Clinical manifestations of hyperkalemia in adults

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Contributor Disclosures

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Literature review current through: Feb 2018. | **This topic last updated:** Dec 12, 2017.

INTRODUCTION — Hyperkalemia is a common clinical problem that is most often due to impaired urinary potassium excretion due to acute or chronic kidney disease and/ordisorders or drugs that inhibit the renin-angiotensin-aldosterone axis. 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). (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment", section on 'Potassium replacement'.)

The clinical manifestations of hyperkalemia will be reviewed here. The causes, diagnosis, treatment, and prevention of hyperkalemia are discussed separately. (See "Causes and evaluation of hyperkalemia in adults" and "Treatment and prevention of hyperkalemia in adults".)

CLINICAL MANIFESTATIONS — The most serious manifestations of hyperkalemia are muscle weakness or paralysis, cardiac conduction abnormalities, and cardiac arrhythmias. These manifestations usually occur when the serum potassium concentration is **≥7.0 mEq/L** with chronic hyperkalemia or possibly at lower levels with an acute rise in serum potassium. Patients with skeletal muscle or cardiac manifestations typically have one or more of the characteristic ECG abnormalities associated with hyperkalemia.

Other manifestations in hyperkalemic patients may be related to the cause of the hyperkalemia, such as polyuria and polydipsia with uncontrolled diabetes.

Severe muscle weakness or paralysis — Hyperkalemia can cause ascending muscle weakness that begins with the legs and progresses to the trunk and arms [4-6]. This can progress to flaccid paralysis, mimicking Guillain-Barré syndrome [5,6]. Sphincter tone and cranial nerve function are typically intact, and respiratory muscle weakness is rare [7]. These manifestations resolve with correction of the hyperkalemia.

In addition to acquired hyperkalemia, there is a genetic disorder hyperkalemic periodic paralysis that is caused by autosomal dominant mutations in the skeletal muscle cell sodium channel. Patients with this disorder develop myopathic weakness during hyperkalemia induced by increased potassium intake or rest after heavy exercise. (See "Hyperkalemic periodic paralysis".)

Cardiac manifestations — Hyperkalemia may be associated with electrocardiographic changes that, if present, may suggest the diagnosis before blood test results. Other manifestations include conduction abnormalities and cardiac arrhythmias.

ECG changes — Hyperkalemia may be associated with a variety of changes on the electrocardiogram (ECG). Tall peaked T waves with a shortened QT interval are usually the first findings (waveform 1). As the hyperkalemia gets more severe, there is progressive lengthening of the PR interval and QRS duration, the P wave may disappear, and ultimately the QRS widens further to a sine wave pattern. 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 as illustrated by the following observations:

●In a review of 90 patients with hyperkalemia (80 percent with a serum potassium below 7.2 mEq/L), the probability of ECG abnormalities increased with increasing serum potassium, but the ECG was insensitive for the diagnosis of hyperkalemia [8].
●In another report, the prevalence of ECG changes suggestive of hyperkalemia was independent of severity (43 and 55 percent in patients with a serum potassium less than 6.8 mEq/L and those with higher values, respectively) [9].
●Rare patients have a normal ECG despite a serum potassium above 9.0 mEq/L [10].
●ECG manifestations are more likely with rapid onset hyperkalemia [11] and the presence of concomitant hypocalcemia, acidemia, and/or hyponatremia [8,12].

Given the unreliable sensitivity, serial measurements of the serum potassium concentration should guide therapy in stable patients with hyperkalemia. The ECG cannot be reliably used to monitor the efficacy of hyperkalemia therapy [10]. In addition, peaked T waves alone are not specific for hyperkalemia, being seen in the early phase of acute myocardial infarction and with early repolarization, and some patients with left ventricular hypertrophy (table 1) [13,14].

Hyperkalemia can also cause a type I Brugada pattern in the ECG, with a pseudo-right bundle branch block and persistent "coved" ST segment elevation in at least two precordial leads. This "hyperkalemic Brugada sign" occurs in critically ill patients with significant hyperkalemia (serum potassium concentration >7.0 mEq/L), and can be differentiated from genetic Brugada syndrome by an absence of P waves, marked QRS widening, and/or an abnormal QRS axis [15]. (See "Brugada syndrome: Clinical presentation, diagnosis, and evaluation".)

Conduction abnormalities and arrhythmias — Hyperkalemia can lead to a variety of conduction abnormalities and arrhythmias:

●Conduction abnormalities that may be seen include right bundle branch block, left bundle branch block, bifascicular block, and advanced atrioventricular block [16].
●Cardiac arrhythmias associated with hyperkalemia include sinus bradycardia, sinus arrest, slow idioventricular rhythms, ventricular tachycardia, ventricular fibrillation, and asystole [17,18].

Reduced urinary acid excretion — Hyperkalemia interferes with renal ammonium (NH4+) excretion, thereby limiting acid excretion and possibly leading to the development of metabolic acidosis [19-23]. This association has been well described in humans as illustrated by the following observations; similar findings have been described in animal models [23]:

●Two case reports described patients with isolated hyporeninemic hypoaldosteronism and mild to moderate chronic kidney disease who had hyperkalemia, metabolic acidosis, and reduced urinary NH4+ excretion [20]. Correction of the hyperkalemia with a potassium-sodium exchange resin led to resolution of the acidemia and normalization of urinary NH4+ excretion.
●In a study in normal men, ingesting a high potassium diet for five days was associated with a significant reduction in both ammonium and net acid excretion [22].
●Correction of hyperkalemia with the potassium binder ZS-9 is associated with an increase in the serum bicarbonate concentration [24,25]. However, in addition to potential indirect effects on renal ammonium excretion, ZS-9 binds intestinal ammonium [26].

At least three mechanisms are thought to contribute to the hyperkalemia-induced diminution in ammonium secretion:

●An intracellular alkalosis as entry of some of the excess potassium into the cells is associated with hydrogen ion movement out the cells to maintain electroneutrality. The intracellular alkalosis will reduce both ammonium excretion and bicarbonate reabsorption [20,22,23,27,28].
●Reduced NH4+ reabsorption in the thick ascending limb of the loop of Henle [23,29]. In normal subjects, NH4+ can substitute for potassium on the Na-K-2Cl cotransporter in the luminal membrane, a process that is essential for medullary recycling of NH4+, which is subsequently secreted into the medullary collecting duct [30]. With hyperkalemia, potassium competes with NH4+ for transport by the Na-K-2Cl cotransporter, resulting in reductions in medullary recycling and NH4+ secretion and the development of metabolic acidosis.
●Diminished ammoniagenesis, mediated in part by reduced glutamate deamination [31].

PATHOGENESIS — The muscle weakness and cardiac manifestations induced by hyperkalemia are related to impaired neuromuscular transmission [2,32]. The generation of an action potential (called membrane excitability) is related both to the magnitude of the resting membrane potential and to the activation state of membrane sodium channels. Opening of these sodium channels, leading to the passive diffusion of extracellular sodium into the cells, is the primary step in this process.

According to the Nernst equation, the resting electrical potential across the cell membrane is related to the ratio of the extracellular to intracellular potassium concentration. An elevation in the extracellular (plasma) potassium concentration decreases this ratio; makes the resting potential less electronegative and partially depolarizing the cell membrane.

The less negative resting potential will initially increase membrane excitability since a lesser depolarizing stimulus is required to generate an action potential. However, the later effect is different. Persistent depolarization inactivates sodium channels in the cell membrane, thereby producing a net decrease in membrane excitability that may be manifested clinically by impaired cardiac conduction and/or neuromuscular weakness or paralysis [32].

Increases in extracellular potassium also affect the repolarization phase of the cardiac action potential via activation of the rapidly activating delayed rectifier potassium channel (I_{Kr}). The HERG (human ether-a-go-go-related) gene encodes the pore-forming subunits of I_{Kr}, which is largely responsible for potassium efflux during phases 2 and 3 of the cardiac action potential [33]. HERG channels are highly sensitive to changes in extracellular potassium, with inhibition in hypokalemia and activation during hyperkalemia [34,35]. This effect of hyperkalemia on repolarization is thought to underlie the "early" signs of hyperkalemia [18], including ST-T segment depression, peaked T waves, and QT interval shortening [33].

PATIENT ASSESSMENT — Careful monitoring of the ECG and muscle strength are indicated to assess the functional consequences of hyperkalemia. Severe muscle weakness and/or marked electrocardiographic changes, including conduction abnormalities and arrhythmias, are potentially life-threatening and require immediate treatment. These manifestations usually occur when the serum potassium concentration is **≥7.0 mEq/L** with chronic hyperkalemia or possibly at lower levels with an acute rise in serum potassium. (See "ECG tutorial: Miscellaneous diagnoses", section on 'Hyperkalemia'.)

Rapid increases in serum potassium cause more pronounced cardiac toxicity [36]. A careful history should assess the probable cause of the hyperkalemia (eg, tissue breakdown) and the expected rate of change in serum potassium; treatment should be adjusted accordingly [37]. (See "Treatment and prevention of hyperkalemia in adults".)

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".)

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)")

SUMMARY

●The most serious manifestations of hyperkalemia are ascending muscle weakness or paralysis, cardiac conduction abnormalities, and cardiac arrhythmias. These usually occur when the serum potassium concentration is ≥7.0 mEq/L if hyperkalemia is chronic or lower if hyperkalemia is acute. (See 'Clinical manifestations' above.)

●Electrocardiogram (ECG) changes associated with hyperkalemia include tall peaked T waves with a shortened QT interval; progressive lengthening of the PR interval and QRS duration; disappearance of the P wave; and widening of the QRS complex to a sine wave pattern. The progression and severity of ECG changes do not correlate well with the serum potassium concentration. (See 'ECG changes' above.)

●Conduction abnormalities associated with hyperkalemia include right bundle branch block, left bundle branch block, bifascicular block, and advanced atrioventricular block. Cardiac arrhythmias associated with hyperkalemia include sinus bradycardia, sinus arrest, slow idioventricular rhythms, ventricular tachycardia, ventricular fibrillation, and asystole. (See 'Conduction abnormalities and arrhythmias' above.)

●Hyperkalemia may cause metabolic acidosis by interfering with renal ammonium (NH_4^+) excretion. (See 'Reduced urinary acid excretion' above.)

●The functional consequences of hyperkalemia are assessed by careful monitoring of the ECG and muscle strength. Severe muscle weakness and/or marked electrocardiographic changes may require immediate treatment. Rapid increases in serum potassium cause more pronounced cardiac toxicity. (See 'Patient assessment' above.)

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