have mild to moderate CKD (GFR, 20–50 mL/min) and acidosis, with elevation in serum [K+] (5.2–6.0 mmol/L), concurrent hypertension, and congestive heart failure. Both the metabolic acidosis and the hyperkalemia are out of proportion to impairment in GFR. Nonsteroidal anti-inflammatory drugs, trimethoprim, pentamidine, and angiotensin-converting enzyme (ACE) inhibitors can also cause non-AG metabolic acidosis in patients with renal insufficiency (Table 66-5).

METABOLIC ALKALOSIS

Metabolic alkalosis is manifested by an elevated arterial pH, an increase in the serum [HCO_3^-], and an increase in $Paco_2$ as a result of compensatory alveolar hypoventilation (Table 66-1). It is often accompanied by hypochloremia and hypokalemia. The arterial pH establishes the diagnosis, because it is increased in metabolic alkalosis and decreased or normal in respiratory acidosis. Metabolic alkalosis frequently occurs in association with other disorders such as respiratory acidosis or alkalosis or metabolic acidosis.

PATHOGENESIS

Metabolic alkalosis occurs as a result of net gain of [HCO_3^-] or loss of nonvolatile acid (usually HCl by vomiting) from the extracellular fluid. For HCO_3^- to be added to the extracellular fluid, it must be administered exogenously or synthesized endogenously, in part or entirely by the kidneys. Because it is unusual for alkali to be added to the body, the disorder involves a generative stage, in which the loss of acid usually causes alkalosis, and a maintenance stage, in which the kidneys fail to compensate by excreting HCO_3^-.

Maintenance of metabolic alkalosis represents a failure of the kidneys to eliminate HCO_3^- in the usual manner. The kidneys will retain, rather than excrete, the excess alkali and maintain the alkalosis if (1) volume deficiency, chloride deficiency, and K^+ deficiency exist in combination with a reduced GFR; or (2) hypokalemia exists because of autonomous hyperaldosteronism. In the first example, alkalosis is corrected by administration of NaCl and KCl, whereas, in the latter, it may be necessary to repair the alkalosis by pharmacologic or surgical intervention, not with saline administration.

DIFFERENTIAL DIAGNOSIS

To establish the cause of metabolic alkalosis (Table 66-6), it is necessary to assess the status of the extracellular fluid volume (ECFV), the recumbent and upright blood pressure, the serum [K^+], and the renin-aldosterone system. For example, the presence of chronic hypertension and chronic hypokalemia in an alkalotic patient suggests either mineralocorticoid excess or that the hypertensive patient is receiving diuretics. Low plasma renin activity and normal urine [Na^+] and [Cl^-] in a patient who is not taking diuretics indicate a primary mineralocorticoid excess syndrome. The combination of hypokalemia and alkalosis in a normotensive, nonedematous patient can be due to Bartter's or Gitelman's syndrome, magnesium deficiency, vomiting, exogenous alkali, or diuretic ingestion. Determination of urine electrolytes (especially the urine [Cl^-]) and screening of the urine for diuretics may be helpful. If the urine is alkaline, with an elevated [Na^+] and [K^+] but low [Cl^-], the diagnosis is usually either vomiting (overt or surreptitious) or alkali ingestion. If the urine is relatively acid and has low concentrations of Na^+, K^+, and Cl^-, the most likely possibilities are prior vomiting, the posthypercapnic state, or prior diuretic ingestion. If, on the other hand, neither the urine sodium, potassium, nor chloride concentrations are depressed, magnesium deficiency, Bartter's or Gitelman's syndrome, or current diuretic ingestion should be considered. Bartter's syndrome is distinguished from Gitelman's syndrome because of hypocalciuria and hypomagnesemia in the latter disorder.

Alkali Administration Chronic administration of alkali to individuals with normal renal function rarely causes alkalosis. However, in patients with coexistent hemodynamic disturbances, alkalosis can develop because the normal capacity to excrete HCO_3^- may be exceeded or there may be enhanced reabsorption of HCO_3^-. Such patients include those who receive HCO_3^- (PO or IV), acetate loads (parenteral hyperalimentation solutions), citrate loads (transfusions), or antacids plus cation-exchange resins (aluminum hydroxide and sodium polystyrene sulfonate). Nursing home patients receiving tube feedings have a higher incidence of metabolic alkalosis than nursing home patients receiving oral feedings.

TABLE 66-6 CAUSES OF METABOLIC ALKALOSIS

- I. Exogenous HCO_3^- loads
  - A. Acute alkali administration
  - B. Milk-alkali syndrome
- II. Effective ECFV contraction, normotension, K^+ deficiency, and secondary hyperreninemic hyperaldosteronism
  - A. Gastrointestinal origin
    1. Vomiting
    2. Gastric aspiration
    3. Congenital chloridorrhea
    4. Villous adenoma
  - B. Renal origin
    1. Diuretics
    2. Posthypercapnic state
    3. Hypercalcemia/hypoparathyroidism
    4. Recovery from lactic acidosis or ketoacidosis
    5. Nonreabsorbable anions including penicillin, carbenicillin
    6. Mg^{2+} deficiency
    7. K^+ depletion
    8. Bartter's syndrome (loss of function mutations of transporters and ion channels in TALH)
    9. Gitelman's syndrome (loss of function mutation in Na^+-Cl^- cotransporter in DCT)
- III. ECFV expansion, hypertension, K^+ deficiency, and mineralocorticoid excess
  - A. High renin
    1. Renal artery stenosis
    2. Accelerated hypertension
    3. Renin-secreting tumor
    4. Estrogen therapy
  - B. Low renin
    1. Primary aldosteronism
       a. Adenoma
       b. Hyperplasia
       c. Carcinoma
    2. Adrenal enzyme defects
       a. 11β-Hydroxylase deficiency
       b. 17α-Hydroxylase deficiency
    3. Cushing's syndrome or disease
    4. Other
       a. Licorice
       b. Carbenoxolone
       c. Chewer's tobacco
- IV. Gain-of-function mutation of renal sodium channel with ECFV expansion, hypertension, K^+ deficiency, and hyporeninemic-hypoaldosteronism
  - A. Liddle's syndrome

Abbreviations: DCT, distal convoluted tubule; ECFV, extracellular fluid volume; TALH, thick ascending limb of Henle's loop.

METABOLIC ALKALOSIS ASSOCIATED WITH ECFV CONTRACTION, K^+ DEPLETION, AND SECONDARY HYPERRENINEMIC HYPERALDOSTERONISM

Gastrointestinal Origin Gastrointestinal loss of H^+ from vomiting or gastric aspiration results in retention of HCO_3^-. During active vomiting, the filtered load of bicarbonate is acutely increased to exceed the reabsorptive capacity of the proximal tubule for HCO_3^- so that the urine becomes alkaline and high in potassium. When vomiting ceases, the persistence of volume, potassium, and chloride depletion causes