TABLE 1. SOME COMMON MEDICAL CAUSES OF HYPERKALEMIA

Impaired Excretion

- Acute kidney injury/chronic kidney disease
- Reduced renal blood flow (i.e. *congestive heart failure; cirrhosis*)
- Hypoaldosteronism (i.e. *adrenal insufficiency; primary hyporeninemia; Hyporeninemic hypoaldosteronism*)
- Primary renal tubular defects (*sickle cell disease; obstructive uropathy; hereditary tubular defects*)

Hyperkalemia Caused by Cellular Shifts in Potassium

- Insulin deficiency
- Acidosis
- Hypertonicity (*i.e. mannitol administration; hyperglycemia*)
- Cellular breakdown or leakage
- Hyperkalemic periodic paralysis

Increased Intake

- Potassium supplementation
- Red blood cell transfusion
- Foods high in potassium
- Potassium-containing salt substitutes
- Protein calorie supplements

Pseudohyperkalemia

- Hemolysis
- Blood sample cooling
- Intravenous fluids with potassium
- Erythrocytosis
- Thrombocytosis
- Familial pseudohyperkalemia

Adapted from references 1-5

TABLE 2. MEDICATIONS THAT CAN CAUSE HYPERKALEMIA

DRUG CLASS--DRUGS	MECHANISM OF HYPERKALEMIA	POTENTIAL INCIDENCE or OTHER INFORMATION
Potassium Supplementation • Oral Potassium (oral potassium chloride; oral potassium acetate etc.) • Intervenus fluids containing potassium (KCl; hyper-alimentation etc.) • Blood products (packed red blood cells)	• These products cause a direct increase in potassium. Hyperkalemia will more common in the presence renal insufficiency. • Stored cells can partially hemolyze and release potassium when infused	• Incidence is quite high in patients with any degree of renal dysfunction.
Beta Adrenergic Blockers (esp. the non-selective agents) • Propranolol; Metoprolol; Carvedilol; Many others	• A reduction in beta 2-driven potassium uptake	• Beta blocker-induced hyperkalemia is estimated at 1-5%
Cardiac Glycosides • Digoxin	• Decreases Na+/K+-ATPase activity	• Happens more frequently with toxic digoxin levels but is not always present in the setting of digoxin toxicity
Muscle Depolarizing Agents • Succinylcholine	• Leakage of potassium out of cells through depolarization of cell membranes	• May be more common with muscle injury/trauma
Diuretics • Spironolactone; Eplerenone • Amiloride, triamterene	• Antagonizes aldosterone • Inhibits sodium reabsorption by blocking the epithelial sodium channel (ENaC) in distal tubule/collecting tubule	• Hyperkalemia is common as doses of drug increase
Drugs Affecting the Renin-Angiotensin Aldosterone System • Angiotensin Converting Enzyme Inhibitors ✓ Lisinopril; Captopril; Enalapril; Many others • Angiotensin Receptor Blockers ✓ Valsartan; Candesartan; Many others • Direct Renin Inhibitor ✓ Aliskiren • Calcineurin i*nhibitors* ✓ Cyclosporine; Tacrolimus	• Blockade of angiotensin II synthesis resulting in a reduction of aldosterone secretion; may also impair the delivery of sodium to the distal nephron • Competitively binds to the angiotensin II receptor resulting in a reduction of aldosterone synthesis • Inhibits the conversion of angiotensinogen to angiotensin I and this results in a reduction of aldosterone secretion • May reduce aldosterone synthesis and Na+/K+-ATPase pump activity	• For ACE-inhibitors and ARBs the incidence of hyperkalemia in clinical trials is estimated at 6% • Incidence increases dramatically as renal function gets worse
Nonsteroidal Anti-inflammatory Drugs (NSAIDs) • Ibuprofen; Naproxen; Indometha :in; Man ' others	• Reduction of prostaglandin-mediated renin release, renal blood flow, and glomerular filtration rate (GFR) • May impair angiotensin-II induced aldosterone release • May cause direct renal toxicity	• Directly causes nephrotoxicity. • Hyperkalemia may be more common in cardiac patients on NSAIDs
Anticoagulants • Heparin	• Reduces aldosterone synthesis	• Hyperkalemia is not common but there are many case reports
Antibiotics • Penicillin • Pentamidine • Trimethoprim	• Direct source of potassium • Blocks luminal sodium channels • Blocks luminal sodium channels	• Penicillin-induced hyperkalemia not as common as penicillin use has subsided
Calcium Channel Blockers • Amlodipine; Nifedipine	• Inhibition of adrenal aldosterone biosynthesis • Reduction in aldosterone secretion	• Very sporadic reports
Other Drugs • Mannitol • Azole antifungal Drugs • Ethinyl estradiol/drospirenone • Fluoride toxicity • Glucose infusion or insulin deficiency • Amino acids (part of total parenteral nutrition administered intravenously)	• Mannitol is an osmotic diuretic. Administration of mannitol may cause hypertonicity which can drive potassium out of the intracellular space • May inhibit adrenal steroid synthesis, which can lead to aldosterone deficiency • Spironolactone analogue • May reduce aldosterone synthesis; most common in patients on dialysis who drink water with high fluoride levels • Infusions may drive K^+ from intracellular space to extracellular space • Lysine or arginine enters cells in exchange for K^+ leading to hyperkalemia	• Very sporadic reports
Herbal Therapy Milkweed; Lily of the Valley; Siberian ginseng; Hawthorn berries	• All of these substances possess cardiac glycoside activity and may cause hyperkalemia via inhibition of Na+/K+-ATPase pump.	• Hyperkalemia not always evident in cardiac glycoside toxicity
Adapted from references: 6-12		

TABLE 3. PHARMACOTHERAPY FOR THE TREATMENT OF HYPERKALEMIA

MEDICATION And GENERAL USE	MECHANISM	ADULT DOSE	PED DOSE	ONSET	DURA-TION	EFFECT ON SERUM K	EFFECT ON TOTAL K	OTHER COMMENTS
Calcium • Calcium gluconate • Calcium chloride ***Treating/preventing cardiac arrhythmias in patients with ↑K⁺***	Provides cardiac membrane stabilization induced by toxic effects of potassium	10 ml (one ampule of 10% solution) of calcium gluconate or calcium chloride given IV over 5-10 minutes. May repeat dose in 5-10	CaCl: 20 mg/kg IV CaGluc: 50-100 mg/kg IV	1-3 min	30-60 min	NONE	NONE	• Calcium is indicated for all patients with severe hyperkalemia (K≥7 mEq/L) or in patients with documented hyperkalemia AND ECG changes consistent with ↑ K+ • Reverses ECG effects caused ↑K⁺ by antagonizing membrane excitability • Calcium **WILL NOT** affect potassium concentration • The chloride salt contains 3x the amount of elemental calcium per 10cc • Calcium chloride must be administered through a central line • Constant ECG monitoring is necessary
Insulin + Glucose ***ACUTE HYPERKALEMIA***	Activation of Na+/K+-ATPase causes potassium shift from extravascular space to intravascular space	Dextrose 25 g (50 ml of 50% solution) plus 5-10 units Regular (or rapid acting) Insulin IV.	Reg or rapid acting insulin 0.1 units/kg given with glucose 0.5 g/kg as D25 at 2 ml/kg (in >5 y/o) or D10 at 5 ml/kg (if <5 y/o)	15-30 min	2-4 hrs.	REDUCE	NONE	• Dose can be repeated every 15 minutes if necessary • Blood glucose monitoring is necessary • Does not reduce total potassium • Dextrose may be unnecessary if patient is hyperglycemic (glucose>250 mg/dL)
Beta adrenergic agonists ***ACUTE HYPERKALEMIA***	Activation of Na+/K+-ATPase causes potassium shift from extravascular space to intravascular space	Albuterol 10-20 mg (mixed with 4 ml of normal saline) administered via nebulizer	Albuterol neb sol 0.4 mg in 2 ml saline (if neonate) 2.5 mg in 2 ml saline (if <25 kg) and 5 mg in 2 ml saline (if >25 kg)	15-30 min	1-2 hrs.	REDUCE	NONE	• May cause tachycardia, tremor etc. Use with caution in patients with coronary artery disease or hypertension. • Effect on potassium may be inconsistent from patient to patient • Relatively short duration of effect
Loop Diuretics (i.e. furosemide) ***ACUTE OR CHRONIC HYPERKALEMIA***	Increases the urinary excretion of potassium	Furosemide 40-80 mg IV bolus	Furosemide: 1 mg/kg IV (max 40 mg/dose with normal renal function to up to 80 mg with decreased kidney function)	5-10 min	4-6 hrs.	REDUCE	REDUCE	• Most useful if hyperkalemia is caused by inadequate potassium excretion • Patients must have adequate renal function for diuretics to be beneficial • ↑excretion of other electrolytes (magnesium, sodium, calcium etc.) • ↑ fluid loss which can cause dehydration and contribute to renal dysfunction
Sodium Bicarbonate ***ACUTE HYPERKALEMIA WITH ACIDOSIS***	Temporarily shifts potassium from the extracellular space to the intracellular space	50-100 mEq intravenously	1mEq/kg IV (max dose 50 mEq) As 1 ml/kg of 8.4% solution or, if <6 months of age, as 2 ml/kg of a 4.2% solution	5-10 min.	1-2 hrs.	REDUCE	NONE	• Only effective if patient is acidotic. • May not be effective in patients with poor renal function or dialysis patient. • May have variable, inconsistent effect on potassium • Use caution in patients with heart failure as it can increase sodium load • Use caution in patients who are hypernatremic

TABLE 3. PHARMACOTHERAPY FOR THE TREATMENT OF HYPERKALEMIA (continued)

MEDICATION And GENERAL USE	MECHANISM	ADULT DOSE	PED DOSE	ONSET	DURA-TION	EFFECT ON SERUM K	EFFECT ON TOTAL K	OTHER COMMENTS
Sodium Polystyrene Sulfonate {SPS---- (Kayexalate®)} ***CHRONIC HYPERKALEMIA***	Cation exchange resin which exchanges potassium for sodium in the gut. The K+-resin complex is then excreted in the stool.	Oral: 15-30 g Rectal: 30-50 g as a retention enema	1 g/kg every 4 hours (max dose 30g)	1-2 hrs.	4-6 hrs.	REDUCE	REDUCE	• May have variable, inconsistent effect on K+ concentrations effects • Can take 1-2 hrs. to work • Has been associated with colonic necrosis and fecal impaction • May be constipating but void using with sorbitol, if possible • SPS dose should be separated from other oral meds by at least 3 hours (before or after) to avoid potential binding of other meds
Patiromer (Veltassa®) ***CHRONIC HYPERKALEMIA***	Cation exchange resin—exchanges K+ for calcium.	Initial dose-8.4 g once daily; to a maximum dose of 25.2 g	NOT APPROVED	7 hrs.	48 hrs. ++	REDUCE	REDUCE	• Does not work acutely to reduce K+ • Can cause constipation and hypomagnesemia (monitor Mg+) • Exchanges K+ for calcium so may be safer for patients who cannot tolerate Na (with SPS) • May cause hypomagnesemia; constipation; nausea; abdominal discomfort • Should be separated from other oral meds by at least 3 hours (before or after) to avoid potential binding of other meds
Sodium Zirconium Cyclosilicate—ZS-9 (Lokelma®) ***CHRONIC HYPERKALEMIA***	Entraps monovalent cations (specifically K+ throughout the GI tract	Initial dose: 10 g TID for 48 hrs. Then 10 g daily	NOT APPROVED	About 1 hr.	2.2 hrs.	REDUCE	REDUCE	• May be safer than exchange resins • Faster acting and works throughout GI tract • Avoid in patients with severe constipation, bowel obstruction or impaction, including abnormal postoperative bowel motility disorders • Contains some sodium so monitor for edema

CaCl=calcium Chloride; CaGluc=Calcium Gluconate; adapted from references: 2, 4, 5, 13-23

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