is respiratory compensation; the P_{CO_2} decreases during a metabolic acidosis and increases during a metabolic alkalosis. With metabolic acidosis, the decrease in the pH increases the ventilatory drive, causing a decrease in the P_{CO_2}. The fall in the CO_2 concentration leads to an increase in the pH. This **appropriate respiratory compensation** for a metabolic process happens quickly and is complete within 12 to 24 hours.

During a primary respiratory process, there is metabolic compensation mediated by the kidneys. The kidneys respond to a respiratory acidosis by increasing hydrogen ion excretion, increasing bicarbonate generation, and raising the serum bicarbonate concentration. The kidneys increase bicarbonate excretion to compensate for a respiratory alkalosis; the serum bicarbonate concentration decreases. In contrast to a rapid respiratory compensation, it takes 3 to 4 days for the kidneys to complete **appropriate metabolic compensation.** However, there is a small and rapid compensatory change in the bicarbonate concentration during a primary respiratory process. The expected appropriate metabolic compensation for a respiratory disorder depends on whether the process is acute or chronic.

A **mixed acid-base disorder** is present when there is more than one primary acid-base disturbance. An infant with bronchopulmonary dysplasia may have a respiratory acidosis from chronic lung disease and a metabolic alkalosis from a diuretic used to treat the chronic lung disease. Formulas are available for calculating the appropriate metabolic or respiratory compensation for the six primary simple acid-base disorders (Table 37-1). Appropriate compensation is expected in a simple disorder; it is not optional. If a patient does not have appropriate compensation, a mixed acid-base disorder is present.

METABOLIC ACIDOSIS

Decision-Making Algorithm
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Acidemia

Metabolic acidosis occurs frequently in hospitalized children; diarrhea is the most common cause. For a patient with an unknown medical problem, the presence of a metabolic acidosis is often helpful diagnostically because it suggests a relatively narrow differential diagnosis (Table 37-2).

Table 37-1 Appropriate Compensation During Simple Acid-Base Disorders

DISORDER	EXPECTED COMPENSATION*
Metabolic acidosis	$P_{CO_2} = 1.5 \times [HCO_3^-] + 8 \pm 2$
Metabolic alkalosis	P_{CO_2} increases by 7 mm Hg for each 10-mEq/L increase in the serum $[HCO_3^-]$
Respiratory acidosis	
Acute	$[HCO_3^-]$ increases by 1 for each 10-mm Hg increase in the P_{CO_2}
Chronic	$[HCO_3^-]$ increases by 3.5 for each 10-mm Hg increase in the P_{CO_2}
Respiratory alkalosis	
Acute	$[HCO_3^-]$ falls by 2 for each 10-mm Hg decrease in the P_{CO_2}
Chronic	$[HCO_3^-]$ falls by 4 for each 10-mm Hg decrease in the P_{CO_2}

*$[HCO_3^-]$ is expressed in mEq/L.

Etiology

Diarrhea causes a loss of bicarbonate from the body. The amount of bicarbonate lost in the stool depends on the volume of diarrhea and the bicarbonate concentration of the stool, which tends to increase with more severe diarrhea. Diarrhea often causes volume depletion because of losses of sodium and water, potentially exacerbating the acidosis by causing hypoperfusion (shock) and a lactic acidosis. There are three forms of renal tubular acidosis (RTA):

- Distal (type I)
- Proximal (type II)
- Hyperkalemic (type IV)

In **distal RTA,** children may have accompanying hypokalemia, hypercalciuria, nephrolithiasis, and nephrocalcinosis; rickets is a less common finding. Failure to thrive, resulting from chronic metabolic acidosis, is the most common presenting complaint. Autosomal dominant and autosomal recessive forms of distal RTA exist. The autosomal dominant form is relatively mild. Autosomal recessive distal RTA is more severe and often associated with deafness secondary to a defect in the gene for a H^+-ATPase that is present in the kidney and the inner ear. Distal RTA also may be secondary to medications or congenital or acquired renal disease. Patients with distal RTA cannot acidify their urine and have a urine pH greater than 5.5, despite a metabolic acidosis.

Proximal RTA is rarely present in isolation. In most patients, proximal RTA is part of **Fanconi syndrome**, a generalized dysfunction of the proximal tubule. Along with renal wasting of bicarbonate, Fanconi syndrome causes glycosuria, aminoaciduria, and excessive urinary losses of phosphate and uric acid. The chronic hypophosphatemia is more clinically significant because it ultimately leads to rickets in children. Rickets or failure to thrive may be the presenting complaint. Fanconi syndrome is rarely an isolated genetic disorder, with pediatric cases usually secondary to an underlying genetic disorder, most commonly **cystinosis.** Medications, such as ifosfamide or valproate, may cause Fanconi syndrome. The ability to acidify the urine is intact in proximal RTA, and untreated patients have a urine pH less than 5.5. However, bicarbonate therapy increases bicarbonate losses in the urine, and the urine pH increases.

In **hyperkalemic RTA,** renal excretion of acid and potassium is impaired because of either an absence of aldosterone

Table 37-2 Causes of Metabolic Acidosis

NORMAL ANION GAP
Diarrhea Renal tubular acidosis Urinary tract diversions Posthypocapnia Ammonium chloride intake
INCREASED ANION GAP
Lactic acidosis (shock) Ketoacidosis (diabetic, starvation, or alcoholic) Kidney failure Poisoning (e.g., ethylene glycol, methanol, or salicylates) Inborn errors of metabolism