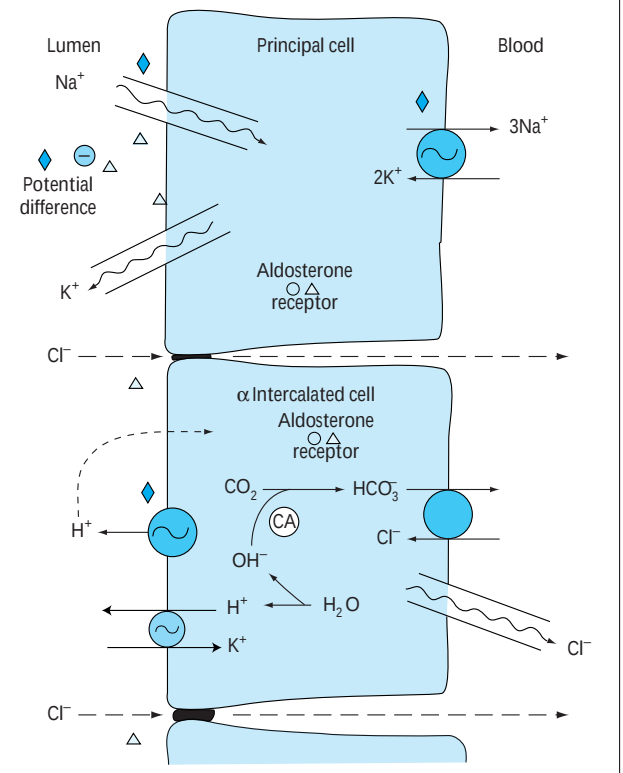

B. CAUSES OF HYPERKALEMIC DISTAL RENAL TUBULAR ACIDOSIS

- Deficiency of aldosterone
  - Associated with glucocorticoid deficiency
    - Addison's disease
    - Bilateral adrenalectomy
    - Enzymatic defects
      - 21-Hydroxylase deficiency
      - 3-β-ol-Dehydrogenase deficiency
      - Desmolase deficiency
    - Acquired immunodeficiency syndrome
  - Isolated aldosterone deficiency
    - Genetically transmitted
      - Corticosterone methyl oxidase deficiency
    - Transient (infants)
    - Sporadic
    - Heparin
    - Deficient renin secretion
      - Diabetic nephropathy
      - Tubulointerstitial renal disease
      - Nonsteroidal antiinflammatory drugs
      - β-adrenergic blockers
      - Acquired immunodeficiency syndrome
      - Renal transplantation
  - Angiotensin I-converting enzyme inhibition
    - Endogenous
    - Captopril and related drugs
  - Angiotensin AT, receptor blockers
- Resistance to aldosterone action
  - Pseudohypoaldosteronism type I (with salt wasting)
    - Childhood forms with obstructive uropathy
    - Adult forms with renal insufficiency
  - Spironolactone
  - Pseudohypoaldosteronism type II (without salt wasting)
  - Combined aldosterone deficiency and resistance
    - Deficient renin secretion
    - Cyclosporine nephrotoxicity
    - Uncertain renin status
  - Voltage-mediated defects
    - Obstructive uropathy
    - Sickle cell anemia
    - Lithium
    - Triamterene
    - Amiloride
    - Trimethoprim, pentamidine
  - Renal transplantation

FIGURE 6-28

A and **B**, Potential defects and causes of hyperkalemic distal renal tubular acidosis (RTA) (type 4). This syndrome represents the most common type of RTA encountered in adults. The characteristic hyperchloremic metabolic acidosis in the company of hyperkalemia emerges as a consequence of generalized dysfunction of the collecting tubule, including diminished sodium reabsorption and impaired hydrogen ion and potassium secretion. The resultant hyperkalemia causes impaired ammonium excretion that is an important contribution to the generation of the metabolic acidosis. The causes of this syndrome are broadly classified into disorders resulting in aldosterone deficiency and those that impose resistance to the action of aldosterone. Aldosterone deficiency can arise from hyporeninemia, impaired conversion of angiotensin I to angiotensin II, or abnormal aldosterone synthesis. Aldosterone resistance can reflect the following: blockade of the mineralocorticoid receptor; destruction of the target cells in the collecting tubule (*tubulointerstitial nephropathies*); interference with the sodium channel of the principal cell, thereby decreasing the lumen-negative potential difference and thus the secretion of potassium and hydrogen ions (voltage-mediated defect); inhibition of the basolateral sodium ion, potassium ion–adenosine triphosphatase; and enhanced chloride ion permeability in the collecting tubule, with consequent shunting of the transepithelial potential difference. Some disorders cause combined aldosterone deficiency and resistance [20].

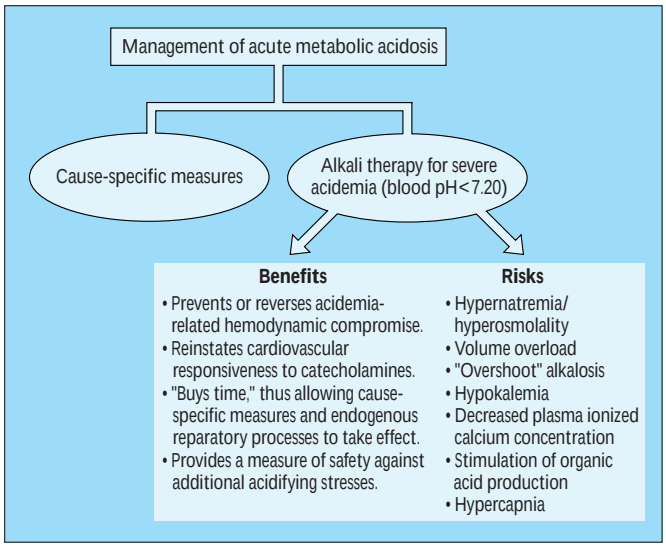

FIGURE 6-29

Treatment of acute metabolic acidosis. Whenever possible, cause-specific measures should be at the center of treatment of metabolic acidosis. In the presence of severe acidemia, such measures should be supplemented by judicious administration of sodium bicarbonate. The goal of alkali therapy is to return the blood pH to a safer level of about 7.20. Anticipated benefits and potential risks of alkali therapy are depicted here [1].

Metabolic Alkalosis

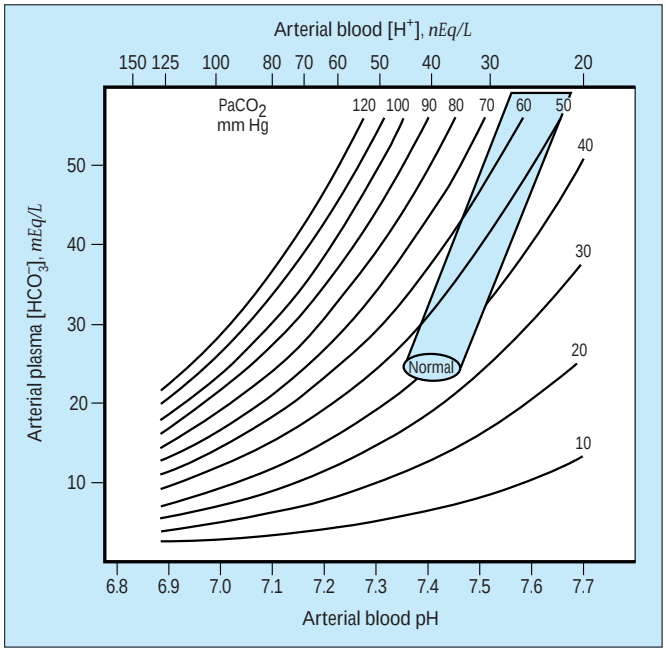

FIGURE 6-30

Ninety-five percent confidence intervals for metabolic alkalosis. Metabolic alkalosis is the acid-base disturbance initiated by an increase in plasma bicarbonate concentration ($[HCO_3^-]$). The resultant alkalemia dampens alveolar ventilation and leads to the secondary hypercapnia characteristic of the disorder. Available observations in humans suggest a roughly linear relationship between the steady-state increase in bicarbonate concentration and the associated increment in the arterial carbon dioxide tension ($PaCO_2$). Although data are limited, the slope of the steady-state $\Delta PaCO_2$ versus $\Delta[HCO_3^-]$ relationship has been estimated as about a 0.7 mm Hg per mEq/L increase in plasma bicarbonate concentration. The value of this slope is virtually identical to that in dogs that has been derived from rigorously controlled observations [21]. Empiric observations in humans have been used for construction of 95% confidence intervals for graded degrees of metabolic alkalosis represented by the area in color in the acid-base template. The black ellipse near the center of the figure indicates the normal range for the acid-base parameters [3]. Assuming a steady state is present, values falling within the area in color are consistent with but not diagnostic of simple metabolic alkalosis. Acid-base values falling outside the area in color denote the presence of a mixed acid-base disturbance [4]. $[H^+]$—hydrogen ion concentration.

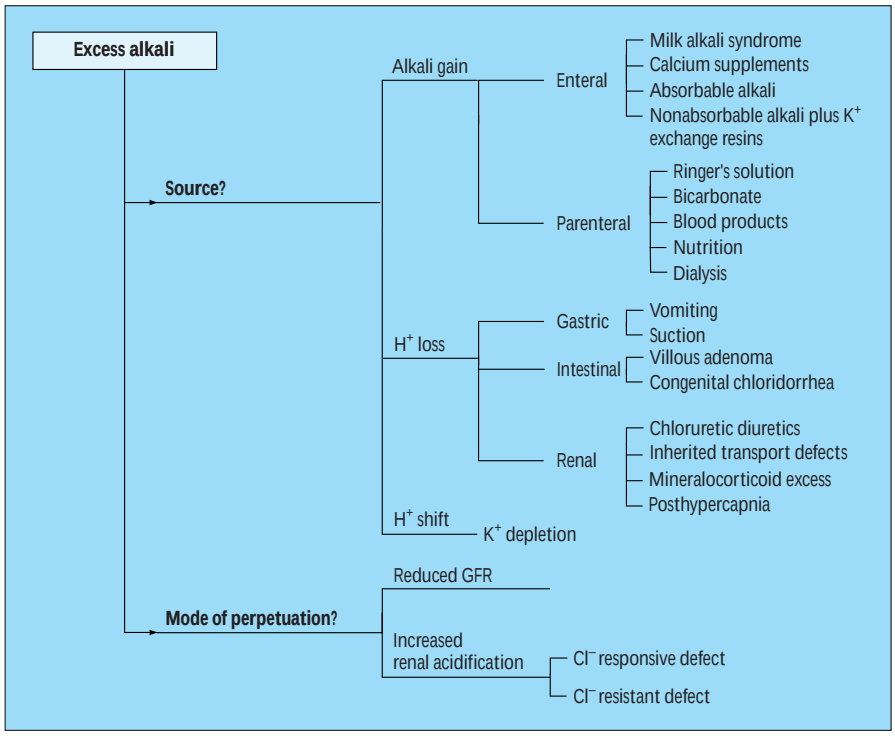

FIGURE 6-31

Pathogenesis of metabolic alkalosis. Two crucial questions must be answered when evaluating the pathogenesis of a case of metabolic alkalosis. 1) What is the source of the excess alkali? Answering this question addresses the primary event responsible for *generating* the hyperbicarbonatemia. 2) What factors perpetuate the hyperbicarbonatemia? Answering this question addresses the pathophysiologic events that *maintain* the metabolic alkalosis.

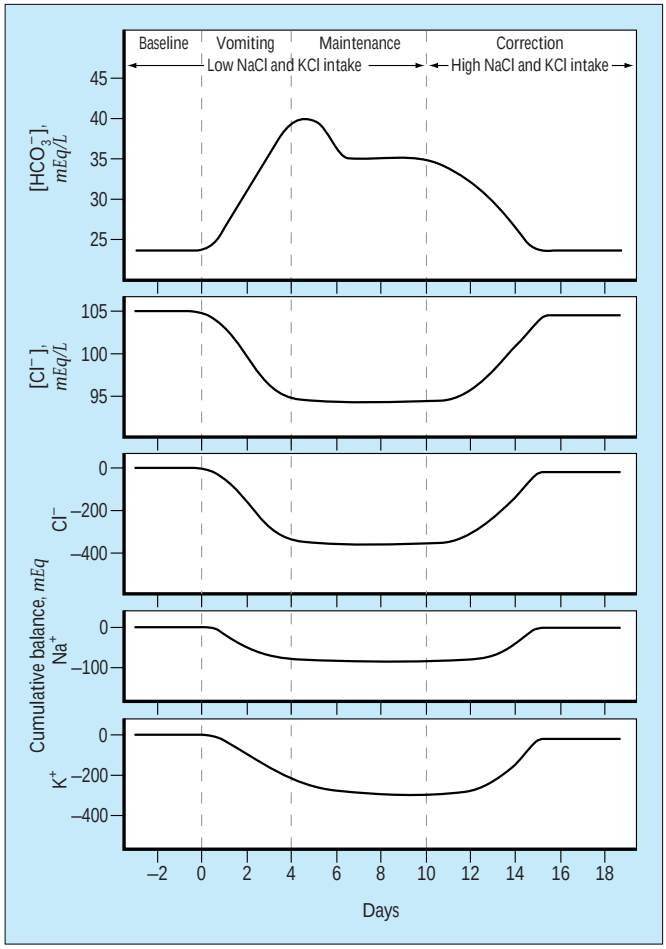

FIGURE 6-32

Changes in plasma anionic pattern and body electrolyte balance during development, maintenance, and correction of metabolic alkalosis induced by vomiting. Loss of hydrochloric acid from the stomach as a result of vomiting (or gastric drainage) generates the hypochloremic hyperbicarbonatemia characteristic of this disorder. During the generation phase, renal sodium and potassium excretion increases, yielding the deficits depicted here. Renal potassium losses continue in the early days of the maintenance phase. Subsequently, and as long as the low-chloride diet is continued, a new steady state is achieved in which plasma bicarbonate concentration ($[HCO_3^-]$) stabilizes at an elevated level, and renal excretion of electrolytes matches intake. Addition of sodium chloride (NaCl) and potassium chloride (KCl) in the correction phase repairs the electrolyte deficits incurred and normalizes the plasma bicarbonate and chloride concentration ($[Cl^-]$) levels [22,23].