TYPE 4 RTA IN DIABETES MELLITUS

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INTRODUCTION

- **Diabetes mellitus**—especially long-standing type 1 or type 2—can cause:

  Hyporeninemic hypoaldosteronism

  – ↓ Renin → ↓ Aldosterone → impaired potassium & hydrogen ion excretion.

- Autonomic neuropathy → ↓ renin release.

- Diabetic nephropathy → affects juxtaglomerular apparatus → ↓ renin-angiotensin-aldosterone system (RAAS) activation.

RENAL TUBULAR ACIDOSIS

NONGAP METABOLIC ACIDOSIS WITH HYPERCHLOREMIA

	DISTAL RTA (T1)	PROXIMAL RTA (T2)	HYPERKALEMIC RTA (T4)
DEFECT	DECREASED DISTAL H+ SECRETION. ↳ No new HCO3- is generated.	DECREASED PROXIMAL HCO3- REABSORPTION.	ALDOSTERONE DEFICIENCY/RESISTANCE ↳ Hyperkalemia, Reduced NH4+ excretion
CAUSES	Amphotericin B tox., Analgesic nephropathy Autoimmune disease (SLE, Sjögren's) Urinary tract obst.	Fanconi syndrome Carbonic anhydrase inhibs. Multiple myeloma	Diabetic or obstructive nephropathy, Chronic interstitial nephritis, Adrenal insufficiency. ACE inhibs/ARBs, K+-sparing diuretics, TMP-SMX
S/SX	Polydipsia, polyuria. Muscle weakness Nephrolithiasis (hypercalciuria, hypocitraturia) Growth retardation, Rickets	Muscle weakness Growth retardation, Rickets	Poss. muscle weakness, cardiac arrythmias (if hyperkalemia is severe)
URINE PH	> 5.5	> 7 IF PLASMA HCO3- IS NORMAL < 5.5 IF PLASMA HCO3- IS DEPLETED	< 5.5
SERUM HCO3- & K+	HCO3-= 10-15 MMOL/L K+ ↓	HCO3-= 16 -20 MMOL/L K+ ↓	HCO3-= > 17 MMOL/L K+ ↑
DIAGNOSIS	NH4+ loading test -> positive urinary anion gap.	HCO3- loading test -> FE HCO3- > 15%, urine pH > 7.5	Urinary K+< 40 mmol/L or FE K+< 20% Abnormal serum aldosterone
TREATMENT	Sodium HCO3- or Potassium citrate Thiazide diuretics	Sodium HCO3- or Potassium citrate Thiazide diuretics	Volume expansion, dietary K+ restriction K+-wasting diuretics

Typical biochemical features
TYPE 4 RTA

Parameter	Finding
Serum K^+	↑ (hyperkalemia)
Serum HCO_3^-	↓ (mild metabolic acidosis, usually 15–20 mmol/L)
Anion gap	Normal (non-anion gap metabolic acidosis)
Urine pH	< 5.5 (kidneys can acidify urine, unlike type 1 RTA)
Urinary ammonium excretion	Low (despite acidosis)
Trans tubular potassium gradient (TTKG)	Low (inappropriately low in hyperkalemia)

TTKG- TRANSTUBULAR POTASSIUM GRADIENT

- **Formula for TTKG**
- TTKG $= \frac{\text{Urine } K^+ \times \text{Plasma osmolality}}{\text{Plasma } K^+ \times \text{Urine osmolality}}$

- **Urine K^+** = urinary potassium concentration (mmol/L).
- **Plasma K^+** = plasma potassium concentration (mmol/L).
- **Urine osmolality** = urine osmolality (mOsm/kg).
- **Plasma osmolality** = plasma osmolality (mOsm/kg).

TTKG INTERPRETATION

- **Normal TTKG values :**
- **In hyperkalemia**: TTKG should be **>7–10** → indicates appropriate renal K^+ excretion.
- **In hypokalemia**: TTKG should be **<3** → indicates appropriate renal K^+ conservation.

- **In Type 4 RTA**, despite hyperkalemia:
- The TTKG is low (<7), showing impaired K^+ secretion.
- This suggests either:
  - Low aldosterone levels (hypoaldosteronism).
  - Aldosterone resistance (tubular dysfunction).

TREATMENT

- Dietary potassium restriction.
- Loop or thiazide diuretics (enhance K^+ excretion).
- Fludrocortisone (mineralocorticoid replacement, if no contraindications like hypertension or fluid overload).
- Sodium bicarbonate to correct acidosis.