

Disorders of Potassium Homeostasis: Review Questions

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QUESTIONS

Choose the single best answer for each question.

1. A 69-year-old woman with a history of chronic bronchitis, hypertension, and mild chronic renal insufficiency is admitted to the hospital with a pulmonary infection and exacerbation of her underlying lung disease. Treatment with β_2 -agonist nebulizers, corticosteroids, and trimethoprim-sulfamethoxazole (1 double-strength tablet twice daily) is initiated. After 7 days of therapy, the patient improves. Routine blood chemistry values are shown below.

On admission	After 7 days of therapy
Na ⁺ , 140 mEq/L	Na ⁺ , 138 mEq/L
K ⁺ , 4.5 mEq/L	K ⁺ , 6.3 mEq/L
BUN, 28 mg/dL	BUN, 32 mg/dL
Cr, 1.5 mg/dL	Cr, 1.7 mg/dL

BUN = blood urea nitrogen; Cr = serum creatinine; K⁺ = serum potassium; Na⁺ = serum sodium.

Which of the following is the most likely cause of this patient's hyperkalemia?

- A) Acute adrenal insufficiency
 B) Corticosteroid therapy
 C) Renal failure-associated potassium excretory defect
 D) Trimethoprim-sulfamethoxazole therapy
2. A 58-year-old man is evaluated for treatment of pain in his hands. He has a history of hypertension, chronic renal insufficiency, and gout. Medications include amlodipine 10 mg daily, enalapril 20 mg daily, furosemide 60 mg twice daily, and allopurinol 100 mg daily. On physical examination, his blood pressure is 138/78 mm Hg, and his pulse is 80 bpm. Examination of the small hand joints reveals swollen, tender, and warm areas with gouty tophi. The patient is prescribed naproxen 500 mg twice

daily for 10 days to treat the pain and inflammation. Routine blood chemistry values are shown below.

Initial values	After 10 days of therapy
Na ⁺ , 137 mEq/L	Na ⁺ , 132 mEq/L
K ⁺ , 4.6 mEq/L	K ⁺ , 6.7 mEq/L
HCO ₃ ⁻ , 21 mEq/L	HCO ₃ ⁻ , 16 mEq/L
BUN, 38 mg/dL	BUN, 56 mg/dL
Cr, 1.8 mg/dL	Cr, 2.9 mg/dL

BUN = blood urea nitrogen; Cr = serum creatinine; HCO₃⁻ = serum bicarbonate; K⁺ = serum potassium; Na⁺ = serum sodium.

What is the most likely mechanism by which naproxen induced the development of hyperkalemia in this patient?

- A) Decrease in renal potassium excretion from acute renal failure
 B) Direct tubular injury with development of aldosterone resistance
 C) Erythrocyte lysis with release of intracellular potassium into the serum
 D) Induction of hyporeninemic hypoaldosteronism
3. A 15-year-old boy is evaluated for hypertension after his blood pressure was elevated on multiple occasions. He also reports generalized weakness and fatigue. His family history is positive for hypertension. Physical examination reveals a blood pressure of 185/110 mm Hg and a pulse of 91 bpm. Heart, lung, abdominal, and extremity examinations are unremarkable. The patient has no thyromegaly or abdominal/flank bruits. Results of a laboratory evaluation are as follows: serum sodium, 140 mEq/L; serum potassium, 2.1 mEq/L; serum chloride,

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98 mEq/L; serum bicarbonate, 34 mEq/L; thyrotropin, 2.5 μ U/mL; free thyroxine, 1.3 ng/dL; plasma renin activity (supine), 0.15 ng/mL/hour; plasma renin activity (upright), 0.2 ng/mL/hour; plasma aldosterone (supine), 2.1 ng/dL; plasma aldosterone (upright), 2.4 ng/dL; urine aldosterone, 5 μ g/24 hours; urine potassium, 54 mEq/L. Which of the following is the most likely etiology of severe hypokalemia and hypertension in this patient?

- A) Adrenal adenoma
- B) Fibromuscular dysplasia of the renal arteries
- C) Glucocorticoid remediable aldosteronism
- D) Liddle's syndrome

4. In a patient who has developed severe hyperkalemia and associated changes on electrocardiogram (ie, peaked T waves, widened QRS complex), administration of which of the following agents is the most appropriate initial therapy?

- A) A β_2 -agonist, via a nebulizer
- B) Calcium gluconate, intravenously
- C) Insulin plus glucose, intravenously
- D) Sodium polystyrene sulfonate, orally

EXPLANATION OF ANSWERS

1. (D) **Trimethoprim-sulfamethoxazole therapy.**

Trimethoprim-sulfamethoxazole (TMP-SMX), which is structurally similar to amiloride, causes hyperkalemia by blocking the apical membrane sodium channel in the principal cell (similar to amiloride and triamterene). Significantly, hyperkalemia occurs with high-dose TMP-SMX in patients with AIDS and with standard-dose TMP-SMX in patients with mild renal impairment. Adrenal insufficiency is more classically associated with hyperkalemia, hyponatremia, and hypotension. The level of hyperkalemia in this patient is excessive for the modest change in serum creatinine, which is elevated from the effect of trimethoprim to competitively inhibit proximal tubular creatinine secretion.

2. (D) **Induction of hyporeninemic hypoaldosteronism.**

Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause a number of adverse renal effects. Hyperkalemia is one of the most common electrolyte disorders associated with NSAID therapy. NSAIDs reduce endogenous prostaglandin-E synthesis,

which stimulates renin and subsequent aldosterone synthesis. Aldosterone significantly increases renal potassium excretion and is the primary regulatory hormone produced for this purpose. Thus, NSAIDs induce a state of hyporeninemic hypoaldosteronism and precipitate hyperkalemia through a reduction in renal potassium excretion.

3. (D) **Liddle's syndrome.** The diagnosis of Liddle's syndrome, a genetic disorder caused by an activating mutation of the epithelial sodium channel in the principal cell, is supported by the early onset of hypertension and severe hypokalemia in the presence of low renin and aldosterone levels. Identification of secondary causes of hypertension requires recognition of clinical clues such as severe hypokalemia, metabolic alkalosis, and hypertension at a young age. In this particular case, the hypertensive syndromes associated with hypokalemia and metabolic alkalosis should be recognized and distinguished on the basis of both serum and laboratory studies. Fibromuscular dysplasia of the renal arteries is excluded from the diagnosis by the absence of an abdominal bruit, the low plasma renin activity, and the low aldosterone concentrations. Hyperaldosteronism from either an adrenal adenoma or glucocorticoid remediable aldosteronism is excluded from the diagnosis based on the low levels of aldosterone in the blood and urine.

4. (B) **Calcium gluconate, intravenously.** Rapid treatment of severe hyperkalemia is required to prevent the occurrence of life-threatening cardiac arrhythmias. The most appropriate initial therapy entails the stabilization of excitable cardiac membranes with calcium gluconate, administered intravenously. This intervention often reverses the abnormal changes on electrocardiogram. However, this effect is short-lived (approximately 30 minutes), and administration may need to be repeated. A reduction in serum potassium is the next step in treatment. Intravenous administration of insulin plus glucose and administration of a nebulized β_2 -agonist are the most effective therapies to lower serum potassium by shifting this cation into cells. Removal of excess potassium from the body can be achieved through the gastrointestinal tract with sodium polystyrene sulfonate resin or through the blood by hemodialysis.