Hypokalemia and Hyperkalemia

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KEYWORDS

• Potassium • Hypokalemia • Hyperkalemia • Electrolyte disorders

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Serum potassium concentration is used to diagnose hypokalemia and hyperkalemia. In the setting of low clinical suspicion of hypokalemia or hyperkalemia, abnormal serum potassium results need to be confirmed.
2. In individuals with hypokalemia or hyperkalemia, evaluate a 12-lead electrocardiogram for evidence of conduction abnormalities or arrhythmias. Telemetry is indicated in individuals with severe potassium derangement, with electrocardiographic abnormalities, or who are at risk of developing arrhythmias.
3. Attempt to identify the cause of hypokalemia or hyperkalemia based on history, medication review, examination, and other laboratory results.
4. In hypokalemia and hyperkalemia, evaluate medications and discontinue or dose reduce any causal or contributing medications.
5. In hypokalemia, determine if the individual needs potassium deficit replacement. In the case of a reversible redistribution of potassium into the intracellular compartment, be careful to avoid rebound hyperkalemia.
6. When potassium deficit replacement is indicated, use oral potassium replacement, unless there is a severe deficit, signs or symptoms of hypokalemia, or the individual cannot tolerate oral intake.
7. In individuals with hypokalemia from ongoing urinary potassium losses, consider use of potassium-sparing diuretics.
8. In severe hyperkalemia with electrocardiographic features of hyperkalemia, administer calcium salt to stabilize the cardiac membrane.

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9. In severe hyperkalemia, administer therapy to redistribute serum potassium into the intracellular space and concomitantly give therapy to remove potassium from the body.
10. After treatment of severe hypokalemia or hyperkalemia, close monitoring of serum potassium is indicated. In addition, repeat electrocardiogram, blood glucose monitoring, or other laboratory studies may be indicated.

DEFINITION

What is a normal potassium level?

Most potassium is intracellular and has a normal concentration of approximately 150 mmol (mEq)/L. Serum potassium has a normal concentration of 3.5 to 5.0 mmol/L. Hypokalemia is defined as a serum potassium concentration less than 3.5 mmol/L, and hyperkalemia is defined as a serum potassium concentration of higher than 5.0 mmol/L.[1] There are no agreed definitions of severe hypokalemia or hyperkalemia. However, most experts define severe hypokalemia as less than 2.5 to 3.0 mmol/L.[2,3] and severe hyperkalemia as higher than 6.0 to 6.5 mmol/L[4–8] However, others argue that hyperkalemia should not be considered severe until higher than 8.0 mmol/L.[9]

EPIDEMIOLOGY

How common are hypokalemia and hyperkalemia in hospitalized patients?

Hypokalemia and hyperkalemia are common clinical problems in hospitalized patients. Hypokalemia is present in up to 21% of hospitalized patients. Most of those patients have serum potassium levels between 3.0 and 3.5 mmol/L. However, around 2.5% to 5% of patients have serum potassium levels less than 3.0 mmol/L.[10,11] Hyperkalemia occurs in 1.1% to 10% of hospitalized patients.[12,13]

PHYSIOLOGY OF POTASSIUM REGULATION

What is the physiology of potassium regulation?

Serum potassium concentrations are highly regulated, because they are essential for normal neuromuscular function.[1] When potassium is ingested in the diet, approximately 90% is absorbed in the gastrointestinal tract. This process leads to an increase in the serum potassium concentration. In response to an increased serum potassium concentration, insulin, catecholamines, and aldosterone are secreted. Insulin and catecholamines serve to acutely decrease serum potassium levels by activating the sodium-potassium-adenosine triphosphatase pumps, which transport potassium into muscle and liver cells.[1,14] Aldosterone, in addition to increased serum potassium levels and increased delivery of sodium and water to the distal nephron, causes urinary potassium excretion.[1,14,15] This process leads to a near complete excretion of the potassium load within 6 to 8 hours of ingestion.[14,15] Normally, the kidney is responsible for 90% to 95% of potassium excretion, with the remaining 5% to 10% lost in stool and sweat.[15]

Hypokalemia is uncommon in the absence of underlying disease. Even in low dietary intake, the serum potassium level is maintained because of the ability of the kidneys to retain potassium.[1,15,16] Low serum potassium levels lead to decreased levels of insulin, catecholamines, and aldosterone.[7,15] In addition, there is often decreased delivery of sodium and water to the distal nephron. These factors lead to a decreased signal for cellular uptake and a very low level of urinary potassium excretion to maintain appropriate potassium concentrations.[1,15]

MECHANISMS AND CAUSES OF HYPOKALEMIA

What are the mechanisms of hypokalemia?

Common mechanisms of serum hypokalemia are listed in **Table 1**.

What are the causes of hypokalemia?

The common causes of hypokalemia are listed in **Table 2**.

MECHANISMS AND CAUSES OF HYPERKALEMIA

What are the main mechanisms of hyperkalemia?

The common mechanisms of serum hyperkalemia are listed in **Table 3**.

What are the causes of hyperkalemia?

The common causes of hyperkalemia are listed in **Table 4**.

Table 1
Common mechanisms of hypokalemia

Low dietary potassium intake	Prolonged and extremely low dietary potassium intake can decrease serum potassium levels. In normal individuals, it is uncommon for low dietary intake alone to cause significant hypokalemia. However, when other mechanisms of hypokalemia are present, it may contribute to the severity of hypokalemia[1,15,16]
Redistribution of potassium into cells	An increase in potassium uptake into the intracellular compartment can lead to low serum potassium concentrations[1,16]
Gastrointestinal loss of potassium	Loss of upper or lower gastrointestinal fluids, such as with vomiting or diarrhea, leads to potassium losses and can result in hypokalemia. In addition to potassium losses in gastrointestinal fluid, resultant hypovolemia induces aldosterone release, which results in urinary potassium losses.[1,16] Vomiting also leads to metabolic alkalosis, which leads to a redistribution of potassium into the intracellular compartment[16]
Urinary loss of potassium	Urinary loss of potassium can be caused by aldosterone or increased flow of nonreabsorbable anions through the collecting tubules[16]
Other mechanisms	Increased sweat losses, dialysis, and plasmapheresis can cause hypokalemia[1,16]

Data from Refs.[1,15,16]

Table 2
Causes of hypokalemia

Dietary	Anorexia/starvation (low dietary potassium intake) Clay ingestion
Redistribution of potassium into cells	Metabolic alkalosis Increased insulin or endogenous insulin use Increased β-adrenergic activity or endogenous β-adrenergic use α-Adrenergic antagonists Increased red or white blood cell production Total parenteral nutrition Drugs (partial list) Bronchodilators (eg, albuterol) Theophylline Caffeine Chloroquine intoxication Hypokalemic periodic paralysis Hypothermia Barium toxicity
Gastrointestinal loss of potassium	Vomiting Nasogastric tube with stomach content removal Infectious diarrhea Other increased stool output (tumors, jejunoileal bypass, enteric fistula, malabsorption, chemotherapy) Drugs Laxative abuse Sodium polystyrene sulfonate
Urinary loss of potassium	Diuretics Osmotic diuresis Salt-wasting nephropathies Mineralocorticoid excess Primary and secondary hyperaldosteronism Apparent mineralocorticoid excess (licorice, chewing tobacco, carbenoxolone) Congenital adrenal hyperplasia Cushing syndrome Loss of gastric secretions Proximal renal tubular acidosis Diabetic ketoacidosis Glue sniffing (toluene abuse) Penicillin derivatives Bartter syndrome Gitelman syndrome Liddle syndrome Hypomagnesemia Amphotericin B Polyuria
Other mechanisms	Sweat losses Dialysis Plasmapheresis

Data from Refs.[1,3,16]

Table 3
Common mechanisms of hyperkalemia

High dietary potassium intake	High dietary potassium intake, or endogenous potassium administration, can lead to transient increase in serum potassium levels. In normal physiology, this is transient because of cellular and urinary responses to an increase in serum potassium levels. However, in an individual with impaired urinary potassium excretion, potassium intake can lead to the development of hyperkalemia[1,14]
Redistribution of potassium out of cells	A redistribution of potassium out of the cells (or impaired entry into cells) can cause an increase in serum potassium level[14]
Decreased urinary excretion of potassium	Impaired urinary potassium excretion is caused by hypoaldosterone (or reduced response to aldosterone in the kidney), decreased sodium, and water delivery to the distal nephron, and acute or chronic kidney disease.[14] In rare cases, hyperkalemia can be caused by other mechanisms (see **Table 4**)

Data from Singer GG, Brenner BM. Fluid and electrolyte disturbances. In: Kasper DL, Fauci AS, Longo DL, et al, editors. Harrison's principles of internal medicine, 16th edition. New York: McGraw-Hill; 2005. p. 258–63; and Mount DB. Causes and evaluation of hyperkalemia in adults. In: Basow DS, editor. UpToDate. Waltham (MA): UpToDate; 2013.

Table 4
Causes of hyperkalemia

High dietary potassium intake	High dietary intake Potassium supplementation
Redistribution of potassium out of cells	Pseudohyperkalemia Metabolic acidosis Insulin deficiency, hyperglycemia, and hyperosmolarity Increased tissue catabolism Exercise Hyperkalemic periodic paralysis Drugs β-Blockers Digitalis Succinylcholine Arginine hydrochloride Activators of adenosine triphosphate–dependent potassium channels (calcineurin inhibitors, minoxidil) Red blood cell transfusion
Decreased urinary excretion of potassium	Acute kidney injury Chronic kidney disease Decreased distal nephron flow (hypovolemia) Reduced aldosterone secretion Adrenal insufficiency or adrenal enzyme deficiency Hyporeninemia Drugs (angiotensin-converting enzyme inhibitors, nonsteroidal antiinflammatory drugs, heparin) Reduced response to aldosterone Pseudohypoaldosteronism Tubulointerstitial disease Drugs (potassium-sparing diuretics, trimethoprim, pentamidine) Selective impairment of potassium secretion Chloride shunt Gordon syndrome Cyclosporine Ureterojejunostomy

Data from Refs.[1,2,4,14,17]

CLINICAL FEATURES, HISTORY, EXAMINATION, AND DIAGNOSIS

What are the clinical features of hypokalemia?

The clinical manifestations of hypokalemia vary greatly between individuals and can range from subtle to clinically apparent (**Table 5**).[1] Manifestations are more likely to occur in individuals with a rapid rate of depletion, a very low level of potassium (in general, <3.0 mmol/L), or other predisposing factor, such as use of digoxin.[1,18]

What are the clinical features of hyperkalemia?

Similar to hypokalemia, the clinical manifestations usually develop with very abnormal levels (higher than 6.9 mmol/L) or rapid serum potassium change (**Table 6**).[19]

What historical information is important?

Hypokalemia and hyperkalemia are difficult to diagnose based on history or physical examination findings alone. Often, they are found incidentally on laboratory testing. History should include evaluation for symptoms, such as weakness and syncope (see **Tables 5** and **6**), and potential causes, such as medications or gastrointestinal losses (see **Tables 2** and **4**).

Which aspects of the physical examination are important?

The immediate physical examination should include an assessment of muscle strength (with particular attention to distal muscle strength and respiratory muscle

Table 5
Clinical manifestations of hypokalemia

Muscle weakness, myalgias, and rhabdomyolysis	Muscle weakness and myalgias usually occur at serum potassium concentrations <2.5 mEg/L.[3,18] They generally start in the lower extremities and can progress to the upper extremities and total paralysis.[18] They can affect the respiratory muscles, causing hypoventilation and respiratory paralysis.[1,3,18] They also affect the smooth muscle of the gastrointestinal tract and can cause ileus.[1,18] Impaired muscle hyperemic response and muscle metabolism can lead to ischemic rhabdomyolysis during exercise[1]
Cardiac arrhythmias	Hypokalemia can lead to arrhythmias including premature atrial and ventricular beats, sinus bradycardia, atrial tachycardia, atrioventricular block, and ventricular tachycardia or fibrillation.[18] Ventricular arrhythmias are associated with myocardial ischemia, heart failure, or left ventricular hypertrophy.[1,3] In addition, hypokalemia can lead to digoxin toxicity.[1] Electrocardiographic changes are listed in **Table 7**
Renal abnormalities	Hypokalemia leads to increased ammonia production and increased bicarbonate reabsorption, leading to metabolic alkalosis.[1,18] In addition, prolonged hypokalemia can lead to impaired urinary concentrating ability, hypokalemic nephropathy, and increase in blood pressure[18]
Glucose intolerance	Glucose intolerance has been attributed to either impaired insulin secretion or peripheral insulin resistance[1]
Hepatic encephalopathy	In individuals with cirrhosis, the increased ammonia production may cause hepatic encephalopathy[18]

Data from Refs.[1,3,18]

Table 6
Clinical manifestations of hyperkalemia

Neuromuscular effects, weakness, paralysis	Hyperkalemia causes muscle weakness, which typically involves the lower extremities. When severe, the weakness can involve the upper extremities or respiratory muscles or cause paralysis.[1,19] Hyperkalemia can cause parasthesias and decreased or absent deep tendon reflexes[5]
Cardiac arrhythmias	Hyperkalemia can manifest with palpitations, syncope, or sudden cardiac death.[4,6] It is associated with the following arrhythmias: sinus bradycardia, sinus arrest, slow idioventricular rhythms, ventricular tachycardia, ventricular fibrillation, and asystole.[1,19] Electrocardiographic changes are listed in **Table 7**
Renal abnormalities	Hyperkalemia interferes with renal ammonium excretion and can lead to metabolic acidosis[1,19]

Data from Refs.[1,4,5,19]

strength), cardiac examination (for evidence of ectopy or arrhythmia), volume status (for evidence of hypovolemia), and gastrointestinal examination (for evidence of ileus or gastrointestinal losses). Further examination should be based on suspected underlying cause of hypokalemia or hyperkalemia.

Which other studies are necessary?

In individuals with symptoms or clinical concern for hypokalemia or hyperkalemia, an initial laboratory value may be sufficient to make the diagnosis. However, if the result is unexpected, the value may need to be verified with repeat testing. For example, in an individual with an unexpected increased serum potassium level without evidence of hyperkalemia, the diagnosis of pseudohyperkalemia (also known as spurious hyperkalemia) must be considered. This condition is common and occurs because of an extracellular potassium shift from the cells in the laboratory specimen, leading to an increased serum potassium measurement, which does not reflect the in vivo serum potassium concentration.[4,20]

An electrocardiogram should be performed in individuals with hypokalemia and hyperkalemia to evaluate for conduction abnormalities or arrhythmias. Electrocardiographic findings are discussed in **Table 7**.

Table 7
Electrocardiographic features of hypokalemia and hyperkalemia

Hypokalemia	Most commonly seen in serum potassium concentrations <2.7 mmol/L. The common changes are decreased or flattening of T wave, ST segment depression, and presence of a U wave (see **Fig. 1**). Other findings include prolonged QT interval (often seen with coexisting hypomagnesemia) and ventricular extrasystoles
Hyperkalemia	The first electrocardiographic changes are tall, sometimes peaked, T waves seen in II, III, V2–V4. Later changes include P wave widening and flattening, PR interval prolongation, loss of P waves, QRS complex widening, and sine wave formation (see **Fig. 2**). Sine wave is a sign of impending cardiac arrest

Adapted from Slovis C, Jenkins R. ABC of clinical electrocardiography: conditions not primarily affecting the heart. BMJ 2002;324:1320, 1321; with permission.

If the cause of hypokalemia is not clinically apparent based on history, examination, and routine laboratory tests, a few laboratory tests can help focus the differential diagnoses. The urinary potassium excretion is best evaluated with a 24-hour urine potassium collection but can be estimated in many cases with spot urine potassium concentration or urine potassium/creatinine ratio. Characterization of the acid-base status can further narrow the differential diagnosis. For example, a spot urine potassium level higher than 40 mmol/L (indicating urinary potassium losses) in the setting of metabolic acidosis can be suggestive of diabetic ketoacidosis, type 1 (distal) renal tubular acidosis or type 2 (proximal) renal tubular acidosis.[21]

In hyperkalemia, laboratory workup should be aimed at finding the underlying cause. Further testing, such as assessment of fractional excretion of potassium and the transtubular potassium gradient, is controversial. Some experts recommend calculation of fractional excretion of potassium and transtubular potassium gradient, because they can be suggestive of inappropriate renal response to hyperkalemia.[4,22] However, other experts argue that urinary potassium excretion in stable hyperkalemia is of limited usefulness because excretion is roughly equal to intake.[14] Furthermore, the calculation of transtubular potassium gradient has been found to produce unreliable results.[14]

What are the electrocardiographic features seen in hypokalemia and hyperkalemia?

There are several electrocardiographic features that sometimes occur in hypokalemia and hyperkalemia (**Figs. 1** and **2**; see **Table 7**). These findings tend to be more pronounced with severe hypokalemia or hyperkalemia but may not be present even in severe cases. An electrocardiogram alone is not sensitive for diagnosing hypokalemia or hyperkalemia.[3,13,23,24]

It is essential to recognize electrocardiographic changes, because this is evidence of action potential derangement in the cardiac tissue and may lead to arrhythmias (see **Tables 5** and **6**).

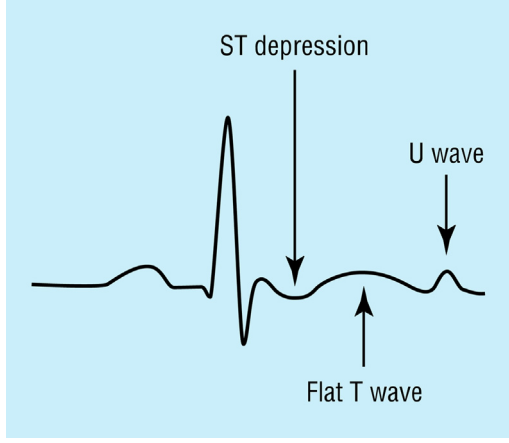

Fig. 1. Electrocardiographic features of hypokalemia. (*From* Slovis C, Jenkins R. ABC of clinical electrocardiography: conditions not primarily affecting the heart. BMJ 2002;324:1320–3; with permission.)

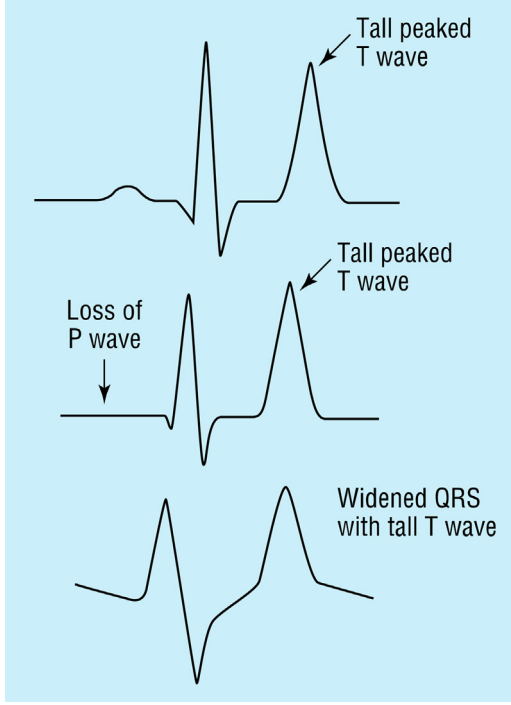

Fig. 2. Electrocardiographic features of hyperkalemia. (*From* Slovis C, Jenkins R. ABC of clinical electrocardiography: conditions not primarily affecting the heart. BMJ 2002;324:1320–3; with permission.)

TREATMENT OF HYPOKALEMIA

What are the general approaches to treating hypokalemia?

To properly treat hypokalemia, it is important to determine the severity, cause, and presence of signs or symptoms. Most individuals require potassium deficit replacement with oral or intravenous potassium salts. In individuals with urinary potassium losses, potassium-sparing diuretics may be beneficial to maintain normal serum potassium levels.[18] The potassium deficit can be roughly estimated by the following formula: serum potassium decreases 0.3 mmol/L per 100 mmol reduction in total body stores.[1,3,18] For example, a serum potassium level of 3.1 mmol/L indicates a body potassium deficit of roughly 300 mmol. This formula does not apply to intracellular redistribution or diabetic ketoacidosis.[18]

Some individuals with hypokalemia have concomitant hypomagnesemia. If hypomagnesemia persists untreated, it can lead to hypokalemia that is refractory to potassium replacement. Thus, magnesium deficit needs to be evaluated and treated in individuals with hypokalemia.[18,25]

How should hypokalemia be treated with potassium deficit replacement?

Most individuals with hypokalemia require potassium deficit replacement. Individuals with serum potassium levels less than 3.0 mmol/L or with symptoms require aggressive

replacement, whereas individuals with mild potassium deficit (3.0–3.5 mmol/L) can be replaced over days to weeks.[1,2,18,26] Individuals with ongoing potassium losses, such as continued diarrhea or urinary losses, may require more potassium replacement until the underlying cause is treated.[18] General treatment recommendations are shown in Table 8.

There are a few notable exceptions to Table 8:

- In individuals who are unable to tolerate oral replacement, intravenous potassium replacement can be considered.
- Certain high-risk groups warrant more aggressive potassium deficit replacement to a goal level of at least 4.0 mmol/L. These high-risk groups include individuals with asymptomatic hypertension, congestive heart failure, cardiac arrhythmias, digoxin use, and myocardial ischemia or myocardial infarction.[26] In addition, individuals with cirrhosis may warrant more aggressive replacement, because hypokalemia can lead to increased ammonia production and the development of hepatic encephalopathy.[18]
- In diabetic ketoacidosis or hyperosmolar hyperglycemia, potassium replacement goals are more aggressive. Insulin therapy should be delayed until the serum potassium level is higher than 3.3 mmol/L, and potassium replacement can begin at serum potassium concentrations 4.5 mmol/L.[18]
- In intracellular redistribution of potassium, such as hypokalemia periodic paralysis, potassium supplementation must be taken with great caution, because rebound hyperkalemia often occurs.[18]

Telemetry should be used in individuals with electrocardiographic features of hypokalemia or who are at risk of developing cardiac arrhythmias or rebound hyperkalemia. In addition, it should be used during intravenous potassium replacement treatment.[13]

Table 8
Treatment of hypokalemia with potassium deficit replacement

Potassium Level (in Mmol/L)	Suggested Treatment
3.6–4.0	Consider increase oral intake of high potassium containing foods (see Table 9)[26]
3.1–3.5	Oral replacement in 10-mmol 20-mmol doses 2 to 4 times per day.[18] Goal replacement is over days to weeks[3,18]
2.6–3.0	Oral replacement in 40-mmol doses 3 to 4 times per day. Can consider IV replacement as well, although some groups recommend IV replacement only for symptomatic hypokalemia or serum potassium levels <2.6 mmol/L.[2] Goal is for rapid correction of serum potassium until symptoms resolve or potassium is >3.0 mmol/L and then continue with reduced dosing. Serum potassium should be checked 2–4 h after dose and should be monitored frequently thereafter[18]
<2.6	Oral replacement in 40-mmol doses 3 or 4 times per day in addition to IV replacement in 10–20 mmol every 2–3 h. Goal replacement is for rapid correction of serum potassium until symptoms resolve or potassium is >3.0 mmol/L and then continue with reduced dosing. Serum potassium should be checked 2–4 h after dose and should be monitored frequently thereafter[18]

Abbreviation: IV, intravenous.
Data from Refs.[2,3,18,26]

Table 9
Potassium content of selected high content foods

Highest content (>25 mmol/100 g)	Dried figs Molasses Seaweed
Very high content (>12.5 mmol/100 g)	Dried fruits Dates Prunes Nuts Avocados Bran cereals Wheat germ Lima beans
High content (>6.2 mmol/100 g)	Vegetables Spinach Tomatoes Broccoli Winter squash Beets Carrots Cauliflower Potatoes Fruits Bananas Cantaloupe Kiwis Oranges Mangos Meats Ground beef Steak Pork Veal Lamb

Data from Refs.[3,18,26]

What are the different types of potassium salts?

The common types and uses of potassium salts are noted in **Table 10**.

What are the risks of oral and intravenous potassium replacement therapy?

Significant hyperkalemia can occur with potassium replacement therapy. The risk is increased with intravenous replacement and in patients with comorbid conditions such as renal insufficiency.[27]

Oral potassium supplementation with potassium chloride is in general well tolerated but is associated with gastric ulceration, gastrointestinal bleeding, nausea, vomiting, abdominal discomfort, diarrhea, and flatulence.[3,18,26]

Intravenous potassium supplementation can commonly cause pain and phlebitis when infused into a peripheral vein. If these symptoms occur, the rate of infusion needs to be slowed or the potassium concentration needs to be decreased.[18] In addition, fatalities have occurred as a result of improper rate or concentration of potassium chloride infusion.[28]

Table 10
Common types of potassium salts

Potassium chloride	The most commonly used potassium replacement regimen. It is an effective treatment regimen for the most common causes of hypokalemia
Potassium phosphate	Indicated for concomitant potassium and phosphate deficiencies
Potassium bicarbonate	Indicated for potassium deficiency in the setting of metabolic acidosis. Potassium acetate is used for intravenous replacement

Data from Refs.[3,18,26]

Which individuals warrant use of potassium-sparing diuretics?

Potassium-sparing diuretics can be used in individuals with renal potassium losses. For instance, some individuals on diuretics require significant daily potassium replacement therapy to match urinary potassium losses. These individuals may require less potassium replacement, or none at all, with the addition of a potassium-sparing diuretic.[3,18] Potassium-sparing diuretics include amiloride, triamterene, spironolactone, and eplerenone. Once initiated, close monitoring of serum potassium is indicated, because hyperkalemia can occur.[3,18]

TREATMENT OF HYPERKALEMIA

What are the general approaches to treating hyperkalemia?

The treatment approach for hyperkalemia is based on the degree and rate of increase, cause, and presence of signs or symptoms. In all cases of hyperkalemia, dietary potassium restriction and discontinuation or dose reduction of medications that cause hyperkalemia may be indicated.

In cases of mild or moderate hyperkalemia without signs or symptoms, treatment may include dietary potassium restriction, discontinuation or dose reduction of medication, and use of diuretic or potassium exchange resin.[4]

In cases of severe hyperkalemia, in addition to dietary and medication adjustments, emergent treatment is indicated. This treatment can include cardiac membrane stabilization, redistribution of potassium into intracellular compartments, and removal of potassium from the body (see **Tables 11** and **12**).[4–7] In addition, these individuals should be monitored with continuous telemetry and serial electrocardiograms.[7]

Which individuals need cardiac membrane stabilization?

Calcium salts antagonize the effects of potassium on cardiac muscle, which reduces membrane excitability and prevents potentially fatal cardiac arrhythmias.[1,4,6,7] There is some disagreement in the literature about when to administer calcium salts for this indication. There is consensus to give calcium supplementation when significant electrocardiographic features of hyperkalemia are present, such as loss of P waves or QRS interval prolongation (but not for peaked T waves alone).[7] Some experts also recommend calcium salt infusion for severe hyperkalemia regardless of the presence of electrocardiographic findings.[4–6]

Calcium gluconate (1000 mg intravenous infusion over 2–5 minutes) or calcium chloride (500–1000 mg intravenous infusion over 2–5 minutes) can be administered for

cardiac membrane stabilization.[7,29] This treatment should always be performed with telemetry, and the dose can be repeated after 5 minutes if electrocardiographic changes persist or recur.[7] The effect lasts for 30 to 60 minutes, so the dose should be given with other therapies to decrease serum potassium levels (see **Table 10**; **Table 11**).[4,6,7]

Calcium salt needs to be infused carefully in individuals on digoxin, because it can increase the cardiotoxic effects of this medication.[4–7] Calcium salt infusion can be irritating to veins, and extravasation can cause tissue necrosis.[5,7] Furthermore, calcium salt should not be given with bicarbonate, because it can precipitate.[7]

Which treatments decrease serum potassium levels by redistributing potassium into the intracellular compartment?

The treatments and characteristics are outlined in **Table 11**. All these treatments lead to a transient reduction in serum potassium. They should be given with treatments to remove potassium from the body (**Table 12**).[4,6,7]

The use of insulin with glucose is well tolerated and is considered to be first-line therapy. β_2-adrenergic agonists are similarly effective to insulin with glucose in most individuals. However, their use is limited by a poor side effect profile and because

Table 11
Severe hyperkalemia treatment: intracellular redistribution

Treatment	Onset of Action; Duration of Action	Dose	Notes
Insulin with glucose	10–20 min; 2–6 h	Intravenous bolus of 10 units of regular insulin with intravenous bolus of 25–50 g of glucose	Continuous dextrose infusion may be necessary to prevent hypoglycemia in some individuals. Blood sugar level needs to be monitored closely to evaluate for hypoglycemia[4–7,30,31]
β_2-Adrenergic agonist	3–5 min; 1–4 h	Albuterol nebulization of 10–20 mg (significantly higher dose than the dose used for bronchoconstriction) over 10 min[7]	There is no significant difference of the effectiveness of nebulization vs intravenous route of administration.[7,30] Individuals can develop tachycardia and tremors, and when coronary artery disease is present, it can cause angina. It may be less effective in individuals taking β-blockers[4–7,31]
Sodium bicarbonate	30–60 min; 2–6 h	150 mmol of bicarbonate in 1 L of 5% dextrose is infused over 2–4 h	This treatment is effective with metabolic acidosis but is otherwise not indicated because of poor effectiveness. It should be used only in adjunct with another therapy[4–7,31]

Data from Refs[4–7,30,31]

Table 12
Severe hyperkalemia treatment: removal of potassium

Treatment	Onset of Action; Duration of Action	Dose	Notes
Diuretics	5–30 min; 2–6 h[5,6]	Furosemide (intravenous, 40–80 mg) or thiazide diuretics with or without saline hydration	Diuretics promote distal nephron flow and urinary potassium secretion. This situation may be useful in an individual with mild to moderate hyperkalemia with normal kidneys or mild to moderate chronic kidney disease. The short-term potassium decreasing effect is modest, and care must be taken to prevent hypovolemia, because this could worsen the hyperkalemia[4–7]
Exchange resins	2–6 h; 4–6 h[5,6]	Sodium polystyrene sulfonate may be used orally (15–30 g) every 4–6 h or as an enema (50 g) every 2–4 h	Exchange resins work by exchanging sodium for potassium ions in the gut and are then removed in the stool. The short-term effectiveness is poor.[4,7] After multiple doses, there is a decrease in serum potassium levels, but it seems no more effective than the use of laxatives.[7,8] Severe side effects are uncommon but do occur, including intestinal necrosis.[7] Some experts have recommended using only sodium polystyrene sulfonate with or without sorbitol in cases of life-threatening hyperkalemia, in which dialysis is not available and other therapies have failed or are not possible.[7] The medication is contraindicated in the postoperative setting, in individuals with an ileus or bowel obstruction[7]
Hemodialysis	Immediate[5,6]		Hemodialysis is the therapy of choice in severe hyperkalemia when the serum potassium level is expected to increase rapidly, in severe renal dysfunction, or when the above medical therapies were contraindicated or ineffective.[4–7] Postdialysis potassium rebound can occur and may require frequent hemodialysis or continuous renal replacement therapy until sufficient potassium is removed[5,7]

Data from Refs.[4–8]

up to 40% of individuals do not respond to treatment. When β_2-adrenergic agonists are used with insulin, they have an additive affect.[4–7,32]

Which treatments decrease serum potassium levels by eliminating potassium from the body?

The therapies in **Table 11** only transiently decrease potassium levels. If potassium is not removed from the body, hyperkalemia returns (with the exception of hyperkalemia caused by redistribution of potassium out of the cells). The treatments and characteristics are noted in **Table 12**.

What long-term changes should be made to prevent hyperkalemia from recurring?

The initial step in preventing hyperkalemia from recurring is to evaluate medications and when possible dose reduce or discontinue medications that can increase potassium levels.[4,7,31] The use of selective β_1-blockers, such as metoprolol, instead of nonselective β-blockers may be warranted.[28] The use of diuretics, such as thiazide diuretics (in individuals with a glomerular filtration rate $\geq$40 mL/min) or loop diuretics (in individuals with a glomerular filtration rate <40 mL/min) may be beneficial in chronic reduction of serum potassium.[4,7,31] The benefit of sodium bicarbonate therapy for the chronic decrease of serum potassium is not clear. However, patients with metabolic acidosis may have benefits independent of potassium decreasing effects.[7] In addition to medication management, a low potassium diet and frequent meals (avoiding fasting) may be beneficial in preventing hyperkalemia.[7]

PRACTICE IMPROVEMENT

What practice improvement recommendations are available for hypokalemia?

There are no current published practice improvement metrics. Previous improvement recommendations have focused on the storage and distribution of potassium chloride. In addition, limits on the rate and concentration of infusion have been widely adopted.[28]

What practice improvement recommendations are available for hyperkalemia?

There are no current published practice improvement metrics in the United States. The UK Renal Association has released audit measures for hyperkalemia, which include[33]:

- All individuals with serum potassium concentration higher than 5.9 mmol/L should have a 12-lead electrocardiogram before treatment. All individuals with an abnormal electrocardiogram should have a repeat electrocardiogram after treatment.
- All individuals with severe hyperkalemia (defined as >6.4 mmol/L) should be placed on continuous telemetry.
- All individuals with severe hyperkalemia should be treated with insulin (and glucose infusion). All individuals treated with insulin should have blood glucose testing performed.
- All individuals with severe hyperkalemia should have repeat potassium testing within 2 hours of treatment.

CLINICAL GUIDELINES

Cohn JN, Kowey PR, Whelton PK, et al. New guidelines for potassium replacement in clinical practice: a contemporary review by the National Council on Potassium in Clinical Practice. Arch Intern Med 2000;160:2429–39.

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