

# Hyperkalemia

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**Hyperkalemia** (**hyperkalaemia** in British English, *hyper-high*; *kalium*, potassium; *-emia*, "in the blood") refers to the condition in which the concentration of the electrolyte potassium ( $K^+$ ) in the blood is elevated. Extreme hyperkalemia is a medical emergency due to the risk of potentially fatal abnormal heart rhythms (arrhythmia).

Normal serum potassium levels are between 3.5 and 5.0 mEq/L;<sup>[1]</sup> at least 95% of the body's potassium is found inside cells, with the remainder in the blood. This concentration gradient is maintained principally by the  $Na^+/K^+$  pump.

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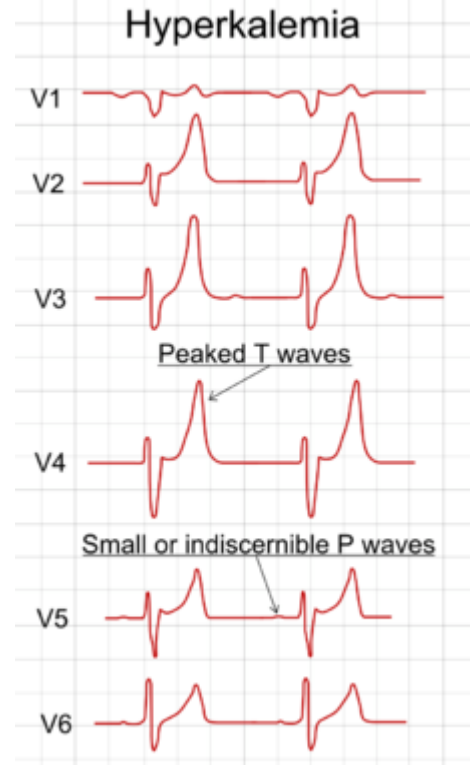
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## Signs and symptoms

Symptoms are fairly nonspecific and generally include malaise, palpitations and muscle weakness; mild hyperventilation may indicate a compensatory response to metabolic acidosis, which is one of the possible causes of hyperkalemia. Often, however, the problem is detected during screening blood tests for a medical disorder, or it only

## Hyperkalemia

*Classification and external resources*



Electrocardiography showing precordial leads in hyperkalemia.

**ICD-10** E87.5 (<http://apps.who.int/classifications/apps/icd/icd10online/?ge70.htm#e875>)

**ICD-9** 276.7 (<http://www.icd9data.com/getICD9Code.aspx?icd9=276.7>)

**DiseasesDB** 6242 (<http://www.diseasesdatabase.com/ddb6242.htm>)

**MedlinePlus** 001179 (<http://www.nlm.nih.gov/medlineplus/ency/article/001179.htm>)

**eMedicine** emerg/261 (<http://www.emedicine.com/emerg/topic261.htm>)

comes to medical attention after complications have developed, such as cardiac arrhythmia or sudden death.

During the medical history taking, a physician will focus on kidney disease and medication use (see below), as these are the main causes. The combination of abdominal pain, hypoglycemia and hyperpigmentation, often in the context of a history of other autoimmune disorders, may be signs of Addison's disease, itself a medical emergency.

<b>MeSH</b>	D006947 ( <a href="http://www.nlm.nih.gov/cgi/mesh/2011/MB_cgi?field=uid&amp;term=D006947">http://www.nlm.nih.gov/cgi/mesh/2011/MB_cgi?field=uid&amp;term=D006947</a> )
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## Causes

### Ineffective elimination

- Renal insufficiency
- Medication that interferes with urinary excretion:
  - ACE inhibitors and angiotensin receptor blockers
  - Potassium-sparing diuretics (e.g. amiloride and spironolactone)
  - NSAIDs such as ibuprofen, naproxen, or celecoxib
  - The calcineurin inhibitor immunosuppressants ciclosporin and tacrolimus
  - The antibiotic trimethoprim
  - The antiparasitic drug pentamidine
- Mineralocorticoid deficiency or resistance, such as:
  - Addison's disease
  - Aldosterone deficiency
  - Some forms of congenital adrenal hyperplasia
  - Type IV renal tubular acidosis (resistance of renal tubules to aldosterone)
- Gordon's syndrome (“familial hypertension with hyperkalemia”), a rare genetic disorder caused by defective modulators of salt transporters, including the thiazide-sensitive Na-Cl cotransporter.

### Excessive release from cells

- Rhabdomyolysis, burns or any cause of rapid tissue necrosis, including tumor lysis syndrome
- Massive blood transfusion or massive hemolysis
- Shifts/transport out of cells caused by acidosis, low insulin levels, beta-blocker therapy, digoxin overdose, or the paralyzing agent succinylcholine

### Excessive intake

- Excess intake with salt-substitute, potassium-containing dietary supplements, or potassium chloride (KCl) infusion. Note that for a person with normal kidney function and nothing interfering with normal elimination (see above), hyperkalemia by potassium intake would be seen only with large infusions of KCl or oral doses of several hundred milliequivalents of KCl.<sup>[2]</sup>

### Lethal injection

In the United States of America, hyperkalemia is intentionally brought about in an execution by lethal injection. A lethal dose of potassium chloride is the third and last of the three drugs administered, and the one that actually causes death.

## Pseudohyperkalemia

Pseudohyperkalemia is a rise in the amount of potassium that occurs due to excessive leakage of potassium from cells, during or after blood is drawn. It is a laboratory artifact rather than a biological abnormality and can be misleading to caregivers.<sup>[3]</sup> Pseudohyperkalemia is typically caused by hemolysis during venipuncture (by either excessive vacuum of the blood draw or by a collection needle that is of too fine a gauge); excessive tourniquet time or fist clenching during phlebotomy (which presumably leads to efflux of potassium from the muscle cells into the bloodstream),<sup>[4]</sup> or by a delay in the processing of the blood specimen. It can also occur in specimens from patients with abnormally high numbers of platelets ( $>500,000/\text{mm}^3$ ), leukocytes ( $> 70\,000/\text{mm}^3$ ), or erythrocytes (hematocrit  $> 55\%$ ). People with "leakier" cell membranes have been found, whose blood must be separated immediately to avoid pseudohyperkalemia.<sup>[5]</sup>

## Pathophysiology

Potassium is the most abundant intracellular cation. It is critically important for many physiological processes, including maintenance of cellular membrane potential, homeostasis of cell volume, and transmission of action potentials in nerve cells. Its main dietary sources are vegetables (tomato and potato), fruits (orange and banana) and meat. Elimination is through the gastrointestinal tract and the kidney.

The renal elimination of potassium is passive (through the glomeruli), and reabsorption is active in the proximal tubule and the ascending limb of the loop of Henle. There is active excretion of potassium in the distal tubule and the collecting duct; both are controlled by aldosterone.

Hyperkalemia develops when there is excessive production (oral intake, tissue breakdown) or ineffective elimination of potassium. Ineffective elimination can be hormonal (in aldosterone deficiency) or due to causes in the renal parenchyma that impair excretion.

Increased extracellular potassium levels result in depolarization of the membrane potentials of cells. This depolarization opens some voltage-gated sodium channels, but not enough to generate an action potential. After a short while, the open sodium channels inactivate and become refractory, increasing the threshold needed to generate an action potential. This leads to the impairment of neuromuscular, cardiac, and gastrointestinal organ systems. Of most concern is the impairment of cardiac conduction which can result in ventricular fibrillation or asystole.

During extreme exercise, potassium is released from active muscle and the serum potassium rises to a point that would be dangerous at rest. For unclear reasons, it appears as if the high levels of adrenaline and noradrenaline have a protective effect on the cardiac electrophysiology.<sup>[6]</sup>

Patients with the rare hereditary condition of hyperkalemic periodic paralysis appear to have a heightened sensitivity of muscular symptoms that are associated with transient elevation of potassium levels. Episodes of muscle weakness and spasms can be precipitated by exercise or fasting in these subjects.

## Diagnosis

To gather enough information for diagnosis, the measurement of potassium needs to be repeated, as the elevation can be due to hemolysis in the first sample. The normal serum level of potassium is 3.5 to 5 mEq/L. Generally, blood tests for renal function (creatinine, blood urea nitrogen), glucose and occasionally creatine kinase and cortisol will be performed. Calculating the trans-tubular potassium gradient can sometimes help in

distinguishing the cause of the hyperkalemia.

In many cases, renal ultrasound will be performed, since hyperkalemia is highly suggestive of renal failure.

Also, electrocardiography (EKG/ECG) may be performed to determine if there is a significant risk of cardiac arrhythmias.

## ECG findings

With mild to moderate hyperkalemia, there is reduction of the size of the P wave and development of peaked T waves. Severe hyperkalemia results in a widening of the QRS complex, and the EKG complex can evolve to a sinusoidal shape. There appears to be a direct effect of elevated potassium on some of the potassium channels that increases their activity and speeds membrane repolarization. Also, (as noted above), hyperkalemia causes an overall membrane depolarization that inactivates many sodium channels. The faster repolarization of the cardiac action potential causes the tenting of the T waves, and the inactivation of sodium channels causes a sluggish conduction of the electrical wave around the heart, which leads to smaller P waves and widening of the QRS complex.

The serum  $K^+$  concentration at which electrocardiographic changes develop is somewhat variable.<sup>[7][8]</sup> Although the factors influencing the effect of serum potassium levels on cardiac electrophysiology are not entirely understood, the concentrations of other electrolytes, as well as levels of catecholamines, play a major role.<sup>[9][10]</sup>

## Treatment

When arrhythmias occur, or when potassium levels exceed 6.5 mmol/l, emergency lowering of potassium levels is mandated. Several agents are used to transiently lower  $K^+$  levels. Choice depends on the degree and cause of the hyperkalemia, and other aspects of the patient's condition.

### Myocardial excitability

Calcium (Calcium chloride or calcium gluconate) increases threshold potential through a mechanism that is still unclear, thus restoring normal gradient between threshold potential and resting membrane potential, which is elevated abnormally in hyperkalemia. One ampule of Calcium chloride has approximately 3 times more calcium than calcium gluconate. Onset of action is <5 min and lasts about 30-60 min. Doses should be titrated with constant monitoring of ECG changes during administration and the dose should be repeated if ECG changes do not normalize within 3 to 5 min.

### Lowering $K^+$ temporarily

Several medical treatments shift potassium ions from the bloodstream into the cellular compartment, thereby reducing the risk of complications. The effect of these measures tends to be short-lived, but may temporize the problem until potassium can be removed from the body.<sup>[11]</sup>

- Insulin (e.g. intravenous injection of 10-15 units of regular insulin along with 50ml of 50% dextrose to prevent hypoglycemia) will lead to a shift of potassium ions into cells, secondary to increased activity of the sodium-potassium ATPase.<sup>[12]</sup> Its effects last a few hours, so it sometimes needs to be repeated while other measures are taken to suppress potassium levels more permanently.

- Bicarbonate therapy (e.g. 1 ampule (50mEq) infused over 5 minutes) is effective in shifting potassium into the cell.<sup>[12]</sup> The bicarbonate ion will stimulate an exchange of cellular H<sup>+</sup> for Na<sup>+</sup>, thus leading to stimulation of the sodium-potassium ATPase.
- Salbutamol (albuterol, Ventolin) is a β<sub>2</sub>-selective catecholamine that is administered by nebulizer (e.g. 10–20 mg). This drug also lowers blood levels of K<sup>+</sup> by promoting its movement into cells.<sup>[12]</sup>

## Increasing elimination

Severe cases require hemodialysis or hemofiltration, which are the most rapid methods of removing potassium from the body.<sup>[12]</sup> These are typically used if the underlying cause cannot be corrected swiftly while temporizing measures are instituted or there is no response to these measures.

Polystyrene sulfonate with sorbitol (Kayexalate) either orally or rectally is widely used with the goal to lower potassium over several hours.<sup>[12]</sup> Removal of potassium is assumed to require defecation. However, careful clinical trials to demonstrate the effectiveness of Kayexalate are lacking, and there are small risks of necrosis of the colon.<sup>[13]</sup>

Furosemide may also be used to promote excretion of potassium in the urine.<sup>[12]</sup>

## Long-term prevention

Preventing recurrence of hyperkalemia typically involves reduction of dietary potassium, removal of an offending medication, and/or the addition of oral bicarbonate or a diuretic (such as furosemide or hydrochlorothiazide). Polystyrene sulfonate and sorbitol (Kayexalate) is occasionally used on an ongoing basis to maintain lower serum levels of potassium. Concerns regarding its use are noted in the previous section.

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