accounts for as much as 80% of clinically significant cases seen in the ED. Hypokalemia is defined as a serum potassium level lower than 3.5 mEq/L. It is further classified as mild (3 to 3.5 mEq/L), moderate (2.5 to 2.9 mEq/L), and severe (<2.5 mEq/L).

Hyperkalemia, a disorder that affects patients with underlying renal insufficiency almost exclusively, is defined as a potassium level higher than 5.0 mEq/L. Hyperkalemia is further classified as mild (5 to 6 mEq/L), moderate (6.1 to 7 mEq/L), and severe (>7 mEq/L).

Both disorders can result in cardiac dysfunction, arrhythmia, and death.

**PATHOPHYSIOLOGY**

Total body potassium (K⁺) is approximately 50 mEq/kg, or 3500 to 4000 mEq, in a normal-sized adult. For conversion purposes, 1 mEq of potassium is equivalent to 39.09 mg. Potassium is the major intracellular cation, and more than 98% of total body potassium is stored in the intracellular space. Intracellular fluid concentrations of potassium range from 150 to 160 mEq/L, with the highest amounts sequestered either in muscle (75%) or in bones and cartilage (8% to 10%).

Extracellular potassium makes up less than 2% of total body stores, only two thirds of which is measurable in serum sampling. The normal range of plasma concentrations reported by most laboratory testing is 3.5 to 5 mEq/L; this small fraction is not reflective of total body potassium. Strict regulation of the ratio of intracellular to extracellular potassium (150 to 4 mEq/L) maintains a critical voltage gradient across cell membranes and plays a crucial role in establishing membrane potentials in cardiac and neuromuscular cells. The Na⁺,K⁺-ATPase transmembrane pump continuously maintains this gradient by actively transporting potassium into and sodium (Na⁺) out of cells (Fig. 165.1). Large changes in the intracellular potassium concentration have little effect on the ratio of intracellular to extracellular potassium. Conversely, even small changes in the extracellular concentration significantly affect this ratio, the transmembrane potential gradient, and the function of cardiac and neuromuscular tissue.

All potassium disorders result from one of three disturbances: impaired potassium intake, impaired distribution of potassium between the intracellular and extracellular spaces, and impaired renal excretion of potassium (Fig. 165.2).
Mild Hypokalemia (3 to 3.5 mEq/L)

Patients without significant comorbid conditions tolerate mild hypokalemia very well. Muscular symptoms are generally absent, although occasionally patients experience mild cramping or early muscle fatigue. Hypokalemia may affect smooth muscle function in the gastrointestinal tract with resultant constipation or abdominal cramping, or both. Cardiac and neurologic symptoms are absent.

Moderate Hypokalemia (2.5 to 2.9 mEq/L)

Muscular symptoms become more pronounced as the degree of hypokalemia worsens; the weakness is generalized, but proximal and lower extremity muscle groups are typically affected to a greater degree. Cardiac manifestations may include palpitations, non–life-threatening dysrhythmias (premature atrial contractions, premature ventricular contractions), and atrial fibrillation. Electrocardiographic (ECG) changes occur but do not correlate with the degree of hypokalemia (Box 165.2; Fig. 165.3).

Hypokalemia may precipitate or worsen encephalopathy in patients with severe liver disease. Potassium depletion increases renal production of ammonia, which readily crosses the blood-brain barrier in the setting of alkalosis. Hypokalemia also inhibits the release of insulin and may cause hyperglycemia in patients with preexisting glucose intolerance or non–insulin-dependent diabetes mellitus. The renal complications of moderate hypokalemia reflect vasopressin resistance to the tubular reabsorption of water; symptoms include nocturia, polydipsia, and polyuria.

Severe Hypokalemia (<2.5 mEq/L)

Alcoholics have the greatest risk for severe hypokalemia. Musculoskeletal symptoms include pronounced fasciculations, tetany, and rhabdomyolysis. Myolysis may cause a transient release of intracellular potassium that can mask the inciting hypokalemic state. In rare cases, life-threatening ascending paralysis and loss of deep tendon reflexes can result in quadriplegia.

Cardiac manifestations of severe hypokalemia worsen the previously mentioned ECG abnormalities. Of great
neuromuscular findings. ECG abnormalities may not be present even with severe hyperkalemia; ventricular fibrillation may be the first cardiac manifestation.

**Mild Hyperkalemia (5 to 6 mEq/L)**

Mild hyperkalemia is generally asymptomatic. Patients with underlying cardiac disease occasionally report palpitations or other well-tolerated disturbances in rhythm.

**Moderate Hyperkalemia (6.1 to 7 mEq/L)**

Patients with moderate hyperkalemia may exhibit ECG abnormalities, including peaked T waves and prolongation of the PR interval and QRS complex (Figs. 165.4 to 165.7; Box 165.3).

Neuromuscular symptoms similar to those seen with hypokalemia can occur. Muscle cramps and weakness are the most commonly reported complaints.
Severe Hyperkalemia (>7 mEq/L)
Progressively worsening hyperkalemia can result in significant conduction abnormalities, heart block, potentially life-threatening arrhythmias, and asystole. Symptoms such as palpitations, syncope, chest pain, and dyspnea (from left-sided heart failure) may be present. Ascending paralysis and tetany may result.

**DIAGNOSTIC TESTING**

**HYPOKALEMIA**
Historical elements that may mandate measurement of serum potassium include potential causes of inadequate intake (malnutrition, alcoholism) and excessive wasting (diarrhea, vomiting, polyuria). Long-standing use of diuretics, β2-agonists, or laxatives should also prompt potassium screening.

In the ED, evaluation should focus on identification of hypokalemia by laboratory testing, classification of disease severity, correlation with findings on physical examination,

**BOX 165.3 Electrocardiographic Manifestations of Hyperkalemia**

<table>
<thead>
<tr>
<th>Mild Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peaked T waves</td>
</tr>
<tr>
<td>Shortened QT interval (early repolarization)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged PR interval</td>
</tr>
<tr>
<td>Diminished P-wave amplitude</td>
</tr>
<tr>
<td>Widened QRS</td>
</tr>
<tr>
<td>Bundle branch blocks</td>
</tr>
<tr>
<td>Second- and third-degree heart block</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of P wave</td>
</tr>
<tr>
<td>Atrioventricular nodal block</td>
</tr>
<tr>
<td>Widened QRS</td>
</tr>
<tr>
<td>Sine wave</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
</tr>
<tr>
<td>Asystole</td>
</tr>
</tbody>
</table>


**Fig. 165.4 Electrocardiographic findings in hyperkalemia.**

**Fig. 165.5 Baseline electrocardiogram in a patient 1 month before emergency department evaluation (K+ = 4.3 mmol/L).**
and correction or stabilization of potentially life-threatening conditions.

If hypokalemia is identified, screening for hypomagnesemia and hypophosphatemia is necessary; these coexistent entities are difficult to distinguish from hypokalemia by physical examination alone. Urine pH higher than 6 suggests type I renal tubular acidosis; urine electrolytes and venous blood gas analysis should be obtained to search for a corresponding normal–anion gap metabolic acidosis.

If the patient is taking digoxin, a serum digoxin level is indicated; hypokalemia potentiates digitalis toxicity and increases the likelihood of cardiac dysrhythmias. Additional laboratory testing and imaging can be performed later in the inpatient or outpatient setting.

**HYPERKALEMIA**

Patients with hyperkalemia be asymptomatic or have life-threatening cardiovascular disturbances. Historical features that should raise suspicion for hyperkalemia include known acute or chronic renal insufficiency, potassium supplementation, and ECG changes following an incomplete hemodialysis session. End-stage renal dialysis patients who have missed a scheduled dialysis session should be placed on a cardiac monitor and immediately be screened for ECG abnormalities and electrolyte disturbances.

The first sign of hyperkalemia may be abnormal ECG findings on arrival at the ED. If hyperkalemia is suspected in an asymptomatic renal patient with abnormal ECG findings, a complete serum chemistry panel should be obtained, as well
as a whole blood potassium level measured by venous blood gas analysis. Arterial or venous blood gas sampling is generally the most efficient method of obtaining an accurate measurement of the potassium concentration. Additional laboratory tests useful in the ED evaluation of hyperkalemia include serum calcium, creatinine, digoxin, and blood pH. Other testing can be deferred to the inpatient setting.

TREATMENT (Table 165.1)

<table>
<thead>
<tr>
<th>FORMULATION</th>
<th>DOSAGE REGIMEN</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral KCl</td>
<td>20-80 mEq/day divided 2-3 times per day</td>
<td>Non-urgent correction and/or maintenance therapy with diuretic use</td>
</tr>
<tr>
<td>Oral KCl liquid (recheck serum K+ in 24-72 hr)</td>
<td>40-60 mEq per dose</td>
<td>Rapid elevation in patients requiring urgent, but not emergency correction</td>
</tr>
<tr>
<td>Intravenous KCl</td>
<td>10-20 mEq/hr (recheck serum K+ after giving 60 mEq)</td>
<td>For patients with severe symptoms or inability to tolerate oral therapy</td>
</tr>
</tbody>
</table>


**HYPOKALEMIA**

**Patients with Cardiovascular Disease**

Optimal goals for serum potassium repletion are predicated on the underlying pathology. Patients with a history of congestive heart failure, coronary artery disease, or dysrhythmias and hypertensive patients being treated with diuretic medications should have a serum potassium level of at least 4 mEq/L. These patients require oral supplementation for even mild, asymptomatic hypokalemia with potassium chloride tablets (20 to 40 mEq daily).³ If the patient is taking a potassium-sparing diuretic, the dose should be decreased.

**Asymptomatic Mild Hypokalemia**

Healthy patients with asymptomatic, mild hypokalemia (3 to 3.5 mEq/L) do not require pharmacologic potassium supplementation. Treatment should be focused on minimizing further potassium loss and increasing oral intake. Patients should be encouraged to eat a diet rich in potassium (Box 165.4). Potassium-wasting diuretics should be decreased or eliminated, as blood pressure allows. Use of substances that contain glycyrrhizic acid (e.g., licorice, chewing tobacco, laxatives) should be avoided.²,⁶

**Symptomatic Mild and Moderate Hypokalemia**

Potassium supplementation is required for patients with symptomatic mild or moderate (<3 mEq/L) hypokalemia. Potassium supplements are available in several forms: potassium chloride, potassium phosphate, potassium citrate, potassium acetate, potassium gluconate, and potassium bicarbonate. Potassium chloride is the preferred formulation for most ED cases of hypokalemia. Potassium phosphate may be beneficial in certain cases of diabetic ketoacidosis.⁶ Oral potassium supplements are available as tablets, powder, or elixir.

Dosing ranges from 20 to 80 mEq/day; doses greater than 40 mEq should be divided and given either two or three times per day. Oral therapy should be monitored daily because serum potassium levels will rise within 48 to 72 hours.⁶ Healthy patients who require daily oral supplementation can be discharged from the ED safely if repeated serum potassium measurements can be monitored by the primary care physician for 1 to 2 days. Patients who are elderly, have significant comorbid conditions, or have poor access to follow-up should be admitted to the hospital for a 24-hour observation period. Magnesium deficiency should be suspected in patients who fail to respond to oral potassium therapy within 96 hours. Magnesium promotes activity of the Na⁺,K⁺-ATPase pump, which will replenish intracellular fluid concentrations in the first days of potassium supplementation.⁶

**Severe Hypokalemia**

Intravenous (IV) potassium replacement is indicated for patients with severe hypokalemia (<2.5 mEq/L) or moderate hypokalemia accompanied by cardiac arrhythmias, familial periodic paralysis, or severe myopathy.⁷ Replacement consists of 100 mEq of potassium chloride in 1 L of normal saline (or 5% dextrose in water [D₅W]) infused...
Calcium Supplementation
Calcium chloride may cause significant skin necrosis if extravasated. Calcium should not be administered with solutions that contain sodium bicarbonate because calcium carbonate (CaCO₃) will precipitate. Intravenous calcium boluses should be avoided in hyperkalemic patients with suspected digoxin toxicity because of the risk for cardiac tetany or fatal arrhythmia. Slow calcium infusions (over a 30-minute period) require close monitoring of these patients.

### Table 165.2 Treatment of Hyperkalemia

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOSAGE REGIMEN</th>
<th>ONSET</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac Stabilization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium chloride</td>
<td>1 ampule (10 mL) over 2-5 min</td>
<td>1-3 min</td>
<td>30-40 min</td>
</tr>
<tr>
<td>Calcium gluconate</td>
<td>10 mL of a 10% solution</td>
<td>1-3 min</td>
<td>20-60 min</td>
</tr>
<tr>
<td><strong>Transcellular Shift</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>10 units IV with 50 mL of 50% dextrose (one ampule of D₅₀W) or 10 units in 500 mL D₅₀W over a 1-hr infusion</td>
<td>10-20 min</td>
<td>2-4 hr</td>
</tr>
<tr>
<td>Albuterol nebulized over 20-60 min</td>
<td>10-20 mg in 4 mL NS</td>
<td>20-30 min</td>
<td>2-4 hr</td>
</tr>
<tr>
<td><strong>Elimination</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kayexalate</td>
<td>30 g PO</td>
<td>2 hr</td>
<td>4-6 hr</td>
</tr>
<tr>
<td></td>
<td>50 g PR</td>
<td>1 hr</td>
<td>4-6 hr</td>
</tr>
<tr>
<td>Lasix (furosemide)</td>
<td>20-40 mg IVP</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td></td>
<td>Minutes</td>
<td>Variable</td>
</tr>
</tbody>
</table>


HYPERKALEMIA
Management of hyperkalemia focuses on three goals of care: cardiac stabilization, transcellular shift of potassium from extracellular fluid to intracellular fluid, and elimination of excess potassium (Table 165.2). Only potassium excretion is a definitive treatment step—other actions serve to temporarily stabilize the cell membrane in an effort to prevent hemodynamic collapse.

CARDIAC STABILIZATION: CALCIUM
IV calcium rapidly antagonizes the adverse effects of moderate to severe hyperkalemia on cell membrane potential in cardiac myocytes. Calcium can be administered as IV calcium chloride or calcium gluconate, even in patients who are normocalcemic. IV preparations of calcium chloride contain three times more calcium per ampule than do calcium gluconate formulations. Calcium chloride is more likely than calcium gluconate to cause tissue necrosis if it extravasates. Calcium normalizes ECG manifestations of hyperkalemia at a rate of 100 to 200 mL/hr (10 to 20 mEq/hr). If the patient has any form of heart block or renal insufficiency, the initial infusion rate should be reduced to 50 mL/hr (5 mEq/hr).

In rare instances of extreme hypokalemia or life-threatening clinical findings, potassium may be infused at a rate of 40 to 60 mEq/hr (400 to 600 mEq/L of normal saline at 100 mL/hr) for a short period (10 to 20 minutes). Therapy should be monitored with great caution. Serum potassium levels should be rechecked after every 40 to 60 mEq infused.

IV potassium supplementation can cause excruciating phlebitis and cardiac arrest if directly injected into a vessel—potassium should never be administered as an IV push. Peripheral IV lines can be used for rates of 10 to 20 mEq/hr or less. In cases of moderate hypokalemia, potassium infusions should remain at 10 mEq/hr. To minimize the risk for phlebitis, a central line is necessary for infusion rates greater than 20 mEq/hr (see earlier indications). There is a theoretic concern for cardiac arrest when potassium is administered via central venous access—splitting the potassium infusion rate over two peripheral lines may be preferable.

In general, patients receiving IV potassium supplementation require telemetry monitoring and frequent repeated potassium measurements (up to every 1 to 3 hours after the initial infusion begins). Significant potassium depletion may take days to correct. As serum potassium levels approach 3.5 mEq/L, patients should be converted to oral therapy if possible. IV potassium supplementation should be discontinued if any ECG signs of hyperkalemia are noted or if a single potassium measurement is higher than 3.5 mEq/L.

Unstable ventricular arrhythmias resulting from severe hypokalemia should be managed according to standard practice guidelines. Severe neuromuscular manifestations may endanger adequate respiratory effort and therefore mandate aggressive airway stabilization. Any volume depletion should be corrected, and coexisting medical conditions that may exacerbate the effects of hypokalemia should be addressed.

RED FLAGS
Calcium Supplementation
Calcium chloride may cause significant skin necrosis if extravasated. Calcium should not be administered with solutions that contain sodium bicarbonate because calcium carbonate (CaCO₃) will precipitate. Intravenous calcium boluses should be avoided in hyperkalemic patients with suspected digoxin toxicity because of the risk for cardiac tetany or fatal arrhythmia. Slow calcium infusions (over a 30-minute period) require close monitoring of these patients.
within minutes of administration; however, the clinical effects are generally short-lived. Doses may need to be repeated within 30 minutes or if no effects are observed within 5 to 10 minutes of the initial dose. Calcium should be administered to patients with hyperkalemia-induced ECG changes, and caution should be exercised in patients taking digoxin.

Transcellular Shift: Insulin and Albuterol

Potassium can be temporarily shifted from the extracellular to the intracellular compartment through stimulation of the Na⁺,K⁺-ATPase pump by insulin or a β₂-agonist such as albuterol. Although either of these agents can temporize moderate hyperkalemia when given alone, studies suggest that combination therapy with both agents may be more efficacious.

Insulin forces a transcellular shift of potassium into liver and muscle cells. Regular (short-acting) insulin administered as a 10-unit IV bolus will begin to lower serum potassium concentrations within 10 to 20 minutes, and the clinical effect lasts several hours. An ampule of D₅₀W should be given concurrently to prevent hypoglycemia; patients who are already hyperglycemic (>250 mg/dL) do not require supplemental dextrose. Blood glucose should be rechecked 1 hour after insulin administration because hypoglycemia may develop despite initial supplementation with dextrose.

Albuterol is the most readily available β₂-agonist used to treat hyperkalemia in the ED. Nebulized albuterol in 10- to 20-mg continuous treatments will decrease serum potassium by 1 mEq/L over a 1- to 2-hour period. Though not approved for use in the United States, IV administration of albuterol shifts potassium into the intracellular fluid compartment even more rapidly. Once routinely used for treatment of hyperkalemia, the use of sodium bicarbonate has been challenged. Recent studies have demonstrated that sodium bicarbonate may only enhance urinary elimination of potassium and does not function at a cellular level. It may have especially a deleterious effect on anuric patients and worsen the degree of intracellular acidosis.

Elimination: Resin Exchange (Kayexalate) and Dialysis

Definitive treatment of hyperkalemia is elimination of potassium. For patients with renal insufficiency, resin exchange (Kayexalate) and dialysis are the mainstays of therapy. Potassium-wasting diuretics (thiazides, loop diuretics) may be taken by patients with normal renal function and mild asymptomatic hyperkalemia. Sodium bicarbonate infusion may also promote renal secretion of potassium but is no longer considered a first-line agent in the treatment of hyperkalemia.

Sodium polystyrene sulfonate (Kayexalate) is an inert resin that exchanges sodium for potassium in the intestinal tract. One gram of Kayexalate removes approximately 0.5 to 1 mEq of potassium in exchange for 2 to 3 mEq of sodium. The usual dose of Kayexalate is 30 to 60 g given orally or rectally. Oral Kayexalate begins to reduce total body potassium within several hours of administration, and the clinical effect lasts 4 to 6 hours. Rectal Kayexalate has a shorter time to onset than the oral formulation but is less efficacious.

Emerging literature questions the efficacy and safety of Kayexalate. Although Kayexalate reliably decreases serum potassium when administered over a period of several days, recent literature reviews suggest that the acute effects of the resin may not be as significant as once thought. Colonic necrosis, ischemic colitis, colonic bleeding, and perforation have been reported when Kayexalate is combined with 70% sorbitol. Kayexalate is often premixed with 33% sorbitol to prevent resin-induced constipation, and there is little evidence to suggest that Kayexalate with 33% sorbitol causes significant colonic pathology at standard doses. Very rare instances of colonic injury have been observed when 33% sorbitol is coadministered with Kayexalate as an enema to patients after recent colon surgery. High-dose Kayexalate precipitates pulmonary edema by increasing extracellular sodium in fluid-overloaded patients.

Hemodialysis is the most rapid method of potassium elimination in patients with persistent, symptomatic, or severe hyperkalemia. If a potassium-free dialysate is used, serum potassium may decrease as much as 1.5 mEq/L/hr. Stable patients may be transferred to an inpatient hemodialysis unit for therapy under strict cardiac monitoring. Patients with ECG abnormalities, hypotension, significant volume overload, or respiratory distress should undergo dialysis in the ED or intensive care unit. Cell membrane stabilization with IV calcium, IV insulin or glucose, and inhalational albuterol is necessary to prevent arrhythmia while awaiting emergency hemodialysis.

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES