Potassium Balance and Management of Hypokalemia

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Objectives

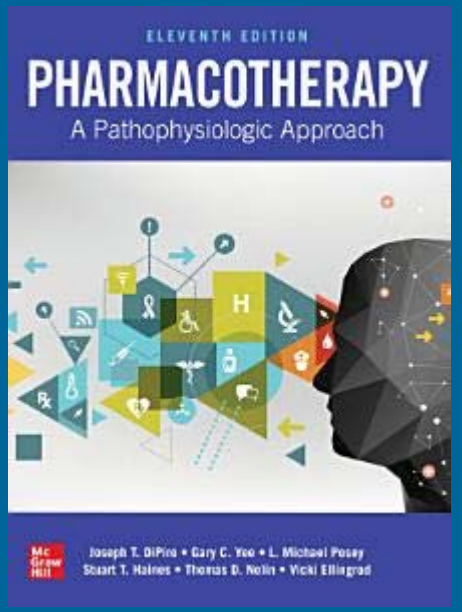
1. Understand normal potassium homeostasis, ICF/ECF balance, and the relationship of serum K to total body K
2. Understand how disease and drug therapy can cause hypokalemia
3. Recognize the clinical manifestations of hypokalemia
4. Design K-replacement therapy appropriate for an individual patient
5. Know commonly used drugs that may alter distribution or excretion of K

Suggested Reading

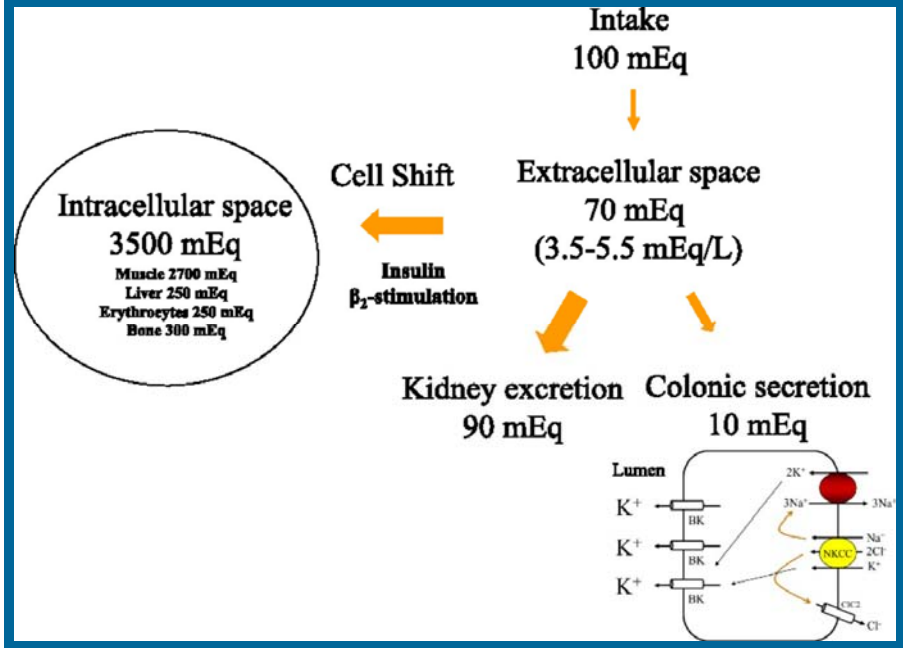
Pharmacotherapy - 11th edition

Chapter 68 – Disorders of Potassium and Magnesium Homeostasis

Pages 797-811



Potassium Homeostasis

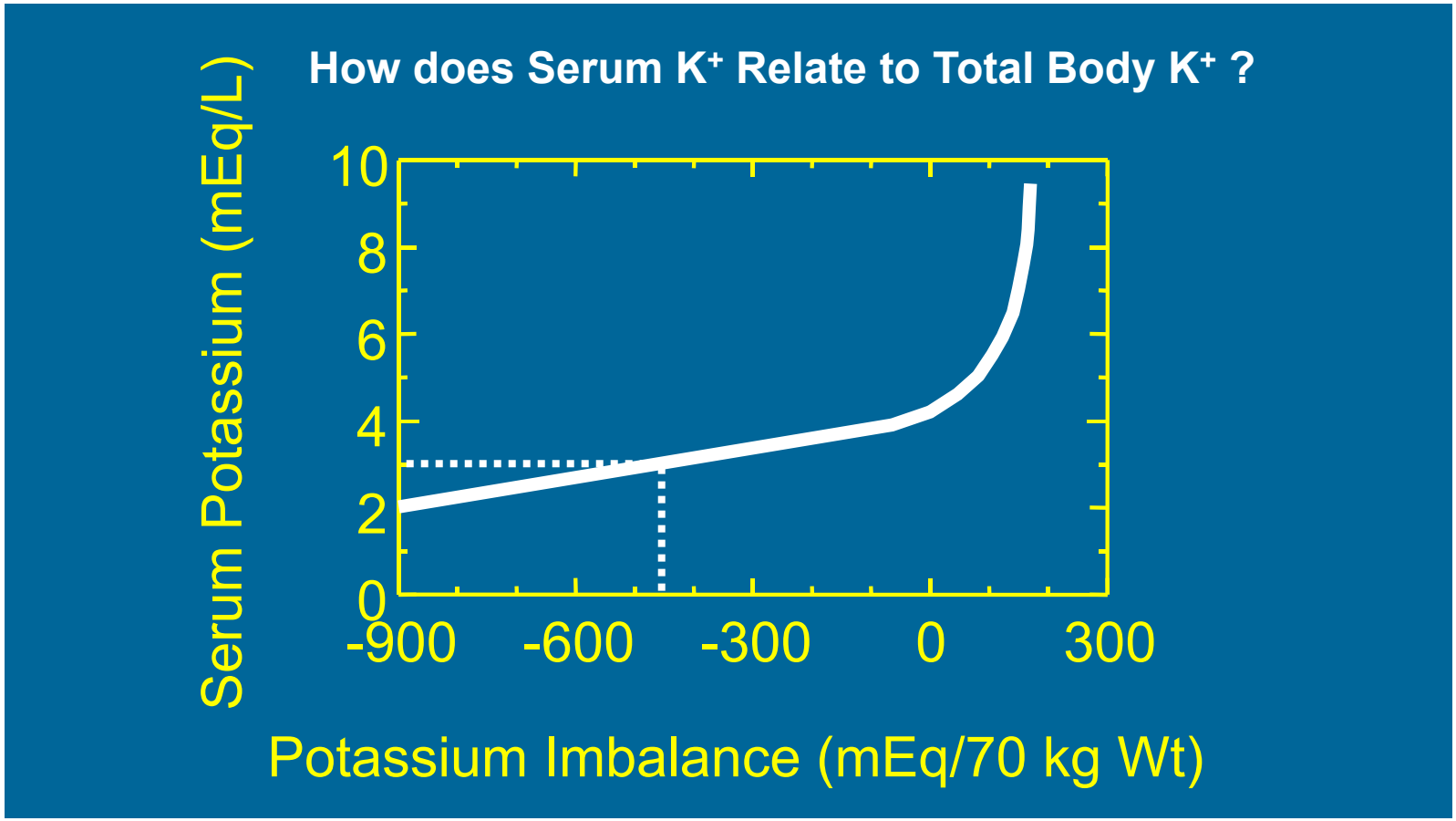


- Normal adult total body K^+ 50-55 mMol/kg;
- >95% intracellular
- Avg daily turnover 50-150 mMol; excretion
- 90% renal, 10% GI;
- aldosterone ↑'s excretion

Kidney 360 2020;1:65-71

Potassium Homeostasis

- Aldosterone secretion is modulated by K level
- ICF / ECF distribution
  - Na/K ATPase in cell membranes
  - Insulin increases intracellular K
  - β_2 adrenergic receptor stim. (e.g. epinephrine) ↑ intracellular K
  - exchange with H^+ (variable effect of pH on K)
- Serum K^+ normally 3.5-4.8 mMol/L


How does Serum K+ Relate to Total Body K+ ?
Serum Potassium (mEq/L)
10
8
6
4
2
0
-900
-600
-300
0
300
Potassium Imbalance (mEq/70 kg Wt)

Classification of Hypokalemia

Category	Serum Potassium Range (mmol/L)
Mild	3.1 – 3.5
Moderate	2.5 – 3.0
Severe	< 2.5

- Hypokalemia is a serious occurrence and problem
- Hypokalemia increases mortality in patients with heart failure or CKD

Circ Heart Fail 2010;3:253-260

Causes of Hypokalemia

- **Poor diet**
  - unlikely as sole cause, unless marked, prolonged reduction in food intake
- **Intracellular shift**
  - Insulin;
  - β_2 agonist use, endogenous sympathetic tone (epinephrine);
  - alkalemia;
  - xanthines
- **GI losses:**
  - diarrhea, vomiting, laxative or enema abuse

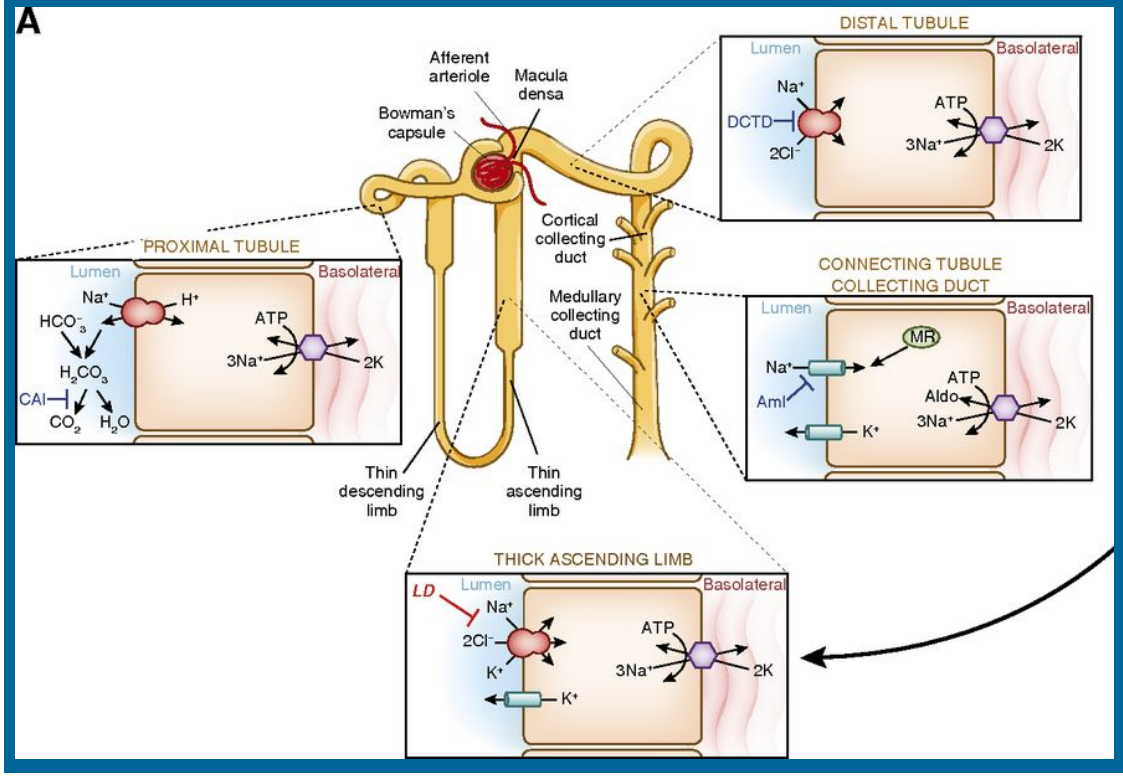
Causes of Hypokalemia

- **Urinary losses**
  - mineralocorticoid excess (aldosterone; steroid Rx)
  - ↑'d Na excretion- high Na intake, diuretic Rx, osmotic diuresis, salt-wasting nephropathies
  - magnesium deficiency
  - metabolic alkalosis
  - high dose Rx with penicillin class; amphotericin B Rx

Potassium and Diuretic Therapy

- K losses are *related to the amount of Na excreted:*
  - greatest during Rx of edema or when Na intake high
- Hypokalemia associated with diuretics most common early after start of Rx or after increase in dose- not common during chronic maintenance diuretic Rx for hypertension
- K-sparing diuretics are effective to avoid hypokalemia, but risk of *hyper*kalemia if K intake increases or reduced renal function

Diuretic Pharmacology



LD – loop diuretic

DCTD – distal convoluted tubule diuretic (thiazide)

Aml – amiloride

CAI – carbonic anhydrase inhibitor

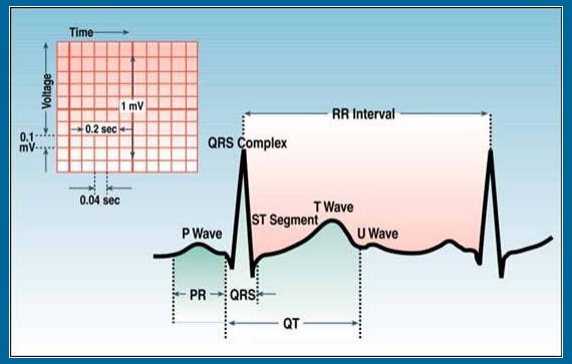
CJASN 2019;14:1248-1257

Manifestations of Hypokalemia

- **Muscle weakness/paralysis**
  - associated with serum K < 2.5 mMol/L
  - gut (constipation or ileus)
  - skeletal muscle
    - lower extremities most sensitive;
    - cramps, tetany, paresthesia, weakness, tenderness; ischemia-rhabdomyolysis, myoglobinuria

Manifestations of Hypokalemia

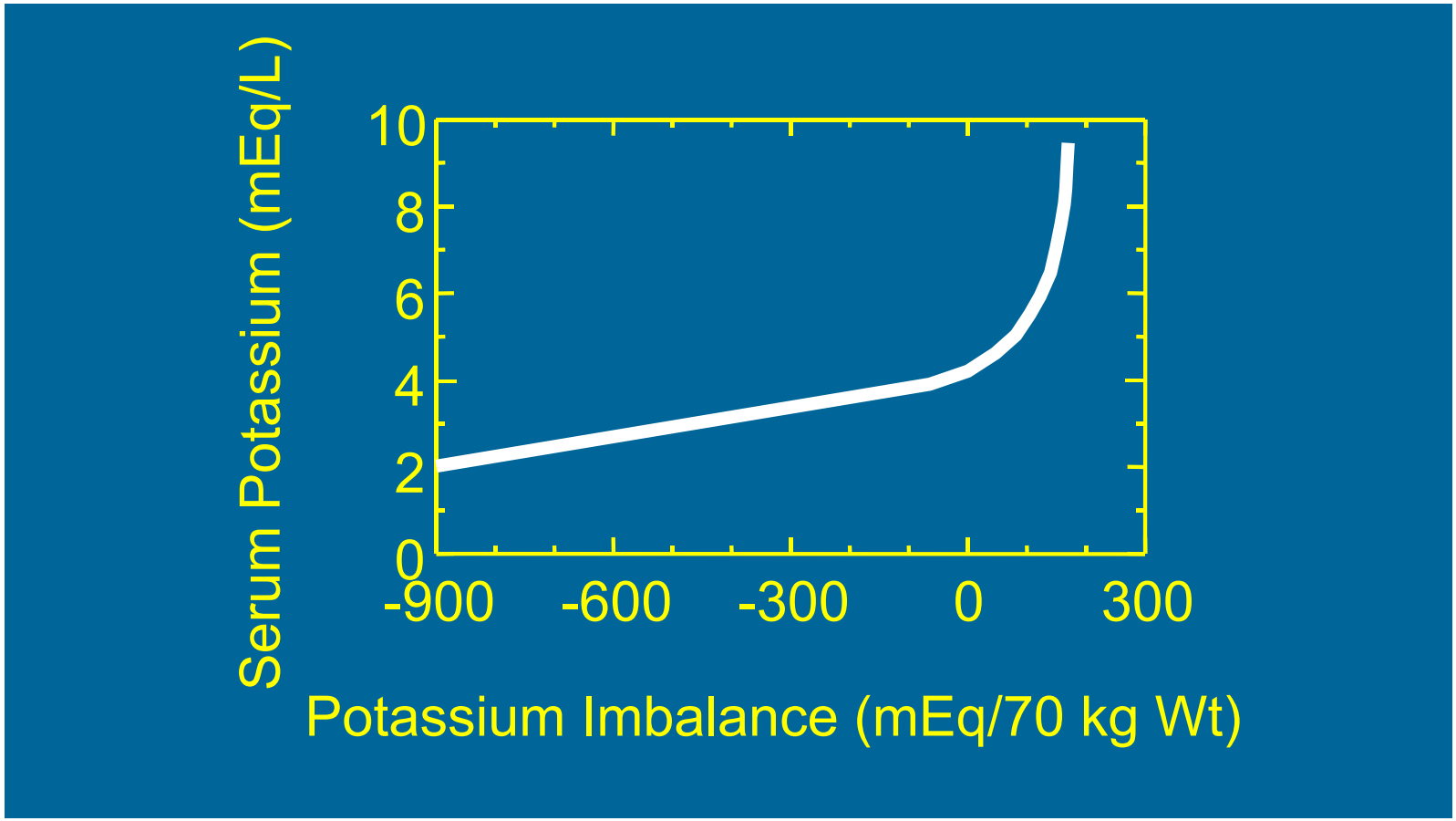
- Cardiac effects
  - U-waves; digitalis toxicity;
  - arrhythmias in *unhealthy* hearts
- Renal effects
  - impaired concentrating ability;
  - metabolic alkalosis
- Glucose intolerance
  - depressed insulin secretion



https://ecg.utah.edu/lesson/12

Management of Hypokalemia

Serum K^+	Treatment
3.0<K<3.5	Usu asymptomatic; p.o. supplement if on digitalis, otherwise dietary K adequate
2.5<K<3.0	Treat with p.o. supplements (40-60 mMol, 3-4X/day until serum K >3.0)
2.0<K<2.5	Some clinical manifestations likely; Rx promptly with p.o. supplements; i.v. supplement if p.o. route questionable or if receiving i.v. fluids
K<2.0	Severe hypokalemia with probable total body deficit 400-900 mMol K; i.v. supplement should start immediately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Oral Potassium Supplements

- **Choice of salt**
  - **See table on next slide**
- **Choice of dosage form**
  - Solutions effective, inexpensive, unpalatable
  - Wax matrix tablets (8, 10 mMol)
  - Microencapsulated capsules (8, 10 mMol) **
  - Sustained release microencapsulated particles (10, 20 mMol) **

** microencapsulated formulations produce fewer GI erosions compared to wax-matrix tablets

Supplement	Comments/Uses
KCl	• preferred in most cases; • Cl^- deficit commonly accompanies K^+ deficit (e.g. gastric losses, diuretics)
Non-Chloride salts - Bicarbonate - Citrate - Gluconate	• Bicarbonate useful when bicarbonate deficit (metabolic acidosis) also present (e.g. lower GI losses) • Citrate largely used for kidney stones not as potassium supplement
K Phosphate	• Useful when phosphate deficit also present

Oral Potassium Supplements

- In acute care – 10 mmol of IV or oral K should increase serum K by 0.1 mmol/L.

- Oral supplementation should be used when possible

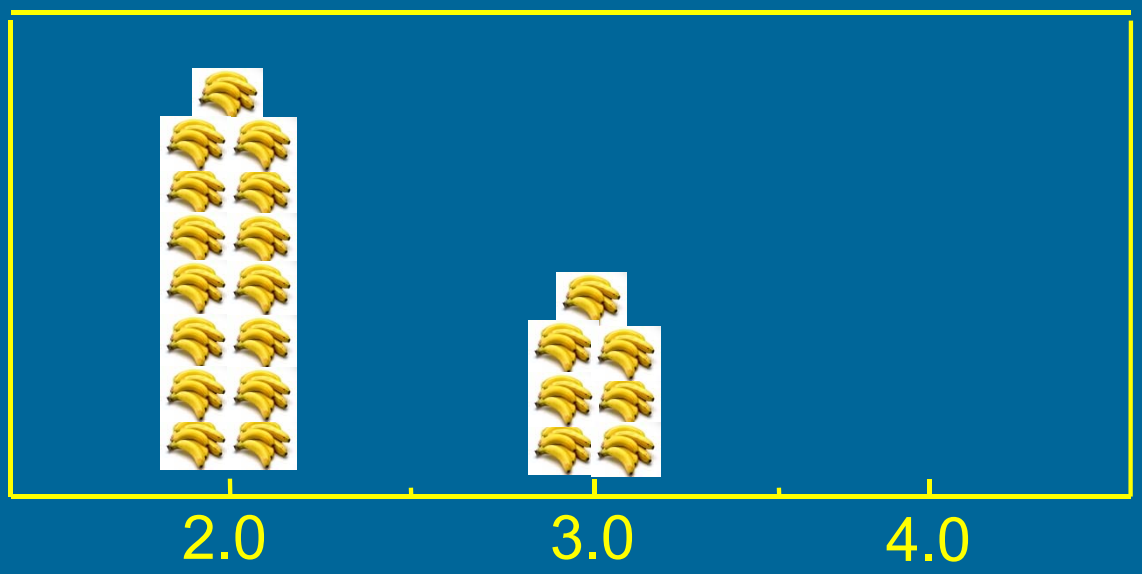
- Oral daily dose should be divided TID or QID with food

Dietary Sources of Potassium

Grams of food needed to obtain 10-12 mMol K^+

- **Lean meat or chicken 120 g**
- **Fruits**
  - **banana 150 g; orange juice 250 g; oranges 200 g; grapes 200 g; pears 400 g; apples 450 g**
- **Vegetables**
  - **cauliflower 150g; mushrooms 100g; potatoes 100g; broccoli 150g; carrots 250g; lettuce 200 g; spinach 100g; tomatoes 200g**
- **Legumes**
  - **canned beans 230g; peas 260g; dry chickpeas 60g**
- **Salt Substitute 1 g KCl**

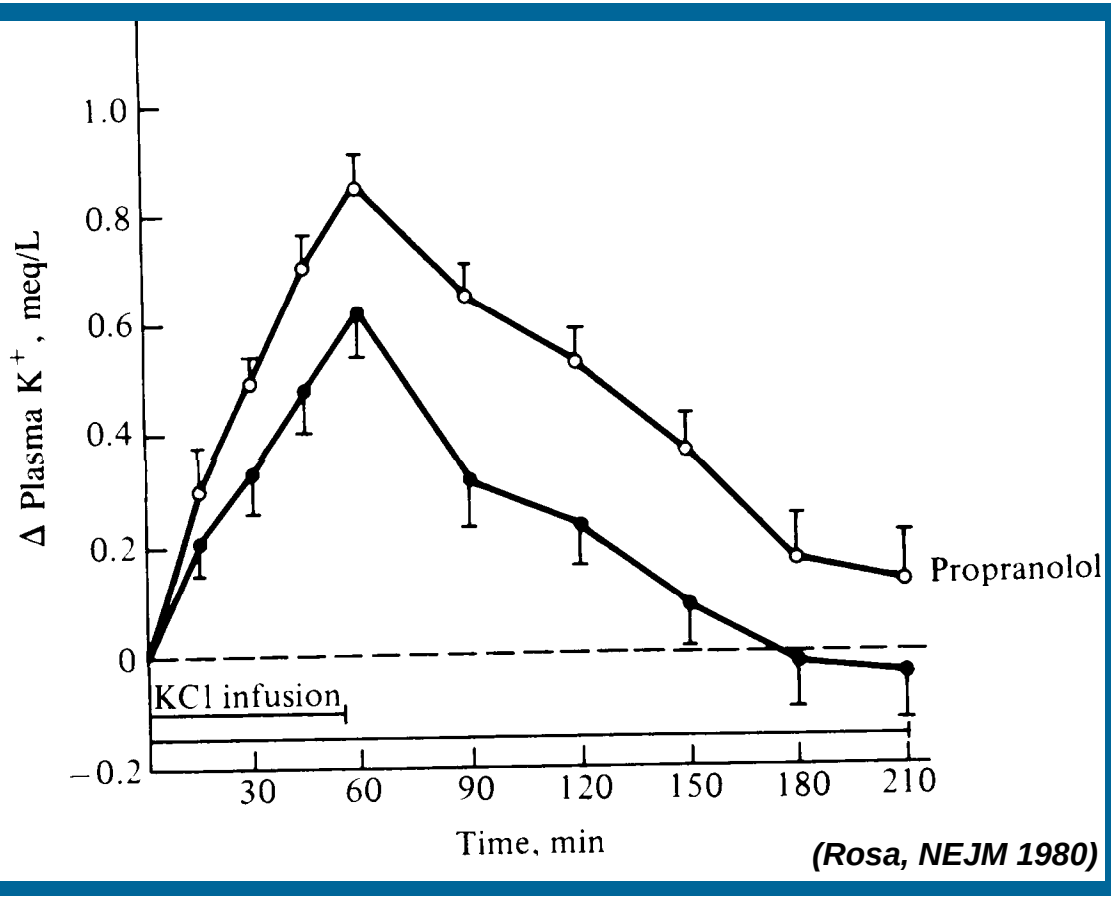
Number of Bananas Needed to Restore Potassium Balance



Cautions for Potassium Rx

Potassium levels may rise higher than expected if compromised ability to excrete K or shift K into ICF normally

- Decreased renal function
- K-sparing diuretic
  - spironolactone, amiloride, triamterene
- Trimethoprim
- Heparin
- ACE inhibitor or ARB
- Beta-2-blocker



(Rosa, NEJM 1980)

Intravenous Potassium Therapy

- In patients receiving i.v. fluid via peripheral vein, may include up to 40 mMol K per liter
- Higher concentrations tolerated via central vein- use pump for safety
- Often administered as piggyback i.v. in 10 mMol increments, infused over an hour

Intravenous Potassium Therapy

- For urgent situations:
  - 10-20 mMol/hr infusion rate via central vein
  - Use dextrose-free i.v. fluid (normal saline)
  - Dextrose solutions stimulate insulin secretion – worsens hypokalemia by shifting K intracellularly
  - Monitor ECG for ≥10 mMol/hr
  - 40 mMol/hr- extreme emergency
  - Measure serum K every 2-4 hours