



# It's A Trap!

Core Content Lecture – Hyperkalemia

Vincent Fu, MD (PGY-1) | 08 November 2022



LOYOLA  
MEDICINE

## DISCLOSURES

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No financial disclosures to report.



CORE CONTENT: HYPERKALEMIA

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# Session Overview



THE HYPERKALEMIA PATIENT

PATHOPHYSIOLOGY OF POTASSIUM

CLINICAL FEATURES

EVIDENCE-BASED MANAGEMENT

NEW KID ON THE BLOCK

CORE CONTENT: HYPERKALEMIA

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# Patient Case



## CHIEF COMPLAINT

72yo M found down at  
apartment, incontinent.

He c/o R hip pain on flexion, rotation.  
Last family contact was 3 days ago.

Confused & combative  
on arrival. **GCS 13.**

VS: **78/60** **74** **32** **91%** NRB **15L**  
ABG: K **9.0** pH **7.23** BGL **32**

# PMHx

CHF

HTN

DM2

OA

# Meds

spironolactone, metoprolol

lisinopril

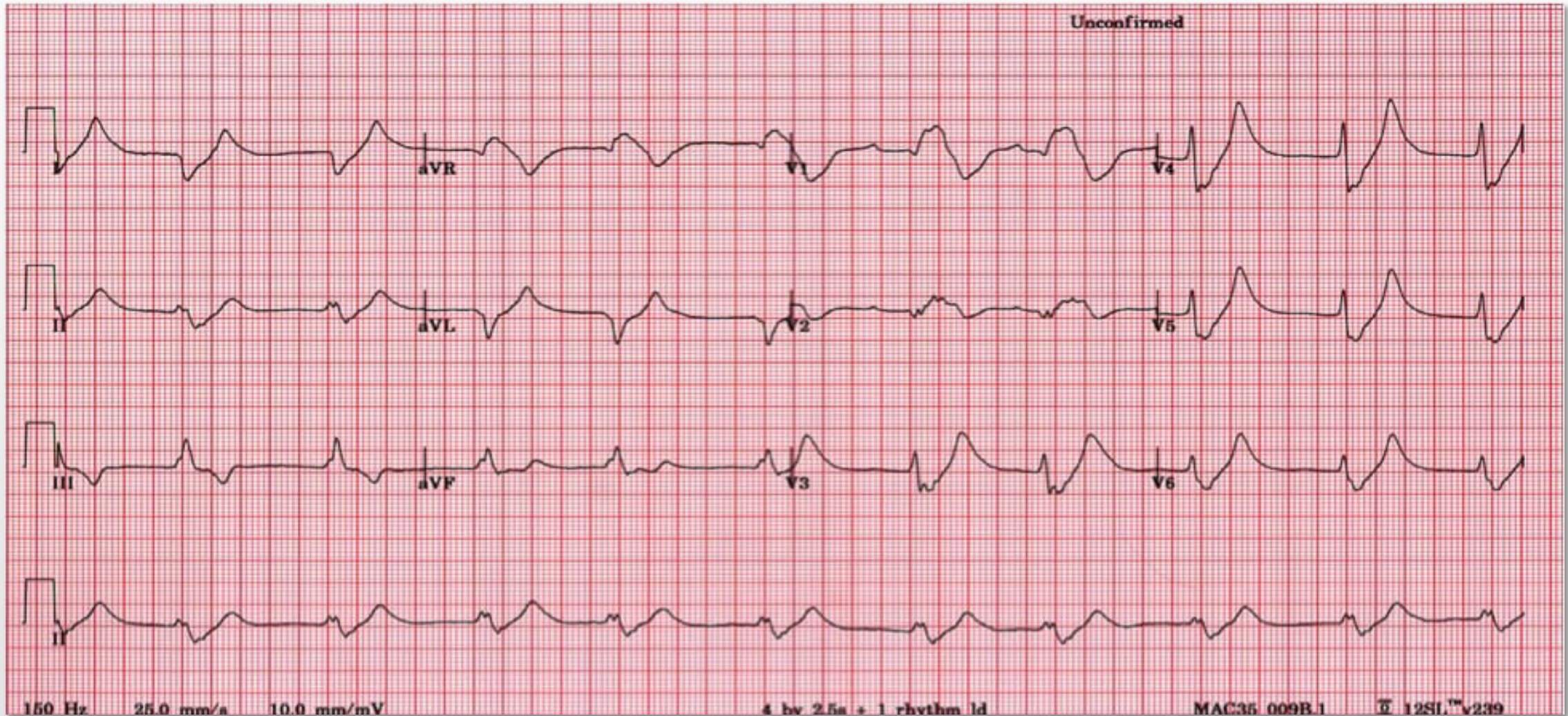
diet controlled

Celebrex





# STAT ECG



Source: Mike Cadogan, *Hyperkalaemia Clinical Case*, LITFL Compendium of Critical Care

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# Pathophysiology



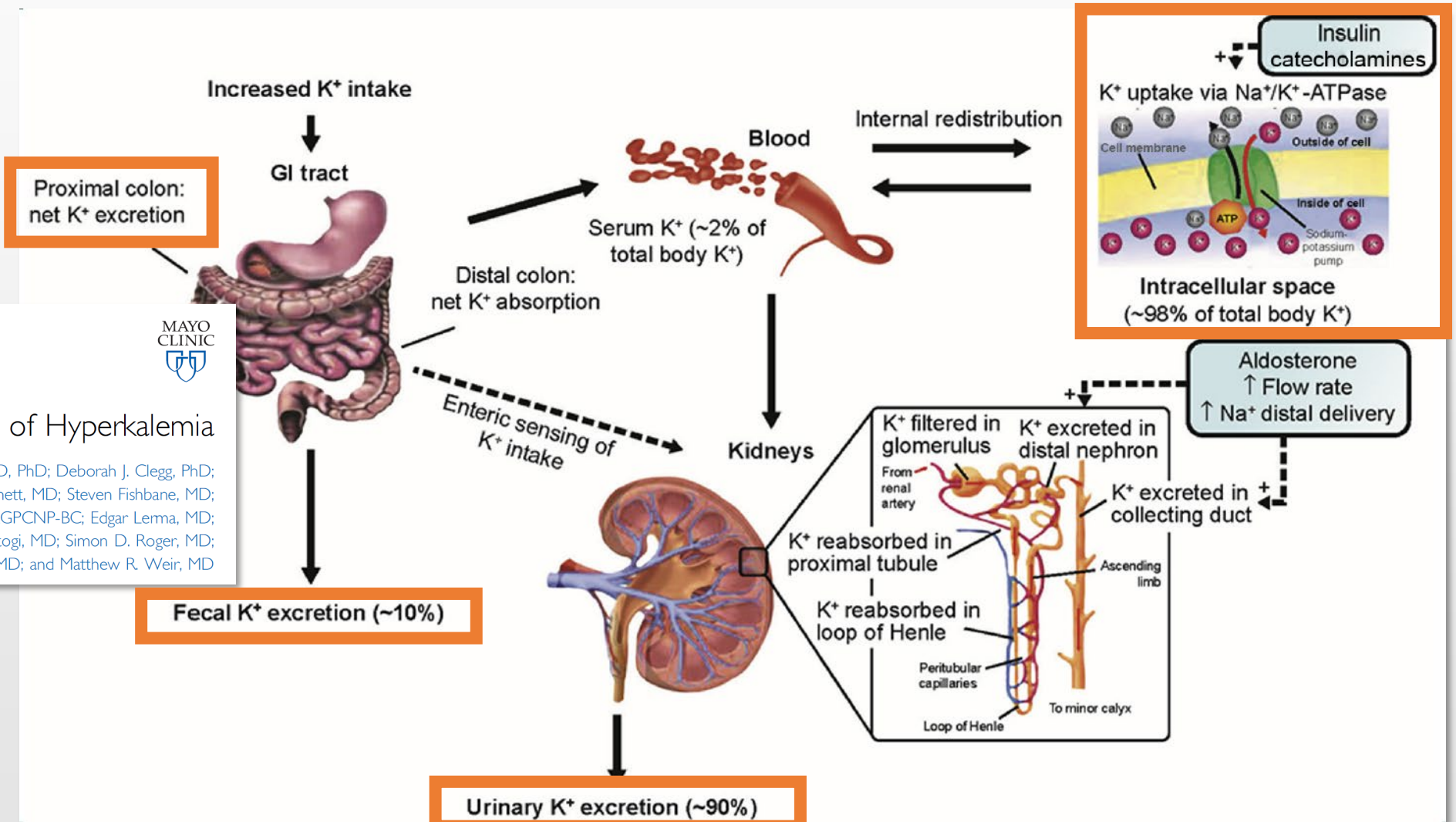
Normal serum K **3.5–5.0 mmol/L**

Hyperkalemia **> 5.5 mmol/L**

- impaired excretion via kidneys
- impaired shift into cells from serum
- combination of both



# REGULATION OF POTASSIUM HOMEOSTASIS



## Clinical Management of Hyperkalemia

Biff F. Palmer, MD; Juan Jesus Carrero, PharmD, PhD; Deborah J. Clegg, PhD;  
Gates B. Colbert, MD; Michael Emmett, MD; Steven Fishbane, MD;  
Debra J. Hain, PhD, APRN, AGPCNP-BC; Edgar Lerma, MD;  
Macaulay Onuigbo, MD; Anjay Rastogi, MD; Simon D. Roger, MD;  
Bruce S. Spinowitz, MD; and Matthew R. Weir, MD

## INCREASED INTAKE

Potassium supplements (IV or PO)  
Excess in diet  
Salt substitutes (K<sup>+</sup> salts of penicillin)

## INCREASED PRODUCTION

Rhabdomyolysis / intense physical activity  
Hemolysis / Tumor Lysis Syndrome  
Trauma / extensive burns / crush injuries

## SHIFT FROM INTRA TO EXTRACELLULAR

**Acidosis (metabolic or respiratory)**

**Insulin deficiency**

**Rx: succinylcholine, beta-blockers, digoxin OD**

## DECREASED EXCRETION

**AKI/CKD/ESRD: decreased GFR**

**Decreased mineralocorticoid activity**

**Rx: NSAIDs, cyclosporin, K-sparing diuretics, ACEIs**

## PSEUDOHYPERKALEMIA

Hemolysis in lab tube

Thrombocytosis

Leukocytosis

CORE CONTENT: HYPERKALEMIA

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# Clinical Features



Generalized muscle weakness

Flaccid paralysis/paresthesias in UE+LE

Lethargy, confusion, weakness, palpitations

Clinical features often nonspecific

ECG: one of the most important diagnostic tools



# ECG CHANGES IN HYPERKALEMIA



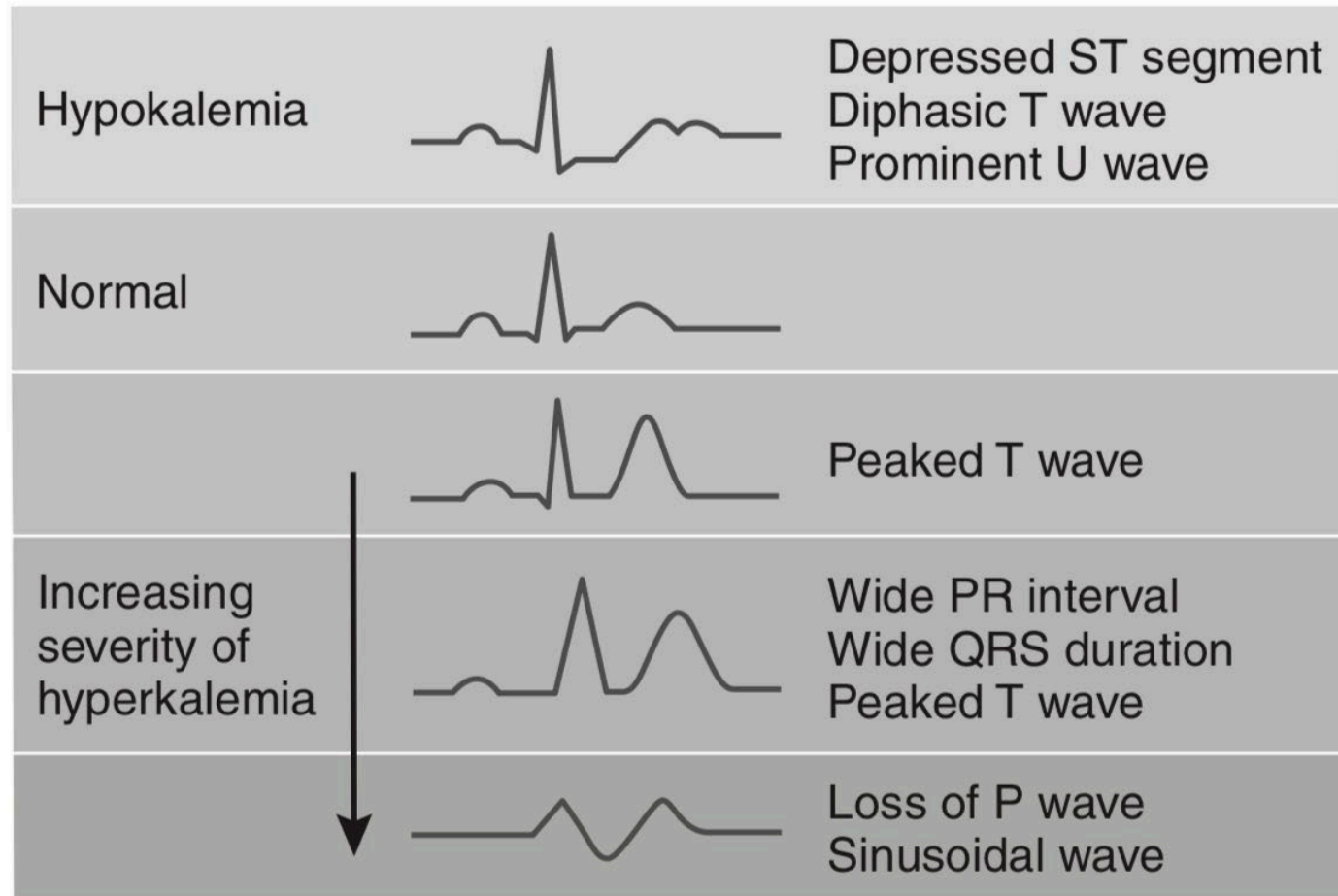
serum K

5.5-6.5

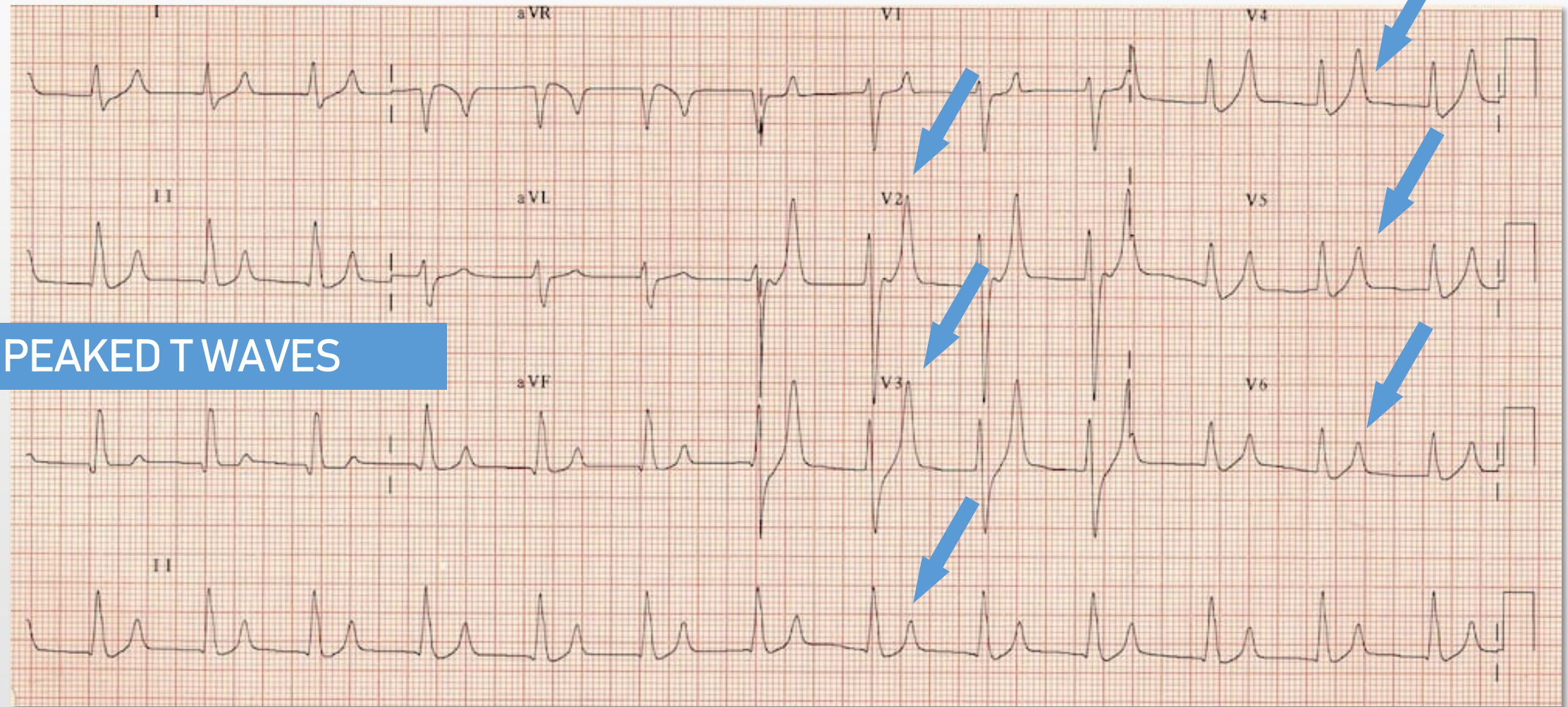
6.5-7.5

7.5-8.5

>8.5



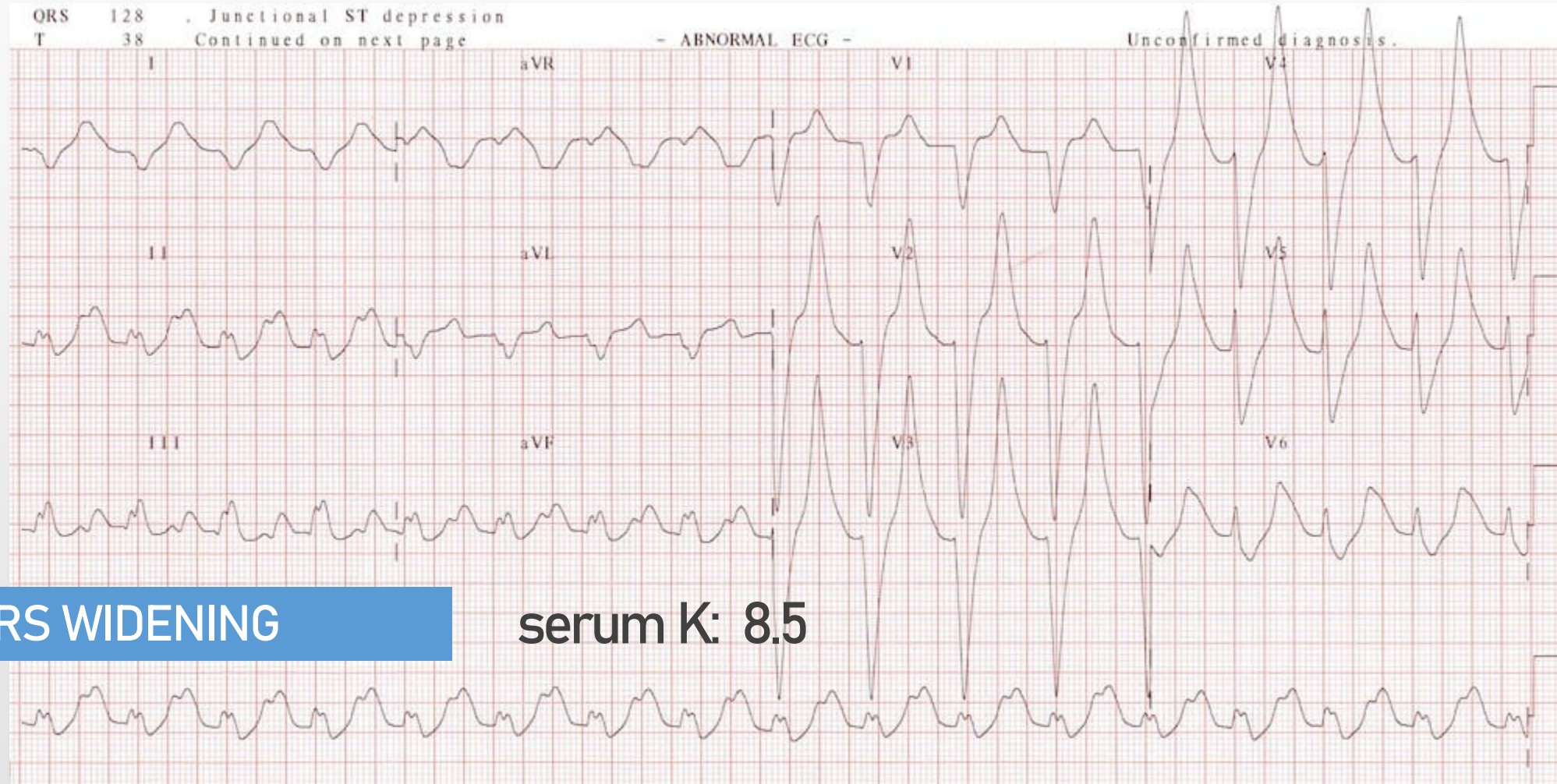
# ECG CHANGES IN HYPERKALEMIA



Source: Mike Cadogan, *Hyperkalaemia Clinical Case*, LITFL Compendium of Critical Care



# ECG CHANGES IN HYPERKALEMIA

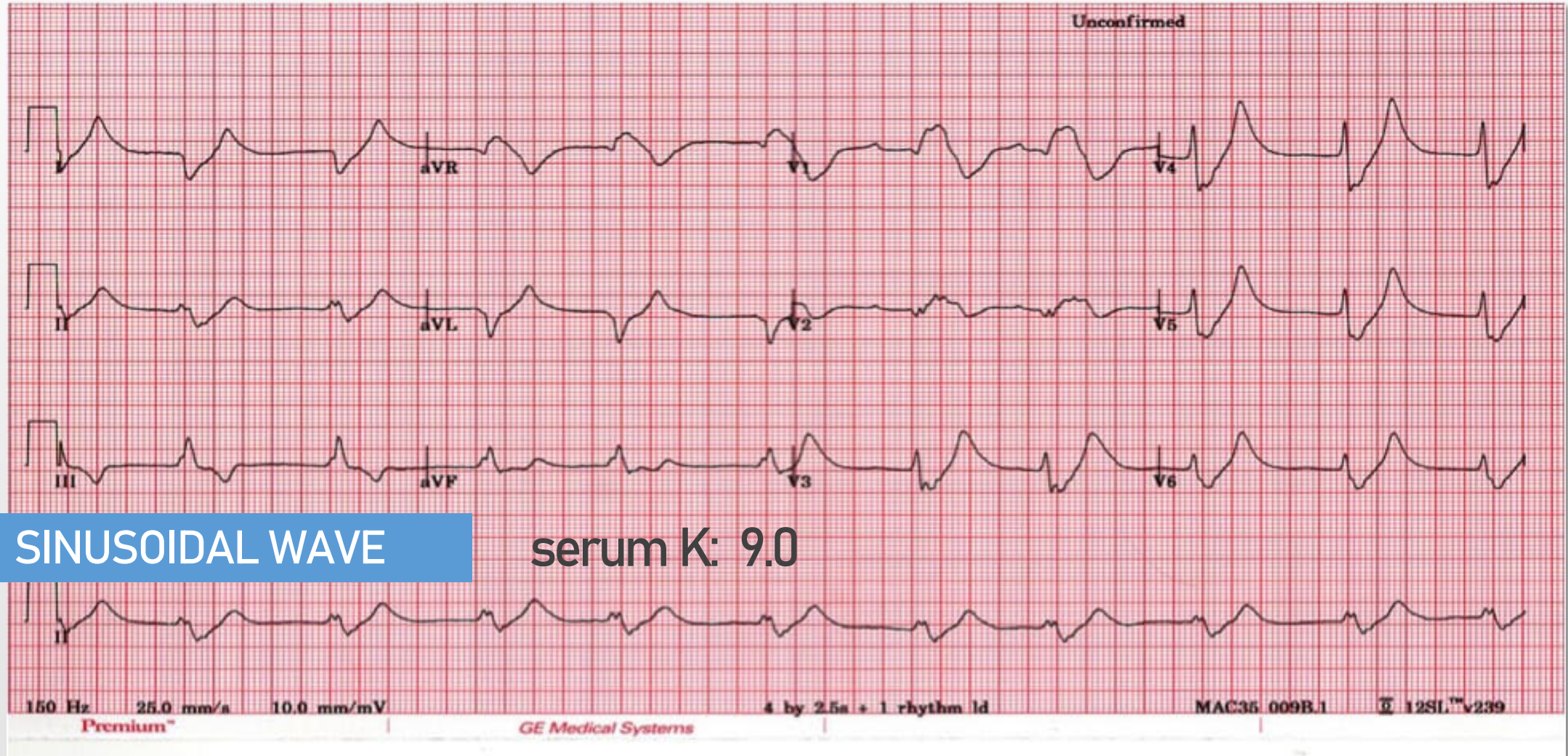


**QRS WIDENING**

**serum K: 8.5**



# ECG CHANGES IN HYPERKALEMIA



SINUSOIDAL WAVE

serum K: 9.0

CORE CONTENT: HYPERKALEMIA

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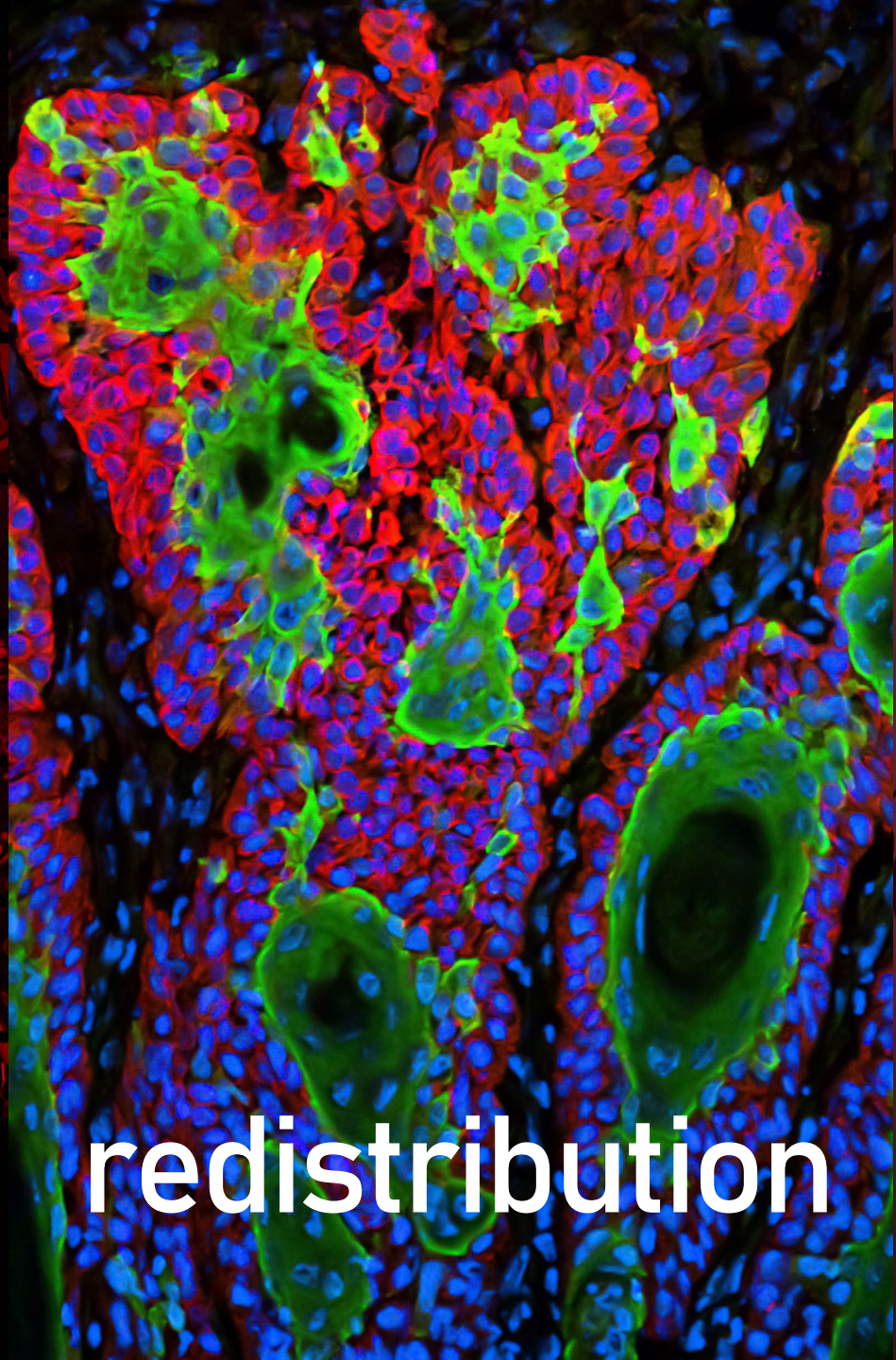
# Evidence Based Management







**stabilization**



**redistribution**



**elimination**



EVIDENCE BASED MANAGEMENT

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# Stabilization



## LR / Plasmalyte

use if hypovolemic, and bicarbonate is normal/high

[!] do not give NS; it will increase the potassium  
if bicarbonate is low... give bicarb (coming up next)



## Calcium

indicated for wide QRS, sine wave pattern, or hyperK cardiac arrest

**Calcium chloride:** 1g IV over 10 min

- 3x more potent than Ca gluconate
- [!] severe thrombophlebitis; best w/ central access

**Calcium gluconate:** 3g IV over 10 min

- less potent, less irritating to veins, OK with PIV

## Calcium

indicated for wide QRS, sine wave pattern, or hyperK cardiac arrest

- [!] bradycardia, hypotension, peripheral vasodilation
  - administer slowly to avoid these complications
  - avoid Ca in digoxin toxicity (use Mg instead)

\* calcium does not lower the serum K level

EVIDENCE BASED MANAGEMENT

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# Redistribution



**Insulin + Glucose/Dextrose**  
drives K<sup>+</sup> into cells + protects from hypoglycemia

**Insulin:**

5 units IV bolus

**Dextrose:**

500ml D10 over 4 hours

## Sodium Bicarbonate

drives K<sup>+</sup> into cells for several hours

only effective at driving K<sup>+</sup> into cells if pt is acidotic

**Isotonic bicarbonate:** D5W + 150 mEq/L NaHCO<sub>3</sub>  
- use for volume resuscitation if bicarbonate is low

# Albuterol

beta-2 agonist, nebulizer route

**Albuterol nebulizer:** 10-20mg continuous

effective in renal patients who are fluid overloaded

EVIDENCE BASED MANAGEMENT

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# Elimination



## Diuretic/Nephron Bomb

might try for patients with normal renal function/mild dysfunction

<b>Loop diuretic:</b>	160mg IV Lasix / 4mg IV Bumex
<b>Thiazide:</b>	0.5-1.0g IV chlorothiazide
<b>+/- Acetazolamide:</b>	250-1000mg IV/PO
<b>+/- Fludrocortisone:</b>	0.2mg PO (esp pt on ACEI/ARB)

\* replace urine losses with crystalloid to avoid hypovolemia!



**Kayexalate / SPS**  
sodium polystyrene sulfonate

**Veltassa / patiromer**  
sodium-free cation-exchange polymer

**Lokelma / SZC**  
sodium zirconium cyclosilicate

NEW KID ON THE BLOCK

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Lokelma / SZC



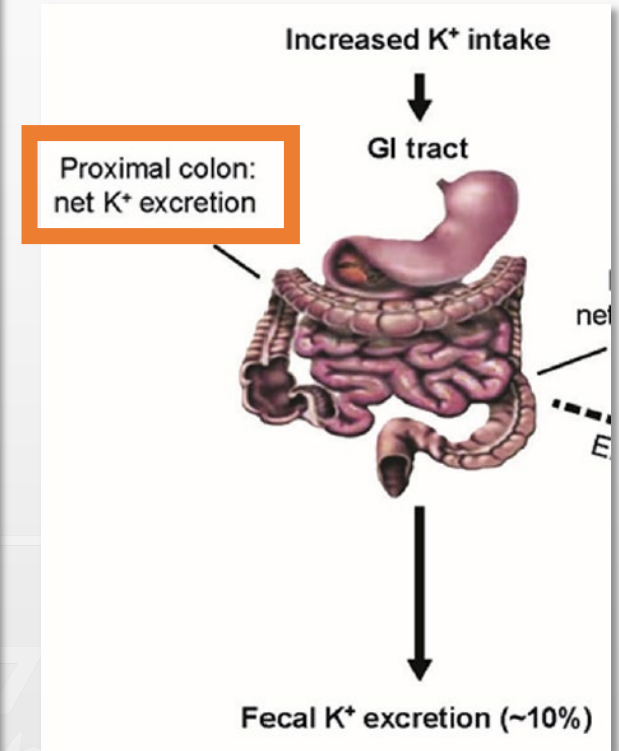
# CHARACTERISTICS OF K<sup>+</sup> BINDING AGENTS FOR HYPERKALEMIA



	Kayexalate	Veltassa	Lokelma
Characteristic	SPS	Patiromer	SZC
Approval date	1958	US, 2015; EU, 2017	US, 2018; EU, 2018
Mechanism of action	K <sup>+</sup> binding in exchange for Na <sup>+</sup> in GI tract (↑ fecal excretion)	K <sup>+</sup> binding in exchange for Ca <sup>2+</sup> in GI tract (↑ fecal excretion)	K <sup>+</sup> binding in exchange for H <sup>+</sup> and Na <sup>+</sup> in GI tract (↑ fecal excretion)
Site of action	Colon	Colon	Small and large intestines
Selectivity for K <sup>+</sup>	Nonselective; also binds Ca <sup>2+</sup> and Mg <sup>2+</sup>	Nonselective; also binds Na <sup>+</sup> and Mg <sup>2+</sup>	Highly selective; also binds NH <sub>4</sub> <sup>+</sup>
Onset of action	Variable; several hours	7 h	1 h
Na <sup>+</sup> content	1500 mg per 15-mg dose	None	400 mg per 5-g dose
Ca <sup>2+</sup> content	None	1.6 g per 8.4-g dose	None
Sorbitol content	20,000 mg per 15-g dose	4000 mg per 8.4-g dose	No sorbitol content
Dosing	15 g 1-4 times (oral); 30-50 g 1-2 times (rectal)	8.4 g QD (oral), titrate up to 16.8 g or 25.2 g QD	10 g TID (oral) for initial correction of hyperkalemia (for ≤48 h), then 5 g QOD to 15 g QD for maintenance
Serious AEs	Cases of fatal GI injury reported	None reported	None reported
Most common AEs	GI disorders (constipation, diarrhea, nausea, vomiting, gastric irritation), hypomagnesemia, hypokalemia, hypocalcemia, systemic alkalosis	GI disorders (abdominal discomfort, constipation, diarrhea, nausea, flatulence), hypomagnesemia	GI disorders (constipation, diarrhea, nausea, vomiting), mild to moderate edema

AE = adverse event; Ca<sup>2+</sup> = calcium; EU = European Union; GI = gastrointestinal; H<sup>+</sup> = hydrogen ion; K<sup>+</sup> = potassium; Mg<sup>2+</sup> = magnesium; Na<sup>+</sup> = sodium; NH<sub>4</sub><sup>+</sup> = ammonium; QD = once daily; QOD = every other day; SPS = sodium polystyrene sulfonate; SZC = sodium zirconium cyclosilicate; TID = three times daily; US = United States; ↑ = increased.

Data from references 12, 59, 60, and 79 to 81.



Source: Palmer et al. *Clinical Management of Hyperkalemia*. Mayo Clin Proc. March 2021

# Lokelma / SZC

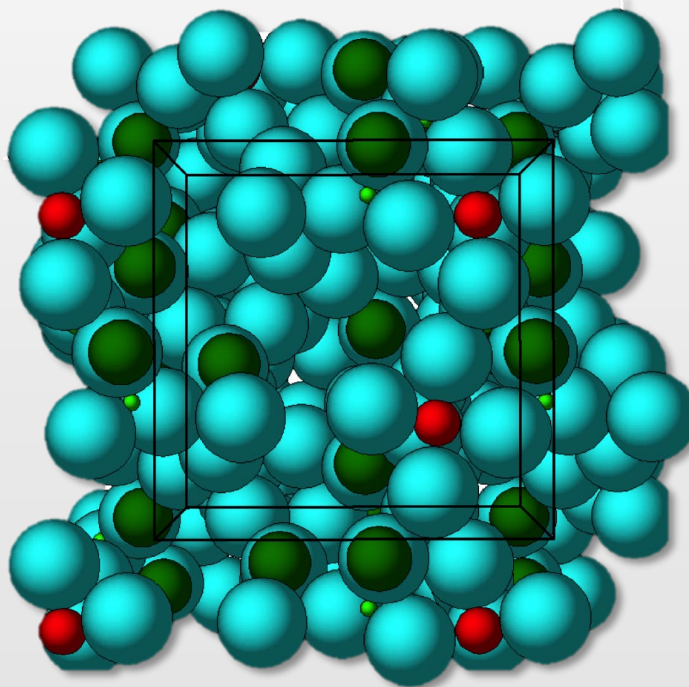
sodium zirconium cyclosilicate

RESEARCH ARTICLE

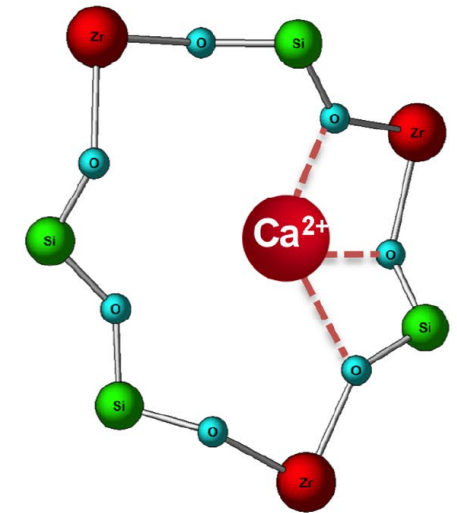
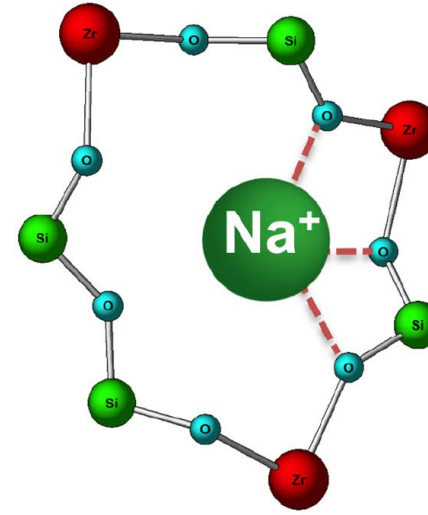
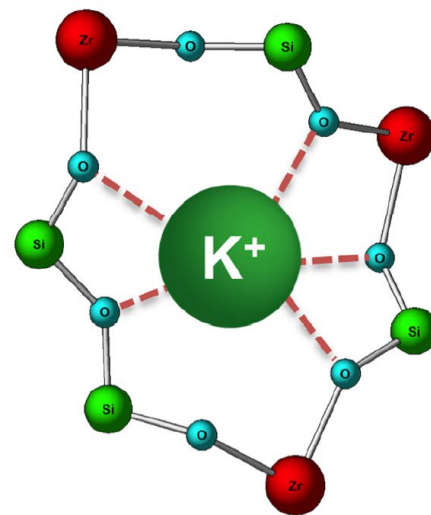
## Characterization of Structure and Function of ZS-9, a $K^+$ Selective Ion Trap

Fiona Stavros<sup>1\*</sup>, Alex Yang<sup>2</sup>, Alejandro Leon<sup>1</sup>, Mark Nuttall<sup>1</sup>, Henrik S. Rasmussen<sup>1</sup>

1. ZS Pharma Inc., Coppell, Texas, United States of America, 2. Xelay Acumen, Inc., Belmont, California, United States of America



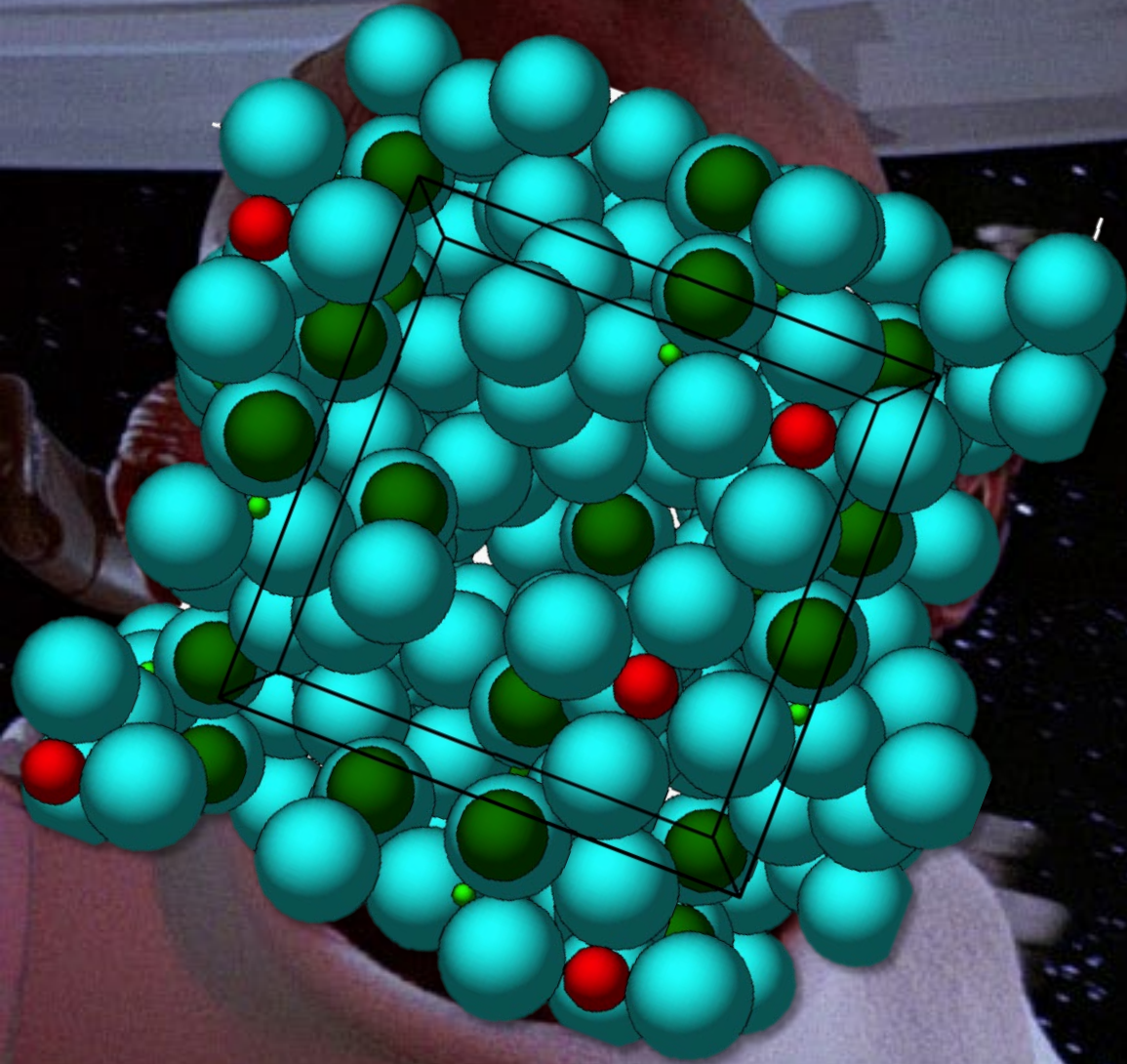
O | Zr | Si



Average Width of  
Micropore Opening 3Å

Source: Stavros et al. PLOS ONE, 2014.





IT'S A  
selective ion  
TRAP



# HEAD TO HEAD COMPARISON



## Kayexalate / SPS

sodium polystyrene sulfonate

Approved 1958 | 7 day trial (n = 33)

**Mean  $\Delta$ :** -0.125 mEq/L  
**Onset:** up to 7 hours  
**Binds:** K<sup>+</sup>, Ca<sup>2+</sup>, Mg<sup>2+</sup> (sloppy!)

[!] colonic ulcers, ischemia,  
necrosis; 30g dose as studied

## Lokelma / SZC

sodium zirconium cyclosilicate

Approved 2018 | 12 mo trial (n = 70)

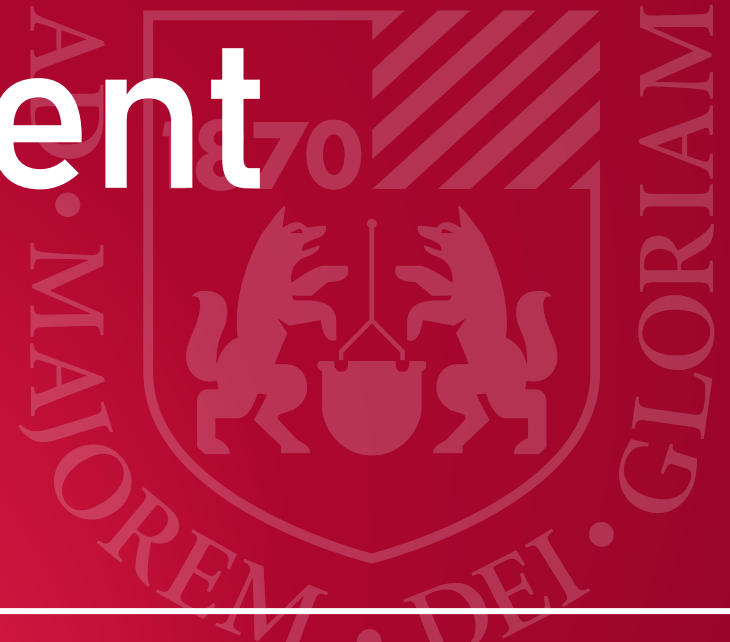
**Mean  $\Delta$ :** -0.410 mEq/L (4 hr)  
**Onset:** 1 hour  
**Binds:** K<sup>+</sup> selectively (nice!)

[+] acts in small & large bowel,  
10g dose as studied

CORE CONTENT: HYPERKALEMIA

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# Recommended Management



Ca<sup>2+</sup>

**Pump / Stabilization**  
LR + calcium chloride/gluconate

Bicarb  
Insulin  
Glucose

**Clump / Redistribution**  
insulin+glucose / sodium bicarb / albuterol

Lokelma

**Dump / Excretion**  
Lokelma aka SZC aka ZS-9



LOYOLA EM CONFERENCE

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thank you

inline references provided throughout deck



## ACKNOWLEDGEMENTS

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**Kristin Larson, MSN, RN, AGNP-BC, CNN**  
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**Russell Attridge, PharmD, MSc, BCPS**  
Medical Science Liaison – Renal | AstraZeneca Pharmaceuticals LP

