# Potassium Disorders: Hypokalemia and Hyperkalemia

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**Hypokalemia and hyperkalemia are common electrolyte disorders caused by changes in potassium intake, altered excretion, or transcellular shifts. Diuretic use and gastrointestinal losses are common causes of hypokalemia, whereas kidney disease, hyperglycemia, and medication use are common causes of hyperkalemia. When severe, potassium disorders can lead to life-threatening cardiac conduction disturbances and neuromuscular dysfunction. Therefore, a first priority is determining the need for urgent treatment through a combination of history, physical examination, laboratory, and electrocardiography findings. Indications for urgent treatment include severe or symptomatic hypokalemia or hyperkalemia; abrupt changes in potassium levels; electrocardiography changes; or the presence of certain comorbid conditions. Hypokalemia is treated with oral or intravenous potassium. To prevent cardiac conduction disturbances, intravenous calcium is administered to patients with hyperkalemic electrocardiography changes. Insulin, usually with concomitant glucose, and albuterol are preferred to lower serum potassium levels in the acute setting; sodium polystyrene sulfonate is reserved for subacute treatment. For both disorders, it is important to consider potential causes of transcellular shifts because patients are at increased risk of rebound potassium disturbances. (*Am Fam Physician*. 2015;92(6):487-495. Copyright © 2015 American Academy of Family Physicians.)**

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**Patient information:** A handout on this topic, written by the authors of this article, is available at http://www.aafp.org/afp/2015/0915/p487-s1.html.

Potassium disorders are common. Hypokalemia (serum potassium level less than 3.6 mEq per L [3.6 mmol per L]) occurs in up to 21% of hospitalized patients and 2% to 3% of outpatients.[1-3] Hyperkalemia (serum potassium level more than 5 mEq per L [5 mmol per L] in adults, more than 5.5 mEq per L [5.5 mmol per L] in children, and more than 6 mEq per L [6 mmol per L] in neonates) occurs in up to 10% of hospitalized patients and approximately 1% of outpatients.[4,5] The body's plasma potassium concentration is closely regulated by a variety of mechanisms.

## Causes of Hypokalemia

Hypokalemia results from abnormal losses, transcellular shifts, or insufficient intake *(Table 1)*.[6-8] Abnormal losses are most common.[9] Because the kidney can significantly lower potassium excretion in response to decreased intake, insufficient intake is rarely the sole cause of hypokalemia, but it often contributes to hypokalemia in hospitalized patients.[9]

### RENAL LOSSES

Diuretic use is a common cause of renally mediated hypokalemia.[10] When given in the same dosage, chlorthalidone is more likely to induce hypokalemia than hydrochlorothiazide, which is more often implicated because of its widespread use.[11,12] Diuretic-induced hypokalemia is dose-dependent and tends to be mild (3 to 3.5 mEq per L [3 to 3.5 mmol per L]), although it can be more severe when accompanied by other causes (e.g., gastrointestinal [GI] losses).[13]

### GI LOSSES

GI losses are another common cause of hypokalemia, particularly among hospitalized patients.[9] The mechanism by which upper GI losses induce hypokalemia is indirect and stems from the kidney's response to the associated alkalosis. As a portion of daily potassium is excreted in the colon, lower GI losses in the form of persistent diarrhea can also result in hypokalemia and may be accompanied by hyperchloremic acidosis.[6]

## Evaluation and Management of Hypokalemia

### GENERAL PRINCIPLES

Hypokalemia is often asymptomatic. Evaluation begins with a search for warning signs or symptoms warranting urgent treatment

*(Figure 1)*.[7,14] These include weakness or palpitations, changes on electrocardiography (ECG), severe hypokalemia (less than 2.5 mEq per L [2.5 mmol per L]), rapid-onset hypokalemia, or underlying heart disease or cirrhosis.[7,15] Most cases of hypokalemia-induced rhythm disturbances occur in individuals with underlying heart disease.[10] Early identification of transcellular shifts is important because management may differ. Identification and treatment of concurrent hypomagnesemia are also important because magnesium depletion impedes potassium repletion and can exacerbate hypokalemia-induced rhythm disturbances.[16,17]

**Table 1. Causes of Hypokalemia**

| |
|---|
| **Abnormal losses** |
| Medications |
| Diuretics |
| Laxatives and enemas |
| Corticosteroids |
| Gastrointestinal losses |
| Renal losses |
| Osmotic diuresis |
| Mineralocorticoid excess |
| Types I and II renal tubular acidosis |
| Polydipsia |
| Intrinsic renal transport defects |
| Hypomagnesemia |
| Dialysis/plasmapheresis |
| **Transcellular shifts** |
| Medications |
| Insulin overdose |
| Beta$_2$ sympathomimetics |
| Decongestants |
| Xanthines |
| Amphotericin B |
| Verapamil intoxication |
| Chloroquine (Aralen) intoxication |
| Barium intoxication |
| Cesium intoxication |
| **Transcellular shifts** *(continued)* |
| Alkalosis |
| Refeeding syndrome |
| Increased beta$_2$ adrenergic stimulation |
| Delirium tremens |
| Head injury |
| Myocardial ischemia |
| Thyrotoxicosis |
| Familial hypokalemic periodic paralysis |
| Hypothermia |
| **Inadequate intake** |
| Anorexia |
| Dementia |
| Starvation |
| Total parenteral nutrition |
| **Pseudohypokalemia** |
| Delayed sample analysis |
| Significant leukocytosis (> 75,000 cells per mm$^3$ [75.0 × 10$^9$ per L]) |

NOTE: *Listed in approximate order of frequency.*

*Information from references 6 through 8.*

### HISTORY AND PHYSICAL EXAMINATION

A focused history includes evaluation for possible GI losses, review of medications, and assessment for underlying cardiac comorbidities. A history of paralysis, hyperthyroidism, or use of insulin or beta agonists suggests possible transcellular shifts leading to redistributive hypokalemia. The physical examination should focus on identifying cardiac arrhythmias and neurologic manifestations, which range from generalized weakness to ascending paralysis.

### LABORATORY ANALYSIS AND ECG

The diagnosis should be confirmed with a repeat serum potassium measurement. Other laboratory tests include serum glucose and magnesium levels, urine electrolyte and creatinine levels, and acid-base balance. The most accurate method for evaluating urinary potassium excretion is a 24-hour timed urine potassium collection; normal kidneys excrete no more than 15 to 30 mEq per L (15 to 30 mmol per L) of potassium per day in response to hypokalemia. A more practical approach is calculation of the urine potassium-to-creatinine ratio from a spot urine specimen; a ratio greater than 1.5 mEq per mmol (13 mEq per g) is indicative of renal potassium wasting.[18] If no cause is identified with the initial workup, assessment of thyroid and adrenal function should be considered.

Typically, the first ECG manifestation of hypokalemia is decreased T-wave amplitude. Further progression can lead to ST-interval depression, T-wave inversions, PR-interval prolongation, and U waves. Arrhythmias associated with hypokalemia include sinus bradycardia, ventricular tachycardia or fibrillation, and torsade de pointes.[19] Although the risk of ECG changes and arrhythmias increases as serum potassium concentration decreases, these findings are not reliable because some patients with severe hypokalemia do not have ECG changes.[20]

## Treatment of Hypokalemia

The immediate goal of treatment is the prevention of potentially life-threatening cardiac conduction disturbances and neuromuscular dysfunction by raising serum potassium to a safe level. Further replenishment can proceed more slowly, and attention can turn to the diagnosis and management of the underlying disorder.[15] Patients with a history of congestive heart failure or myocardial infarction should maintain a serum potassium concentration of at least 4 mEq per L (4 mmol per L), based on expert opinion.[15]

Careful monitoring during treatment is essential because supplemental potassium is a common cause of hyperkalemia in hospitalized patients.[21] The risk of rebound hyperkalemia is higher when treating redistributive hypokalemia. Because serum potassium concentration drops approximately 0.3 mEq per L (0.3 mmol per L) for every 100-mEq (100-mmol) reduction in total body potassium, the approximate potassium

deficit can be estimated in patients with abnormal losses and decreased intake. For example, a decline in serum potassium from 3.8 to 2.9 mEq per L (3.8 to 2.9 mmol per L) roughly corresponds to a 300-mEq (300-mmol) reduction in total body potassium. Additional potassium will be required if losses are ongoing. Concomitant hypomagnesemia should be treated concurrently.

For hypokalemia associated with diuretic use, stopping the diuretic or reducing its dosage may be effective.[15] Another strategy, if otherwise indicated to treat a comorbid condition, is use of an angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), beta blocker, or potassium-sparing diuretic because each of these drugs is associated with an elevation in serum potassium.

It is appropriate to increase dietary potassium in patients with low-normal and mild hypokalemia, particularly in those with a history of hypertension or heart disease.[15] The effectiveness of increased dietary potassium is limited, however, because most of the potassium contained in foods is coupled with phosphate, whereas most cases of hypokalemia involve chloride depletion and respond best to supplemental potassium chloride.[6,15]

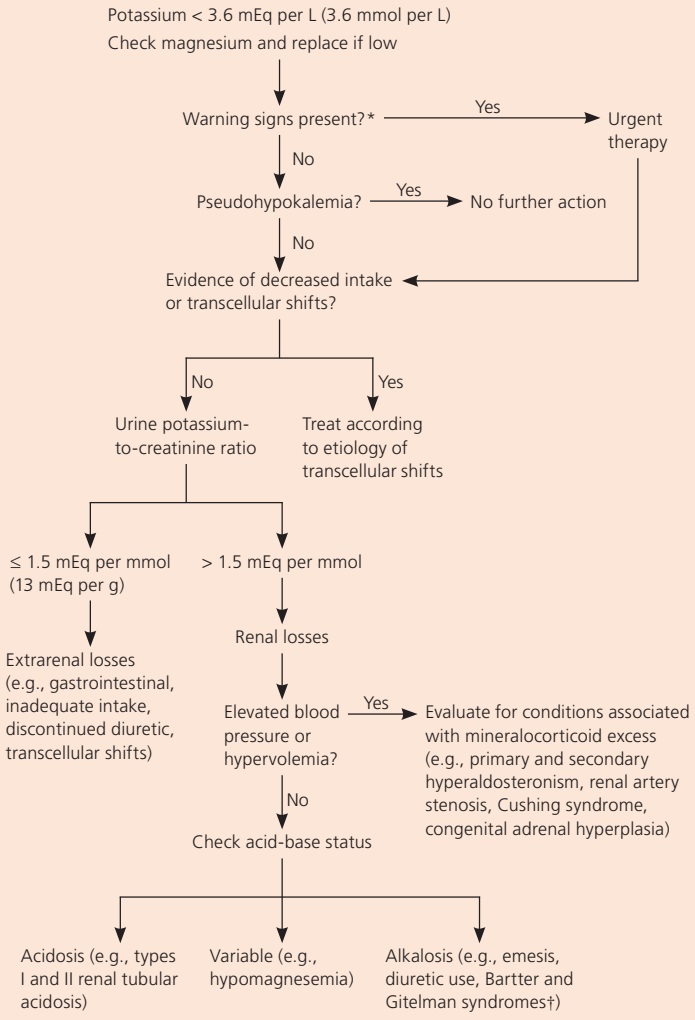
Because use of intravenous potassium increases the risk of hyperkalemia and can cause pain and phlebitis, intravenous potassium should be reserved for patients with severe hypokalemia, hypokalemic ECG changes, or physical signs or symptoms of hypokalemia, or for those unable to tolerate the oral form. Rapid correction is possible with oral potassium; the fastest results are likely best achieved by combining oral (e.g., 20 to 40 mmol) and intravenous administration.[22]

When intravenous potassium is used, standard administration is 20 to 40 mmol of potassium in 1 L of normal saline. Correction typically should not exceed 20 mmol per hour, although higher rates using central venous catheters have been successful in emergency situations.[22] Continuous cardiac monitoring is indicated if the rate exceeds 10 mmol per hour. In children, dosing is 0.5 to 1.0 mmol per L per kg over one hour (maximum of 40 mmol).[23]

Potassium should not be given in dextrose-containing solutions because dextrose-stimulated insulin secretion can exacerbate hypokalemia.

Nonurgent hypokalemia is treated with 40 to 100 mmol of oral potassium per day over days to weeks. For the prevention of hypokalemia in patients with persistent losses,

## Evaluation of Hypokalemia




*—Symptoms of hypokalemia, changes on electrocardiography, severe hypokalemia (less than 2.5 mEq per L [2.5 mmol per L]), rapid-onset hypokalemia, or underlying heart disease or cirrhosis.*

†—*Autosomal recessive disorders of renal tubular transport.*

**Figure 1.** Suggested algorithm for the evaluation of hypokalemia.

*Information from references 7 and 14.*

as with ongoing diuretic therapy or hyperaldosteronism, 20 mmol per day is usually sufficient.[15]

## Causes of Hyperkalemia

Hyperkalemia is caused by excess potassium intake, impaired potassium excretion, or transcellular shifts *(Table 2)*.[8,24] The etiology of hyperkalemia is often multifactorial, with impaired renal function, medication use, and hyperglycemia as the most common contributors.[25] Because healthy individuals can adapt to excess potassium consumption by increasing excretion, increased potassium intake is rarely the sole cause of hyperkalemia, and underlying renal dysfunction is common.[24]

### IMPAIRED POTASSIUM EXCRETION

Renally mediated hyperkalemia results from derangement of one or more of the following processes: rate of flow in the distal nephron, aldosterone secretion and its effects, and functioning potassium secretory pathways. Hyperkalemia secondary to decreased distal delivery of sodium and water occurs with congestive heart failure, cirrhosis, acute kidney injury, and advanced chronic kidney disease. Conditions that cause hypoaldosteronism, such as adrenal insufficiency and hyporeninemic hypoaldosteronism (a common complication of diabetic nephropathy and tubulointerstitial diseases), can lead to hyperkalemia.

**Table 2. Causes of Hyperkalemia**

| | |
|---|---|
| **Impaired excretion** | **Transcellular shifts** |
| Acute kidney injury/chronic kidney disease | Insulin deficiency/resistance |
| Medications | Acidosis |
| Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers | Hypertonicity |
| Nonsteroidal anti-inflammatory drugs | Hyperglycemia |
| Potassium-sparing diuretics | Mannitol |
| Trimethoprim | Medications |
| Heparin | Beta blockers |
| Lithium | Digoxin toxicity |
| Calcineurin inhibitors | Somatostatin |
| Decreased distal renal flow | Succinylcholine (Anectine) |
| Acute kidney injury/chronic kidney disease | Cell breakdown/leakage |
| Congestive heart failure | Hyperkalemic periodic paralysis |
| Cirrhosis | **Increased intake** |
| Hypoaldosteronism | Potassium supplementation |
| Hyporeninemic hypoaldosteronism | Red blood cell transfusion |
| Adrenal insufficiency | Foods high in potassium* |
| Adrenocorticotropic hormone deficiency | Potassium-containing salt substitutes |
| Primary hyporeninemia | Protein calorie supplements |
| Primary renal tubular defects | Penicillin G potassium |
| Sickle cell disease | Certain forms of pica |
| Systemic lupus erythematosus | **Pseudohyperkalemia** |
| Obstructive uropathy | Hemolysis |
| Hereditary tubular defects | Tourniquet use |
| Amyloidosis | Fist clenching |
| | Blood sample cooling |
| | Intravenous fluids with potassium |
| | Cell hyperplasia |
| | Significant leukocytosis (> 75,000 cells per $mm^3$ [75.0 × $10^9$ per L]) |
| | Erythrocytosis |
| | Thrombocytosis |
| | Familial pseudohyperkalemia |

NOTE: *Listed in approximate order of frequency.*

**—Dietary-induced hyperkalemia usually involves concurrent renal insufficiency.*

*Information from references 8 and 24.*

### TRANSCELLULAR SHIFTS

Various mechanisms promote the exit of potassium from cells or impede its entrance, thereby raising the plasma potassium concentration (redistributive hyperkalemia). Increased plasma osmolality, such as with uncontrolled diabetes mellitus, establishes a concentration gradient wherein potassium follows water out of cells. Relative insulin deficiency or insulin resistance, which also occurs in persons with diabetes, prevents potassium from entering cells. In response to acidosis, extracellular hydrogen is exchanged for intracellular potassium, although the net result is highly variable and depends in part on the type of acidosis; metabolic acidosis produces the greatest effect.[26] Because 98% of total body potassium is intracellular, any process that increases cell turnover, such as rhabdomyolysis, tumor lysis syndrome, or red blood cell transfusions, can result in hyperkalemia.

### MEDICATION-INDUCED HYPERKALEMIA

Medication use is a common cause of hyperkalemia, particularly in patients with baseline renal dysfunction or hypoaldosteronism.[27] Medication-induced hyperkalemia is most often a result of the medication interfering with potassium excretion. Also, the administration of potassium to treat or prevent hypokalemia can inadvertently cause hyperkalemia.[19]

ACE inhibitors contributed to one-half of all cases of drug-induced hyperkalemia in one sample, and approximately 10% of outpatients who start an ACE inhibitor or an ARB will develop hyperkalemia within one year.[23,28]

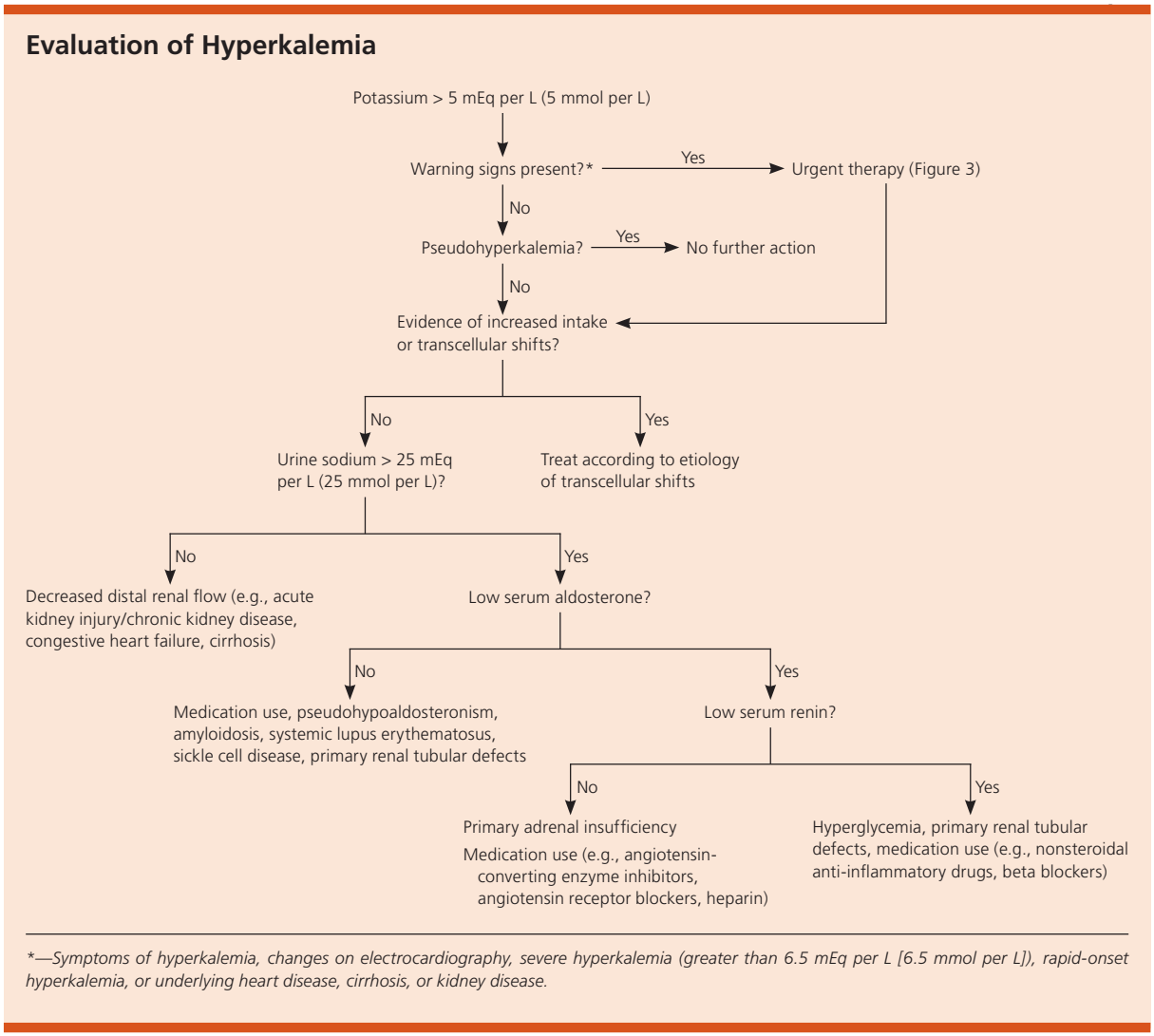



**Figure 2.** Suggested algorithm for the evaluation of hyperkalemia.

*Information from references 14 and 30.*

The incidence of hyperkalemia associated with use of potassium-sparing diuretics has risen since adding spironolactone to standard therapy was shown to reduce morbidity and mortality in patients with congestive heart failure.[29] Dual treatment with an ACE inhibitor and an ARB increases the risk of harmful adverse effects, including hyperkalemia, and should be avoided.[11] Other commonly used medications known to cause hyperkalemia include trimethoprim, heparin, beta blockers, digoxin, and nonsteroidal anti-inflammatory drugs.[3]

## Evaluation and Management of Hyperkalemia

### GENERAL PRINCIPLES

As with hypokalemia, the immediate danger of hyperkalemia is its effect on cardiac conduction and muscle strength, and initial efforts should focus on determining the need for urgent intervention *(Figure 2)*.[14,30] The absence of symptoms does not exclude severe hyperkalemia, because hyperkalemia is often asymptomatic. Because of their increased risk of developing hyperkalemia, patients with underlying renal dysfunction merit special attention.[22]

### HISTORY AND PHYSICAL EXAMINATION

Severe hyperkalemia (more than 6.5 mEq per L [6.5 mmol per L]) can cause muscle weakness, ascending paralysis, heart palpitations, and paresthesias. Chronic kidney disease, diabetes, heart failure, and liver disease all increase the risk of hyperkalemia. Clinicians should review patients' medications to identify those known to cause hyperkalemia, and ask patients about the use of salt substitutes that contain potassium. The physical examination should include assessment of blood pressure and intravascular volume status to identify potential causes

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