Renal Tubular Acidosis

Normal anion gap acidosis with normal-ish kidneys · The potassium and the urine pH name the type

URINE ANION GAP
positive = renal, negative = gut

GET TO RTA IN THREE STEPS *most normal-gap acidosis is diarrhea, not tubular disease*

1. CONFIRM A NORMAL GAP

Metabolic acidosis with a normal serum anion gap, meaning bicarbonate has been lost or acid retained without an unmeasured anion. **Correct the gap for albumin** — a low albumin lowers the calculated gap by roughly 2.5 for every 1 g/dL below normal and can disguise a raised-gap acidosis entirely.

2. GUT OR KIDNEY?

The urine anion gap answers it: urine sodium plus potassium minus chloride. It is an indirect measure of **ammonium excretion**. **Negative means the kidney is excreting acid appropriately**, so the loss is gastrointestinal. **Positive means the kidney is failing to excrete acid**, which is RTA. Remember **"NEGUTIVE"** — negative points to the gut.

3. THEN THE POTASSIUM

The serum potassium separates the types faster than anything else. Low potassium points to **type 1 or type 2**. **High potassium** points to **type 4**, which is by far the commonest in practice and the one you will actually meet on the wards.

THE THREE TYPES *type 3 is a historical hybrid and is not used clinically*

Feature	Type 1 — distal	Type 2 — proximal	Type 4 — hyperkalemic
Defect	**Cannot excrete acid** in the distal tubule	**Cannot reabsorb bicarbonate** in the proximal tubule	**Aldosterone deficiency or resistance**
Potassium	**Low**, sometimes severely	**Low**	**High** — the giveaway
Urine pH	**Stays above 5.5** despite acidemia — the defining feature	**Variable**: high while bicarbonate is spilling, then **falls below 5.5** once serum bicarbonate drops below the reabsorptive threshold	**Below 5.5** — acidification works; ammonia production is the problem
Serum bicarbonate	Can fall **very low**	**Plateaus around 12–18**, because reabsorption resumes below the threshold	**Mild**, usually above 17
Complications	**Nephrocalcinosis, calcium phosphate stones, rickets and osteomalacia**	**Rarely stones**; often part of **Fanconi syndrome** with glycosuria, phosphaturia, aminoaciduria and uricosuria	Usually none beyond the **hyperkalemia** itself
Typical causes	**Sjögren's syndrome, lupus, rheumatoid arthritis, amphotericin B, lithium, sickle cell disease**, hereditary	**Myeloma, acetazolamide, tenofovir, ifosfamide, heavy metals**, hereditary and Wilson's disease	**Diabetic nephropathy** (much the commonest), **ACE inhibitors and ARBs, spironolactone, NSAIDs, trimethoprim, calcineurin inhibitors, heparin**, adrenal insufficiency

TREAT BY TYPE *the alkali requirement differs by an order of magnitude*

Type	Approach
Type 1	**Oral alkali, in modest doses**, which usually corrects both the acidosis and the potassium because acidosis itself drives the renal potassium wasting. **Alkali also reduces stone formation and nephrocalcinosis**, and improves growth in children. **Treat the underlying cause** — screen for Sjögren's syndrome and review lithium and amphotericin.
Type 2	**Requires far larger alkali doses**, because the bicarbonate you give is promptly spilled into the urine. **Alkali worsens the hypokalemia** by increasing distal delivery, so **give potassium citrate rather than sodium bicarbonate**, and monitor closely. **A thiazide** can help by inducing mild volume contraction. **Look hard for myeloma and for a causative drug**, and check for the other features of Fanconi syndrome.
Type 4	**Treat the hyperkalemia and the cause. Review the drug chart first** — stopping or reducing the offending agent is often the whole treatment. Add **dietary potassium restriction**, a **loop diuretic**, and a **potassium binder** where needed. **Fludrocortisone** is used in genuine mineralocorticoid deficiency, with care where there is hypertension or heart failure. **Modest alkali** also lowers potassium.
Before you commit	**Confirm you are not simply dealing with chronic kidney disease.** Advanced CKD produces acidosis on its own, and the RTA label should be reserved for a tubular defect out of proportion to the eGFR. **Recheck the gas, the electrolytes and the urine pH off any interfering drug** before making it a lifelong diagnosis.

TRAPS IN THE MEASUREMENT *most wrong diagnoses come from the sample, not the physiology*

THE URINE pH

Measure it on a fresh sample, ideally with a pH meter rather than a dipstick, and **test it promptly** — carbon dioxide escapes from a standing sample and drives the pH up, manufacturing a false type 1. **A urinary tract infection with a urea-splitting organism raises the pH** and does the same. **Interpret the pH only in the presence of genuine acidemia**: an alkaline urine in a non-acidotic patient means nothing.

THE URINE ANION GAP

It is invalid whenever an unmeasured anion is present in the urine — diabetic or starvation ketoacidosis, toluene or glue sniffing, high-dose penicillins, or a drug being excreted as an anion. In those settings the gap can read positive despite normal acidification. **The urine osmolar gap is the more reliable estimate of ammonium** in ambiguous cases. **It also needs a reasonable urine sodium**, so a very avid, sodium-poor urine makes it uninterpretable.

PEARLS & PITFALLS

- **The three numbers that separate the types: type 1 distal** — urine pH stays **above 5.5** despite acidemia, potassium **low**, with nephrocalcinosis and stones; **type 2 proximal** — urine pH **falls below 5.5** once the filtered load drops, potassium **low**, often with Fanconi features; **type 4** — urine pH **below 5.5** but potassium **high**, which is the giveaway. **A positive urine anion gap points to the kidney, a negative one to GI losses.**
- **Check the potassium first.** High points to type 4, low to types 1 and 2, and that single number does most of the sorting.
- **Type 4 is the one you will actually see** — diabetic nephropathy plus an ACE inhibitor, spironolactone or trimethoprim.
- **Negative urine anion gap means the gut.** Diarrhea is far commoner than any tubular defect.
- **Correct the serum anion gap for albumin** before calling it normal, or you will miss a raised-gap acidosis.
- **Type 2 needs large alkali doses and potassium citrate**, since bicarbonate alone worsens the hypokalemia.
- **Test urine pH on a fresh sample.** A standing specimen or a urea-splitting infection fabricates type 1 RTA.

References: KDIGO and major nephrology reference guidance on the diagnosis and management of renal tubular acidosis · reviews of the urine anion and osmolar gaps in normal-anion-gap metabolic acidosis · consensus guidance on distal RTA and its inherited forms.