maintenance of the alkalosis because of an enhanced capacity of the nephron to reabsorb HCO_3^-. Correction of the contracted ECFV with NaCl and repair of K^+ deficits corrects the acid-base disorder by restoring the ability of the kidney to excrete the excess bicarbonate.

Renal Origin • ***DIURETICS*** (See also Chap. 279) Drugs that induce chloruresis, such as thiazides and loop diuretics (furosemide, bumetanide, torsemide, and ethacrynic acid), acutely diminish the ECFV without altering the total body bicarbonate content. The serum [HCO_3^-] increases because the reduced ECFV "contracts" the [HCO_3^-] in the plasma (contraction alkalosis). The chronic administration of diuretics tends to generate an alkalosis by increasing distal salt delivery, so that K^+ and H^+ secretion are stimulated. The alkalosis is maintained by persistence of the contraction of the ECFV, secondary hyperaldosteronism, K^+ deficiency, and the direct effect of the diuretic (as long as diuretic administration continues). Repair of the alkalosis is achieved by providing isotonic saline to correct the ECFV deficit.

SOLUTE LOSING DISORDERS: BARTTER'S SYNDROME AND GITELMAN'S SYNDROME See Chap. 339.

NONREABSORBABLE ANIONS AND MAGNESIUM DEFICIENCY Administration of large quantities of nonreabsorbable anions, such as penicillin or carbenicillin, can enhance distal acidification and K^+ secretion by increasing the transepithelial potential difference. Mg^{2+} deficiency results in hypokalemic alkalosis by enhancing distal acidification through stimulation of renin and hence aldosterone secretion.

POTASSIUM DEPLETION Chronic K^+ depletion may cause metabolic alkalosis by increasing urinary acid excretion. Both NH_4^+ production and absorption are enhanced and HCO_3^- reabsorption is stimulated. Chronic K^+ deficiency upregulates the renal H^+, K^+-ATPase to increase K^+ absorption at the expense of enhanced H^+ secretion. Alkalosis associated with severe K^+ depletion is resistant to salt administration, but repair of the K^+ deficiency corrects the alkalosis.

AFTER TREATMENT OF LACTIC ACIDOSIS OR KETOACIDOSIS When an underlying stimulus for the generation of lactic acid or ketoacid is removed rapidly, as with repair of circulatory insufficiency or with insulin therapy, the lactate or ketones are metabolized to yield an equivalent amount of HCO_3^-. Other sources of new HCO_3^- are additive with the original amount generated by organic anion metabolism to create a surfeit of HCO_3^-. Such sources include (1) new HCO_3^- added to the blood by the kidneys as a result of enhanced acid excretion during the preexisting period of acidosis, and (2) alkali therapy during the treatment phase of the acidosis. Acidosis-induced contraction of the ECFV and K^+ deficiency act to sustain the alkalosis.

POSTHYPERCAPNIA Prolonged CO_2 retention with chronic respiratory acidosis enhances renal HCO_3^- absorption and the generation of new HCO_3^- (increased net acid excretion). Metabolic alkalosis results from the effect of the persistently elevated [HCO_3^-] when the elevated $Paco_2$ is abruptly returned toward normal.

METABOLIC ALKALOSIS ASSOCIATED WITH ECFV EXPANSION, HYPERTENSION, AND HYPERALDOSTERONISM

Increased aldosterone levels may be the result of autonomous primary adrenal overproduction or of secondary aldosterone release due to renal overproduction of renin. Mineralocorticoid excess increases net acid excretion and may result in metabolic alkalosis, which may be worsened by associated K^+ deficiency. ECFV expansion from salt retention causes hypertension. The kaliuresis persists because of mineralocorticoid excess and distal Na^+ absorption causing enhanced K^+ excretion, continued K^+ depletion with polydipsia, inability to concentrate the urine, and polyuria.

Liddle's syndrome (Chap. 339) results from increased activity of the collecting duct Na^+ channel (ENaC) and is a rare monogenic form of hypertension due to volume expansion manifested as hypokalemic alkalosis and normal aldosterone levels.

Symptoms With metabolic alkalosis, changes in CNS and peripheral nervous system function are similar to those of hypocalcemia (Chap. 423); symptoms include mental confusion; obtundation; and a predisposition to seizures, paresthesia, muscular cramping, tetany, aggravation of arrhythmias, and hypoxemia in chronic obstructive pulmonary disease. Related electrolyte abnormalities include hypokalemia and hypophosphatemia.

TREATMENT METABOLIC ALKALOSIS

This is primarily directed at correcting the underlying stimulus for HCO_3^- generation. If primary aldosteronism, renal artery stenosis, or Cushing's syndrome is present, correction of the underlying cause will reverse the alkalosis. [H^+] loss by the stomach or kidneys can be mitigated by the use of proton pump inhibitors or the discontinuation of diuretics. The second aspect of treatment is to remove the factors that sustain the inappropriate increase in HCO_3^- reabsorption, such as ECFV contraction or K^+ deficiency. K^+ deficits should always be repaired. Isotonic saline is usually sufficient to reverse the alkalosis if ECFV contraction is present.

If associated conditions preclude infusion of saline, renal HCO_3^- loss can be accelerated by administration of acetazolamide, a carbonic anhydrase inhibitor, which is usually effective in patients with adequate renal function but can worsen K^+ losses. Dilute hydrochloric acid (0.1 *N* HCl) is also effective but can cause hemolysis, and must be delivered slowly in a central vein.

RESPIRATORY ACIDOSIS

Respiratory acidosis can be due to severe pulmonary disease, respiratory muscle fatigue, or abnormalities in ventilatory control and is recognized by an increase in $Paco_2$ and decrease in pH (Table 66-7). In acute respiratory acidosis, there is an immediate compensatory elevation (due to cellular buffering mechanisms) in HCO_3^-, which increases 1 mmol/L for every 10-mmHg increase in $Paco_2$. In chronic respiratory acidosis (>24 h), renal adaptation increases the [HCO_3^-] by 4 mmol/L for every 10-mmHg increase in $Paco_2$. The serum HCO_3^- usually does not increase above 38 mmol/L.

The clinical features vary according to the severity and duration of the respiratory acidosis, the underlying disease, and whether there is accompanying hypoxemia. A rapid increase in $Paco_2$ may cause anxiety, dyspnea, confusion, psychosis, and hallucinations and may progress to coma. Lesser degrees of dysfunction in chronic hypercapnia include sleep disturbances; loss of memory; daytime somnolence; personality changes; impairment of coordination; and motor disturbances such as tremor, myoclonic jerks, and asterixis. Headaches and other signs that mimic raised intracranial pressure, such as papilledema, abnormal reflexes, and focal muscle weakness, are due to vasoconstriction secondary to loss of the vasodilator effects of CO_2.

Depression of the respiratory center by a variety of drugs, injury, or disease can produce respiratory acidosis. This may occur acutely with general anesthetics, sedatives, and head trauma or chronically with sedatives, alcohol, intracranial tumors, and the syndromes of sleep-disordered breathing including the primary alveolar and obesity-hypoventilation syndromes (Chaps. 318 and 319). Abnormalities or disease in the motor neurons, neuromuscular junction, and skeletal muscle can cause hypoventilation via respiratory muscle fatigue. Mechanical ventilation, when not properly adjusted and supervised, may result in respiratory acidosis, particularly if CO_2 production suddenly rises (because of fever, agitation, sepsis, or overfeeding) or alveolar ventilation falls because of worsening pulmonary function. High levels of positive end-expiratory pressure in the presence of reduced cardiac output may cause hypercapnia as a result of large increases in alveolar dead space (Chap. 306e). Permissive hypercapnia is being used with increasing frequency because of studies suggesting lower mortality rates than with conventional mechanical ventilation, especially with severe CNS or heart disease. The respiratory acidosis associated with permissive hypercapnia may require administration of $NaHCO_3$ to increase the arterial pH to 7.25, but overcorrection of the acidemia may be deleterious.

Acute hypercapnia follows sudden occlusion of the upper airway or generalized bronchospasm as in severe asthma, anaphylaxis,