Treatment and prevention of hyperkalemia in adults

AUTHOR: David B Mount, MD
SECTION EDITOR: Richard H Sterns, MD
DEPUTY EDITOR: John P Forman, MD, MSc

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Jan 2024.**
This topic last updated: **Feb 05, 2024.**

INTRODUCTION

Hyperkalemia is a common clinical problem that is most often a result of impaired urinary potassium excretion due to acute or chronic kidney disease (CKD) and/or disorders or drugs that inhibit the renin-angiotensin-aldosterone system (RAAS). Therapy for hyperkalemia due to potassium retention is ultimately aimed at inducing potassium loss [1-3].

In some cases, the primary problem is movement of potassium out of the cells, even though the total body potassium may be reduced. Redistributive hyperkalemia most commonly occurs in uncontrolled hyperglycemia (eg, diabetic ketoacidosis or hyperosmolar hyperglycemic state). In these disorders, hyperosmolality and insulin deficiency are primarily responsible for the transcellular shift of potassium from the cells into the extracellular fluid, which can be reversed by the administration of fluids and insulin. Many of these patients have a significant deficit in whole body potassium and must be monitored carefully for the development of hypokalemia during therapy. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment", section on 'Potassium replacement'.)

The treatment and prevention of hyperkalemia will be reviewed here. The causes, diagnosis, and clinical manifestations of hyperkalemia are discussed separately:

- (See "Causes and evaluation of hyperkalemia in adults".)
- (See "Clinical manifestations of hyperkalemia in adults".)

DETERMINING THE URGENCY OF THERAPY

The urgency of treatment of hyperkalemia varies with the presence or absence of the symptoms and signs associated with hyperkalemia, the severity of the potassium elevation, and the cause of hyperkalemia.

Our approach to therapeutic urgency is as follows (algorithm 1):

- **Hyperkalemic emergency** – In general, the following patients should be considered to have a hyperkalemic emergency and should therefore be treated with rapidly acting therapies (ie, intravenous calcium, insulin, and glucose) in addition to therapies that remove potassium from the body (such as hemodialysis, gastrointestinal potassium binders, or diuretics) (see 'Patients with a hyperkalemic emergency' below):

  - Patients who have clinical signs or symptoms of hyperkalemia. The most serious manifestations of hyperkalemia are muscle weakness or paralysis, cardiac conduction abnormalities, and cardiac arrhythmias, including sinus bradycardia, sinus arrest, slow idioventricular rhythms, ventricular tachycardia, ventricular fibrillation, and asystole. These manifestations usually occur when the serum potassium concentration is ≥7 mEq/L with chronic hyperkalemia, or possibly at lower levels in patients with an acute rise in serum potassium and/or underlying cardiac conduction disease. (See "Clinical manifestations of hyperkalemia in adults".)

    There are several characteristic electrocardiogram (ECG) abnormalities associated with hyperkalemia (figure 1). A tall peaked T wave with a shortened QT interval is the earliest change (waveform 1), followed by progressive lengthening of the PR interval and QRS duration (waveform 2). The P wave may disappear, and ultimately, the QRS widens further to a sine wave. Ventricular standstill with a flat line on the ECG ensues with complete absence of electrical activity. The progression and severity of ECG changes do not correlate well with the serum potassium concentration. Conduction abnormalities, such as bundle branch blocks and arrhythmias (sinus bradycardia, sinus arrest, slow idioventricular rhythms, ventricular tachycardia, ventricular fibrillation, pseudo-ST-elevation myocardial infarction, pseudo-Brugada patterns, and asystole) may also occur in hyperkalemia [4]. (See "Clinical manifestations of hyperkalemia in adults", section on 'ECG changes'.)

  - Patients with severe hyperkalemia (serum potassium greater than 6.5 mEq/L), especially if there is concurrent tissue breakdown or gastrointestinal bleeding, even if there are no clinical signs or symptoms.

- Some patients with moderate hyperkalemia (>5.5 mEq/L) who have significant kidney function impairment and marked, ongoing tissue breakdown (eg, rhabdomyolysis or crush injury, tumor lysis syndrome), ongoing potassium absorption (eg, from substantial gastrointestinal bleeding), or a significant nonanion gap metabolic acidosis or respiratory acidosis. Tissue breakdown can release large amounts of potassium from cells, which can lead to rapid and substantial elevations in serum potassium. Potassium absorption from the blood in the gastrointestinal tract or soft tissues can produce similar rapid increases in the serum potassium. Patients with a nongap acidosis or respiratory acidosis may develop severe hyperkalemia quickly if the acidosis worsens, or if they develop an additional superimposed metabolic or respiratory acidosis, particularly when kidney function is impaired. (See "Crush-related acute kidney injury" and "Tumor lysis syndrome: Pathogenesis, clinical manifestations, definition, etiology and risk factors" and "Prevention and treatment of heme pigment-induced acute kidney injury (including rhabdomyolysis)" and "Potassium balance in acid-base disorders".)

- **Patients needing prompt therapy** – Some patients without a hyperkalemic emergency should, nonetheless, have their potassium lowered promptly (ie, within 6 to 12 hours). Such patients include hemodialysis patients who present outside of regular dialysis hours, patients with marginal kidney function and/or marginal urine output, or hyperkalemic patients who need to be optimized for surgery. Measures such as isotonic bicarbonate infusion, intravenous 5 percent dextrose in water infusion overnight (to stimulate insulin in a fasting patient), or hemodialysis may be appropriate in these settings. Additional measures can include oral potassium binders or kaliuresis induced by intravenous saline with diuretic therapy. (See 'Patients who need prompt serum potassium reduction' below.)

- **Patients who can have the potassium lowered slowly** – Most patients with hyperkalemia have chronic, mild (≤5.5 mEq/L) or moderate (5.5 to 6.5 mEq/L) elevations in serum potassium due to chronic kidney disease (CKD) or the use of medications that inhibit the renin-angiotensin-aldosterone system ([RAAS] or both). Such patients do not require urgent lowering of the serum potassium and can often be treated with dietary modification, use of diuretics (if otherwise appropriate), treatment of chronic metabolic acidosis, or reversal of factors that can cause hyperkalemia (eg, nonsteroidal antiinflammatory drugs, hypovolemia). In some instances, drugs that inhibit the RAAS are reduced or discontinued, and drugs that remove potassium by gastrointestinal cation exchange are prescribed for chronic use. (See 'Patients who can have the serum potassium lowered slowly' below.)

PATIENTS WITH A HYPERKALEMIC EMERGENCY

Identifying patients who have a hyperkalemic emergency is presented above (algorithm 1). (See 'Determining the urgency of therapy' above.)

A table summarizing the initial assessment and management of patients with a hyperkalemic emergency is provided (table 1).

Treatment approach to hyperkalemic emergencies — Patients with a hyperkalemic emergency should generally receive (table 1 and table 2):

- Intravenous calcium to antagonize the membrane actions of hyperkalemia (if electrocardiogram (ECG) changes consistent with hyperkalemia are present). In addition, some experts give intravenous calcium to all patients with a potassium >6.5 mEq/L (even if notable ECG changes are absent), an approach supported by the Kidney Disease: Improving Global Outcomes (KDIGO) expert panel [1]. However, other experts administer intravenous calcium only if ECG abnormalities associated with hyperkalemia are present. (See 'Calcium' below.)

- Intravenous insulin (typically given with intravenous glucose to avoid hypoglycemia) to drive extracellular potassium into cells. (See 'Insulin with glucose' below.)

- Therapy to rapidly remove excess potassium from the body (ie, loop or thiazide diuretics if kidney function is not severely impaired, a gastrointestinal cation exchanger, and/or dialysis [preferably hemodialysis] if kidney function is severely impaired). (See 'Remove potassium from the body' below.)

  Urgent nephrology consultation to coordinate these therapies is appropriate in patients with a hyperkalemic emergency in the setting of kidney function impairment.

- Treatment of reversible causes of hyperkalemia, such as correcting hypovolemia and discontinuing drugs that increase the serum potassium (eg, nonsteroidal antiinflammatory drugs, inhibitors of the renin-angiotensin-aldosterone system) (table 3 and table 4). (See "Causes and evaluation of hyperkalemia in adults" and 'Drug-induced hyperkalemia' below.)

Intravenous calcium and insulin are rapidly acting treatments that provide time for the initiation of therapies that remove the excess potassium from the body (table 1).

Monitoring — Continuous cardiac monitoring and serial ECGs are warranted in patients with hyperkalemia who require rapidly acting therapies. The serum potassium should be measured at one to two hours after the initiation of treatment. The timing of further measurements is determined by the serum potassium concentration and the response to therapy. Patients who receive insulin, with or without dextrose, should undergo hourly glucose measurements for up to six hours in order to monitor for hypoglycemia.

Administer rapidly acting therapies

Calcium — Calcium directly antagonizes the membrane actions of hyperkalemia [5], while hypocalcemia increases the cardiotoxicity of hyperkalemia [6]. As discussed elsewhere, hyperkalemia-induced depolarization of the resting membrane potential leads to inactivation of sodium channels and decreased membrane excitability. (See "Clinical manifestations of hyperkalemia in adults", section on 'Pathogenesis'.)

The effect of intravenous calcium administration begins within minutes but is relatively short lived (30 to 60 minutes). As a result, calcium should not be administered as monotherapy for hyperkalemia but should rather be combined with therapies that drive extracellular potassium into cells. Administration of calcium can be repeated every 30 to 60 minutes if the hyperkalemic emergency persists and the serum calcium does not become elevated. (See 'Insulin with glucose' below.)

Calcium can be given as either calcium gluconate or calcium chloride. Calcium chloride contains three times the concentration of elemental calcium compared with calcium gluconate (13.6 versus 4.6 mEq in 10 mL of a 10 percent solution). However, calcium gluconate is generally preferred because calcium chloride may cause local irritation at the injection site [3].

The usual dose of calcium gluconate is 1000 mg (10 mL of a 10 percent solution) infused over two to three minutes, with constant cardiac monitoring. The usual dose of calcium chloride is 500 to 1000 mg (5 to 10 mL of a 10 percent solution), also infused over two to three minutes, with constant cardiac monitoring. The dose of either formulation can be repeated after five minutes if the ECG changes persist or recur.

Concentrated calcium infusions (particularly calcium chloride) are irritating to veins, and extravasation can cause tissue necrosis. As a result, a central or deep vein is preferred for administration of calcium chloride. Calcium gluconate can be given peripherally, ideally through a small needle or catheter in a large vein. Calcium should **not** be given in bicarbonate-containing solutions, which can lead to the precipitation of calcium carbonate.

When hyperkalemia occurs in patients treated with digitalis, calcium should be administered for the same indications as in patients not treated with digitalis (eg, widening of the QRS complex or loss of P waves) even though hypercalcemia potentiates the cardiotoxic effects of digitalis. In such patients, a dilute solution can be administered slowly, infusing 10 mL of 10 percent calcium gluconate in 100 mL of 5 percent dextrose in water over 20 to 30 minutes, to avoid acute hypercalcemia [2]. In patients with hyperkalemia due to digitalis toxicity, the administration of digoxin-specific antibody fragments is the preferred therapy. (See "Digitalis (cardiac glycoside) poisoning", section on 'Electrolyte abnormalities'.)

Insulin with glucose — Insulin administration lowers the serum potassium concentration by driving potassium into the cells, primarily by enhancing the activity of the Na-K-ATPase pump in skeletal muscle [2,7]. Glucose is usually given with insulin to prevent the development of hypoglycemia. However, insulin should be given alone if the serum glucose is ≥250 mg/dL (13.9 mmol/L) [8]. The serum glucose should be measured every hour for five to six hours after the administration of insulin, given the risk of hypoglycemia.

The potassium-lowering effect of insulin is greatest at the high insulin levels achieved by a bolus injection. Administration of 10 units of regular insulin, followed immediately by 50 mL of 50 percent dextrose (25 g of glucose) leads to a relatively rapid reduction in serum potassium by approximately 1 mEq/L. However, high insulin levels, which are required for the maximal hypokalemic effect, are not sustained long after a single 10 unit bolus [9,10]. Yet the insulin levels remain high enough to cause hypoglycemia, which occurred in 6 to 19 percent of patients in two studies [11,12]. Thus, when glucose is given as a single bolus, hypoglycemia often develops an hour or more after the start of therapy for two reasons:

- The amount of glucose in a single bolus is insufficient to replace the glucose utilized in response to exogenous insulin.
- Insulin's prolonged half-life in patients with kidney disease leads to insulin levels high enough to promote glucose utilization for more than an hour.

The incidence of hypoglycemia depends more upon the dose of glucose than upon the dose of insulin [9,10]. To avoid hypoglycemia, we recommend infusion of 10 percent dextrose at 50 to 75 mL/hour after the initial 25 g bolus and close monitoring of blood glucose levels every hour for five to six hours.

The administration of glucose without insulin is **not** recommended, since the release of endogenous insulin can be variable and the attained insulin levels are generally lower with a glucose infusion alone [13]. Furthermore, in susceptible patients (primarily diabetic patients with hyporeninemic hypoaldosteronism), hypertonic glucose in the absence of insulin may

acutely increase the serum potassium concentration by raising the plasma osmolality, which promotes water and potassium movement out of the cells [14-16].

The effect of insulin begins in 10 to 20 minutes, peaks at 30 to 60 minutes, and lasts for four to six hours [17-20]. In almost all patients, the serum potassium concentration drops by 0.5 to 1.2 mEq/L [20-23]. In particular, although patients with kidney failure are resistant to the glucose-lowering effect of insulin, they are not resistant to the hypokalemic effect, because Na-K-ATPase activity is still enhanced [24,25]. (See "Carbohydrate and insulin metabolism in chronic kidney disease".)

Repeated dosing — Removal of excess potassium from the body (eg, with hemodialysis or a gastrointestinal cation exchanger) is sometimes not feasible or must be delayed. Such patients can be treated with either a continuous infusion of insulin and glucose or bolus infusions of insulin with glucose, repeated every two to four hours, with serial monitoring of blood glucose levels. Compared with single-dose management, the risk of hypoglycemia is higher with repeated doses [12].

Remove potassium from the body — The effective modalities described above only transiently lower the serum potassium concentration. Thus, additional therapy is typically required to remove excess potassium from the body, except in patients who have reversible hyperkalemia resulting from increased potassium release from cells due, for example, to metabolic acidosis or insulin deficiency and hyperglycemia. (See "Causes and evaluation of hyperkalemia in adults", section on 'Increased potassium release from cells'.)

The three available modalities for potassium removal are diuretics, gastrointestinal cation exchangers (eg, patiromer, sodium polystyrene sulfonate [SPS], and sodium zirconium cyclosilicate [SZC]), and dialysis (which, if available, is the most efficient method to remove potassium). In patients with a hyperkalemic emergency, diuretics should **not** be the only method used to remove potassium from the body.

Loop diuretics in patients without severe kidney function impairment — Loop diuretics increase potassium loss in the urine in patients with normal or mild to moderately impaired kidney function, particularly when combined with saline hydration to maintain distal sodium delivery and flow. However, patients with persistent hyperkalemia typically have impaired renal potassium secretion, and there are no data demonstrating a clinically important short-term kaliuretic response to diuretic therapy. Thus, diuretics should **not** be used as the only means to remove potassium from the body in patients with a hyperkalemic emergency.

In hypervolemic patients with preserved kidney function (eg, patients with heart failure), we administer 40 mg of intravenous furosemide every 12 hours or a continuous furosemide

infusion. In euvolemic or hypovolemic patients with preserved kidney function, we administer isotonic saline at a rate that is appropriate to replete hypovolemia and maintain euvolemia, followed by 40 mg of intravenous furosemide every 12 hours or a continuous furosemide infusion.

If kidney function is not preserved, we use a combination of an intravenous isotonic bicarbonate or isotonic saline infusion plus intravenous furosemide at doses that are appropriate for the patient's kidney function. (See "Loop diuretics: Dosing and major side effects".)

Dialysis and gastrointestinal cation exchangers — Gastrointestinal cation exchangers, including patiromer, SZC, and SPS, bind potassium in the gastrointestinal tract in exchange for other cations, such as sodium or calcium. Such therapies can be used to treat hyperkalemia in patients with or without severe kidney function impairment.

Hemodialysis in patients with severe kidney dysfunction — Urgent nephrology consultation is appropriate for all patients with a hyperkalemic emergency and kidney function impairment (regardless of severity). Hemodialysis is indicated in hyperkalemic patients with severe kidney function impairment, and is preferable to cation exchangers if the patient has functioning vascular access for dialysis and if the procedure can be performed without delay. However, if hemodialysis cannot be performed promptly (eg, within six hours), we administer gastrointestinal cation exchange therapy (preferably **not** SPS) and then perform hemodialysis as soon as possible.

Patiromer or sodium zirconium cyclosilicate (SZC) — When using a cation exchanger in patients with a hyperkalemic emergency, we use SZC (10 g three times daily for 48 hours) or patiromer (8.4 g, repeated daily as needed) rather than SPS. If available, SZC is generally preferred over patiromer because of its more rapid onset of action. Both SZC and patiromer can acutely reduce serum potassium in patients with hyperkalemic emergency [26-28], although data are somewhat limited. The hypokalemic effect of SZC, for example, can be appreciated within one hour, with a mean reduction in serum potassium of 0.37 mEq/L four hours after a 10 g dose [29]. Our approach to dosing is based upon short-term effects of these drugs in a separate patient population (ie, those treated for chronic moderate hyperkalemia). (See 'Patiromer' below and 'Sodium zirconium cyclosilicate (SZC)' below.)

Sodium polystyrene sulfonate (SPS) in rare settings — We do **not** use sodium polystyrene sulfonate (SPS) if patiromer or SZC are available [30,31]. If necessary, SPS can lower the serum potassium in patients presenting with a hyperkalemic emergency [32,33]. In one retrospective uncontrolled study, for example, 501 patients with acute hyperkalemia were

treated with 15 to 60 g of SPS; serum potassium decreased by a mean of 0.93 mEq/L by the time the serum potassium was measured again (typically within 24 hours) [33]. However, adverse effects were common and two patients developed bowel necrosis, a well-described complication of SPS [34-38].

SPS with or without sorbitol should **not** be given to the following patients because they may be at high risk for intestinal necrosis [35,36,39,40]:

- Postoperative patients
- Patients with an ileus
- Patients with a large or small bowel obstruction
- Patients with constipation or at risk of becoming constipated (eg, due to opioid use)
- Patients with underlying bowel disease, eg, ulcerative colitis or *Clostridioides difficile* colitis

Even if restoration of kidney function or dialysis is not possible or immediately available, SPS should **not** be given in these high-risk settings; if other cation exchangers are not available, such patients can be managed with repeated doses of insulin and glucose (or continuous infusions) until dialysis can be performed. Other measures include the administration of isotonic bicarbonate and high-dose diuretics (if there is residual urine output). (See 'Sodium bicarbonate' below.)

Thus, we suggest that SPS be used (in conjunction with the rapidly acting transient therapies mentioned above) **only** in a patient who meets **all** of the following criteria:

- Patient has potentially life-threatening hyperkalemia
- Dialysis is not readily available
- Newer cation exchangers (ie, patiromer or SZC) are not available
- Other therapies to remove potassium (eg, diuretics, rapid restoration of kidney function) have failed or are not possible

In addition, if SPS is used, other orally administered drugs should be taken at least three hours before or three hours after the dose of SPS [41]. SPS binds to and prevents the absorption of many common medications.

The majority of intestinal necrosis cases associated with SPS occurred when the resin was administered with sorbitol [34-38]. In addition, intestinal necrosis was induced in a rat model by sorbitol alone or by sorbitol mixed with SPS but not with SPS alone [37]. Thus, it was presumed that sorbitol was required for the intestinal injury. As a result, the US Food and Drug Association (FDA) issued a recommendation in September 2009 that SPS should no longer be administered in sorbitol [34]. Despite this, many hospitals and pharmacies only stock sodium polystyrene

sulfonate premixed in sorbitol. SPS alone is not always available and, when available, comes as a powder that must be reconstituted.

However, the association of SPS in sorbitol with intestinal necrosis may be coincidental since sorbitol is so widely used in conjunction with SPS. In addition, contemporary studies have found that SPS alone can cause intestinal necrosis in rats and have suggested that the previously noted toxicity of sorbitol alone in rats may have resulted from the hypertonic solution in which it was suspended [42].

Multiple clinical cases of intestinal necrosis with SPS and similar cation exchange resins without sorbitol have been reported [43-46]. Intestinal necrosis has also been reported in patients receiving SPS in a reduced concentration (33 percent) of sorbitol [34]. Evidence of gastrointestinal toxicity with SPS has also been noted in large observational studies:

- In a propensity-matched case-control study of more than 40,000 older adults spanning periods before and after the recommendation against mixing SPS with sorbitol [47], the incidence of serious adverse gastrointestinal events at 30 days, defined as hospitalization or emergency evaluation for intestinal ischemia, thrombosis, ulceration, perforation, resection, or ostomy, was twice as high among those treated with SPS compared with those who were not (0.2 versus 0.1 percent; hazard ratio 1.94, 95% CI 1.10-3.41).

- A Swedish study of 19,530 SPS-naïve patients with stage 4 or 5 chronic kidney disease (CKD), including patients with end-stage kidney disease (ESKD), identified 202 severe and 1149 minor gastrointestinal events among 3690 patients who received SPS without sorbitol [48]. Initiation of SPS was associated with a higher incidence of severe adverse events (adjusted hazard ratio 1.25, 95% CI 1.05-1.49), primarily ulcers and perforations. Most patients (85 percent) were given lower dosages than specified on the product label, and patients receiving higher doses had a higher incidence of adverse events. Notably, SPS is commonly prescribed on a chronic basis to dialysis patients in Sweden (20 to 25 percent) and France (40 to 45 percent), while in the United Kingdom and the United States, SPS is prescribed to less than 5 percent of dialysis patients.

Thus, intestinal injury appears to be an important complication of SPS and is likely independent of sorbitol.

If given, SPS with or without sorbitol can be administered orally, and SPS without sorbitol can be administered as a retention enema. Oral dosing is probably more effective if intestinal motility is not impaired. The oral dose is usually 15 to 30 g, which can be repeated every four to six hours as necessary. Single doses are probably less effective [49].

If given as an enema, 50 g of SPS is mixed with 150 mL of tap water (**not** sorbitol). After cleansing enema with tap water at body temperature, the resin emulsion should be administered at body temperature through a rubber tube placed at approximately 20 cm from the rectum with the tip well into the sigmoid colon. The emulsion should be introduced by gravity and flushed with an additional 50 to 100 mL of non-sodium-containing fluid. The emulsion should be kept in the colon for at least 30 to 60 minutes and, preferably, two to four hours, followed by a cleansing enema (250 to 1000 mL of tap water at body temperature) [50]. The enema can be repeated every two to four hours, as necessary.

Other therapies — Beta-2-adrenergic agonists (eg, inhaled albuterol) and intravenous sodium bicarbonate have been studied as potential rapidly acting therapies to reduce the serum potassium in hyperkalemic patients. Although they can be used in addition to calcium, insulin (with glucose), and potassium removal therapy, they should **not** be used in place of these treatments.

Beta-2-adrenergic agonists — Given the potential adverse effects described below, the authors and reviewers of this topic believe that intravenous epinephrine should **not** be used in the treatment of hyperkalemia. Albuterol is not frequently used but can be considered as transient therapy in patients who have symptoms or serious ECG manifestations of hyperkalemia despite therapy with calcium and insulin with glucose, or in patients in whom dialysis is not appropriate or not feasible.

Like insulin, the beta-2-adrenergic agonists drive potassium into the cells by increasing the activity of the Na-K-ATPase pump in skeletal muscle [2,51]. Beta-2-adrenergic receptors in skeletal muscle also activate the inwardly directed Na-K-2Cl cotransporter, which may account for as much as one-third of the uptake response to catecholamines [52].

Beta-2-adrenergic agonists can be effective in the acute treatment of hyperkalemia, lowering the serum potassium concentration by 0.5 to 1.5 mEq/L [13,17,22,53,54]. Albuterol, which is relatively selective for the beta-2-adrenergic receptors, can be given as 10 to 20 mg in 4 mL of saline by nebulization over 10 minutes (which is 4 to 8 times the dose used for bronchodilation). Alternatively and where available, albuterol 0.5 mg can be administered by intravenous infusion. In patients who cannot tolerate nebulized albuterol, and if intravenous therapy is not available, subcutaneous terbutaline is a potential alternative [54]. The peak effect is seen within 30 minutes with intravenous infusion and at 90 minutes with nebulization [53].

Albuterol and insulin with glucose have an additive effect, reducing serum potassium concentration by approximately 1.2 to 1.5 mEq/L [17,20,55]. Thus, although albuterol should not be used as monotherapy in hyperkalemic patients with ESKD, it can be added to insulin plus

glucose to maximize the reduction in serum potassium [17]. One problem in patients on maintenance hemodialysis is that lowering the serum potassium concentration by driving potassium into the cells can diminish subsequent potassium removal during the dialysis session (from 50 to 29 mEq in one report), possibly leading to rebound hyperkalemia after dialysis [56].

Potential side effects of the beta-2 agonists include mild tachycardia and the possible induction of angina in susceptible subjects. Thus, these agents should probably be avoided in patients with active coronary disease. In addition, all patients with ESKD should be monitored carefully since they may have subclinical or overt coronary disease. (See "Risk factors and epidemiology of coronary heart disease in end-stage kidney disease (dialysis)".)

Sodium bicarbonate — Sodium bicarbonate has limited efficacy in lowering the serum potassium in the acute setting, even in patients with metabolic acidosis [22,57-59]; therefore, we do not use bicarbonate therapy as the only treatment in the acute management of hyperkalemia.

Raising the systemic pH with sodium bicarbonate results in hydrogen ion release from the cells as part of the buffering reaction. This change is accompanied by potassium movement into the cells to maintain electroneutrality. The use of bicarbonate for the treatment of hyperkalemia was mainly based upon small uncontrolled clinical studies [60-62]. However, in a study that compared different potassium-lowering modalities in 10 patients undergoing maintenance hemodialysis, a bicarbonate infusion (isotonic or hypertonic) for up to 60 minutes had no effect on the serum potassium concentration [22]. This lack of benefit was confirmed in several subsequent studies of hemodialysis patients [57-59].

However, bicarbonate therapy appears to be beneficial in patients with metabolic acidosis, particularly when administered as an isotonic infusion rather than bolus ampules of hypertonic sodium bicarbonate [22]. In one series, for example, the administration of isotonic sodium bicarbonate in a constant infusion to patients with a baseline serum bicarbonate of 18 mEq/L had little effect at one and two hours but significantly lowered the serum potassium from 6 mEq/L at baseline to 5.4 and 5.3 mEq/L at four and six hours, respectively; the serum bicarbonate increased to 28 mEq/L at one hour and 30 mEq/L at six hours [58].

In addition, acute or chronic bicarbonate (alkali) therapy may be warranted to treat acidemia independent of hyperkalemia [61]. (See "Approach to the adult with metabolic acidosis", section on 'Overview of therapy' and "Pathogenesis, consequences, and treatment of metabolic acidosis in chronic kidney disease".)

When bicarbonate is given in the acute setting, we recommend the administration of an isotonic solution (eg, 150 mEq in 1 L of 5 percent dextrose in water over two to four hours),

assuming the patient can tolerate the volume load. There is a potential hazard of giving hypertonic solutions, such as the standard ampule of 50 mEq of sodium bicarbonate in 50 mL. In addition, multiple doses can lead to hypernatremia [22].

Over the long term, in patients with chronic kidney disease (CKD), there are a variety of benefits from treating metabolic acidosis, and alkali therapy is recommended to maintain a near-normal serum bicarbonate, independent of any effect on the serum potassium concentration. (See "Pathogenesis, consequences, and treatment of metabolic acidosis in chronic kidney disease", section on 'Treatment of metabolic acidosis in CKD'.)

PATIENTS WITHOUT A HYPERKALEMIC EMERGENCY

Identifying patients who do **not** have a hyperkalemic emergency is presented above. (See 'Determining the urgency of therapy' above.)

Patients who do not have a hyperkalemic emergency can generally be divided into two groups (algorithm 1) (see 'Determining the urgency of therapy' above):

- Those who, despite needing to have their potassium lowered promptly, do not require rapidly acting therapy with calcium and insulin with glucose. Such patients with severe kidney function impairment are typically treated with dialysis (preferably hemodialysis) with or without the use of a gastrointestinal cation exchanger (eg, patiromer). In patients with normal kidney function or mild to moderate kidney function impairment, correcting the cause of hyperkalemia (eg, drugs, hypovolemia) will generally suffice, in addition to treatment with saline infusion and loop diuretics.

- Those who can safely have their serum potassium lowered slowly. Such patients can usually be treated with therapies that gradually reduce the serum potassium, such as a low-potassium diet, loop or thiazide diuretics, or a reduction or cessation of medicines that can increase the serum potassium. With the introduction of patiromer and sodium zirconium cyclosilicate (SZC), it is anticipated that gastrointestinal cation exchangers will be utilized more frequently in these patients for chronic control of the serum potassium.

Patients who need prompt serum potassium reduction — Identifying patients who should have their serum potassium promptly lowered but who do not require rapidly acting therapy (ie, calcium and insulin with glucose), is presented above. (See 'Determining the urgency of therapy' above.)

Those with severe kidney function impairment — In patients with severe kidney function impairment who need prompt serum potassium reduction (ie, within 6 to 12 hours), dialysis should be performed right away if it is logistically feasible (ie, regular working hours, availability of staff, and presence of a suitable vascular access). Hemodialysis can normalize the serum potassium within four hours [63]. If prompt dialysis is not logistically feasible, then a gastrointestinal cation exchanger (preferably patiromer or SZC, if and when available) can be used to remove potassium from the body until such time that dialysis can be performed. (See 'Gastrointestinal cation exchangers' below.)

Dialysis — Dialysis is indicated in hyperkalemic patients with severe kidney function impairment. Hemodialysis is preferred since the rate of potassium removal is many times faster than with peritoneal dialysis [64]. Hemodialysis can remove 25 to 50 mEq of potassium per hour, with variability based upon the initial serum potassium concentration, the type and surface area of the dialyzer used, the blood flow rate, the dialysate flow rate, the duration of dialysis, the potassium concentration of the dialysate, and the patient's muscle mass [2,18].

One of the major determinants of the rate of potassium removal is the potassium gradient between the plasma and dialysate. Issues related to the removal of potassium with hemodialysis and potential adverse effects are discussed in detail separately. (See "Acute hemodialysis prescription".)

A rebound increase in serum potassium concentration occurs after hemodialysis in all patients in whom potassium is removed since the reduction in serum potassium during dialysis creates a gradient for potassium movement out of the cells. The magnitude of this effect was evaluated in a study of 14 stable maintenance hemodialysis patients [65]. The average serum potassium concentrations at baseline, during hemodialysis, and up to six hours after hemodialysis were 5.7, 3.6, and 5 mEq/L, respectively. Thus, the serum potassium concentration should usually not be measured soon after the completion of hemodialysis, since the results are likely to be misleading.

The postdialysis rebound after hemodialysis is more pronounced in patients undergoing acute hemodialysis for hyperkalemia due to massive release of potassium from injured cells (eg, tumor lysis, rhabdomyolysis) and after regular maintenance hemodialysis in patients with a high predialysis serum potassium concentration [65].

Rapidly acting transient therapies given before dialysis, such as insulin with glucose or albuterol, have a twofold effect: Total potassium removal is reduced due to lowering of the serum potassium concentration [56,66]; and the potassium rebound is greater because of the wearing off of the effect of the transient therapies. The potassium rebound is also increased

with a high-sodium dialysate since the increase in plasma osmolality creates a gradient for water and then potassium efflux from the cells [67].

Patients who have a large postdialysis rebound may require daily dialysis or continuous kidney replacement therapy to avoid recurrent severe hyperkalemia.

Those without severe kidney function impairment — Patients who have moderate hyperkalemia and either normal kidney function or mild to moderate kidney function impairment can usually be managed without dialysis. Treatment of such patients typically includes a gastrointestinal cation exchanger in addition to reversing the cause of hyperkalemia. As an example, a patient with moderate chronic kidney disease (CKD) treated with a renin-angiotensin-aldosterone system (RAAS) inhibitor who presents with a serum potassium of 6.0 mEq/L may be treated with a cation exchanger (such as patiromer), temporary discontinuation of the RAAS inhibitor, as well as other therapies that are appropriate for the clinical setting (ie, bicarbonate therapy if the patient has metabolic acidosis, and diuretic therapy if the patient is hypervolemic).

Patients who can have the serum potassium lowered slowly — Identifying patients who do not need prompt lowering of the serum potassium and can be safely treated with therapy that gradually lowers the serum potassium is presented above. (See 'Determining the urgency of therapy' above.)

Hyperkalemia can be corrected in these patients over a matter of days to weeks, depending upon the clinical circumstance. Serum potassium should be monitored over the equivalent time frame, so as to follow the response to therapy and detect iatrogenic hypokalemia.

In addition to correcting reversible causes of hyperkalemia, our approach in such patients is as follows:

- All such patients should receive dietary counseling to reduce potassium intake (table 5). (See "Patient education: Low-potassium diet (The Basics)" and "Patient education: Low-potassium diet (Beyond the Basics)" and 'Dietary modification' below.)
- In addition, thiazide or loop diuretics can be used in patients who have hypertension or hypervolemia. (See 'Diuretics' below.)
- Patients who continue to have moderate hyperkalemia despite dietary modification and diuretics can be treated chronically with newer gastrointestinal cation exchangers (eg, patiromer). (See 'Gastrointestinal cation exchangers' below.)

Dietary modification — It is rare for hyperkalemia to occur exclusively due to excessive intake, although such cases have been described [68,69]. By contrast, the presence of kidney disease predisposes to hyperkalemia in patients consuming potassium [70]. In addition to kidney function impairment, other predisposing factors include hypoaldosteronism and drugs that inhibit the RAAS can result in significant hyperkalemia after only modest intake of potassium. Such patients should be assessed for their intake of potassium-rich foods (refer to https://www.kidney.org/atoz/content/potassium), and counseled to avoid these foods (table 6). Other, occult sources of excessive potassium include salt substitutes [71,72], various forms of pica [73], and "alternative" nutritional therapies [74,75]. Often, the adoption of a potassium-restricted diet (refer to https://www.kidney.org/atoz/content/potassium) normalizes serum potassium levels and affords the resumption of RAAS antagonists (table 7), even in patients with CKD.

Diuretics — Loop and thiazide diuretics increase potassium loss in the urine in patients with normal or mild to moderately impaired kidney function, particularly when combined with saline hydration to maintain distal sodium delivery and flow. However, patients with persistent hyperkalemia typically have impaired renal potassium secretion, and there are no data demonstrating a clinically important short-term kaliuretic response to diuretic therapy.

Although data are limited, chronic diuretic therapy is probably effective over the long term by increasing urinary potassium excretion, particularly in patients with mild to moderate CKD [76]. For patients with moderate hyperkalemia whose kidney function is not severely impaired, we suggest a trial of diuretics if otherwise appropriate (eg, hypertension or hypervolemia). Among patients with hyperkalemia due to angiotensin inhibitors, many can be controlled with a low-potassium diet and diuretic therapy.

Gastrointestinal cation exchangers — Patiromer and SZC are nonabsorbable compounds that exchange calcium or sodium and hydrogen, respectively. We do **not** use sodium polystyrene sulfonate (a cation exchange resin) as chronic therapy for such patients.

Patiromer — Patiromer is a spherical, nonabsorbable organic polymer, formulated as a powder for suspension, which binds potassium in the colon in exchange for calcium [77,78].

In a phase II, open-label dose-finding trial (AMETHYST-DN), 306 diabetic patients with an estimated glomerular filtration rate (eGFR) of 15 to 59 mL/min/1.73 m^2 and either mild or moderate hyperkalemia (serum potassium of 5.1 to 5.5, or 5.6 to 5.9 mEq/L, respectively) were randomly assigned to a range of initial patiromer doses (4.2 g twice daily to 16.8 g twice daily) [79]; follow-up was 52 weeks. All patients were also treated with stable doses of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB), or both, often in

combination with spironolactone. At four weeks, the change in serum potassium from baseline ranged from -0.35 to -0.55 mEq/L with initial doses of 4.2 g twice daily to 12.6 g twice daily among those with mild hyperkalemia, and from -0.87 to -0.97 mEq/L with initial doses of 8.4 g twice daily to 12.6 g twice daily among those with moderate hyperkalemia. Approximately one-third of patients had a single adjustment (up or down) to their patiromer dose; most required no adjustment. At 52 weeks, serum potassium concentrations remained in the normal range with continued patiromer therapy. Discontinuation of patiromer resulted in an increase in the serum potassium within three days.

There were no treatment-related serious adverse events in AMETHYST-DN. The most common treatment-related side effects included constipation (6.3 percent of patients) and hypomagnesemia (8.6 percent of patients). Hypomagnesemia occurred more commonly with higher doses of patiromer (16.7 percent among those assigned 33.6 g/day compared with 5.4 percent among those assigned 8.4 g/day). Severe hypomagnesemia (a serum magnesium <1.2 mg/dL) developed in 13 patients (4.3 percent).

The OPAL-HK study extended these observations in a phase III, randomized placebo-controlled trial in outpatients with CKD and hyperkalemia [80]. In OPAL-HK, 243 patients with an eGFR of 15 to 59 mL/min/1.73 m^2 and a serum potassium of 5.1 to 6.4 mEq/L on two occasions while receiving a stable dose of an ACE inhibitor or ARB received either 4.2 or 8.4 g of patiromer twice daily for four weeks, depending upon whether their serum potassium was below or above 5.5 mEq/L. The mean decrease in serum potassium at four weeks was 1.0 mEq/L (0.6 and 1.2 mEq/L with lower and higher doses, respectively); approximately 75 percent of patients achieved the target serum potassium of 3.8 to 5.0 mEq/L. The decline in serum potassium was steepest during the first three days.

The 107 patients whose baseline serum potassium was 5.5 mEq/L or greater and who achieved the target serum potassium during the initial four-week treatment period were randomly assigned to patiromer or placebo for another eight weeks. Serum potassium remained the same in patients continuing patiromer and increased by 0.7 mEq/L in those assigned to placebo. The incidence of hyperkalemia (5.5 mEq/L or greater) was significantly higher in the placebo group (60 versus 15 percent). Serious adverse events were rare and not likely to be related to treatment; constipation was the most common side effect, occurring in 11 percent of patients during the initial four-week period. As with the AMETHYST-DN trial, hypomagnesemia developed in some patients (eight patients [3 percent] developed magnesium levels <1.4 mg/dL).

There are several limitations of the OPAL-HK and AMETHYST-DN trials. The effect of patiromer in patients with acute hyperkalemia or end-stage kidney disease (ESKD) was not evaluated,

although this drug effectively reduced potassium among hemodialysis patients in a nonrandomized study [81]. In addition, patients in these trials were not routinely prescribed a low-potassium diet, only one-half of patients in the OPAL-HK trial were receiving loop or thiazide diuretics, and the number of patients in the AMETHYST-DN trial who received diuretics was not reported. Both a low-potassium diet and the use of loop or thiazide diuretics can be long-term strategies to prevent hyperkalemia in many patients with CKD who are treated with ACE inhibitors or ARBs. (See 'Diuretics' above.)

Patiromer has been used successfully to minimize hyperkalemia in other patient groups, including those with resistant hypertension treated with spironolactone and those with heart failure with reduced ejection fraction (HFrEF) treated with several RAAS inhibitors [82,83]. (See "Treatment of resistant hypertension" and "Primary pharmacologic therapy for heart failure with reduced ejection fraction".)

In addition to binding cations, patiromer can bind other drugs in the gastrointestinal tract. Clinically important interactions with ciprofloxacin, thyroxine, and metformin have been identified; these three drugs need to be administered more than three hours before or after patiromer [84].

Sodium zirconium cyclosilicate (SZC) — Sodium zirconium cyclosilicate (also known as zirconium cyclosilicate, SZC, and ZS-9) is an inorganic, nonabsorbable crystalline compound that exchanges both sodium and hydrogen ions for potassium throughout its intestinal transit [77]. The efficacy of SZC in hyperkalemic outpatients was evaluated in two nearly identical phase III, randomized placebo-controlled trials:

- In the Hyperkalemia Randomized Intervention Multidose ZS-9 Maintenance (HARMONIZE) study, 258 adult patients with persistent hyperkalemia (serum potassium that is greater than or equal to 5.1 mEq/L) entered a 48-hour open-label run-in during which they received 10 g of SZC three times daily; 69 percent had CKD (although patients with ESKD were excluded), 70 percent were taking a renin-angiotensin system inhibitor, and the majority had heart failure, diabetes mellitus, or both [85]. Of the 258 patients who entered the open-label run-in, 237 (92 percent) achieved a normal serum potassium (3.5 to 5.0 mEq/L) at 48 hours and were then randomly assigned to placebo or 5 g, 10 g, or 15 g of SZC once daily for four weeks. During randomized therapy, the mean serum potassium was significantly lower with SZC (4.8, 4.5, and 4.4 mEq/L with 5, 10, and 15 g dosing, respectively) as compared with placebo (5.1 mEq/L). Similarly, the proportion of normokalemic patients at the end of the study was significantly greater with SZC (71 to 85 percent as compared with 48 percent with placebo). Serious adverse events were uncommon and were not significantly increased with SZC. However, edema was more

common with the 10 g and 15 g doses compared with placebo (6 and 14 versus 2 percent), as was hypokalemia (10 and 11 versus 0 percent). Among a subgroup of 87 patients with heart failure, edema occurred in eight (15 percent) of those receiving SZC and in one (4 percent) receiving placebo [86]. Higher edema rates with SZC are likely due to an increased sodium load (which, as noted above, would be expected since SZC exchanges sodium for potassium).

- In another trial, 753 adult patients with a serum potassium of 5.0 to 6.5 mEq/L were randomly assigned to receive 1.25, 2.5, 5, or 10 g of SZC three times daily for 48 hours; 62 percent had CKD (patients with ESKD were excluded), 67 percent were receiving a renin-angiotensin system inhibitor, and most patients had diabetes, heart failure, or both [29]. A normal serum potassium (3.5 to 4.9 mEq/L) at 48 hours was attained by 543 patients (72 percent), and these individuals were then reassigned to receive placebo or 1.25, 2.5, 5, or 10 g of SZC once daily for two weeks. The serum potassium at two weeks was significantly lower in patients receiving 5 and 10 g doses of SZC as compared with placebo (by approximately 0.3 and 0.5 mEq/L, respectively) but not with 1.25 and 2.5 g doses. Adverse events were similar with placebo and SZC.

In these trials, the steepest decline in serum potassium with SZC occurred during the first four hours of therapy [29,85]. This suggests an acute effect on intestinal potassium secretion, rather than simply a reduction in potassium absorption.

The long-term efficacy of SZC was examined in an open-label trial of 751 outpatients with sustained hyperkalemia (5.1 mEq/L or greater); mean eGFR was 47 mL/min/1.73 m^2 and 65 percent were receiving a renin-angiotensin system inhibitor (ie, an ACE inhibitor, ARB, or mineralocorticoid receptor antagonist) [87]. Patients were treated with 10 g three times daily of SZC for three days; the serum potassium corrected to the normal range in 99 percent, and these patients received a maintenance dose of 5 to 15 g once daily for up to 12 months. During maintenance treatment, 88 percent had a mean serum potassium of 5.1 mEq/L or less, 87 percent of those taking a renin-angiotensin system inhibitor continued on these medications, and renin-angiotensin system inhibitors were initiated in 14 percent of those not taking them at baseline.

SZC is also effective for management of hyperkalemia among patients receiving maintenance hemodialysis. In the DIALYZE study, 196 patients receiving maintenance hemodialysis who had persistent predialysis hyperkalemia were randomly assigned to treatment with SZC (5 to 15 g orally on nondialysis days) or placebo for eight weeks [88]. Treatment success, defined as a predialysis serum potassium (following the long interdialytic interval) of 4.0 to 5.0 mEq/L during the last four weeks of therapy, was more common with SZC (41 versus 1 percent). However, the

more clinically important endpoint of "rescue therapy," defined as an intervention (such as dialysis, insulin plus glucose, other cation exchangers) to urgently reduce the serum potassium, was infrequent in both groups and not statistically different (2 versus 5 percent). Adverse event rates were similar in both groups.

Do not use sodium polystyrene sulfonate (SPS) or other resins — The most widely used cation exchange resin has been sodium polystyrene sulfonate (SPS). Although "SPS" is often used as an abbreviation for sodium polystyrene sulfonate, SPS is actually a brand name for sodium polystyrene sulfonate in sorbitol.

Cation exchange resins do not appear to be more effective in removing potassium from the body than laxative therapy. Although uncommon, cation exchange resins can produce severe side effects, particularly intestinal necrosis, which may be fatal. (See 'Sodium polystyrene sulfonate (SPS) in rare settings' above.)

Given these concerns, SPS or other resins should **not** be used in patients with chronic mild or moderate hyperkalemia who do not have a hyperkalemic emergency and who do not require a prompt reduction in serum potassium. (See 'Determining the urgency of therapy' above.)

DRUG-INDUCED HYPERKALEMIA

A variety of drugs can raise the serum potassium, primarily by interfering with the renin-angiotensin-aldosterone system (RAAS). Probably the most common are angiotensin inhibitors (eg, angiotensin-converting enzyme [ACE] inhibitors and angiotensin II receptor blockers [ARBs]), aldosterone antagonists and other potassium sparing diuretics (eg, spironolactone, eplerenone, and amiloride), digitalis, and nonsteroidal antiinflammatory drugs (table 4). (See "Causes and evaluation of hyperkalemia in adults", section on 'Reduced aldosterone secretion'.)

These drugs should be discontinued, or the dose reduced, at least temporarily, until the hyperkalemia is controlled.

In patients with heart failure with reduced ejection fraction or albuminuric chronic kidney disease, it is important to resume therapeutic doses of RAAS antagonists since cessation or permanent dose reduction of these agents is associated with higher rates of mortality and adverse cardiovascular events [89,90]. (See "Primary pharmacologic therapy for heart failure with reduced ejection fraction" and "Antihypertensive therapy and progression of nondiabetic chronic kidney disease in adults" and "Treatment of diabetic kidney disease".)

Strategies to prevent the recurrence of hyperkalemia when RAAS inhibition is reinstituted are presented below. (See 'Prevention' below.)

If hyperkalemia recurs, strategies other than RAAS inhibitor discontinuation should be implemented, as described above. (See 'Patients who can have the serum potassium lowered slowly' above.)

PREVENTION

There are several measures that can help to prevent hyperkalemia in patients with chronic kidney disease (CKD), particularly those with end-stage kidney disease (ESKD). In addition to a low-potassium diet, the following modalities have been effective in stable maintenance hemodialysis patients (see "Patient education: Low-potassium diet (Beyond the Basics)"):

- Avoid episodes of fasting, which can increase potassium movement out of the cells due, at least in part, to reduced insulin secretion [13,91]. In a study of 10 stable patients on maintenance hemodialysis who did not have diabetes mellitus, fasting for 18 hours led to a mean 0.6 mEq/L rise in the serum potassium concentration, which was completely prevented when the protocol was repeated with the administration of low-dose insulin with dextrose [91]. Thus, nondiabetic patients with ESKD who are undergoing elective surgery should, if they are in the hospital, receive parenteral glucose-containing solutions when fasting overnight.

- Avoid, if possible, drugs that raise the serum potassium concentration in patients with a serum potassium ≥5.5 mEq/L. These include inhibitors of the renin-angiotensin-aldosterone system (RAAS), such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), direct renin inhibitors, aldosterone antagonists, and nonselective beta blockers (eg, propranolol and labetalol) [92,93]. Beta-1-selective blockers such as metoprolol and atenolol are much less likely to cause hyperkalemia [13,94]. (See "Causes and evaluation of hyperkalemia in adults", section on 'Beta blockers'.)

Patients with CKD or heart failure are often treated with RAAS inhibitors. A variety of preventive measures can diminish the risk of hyperkalemia [92]. These include:

- Close monitoring of the serum potassium concentration and estimated glomerular filtration rate (eGFR), particularly after changes in RAAS inhibitor therapy.

- Dietary restriction of potassium. (See "Patient education: Low-potassium diet (Beyond the Basics)".)

- Avoidance or discontinuation of other drugs that impair potassium excretion (eg, nonsteroidal antiinflammatory drugs).
- The utilization of low initial doses and evidence-based final doses of RAAS inhibitors for specific indications (eg, heart failure, proteinuric CKD). The dose should be reduced with moderate hyperkalemia (serum potassium of ≤5.5 mEq/L) and therapy should be discontinued if the serum potassium rises above 5.5 mEq/L unless the serum potassium can be reduced by diuretic therapy.
- The use of thiazide or loop diuretics whenever otherwise indicated.
- There are no good data on the chronic efficacy of oral alkali therapy (sodium bicarbonate or sodium citrate) for the treatment of persistent hyperkalemia. Most such patients have CKD with or without hypoaldosteronism. There are a variety of benefits from treating metabolic acidosis in such patients, and alkali therapy is typically recommended, independent of any effect on the serum potassium concentration. (See "Pathogenesis, consequences, and treatment of metabolic acidosis in chronic kidney disease", section on 'Treatment of metabolic acidosis in CKD'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Fluid and electrolyte disorders in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a

variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Hyperkalemia (The Basics)" and "Patient education: Low-potassium diet (The Basics)")
- Beyond the Basics topic (see "Patient education: Low-potassium diet (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Determining the urgency of treatment** – The urgency of treatment of hyperkalemia varies with the presence or absence of the symptoms and signs associated with hyperkalemia, the severity of the potassium elevation, and the cause of hyperkalemia. Our approach to therapeutic urgency is as follows (algorithm 1) (see 'Determining the urgency of therapy' above):

  - Hyperkalemic emergency − Patients who have clinical signs or symptoms of hyperkalemia (eg, muscle weakness or paralysis, cardiac conduction abnormalities, cardiac arrhythmias), patients with severe hyperkalemia (serum potassium >6.5 mEq/L), and patients with moderate hyperkalemia (serum potassium >5.5 mEq/L) plus significant kidney function impairment and ongoing tissue breakdown or potassium absorption) have a hyperkalemic emergency.

  - Patients needing prompt therapy − Some patients with moderate hyperkalemia but without a hyperkalemic emergency should, nonetheless, have their potassium lowered promptly (ie, within 6 to 12 hours). Such patients include hemodialysis patients who present outside of regular dialysis hours, patients with marginal kidney function and/or marginal urine output, or hyperkalemic patients who need to be optimized for surgery.

  - Patients who can have the potassium lowered slowly − Most patients with hyperkalemia have chronic, mild (≤5.5 mEq/L) or moderate (5.5 to 6.5 mEq/L) elevations in serum potassium due to chronic kidney disease (CKD) or the use of medications that inhibit the renin-angiotensin-aldosterone system ([RAAS] or both). Such patients do not require urgent lowering of the serum potassium.

- **Patients with a hyperkalemic emergency** – Patients with a hyperkalemic emergency should receive (table 1 and table 2) (see 'Patients with a hyperkalemic emergency' above):

  - Intravenous calcium to antagonize the membrane actions of hyperkalemia if electrocardiogram (ECG) changes consistent with hyperkalemia are present. In

addition, some, although not all, experts give intravenous calcium to patients with a potassium >6.5 mEq/L (even if notable ECG changes are absent). (See 'Calcium' above.)

- Intravenous insulin (typically given with intravenous glucose) to drive extracellular potassium into cells. (See 'Insulin with glucose' above.)

- Therapy to rapidly remove excess potassium from the body (ie, loop or thiazide diuretics if kidney function is not severely impaired, a gastrointestinal cation exchanger, and/or dialysis [preferably hemodialysis] if kidney function is severely impaired). (See 'Remove potassium from the body' above.)

- Treatment of reversible causes of hyperkalemia, such as correcting hypovolemia and discontinuing drugs that increase the serum potassium (eg, nonsteroidal antiinflammatory drugs [NSAIDs], inhibitors of the RAAS). (See "Causes and evaluation of hyperkalemia in adults" and 'Drug-induced hyperkalemia' above.)

- Continuous cardiac monitoring and serial ECGs. The serum potassium should be measured at one to two hours after the initiation of treatment. The timing of further measurements is determined by the serum potassium concentration and the response to therapy. Patients who receive insulin, with or without dextrose, should undergo hourly glucose measurements for up to six hours in order to monitor for hypoglycemia. (See 'Monitoring' above.)

- **Patients without a hyperkalemic emergency** – Treatment of patients who do not have a hyperkalemic emergency generally depends upon how promptly the serum potassium should be lowered (algorithm 1) (see 'Patients without a hyperkalemic emergency' above):

  - Patients needing prompt potassium lowering are typically treated with hemodialysis (if they have severe kidney dysfunction) with or without the use of a gastrointestinal cation exchanger (preferably sodium zirconium cyclosilicate [SZC] or patiromer). In patients with normal kidney function or mild to moderate kidney function impairment, correcting the cause of hyperkalemia (eg, drugs, hypovolemia) will generally suffice, in addition to treatment with saline infusion and loop diuretics; a gastrointestinal cation exchanger is sometimes used in such patients. (See 'Patients who need prompt serum potassium reduction' above.)

  - Patients who can safely have their serum potassium lowered slowly are usually treated with therapies that gradually reduce the serum potassium, such as a low-potassium diet, loop or thiazide diuretics, or a reduction or cessation of medicines that can

increase the serum potassium. With the introduction of patiromer and SZC, it is anticipated that gastrointestinal cation exchangers will be utilized more frequently in these patients for chronic control of the serum potassium. (See 'Patients who can have the serum potassium lowered slowly' above.)

- **Prevention** – There are several measures that can help to prevent hyperkalemia or worsening of hyperkalemia in patients with CKD, particularly those with end-stage kidney disease (ESKD). In addition to a low-potassium diet, the following modalities have been effective in stable maintenance hemodialysis patients (see 'Prevention' above and "Patient education: Low-potassium diet (Beyond the Basics)"):

  - Avoid episodes of fasting, which can increase potassium movement out of the cells due, at least in part, to reduced insulin secretion.

  - In patients with moderate hyperkalemia, avoid, if possible, drugs that raise the serum potassium concentration. These include RAAS inhibitors, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), direct renin inhibitors, aldosterone antagonists, and nonselective beta blockers (eg, propranolol and labetalol) (table 4).

  - Avoidance or discontinuation of other drugs that impair potassium excretion (eg, NSAIDs).

  - The use of thiazide or loop diuretics whenever otherwise indicated.

REFERENCES

1. Clase CM, Carrero JJ, Ellison DH, et al. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int 2020; 97:42.
2. Mount DB. Disorders of potassium balance. In: Brenner and Rector's The Kidney, 11th ed, Y u A, Chertow G, Luyckx V, et al (Eds), W.B. Saunders & Company, Philadelphia 2020. p.537.
3. Long B, Warix JR, Koyfman A. Controversies in Management of Hyperkalemia. J Emerg Med 2018; 55:192.
4. Littmann L, Gibbs MA. Electrocardiographic manifestations of severe hyperkalemia. J Electrocardiol 2018; 51:814.

5. Winkler AW, Hoff HE, Smith PK. Factors affecting the toxicity of potassium. Am J Physiol 1939; 127:430.
6. BRAUN HA, VAN HORNE R, BETTINGER JC, BELLET S. The influence of hypocalcemia induced by sodium ethylenediamine tetraacetate on the toxicity of potassium; an experimental study. J Lab Clin Med 1955; 46:544.
7. Ferrannini E, Taddei S, Santoro D, et al. Independent stimulation of glucose metabolism and Na+-K+ exchange by insulin in the human forearm. Am J Physiol 1988; 255:E953.
8. Pergola PE, DeFronzo R. Clinical disorders of hyperkalemia. In: The Kidney: Physiology and Pathophysiology, Seldin DW, Giebisch G (Eds), Lippincott Williams & Wilkins, 2000. Vol 2, p.1647.
9. Harel Z, Kamel KS. Optimal Dose and Method of Administration of Intravenous Insulin in the Management of Emergency Hyperkalemia: A Systematic Review. PLoS One 2016; 11:e0154963.
10. Sterns RH, Grieff M, Bernstein PL. Treatment of hyperkalemia: something old, something new. Kidney Int 2016; 89:546.
11. Tee SA, Devine K, Potts A, et al. Iatrogenic hypoglycaemia following glucose-insulin infusions for the treatment of hyperkalaemia. Clin Endocrinol (Oxf) 2021; 94:176.
12. Humphrey TJL, James G, Wilkinson IB, Hiemstra TF. Clinical outcomes associated with the emergency treatment of hyperkalaemia with intravenous insulin-dextrose. Eur J Intern Med 2022; 95:87.
13. Allon M. Hyperkalemia in end-stage renal disease: mechanisms and management. J Am Soc Nephrol 1995; 6:1134.
14. Goldfarb S, Strunk B, Singer I, Goldberg M. Paradoxical glucose-induced hyperkalemia. Combined aldosterone-insulin deficiency. Am J Med 1975; 59:744.
15. Nicolis GL, Kahn T, Sanchez A, Gabrilove JL. Glucose-induced hyperkalemia in diabetic subjects. Arch Intern Med 1981; 141:49.
16. Magnus Nzerue C, Jackson E. Intractable life-threatening hyperkalaemia in a diabetic patient. Nephrol Dial Transplant 2000; 15:113.
17. Allon M, Copkney C. Albuterol and insulin for treatment of hyperkalemia in hemodialysis patients. Kidney Int 1990; 38:869.
18. Ahmed J, Weisberg LS. Hyperkalemia in dialysis patients. Semin Dial 2001; 14:348.
19. Kim HJ, Han SW. Therapeutic approach to hyperkalemia. Nephron 2002; 92 Suppl 1:33.
20. Lens XM, Montoliu J, Cases A, et al. Treatment of hyperkalaemia in renal failure: salbutamol

v. insulin. Nephrol Dial Transplant 1989; 4:228.

21. Emmett M. Non-dialytic treatment of acute hyperkalemia in the dialysis patient. Semin Dial 2000; 13:279.
22. Blumberg A, Weidmann P, Shaw S, Gnädinger M. Effect of various therapeutic approaches on plasma potassium and major regulating factors in terminal renal failure. Am J Med 1988; 85:507.
23. De Wolf A, Frenette L, Kang Y, Tang C. Insulin decreases the serum potassium concentration during the anhepatic stage of liver transplantation. Anesthesiology 1993; 78:677.
24. Alvestrand A, Wahren J, Smith D, DeFronzo RA. Insulin-mediated potassium uptake is normal in uremic and healthy subjects. Am J Physiol 1984; 246:E174.
25. Goecke IA, Bonilla S, Marusic ET, Alvo M. Enhanced insulin sensitivity in extrarenal potassium handling in uremic rats. Kidney Int 1991; 39:39.
26. Rafique Z, Liu M, Staggers KA, et al. Patiromer for Treatment of Hyperkalemia in the Emergency Department: A Pilot Study. Acad Emerg Med 2020; 27:54.
27. Peacock WF, Rafique Z, Vishnevskiy K, et al. Emergency Potassium Normalization Treatment Including Sodium Zirconium Cyclosilicate: A Phase II, Randomized, Double-blind, Placebo-controlled Study (ENERGIZE). Acad Emerg Med 2020; 27:475.
28. Lewis H, Stamper B, Yungkurth AC. Serum potassium response to single-dose sodium zirconium cyclosilicate for the treatment of asymptomatic hyperkalemia in hospitalized patients. Pharmacotherapy 2024; 44:13.
29. Packham DK, Rasmussen HS, Lavin PT, et al. Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med 2015; 372:222.
30. Gupta AA, Self M, Mueller M, et al. Dispelling myths and misconceptions about the treatment of acute hyperkalemia. Am J Emerg Med 2022; 52:85.
31. Rossignol P, Pitt B. Sodium polystyrene is unsafe and should not be prescribed for the treatment of hyperkalaemia: primum non nocere! Clin Kidney J 2023; 16:1221.
32. Mistry M, Shea A, Giguère P, Nguyen ML. Evaluation of Sodium Polystyrene Sulfonate Dosing Strategies in the Inpatient Management of Hyperkalemia. Ann Pharmacother 2016; 50:455.
33. Hagan AE, Farrington CA, Wall GC, Belz MM. Sodium polystyrene sulfonate for the treatment of acute hyperkalemia: a retrospective study. Clin Nephrol 2016; 85:38.
34. Sterns RH, Rojas M, Bernstein P, Chennupati S. Ion-exchange resins for the treatment of hyperkalemia: are they safe and effective? J Am Soc Nephrol 2010; 21:733.

35. Gerstman BB, Kirkman R, Platt R. Intestinal necrosis associated with postoperative orally administered sodium polystyrene sulfonate in sorbitol. Am J Kidney Dis 1992; 20:159.
36. McGowan CE, Saha S, Chu G, et al. Intestinal necrosis due to sodium polystyrene sulfonate (Kayexalate) in sorbitol. South Med J 2009; 102:493.
37. Lillemoe KD, Romolo JL, Hamilton SR, et al. Intestinal necrosis due to sodium polystyrene (Kayexalate) in sorbitol enemas: clinical and experimental support for the hypothesis. Surgery 1987; 101:267.
38. Rashid A, Hamilton SR. Necrosis of the gastrointestinal tract in uremic patients as a result of sodium polystyrene sulfonate (Kayexalate) in sorbitol: an underrecognized condition. Am J Surg Pathol 1997; 21:60.
39. Scott TR, Graham SM, Schweitzer EJ, Bartlett ST. Colonic necrosis following sodium polystyrene sulfonate (Kayexalate)-sorbitol enema in a renal transplant patient. Report of a case and review of the literature. Dis Colon Rectum 1993; 36:607.
40. Wootton FT, Rhodes DF, Lee WM, Fitts CT. Colonic necrosis with Kayexalate-sorbitol enemas after renal transplantation. Ann Intern Med 1989; 111:947.
41. https://www.fda.gov/Drugs/DrugSafety/ucm572484.htm.
42. Ayoub I, Oh MS, Gupta R, et al. Colon Necrosis Due to Sodium Polystyrene Sulfonate with and without Sorbitol: An Experimental Study in Rats. PLoS One 2015; 10:e0137636.
43. Cheng ES, Stringer KM, Pegg SP. Colonic necrosis and perforation following oral sodium polystyrene sulfonate (Resonium A/Kayexalate in a burn patient. Burns 2002; 28:189.
44. Goutorbe P, Montcriol A, Lacroix G, et al. Intestinal Necrosis Associated with Orally Administered Calcium Polystyrene Sulfonate Without Sorbitol. Ann Pharmacother 2011; 45:e13.
45. Rugolotto S, Gruber M, Solano PD, et al. Necrotizing enterocolitis in a 850 gram infant receiving sorbitol-free sodium polystyrene sulfonate (Kayexalate): clinical and histopathologic findings. J Perinatol 2007; 27:247.
46. Joo M, Bae WK, Kim NH, Han SR. Colonic mucosal necrosis following administration of calcium polystryrene sulfonate (Kalimate) in a uremic patient. J Korean Med Sci 2009; 24:1207.
47. Noel JA, Bota SE, Petrcich W, et al. Risk of Hospitalization for Serious Adverse Gastrointestinal Events Associated With Sodium Polystyrene Sulfonate Use in Patients of Advanced Age. JAMA Intern Med 2019; 179:1025.
48. Laureati P, Xu Y, Trevisan M, et al. Initiation of sodium polystyrene sulphonate and the risk of gastrointestinal adverse events in advanced chronic kidney disease: a nationwide study.

Nephrol Dial Transplant 2020; 35:1518.

49. Gruy-Kapral C, Emmett M, Santa Ana CA, et al. Effect of single dose resin-cathartic therapy on serum potassium concentration in patients with end-stage renal disease. J Am Soc Nephrol 1998; 9:1924.
50. Gales MA, Gales BJ, Dyer ME, Orr SR. Rectally administered sodium polystyrene sulfonate. Am J Health Syst Pharm 1995; 52:2813.
51. Clausen T, Everts ME. Regulation of the Na,K-pump in skeletal muscle. Kidney Int 1989; 35:1.
52. Gosmanov AR, Wong JA, Thomason DB. Duality of G protein-coupled mechanisms for beta-adrenergic activation of NKCC activity in skeletal muscle. Am J Physiol Cell Physiol 2002; 283:C1025.
53. Liou HH, Chiang SS, Wu SC, et al. Hypokalemic effects of intravenous infusion or nebulization of salbutamol in patients with chronic renal failure: comparative study. Am J Kidney Dis 1994; 23:266.
54. Sowinski KM, Cronin D, Mueller BA, Kraus MA. Subcutaneous terbutaline use in CKD to reduce potassium concentrations. Am J Kidney Dis 2005; 45:1040.
55. Ahee P, Crowe AV. The management of hyperkalaemia in the emergency department. J Accid Emerg Med 2000; 17:188.
56. Allon M, Shanklin N. Effect of albuterol treatment on subsequent dialytic potassium removal. Am J Kidney Dis 1995; 26:607.
57. Gutierrez R, Schlessinger F, Oster JR, et al. Effect of hypertonic versus isotonic sodium bicarbonate on plasma potassium concentration in patients with end-stage renal disease. Miner Electrolyte Metab 1991; 17:297.
58. Blumberg A, Weidmann P, Ferrari P. Effect of prolonged bicarbonate administration on plasma potassium in terminal renal failure. Kidney Int 1992; 41:369.
59. Allon M, Shanklin N. Effect of bicarbonate administration on plasma potassium in dialysis patients: interactions with insulin and albuterol. Am J Kidney Dis 1996; 28:508.
60. BURNELL JM, SCRIBNER BH, UYENO BT, VILLAMIL MF. The effect in humans of extracellular pH change on the relationship between serum potassium concentration and intracellular potassium. J Clin Invest 1956; 35:935.
61. SCHWARZ KC, COHEN BD, LUBASH GD, RUBIN AL. Severe acidosis and hyperpotassemia treated with sodium bicarbonate infusion. Circulation 1959; 19:215.
62. Fraley DS, Adler S. Correction of hyperkalemia by bicarbonate despite constant blood pH. Kidney Int 1977; 12:354.

63. Peacock WF, Rafique Z, Clark CL, et al. Real World Evidence for Treatment of Hyperkalemia in the Emergency Department (REVEAL-ED): A Multicenter, Prospective, Observational Study. J Emerg Med 2018; 55:741.
64. Nolph KD, Popovich RP, Ghods AJ, Twardowski Z. Determinants of low clearances of small solutes during peritoneal dialysis. Kidney Int 1978; 13:117.
65. Blumberg A, Roser HW, Zehnder C, Müller-Brand J. Plasma potassium in patients with terminal renal failure during and after haemodialysis; relationship with dialytic potassium removal and total body potassium. Nephrol Dial Transplant 1997; 12:1629.
66. Allon M. Medical and dialytic management of hyperkalemia in hemodialysis patients. Int J Artif Organs 1996; 19:697.
67. De Nicola L, Bellizzi V, Minutolo R, et al. Effect of dialysate sodium concentration on interdialytic increase of potassium. J Am Soc Nephrol 2000; 11:2337.
68. John SK, Rangan Y, Block CA, Koff MD. Life-threatening hyperkalemia from nutritional supplements: uncommon or undiagnosed? Am J Emerg Med 2011; 29:1237.e1.
69. Parisi A, Alabiso A, Sacchetti M, et al. Complex ventricular arrhythmia induced by overuse of potassium supplementation in a young male football player. Case report. J Sports Med Phys Fitness 2002; 42:214.
70. Smillie WG. Potassium poisoning in nephritis. Arch Intern Med 1915; 16:330.
71. Doorenbos CJ, Vermeij CG. Danger of salt substitutes that contain potassium in patients with renal failure. BMJ 2003; 326:35.
72. Sopko JA, Freeman RM. Salt substitutes as a source of potassium. JAMA 1977; 238:608.
73. Abu-Hamdan DK, Sondheimer JH, Mahajan SK. Cautopyreiophagia. Cause of life-threatening hyperkalemia in a patient undergoing hemodialysis. Am J Med 1985; 79:517.
74. Nagasaki A, Takamine W, Takasu N. Severe hyperkalemia associated with "alternative" nutritional cancer therapy. Clin Nutr 2005; 24:864.
75. Mueller BA, Scott MK, Sowinski KM, Prag KA. Noni juice (Morinda citrifolia): hidden potential for hyperkalemia? Am J Kidney Dis 2000; 35:310.
76. Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. How much should we worry? Arch Intern Med 1998; 158:26.
77. Ingelfinger JR. A new era for the treatment of hyperkalemia? N Engl J Med 2015; 372:275.
78. Bushinsky DA, Spiegel DM, Gross C, et al. Effect of Patiromer on Urinary Ion Excretion in Healthy Adults. Clin J Am Soc Nephrol 2016; 11:1769.

79. Bakris GL, Pitt B, Weir MR, et al. Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease: The AMETHYST-DN Randomized Clinical Trial. JAMA 2015; 314:151.

80. Weir MR, Bakris GL, Bushinsky DA, et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med 2015; 372:211.

81. Amdur RL, Paul R, Barrows ED, et al. The potassium regulator patiromer affects serum and stool electrolytes in patients receiving hemodialysis. Kidney Int 2020; 98:1331.

82. Agarwal R, Rossignol P, Romero A, et al. Patiromer versus placebo to enable spironolactone use in patients with resistant hypertension and chronic kidney disease (AMBER): a phase 2, randomised, double-blind, placebo-controlled trial. Lancet 2019; 394:1540.

83. Butler J, Anker SD, Lund LH, et al. Patiromer for the management of hyperkalemia in heart failure with reduced ejection fraction: the DIAMOND trial. Eur Heart J 2022; 43:4362.

84. Lesko LJ, Offman E, Brew CT, et al. Evaluation of the Potential for Drug Interactions With Patiromer in Healthy Volunteers. J Cardiovasc Pharmacol Ther 2017; 22:434.

85. Kosiborod M, Rasmussen HS, Lavin P, et al. Effect of sodium zirconium cyclosilicate on potassium lowering for 28 days among outpatients with hyperkalemia: the HARMONIZE randomized clinical trial. JAMA 2014; 312:2223.

86. Anker SD, Kosiborod M, Zannad F, et al. Maintenance of serum potassium with sodium zirconium cyclosilicate (ZS-9) in heart failure patients: results from a phase 3 randomized, double-blind, placebo-controlled trial. Eur J Heart Fail 2015; 17:1050.

87. Spinowitz BS, Fishbane S, Pergola PE, et al. Sodium Zirconium Cyclosilicate among Individuals with Hyperkalemia: A 12-Month Phase 3 Study. Clin J Am Soc Nephrol 2019; 14:798.

88. Fishbane S, Ford M, Fukagawa M, et al. A Phase 3b, Randomized, Double-Blind, Placebo-Controlled Study of Sodium Zirconium Cyclosilicate for Reducing the Incidence of Predialysis Hyperkalemia. J Am Soc Nephrol 2019; 30:1723.

89. Leon SJ, Whitlock R, Rigatto C, et al. Hyperkalemia-Related Discontinuation of Renin-Angiotensin-Aldosterone System Inhibitors and Clinical Outcomes in CKD: A Population-Based Cohort Study. Am J Kidney Dis 2022; 80:164.

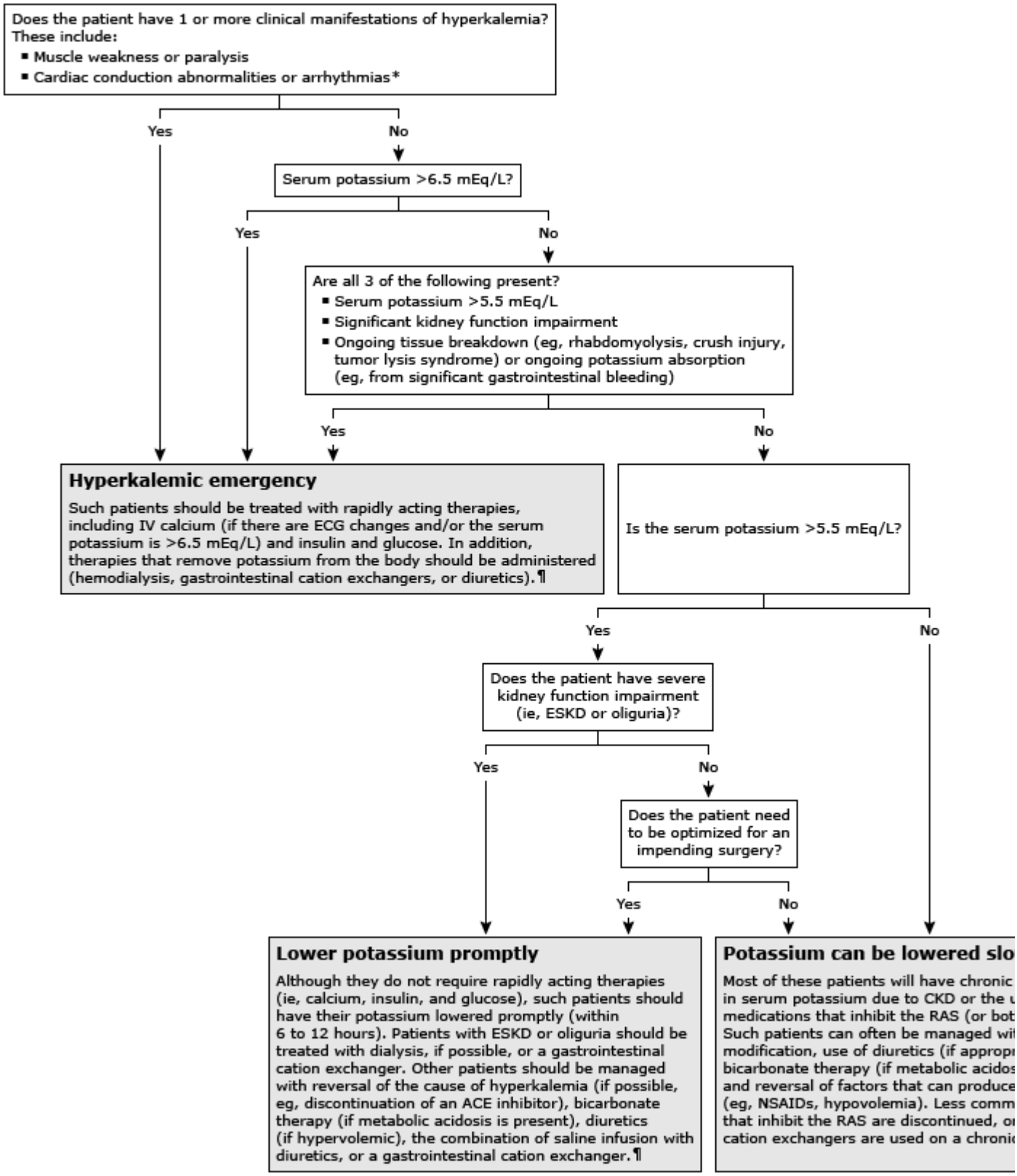
90. Linde C, Bakhai A, Furuland H, et al. Real-World Associations of Renin-Angiotensin-Aldosterone System Inhibitor Dose, Hyperkalemia, and Adverse Clinical Outcomes in a Cohort of Patients With New-Onset Chronic Kidney Disease or Heart Failure in the United Kingdom. J Am Heart Assoc 2019; 8:e012655.

91. Allon M, Takeshian A, Shanklin N. Effect of insulin-plus-glucose infusion with or without epinephrine on fasting hyperkalemia. Kidney Int 1993; 43:212.
92. Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. N Engl J Med 2004; 351:585.
93. Knoll GA, Sahgal A, Nair RC, et al. Renin-angiotensin system blockade and the risk of hyperkalemia in chronic hemodialysis patients. Am J Med 2002; 112:110.
94. Castellino P, Bia MJ, DeFronzo RA. Adrenergic modulation of potassium metabolism in uremia. Kidney Int 1990; 37:793.

Topic 2332 Version 57.0

GRAPHICS

Treatment of hyperkalemia in adults



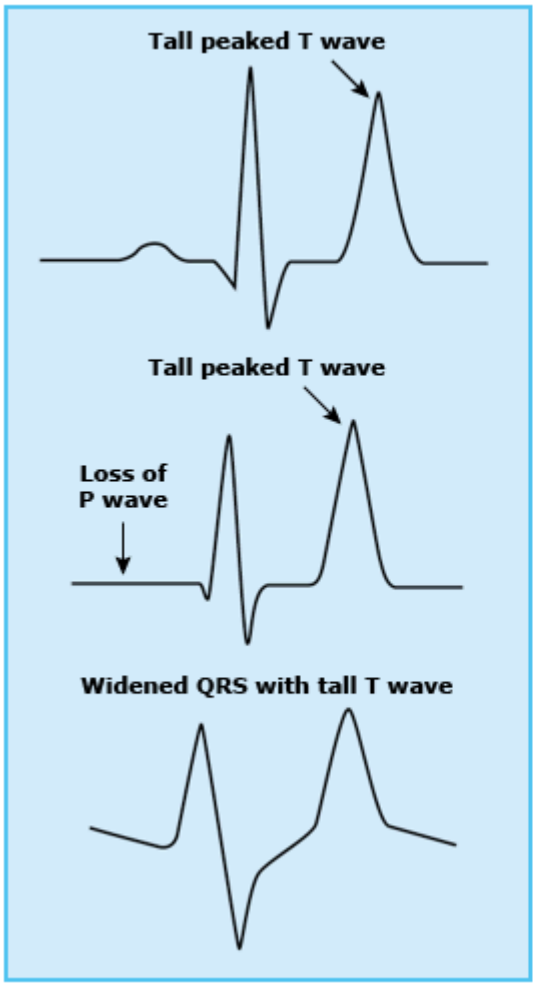
ESKD: end-stage kidney disease; ACE: angiotensin-converting enzyme; CKD: chronic kidney disease; RAS: renin-angiotensin system; NSAIDs: nonsteroidal antiinflammatory drugs; IV: intravenous; ECG: electrocardiogram.

* Cardiac manifestations of hyperkalemia are discussed in detail in the topic on clinical manifestations of hyperkalemia.

¶ Some experts given IV calcium only to patients with ECG changes. Details are presented in the topic on treatment of hyperkalemia.

Graphic 109740 Version 3.0

Typical electrocardiographic features of hyperkalemia

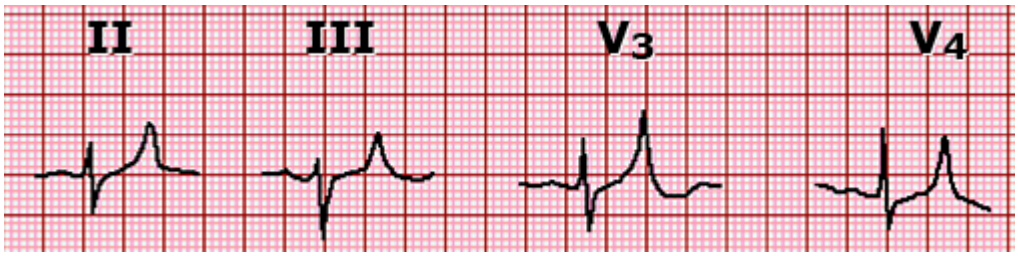


Serum potassium	Major change
5.5-6.5	Tall peaked T waves
6.5-7.5	Loss of P waves
7.0-8.0	Widening of QRS
8.0-10.0	Sine wave, ventricular arrhythmia, asystole

Adapted from: Mattu A, Brady WJ, Robinson DA. Electrocardiographic manifestations of hyperkalemia. Am J Emerg Med 2000; 18:721.

Graphic 109443 Version 1.0

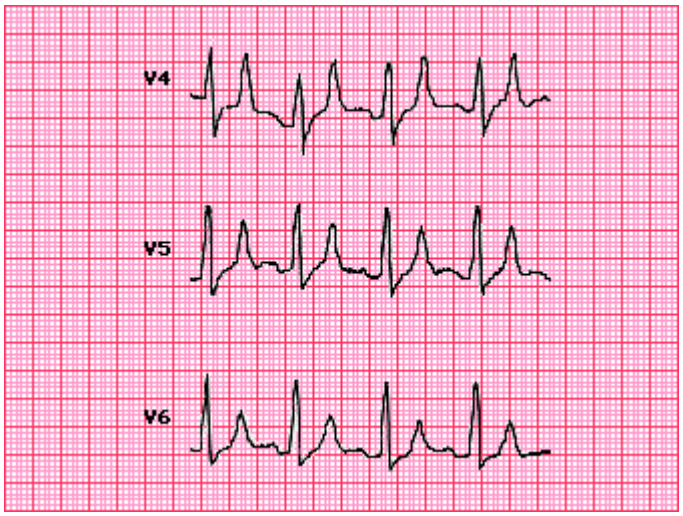
Peaked T waves as first sign of hyperkalemia on electrocardiogram



A tall peaked and symmetrical T wave is the first change seen on the electrocardiogram in a patient with hyperkalemia.

Graphic 80441 Version 7.0

Hyperkalemia



Lateral precordial leads showing peaked, narrow (tented) T waves and prolongation of the QRS complex (0.14 to 0.16 seconds) associated with moderate to severe hyperkalemia.

Courtesy of Ary Goldberger, MD.

Graphic 63569 Version 2.0

Hyperkalemia in adults: Rapid overview of emergency management

Clinical features
Signs and symptoms are uncommon and tend to occur only when serum potassium is >7.0 meq/L; can include muscle weakness and ventricular arrhythmias.
There are two major mechanisms of hyperkalemia:
Increased potassium release from cells (eg, severe hyperglycemia, rhabdomyolysis).
Reduced potassium excretion in urine (eg, hypoaldosteronism, kidney failure).
Pseudohyperkalemia is a common cause of a reported elevation in serum potassium and must be excluded. It does not reflect true hyperkalemia and does not produce ECG changes.
ECG manifestations
The relationship between the degree of serum potassium elevation and ECG changes varies from patient to patient, and changes are more common with acute-onset hyperkalemia.
ECG findings that are commonly observed with more severe elevation of the serum potassium include:
Tall peaked T waves.
Shrinking and then loss of P waves.
Widening of the QRS interval and then "sine wave," ventricular arrhythmia, and asystole.
Early management
Exclude pseudohyperkalemia.
Obtain ECG and place patients with hyperkalemic emergency on continuous cardiac monitoring. Patients with hyperkalemic emergency include:
Those with clinical manifestations or ECG changes.
Those with serum potassium of >6.5 meq/L.
Those with serum potassium of >5.5 meq/L plus kidney function impairment and ongoing tissue breakdown or potassium absorption.
In patients with a hyperkalemic emergency:
If ECG changes present and/or serum potassium >6.5 meq/L: Give **calcium gluconate** 1000 mg (10 mL of 10% solution) **or** calcium chloride 500 to 1000 mg IV over two to three minutes to stabilize cardiac membranes.
For ALL hyperkalemic emergencies: Give **insulin and glucose** to shift K^+ intracellularly (give insulin only, without glucose, if serum glucose is >250 mg/dL [13.9 mmol/L]). A common regimen consists of a bolus injection of 10 units of regular insulin, followed immediately by 50 mL of 50% dextrose (25 g of glucose) over 5 minutes. We subsequently infuse 10% dextrose at 50 to 75 mL/hou and closely monitor blood glucose levels every hour for five to six hours.
Give therapy to remove potassium from the body (refer below).

Remove potassium from the body
Hemodialysis should be performed in patients with ESKD or severe kidney function impairment.
Loop diuretics (in hypervolemic patients) or saline infusion with IV loop diuretics can be administered (eg, 40 mg of furosemide every 12 hours) to nonoliguric patients without severe kidney function impairment.
A gastrointestinal cation exchanger (eg, sodium zirconium cyclosilicate 10 g orally or patiromer 8.4 g orally) can be given, especially in patients with severe kidney function impairment in whom hemodialysis cannot be swiftly performed. Sodium polystyrene sulfonate (15 to 30 g orally) **should not** be given unless there are no other options to effectively remove potassium from the body in a timely fashion.

ECG: electrocardiogram; IV: intravenous; ESKD: end-stage kidney disease; K^+: potassium ion.

Graphic 74169 Version 15.0

Treatment of hyperkalemia

Antagonism of membrane actions of potassium
Calcium
Drive extracellular potassium into the cells
Insulin and glucose
Sodium bicarbonate, primarily if metabolic acidosis
Beta-2-adrenergic agonists
Removal of potassium from the body
Loop or thiazide diuretics
Cation exchange resin
Dialysis, preferably hemodialysis if severe

Graphic 52694 Version 2.0

Major causes of hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality
Increased tissue catabolism
Beta blockers
Exercise
Hyperkalemic periodic paralysis
Other
Overdose of digitalis or related digitalis glycosides
Red cell transfusion
Succinylcholine
Arginine hydrochloride
Activators of ATP-dependent potassium channels (eg, calcineurin inhibitors, diazoxide, minoxidil, and some volatile anesthetics)
Reduced urinary potassium excretion
Reduced aldosterone secretion
Reduced response to aldosterone
Reduced distal sodium and water delivery
Effective arterial blood volume depletion
Acute and chronic kidney disease
Other
Selective impairment in potassium secretion
Gordon's syndrome
Ureterojejunostomy

Graphic 58157 Version 6.0

Major causes of hypoaldosteronism

Reduced aldosterone production
Hyporeninemic hypoaldosteronism
Kidney disease, most often diabetic nephropathy
Nonsteroidal antiinflammatory drugs
Calcineurin inhibitors
Volume expansion, as in acute glomerulonephritis
Angiotensin inhibitors, such as ACE inhibitors, angiotensin II receptor blockers, and direct renin inhibitors
Chronic heparin therapy (impairs aldosterone synthesis)
Primary adrenal insufficiency
Severe illness
Inherited disorders
Congenital hypoaldosteronism (21-hydroxylase deficiency and isolated hypoaldosteronism)
Pseudohypoaldosteronism type 2 (Gordon's syndrome)
Aldosterone resistance
Inhibition of the epithelial sodium channel
Potassium-sparing diuretics, such as spironolactone, eplerenone, amiloride, and triamterene
Antibiotics, trimethoprim, and pentamidine
Pseudohypoaldosteronism type 1
Voltage defects
Markedly reduced distal sodium delivery
Acquired or congenital defects in sodium reabsorption by the distal tubule principal cells (obstructiv uropathy), SLE, and sickle cell disease

ACE: angiotensin-converting enzyme; SLE: systemic lupus erythematosus.

Graphic 82440 Version 17.0

Sample lower-potassium diet

Food	Calories	Sodium content (mg)	Potassium content (mg)
Breakfast			
English muffin, white	129	242	62
Low-calorie, nonhydrogenated margarine, 2 teaspoons	58	65	4
Puffed corn cereal (non-sweetened), 1.5 cups	135	247	45
Eggs, 2 medium fresh	126	123	118
Coffee, 1.25 cups	3	6	145
Non-dairy, fat-free coffee creamer, 1 ounce	20	3	0
Snack			
Cheddar cheese (reduced fat), 1 ounce	49	270	19
Apple, 1 medium	72	1	148
Lunch			
White bread, 2 slices	108	234	44
Turkey breast, 3 ounces	119	189	236
Mayonnaise (low fat), 1 tablespoon	25	140	2
Cheddar cheese (reduced fat), 1 ounce	49	270	19
Egg, hard boiled	78	62	63
Lettuce (iceberg; shredded), 1 cup	8	6	80

Cucumber, peeled, 1/2 medium	12	2	137
Water chestnuts, canned & drained, 5 pieces	17	5	54
Salad dressing (Italian, low fat), 1 tablespoon	27	192	4
Snack			
Clementine, 1	35	1	131
Dinner			
Chicken breast (skin removed, baked with breadcrumb coating and no fat), 4 ounces	221	87	287
Green beans, cooked, no salt added, 1 cup	60	46	184
Low-fat, nonhydrogenated margarine, 1 teaspoon	29	33	2
Rice, white, cooked in unsalted water, 1 cup after cooking	234	3	89
Extra virgin olive oil, 2 teaspoons	40	0	0
Snack			
Oatmeal cookies (reduced fat), 2 small	56	58	22
TOTALS	**1710**	**2285**	**1895**

This sample diet is calorically adequate for people of smaller stature and activity levels. People who are active or larger may require additional nutrients and calories. This diet contains less than 7% of calories from saturated fat, which meets the American Heart Association (AHA) guidelines for that nutrient.

Graphic 82742 Version 8.0

Foods with high levels of potassium

Highest content (>25 mEq/100 g)
Dried figs
Molasses
Seaweed
Very high content (>12.5 mEq/100 g)
Dried fruits (dates, prunes)
Nuts
Avocados
Bran cereals
Wheat germ
Lima beans

High content (>6.2 mEq/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

Adapted from: Gennari FJ. Hypokalemia. N Engl J Med 1998; 339:451.

Graphic 53492 Version 5.0

Foods with lower levels of potassium

Grains	Foods prepared with white flour (eg, pasta, bread), white rice
Beverages	Non-dairy creamer, fruit punch, drink mixes (eg, Kool-Aid), tea (<2 cups or 16 ounces per day), coffee (<1 cup or 8 ounces per day)
Sweets	Angel or yellow cake, pies without chocolate or high-potassium fruit, cookies without nuts or chocolate
Fruits	Apples (1), apple juice, applesauce, apricots (canned), blackberries, blueberries, cherries, cranberries, fruit cocktail (drained), grapes, grape juice, grapefruit (½), mandarin oranges, peaches (½ fresh or ½ cup canned), pears (½ cup canned), pineapple and juice, plums (1 whole), raspberries, strawberries, tangerine (1 whole), watermelon (1 cup), lemons
Vegetables	Alfalfa sprouts, asparagus (6 spears), green or wax beans, cabbage (cooked), carrots (cooked), cauliflower, celery (1 stalk), corn (½ fresh ear or ½ cup), cucumber, eggplant, kale iceberg lettuce, mushrooms (fresh), okra, onions, parsley, green peas, green peppers, radish, rhubarb, water chestnuts (canned, drained), watercress, spinach (raw, 1 cup), squash (yellow), zucchini, scallions, turnips, turnip greens
Proteins	Chicken, turkey (3 ounces), tuna, eggs, baloney, shrimp (all 1 ounce), unsalted peanut butter (1 tablespoon)
Dairy products	Cheddar or swiss cheese (1 ounce), cottage cheese (½ cup)
Nuts, seeds, and legumes	Macadamia nuts, pecans, cashews, walnuts, almonds, peanuts, sesame seeds, sunflower or pumpkin seeds, chia seeds, flax seeds (all 1 ounce)

Unless noted, one serving is ½ cup (4 ounces). These foods have a lower level of potassium (less than 200 mg potassium per serving on average). Be sure to measure the portion sizes of each food and calculate the total amount in each meal to maintain your lower-potassium diet (eg, average of 2000 mg potassium per day).

Graphic 63021 Version 7.0