K^+ rapidly enough in this setting to prevent life-threatening hyperkalemia. This excess K^+ must be rapidly shifted and stored in cells until the kidney has successfully excreted the K^+ load. The major regulators of K^+ shift into cells are insulin and catecholamines.

Insulin excess can lower the serum K^+ level when given exogenously to a diabetic patient or when it occurs as an endogenous secretion in a normal person given a high-glucose load. β-Adrenergic agonists used in the treatment of bronchospasm or in treating premature labor can effect similar K^+ shifts. In the setting of an acute myocardial infarction, hypokalemia may result as a sequela of high circulating epinephrine levels and may predispose patients to arrhythmias. Other clinical disorders resulting in an intracellular sequestration of K^+ are treatment of megaloblastic anemia with vitamin B_{12}, hypothermia, and barium poisoning. Hypokalemic periodic paralysis is inherited in an autosomal dominant pattern and is characterized by episodic hypokalemia resulting in muscle weakness. An acquired form of the disorder is seen in thyrotoxic patients, who are often of Japanese or Mexican descent.

Decreased Total Body Potassium

In the absence of a cellular shift, a low serum K^+ level can result from inadequate dietary intake, extrarenal losses through the gastrointestinal tract or skin, or renal losses. The urinary K^+ concentration is a useful guide for deciding among these possibilities. A urine K^+ concentration of less than 20 mEq/L suggests extrarenal losses, whereas a concentration of more than 20 mEq/L suggests renal K^+ losses. Calculation of the transtubular K^+ gradient has also been used for this purpose.

Inadequate dietary intake is an unusual cause of hypokalemia. Clinical situations associated with extreme K^+-deficient diets include anorexia nervosa, crash diets, alcoholism, and intestinal malabsorption. Increased renal K^+ excretion due to magnesium deficiency (which occurs often in these clinical situations) may contribute to the observed hypokalemia.

Extrarenal Potassium Losses

Sweat has a low K^+ concentration and is an unusual cause of K^+ depletion. However, during physical training, sweat losses can become substantial, and K^+ depletion may result. Gastrointestinal syndromes are the most common clinical sources of extrarenal K^+ losses. Diarrhea leads to fecal K^+ wastage and is associated with a normal anion gap acidosis. Acidosis results in K^+ redistribution out of cells, leading to a degree of hypokalemia that is not as severe as the degree of K^+ depletion.

Renal Potassium Losses

Increased distal delivery of Na^+ and water and increased mineralocorticoid activity can each stimulate renal K^+ secretion. Under normal physiologic conditions, these two determinants are inversely regulated by the EABV (Fig. 27-4). Decreased EABV is associated with increased aldosterone secretion but with lower distal delivery of Na^+ and water due to enhancement of reabsorption in the proximal nephron. Renal K^+ excretion is relatively independent of volume status. It is only under pathophysiologic conditions that distal Na^+ delivery and aldosterone become coupled, and in this setting, renal K^+ wasting occurs. The coupling can result from a primary increase in mineralocorticoid activity or a primary increase in distal Na^+ delivery. The term *primary* means that the changes do not depend on changes in the EABV. The causes of hypokalemia, grouped according to the physiologic determinants of renal K^+ excretion, are given in Figure 27-5.

Primary Increase in Mineralocorticoid Activity

Increases in mineralocorticoid activity can result from primary increases in renin or aldosterone secretion, increases in a nonaldosterone mineralocorticoid, or an increased mineralocorticoid-like effect. In these conditions, ECF volume is expanded, and hypertension typically occurs. The differential diagnosis for the patient with hypertension, hypokalemia, and metabolic alkalosis rests on the measurement of plasma renin activity and plasma aldosterone levels.

Primary Increase in Distal Sodium Delivery

Conditions that give rise to primary increases in distal Na^+ delivery are characterized by normal or low ECF volume. Blood pressure is typically normal.

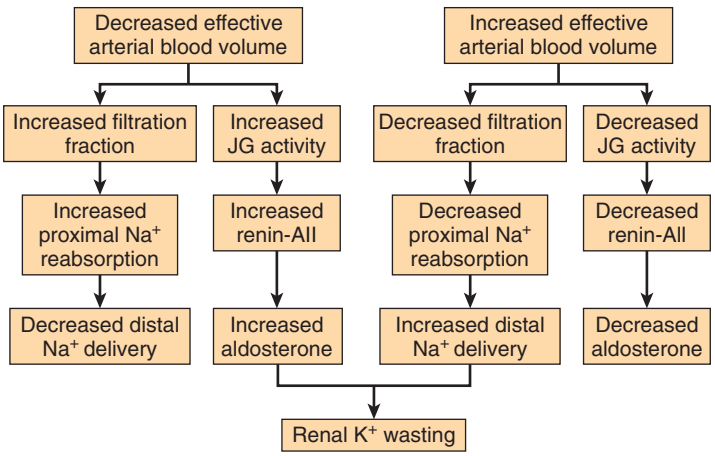

FIGURE 27-4 The relationship between effective arterial volume and distal sodium (Na^+) delivery in determining renal potassium (K^+) excretion. AII, Angiotensin II; JG, Juxtaglomerular.