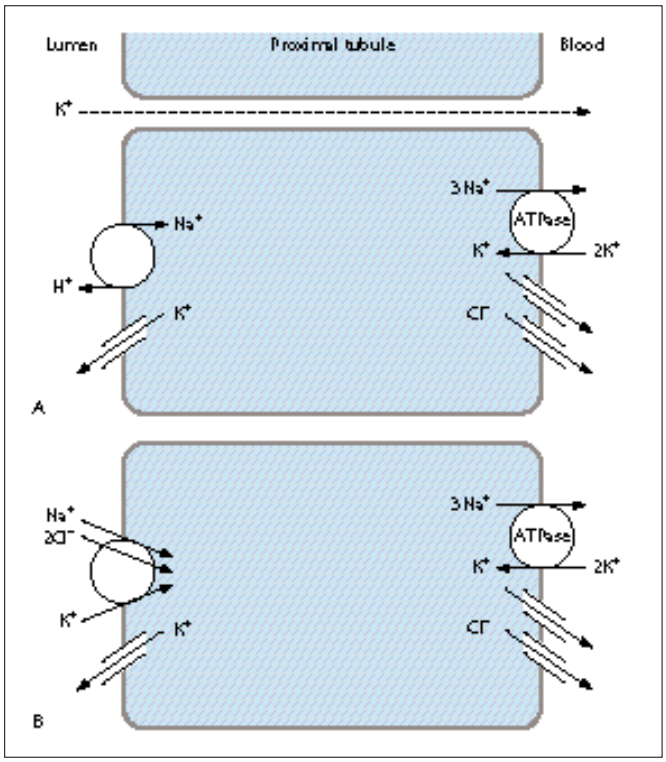

FIGURE 3-5

Cellular mechanisms of renal potassium transport: proximal tubule and thick ascending limb. **A**, Proximal tubule potassium reabsorption is closely coupled to proximal sodium and water transport. Potassium is reabsorbed through both paracellular and cellular pathways. Proximal apical potassium channels are normally almost completely closed. The lumen of the proximal tubule is negative in the early proximal tubule and positive in late proximal tubule segments. Potassium transport is not specifically regulated in this portion of the nephron, but net potassium reabsorption is closely coupled to sodium and water reabsorption. **B**, In the thick ascending limb of Henle's loop, potassium reabsorption proceeds by electroneutral Na^+-K^+-$2Cl^-$ cotransport in the thick ascending limb, the low intracellular sodium and chloride concentrations providing the driving force for transport. In addition, the positive lumen potential allows some portion of luminal potassium to be reabsorbed via paracellular pathways [11]. The apical potassium channel allows potassium recycling and provides substrate to the apical Na^+-K^+-$2Cl^-$ cotransporter [12]. Loop diuretics act by competing for the Cl^- site on this carrier.

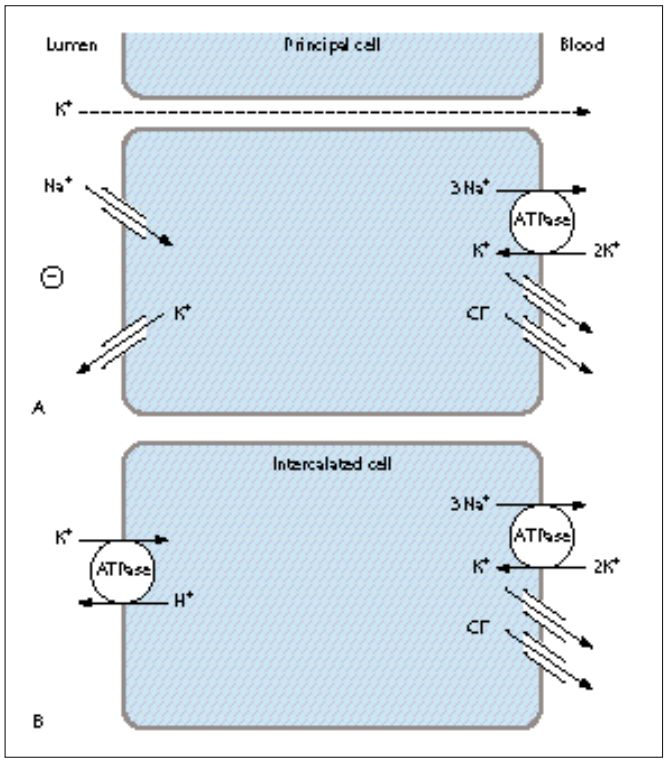

FIGURE 3-6

Cellular mechanisms of renal potassium transport: cortical collecting tubule. **A**, Principal cells of the cortical collecting duct: apical sodium channels play a key role in potassium secretion by increasing the intracellular sodium available to Na^+-K^+-ATPase pumps and by creating a favorable electrical potential for potassium secretion. Basolateral Na^+-K^+-ATPase creates a favorable concentration gradient for passive diffusion of potassium from cell to lumen through potassium-selective channels. **B**, Intercalated cells. Under conditions of potassium depletion, the cortical collecting duct becomes a site for net potassium reabsorption. The H^+-K^+-ATPase pump is regulated by potassium intake. Decreases in total body potassium increase pump activity, resulting in enhanced potassium reabsorption. This pump may be partly responsible for the maintenance of metabolic alkalosis in conditions of potassium depletion [11].

Hypokalemia: Diagnostic Approach

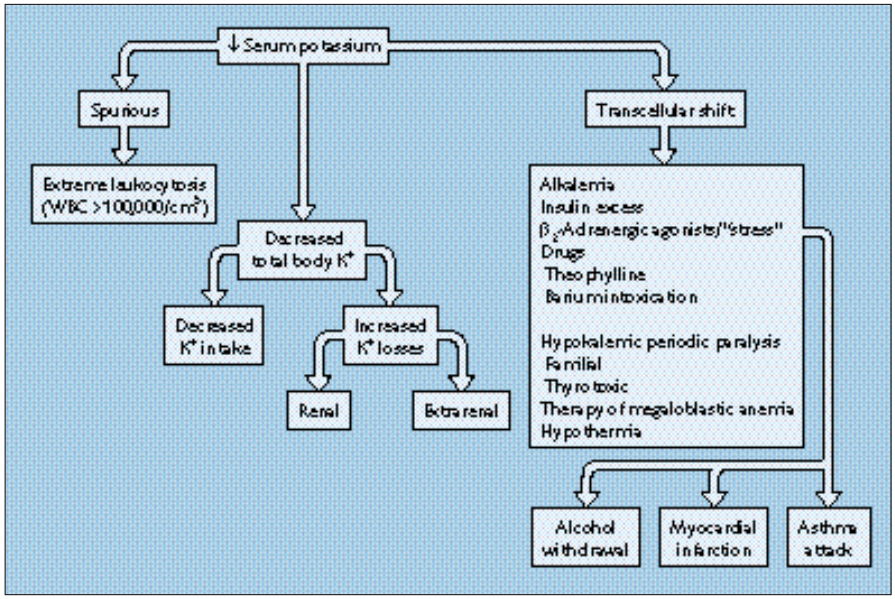

FIGURE 3-7

Overview of diagnostic approach to hypokalemia: hypokalemia without total body potassium depletion. Hypokalemia can result from transcellular shifts of potassium into cells without total body potassium depletion or from decreases in total body potassium. Perhaps the most dramatic examples occur in catecholamine excess states, as after administration of $\beta_2$adreneric receptor (β_2AR) agonists or during "stress." It is important to note that, during some conditions (*eg*, ketoacidosis), transcellular shifts and potassium depletion exist simultaneously. Spurious hypokalemia results when blood specimens from leukemia patients are allowed to stand at room temperature; this results in leukocyte uptake of potassium from serum and artifactual hypokalemia. Patients with spurious hypokalemia do not have clinical manifestations of hypokalemia, as their in vivo serum potassium values are normal. Theophylline poisoning prevents cAMP breakdown (*see* Fig. 3-3). Barium poisoning from the ingestion of soluble barium salts results in severe hypokalemia by blocking channels for exit of potassium from cells. Episodes of hypokalemic periodic paralysis can be precipitated by rest after exercise, carbohydrate meal, stress, or administration of insulin. Hypokalemic periodic paralysis can be inherited as an autosomal-dominant disease or acquired by patients with thyrotoxicosis, especially Chinese males. Therapy of megaloblastic anemia is associated with potassium uptake by newly formed cells, which is occasionally of sufficient magnitude to cause hypokalemia [13].

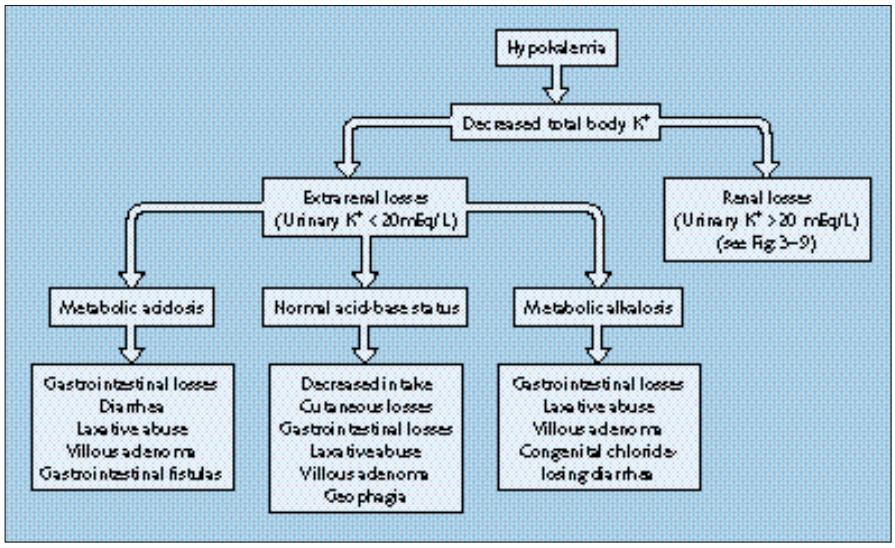

FIGURE 3-8

Diagnostic approach to hypokalemia: hypokalemia with total body potassium depletion secondary to extrarenal losses. In the absence of redistribution, measurement of urinary potassium is helpful in determining whether hypokalemia is due to renal or to extrarenal potassium losses. The normal kidney responds to several (3 to 5) days of potassium depletion with appropriate renal potassium conservation. In the absence of severe polyuria, a "spot" urinary potassium concentration of less than 20 mEq/L indicates renal potassium conservation. In certain circumstances (*eg*, diuretics abuse), renal potassium losses may not be evident once the stimulus for renal potassium wasting is removed. In this circumstance, urinary potassium concentrations may be deceptively low despite renal potassium losses. Hypokalemia due to colonic villous adenoma or laxative abuse may be associated with metabolic acidosis, alkalosis, or no acid-base disturbance. Stool has a relatively high potassium content, and fecal potassium losses could exceed 100 mEq per day with severe diarrhea. Habitual ingestion of clay (pica), encountered in some parts of the rural southeastern United States, can result in potassium depletion by binding potassium in the gut, much as a cation exchange resin does. Inadequate dietary intake of potassium, like that associated ith anorexia or a "tea and toast" diet, can lead to hypokalemia, owing to delayed renal conservation of potassium; however, progressive potassium depletion does not occur unless intake is well below 15 mEq of potassium per day.

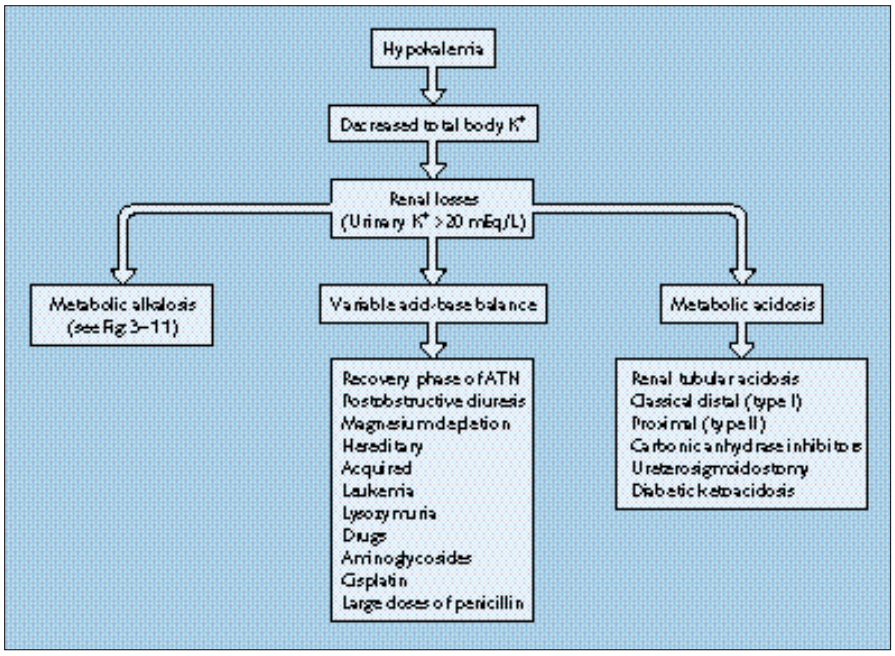

FIGURE 3-9

Diagnostic approach to hypokalemia: hypokalemia due to renal losses with normal acid-base status or metabolic acidosis. Hypokalemia is occasionally observed during the diuretic recovery phase of acute tubular necrosis (ATN) or after relief of acute obstructive uropathy, presumably secondary to increased delivery of sodium and water to the distal nephrons. Patients with acute monocytic and myelomonocytic leukemias occasionally excrete large amounts of lysozyme in their urine. Lysozyme appears to have a direct kaliuretic effect on the kidneys (by an undefined mechanism). Penicillin in large doses acts as a poorly reabsorbable anion, resulting in obligate renal potassium wasting. Mechanisms for renal potassium wasting associated with aminoglycosides and cisplatin are ill-defined. Hypokalemia in type I renal tubular acidosis is due in part to secondary hyperaldosteronism, whereas type II renal tubular acidosis can result in a defect in potassium reabsorption in the proximal nephrons. Carbonic anhydrase inhibitors result in an acquired form of renal tubular acidosis. Ureterosigmoidostomy results in hypokalemia in 10% to 35% of patients, owing to the sigmoid colon's capacity for net potassium secretion. The osmotic diuresis associated with diabetic ketoacidosis results in potassium depletion, although patients may initially present with a normal serum potassium value, owing to altered transcellular potassium distribution.

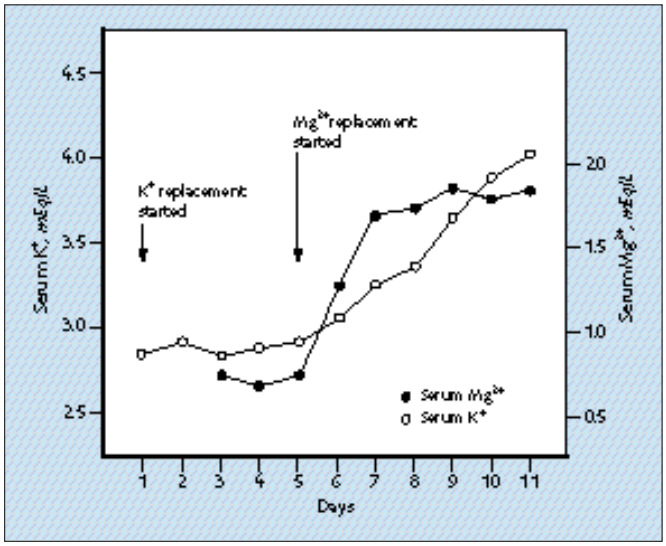

FIGURE 3-10

Hypokalemia and magnesium depletion. Hypokalemia and magnesium depletion can occur concurrently in a variety of clinical settings, including diuretic therapy, ketoacidosis, aminoglycoside therapy, and prolonged osmotic diuresis (as with poorly controlled diabetes mellitus). Hypokalemia is also a common finding in patients with congenital magnesium-losing kidney disease. The patient depicted was treated with cisplatin 2 months before presentation. Attempts at oral and intravenous potassium replacement of up to 80 mEq/day were unsuccessful in correcting the hypokalemia. Once serum magnesium was corrected, however, serum potassium quickly normalized [14].