Derangements of Potassium

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KEYWORDS
- Potassium • Hypokalemia • Hyperkalemia • Peaked T waves

KEY POINTS
- Potassium balance regulates the excitability of cardiac cells, and both hypokalemia and hyperkalemia can cause cardiac arrest when severe.
- Treatment of hyperkalemia includes cardiac membrane stabilization, transcellular shifting, and total body potassium elimination. Sodium bicarbonate and Kayexalate are not recommended for management.
- Treatment of symptomatic hypokalemia consists of repletion with potassium chloride, which is available in liquid, pill, and intravenously (IV) administrable forms. Magnesium should be repleted simultaneously to potentiate potassium absorption and avoid further potassium losses.
- Determine and treat the underlying cause of potassium derangement to prevent recurrence.
  - Avoid potentiating medications.
  - Consider the dietary potassium contribution.
  - Consider problems with potassium excretion from the gastrointestinal (GI) tract or kidneys.
  - Consider transcellular potassium shifts across cell membranes.

INTRODUCTION AND PATHOPHYSIOLOGY
About 98% of total body potassium (K\textsuperscript{+}) is intracellular,\textsuperscript{1,2} and 75% of the intracellular potassium is contained in skeletal muscle cells.\textsuperscript{3,4} The body maintains the remaining 2% extracellular component within a tight range of 3.5 to 5.0 mEq/L (1 mmol equals 1 mEq K\textsuperscript{+}).\textsuperscript{3} The main mechanism for maintaining this transcellular ratio is the sodium-potassium (Na-K) adenosine triphosphatase (ATPase) pump, which uses energy in the form of adenosine triphosphate to drive K\textsuperscript{+} into cells in exchange for sodium (Na). The resulting K\textsuperscript{+} gradient creates a resting membrane potential that determines cardiac and neuromuscular cell excitability and signal conduction.

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Because the extracellular K\textsuperscript{+} level is proportionally so much less than the intracellular level, even a small change in the extracellular level significantly alters the resting membrane potential. Hyperkalemia is less tolerated by the body and causes more significant extracellular shifts than hypokalemia. A 100 mEq excess of total body K\textsuperscript{+} increases extracellular levels by 0.5 mEq, whereas a 100 mEq deficit decreases extracellular levels by just 0.3 mEq.\textsuperscript{3} Three different mechanisms alter the extracellular K\textsuperscript{+} concentration: K\textsuperscript{+} intake, K\textsuperscript{+} excretion, and transcellular shift of K\textsuperscript{+} into or out of cells.\textsuperscript{3} Many common medications affect one of these 3 mechanisms and can provoke a potassium imbalance (Boxes 1 and 2).

Usually the body’s regulatory mechanisms can resist large fluctuations in daily potassium intake. However, over time or in those persons predisposed to K\textsuperscript{+} disorders, diet can affect the extracellular K\textsuperscript{+} level. Patients with altered total-body potassium stores, who chronically take medications that alter K\textsuperscript{+} balance, or who have a disease predisposing them to K\textsuperscript{+} imbalance may need to either increase or avoid intake of potassium-rich foods (Box 3).

Excretion of K\textsuperscript{+} from the body is primarily managed by the kidneys, which are responsible for 90% of excretion in normal physiology.\textsuperscript{2,4} The other 10% is excreted mostly by the intestine into stool, with a small contribution from sweat. In cases of severe burns or extreme exercise, sweat and skin losses increase. Similarly, in end-stage renal disease when the kidneys no longer function, the gut upregulates to perform 25% of excretion.\textsuperscript{2}

### Box 1
**Medications causing hyperkalemia**

*Inhibit excretion*

- Decrease aldosterone
  - Angiotensin converting enzyme inhibitors
  - Angiotensin receptor blockers
  - Potassium-sparing diuretics (spironolactone)
  - Nonsteroidal antiinflammatory drugs (NSAIDs)
  - Heparin
  - Nonselective β-blockers

*Block sodium channels*

- Potassium-sparing diuretics (amiloride, triamterene)
- Antibiotics (trimethoprim, pentamidine)

*Transcellular shift*

- Inhibit Na-K ATPase pump
  - Digoxin (dose dependent)
  - NSAIDs
  - Nonselective β-blockers
  - Anesthetics (succinylcholine, suxamethonium)

Na-K ATPase exchangers are present both in the intestine and in the distal renal nephron to excrete K+. In the kidney, high amounts of urine and sodium arriving to the distal nephron stimulate the Na-K ATPase to excrete more K+, as does aldosterone. Low renal perfusion, hypovolemia, low sodium levels, or high potassium levels trigger renal renin release, which leads to aldosterone release by the adrenal glands, increasing renal excretion of K+.

Finally, certain physiologic states and medications affect the transport of K+ across the cell membrane, leading to transcellular shifts that can alter extracellular K+ levels. These shifts can be caused by alterations in the Na-K ATPase pump, pH and acid-base status in the body, and toxicity of the serum. Hyperglycemia and hypernatremia are 2 examples of hypertonic states that drive potassium out of cells.

The symptoms of potassium alterations are typically vague, so a careful history is important to raise clinical suspicion of the diagnosis. Symptoms of both hypokalemia and hyperkalemia affect the cardiac, muscular, and GI systems. The rate of change in extracellular K+ levels is more important than the absolute K+ level in determining severity of symptoms and risk for deterioration, so symptoms are unreliable predictors of absolute K+ values. Workup of any patient whose history suggests potassium...
### Box 3
**Foods rich in potassium**

- Legumes and grains
  - Whole-grain bread
  - Wheat bran
  - Granola
  - Beans (kidney, pinto, black, navy, and lima)
  - Nuts, nut butter
- Vegetables
  - Potato
  - Yam, sweet potato
  - Tomato
  - Spinach
  - Beets
  - Broccoli
  - Brussel sprouts
  - Bamboo shoots
  - Winter squash (acorn, butternut, pumpkin)
  - Cabbage
  - Carrots (raw)
  - Spinach
  - Canned mushrooms
  - Pickles
- Fruits
  - Banana, plantain
  - Fig
  - Prune
  - Raisin
  - Date
  - Apricot (especially dried)
  - Avocado
  - Melon (cantaloupe and honey dew)
  - Kiwi
  - Mango
  - Citrus (nectarine and orange)
  - Pear
- Dairy
  - Milk (soy and regular)
  - Yogurt
imbalance should include electrocardiography (ECG), basic metabolic panel (with electrolyte and creatinine levels), complete blood count, and urinalysis. If symptoms are severe, blood gas analysis to determine pH and urine electrolyte levels to differentiate the causes are also suggested (Box 4). Magnesium levels need to be checked in cases of hypokalemia. The ECG may show specific abnormalities that can help make the diagnosis and suggest risk of cardiac deterioration, but it is not sensitive and absence of ECG changes does not rule out a significant potassium abnormality.

HYPERKALEMIA

Etiology

Hyperkalemia, extracellular K+ levels greater than 5.0 mEq/L or 5.5 mEq/L depending on the laboratory assay,1–4 can be caused by failure to excrete enough K+, leading to total body excess, transcellular shifts, or measurement error (Box 5). Many common medications inhibit K+ excretion or shift it out of cells and into the extracellular space (see Box 1). Patients with underlying disorders predisposing them to hyperkalemia

<table>
<thead>
<tr>
<th>Meats</th>
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<tr>
<td>Beef</td>
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<tr>
<td>Clams</td>
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<td>Sardines</td>
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<td>Scallops</td>
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<td>Lobster</td>
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<td>Salmon</td>
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<td>White fish</td>
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</table>

Other

Sports beverages and supplements
Imitation salt (low-sodium products)
Molasses
Chocolate


| Box 4  
<table>
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<tbody>
<tr>
<td>Diagnostic workup</td>
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</table>

| ECG |
| BMP/Chem7 |
| Magnesium<sup>a</sup> |
| CBC |
| UA |
| Blood gas, Urine electrolytes<sup>b</sup> |

<sup>a</sup> In hypokalemia
<sup>b</sup> In severe cases
<table>
<thead>
<tr>
<th>Box 5</th>
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<tbody>
<tr>
<td><strong>Disorders causing hyperkalemia</strong></td>
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<tr>
<td><em>Failure of excretion</em></td>
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<tr>
<td>Decreased glomerular filtration rate</td>
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<tr>
<td>Renal insufficiency</td>
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<tr>
<td>Renal failure</td>
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<tr>
<td>Heart failure</td>
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<tr>
<td>Obstructive uropathy</td>
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<tr>
<td>Low aldosterone level</td>
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<tr>
<td>Adrenal insufficiency (Addison disease)</td>
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<tr>
<td>Low renin level</td>
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<td>Type 4 renal tubular acidosis</td>
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<tr>
<td>Medications that inhibit Na-K ATPase in the distal nephron (see Box 1)</td>
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<tr>
<td><em>Transcellular shifts (Na-K ATPase pump)</em></td>
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<tr>
<td>Hemolysis</td>
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<tr>
<td>Rhabdomyolysis</td>
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<td>Tumor lysis syndrome</td>
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<td>Hematoma reabsorption</td>
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<tr>
<td>Medications that inhibit Na-K ATPase pump (see Box 1)</td>
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<tr>
<td>Insulin deficiency</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Prolonged fasting</td>
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<td>Hypertonicity</td>
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<td>Hyperglycemia</td>
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<tr>
<td>Hypernatremia</td>
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<tr>
<td>Acidosis</td>
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<tr>
<td>Hyperkalemic periodic paralysis (mutation of skeletal muscle Na-K pump)</td>
</tr>
<tr>
<td>Fasting</td>
</tr>
<tr>
<td>Intense exercise</td>
</tr>
<tr>
<td>High-K+ meal</td>
</tr>
<tr>
<td><em>Measurement error (pseudohyperkalemia)</em></td>
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<tr>
<td>Hemolysis during blood draw</td>
</tr>
<tr>
<td>Prolonged tourniquet use</td>
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<td>Small needle caliber</td>
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<td>Excessive fist clenching</td>
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<tr>
<td>Excessive plunger force to pull blood into a syringe</td>
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<tr>
<td>Hemolysis before laboratory analysis</td>
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<tr>
<td>Delay between blood draw and analysis</td>
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<td>Aggressive sample shaking</td>
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are much more sensitive to initiation of these medications. Ingesting too much K+ rarely causes hyperkalemia except in patients with preexisting K+ homeostasis abnormalities.

Renal disorders are the most common cause of hyperkalemia, followed by cell lysis, which releases large intracellular K+ stores.2 High K+ levels stimulate aldosterone secretion, which acts on the renal tubules to increase K+ excretion into the urine, but in primary mineralocorticoid deficiency this homeostasis mechanism fails to activate, whereas in renal failure the kidney is unable to respond to aldosterone.4 High plasma K+ levels also stimulate insulin secretion from the pancreas, which drives K+ intracellularly,4 although patients with diabetes mellitus may not have sufficient insulin production capacity to counteract high K+ levels.

Clinical Presentation

Patients with hyperkalemia may be completely asymptomatic or may have cardiac, muscular, or GI complaints. Hyperkalemia depolarizes the cardiac membrane, slowing conduction.5 Patients may experience palpitations or generalized fatigue and malaise. Muscle cramps,4 paresthesias, and weakness are common.2 Weakness can progress to a flaccid paralysis.2 Nausea, vomiting, and diarrhea can also occur.4

Physical examination findings include bradycardia and/or irregular cardiac rhythm with frequent premature ventricular contractions.2 Neurologic examination may reveal decreased deep tendon reflexes and decreased strength with intact sensation.2,3,5

Diagnostic Testing

An ECG is the first step in the workup of a patient with hyperkalemia. Hyperkalemia increases myocyte sensitivity in different areas of the heart progressively as K+ levels rise:2

1. Atria
2. Ventricles
3. Bundle of His
4. Sinoatrial node
5. Interatrial tracts

Therefore, the ECG progresses through several phases that are loosely correlated with absolute serum K+ levels and with the rate of increase in serum K+ levels.2,6 The first and most common sign is tall, “peaked” T waves with a narrow base (Fig. 1). These occur most frequently in the precordial leads V2-V4. A sensitive sign

<table>
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<th>Hyperviscosity</th>
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<tbody>
<tr>
<td>Extreme leukocytosis</td>
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<tr>
<td>Extreme thrombocytosis</td>
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<tr>
<td>Polycythemia vera</td>
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<tr>
<td>Patient hyperventilation during blood draw (respiratory alkalosis causing transient K+ shift)</td>
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<tr>
<td>Large, rapid potassium load</td>
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<tr>
<td>Massive blood transfusion protocol</td>
</tr>
<tr>
<td>High-dose potassium penicillin</td>
</tr>
<tr>
<td>Poisoning/ingestion</td>
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</tbody>
</table>

Data from Refs.1-4
Fig. 1. ECG with peaked T waves in hyperkalemia.
is if the amplitude of the T exceeds the amplitude of the R. As the atria are affected the PR interval lengthens, and as the ventricles are affected the QRS widens. When hyperkalemia affects the conduction system, the P waves decrease in amplitude until the ECG develops a “nodal” rhythm with absent P waves (Fig. 2). The QRS continues to widen until the S and T waves merge into a “sine wave” pattern (Fig. 3). The sine wave pattern usually shortly precedes ventricular fibrillation (VFib) and cardiac arrest.

However, research has shown poor sensitivity for these changes, with only 32% of ECGs in known hyperkalemia having peaked T waves and only 52% exhibiting any ECG change. If strict measurement criteria were used, just 18% of ECGs displayed a change despite hyperkalemia. When limited to hyperkalemia greater than 6.0 mEq/L rather than 5 mEq/L, 46% to 64% had changes, suggesting a nonsignificant trend with degree of hyperkalemia.

**Treatment**

Most experts agree that ECG changes and/or symptoms should be treated expeditiously, but because these can occur at varying absolute K+ levels and some patients can have K+ levels greater than 7.5 mEq/L without ECG changes or symptoms, it is still undecided whether an absolute K+ threshold exists whereby risk of arrhythmia necessitates treatment in the asymptomatic patient.

In the setting of ECG changes, cardiac membrane stabilization is the first priority to prevent arrhythmias and cardiac arrest. Calcium is the mainstay of cardiac stabilization to restore resting membrane potential, either as gluconate or chloride compounds. Calcium chloride has approximately 3 times more elemental calcium than calcium gluconate (6.8 mEq/10 mL vs 2.2 mEq/10 mL) and it has greater bioavailability because calcium gluconate has to be metabolized into an active form. However, calcium gluconate has less risk of tissue necrosis, which allows faster transfusion. There is no randomized evidence supporting one or the other, and decision on which agent to use remains provider and facility dependent.

Next, potassium levels can be lowered either temporarily by medications that cause an intracellular shift of K+ or by therapies that eliminate K+ from the body to decrease total body stores (Table 1). Insulin and β-agonists stimulate the Na-K ATPase pump to pull more K+ into cells and are the mainstays of evidence-based therapy for transcellular shift. The 2 medications are synergistic, so using both in combination results in a larger reduction of extracellular K+ than using either alone. There is no difference in inhaled or IV forms of β-agonists, although IV forms are not currently available in the United States, nor is there a difference between albuterol and levalbuterol. Both metered-dose inhalers and nebulizers are also equally effective, although it may be easier to deliver consistent dosing with the nebulized form.

Sodium bicarbonate has been used to promote intracellular shift of K+, but no good evidence supports its routine use in hyperkalemia. It is significantly less effective than insulin or β-agonists, with a maximum effect of 0.4 mEq/L, and it has only been helpful in patients with a nongap metabolic acidosis. Furthermore, several studies have found no effect compared with placebo and no additional effect compared with insulin or β-agonists alone.

Reduction of total body K+ can be accomplished by enhancing the body’s renal or GI elimination. Loop diuretics are useful in patients who still produce urine. Sodium polystyrene, or Kayexalate, has been commonly used in practice since studies suggesting its efficacy were published in 1961, with the presumed mechanism of increased Na-K exchange across the bowel wall. Onset of action is delayed by 2 to 6 hours, decreasing its utility in the management of acute hyperkalemia in the
Fig. 2. ECG with nodal rhythm and absent T waves in hyperkalemia.
Derangements of Potassium
It also causes significant constipation and so is usually administered in combination with a stool softener. However, subsequent research has not replicated the 1961 results, instead showing that Kayexalate makes no difference in serum K+ levels and that stool softeners alone are equally effective. A dangerous side effect of Kayexalate is intestinal necrosis, and the US Food and Drug Administration has issued a warning against administering it in combination with the stool softener sorbitol, which is thought to increase the incidence of intestinal necrosis. In light of its delayed onset of action, uncertain efficacy, and high-risk side-effect profile, Kayexalate is not recommended in the treatment of hyperkalemia.

Finally, dialysis is the definitive treatment for removing potassium from the body. Most of the K+ elimination occurs during the first 2 hours of dialysis. However, dialysis only filters the extracellular compartment, minimizing its effect on total body K+ stores, and in cases of elevated total body K+ stores, the body quickly

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Time to Onset (min)</th>
<th>Magnitude of K+ Reduction (mEq/L)</th>
<th>Duration of Effect (h)</th>
<th>Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>1–2 g (10 mL)</td>
<td>Immediate</td>
<td>No effect on K+</td>
<td>0.5–1&lt;sup&gt;2,4,5&lt;/sup&gt;</td>
<td>• May potentiate arrhythmias in digoxin toxicity</td>
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<td></td>
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<td></td>
<td></td>
<td>• Extravasation can cause tissue damage and phlebitis</td>
</tr>
<tr>
<td>β-Agonists</td>
<td>20 mg</td>
<td>Within 30&lt;sup&gt;2,4,5,9,10&lt;/sup&gt;</td>
<td>0.5–1.5&lt;sup&gt;1,2,4,5,9&lt;/sup&gt;</td>
<td>2–6&lt;sup&gt;1–5&lt;/sup&gt;</td>
<td>• Patients taking nonselective β-blockers may be resistant to this effect&lt;sup&gt;2,5&lt;/sup&gt;</td>
</tr>
<tr>
<td>(albuterol)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Tremors, anxiety</td>
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<tr>
<td>Insulin</td>
<td>10 units</td>
<td>15–30&lt;sup&gt;2,4,5,9,10&lt;/sup&gt;</td>
<td>0.6–1.2&lt;sup&gt;2,5,10&lt;/sup&gt;</td>
<td>2–6&lt;sup&gt;2,5,10&lt;/sup&gt;</td>
<td>• Give with Dextrose 50%; monitor glucose closely for hypoglycemia</td>
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<td></td>
<td></td>
<td>• Patients with ESRD are more susceptible to hypoglycemia because of decreased excretion of insulin</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td></td>
<td>15&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1–3&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>Not effective in patients with ESRD who no longer make urine</td>
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<tr>
<td>(Lasix, Bumex)</td>
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<tr>
<td>Dialysis</td>
<td>N/A</td>
<td>Immediate</td>
<td>1–2&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>2–6&lt;sup&gt;2,5&lt;/sup&gt;</td>
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</table>

Abbreviations: ESRD, end-stage renal disease; N/A, not applicable.
reequilibrates to a hyperkalemic state. Within 6 hours, extracellular K+ returns to 70% of its predialysis levels. In situations of resuscitation from cardiac arrest, case reports have demonstrated successful return of spontaneous circulation and good neurologic outcomes despite prolonged arrest when dialysis is initiated during cardiopulmonary resuscitation (CPR) to correct hyperkalemia.

**Key Points**

- Treatment of hyperkalemia includes
  - Cardiac membrane stabilization
  - Transcellular shifts
  - Total body potassium elimination
- Changes in practice
  - Sodium bicarbonate is not an indicated therapy; can consider its use in acidic patients with hyperkalemia
  - Do not give Kayexalate
  - In cases of cardiac arrest due to hyperkalemia, perform prolonged CPR until K+ level is corrected; the patient should not be pronounced dead until their K+ level is normalized.
- Next steps
  - Repeat serial K+ measurements to monitor for rebound hyperkalemia
  - Prevent recurrence
    - Avoid potentiating medications (see Box 1)
    - Determine and treat underlying cause (see Box 5)
      - Failure to excrete enough K+ to maintain a balance
      - Transcellular shifts
      - Suspect measurement error in otherwise normal patients and repeat laboratory analysis before initiating treatment

**HYPOKALEMIA**

**Etiology**

Hypokalemia, extracellular K+ concentration less than 3.5 mEq/L, can be caused by increased K+ loss from the body, transcellular shifts, decreased K+ intake, and sometimes by magnesium depletion (Box 6). K+ is excreted into the stool via Na-K ATPase exchange pumps in the GI tract, and any disease state (eg, diarrhea) or medication (eg, laxatives) that increases stool output increases GI K+ losses.

The kidneys are primarily responsible for maintaining K+ balance via the Na-K ATPase exchange pumps in the distal nephron. Anything that activates these pumps or increases the flow of Na or urine through the distal nephron increases renal K+ losses.

Low magnesium (Mg) levels stimulate Na-K ATPase activity. Some drugs such as amphotericin, aminoglycosides, and cisplatin lower Mg, which secondarily lowers K+ (see Box 2). If Mg remains low, any K+ intake is quickly excreted by the kidneys despite a total body K+ deficit.

Aldosterone via the renin-angiotensin-aldosterone system is a primary activator of the Na-K ATPase pump in the distal nephron. High aldosterone levels occur during dehydration in reaction to hypovolemia and in cases of high cortisol and adrenocorticotropic hormone or aldosterone-secreting tumors (Cushing syndrome; Conn syndrome).

High-urine-flow states increase renal excretion of K+. Diuresis, whether drug induced or driven by the body’s elimination of other substances such as excess glucose or water, therefore increases K+ losses. A high-sodium diet and drugs
Box 6
Disorders causing hypokalemia

*Excessive loss*

GI tract
- Diarrhea
- Laxative abuse
- Fistula
- Ileostomy

Renal
- Increased Na+ delivery to the distal nephron
  - High-sodium diet
  - Drugs (eg, penicillins)
- Increased urinary flow
  - Hyperglycemia
  - Mannitol
    - High-volume IV normal saline
- Activation of Na-K ATPase
  - Hypomagnesemia
  - Renal tubular acidosis types 1 and 2
  - Liddle syndrome
  - High aldosterone levels
    - Primary
      - Conn syndrome
    - Cushing syndrome
    - Secondary
      - Hypovolemia (eg, vomiting)
      - Bartter syndrome
      - Gitelman syndrome
      - Excessive licorice intake (with glycyrrhizic acid, not sold in the United States)

Cutaneous
- Excessive sweating
- Extensive burns

Transcellular shift

Alkalosis

Hypernatremic hypokalemic paralysis

Thyrotoxic periodic paralysis

Other
- Low dietary intake (when chronic)

*Data from Refs.*²⁻⁴,¹³
such as penicillins also increase renal K+ excretion by delivering more Na to the distal nephron where the Na gradient drives the Na-K ATPase exchange. Cutaneous losses are usually negligible except in cases of excessive sweating as happens during extreme exercise or heat exhaustion or when large-surface-area burns break down the skin barrier.

Several common medications can shift K+ intracellularly, causing an apparent hypokalemia despite normal total body K+ stores (see Box 2). Alkalosis, respiratory or metabolic, also drives K+ intracellularly. In addition to stimulating renal losses, a high aldosterone level leads to a metabolic alkalosis, which can perpetuate hypokalemia by simultaneously shifting K+ intracellularly, further reducing extracellular levels. Renal tubular acidosis types 1 and 2 are the only cases in which hypokalemia occurs in the setting of an acidosis rather than an alkalosis. The body can compensate for a low-K+ diet by severely limiting renal excretion of potassium, but if a low-potassium diet continues chronically, it can eventually lead to clinically significant hypokalemia.

**Clinical Presentation**

Like in hyperkalemia, most hypokalemic patients are asymptomatic, particularly at K+ levels greater than 3.0 mEq/L. Patients with heart failure are more likely to be symptomatic, and it is recommended that their levels should remain 4.0 mEq/L or more to prevent arrhythmias. Muscular symptoms include generalized malaise, fatigue, lethargy, and weakness. Fasciculations and tetany also occur. Severe cases may present as an ascending paralysis that can include respiratory muscles. GI complaints include ileus due to impaired smooth muscle activity, which can cause nausea, vomiting, and constipation. Inability to concentrate the urine can also create a nephrogenic diabetes insipidus presentation with polyuria and polydipsia.

On examination, weakness may be evident, with decreased strength typically more pronounced in proximal muscles and lower extremities. Mental status and orientation remain intact. Abdominal examination may reveal distention in cases of ileus.

**Diagnostic Testing**

An ECG is an initial diagnostic test with immediate results that can be used to guide further treatment. Hypokalemia predisposes to several arrhythmias, including first-degree heart block with a prolonged PR interval, second-degree heart block, and atrial fibrillation. These rhythms can deteriorate into ventricular tachycardia (VTach), VFib, torsades de pointes, and cardiac arrest. Patients taking digitalis are more susceptible to arrhythmias in the setting of hypokalemia.

In addition to arrhythmias such as first-degree atrioventricular block with an increased P wave amplitude, there are several more specific signs of hypokalemia that can appear on ECG. The first sign of hypokalemia is usually decreased T wave amplitude, followed by ST depressions or T wave inversions. U waves are the classically taught abnormality and are best seen in V2 and V3 (Fig. 4). As they enlarge, they can merge with and mimic T waves (which are simultaneously decreasing in amplitude), giving the false impression of a prolonged QT. Sometimes U waves grow so tall that they appear similar to the peaked T waves of hyperkalemia, but U waves usually have a broader base.

Additional testing should include a blood gas and pH analysis. In hypokalemia, the kidney cannot excrete bicarbonate and instead excretes protons and chloride, causing a metabolic alkalosis (or perpetuating an existing alkalosis, which may have caused the hypokalemia via transcellular shift initially). All patients with hypokalemia should have a magnesium level checked because of the strong correlation between hypomagnesemia and hypokalemia. It is helpful to determine total body K+ stores...
Fig. 4. ECG with U waves in hypokalemia. (From Dangodara A. ECG interpretation. In: Glasheen JJ, editor. Hospital medicine secrets. Philadelphia: Mosby/Elsevier, 2007; with permission.)
to differentiate between transcellular shifts and total K+ loss, but measuring total body K+ requires a 24-hour urine collection.\textsuperscript{13}

**Treatment**

Treatment of hypokalemia includes both potassium and magnesium repletion. Hypomagnesemia is frequently found in patients with hypokalemia because hypomagnesemia causes hypokalemia via renal wasting, and other common causes of hypokalemia such as diarrhea and diuretic use also cause a simultaneous hypomagnesemia.\textsuperscript{3,4,7} However, in severe cases of symptomatic hypokalemia, concurrent Mg repletion is recommended even with normal Mg levels because Mg activates the Na-K ATPase pump to promote cellular uptake of dosed K+.\textsuperscript{4}

Although asymptomatic hypokalemia greater than 3.0 mEq/L can be safely discharged with a high-K+ diet (see Box 3) and close follow-up after addressing the cause, any symptomatic hypokalemia should be repleted in the emergency department. Patients with recent myocardial infarction or with heart failure should be repleted to levels of at least 4.0 mEq/L.\textsuperscript{3,4} As a guide, a 0.3-mEq/L drop in extracellular K+ levels represents a 100-mEq/L total body deficit.\textsuperscript{4} When K+ is rechecked after repletion but before transcellular equilibration, 10 mEq of K+ is expected to increase extracellular levels by 0.1 mEq/L.

The maximum recommended dose of potassium chloride in low-risk hypokalemia with minimal symptoms and without arrhythmia is 20 to 80 mEq/d.\textsuperscript{4} It is important to consider the likely cause of the hypokalemia, as aggressive repletion in cases of transcellular shift can lead to overcorrection of total body K+ and rebound hyperkalemia once the cause of the shift is resolved. K+ levels should be rechecked periodically during and after repletion to prevent overcorrection.\textsuperscript{4}

Patients with minimal symptoms who are tolerating intake by mouth can receive pill or liquid potassium chloride, which has the advantage of a single large dose. If patients present with nausea or vomiting and are unable to tolerate intake by mouth, IV correction is recommended at a rate of 10 to 20 mEq/h. Patients should be monitored on a telemetry monitor during IV infusion for the development of dysrhythmias. In patients with significant dysrhythmias (VTach) as a presenting symptom, 20 mEq can be pushed over 3 to 10 minutes to prevent deterioration into cardiac arrest.\textsuperscript{2,4} IV potassium chloride causes burning and discomfort at the IV site and can cause phlebitis.\textsuperscript{4} A central line is recommended for rates greater than 10 mEq/h.

**Key Points**

Hypokalemia is a common disorder, but is well tolerated by the body relative to hyperkalemia. However, severe cases of hypokalemia can cause dysrhythmias and cardiac arrest.

- Treatment of symptomatic hypokalemia consists of repletion with potassium chloride
  - Intake by mouth in pill or liquid forms
  - IV
    - Max rate 10 to 20 mEq/h
    - Push rapidly over 5 to 10 minutes in cases of cardiac arrest or impending arrest (VFib, VTach)
- Next steps
  - Repeat serial K+ measurements to monitor for recurrence and prevent overcorrection
  - Remember to replete Mg along with K+
Prevent recurrence
  - Avoid potentiating medications (see Box 2)
  - Determine and treat underlying cause (see Box 6)
    - Increased K+ losses from the body
      - GI
      - Renal
      - Cutaneous
    - Transcellular shifts
    - Decreased K+ intake

SUMMARY

Changes in potassium elimination, primarily due to the renal and GI systems; shifting potassium between the intracellular and extracellular spaces; and dietary potassium intake are the 3 major causes of potassium derangements. Several common medications can contribute to either hyperkalemia or hypokalemia. False laboratory results regarding elevations in potassium value are also a common cause for hyperkalemia, and the test should be repeated if suspicion for pseudohyperkalemia exists. Symptoms of potassium derangement are vague but can be cardiac, musculoskeletal, or GI. There are no absolute guidelines for when to initiate treatment of potassium derangement, but it is generally recommended when the patient is symptomatic and/or has changes on the ECG attributable to potassium derangement. Treatment of hyperkalemia includes cardiac membrane stabilization with IV calcium, pushing potassium intracellularly using insulin (which should be given in combination with glucose to avoid hypoglycemia) and β-antagonists, and removing potassium from the body entirely with dialysis. Neither sodium bicarbonate nor Kayexalate are recommended as evidence-based therapies. Treatment of symptomatic hypokalemia consists of repletion with potassium chloride either by mouth or IV. Magnesium should be repleted when repleting potassium. Repeat potassium levels should be checked after treatment of potassium derangement to monitor effect and guide further therapy. Medications and diet should be adjusted to prevent recurrence, especially in patients predisposed by renal insufficiency.

REFERENCES


