lowers the P_{CO_2}, contributing to the development of respiratory alkalosis. Children primarily have an anion gap metabolic acidosis with toxic salicylate levels, whereas respiratory alkalosis is most evident in adults.

In addition to conservative management, the initial goal of therapy is to correct systemic acidemia and to increase the urine pH. By increasing the systemic pH, the ionized fraction of salicylic acid increases, and there is less accumulation of the drug in the central nervous system. Similarly, an alkaline urine pH favors increased urinary excretion because the ionized fraction of the drug is poorly reabsorbed by the tubule. At serum concentrations greater than 80 mg/dL or in the setting of severe clinical toxicity, hemodialysis can be used to accelerate removal of the drug from the body.

Pyroglutamic Acidosis

Pyroglutamic acidosis is a cause of anion gap metabolic acidosis accompanied by alterations in mental status ranging from confusion to coma. Pyroglutamic acidosis occurs in critically ill patients receiving therapeutic doses of acetaminophen, a setting in which glutathione levels are reduced as a result of acetaminophen metabolism and oxidative stress associated with critical illness. The diagnosis of pyroglutamic acidosis should be considered for patients with unexplained anion gap metabolic acidosis and recent acetaminophen ingestion.

METABOLIC ALKALOSIS

Definition

The pathogenesis of metabolic alkalosis involves generation and maintenance of the disorder. Metabolic alkalosis is caused by the addition of new HCO_3^- ions to the blood as a result of loss of acid or gain of alkali. New HCO_3^- ions may be generated by renal or extrarenal mechanisms. Because the kidneys have an enormous capacity to excrete HCO_3^-, even vigorous HCO_3^- generation may not be sufficient to produce sustained metabolic alkalosis. To maintain a metabolic alkalosis, the kidney's capacity to correct the alkalosis must be impaired, or the capacity to reclaim HCO_3^- ions must be enhanced.

Metabolic alkalosis is considered by most physicians to be a benign condition. However, a high blood pH can result in a number of effects that decrease tissue perfusion. Increases in blood pH (i.e., alkalemia) cause respiratory depression and decrease tissue oxygen delivery through the Bohr effect and vasoconstriction. Alkalosis should be aggressively corrected in critically ill patients in whom perfusion of the heart and brain is essential.

Treatment

The treatment of metabolic alkalosis is best approached according to the mechanism of maintenance because correction of the mechanism remedies the metabolic alkalosis. If the EABV can be restored with saline, the metabolic alkalosis is easily corrected. Several conditions are poorly responsive to the administration of NaCl. Metabolic alkalosis in these conditions usually is maintained by a combination of increased mineralocorticoid levels along with high distal Na^+ delivery and hypokalemia. The distinction between these entities relies on assessment of the EABV (Table 27-4).

Decreased Effective Arterial Blood Volume and Saline-Responsive Metabolic Alkalosis

Gastrointestinal Acid Loss

Loss of acid, as occurs with vomiting or nasogastric suction, is a common cause of metabolic alkalosis that is maintained by volume contraction. The loss of gastric acid generates a metabolic alkalosis, and the loss of NaCl in the gastric fluid leads to volume contraction. During active vomiting, the plasma HCO_3^- concentration tends to be higher than the threshold for reabsorption in the proximal nephron. The resultant bicarbonaturia leads to increased excretion of $NaHCO_3$ and $KHCO_3$, resulting in further total body Na^+ depletion and development of K^+ depletion. During this active phase, urine Cl^- concentration is less than 15 mEq/L in the setting of high levels of urine Na^+ and K^+ and a urine pH of 7 to 8.

When the patient stops vomiting, equilibrium is established such that bicarbonaturia disappears but a metabolic alkalosis is maintained by volume contraction, K^+ depletion, and reduction

TABLE 27-4 METABOLIC ALKALOSIS CLASSIFICATION

	TYPES OF METABOLIC ALKALOSIS		
CLASSIFICATION CHARACTERISTIC	***Decreased EABV, Saline Responsive***	***Decreased EABV, Saline Resistant***	***Increased EABV, Saline Resistant***
EABV	Low	Low	High
Urine Cl^- concentration (mEq/L)	<15	>15	>15
Response to saline	Corrects (saline responsive)	No correction (saline resistant)	No correction (saline resistant)
Maintenance	Low EABV	Low EABV + high distal Na^+ delivery and mineralocorticoid effect	High distal Na^+ delivery and mineralocorticoid effect
Cause	Gastrointestinal acid loss: Vomiting or nasogastric suction Congenital chloridorrhea Villous adenoma Post-hypercapneic alkalosis Diuretics Non-reabsorbable anions	Primary increase in distal delivery of Na^+: Active diuretic use (loop and thiazide) Mg^{2+} deficiency Bartter syndrome Gitelman syndrome	Primary increase in mineralocorticoid or mineralocorticoid-like effect: Conn syndrome Liddle syndrome Glucocorticoid-suppresible hyperaldosteronism

EABV, Effective arterial blood volume.