or an inability of the kidney to respond to aldosterone. In severe aldosterone deficiency, as occurs with congenital adrenal hyperplasia secondary to 21α-hydroxylase deficiency, the hyperkalemia and metabolic acidosis are accompanied by hyponatremia and volume depletion from renal salt wasting. Incomplete aldosterone deficiency causes less severe electrolyte disturbances; children may have isolated hyperkalemic RTA, hyperkalemia without acidosis, or isolated hyponatremia.

Lactic acidosis most commonly occurs when inadequate oxygen delivery to the tissues leads to anaerobic metabolism and excess production of lactic acid. Lactic acidosis may be secondary to shock, severe anemia, or hypoxemia. Inborn errors of carbohydrate metabolism produce a severe lactic acidosis (see Chapter 52). In diabetes mellitus, inadequate insulin leads to hyperglycemia and diabetic ketoacidosis (see Chapter 171). Renal failure (see Chapter 165) causes a metabolic acidosis because the kidneys are unable to excrete the acid produced by normal metabolism.

A variety of **toxic ingestions** cause a metabolic acidosis. Acute **salicylate** intoxication occurs after a large overdose. Chronic salicylate intoxication is possible because of the gradual buildup of the drug. In addition to a metabolic acidosis, some patients may have a respiratory alkalosis. Other symptoms of salicylate intoxication include fever, seizures, lethargy, and coma. Hyperventilation may be particularly marked. Tinnitus, vertigo, and hearing impairment are more likely with chronic salicylate intoxication. **Ethylene glycol,** a component of antifreeze, is converted in the liver to glyoxylic and oxalic acids, causing a severe metabolic acidosis. Excessive oxalate excretion causes calcium oxalate crystals to appear in the urine, and calcium oxalate precipitation in the kidney tubules can cause renal failure. The toxicity of **methanol** ingestion also depends on liver metabolism; formic acid is the toxic end product that causes the metabolic acidosis and other sequelae, which include damage to the optic nerve and central nervous system.

There are many **inborn errors of metabolism** that may cause a metabolic acidosis (see Section 10). The metabolic acidosis may be due to excessive production of ketoacids, lactic acid, or other organic anions. Some patients have accompanying hyperammonemia. In most patients, acidosis occurs only episodically during acute decompensations, which may be precipitated by ingestion of specific dietary substrates (proteins), the stress of a mild illness (fasting, catabolism), or poor compliance with dietary or medical therapy.

Clinical Manifestations

The underlying disorder usually produces most of the signs and symptoms in children with a mild or moderate metabolic acidosis. The clinical manifestations of the acidosis are related to the degree of acidemia; patients with appropriate respiratory compensation and less severe acidemia have fewer manifestations than patients with a concomitant respiratory acidosis. At a serum pH less than 7.20, there is impaired cardiac contractility and an increased risk of arrhythmias, especially if underlying heart disease or other predisposing electrolyte disorders are present. With acidemia, there is a decrease in the cardiovascular response to catecholamines, potentially exacerbating hypotension in children with volume depletion or shock. Acidemia causes vasoconstriction of the pulmonary vasculature, which is especially problematic in neonates with primary pulmonary hypertension of the newborn (see Chapter 61). The normal respiratory response to metabolic acidosis—compensatory hyperventilation—may be subtle with mild metabolic acidosis, but it causes discernible increased respiratory effort with worsening acidemia. Chronic metabolic acidosis causes failure to thrive.

Diagnosis

The plasma **anion gap** is useful for evaluating patients with a metabolic acidosis. It divides patients into two diagnostic groups: normal anion gap and increased anion gap. The following formula determines the anion gap:

$$\text{Anion gap} = [Na^+] - [Cl^-] - [HCO_3^-]$$

A normal anion gap is 3 to 11. A decrease in the albumin concentration of 1 g/dL decreases the anion gap by roughly 4 mEq/L. Similarly, albeit less commonly, an increase in unmeasured cations, such as calcium, potassium, or magnesium, decreases the anion gap. Conversely, a decrease in unmeasured cations is a rare cause of an increased anion gap. Because of these variables, the broad range of a normal anion gap, and other factors, the presence of a normal or increased anion gap is not always reliable in differentiating the causes of a metabolic acidosis, especially when the metabolic acidosis is mild. Some patients have more than one explanation for their metabolic acidosis, such as a child with diarrhea and lactic acidosis secondary to hypoperfusion. The anion gap should not be interpreted in dogmatic isolation; consideration of other laboratory abnormalities and the clinical history improves its diagnostic utility.

Treatment

The most effective therapeutic approach for patients with a metabolic acidosis is correction of the underlying disorder, if possible. The administration of insulin in diabetic ketoacidosis or restoration of adequate perfusion in lactic acidosis from shock eventually results in normalization of acid-base balance. The use of bicarbonate therapy is indicated when the underlying disorder is irreparable; examples include RTA and chronic renal failure. In salicylate poisoning, alkali administration increases renal clearance of salicylate and decreases the amount of salicylate in brain cells. Short-term base therapy is often necessary in other poisonings and inborn errors of metabolism.

METABOLIC ALKALOSIS

Etiology

The causes of a metabolic alkalosis are divided into two categories based on the urinary chloride (Table 37-3). The alkalosis in patients with a low urinary chloride is maintained by volume depletion. They are called **chloride responsive** because volume repletion with fluid containing sodium chloride and potassium chloride is necessary to correct the metabolic alkalosis. Emesis, which causes loss of hydrochloride and volume depletion, is the most common cause of a metabolic alkalosis. Diuretic use increases chloride excretion in the urine. Consequently, while a patient is receiving diuretics, the urinary chloride is typically high (>20 mEq/L). After the diuretic effect resolves, the urinary chloride is low (<15 mEq/L), because of appropriate renal chloride retention in response to volume depletion. Categorization of diuretics based on urinary