HYPOKALEMIA AND POTASSIUM DEPLETION

Hypokalemia and potassium deficiency are frequently encountered, and their consequences are sufficiently serious to merit prompt and effective diagnosis and management. Potassium is lost from the gastrointestinal tract as a result of diarrhea, vomiting, and external drainage of various fluids; it is lost from the kidney in many disease entities and by the action of a large number of diuretics. In certain circumstances, hypokalemia appears in the absence of potassium depletion.

When a potassium deficit is suspected, the first step is to determine from the patient's history if there has been a source of potassium loss and to test muscle strength. A history of diarrhea or vomiting, the use of cathartics or diuretics, and the presence of gross muscle weakness, should trigger the possibility of potassium depletion in the physician's mind. The finding of prominent U waves on the electrocardiogram is often another clue. The diagnosis can be tested further by measurement of serum potassium concentration and, when appropriate, urinary potassium excretion.

Estimating the potassium deficit

Unfortunately, no single readily available test exists that can accurately assess body potassium stores. Isotopic measurements of total body potassium and whole body counting methods do measure body potassium accurately, but they are expensive and are used chiefly for research purposes. Instead, the best way of assessing potassium stores clinically is to measure serum potassium concentration because, as a general rule, the reduction in serum potassium roughly parallels the reduction in total body potassium.

Given that the extracellular fluid potassium represents only approximately 2% of total body potassium, it is not surprising that measurements of serum potassium provide only a gross approximation of intracellular stores.

There are several disorders that disturb the relationship between extracellular and intracellular potassium, (see below) but if these disorders are factored out, a rather predictable pattern emerges that makes it possible to estimate a potassium deficit from the serum potassium concentration. As a guideline, a serum potassium concentration of 3.0 mEq/l corresponds to a deficit of approximately 100–200 mEq. For serum potassium concentrations below 3.0 mEq/l, each 1.0 mEq/l reduction in serum concentration represents approximately an additional 200–400 mEq deficit for an adult of average size (1). Serum potassium concentrations between 1.5 and 2.0 mEq/l are often associated with potassium deficits as large as 800–1200 mEq.

There are many exceptions to the rule that serum potassium and intracellular potassium change in parallel, and because of these exceptions physicians often are bewildered at how to interpret serum potassium concentrations. Recognizing these exceptions is not, however, difficult. In certain circumstances, serum potassium concentration may be remarkably low in the face of normal intracellular potassium stores, or normal in the face of remarkably depleted stores. Marked reductions in serum potassium concentration may occur when total body potassium stores are normal if there has been a substantial shift of potassium from extracellular to intracellular compartments. Such internal shifts of potassium are encountered in hypokalemic periodic paralysis. Because of the disproportionately small quantity of potassium in the extracellular fluid, small internal shifts of potassium across cell membranes in this rare disorder can produce dramatic changes in serum potassium concentration that do not reflect the true state of intracellular potassium stores.

Many acid-base disorders have profound effects on serum potassium concentration and on intracellular potassium stores. Acidemia promotes the shift of potassium from the intracellular to the extracellular compartment and acute alkalemia acts in the opposite fashion. Early studies suggested that serum potassium concentration was altered approximately 0.6 mEq/l for each 0.1 unit change in pH in the opposite direction (2), but we now know this estimate to be an oversimplification. Indeed, many exceptions occur (3). In acute respiratory acidosis and alkalosis, for example, serum potassium concentration changes only approximately 0.1 mEq/l for every change in blood pH of 0.1 unit and in both chronic respiratory acidosis and chronic respiratory alkalosis, little or no change in serum potassium concentration can be identified. Among the metabolic acid-base disturbances, acute lactic acidosis following seizures is another notable exception. In this disorder, abrupt reductions in plasma bicarbonate concentration and blood pH are typically associated with little or no alteration in serum potassium concentration (4). Moreover, although metabolic acidosis may transiently increase serum potassium concentration, persistent acidosis tends to increase renal potassium excretion and deplete body potassium stores (5). The net effect of this alteration is to lower serum potassium concentration.
over time from its initial high value. Finally, disturbances of potassium metabolism often accompany complex metabolic events: in diabetic ketoacidosis, for example, total body potassium is markedly reduced due to profound urinary potassium losses that result from osmotic diuresis, renal excretion of keto-anions, and chronic acidosis (6). Yet, serum potassium concentration may be normal or even elevated as the result of renal insufficiency and the acidemia-induced movement of potassium from the intracellular to the extracellular compartment.

Measurement of urinary potassium excretion is a valuable method to assess not only the extent of the potassium deficit but also the route of potassium loss from the body. When urinary potassium excretion is less than 10–20 mEq/day, the inference can be drawn that depletion is severe, that it is probably long-standing, and that the kidneys are probably not the route of potassium loss. On rare occasions, urinary potassium concentration may be lower than that of the plasma when potassium depletion is extreme. A high urinary potassium excretion in a potassium deficient patient (i.e., 40–80 mEq/day) indicates that the patient has failed to conserve potassium appropriately, as the result of renal tubular disease or hormonal, pharmacologic, or osmotic influences.

Consequences of potassium depletion (Table 1)

Cardiovascular
The most common and potentially serious cardiovascular manifestations of potassium depletion are disturbances of cardiac conduction. Although best described in patients also receiving digitalis or in those with underlying heart disease, conduction abnormalities may occur in patients with normal hearts. Hypokalemia produces typical electrocardiographic alterations, including depression of the S-T segments, flattening of the T waves, and the appearance of prominent U waves. The flattened T waves and increased U wave voltage may give the impression of a prolonged QT interval. Prolongation of the PR interval may also occur in potassium depletion. The electrocardiographic abnormalities in hypokalemia are not pathognomonic, however, and sometimes are absent in patients with well documented hypokalemia. Furthermore, the changes in patients with hypokalemia are not directly proportional to the degree of potassium depletion (7).

A variety of cardiac arrhythmias are associated with severe potassium depletion, particularly a predisposition to atrial and ventricular ectopic beats (8). Hypokalemia per se has not been shown to cause fatal ventricular arrhythmias (9). However, serious supraventricular and ventricular arrhythmias are seen in patients with potassium depletion who are also receiving digitalis glycosides. Indeed, the incidence of all digitalis-induced arrhythmias is increased by concomitant hypokalemia. Because patients receiving digitalis are commonly receiving diuretics and are usually ingesting little salt, they are likely to develop both metabolic alkalosis and potassium deficiency. For this reason, potassium balance must be monitored carefully and controlled meticulously in salt-restricted patients receiving digitalis and diuretics.

Neuromuscular
Hypokalemia exerts its pathophysiological effects by reducing the extracellular to intracellular potassium ratio, thereby hyperpolarizing the membrane of nerves and muscles and impeding nerve conduction and muscle contraction. Distal muscles are affected more than proximal muscles, and in extreme cases respiratory muscle paralysis may produce hypoxia, hypercapnia and death. In advanced cases, deep tendon reflexes may diminish or disappear and the patient may become quadriplegic. Cross striations of skeletal muscle may be lost in moderately severe potassium depletion, and permanent loss of muscle mass may occur in severe cases (10). The rhabdomyolysis occasionally seen in extreme potassium depletion is probably due to a combination of muscle ischemia associated with increased vascular tone and a direct toxic effect on the cellular membranes by hypokalemia itself (11). The severe muscle weakness in the potassium deficient patient can be confused with that seen in primary neuromuscular disease, and therefore measurements of serum potassium concentration always should be obtained in any patient who presents with rapid onset of paresis or paralysis.

Confusional states and affective disorders have also been attributed to severe potassium depletion (12). Symptoms most commonly mentioned include memory impairment, disorientation, and confusion. The extent to which these symptoms are the result of hypokalemia per se rather than to associated disorders such as hypoxemia and metabolic alkalosis (or unrelated conditions) is uncertain.

Renal
Impairment in the capacity to concentrate the urine appears when the total body potassium deficit exceeds

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Table 1. Important consequences of potassium deficiency.

| I. Cardiovascular | a) Cardiac arrhythmias  
b) Enhanced digitalis toxicity |
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| II. Neuromuscular | a) Skeletal muscle weakness  
b) Rhabdomyolysis  
c) Mental confusion (?) |
| III. Renal | a) Impaired concentrating ability  
b) Decline in GFR |
| IV. Acid-Base | a) Mild defect in renal acid excretion  
b) Metabolic alkalosis (rarely) |
| V. Metabolic | |
| VI. Smooth muscle | a) Adynamic ileus (?)  
b) Gastric dilation (?) |