

# Introduction to Clinical Medicine - Potassium Disorders

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Disorders of potassium homeostasis are among the most frequent and potentially lethal of all renal conditions. Both excess potassium and inadequate potassium lead to significant morbidity and mortality.

## Hyperkalemia

Hyperkalemia is the more dramatic than hypokalemia, and more likely to lead to immediate death. Changes in extracellular potassium levels alter membrane potential (see Figure 1). This leads to increased rates of repolarization and decreased conduction velocity of electrical signals.

### Clinical Manifestations

Hyperkalemia's cardiac effects are its most dramatic, and its most life-threatening. Figure 2 shows some of the cardiac changes resulting from hyperkalemia. The first effect of hyperkalemia is peaking of the T waves, followed by prolonged PR interval and slowed QRS conduction.

Ventricular fibrillation can develop, causing sudden cardiac death. The cardiac manifestations of hyperkalemia make it a medical emergency.

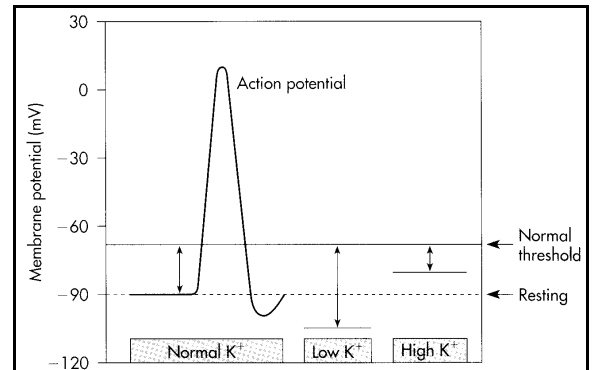
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### Causes

Hyperkalemia can be either spurious or true.

Spurious hyperkalemia is due to release of potassium from either WBC's or platelets during clotting. It should be considered if the WBC count is greater than 70,000 or platelet count is greater than 500,000. This diagnosis can be confirmed by comparing the potassium concentration in blood allowed to clot and blood that is heparinized so that



**Figure 1.** Effect of changes in extracellular potassium on membrane potential.

	Serum potassium mEq/L	P	QRS	T	U	
Hyperkalemia	10					Ventricular fibrillation
	9					Auricular standstill, intraventricular block
	8					Prolonged PR interval, depressed ST segment, high T wave
	7					High T wave
Normal	4-5					Normal
Hypokalemia	3.5					Low T wave
	3					Low T wave, high U wave
	2.5					Low T wave, high U wave, low ST segment

**Figure 2.** Electrocardiographic manifestations of hyper- and hypokalemia.

it does not clot. Under normal conditions the two should be within ~0.3 mEq/L of each other.

True hyperkalemia is due to either decreased renal excretion of potassium or redistribution from the intracellular to extracellular fluid compartments. Pure redistribution rarely causes hyperkalemia, except in the case of digoxin overdose.

Decreased renal excretion of potassium most likely occurs either because the kidneys don't work (renal failure) or because medications are impairing the kidney's normal response to hyperkalemia.

Renal failure should be easy to diagnose and is the subject of the next talk.

The kidney's normal response to hyperkalemia is to increase urinary potassium secretion. This response requires aldosterone to signal the kidneys, prostaglandins to coordinate the renal response and intact functioning of potassium secreting transporters.

	<b>Class</b>	<b>Mechanism</b>
Inhibit aldosterone	β-blockers	Inhibit renin secretion and inhibit β-adrenergic stimulation of cellular potassium uptake
	ACE-inhibitors	Prevent AII formation (AII stimulates aldosterone formation)
	Angiotensin-receptor blockers	Prevent AII formation
	Heparin	Inhibits adrenal aldosterone synthase
	Aldosterone receptor antagonist (spironolactone)	Inhibits aldosterone action
Inhibit prostaglandin formation	NSAIA	Prostaglandins required for increased renal potassium secretion
Inhibit potassium transporters	Potassium-sparing diuretics (amiloride, triamterene)	Block potassium exit from collecting duct cells into the urine
	Certain antibiotics (trimethoprim, pentamidine)	Act as potassium sparing diuretics
	Digoxin overdose	Block potassium uptake into cells on Na <sup>+</sup> -K <sup>+</sup> -ATPase
	Cyclosporine	Still not clear, probably block potassium uptake into cells on Na <sup>+</sup> -K <sup>+</sup> -ATPase

**Treatment of Hyperkalemia**

Mechanism	Therapy	Onset	Duration
Antagonize membrane effects	IV calcium	1-2 minutes	30-60 min
Drive potassium inside cells	Insulin ( $\pm$ glucose)	30 min	4-6 hr
	$\beta$ -agonists	30 min	2-4 hr
Get potassium out of the body	Kayexalate (exchanges sodium for potassium)	1-2 hrs	-
	Dialysis	Immediate, but may take 4-6 hours to institute	-
	Diuretics	Hours (may require high doses, useful for chronic hyperkalemia)	-

## Hypokalemia

Hypokalemia is commonly silent and can cause both long-term and short-term adverse effects.

### Clinical Manifestations

The most profound of hypokalemia's effects is on the cardiovascular system. First, hypokalemia increases myocardial cell sensitivity to arrhythmia, leading to an increased risk of ventricular fibrillation, especially in the setting of myocardial ischemia. Second, hypokalemia causes hypertension. This is due, at least in part, to stimulation of sodium retention and extracellular volume expansion.

Other effects of hypokalemia include decreased insulin sensitivity, muscular weakness, polyuria and, in the presence of liver failure, precipitating hepatic encephalopathy.

### Causes

Broad category	Specifics	Example(s)
Pseudohypokalemia	Abnormal WBC take up $K^+$	Leukemia
Redistribution	Shift from extra- to intracellular fluid compartments	Insulin
		Aldosterone
		$\beta$ -agonists (including epinephrine and norepinephrine during myocardial ischemia)
Renal potassium loss	Diuretics	
	Magnesium deficiency	Inhibits renal $K^+$ retention

Broad category	Specifics	Example(s)
Non-renal loss	Diarrhea, sweating	
Inadequate intake	Dietary	Junk food diet

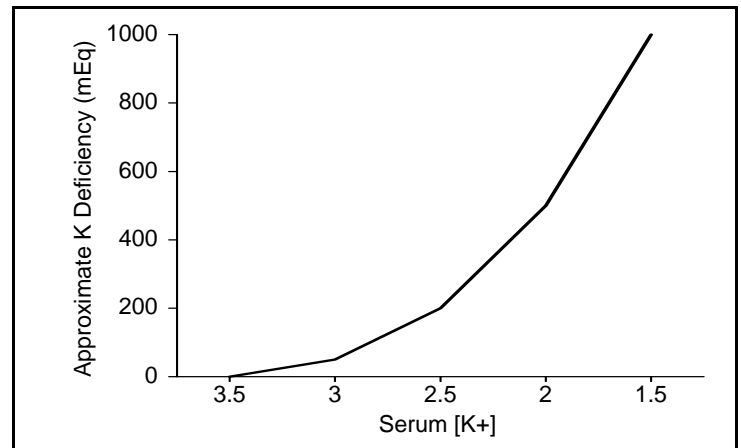
**Treatment**

First, exclude pseudohypokalemia by measuring the WBC.

Second, guesstimate the amount of potassium required. More than 98% of total body potassium is present inside cells. Because cells try to minimize the development of hypokalemia, during potassium depletion they will shift potassium from the intra- to extra-cellular fluid trying to maintain a normal ratio of extra- to intra-cellular potassium to keep membrane potential as close to normal as possible.

Finally, determine the urgency of treatment. Are life-threatening arrhythmias present? If so treat rapidly. To do so, give intravenous KCl at rates of 20-40 mEq per hour via a central line under continuous EKG monitoring in an ICU.

If not life-threatening, then determine whether oral or IV therapy must be used. Whenever possible, try to use oral therapy. If giving IV, then give no faster than 10 mEq/hr unless in an ICU.



**Figure 3** Approximate relationship between degree of hypokalemia and degree of total body potassium depletion.

**Additional reading**

Weiner, I. D. and C. S. Wingo. Hyperkalemia - a potential lethal disorder. *J Am Soc Nephrol* 9: 1535-43, 1998.

Weiner, I. D. and C. S. Wingo. Hypokalemia - consequences, causes and correction. *J Am Soc Nephrol* 8: 1179-88, 1997.