. Between pH 7.2 and 7.5, the $[H^+]$ changes by 1 mmol/L for each 0.01 unit change in pH (Table 1).

Although acid-base status is typically characterized by $[H^+]$ and $[HCO_3^-]$ for current clinical problem-solving, the physicochemical analysis of Stewart more accurately describes the determinants of acid-base status in biological systems. Three independent variables determine acid-base changes.

1. Pa_{CO_2}
2. The strong ion difference (SID)—This is the net electric charge on strong electrolytes. It is the sum of all strong cation concentrations minus the sum of all strong anion concentrations or SID=($[Na^+]+[K^+]+[Ca^{2+}]+[Mg^{2+}]$) – ($[Cl^-]$+[other strong anions]. The normal value is 38-42 mmol/L. The SID is dependent primarily on renal function but may also be impacted by gastrointestinal (GI) function and tissue metabolism.
3. The total concentrations of nonvolatile weak acids—The main weak acids are inorganic phosphate (Pi) and serum proteins, particularly albumin.

Other variables such as $[H^+]$ and $[HCO_3^-]$ are dependent variables that change based on

Table 1—*Relationship Between pH and [H+]*

pH	[H+], mmol/L
7.65	22
7.60	25
7.55	28
7.50	32
7.45	35
7.40	40
7.35	45
7.30	50
7.25	56
7.20	63
7.15	71
7.10	79
7.05	89
7.00	100

primary alterations in the independent variables above. Evaluation of acid-base status by Stewart's approach would require assessment of all the independent variables.

This chapter will primarily review the more traditional analysis of acid-base problems using formulas based on $[H^+]$ and $[HCO_3^-]$. However, some correlates of Stewart's approach will be mentioned and may help in understanding the limitations of current acid-base analysis.

Definitions

Acidemia: An increase in $[H^+]$ and a decrease in arterial pH.

Alkalemia: A decrease in $[H^+]$ and elevation of arterial pH.

Acidosis: A process that, if unopposed, will lead to a decrease in pH.

Alkalosis: A process that, if unopposed, will lead to an increase in pH.

Acid-Base Disturbances

The development of an acid-base disorder is traditionally identified by changes in the bicarbonate concentration (the metabolic or renal component) or by changes in the $Paco_2$ (the respiratory component). A primary metabolic disturbance results from a primary alteration in bicarbonate concentration, whereas a primary respiratory disturbance results from a primary alteration in $Paco_2$. In Stewart's approach, metabolic disturbances result from changes in the strong ion difference and/or concentrations of weak acids.

Features of acid-base disturbances are noted in Table 2. Primary acid-base disturbances also initiate secondary compensatory responses that are predictable. Compensatory processes help normalize the arterial pH but usually never return the pH fully to normal. Appropriate compensatory responses require normal functioning of lungs and kidneys, and failure to develop a compensatory response defines the presence of a second primary disorder.

Metabolic Acidosis

Defect. Increased acid accumulation or decreased extracellular $[HCO_3^-]$; decreased SID, increased concentration of albumin, or increased [Pi].

Laboratory manifestation. Decreased pH, decreased plasma $[HCO_3^-]$.

Compensation. Increased ventilation, decreased $Paco_2$; exchange of intracellular Na^+ and K^+ for extracellular H^+, increased renal H^+ excretion with urinary buffers and regeneration of new bicarbonate (slower process).

The degree of respiratory compensation can be estimated by the following formulas:

$Paco_2 = 1.5 \times [HCO_3^-] + 8 \pm 2$

$\Delta Paco_2 = 1.2 \times \Delta [HCO_3^-]$

During prolonged acidosis where respiratory compensation is complete, the last two digits of pH equal $Paco_2$ (if pH>7). The lower limit of normal compensation is $Paco_2$ = 10 mm Hg.

Etiologies

Metabolic acidosis can result from an increase in endogenous acid production that overwhelms renal excretion (*eg*, ketoacidosis), exogenous acid input, excessive loss of bicarbonate (*eg*, diarrhea) or decreased renal excretion of endogenous acids *eg*, chronic renal failure). Metabolic acidoses are usually further characterized by the anion gap (AG). Unmeasured anions (proteins, phosphates, sulfates, and organic acids) in healthy persons exceed the unmeasured cations (potassium, calcium, and magnesium) and this difference results in the AG. The AG can be estimated by the following formula:

$AG = [Na^+] - ([Cl^-] + [HCO_3^-]) = 10 \pm 4$

Table 2—*Features of Acid-Base Disturbances*

Disorder	Primary Problem	pH	Compensation
Metabolic acidosis	$\downarrow[HCO_3^-]$, ↓SID, ↑alb, ↑Pi	↓	↓ $Paco_2$
Metabolic alkalosis	$\uparrow[HCO_3^-]$, ↑SID, ↓alb	↑	↑ $Paco_2$
Respiratory acidosis	↑ $Paco_2$	↓	$\uparrow[HCO_3^-]$
Respiratory alkalosis	↓ $Paco_2$	↑	$\downarrow[HCO_3^-]$

SID, strong ion difference; alb, albumin; Pi, inorganic phosphate

The AG can be increased because of a decrease in unmeasured cations, an increase in unmeasured anions, or laboratory error in measurement. The classification of metabolic acidoses by the AG is shown in Table 3. Base deficit determined by measured plasma pH and $Paco_2$, and hemoglobin concentration using Siggard-Andersen's algorithms and nomograms, has also been used to evaluate metabolic acidosis. However, this approach is less reliable in critically ill patients.

The AG has several limitations as the sole indicator of a metabolic acidosis. An AG acidosis can exist even with a normal AG in patients who are severely hypoalbuminemic or have pathologic paraproteinemias. In such patients, the normal AG may be as low as 4 to 5 mmol/L. For every decrease of 1 g/dL in albumin, a decrease of 2.5 to 3 mmol in AG will occur. Pathologic paraproteinemias lower the AG because immunoglobulins are largely cationic. Another exception can occur when an elevated AG does not reflect an underlying acidosis. In patients with significant alkalemia (usually pH >7.5), albumin is more negatively charged, which increases unmeasured anions.

Table 3—*Classification of Metabolic Acidosis by Anion Gap*

Increased anion gap
Lactic acidosis
Ketoacidosis
Diabetes
Alcohol-induced
Starvation
Renal failure
Toxin ingestion
Salicylates
Methanol
Ethylene glycol
Paraldehyde
Normal anion gap (hyperchloremic)
GI loss of HCO_3
Ureteral diversion
Diarrhea
Ileostomy
Proximal colostomy
Renal loss of HCO_3
Proximal renal tubular acidosis
Carbonic anhydrase inhibitor
Renal tubular disease
Acute tubular necrosis
Chronic tubulointerstitial disease
Distal renal tubular acidosis (type I and IV)
Hypoaldosteronism, aldosterone inhibitors
Pharmacologic
Ammonium chloride
Hyperalimentation
Dilutional acidosis

Normal AG acidoses can also be categorized by the potassium level. Hypokalemia (<3.5 mmol/L) is associated with ureteral diversion, diarrhea, proximal colostomy, ilestomy, proximal renal tubular acidosis (RTA), type I distal RTA, and hyperalimentation. Hyperkalemia (>4.5 mmol/L) can be found in hypoaldosterone states, ammonium chloride administration, and type IV distal RTA.

A decreased AG implies an increase in unmeasured cations or a decrease in unmeasured anions. Possible etiologies include para-proteinemias, hypoalbuminemia, hyponatremia, lithium toxicity, profound hyperkalemia, hypercalcemia, or hypermagnesemia, and halide poisoning (Br and I).

In an uncomplicated AG metabolic acidosis, every increase of 1 mmol/L in the AG should result in a concomitant decrease of 1 mmol/L in $[HCO_3^-]$. Deviation from this relation suggests a mixed acid-base disorder. The difference between these two values has been termed the delta gap (Δgap) and can be expressed as:

Δgap = (deviation of AG from normal) – (deviation of $[HCO_3^-]$ from normal)

If the normal AG is assumed to be 12 mmol/L and the normal $[HCO_3^-]$ is 24 mmol/L, then the following equation results:

$\Delta gap = (AG–12) – (24–[HCO_3^-])$

The normal value for Δgap should be zero. However, variance in measurements can result in a Δgap of 0 ± 6. If the Δgap is positive, then either a simultaneous metabolic alkalosis or a respiratory acidosis exists. If the decrease in $[HCO_3^-]$ is greater than the increase in AG, which results in a negative Δgap, then a concomitant normal AG acidosis (hyperchloremic) or chronic respiratory alkalosis with compensating hyperchloremic acidosis may exist. Small deviations of the Δgap may not indicate mixed acid-base disorders, and clinical information must always be considered in the evaluation.

In Stewart's approach, a decreased SID in metabolic acidosis results from an elevated $[Cl^-]$ or accumulation of unidentified anions analogous to a normal anion gap or increased anion gap acidosis described above. A simplified formula that can be used to estimate the SID takes into account changes in albumin (alb) and phosphate:

$SID = [HCO_3^-] + 0.28\ [alb\ g/L] + 1.8\ [Pi\ mmol/L]$

Clinical Manifestations

The clinical features of metabolic acidosis depend primarily on the underlying disorder. Some effects of acidosis can be related to the change in pH. The effects of acidemia on the cardiovascular system have been questioned and may not be clinically significant.

Pulmonary. Rapid, deep respiration (Kussmaul's respiration); increase in pulmonary vascular resistance.

Cardiovascular. Decreased myocardial contractility; arrhythmias; potential decreased responsiveness to catecholamines.

Metabolic. Insulin resistance; hyperkalemia; increased protein catabolism. Metabolic acidosis shifts the oxyhemoglobin dissociation curve to the right, which promotes oxygen release at the tissue level.

Treatment

Treatment requires appropriate diagnosis of the etiology of metabolic acidosis and correction of the underlying disorder. Therapy for a non-AG metabolic acidosis requires replacing volume losses with a solution that contains low chloride and bicarbonate. Treatment of most AG metabolic acidoses is well established (*ie*, insulin for ketoacidosis or dialysis for renal failure). Adjunctive therapy with sodium bicarbonate in this setting is controversial. Treatment of lactic acidosis with bicarbonate does not improve survival. In circumstances when pH <7.1 is associated with severe hemodynamic compromise, some studies show that bicarbonate may improve cardiovascular responsiveness. However, myocardial performance is often normal in the setting of metabolic acidosis. Potential complications of bicarbonate administration frequently outweigh possible benefits (Table 4). Other nonbicarbonate buffers, such as tris(hydroxymethyl)aminomethae, dichloroacetate, and carbicarb, may avoid some of the complications, but clinical data do not support their use.

Table 4—*Potential Complications of Bicarbonate Administration*

Volume overload
Paradoxical cerebrospinal fluid/intracellular acidosis
Respiratory acidosis
Impaired O_2 delivery (tissue hypoxia)
Hypokalemia
Hypocalcemia
Hypernatremia
Hyperosmolality
Overshoot alkalemia

Metabolic Alkalosis

Defect. Extracellular fluid increase in base or loss of acid; increased SID or decreased concentration of albumin.

Laboratory Manifestation. Increase in pH and increase in $[HCO_3^-]$.

Compensation. Hypoventilation leading to increased $Paco_2$. The $Paco_2$ may rise 6 to 7 mm Hg for every increase of 10 mmol/L in $[HCO_3^-]$. This response is limited by hypoxemia to a maximum $Paco_2$ of 50 to 55 mm Hg. A characteristic feature of metabolic alkalosis is that the kidneys contribute to the process by adding HCO_3^- to the circulation and hyperabsorbing filtered HCO_3^- rather than enhancing HCO_3^- excretion.

Etiologies

The etiologies of metabolic alkalosis can be divided into those characterized by chloride depletion (hypovolemic) and those characterized by chloride expansion (hypervolemic). These etiologies are also referred to as chloride or saline responsive and chloride or saline resistant, respectively (Table 5). In Stewart's approach, an increased SID in metabolic

Table 5—*Etiologies of Metabolic Alkalosis*

Hypovolemic, Cl^- depleted
GI loss of H^+
Vomiting
Gastric suction
Cl^- rich diarrhea
Villous adenoma
Renal loss of H^+
Diuretics
Posthypercapnia
High-dose carbenicillin
Hypervolemic, Cl^- expanded
Renal loss of H^+
Primary hyperaldosteronism
Primary hypercortisolism
Adrenocorticotropic hormone excess
Pharmacologic hydrocortisone/mineralocorticoid excess
Renal artery stenosis with right-ventricular hypertension
Renin secreting tumor
Hypokalemia
Bicarbonate overdose
Pharmacologic overdose of $NaHCO_3$
Milk–alkali syndrome
Massive blood transfusion

alkalosis is due to decreased [Cl^-]. Hypokalemia is common to both types of metabolic alkalosis. Measurement of urine chloride (UCl) is helpful in distinguishing the two categories: UCl <20 mmol/L in chloride depletion and UCl >20 mmol/L in chloride expansion. In metabolic alkalosis, the UCl is a more accurate reflection of intravascular volume than urine sodium because sodium must be excreted with excess HCO_3. Diuretic use alters the utility of UCl for assessing volume status.

Clinical Manifestations

Severe metabolic alkalosis is associated with a high mortality rate in hospitalized patients.

Cardiovascular. Tachycardia; arrhythmias.

Central Nervous System. Decreased cerebral blood flow; seizures; altered mental status.

Metabolic. Ionized hypocalcemia; hypokalemia.

Treatment

The clinical setting along with measurement of UCl usually allows appropriate classification of the metabolic alkalosis. Etiologies associated with chloride depletion respond to volume replacement (saline-responsive). Normal saline offers more chloride per liter (154 mmol/L) than lactated Ringer's solution (104 to 109 mmol/L). Etiologies associated with chloride expansion usually indicate imbalances in the renal–adrenal axis. Potassium deficiencies should be corrected as appropriate. It is rarely necessary to consider hydrochloric acid (0.1N solution) administration or deliberate hypoventilation to correct severe metabolic alkalosis. Acetazolamide (250-375 mg once or twice daily) will increase excretion of HCO_3^- but may result in acidemia and worsening hypokalemia because of kaliuresis.

Respiratory Acidosis

Defect. Ineffective alveolar ventilation; increase in CO_2 production.

Laboratory manifestation. Increased $PaCO_2$, decreased pH.

Compensation. Buffers (primarily intracellular proteins); increased respiratory rate; slow renal response (>24 to 36 hrs) with increased bicarbonate reabsorption.

The normal respiratory response to hypercapnia is an increase in alveolar ventilation. The stimulus to increase ventilation is mediated by changes in the [H^+] of the cerebrospinal fluid (CSF), which affects chemoreceptors in the medulla. Because CSF is essentially devoid of nonbicarbonate buffers, CO_2 that diffuses readily across the blood–brain barrier results in a marked increase in CSF [H^+]. The CSF pH is corrected toward normal by a slower rise in CSF [HCO_3^-] that results from transfer of cerebral or blood HCO_3^-.

A very small increase in plasma [HCO_3^-] can be seen acutely because of titration of intracellular nonbicarbonate buffers. For each increase of 10 mm Hg in $PaCO_2$, the [HCO_3^-] increases by 1 mmol/L. Acute increases in $PaCO_2$ change the plasma [HCO_3^-] only 4 to 5 mmol/L to a maximum of 30 to 32 mmol/L. If the respiratory acidosis is acute, the pH should decrease by 0.08 units for each increase of 10 mm Hg in $PaCO_2$.

The renal reabsorption of HCO_3^- is slower and plays a minimal role in acute respiratory acidosis. Over hours to days, the kidneys compensate with proximal reabsorption of filtered bicarbonate and secretion of H^+ in the distal tubule, which is trapped by ammonia and excreted. Bicarbonate reabsorption is accompanied by loss of Cl^-. This mechanism provides adequate, although incomplete pH compensation for chronic respiratory acidosis. The transition from acute to chronic respiratory acidosis is defined by HCO_3^- retention due to renal compensation. In chronic respiratory acidosis, the [HCO_3^-] increases 3.5 mmol/L for each increase of 10 mm Hg in $PaCO_2$. The limit of renal compensation in chronic respiratory acidosis is [HCO_3^-] ≈ 45 mmol/L. Higher values suggest an associated secondary metabolic alkalosis. In chronic respiratory acidosis, the pH decreases by 0.03 units for each increase of 10 mm Hg in $PaCO_2$.

Etiologies

Common causes of acute respiratory acidosis include airway obstruction, respiratory center depression, neuromuscular disorders, and pulmonary disorders (Table 6).

Clinical Manifestations

The clinical manifestations of acute respiratory acidosis depend on the absolute increase in $PaCO_2$, the rate of $PaCO_2$ increase, and severity of associated hypoxemia.

Nervous System. Somnolence; anxiety or confusion; psychosis; tremors, myoclonus, or asterixis; headache; papilledema (cerebral vasodilation leads to increased intracranial pressure).

Cardiovascular System. Tachycardia; hypertension; supraventricular/ventricular arrhythmias; peripheral vasodilation.

Treatment

Treatment involves the rapid identification of the etiology of respiratory acidosis and implementation of corrective action. In many circumstances, intubation and mechanical ventilation are necessary to support alveolar ventilation. Administration of $NaHCO_3$ for acute respiratory acidosis is not indicated. Remember that $NaHCO_3$ is metabolized to CO_2, which may worsen acidosis. In addition, normally functioning kidneys excrete most of the bicarbonate in the acute setting.

A therapeutic pitfall to avoid in the treatment of respiratory acidosis is creation of a posthypercapnic alkalosis. This condition most commonly occurs when a patient with compensated chronic respiratory acidosis is overventilated to a normal or near-normal $Paco_2$. A high plasma [HCO_3^-] results in alkalemia. Appropriate ventilator management and goals should prevent this situation.

Table 6—*Etiologies of Respiratory Acidosis*

Airway obstruction
Foreign body
Tongue displacement
Laryngospasm
Obstructed endotracheal tube
Severe bronchospasm
Obstructive sleep apnea
Respiratory center depression
General anesthesia
Sedative, narcotic drugs
Cerebral injury, ischemia
Increased CO_2 production
Malignant hyperthermia
Shivering
Hypermetabolism
High carbohydrate diet
Neuromuscular disorders
Drugs or toxins
Electrolyte disorders
Spinal cord injury
Guillain-Barré syndrome
Myasthenia gravis
Polymyositis
Lung conditions
Restrictive disease
Obstructive disease
Hemothorax or pneumothorax
Flail chest
Acute lung injury
Obesity-hypoventilation syndrome
Inappropriate ventilator settings

Respiratory Alkalosis

Defect. Primary hyperventilation.

Laboratory Manifestation. Decreased $Paco_2$, increased pH.

Compensation. Protein or hemoglobin release of hydrogen ion; slow renal response with bicarbonate loss in urine.

Alveolar ventilation is regulated by several factors: chemoreceptors in the medulla (sensitive to [H^+]) and great vessels (sensitive to oxygen); cortical input (voluntary control); and pulmonary chemoreceptors and stretch receptors. Any of these factors or a combination may lead to hyperventilation. The [HCO_3^-] decreases 2 mmol/L for each decrease of 10 mm Hg in $Paco_2$ in acute respiratory alkalosis. Similarly to changes noted in respiratory acidosis, pH increases 0.08 units for every decrease of 10 mm Hg in $Paco_2$ in acute respiratory alkalosis, and pH increases 0.03 units for each decrease of 10 mm Hg in $Paco_2$ in chronic respiratory alkalosis. However, chronic respiratory alkalosis is unique among acid-base disorders in that pH may return to normal if the condition is prolonged. Persistent hypocapnia results in decreased renal H^+ secretion. Plasma [HCO_3^-] decreases 5 mmol/L for each decrease of 10 mm Hg in $Paco_2$.

Table 7—*Etiologies of Respiratory Alkalosis*

Hypoxemic drive
Pulmonary disease with arterial-alveolar gradient
Cardiac disease with right-to-left shunt
Cardiac disease with pulmonary edema
High altitude
Acute and chronic pulmonary disease
Emphysema
Pulmonary embolism
Pulmonary edema
Mechanical overventilation
Stimulation of respiratory center
Neurologic disorders
Pain
Psychogenic
Liver failure with encephalopathy
Sepsis/infection
Salicylates
Progesterone
Pregnancy
Fever

Etiologies

The etiologies of respiratory alkalosis are listed in Table 7.

Clinical Manifestations

Acute respiratory alkalosis results in neurologic, cardiovascular, muscular, and metabolic abnormalities.

Nervous System. Confusion or dizziness; seizures; paresthesias; circumoral numbness.

Cardiovascular System. Tachycardia; arrhythmias (especially at pH >7.6).

Muscular System. Cramps; carpopedal spasms.

Metabolic Changes. Hypokalemia; hypophosphatemia; ionized hypocalcemia. In chronic respiratory alkalosis, mild hypokalemia (from intracellular shift) and hyperchloremia (from renal retention) result.

Treatment

Severe alkalemia is associated with high mortality and requires aggressive treatment. Therapy is directed at the underlying cause because pharmacologic agents are not available for the alkalemia.

Complex Acid-Base Disorders

When a single process, such as metabolic alkalosis, results in the acid-base disturbance, it is classified as simple. In many patients, multiple acid-base disturbances exist concurrently and are labeled complex acid-base disorders (Table 8). Triple acid-base disorders involve two metabolic disturbances with a superimposed primary respiratory disturbance. Such conditions may be seen in patients with a chronic acid-base disturbance who develop a superimposed mixed disturbance. Clues to the presence of a complex disorder include a normal pH (with the exception of respiratory alkalosis), $Paco_2$ and HCO_3^- deviating in opposite directions, and a pH change in the opposite direction for a known primary disorder.

Complex disorders require an organized approach to interpretation of acid-base parameters for accurate diagnosis. The following considerations are one system that may be useful in determining the disturbances present.

1. Determine the overall acid-base condition by measuring pH. Is acidemia or alkalemia present?
2. Determine if the primary process is metabolic ($[HCO_3^-]$ deviation) or respiratory ($Paco_2$ deviation).
3. If a respiratory disturbance is present, determine if it is acute or chronic.

Table 8—*Mixed Acid-Base Disorders*

Acid-Base Disorder	Clinical Syndromes
Respiratory acidosis with metabolic acidosis	Cardiopulmonary arrest Intoxication with ethanol, methanol,ethylene glycol COPD with lactic acidosis, diabetic ketoacidosis, etc. Severe hypophosphatemia Respiratory failure with renal failure, diarrhea, etc.
Respiratory alkalosis with metabolic alkalosis	Cirrhosis with diuretic use, vomiting Pregnancy with hyperemesis Overventilation in COPD patient
Respiratory acidosis with metabolic alkalosis	COPD with diuretic use, vomiting, gastric suction Severe hypokalemia
Respiratory alkalosis with metabolic acidosis	Sepsis Salicylate intoxication Renal insufficiency with congestive heart failure, pneumonia Advanced liver disease with lactic acidosis
Metabolic acidosis with metabolic alkalosis	Uremia or ketoacidosis with vomiting, gastric suction, diuretics, etc.

Table 9—*Acid-Base Calculations**

Acid-base disorder	Formula
Respiratory acidosis	
Acute	Decrease in pH=0.08× $\frac{(Pa_{CO_2}-40)}{10}$
	Increase in $[HCO_3^-]=\frac{\Delta Pa_{CO_2}}{10}\pm 3$
Chronic	Decrease in pH=0.03× $\frac{(Pa_{CO_2}-40)}{10}$
	Increase in $[HCO_3^-]=3.5\times\frac{\Delta PaCO_2}{10}$
Respiratory alkalosis	
Acute	Increase in pH=0.08× $\frac{(40-Pa_{CO_2})}{10}$
	Decrease in $[HCO_3^-]=2\times\frac{\Delta Pa_{CO_2}}{10}$
Chronic	Increase in pH=0.03× $\frac{(40-Pa_{CO_2})}{10}$
	Decrease in $[HCO_3^-]=5–7\times\frac{\Delta Pa_{CO_2}}{10}$
Metabolic acidosis	AG=[Na]–([Cl^-]+[HCO_3^-] $Pa_{CO_2}=1.5\times[HCO_3^-]+8\pm2$ Δgap=(AG–12)–(24–[HCO_3^-])
Metabolic alkalosis	Increase in $Pa_{CO_2}=0.6–0.7\times\Delta[HCO_3^-]$

*AG=anion gap.

4. If a metabolic disturbance is present, determine if respiratory compensation is adequate.
5. If a metabolic acidosis is present, calculate the AG.
6. If an AG metabolic acidosis is present, calculate the Δgap to determine if other metabolic disturbances are present.

A summary of useful calculations for acid-base evaluation is found in Table 9.

Annotated Bibliography

Adrogue HJ, Madias NE. Management of life-threatening acid-base disorders: first of two parts. N Engl J Med 1998; 338:26-34

Adrogue HJ, Madias NE. Management of life-threatening acid-base disorders: second of two parts. N Engl J Med 1998; 338:107-111

Current review of adverse consequences and management of severe acid-base disorders.

Dubose TD. Acid-base disorders. In: Brenner BM, ed. Brenner and Rector's The Kidney, Sixth Edition. Philadelphia, PA: WB Saunders, 2000; 925-997

A detailed review of all acid-base disorders.

Fencl V, Jabor A, Kazda A, Figge J. Diagnosis of metabolic acid-base disturbances in critically ill patients. Am J Respir Crit Care Med 2000; 162:2246-2251

Use of the strong ion difference compared to anion gap and base excess in analysis of acid-base status.

Forsythe SM, Schmidt GA. Sodium bicarbonate for the treatment of lactic acidosis. Chest 2000; 117:260-67

A review of the literature on the use of bicarbonate to correct lactic acidosis and its lack of benefit.

Morganroth ML. An analytic approach to diagnosing acid-base disorders. J Crit Illness 1990; 5:138-150

A concise, practical approach to analyzing acid-base parameters.

Narins RG, Kupin W, Faber MD, et al. Pathophysiology, classification and therapy of acid-base disturbances. In: Arieff AI, DeFronzo RA, eds. Fluid, electrolyte, and acid-base disorders. New York, NY: Churchill Livingstone, 1995; 105-198

A detailed review of pathophysiology and management of all acid-base disorders.

Narins RG, Emmett M. Simple and mixed acid-base disorders: a practical approach. Medicine (Baltimore) 1980; 59:161-187

An old, but classic review of all acid-base disorders.

Paulson WD. How to interpret the anion gap. J Crit Illness 1997; 12:96-99

Brief review of the use of the anion gap and its limitations.

Salem MM, Mujais SK. Gaps in the anion gap. Arch Intern Med 1992; 152:1625-1629

A detailed review of limitations of the use of the anion gap in clinical practice.

Stewart PA. Modern quantitative acid-base chemistry. Can J Physiol Pharmacol 1983; 61: 1444-1461

The original explanation of physicochemical analysis and use of strong ion difference in acid-base problems.

Wrenn K. The delta Δgap: an approach to mixed acid-base disorders. Ann Emerg Med 1990; 19:1310-1313

A concise review of the derivation, interpretation, and clinical application of the Δgap.

Notes

Notes