hyperkalemia in diabetics by raising extracellular osmolality and causing K^+ to shift into the extracellular space. Through expansion of the ECF space, $NaHCO_3$ administration results in dilution of the serum K^+ concentration. K^+ also is shifted into cells whenever concomitant metabolic acidosis is corrected. Inhalation of β_2-agonists such as albuterol or parenteral use of salbutamol can effect significant K^+ shifts into cells.

The administration of calcium, HCO_3^-, glucose and insulin, and β_2-agonist therapy provides immediate relief of acute toxicity but does not decrease total body K^+. Measures to reduce total body K^+ include the administration of Na^+ polystyrene sulfonate (Kayexalate) and dialysis.

Chronic Hyperkalemia

After a review the patient's medication profile, drugs that can impair renal K^+ excretion should be discontinued if possible. Prescription or over-the-counter NSAIDs are common offenders. Patients should be placed on a low-K^+ diet with specific counseling against the use of K^+-containing salt substitutes.

Diuretics are particularly effective in minimizing hyperkalemia. In patients with an eGFR >30 mL/min, thiazide diuretics can be used, but for more severe renal insufficiency, loop diuretics are required. In chronic kidney disease patients with metabolic acidosis (HCO_3^- concentration <20 mEq/L), $NaHCO_3$ should be given. Intermittent use of a K^+-binding resin can be tried, but this drug is poorly tolerated when used on a chronic basis and has been associated with gastrointestinal ulceration.

METABOLIC ACIDOSIS

Metabolic acidosis is diagnosed by a low serum pH, a reduced plasma HCO_3^- concentration, and respiratory compensation resulting in a decrease in the partial pressure of carbon dioxide (P_{CO_2}). A low HCO_3^- concentration alone is not diagnostic of metabolic acidosis because it also results from renal compensation to chronic respiratory alkalosis. Measurement of the arterial pH differentiates these two possibilities. The pH is low in hyperchloremic metabolic acidosis and high in chronic respiratory alkalosis. The clinical approach to a patient with a low serum HCO_3^- concentration is given in Figure 27-6.

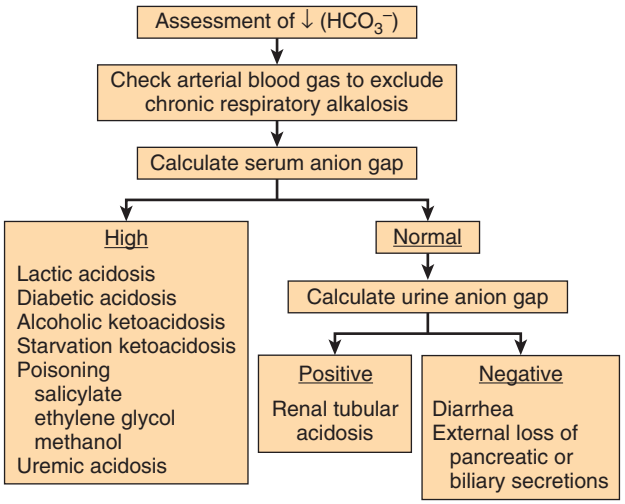

FIGURE 27-6 Approach to the patient with a reduced (↓) serum bicarbonate (HCO_3^-) concentration.

After confirming metabolic acidosis, calculation of the serum anion gap is a useful step in determining the differential diagnosis of the disorder. The anion gap is equal to the difference between the plasma concentrations of the major cation (Na^+) and the major measured anions ($Cl^- + HCO_3^-$).

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

The normal value of the anion gap is approximately 12 ± 2 mEq/L. Most of the unmeasured anions consist of albumin, and the normal anion gap therefore changes in the setting of hypoalbuminemia (i.e., normal anion gap is approximately three times the serum albumin [in g/dL]).

Because the total number of cations must equal the total number of anions, a fall in the serum HCO_3^- concentration must be offset by a rise in the concentration of other anions. If the anion accompanying excess hydrogen ions (H^+) is Cl^-, the decrease in the serum HCO_3^- concentration is matched by an equal increase in the serum Cl^- concentration. The acidosis is classified as a normal anion gap or hyperchloremic metabolic acidosis. If excess H^+ is accompanied by an anion other than Cl^-, the decrease in HCO_3^- is balanced by an increase in the concentration of the unmeasured anion. The Cl^- concentration remains the same. In this setting, the acidosis is a high anion gap metabolic acidosis.

A useful method for differentiating extrarenal from renal causes of metabolic acidosis is measurement of urinary ammonium ion (NH_4^+) excretion. Extrarenal causes of metabolic acidosis are associated with an appropriate increase in net acid excretion, which is primarily reflected by high levels of urinary NH_4^+ excretion. In contrast, net acid excretion and urinary NH_4^+ levels are low in metabolic acidosis of renal origin. Unfortunately, measurement of urinary NH_4^+ is not a test that is commonly available in clinical medicine. However, the amount of urinary NH_4^+ can be indirectly assessed by calculating the urine anion gap (UAG).

$$\text{UAG} = (\text{UNa}^+ + \text{UK}^+) - \text{UCl}^-$$

Under normal circumstances, the UAG is positive, with values ranging from 30 to 50 mEq/L. Metabolic acidosis of extrarenal origin is associated with a marked increase in urinary NH_4^+ excretion, and a large negative value is therefore obtained for the UAG. If the acidosis is of renal origin, urinary NH_4^+ excretion is minimal, and the UAG value usually is positive.

Urine pH cannot reliably differentiate acidosis of renal origin from that of extrarenal origin. For example, an acidic urine pH does not necessarily indicate an appropriate increase in net acid excretion. With a significant reduction in the availability of NH_4^+ to serve as a buffer, only a small amount of distal H^+ secretion leads to a maximal reduction in urine pH. In this setting, the pH of the urine is acidic, but the quantity of H^+ secretion is insufficient to meet daily acid production. Alkaline urine does not necessarily imply a renal acidification defect. In conditions in which availability of NH_4^+ is not limiting, distal H^+ secretion can be massive, but the urine remains relatively alkaline because of the buffering effects of NH_4^+.