in the GFR. Decreased EABV is the main factor in the maintenance of metabolic alkalosis. At this point, urine Na^+ and Cl^- levels are low. Administration of NaCl results in bicarbonaturia, and the metabolic alkalosis is corrected.

Diuretics

Thiazide and loop diuretics are another common cause of metabolic alkalosis. The diuretics produce a metabolic alkalosis that is generated in the distal nephron by the combination of high aldosterone levels and enhanced distal delivery of Na^+. If diuretics are stopped and the patient is maintained on a low-salt diet, the alkalosis is maintained despite the fact that distal delivery is no longer increased. In this setting, patients tend to be volume contracted and K^+ deficient. Contraction of the EABV is the major factor in the maintenance of metabolic alkalosis. Saline infusion in this setting corrects the metabolic alkalosis.

Decreased Effective Arterial Blood Volume and Saline-Resistant Metabolic Alkalosis

In some forms of metabolic alkalosis, the alkalosis is maintained by decreased EABV, but because of other maintenance factors, the alkalosis is not completely saline responsive. In these patients, saline infusions may improve the metabolic alkalosis but do not completely correct it. Patients may have a low EABV but typically do not have a low urine Cl^- level.

Continued use of thiazide or loop diuretics, magnesium deficiency, Gitelman syndrome, and Bartter syndrome can produce this condition. Treatment of the various causes of metabolic alkalosis is summarized in Table 27-5.

Increased Effective Arterial Blood Volume and Saline-Resistant Metabolic Alkalosis

One type of metabolic alkalosis is not maintained by decreased EABV but instead is maintained by K^+ deficiency and high mineralocorticoid levels in the setting of continued distal delivery of Na^+. The most common cause of this saline-resistant alkalosis is a primary increase in mineralocorticoid levels not related to volume contraction. The mechanism of generation of the alkalosis—enhanced Na^+ delivery with high mineralocorticoid activity—is also responsible for maintenance of metabolic alkalosis. The K^+ deficiency that occurs in this setting exacerbates the tendency to produce alkalosis.

The preferred treatment of metabolic alkalosis in patients with volume expansion and primary mineralocorticoid excess is to remove the underlying cause of the persistent mineralocorticoid activity. When this is not possible, therapy is directed at blocking the actions of the mineralocorticoid at the level of the kidney.

RESPIRATORY ALKALOSIS

Definition

Primary respiratory alkalosis results from hypocapnia and is defined by an arterial partial pressure of carbon dioxide ($Paco_2$) of less than 35 mm Hg in the setting of alkalemia. Primary respiratory alkalosis should be differentiated from secondary hypocapnia, which is a compensatory mechanism in the setting of primary metabolic acidosis.

Respiratory alkalosis is the most frequent acid-base disturbance encountered. It is particularly common in hospitalized patients, for whom it can be the initial clue to gram-negative sepsis. Hepatic failure is a common and important cause of primary hypocapnia. The severity of hypocapnia correlates with the level of blood ammonia and has prognostic significance. Respiratory alkalosis can be an important clue to the existence of salicylate intoxication. High progesterone levels (in pregnancy) can also cause respiratory alkalosis.

Clinical Presentation

Mild respiratory alkalosis causes lightheadedness, palpitations, and paresthesia of the extremities and the circumoral area. Acute hypocapnia decreases cerebral blood flow and causes binding of free calcium to albumin in the blood. At clinical presentation, patients with acute respiratory alkalosis may appear similar to patients with hypocalcemia and have positive Chvostek and Trousseau signs. Patients with ischemic heart disease may occasionally develop cardiac arrhythmias, ischemic electrocardiographic changes, and angina pectoris during acute hypocapnia.

Diagnosis

The diagnosis of respiratory alkalosis is made by evaluating the patient's history, performing a physical examination, and obtaining laboratory data, including a blood gas analysis. Tachypnea or Kussmaul breathing can be detected on physical examination, and it may be the first clue to a primary respiratory alkalosis or a compensatory respiratory mechanism in the setting of primary metabolic acidosis.

Changes in serum electrolytes can aid in the diagnosis of respiratory alkalosis. An acute fall in Pco_2 causes an HCO_3^--Cl^- shift in red blood cells and accounts for the small initial compensatory response in acute respiratory alkalosis in which the

TABLE 27-5 TREATMENT OF SALINE-RESISTANT METABOLIC ALKALOSIS

DECREASED EABV		INCREASED EABV	
Cause	***Treatment***	***Cause***	***Treatment***
Thiazide and loop diuretics	Discontinue drug, replete EABV	Renin secreting tumor	Remove tumor
Mg^{2+} deficiency	Replete Mg^{2+} deficit	Primary hyperaldosteronism	Remove tumor, spironolactone for BAH
Gitelman syndrome	Amiloride, triamterene, or spironolactone, K^+ supplements, Mg^{2+} supplements	Glucocorticoid-suppressible hyperaldosteronism	Dexamethasone
Bartter syndrome	Amiloride, triamterene, or spironolactone, K^+ supplements, Mg^{2+} supplements in some	Liddle syndrome	Amiloride or triamterene

BAH, Bilateral adrenal hyperplasia; EABV, effective arterial blood volume; K^+, potassium ion; Mg^{2+}, magnesium ion.