Renal Tubular Acidosis (RTA): Classification, Diagnosis, and Management

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Definition & Epidemiology

Renal tubular acidosis (RTA) = **Primary problem in renal tubule acid secretion or HCO_3 reabsorption**, not glomerular filtration

Key diagnostic feature: **Normal anion gap metabolic acidosis with preserved GFR (eGFR >30)**

- **Anion gap** = Na+ - (Cl- + HCO_3) = normally 8-16 mEq/L
- **In RTA**: AG normal (<12); problem is H+ or HCO_3 handling, not unmeasured anions

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Classification: Four Types

TYPE 1 RTA (DISTAL RTA) — "Can't Acidify Urine"

Location: Alpha-intercalated cells, **distal convoluted tubule (DCT) and collecting duct**

Mechanism: Defect in H+ secretion or secretory pathway - ↓ H+-ATPase pump expression/function - ↓ Urine H+ production → urine cannot acidify below pH 5.5 - **Causes**: Autoimmune (SLE), medications (amphotericin B, NSAIDs, lithium), hereditary (RB1 mutations)

Clinical Features of Type 1 RTA

- **Metabolic acidosis**: Low serum HCO_3, low pH, normal AG
- **Hypokalemia**: Often SEVERE (K+ <3.0); caused by ↑ distal K+ secretion (exchange for Na+ due to H+ pump defect)
- **Inability to acidify urine**: Urine pH >5.5 despite systemic acidosis (pathognomonic)
- **Nephrolithiasis** (50%): Hypocitraturia + high urine pH → calcium phosphate stones
- **Nephrocalcinosis**: Chronic exposure to alkaline urine + high urine calcium → crystal deposition
- **Bone disease**: Chronic acidosis → ↑ bone resorption (osteoporosis, rickets in children)

Diagnostic Tests for Type 1 RTA

Test	Finding	Interpretation
Serum HCO_3	<15 mEq/L	Metabolic acidosis
Serum K+	<3.5 mEq/L	Hypokalemia often SEVERE
Urine AG	Negative	Normal proximal tubule H+ secretion
Urine pH	>5.5 (even with pH <7.20)	Cannot acidify despite acidemia
Urine osmolality	Often low	Inability to concentrate urine (partial NDI)
Serum Cl-	>110 mEq/L	Hyperchloremic acidosis

> [!important] Key Point **Type 1 RTA diagnosis**: You MUST see urine pH >5.5 in setting of systemic acidosis (pH <7.35, HCO_3 <15). This is diagnostic. The kidney is saying "I can't make the urine acidic enough."

TYPE 2 RTA (PROXIMAL RTA) — "Can't Reabsorb HCO_3"

Location: Proximal tubule epithelial cells (S1/S3 segments)

Mechanism: ↓ HCO_3 reabsorption capacity - Normally reabsorbs ~85% of filtered HCO_3 at physiologic levels - Renal threshold for HCO_3 reabsorption lowered (e.g., from 24 mEq/L to 15 mEq/L) - Causes: Carbonic anhydrase II deficiency, acetazolamide use, Fanconi syndrome, medications

Clinical Features of Type 2 RTA

- **Metabolic acidosis**: HCO_3 12-20 mEq/L (less severe than Type 1)
- **Hypokalemia**: Moderate (K+ 3.0-3.5); from urinary K+ wasting in Fanconi syndrome
- **Bicarbonaturia**: PATHOGNOMONIC finding
  - Urine HCO_3 >15-20 mEq/L (renal threshold exceeded)
  - Urine dipstick POSITIVE for protein (actually filtration of HCO_3)
- **Urine pH**: Variable; can acidify normally (pH 5.5-6.0) when serum HCO_3 LOW enough
- **Growth retardation** (in children): Chronic acidosis impairs bone growth

Associated Features: Often Part of FANCONI SYNDROME

- **Fanconi syndrome** = Global proximal tubule dysfunction
- Associated findings: Phosphaturia (↓ serum phosphate), glycosuria (despite normal glucose), aminoaciduria, uricosuria

- Causes: Cystinosis (most common in children), Dent disease, Wilson disease, heavy metal exposure (lead, cadmium), medullary sponge kidney, expired tetracycline

Diagnostic Tests for Type 2 RTA

Test	Finding	Interpretation
Serum HCO_3	12-20 mEq/L	Mild-moderate acidosis
Serum K+	3.0-3.5 mEq/L	Mild hypokalemia
Urine HCO_3	>15 mEq/L	Proximal HCO_3 wasting
Urine pH	5.5-6.0 (can acidify)	Normal H+ secretion
Serum Cl-	105-110 mEq/L	Hyperchloremic
Urine AG	Positive or neutral	From glycosuria, phosphaturia, aminoaciduria
Urine glucose, phosphate, amino acids	Present	Fanconi syndrome features

> [!tip] Clinical Pearl **Type 2 RTA "rule out"**: If serum HCO_3 falls to <15 mEq/L, urine HCO_3 will drop (proximal reabsorption catches up). If still seeing bicarbonaturia despite HCO_3 <15, suspect Type 4 RTA (aldosterone deficiency) or secondary causes.

TYPE 3 RTA — "Hybrid" (Rare, Not on Most Exams)

Rarely discussed; considered variant of Type 1 + Type 2

- Distal secretion defect + proximal reabsorption defect
- Very rare; mostly of historic interest
- Omitted from most modern textbooks

TYPE 4 RTA (HYPERKALEMIC RTA) — "Aldosterone Problem"

Location: Collecting duct and principal cells

Mechanism: ↓ Aldosterone activity or response - **Primary hypoaldosteronism**: Low aldosterone (genetic, adrenal insufficiency, ACE-I/ARB) - **Secondary aldosterone resistance**: Normal aldosterone; tubules don't respond (NSAIDs, K-sparing diuretics, diabetes with hyporeninemia)

Causes: 1. ↓ **Aldosterone production**: - Adrenal insufficiency (Addison disease) - ACE-I/ARB (↓ angiotensin II → ↓ aldo) - NSAIDs (↓ renin → ↓ angiotensin II → ↓ aldo) - Hyporeninemic hypoaldosteronism (type 4A RTA) — seen in diabetics, mild CKD

2. **Aldosterone resistance**:
    - NSAIDs: ↓ prostaglandin-dependent distal K+ secretion
    - K-sparing diuretics (spironolactone, amiloride, triamterene)
    - Kidney disease (tubulointerstitial disease affecting collecting duct)
    - Medications: Trimethoprim (blocks ENaC), pentamidine, topiramate

Clinical Features of Type 4 RTA

- **Metabolic acidosis**: Usually mild (HCO_3 17-24 mEq/L) — hallmark of Type 4
- **HYPERKALEMIA** (K+ >5.5): DISTINGUISHES from Types 1 & 2
    - Mechanism: ↓ distal K+ secretion (aldosterone ↓ or resistant)
    - Severity: Mild-moderate (5.5-7.0 mEq/L usually)
- **Normal urine anion gap**: Indicates H+ secretion intact (not primary defect)
- **Urine pH**: 5.5-6.0 (can acidify normally)
- **Risk of arrhythmia**: Hyperkalemia + acidosis = dangerous combination

Diagnostic Tests for Type 4 RTA

Test	Finding	Interpretation
Serum HCO_3	17-24 mEq/L	Mild acidosis (key feature)
Serum K+	>5.5 mEq/L	HYPERKALEMIA (diagnostic)
Plasma renin activity	↓ or ↑	Check to differentiate (Type 4A vs. 4B)
Serum aldosterone	↓ (Type 4A) or normal (Type 4B)	4A: ↓ aldo; 4B: normal but resistant
Urine K+	Low	Confirms K+ retention (if not due to intake)
Urine AG	Normal or positive	H+ secretion intact; problem is K+ not H+

Diagnostic Algorithm: Which RTA Type?

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STEP 1: Check serum K+
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├─ K+ <3.5 → TYPE 1 or 2 RTA
│   └─ Check urine pH
│       ├─ Urine pH >5.5 → TYPE 1 RTA ("can't acidify")
│       │   └─ Stones? Nephrocalcinosis? Yes → Type 1 confirmed
│       └─ Urine pH <5.5 → TYPE 2 RTA ("can't reabsorb HCO₃")
│           └─ Check urine HCO₃ or Fanconi features
├─ K+ >5.5 → TYPE 4 RTA ("hyperkalemic")
│   └─ Check plasma renin, aldosterone
│       ├─ ↓ Renin + ↓ Aldo → Type 4A (hyporenemic)
│       └─ ↑ Renin + normal/↓ Aldo → Type 4B (aldosterone resistant)
└─ K+ normal (3.5–5.0) → Rarely RTA; consider other diagnoses
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Treatment by Type

TYPE 1 RTA TREATMENT

Goal: Correct acidosis, replace K+, prevent nephrolithiasis

1. **Alkali replacement**: **Sodium or potassium bicarbonate**
   - Dose: 0.5-1 mEq/kg/day (titrate to HCO_3 >20 mEq/L)
   - Form: PO sodium bicarbonate tablets 650-1300 mg TID; or liquid (Shohl solution)
   - Give K+ at same time (often compounded: K-Citrate) — preferentially citrate (↑ urine citrate → ↓ stone risk)
2. **Potassium supplementation**: K-citrate preferred
   - Citrate metabolized to HCO_3 (adds alkali)
   - Citrate in urine ↓ calcium stone formation
   - Typical dose: 40-80 mEq/day K-citrate (often in divided doses)
   - Monitor: Serum K+, HCO_3, Cr (check monthly × 3, then every 3 months)
3. **Monitoring**: Thrice yearly (K+, Cr, urine calcium, bone densitometry annual)

   [!tip] Clinical Pearl **K-citrate in Type 1 RTA**: Kills two birds: replaces K+ AND reduces stone formation (citrate chelates calcium). Superior to separate K+ and HCO_3 replacement. Dosing 40-60 mEq/day typical; titrate to K+ goal 3.5-4.5.

TYPE 2 RTA TREATMENT

Goal: Correct acidosis, treat underlying cause (Fanconi syndrome), replace K+

1. **Alkali replacement**: Sodium bicarbonate similar to Type 1
   - BUT dose usually lower (0.5-1 mEq/kg/day) because proximal tubule reabsorbs more
   - If given excessive alkali, bicarbonaturia worsens (can deplete other electrolytes)
2. **Thiazide diuretic** (counter-intuitive!):
   - Thiazide-induced volume depletion → ↑ proximal tubule reabsorption of HCO_3
   - Typical dose: Hydrochlorothiazide 25 mg daily
   - Mechanism: Hypovolemia enhances proximal reabsorption; net result = higher serum HCO_3
   - Monitor for hypokalemia (may need K+ replacement despite thiazide)
3. **Treat Fanconi syndrome**: Address underlying cause

- Cystinosis: Cysteamine (chelates cystine)
- Dent disease: Genetic; supportive care
- Other causes: Avoid offending agent (expired tetracycline, etc.)

4. **Monitoring**: K+, HCO_3, Cr q 3 months; screen for growth delay (in children)

TYPE 4 RTA TREATMENT

Goal: Lower K+, correct acidosis; treat underlying cause

1. **Remove offending agent** (MOST IMPORTANT)
   - Discontinue K-sparing diuretic if possible
   - Stop NSAID; use acetaminophen instead
   - Hold ACE-I/ARB if tolerated; reassess need if essential
2. **Loop diuretic** (if eGFR adequate):
   - Furosemide 40-80 mg daily → increases distal K+ and H+ secretion
   - Mechanism: Volume contraction → ↑ renin → ↑ aldosterone (if GFR adequate)
   - Goal: Prevent K+ >6.0; maintain eukalemia
3. **Sodium polystyrene sulfonate (Kayexalate)** (if K+ >6.0):
   - 15-30 g PO TID (or 30-50 g PR enema)
   - Cation exchange resin; exchanges K+ for Na+
   - Onset: Hours (PO); minutes (PR)
   - Caution: Risk of intestinal necrosis if used with sorbitol
4. **Alkali replacement**: Usually NOT needed
   - Metabolic acidosis typically mild (HCO_3 >18)
   - If acidosis severe, sodium bicarbonate OK (but K+ rises further)
5. **Treat underlying cause**:
   - Adrenal insufficiency: Glucocorticoid + mineralocorticoid replacement
   - Hyporeninemic hypoaldosteronism (diabetic): Fludrocortisone 0.1-0.2 mg daily (if tolerated; monitor HTN)

> [!warning] High-Yield Board Point **Type 4 RTA + ACE-I/ARB**: Common scenario in diabetes. Must weigh benefit of cardiac protection (ACE-I/ARB) vs. risk of hyperkalemia. If K+ >6.0, discontinue ACE-I/ARB and substitute other agent (CCB, beta-blocker) if no MI/HF. If K+ <5.5 and HCO_3 <20, may continue with close monitoring.

Clinical Pearls & Pitfalls

> [!tip] Clinical Pearl **Anion gap vs. non-anion gap acidosis**: Always calculate AG. If AG normal + HCO_3 low, RTA is likely culprit. If AG high, organic acids (lactate, ketones, uremia) or ingestions at fault.

> [!important] Key Point **Type 1 RTA + stone disease**: ALWAYS check urine pH, citrate, calcium in any patient with "recurrent" kidney stones. If urine pH persistently >6.0 + normal renal function, suspect Type 1 RTA. Treat with K-citrate (alkali + stone prevention).

> [!warning] High-Yield Board Point **Amphotericin B causes Type 1 RTA**: Nephrotoxic antifungal; both AKI AND Type 1 RTA. If receiving amphotericin, monitor UA for

inability to acidify + hypokalemia. Consider liposomal formulation (less renal toxic).

[!tip] Clinical Pearl **SLE + Type 1 RTA**: Autoimmune attack on alpha-intercalated cells. If lupus patient develops hyperchloremic acidosis + inability to acidify urine, consider RTA as lupus manifestation (separate from lupus nephritis). Treat with bicarbonate + loop diuretic.

[!important] Key Point **Type 4 RTA risk in CKD**: As eGFR falls <30-40, mild Type 4 RTA can develop (hyporeninemic hypoaldosteronism). Exacerbated by diabetes, NSAIDs, ACE-I/ARB. Screen with K+ + venous bicarb every 6 months if eGFR <30.

Related Resources

- Acid-Base Formal Review
- BMP Pattern Recognition Master Guide
- CKD Comprehensive Management Pathways

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