ECNG
Extracorporeal Nephrology Group
An Academic Forum for Nephrologists, DM Trainees, Physicians, and Healthcare Professionals

"Knowledge grows when shared, wisdom deepens when discussed."

CPS VS SZC

Comparison of Calcium Polystyrene Sulphonate (CPS) and Sodium Zirconium Cyclosilicate (SZC)

CPS
Calcium Polystyrene Sulphonate
(Sachet / Suspension)

SZC
Sodium Zirconium Cyclosilicate
(Oral Powder for Suspension)

Lower cost Significantly less expensive; more affordable for long-term use.	COST	**Higher cost** More expensive than CPS.
Wider availability Available in most pharmacies and hospitals; included in many formularies and government programs.	AVAILABILITY	**Limited availability** May not be available in all centers; newer and costlier.
No sodium load Exchanges K+ for Ca2+. Useful in patients who need sodium restriction (HTN, HF, fluid overload, advanced CKD).	SODIUM LOAD	**Contains sodium** Sodium load may be a concern in patients with fluid overload, HF or severe hypertension.
Slow onset Onset in hours to days.	ONSET OF ACTION	**Rapid onset** Begins working within ~1 hour.
Variable efficacy Potassium lowering effect is less predictable.	POTASSIUM LOWERING	**Predictable efficacy** More consistent and predictable reduction in serum potassium.
GI tolerability Constipation, nausea, bloating more common.	GI TOLERABILITY	**Better tolerated** Lower rates of constipation and GI side effects.
Serious GI complications Rare but possible (intestinal necrosis, especially with sorbitol).	SERIOUS GI COMPLICATIONS	**Very uncommon** Serious GI events are very rare.
More drug interactions May bind to other oral medications; separate dosing required.	DRUG INTERACTIONS	**Fewer drug interactions** Minimal clinically significant drug interactions.
Limited high-quality RCT evidence Evidence mainly from older studies and observational data.	EVIDENCE	**Strong RCT evidence** Multiple RCTs demonstrating efficacy and safety.
Not suitable for emergency Too slow for acute, life-threatening hyperkalemia.	USE IN URGENT HYPERKALEMIA	**Better option (but not replacement for standard emergency therapy)** Can be used for rapid reduction along with standard care.
Available as suspension Easier to administer; suitable for elderly, swallowing difficulty, or feeding tubes.	FORMULATION	**Oral powder for suspension** Needs to be mixed with water before administration.

When is CPS a reasonable choice?

- Chronic CKD with mild–moderate hyperkalemia
- Cost-sensitive patients
- Patients who should avoid sodium loading
- Settings where newer binders are unavailable
- Maintenance therapy (potassium reduction does not need to be rapid)

Goal for both

Maintain normal serum potassium and enable optimal care (e.g., continuation of RAAS inhibitors)

When is SZC preferred?

- Need for rapid potassium reduction
- Recurrent hyperkalemia while on RAAS inhibitors
- Better GI tolerability desired
- Need for predictable potassium control to allow continuation of ACEi/ARB/MRA

Bottom line: While SZC is generally preferred for faster onset, greater efficacy and better safety, CPS remains valuable because it is less expensive, widely available, sodium-free, and supported by decades of experience, making it a practical option for many patients, especially in low- and middle-income settings.

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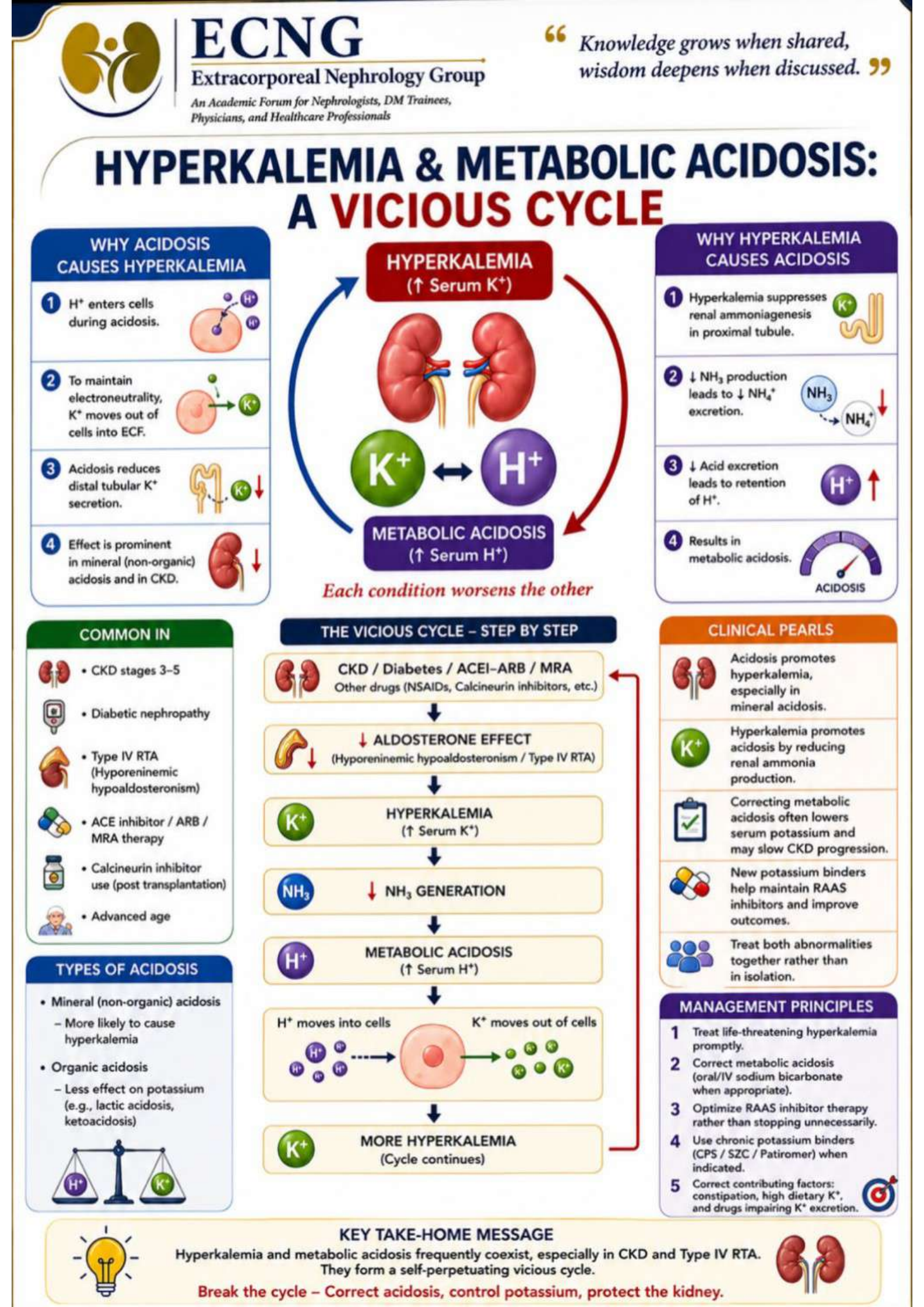
HYPERKALEMIA & METABOLIC ACIDOSIS: A VICIOUS CYCLE

WHY ACIDOSIS CAUSES HYPERKALEMIA

1. H^+ enters cells during acidosis.
2. To maintain electroneutrality, K^+ moves out of cells into ECF.
3. Acidosis reduces distal tubular K^+ secretion.
4. Effect is prominent in mineral (non-organic) acidosis and in CKD.



Each condition worsens the other

WHY HYPERKALEMIA CAUSES ACIDOSIS

1. Hyperkalemia suppresses renal ammoniagenesis in proximal tubule.
2. ↓ NH_3 production leads to ↓ NH_4^+ excretion.
3. ↓ Acid excretion leads to retention of H^+.
4. Results in metabolic acidosis.

ACIDOSIS

COMMON IN

- CKD stages 3–5
- Diabetic nephropathy
- Type IV RTA (Hyporeninemic hypoaldosteronism)
- ACE inhibitor / ARB / MRA therapy
- Calcineurin inhibitor use (post transplantation)
- Advanced age

TYPES OF ACIDOSIS

- Mineral (non-organic) acidosis
  - More likely to cause hyperkalemia
- Organic acidosis
  - Less effect on potassium (e.g., lactic acidosis, ketoacidosis)

THE VICIOUS CYCLE – STEP BY STEP

CKD / Diabetes / ACEI–ARB / MRA
Other drugs (NSAIDs, Calcineurin inhibitors, etc.)

↓

↓ ALDOSTERONE EFFECT
(Hyporeninemic hypoaldosteronism / Type IV RTA)

↓

HYPERKALEMIA
(↑ Serum K^+)

↓

↓ NH_3 GENERATION

↓

METABOLIC ACIDOSIS
(↑ Serum H^+)

↓

H^+ moves into cells — K^+ moves out of cells

↓

MORE HYPERKALEMIA
(Cycle continues)

CLINICAL PEARLS

- Acidosis promotes hyperkalemia, especially in mineral acidosis.
- Hyperkalemia promotes acidosis by reducing renal ammonia production.
- Correcting metabolic acidosis often lowers serum potassium and may slow CKD progression.
- New potassium binders help maintain RAAS inhibitors and improve outcomes.
- Treat both abnormalities together rather than in isolation.

MANAGEMENT PRINCIPLES

1. Treat life-threatening hyperkalemia promptly.
2. Correct metabolic acidosis (oral/IV sodium bicarbonate when appropriate).
3. Optimize RAAS inhibitor therapy rather than stopping unnecessarily.
4. Use chronic potassium binders (CPS / SZC / Patiromer) when indicated.
5. Correct contributing factors: constipation, high dietary K^+, and drugs impairing K^+ excretion.

KEY TAKE-HOME MESSAGE

Hyperkalemia and metabolic acidosis frequently coexist, especially in CKD and Type IV RTA. They form a self-perpetuating vicious cycle.

Break the cycle – Correct acidosis, control potassium, protect the kidney.

HYPERKALEMIA IN DIABETES vs TYPE 4 RTA IN DIABETES

Key Distinction: Presence or Absence of Normal–Anion–Gap Metabolic Acidosis

	HYPERKALEMIA IN DIABETES	TYPE 4 RTA IN DIABETES
Serum K^+	↑ **Elevated** (>5.5 mEq/L)	↑ **Elevated** (>5.5 mEq/L)
Serum HCO_3^- (Bicarbonate)	**Normal** (≥22 mEq/L)	**Low** (<22 mEq/L)
Acid–Base Status	**No acidosis required** (HCO_3^- usually normal)	**Normal–Anion–Gap Metabolic Acidosis** (pH low or normal, HCO_3^- low, AG normal)
Main Mechanism	• Drugs (ACEi, ARB, K^+ sparing diuretics, NSAIDs, Heparin, TMP–SMX) • Reduced GFR / CKD • Insulin deficiency / hypoinsulinemia • Hyperosmolality • Tissue breakdown, acidosis (other causes)	**Hyporeninemic Hypoaldosteronism or Aldosterone Resistance** ↓ Aldosterone effect on distal nephron ↓ ENaC activity & Na^+ reabsorption ↓ K^+ secretion ↓ H^+ secretion ↓ NH_3/NH_4^+ excretion
Kidney Function	**Any stage** (can occur with normal or reduced GFR)	**Usually in mild–moderate Diabetic CKD** (often with GFR <60 mL/min)
Urine Findings	**Variable** (Depends on cause)	• Urine K^+: Often >20 mEq/L • Urine pH: Usually <5.5 • Urine Anion Gap: Positive
Diagnosis	**Hyperkalemia alone**	**Hyperkalemia + Low HCO_3^- + Normal–Anion–Gap Metabolic Acidosis**

PATHOPHYSIOLOGY OF TYPE 4 RTA

↓ Renin secretion (diabetic nephropathy)
↓
↓ Aldosterone secretion or Aldosterone resistance
↓
↓ Na^+ reabsorption in collecting duct (via ENaC)
↓
↓ K^+ secretion (Hyperkalemia) K^+
↓
↓ H^+ secretion
↓
↓ NH_3/NH_4^+ excretion NH_4^+
↓
Normal–Anion–Gap Metabolic Acidosis

KEY CLINICAL DISTINCTION

- Diabetes + Hyperkalemia + Normal Bicarbonate → **DO NOT CALL IT TYPE 4 RTA.**
- Diabetes + Persistent Hyperkalemia + Low Bicarbonate + Normal Anion Gap → **CONSIDER TYPE 4 RTA.**

ONE–LINE TAKE HOME MESSAGE

Type 4 RTA should be suspected in a diabetic patient with persistent hyperkalemia accompanied by a mild normal–anion–gap metabolic acidosis; isolated hyperkalemia without acidosis **is not Type 4 RTA.**