



# HYPER**K**ALEMIA: Evaluation and Management

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Boca Raton Regional Hospital Grand Rounds  
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# OUTLINE

- Physiology
- Causes
- Clinical Presentation
- Workup
- Management
- Cases



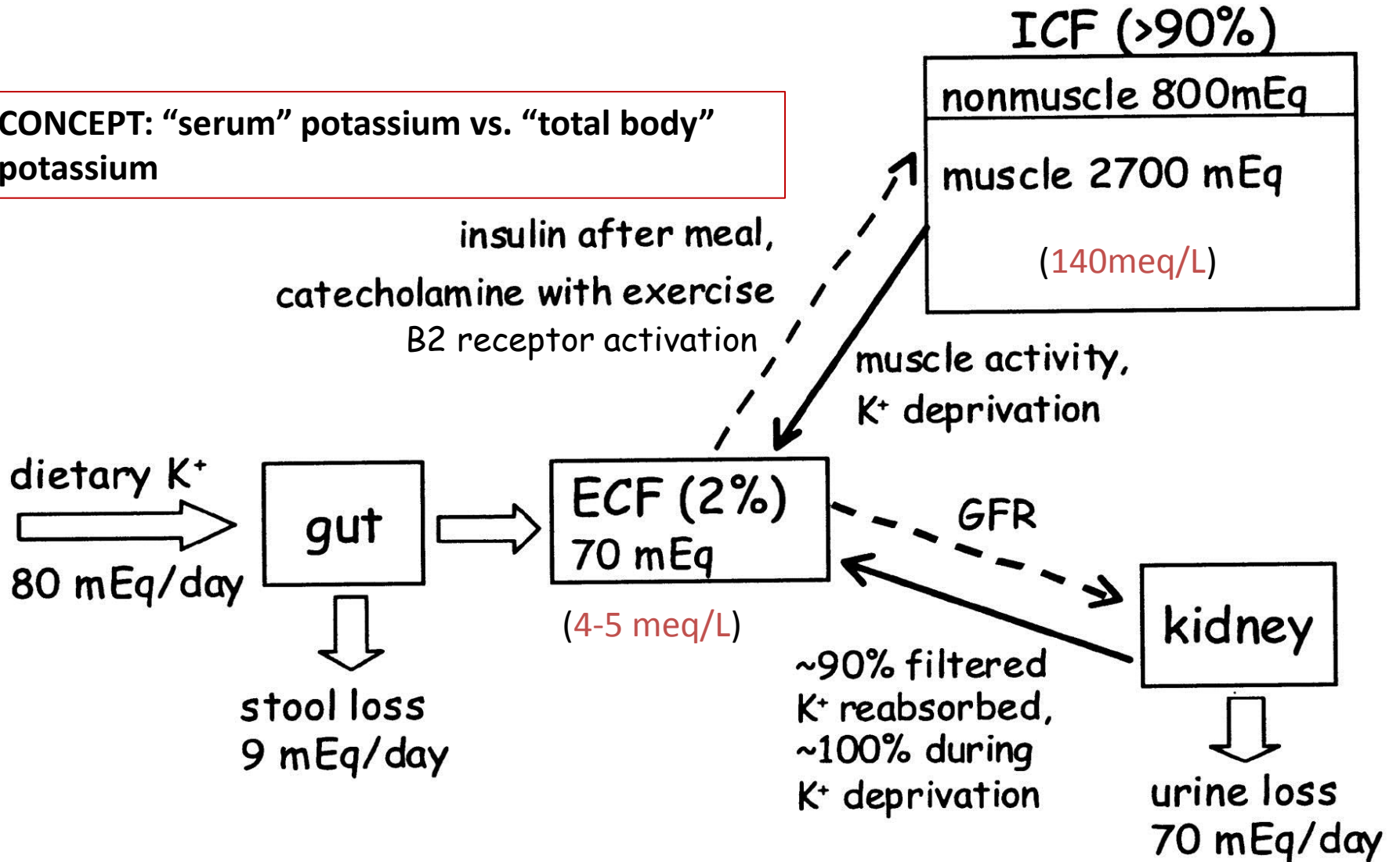
D'Lo Brown

WWE European Champion x4

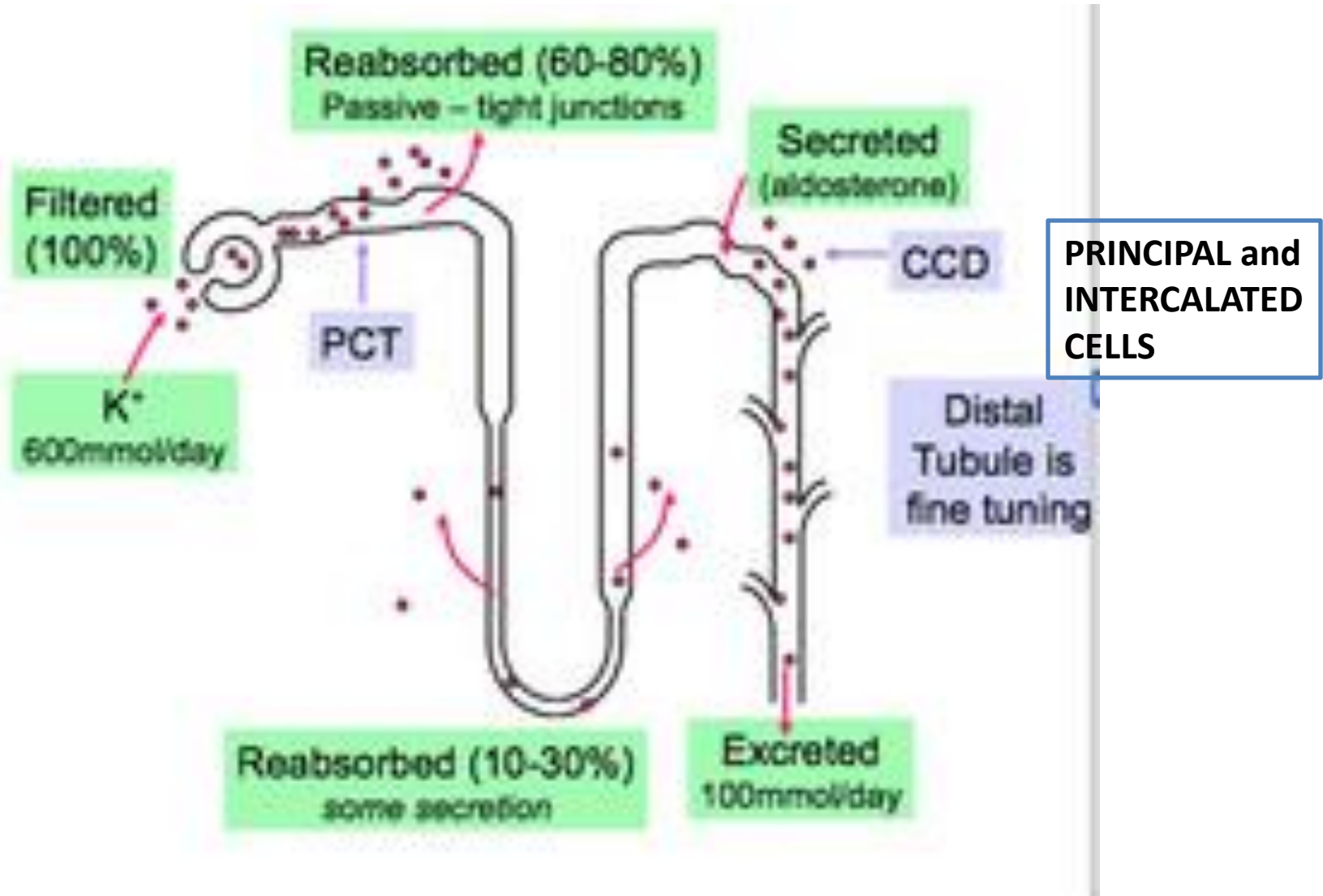
WWE Intercontinental Champion x1

# GENERAL PHYSIOLOGY

CONCEPT: "serum" potassium vs. "total body" potassium

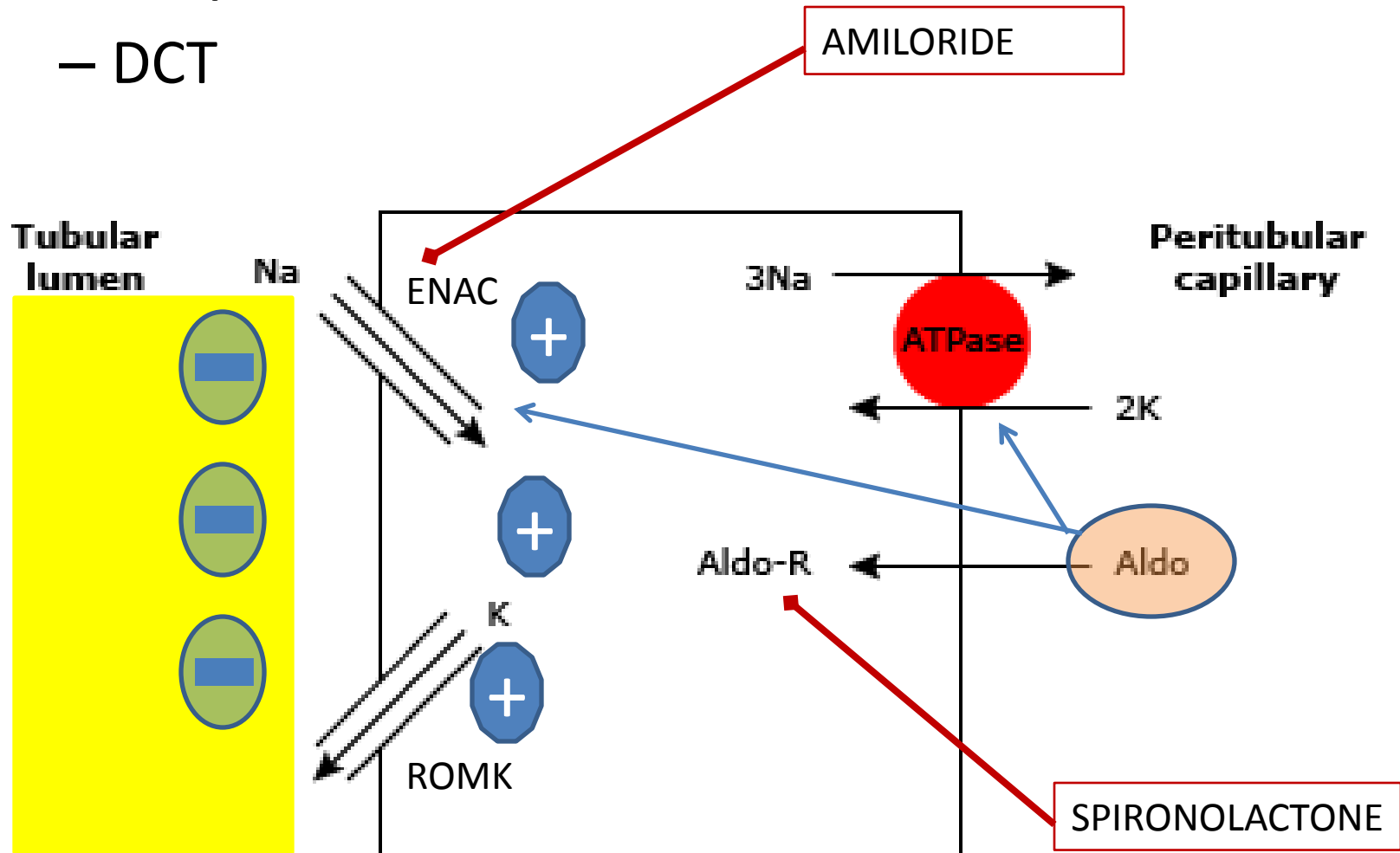


# RENAL PHYSIOLOGY



# RENAL PHYSIOLOGY

- Principal Cell
  - DCT



# CAUSES

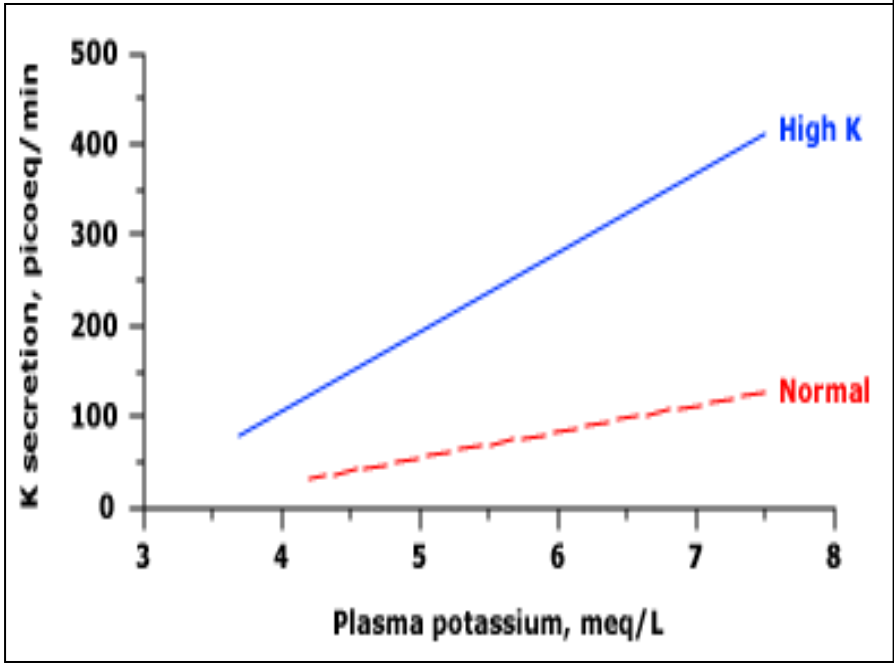
## TOO MUCH IN

- Oral or IV overdose (rare- executions)
- Increased release from cells

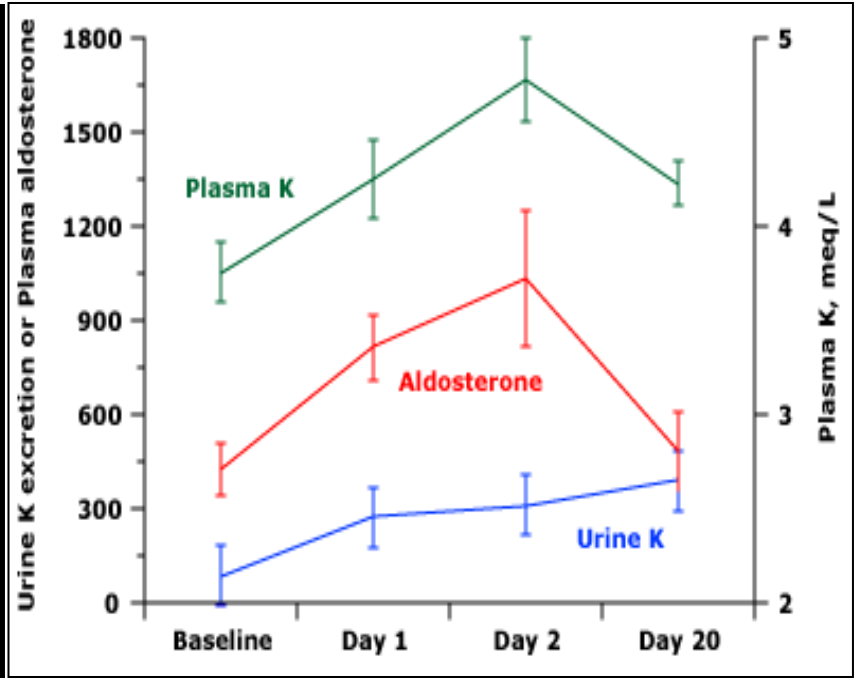
## IMPAIRED RENAL EXCRETION

TOO MUCH  
IN?

# POTASSIUM ADAPTATION



- Stanton- AJP 1989
- Rats
- High K diet led to more K excretion at all K levels while receiving KCl infusion



- Rabelink- KI 1990
- High K diet led to more K excretion
- Plasma K stable
- Aldo levels fell to normal
- More ENaC and Na-K ATPase

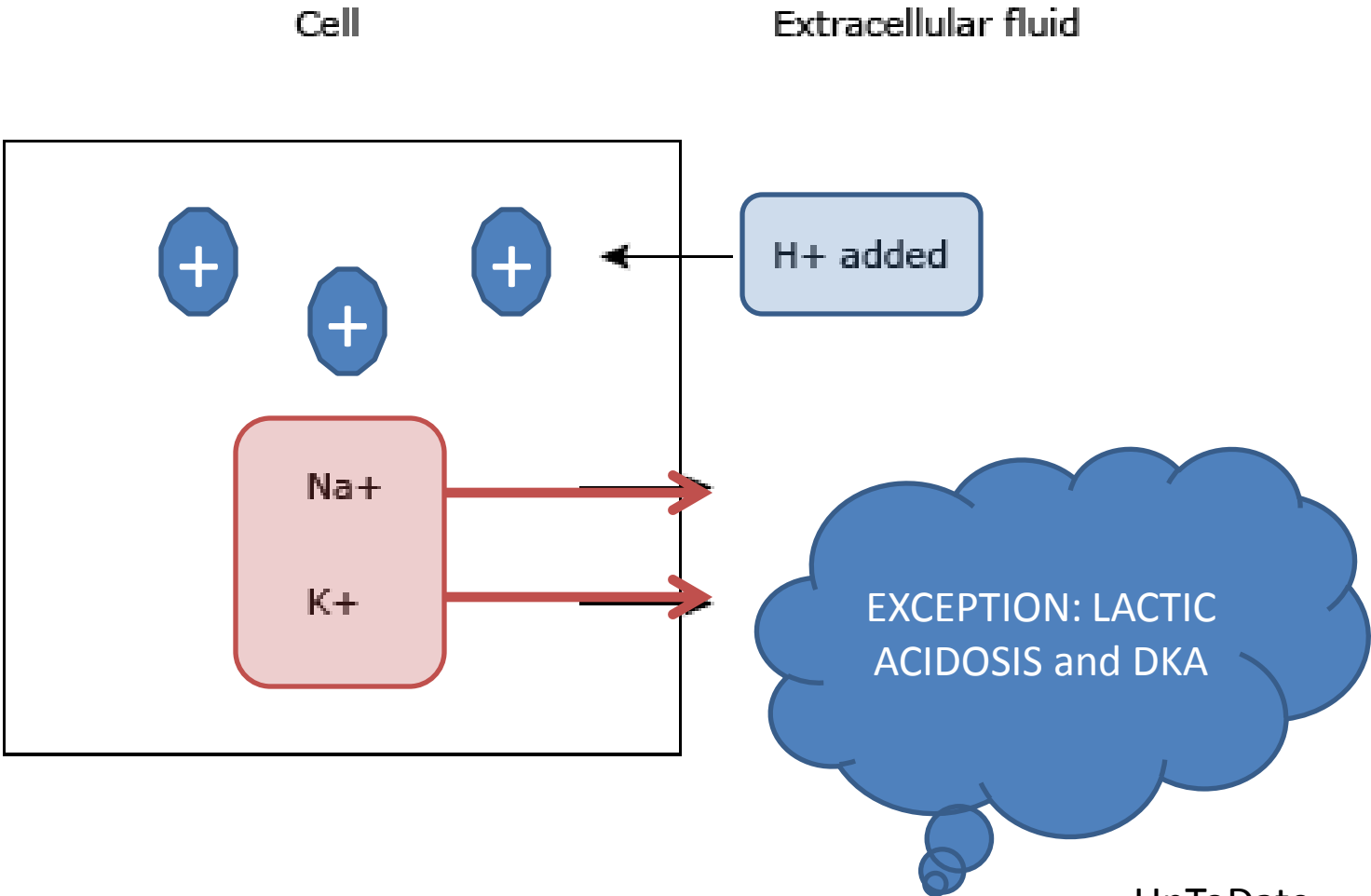
# PSEUDOHYPERKALEMIA

- Is the hyperkalemia *real*?
  - Phlebotomy
  - Exercise/ Fist Clenching
  - Thrombocytosis
    - Normal plasma potassium (post-centrifugation)
  - Leukocytosis (low K more common)
    - Cell fragility



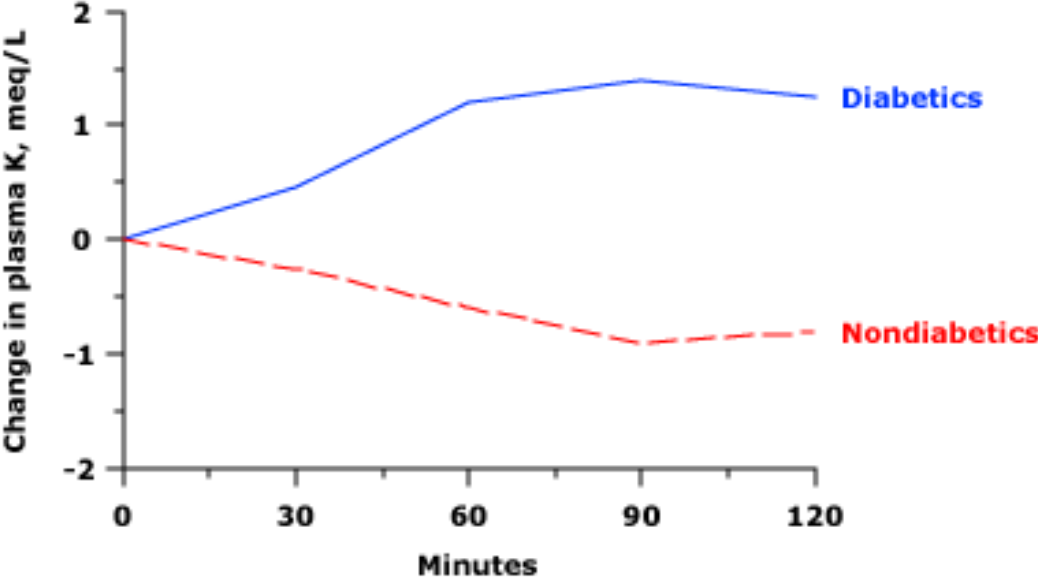


# METABOLIC ACIDOSIS



# HYPERGLYCEMIA, INSULIN DEFICIENCY

- **Nondiabetics:** Glucose consumption increases insulin release
- **Diabetics:** Insulin deficiency or resistance
- Hyperosmolarity

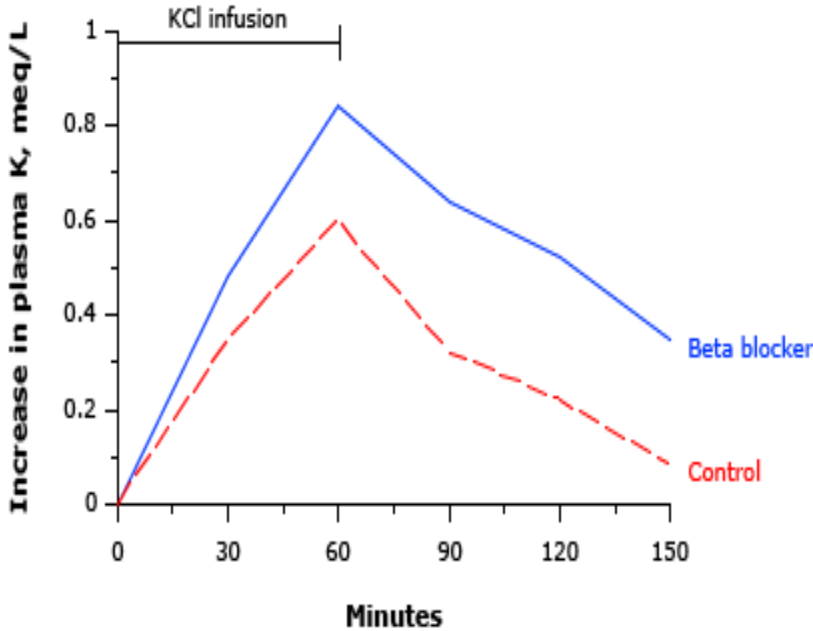


# TISSUE BREAKDOWN

- Rhabdomyolysis
- Crush injury
- Tumor lysis syndrome
- Hypothermia

# BETA BLOCKERS

- Beta 2 activity drives K into cells
- Nonselective BBs can raise K
  - Labetalol
  - Carvedilol
  - Propranolol
- Look for other RFs



# OTHER MEDICATIONS

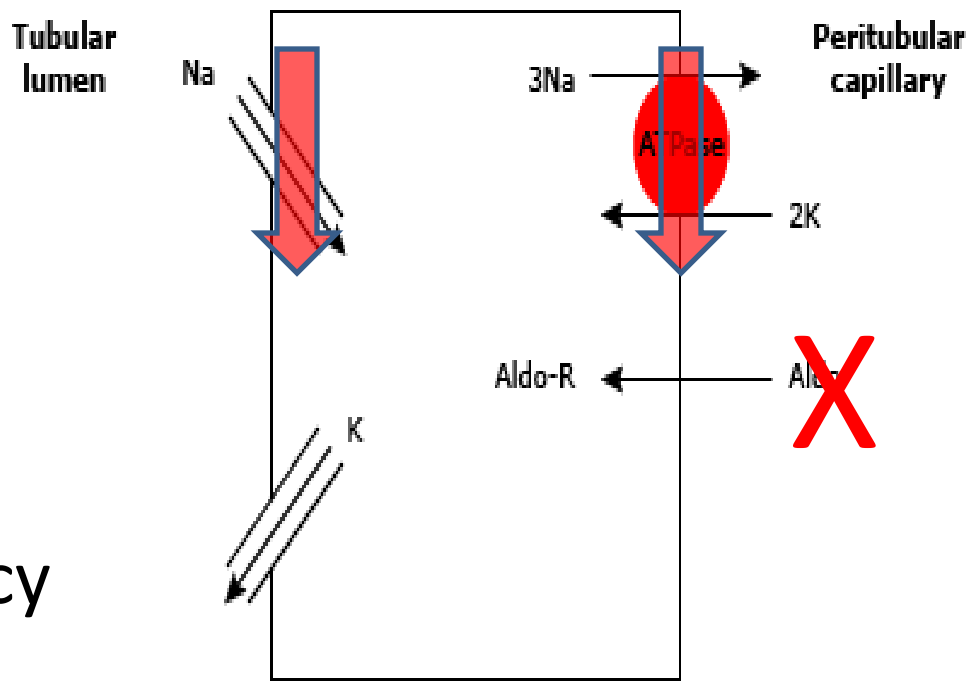
- Digoxin
  - Na-K ATPase pump inhibition
- Succinylcholine
  - Widespread acetylcholine receptor activation
- Etc

# IMPAIRED URINARY EXCRETION

- Decreased Aldosterone
- Aldosterone Resistance
- Diminished distal tubule Na and H<sub>2</sub>O delivery
- Any of above + AKI/CKD

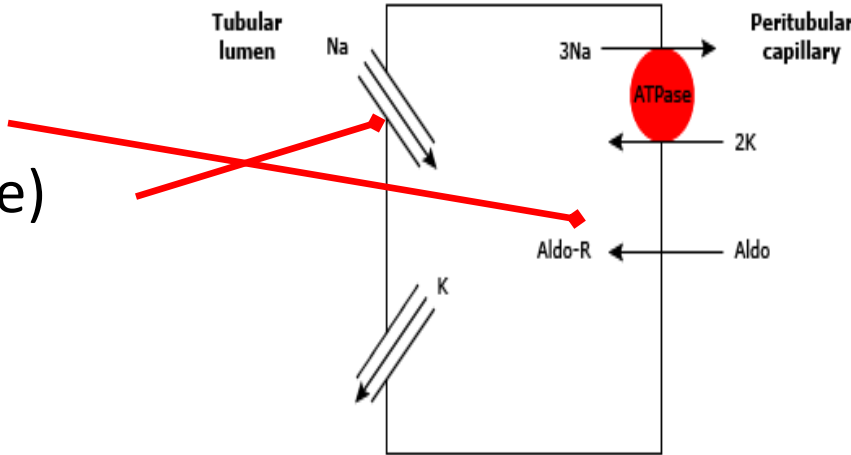
# REDUCED ALDO SECRETION

- “Hyporeninemic Hypoaldosteronism”
  - DM
- DRUGS
  - ACE/ARB
  - NSAIDs
  - CNIs (CsA/Tac)
  - Heparin (+LMWH)
- Adrenal Insufficiency



# REDUCED ALDO RESPONSE

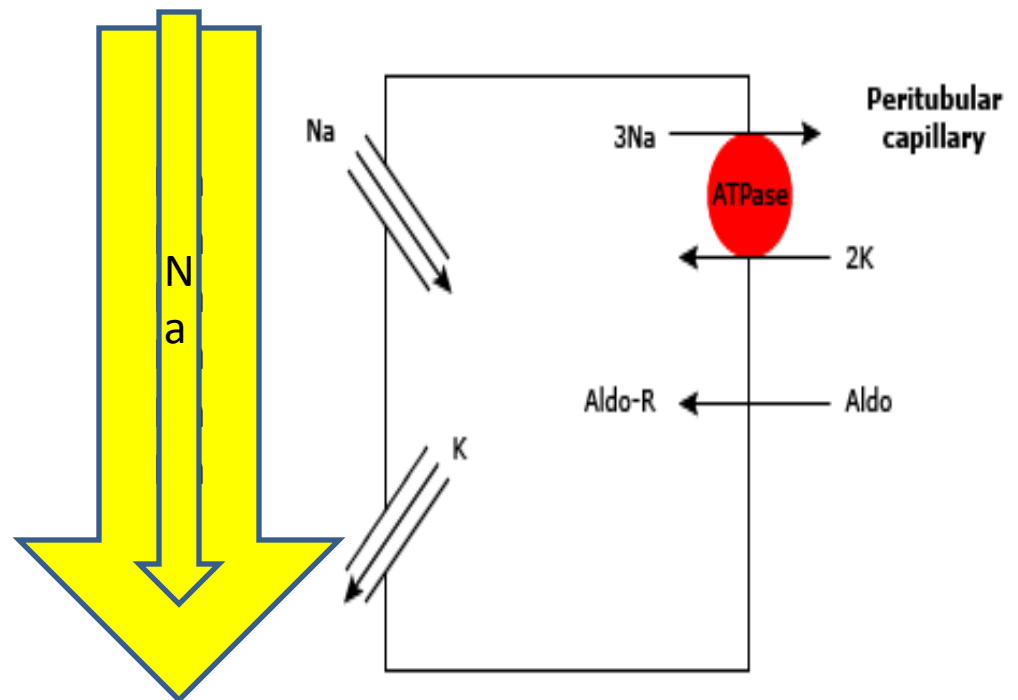
- K sparing diuretics
  - MRBs (Spironolactone)
  - ENAC inhibitors (Amiloride)
- Type 1 RTA (some types)
  - ENACs not effective
  - SLE, Sickle Cell, Obstruction
- ENAC-inhibiting Abx
  - Trimethoprim (Bactrim)
  - Pentamadine





# REDUCED DISTAL NA/H<sub>2</sub>O DELIVERY

- True volume depletion
- Decreased “effective arterial blood volume”
  - CHF
  - Cirrhosis



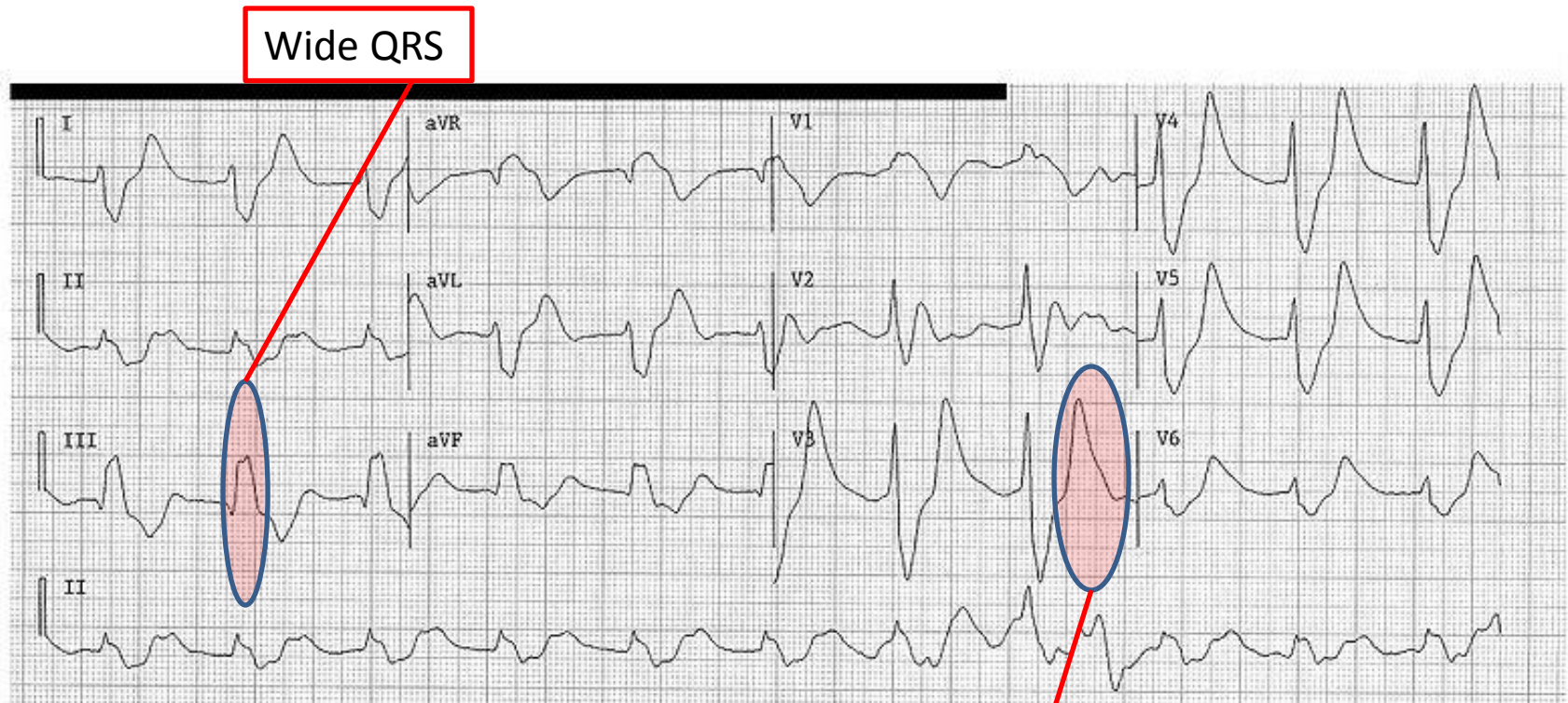
# AKI/CKD

- Often combined with previous topics
- High K diet
- Oliguria
- Uremia?

# CLINICAL PRESENTATION

- EKG Changes
  - “Peaked” T waves
  - Prolonged PR/QRS intervals
  - “sine wave” pattern”
  - BBB
  - Bradycardia
  - Ventricular Rhythms
- Muscle Weakness/Paralysis

# EKG



Courtesy of R. W. Koster, MD, PhD, The Netherlands

Tall T wave

# EVALUATION: HISTORY

- HPI: Muscle weakness? Palpitations? Signs of volume depletion?
- PMH: Kidney Disease? Cancer?
- SH: High K Diet?
- FH: High K in relatives?
  
- EXAM: Pulse, muscle strength

# EVALUATION: MEDS

- ACE/ARB
- K-sparing diuretics
- NSAIDs
- Beta Blockers (nonselective)
- CNIs
- Heparin
- KCl, MVI
- Bactrim

# EVALUATION: LABS

- Normal K: 3.5-5 meq/L
- Hyperkalemia: 5+
- “Worrisome K”: 6+ with EKG changes
  
- Also:
  - Bicarb
  - Anion Gap
  - Glucose
  - Renin, Aldosterone
  - CK
  - Cortisol
  - Uric Acid
  - Digoxin
  - Urine (TTKG)???

# MANAGEMENT

- 1: Calcium to counteract K effects on cardiac membrane
- 2: Drive K into cells
- 3: Removal of K from body
  
- Also: cardiac monitor; hold offending meds; treat underlying cause



# CALCIUM

- Hyperkalemia decreases cardiac membrane excitability
- Ca-Gluc or Ca-Cl 1000mg IV
- Effect starts: Few minutes
- Effect wears off: 30-60 minutes

# INSULIN (+/- GLUCOSE)

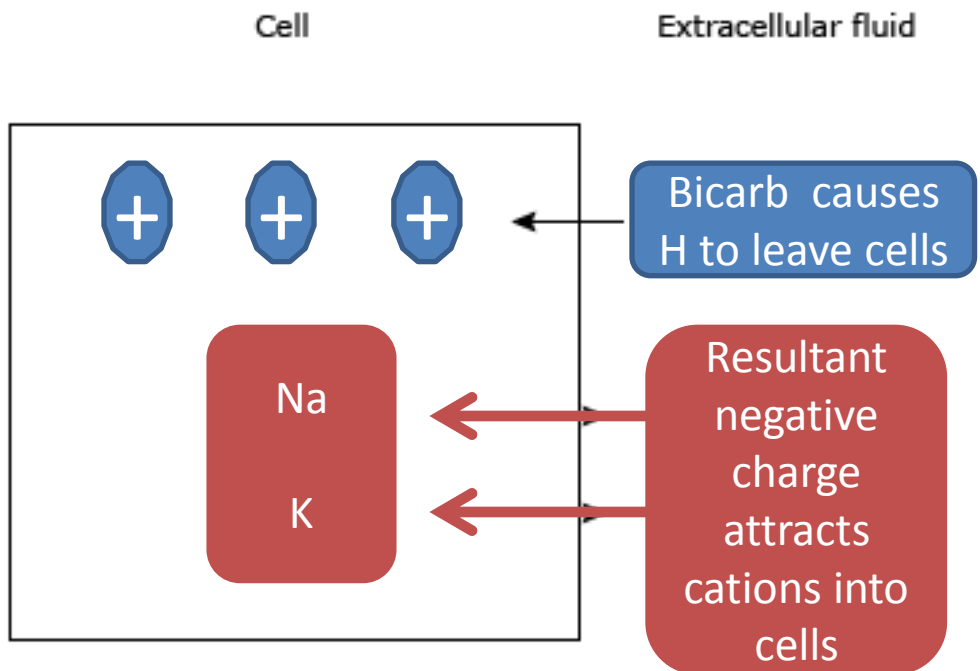
- Enhances Na-K pump in muscle
- 10U Reg Insulin +/- 25g Glucose “1amp”
- Effect: starts at 10min peaks at 30-60min, wears off after 4-6hrs

# BETA AGONISTS (ALBUTEROL)

- Increase Na-K pump in muscle
- Neb over 10 min- 10-20mg in 4mL saline
- Peak effect: 90 min

# BICARBONATE

- Treating acidosis pushes H out of cells in exchange for K
- Can give 1 amp or bicarb gtt mixed in D5W



# DIURETICS

- Loop diuretics
- Thiazide diuretics
  
- Reserved for long term management

# POTASSIUM BINDING RESINS

- Old School:
  - Sodium Polystyrene Sulfate (Kayexelate, Kionex)\*



- New School:
  - Patiromer (Veltassa)
  - Sodium zirconium cyclosilicate (Lokelma)\*



(\* on formulary at BRRH)



# KAYEXELATE

- Most commonly used hyperkalemia tx
- 15-30g, can be repeated
- Single doses often ineffective and take hours to work
- Administration with sorbitol has caused intestinal necrosis
  - High risk pts (post op, SBO)
- Use when other modalities not possible/ineffective

# PATIROMER (VELTASSA)

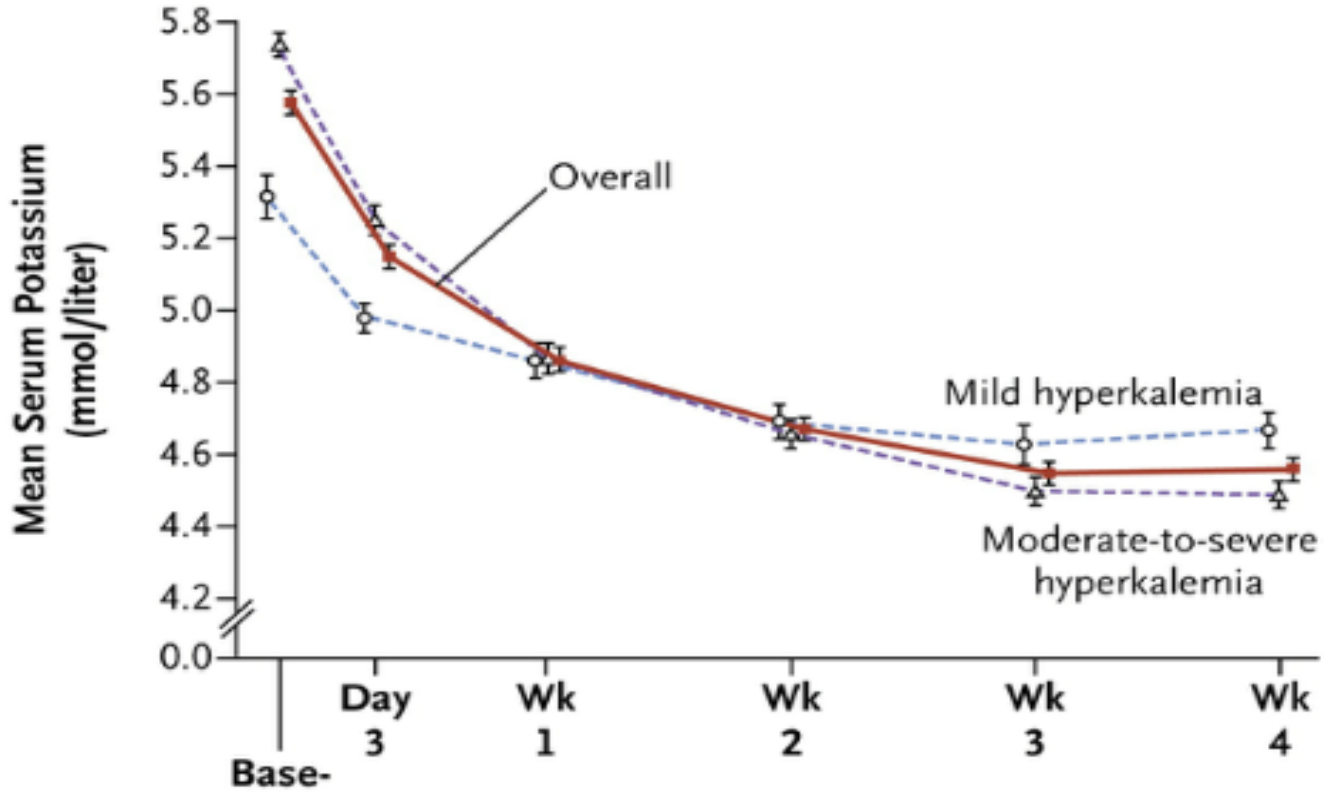
- Nonabsorbable polymer in suspension that binds K in distal colon in exchange for Ca
- Multiple trials noted good efficacy at lowering K chronically with no significant SEs
- Cannot be taken within 3 hours of other meds
- Needs refrigeration



# OPAL-HK TRIAL (NEJM 2015)

- CKD patients with hyperkalemia (K 5.1+)
- On RAAS inhibition- maintained
- 4 weeks of Patiromer, then blinded withdrawal x 8 weeks

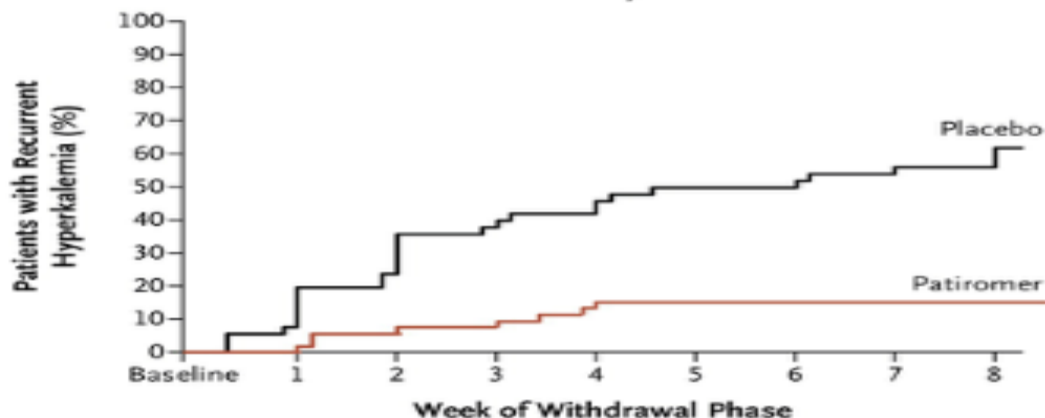
# OPAL-HK: 4 week treatment



No. at Risk	Base-line	Day 3	Wk 1	Wk 2	Wk 3	Wk 4
Overall	243	217	237	228	221	219
Mild hyperkalemia	92	80	90	87	85	85
Moderate-to-severe hyperkalemia	151	137	147	141	136	134

# OPAL-HK: 8 week withdrawal phase

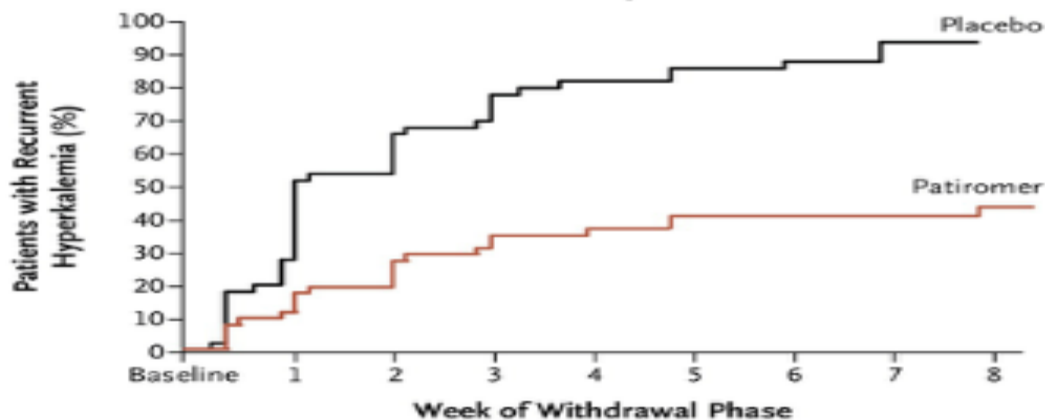
**A Time to First Serum Potassium Level  $\geq 5.5$  mmol/liter**



**No. at Risk**

Placebo	52	46	38	31	29	25	25	23	15
Patiromer	55	53	49	48	45	43	42	42	32

**B Time to First Serum Potassium Level  $\geq 5.1$  mmol/liter**



**No. at Risk**

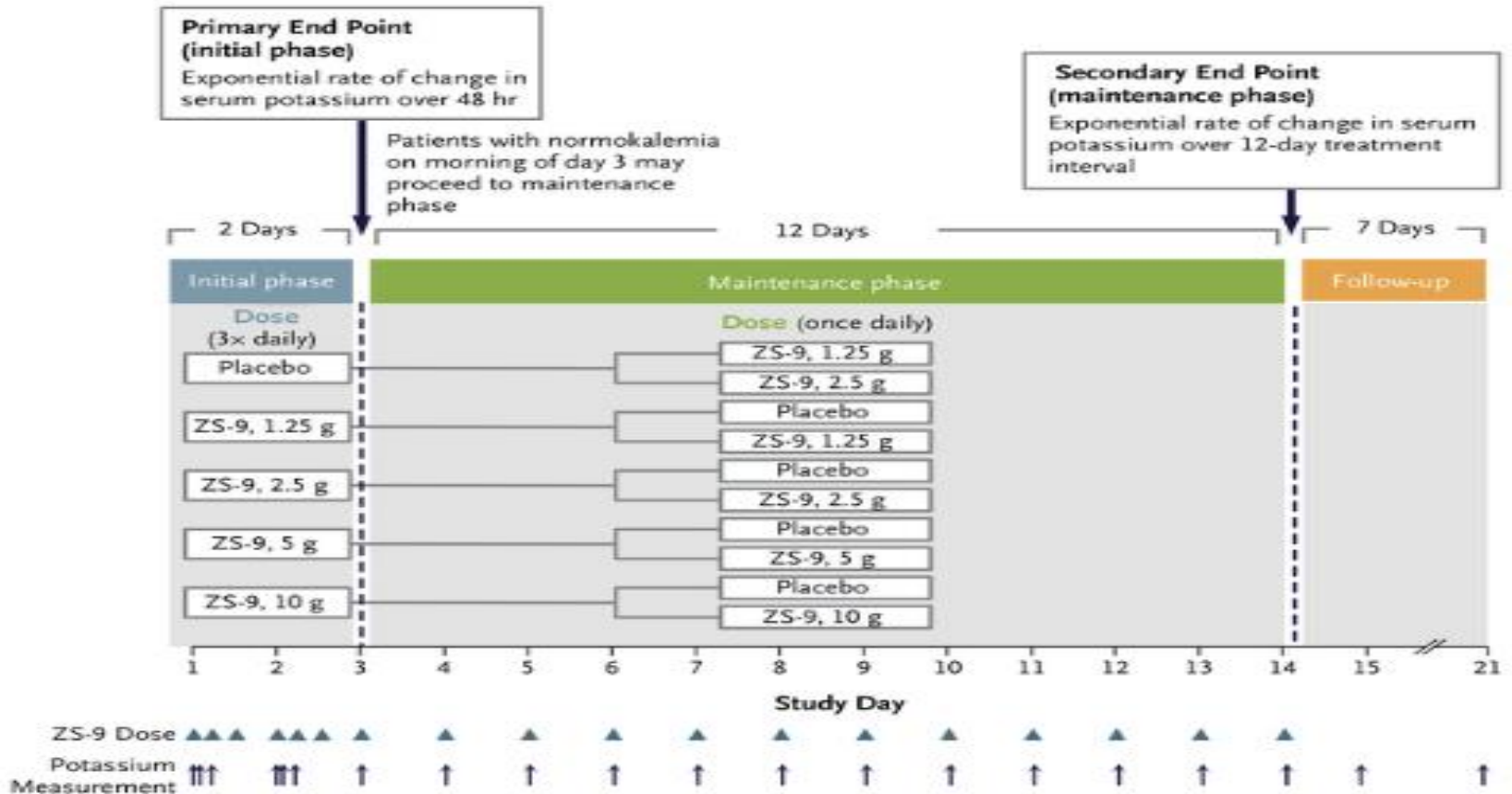
Placebo	52	37	24	16	10	8	8	7	1
Patiromer	55	47	42	36	34	30	29	29	23

# SZC (LOKELMA)

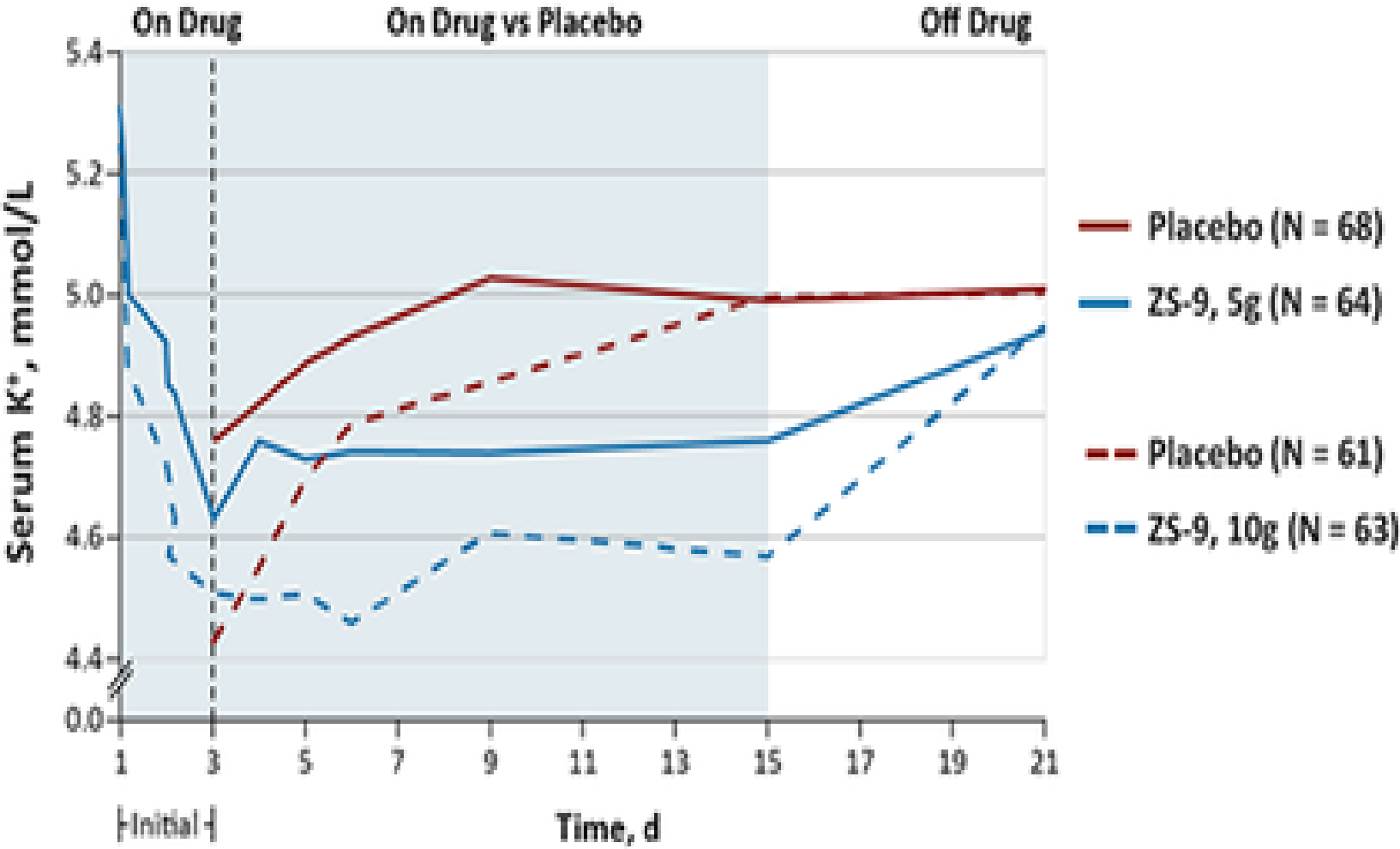
- Inorganic cation exchanger with a crystalline structure that entraps K along the length of the GI tract (exchanges Na and H)
- Minimal SEs (edema, GI)
- Cannot be administered within 2 hours of other medications
- Does not need refrigeration.

# LOKELMA: Packham NEJM 2015

- $K > 5$ , many with CKD and on RAAS blockers



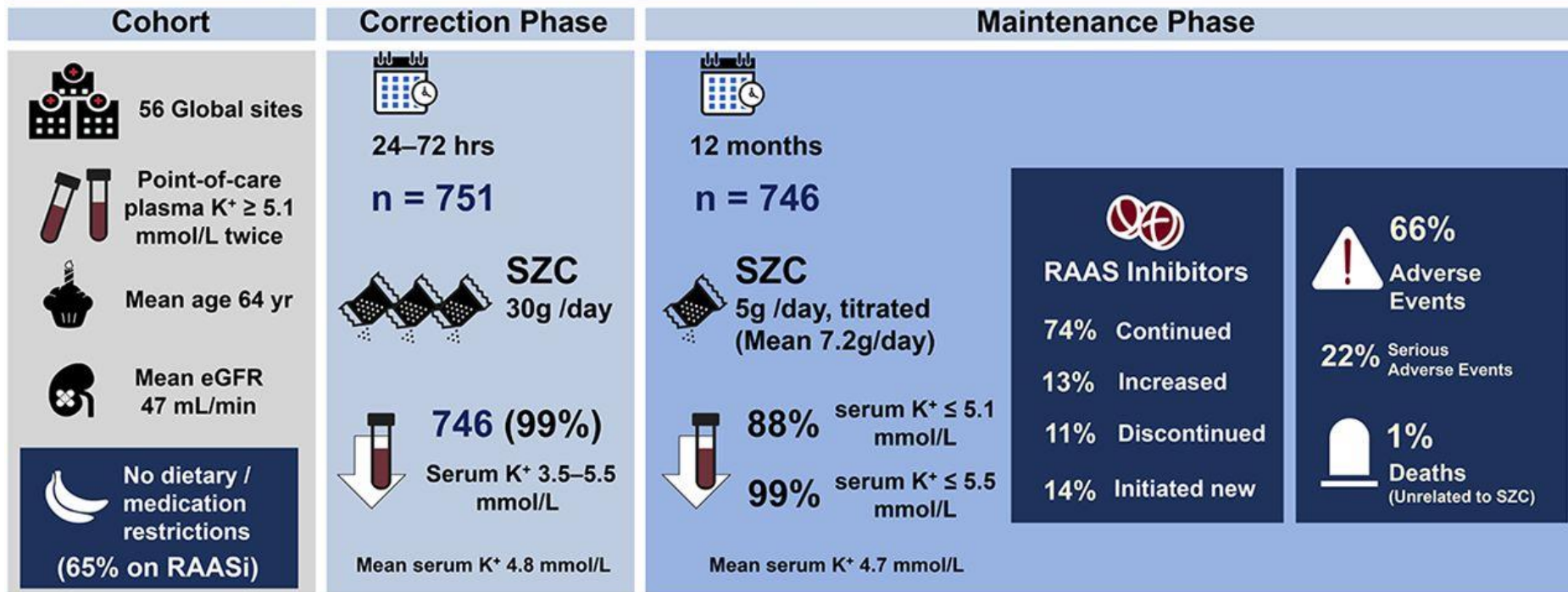
# LOKELMA: Packham NEJM 2015



# LOKELMA- long term use

## Efficacy and Safety of Long-Term Sodium Zirconium Cyclosilicate (SZC) for Hyperkalemia

Prospective, Multicenter, Open-label, Single-arm, Two-Part Phase 3 Trial



**Conclusions:** After achieving normokalemia, individualized once-daily SZC was associated with maintenance of normokalemia without substantial RAASi changes for  $\leq 12$  months.

Bruce Spinowitz, Steven Fishbane, Pablo Pergola, Simon Roger, et al. Sodium Zirconium Cyclosilicate Among Individuals with Hyperkalemia: A 12-Month Phase 3 Study. CJASN doi: 10.2215/CJN.12651018. Visual Abstract by Divya Bajpai, MD, PhD

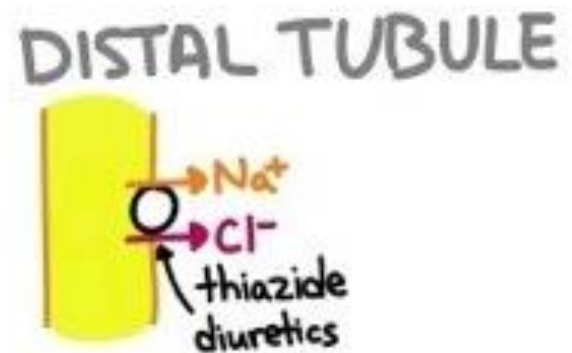
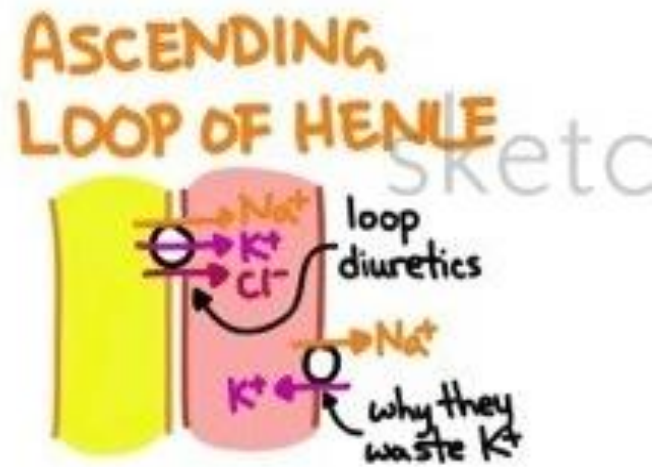
# DIALYSIS

- IHD very efficiently removes K
  - Tx time usually 1.5-2 hours
- Post dialysis “rebound”
  - Especially if treated with transient K lowering therapies
- The myth of “EMERGENT DIALYSIS”



# CHRONIC MANAGEMENT

- Low potassium diet
- Diuretics
  - Loop
  - Thiazide (?efficacy with GFR < 30)
- Mineralocorticoids
  - Limited by BPs and edema
- Sodium Bicarbonate
- K binding resin
  - Patiromer
  - Lokelma (*\*on formulary at BRRH*)



# CASE #1 (adapted from MKSAP)

- 44F presents with worsening fatigue. She has chronic HA and takes APAP and ASA 2-3x/day for the last 12 years. H/O HTN treated with HCTZ.
- Exam: BP 148/88, P 60, BMI 33, o/w normal
- Labs: K 5, Bicarb 22, Cr 1.7, UA 1+ pro, UPC 0.7g
- **What do you do?**

## CASE #2 (adapted from MKSAP)

- 70F presents to office. Known CKD with Cr 1.5. Started PPI 6 weeks ago. No other recent changes.
- Meds: PPI, Atenolol, Enalapril, HCTZ, APAP, baby ASA
- Exam: BP 150/80, P 60, normal exam
- Labs: K 5.5, Bicarb 18, Cr 3.5, UA 1+P, 5-10 WBC/hpf, UPC 0.6g, Hansel stain neg
- **What do you do?**

## CASE #3 (adapted from MKSAP)

- 55M new pt eval. DM x 15 years, HTN, OA on Ibuprofen x 1 year. No other meds (ran out of Rx after last MD visit 3 years ago).
- Old med bottles brought to visit: HCTZ, Losartan, Metformin, Pravastatin
- Exam: BP 146/92, P 70, BMI 31, 2+ edema
- Labs: Na 142, K 5.7, Bicarb 18, Glc 230, Cr 2.5, UPC 1.5g, UA 2+ glucose 3+ protein
- **What do you do?**

# CASE #4 (adapted from MKSAP)

- 23M HIV admitted 1 week ago with PCP. Treated with pentamidine and steroids. On HAART x 2 months,.
- Exam: normal
- Labs: Na 132, K 6.2 (4.8 on admit), Bicarb 18, Cr 1.4, UA nx
- **What do you do?**

# CASE #5

- 90F nursing home resident -> ER with abdominal pain. Recently started on Baclofen for spasms related to a past CVA. No further history due to cognitive impairment
- Meds: Enalapril, Baclofen, Lasix, Flomax
- Exam: BP 160/90, P 110, AAOx1, uncomfortable, lower abdomen tenderness
- Labs: Na 125, K 6.8, Bicarb 14, Cr 10.3
- EKG: tall T waves (new), RBBB (old)
- **What do you do?**



# CASE #6

- 65M dialysis patient, last dialyzed 3d ago, presents to ED with fever and weeping foot ulcer. No other complaints.
- Meds: ASA, Zocor, Atenolol, Epogen, Sevelamer, Sensipar
- Exam: BP 150/70, P 75, T 101, weeping foot ulcer, fistula with thrill but augments on elevating arm
- Labs: Na 135, K 7.2, bicarb 19, Cr 8.5
- EKG: Tall T waves, RBBB (no past EKGs available)
- **What do you do?**

# THANK YOU!!!

