Renal Tubular Acidosis: A Drug-Centric Perspective
compiled by Peter Loewen, R.Ph., ACPR, Pharm.D., FCSHP
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**Goals of therapy:**
1. prevent nephrocalcinosis, osteomalacia, rickets
2. prevent severe acidosis, respiratory failure & death
3. prevent hypokalemic paralysis (with rhabdomyolysis), hypokalemia & death
4. prevent irreversible renal damage (if drug-induced)
5. prevent fatigue

**NOTES:**
- > UAG = urine (Na + K) - urine Cl
- > urine pH must be measured promptly (it increases as it sits since CO2 evaporates & bacteria produce urea, > increases urea, can't run pH on previously obtained sample)
- > most labs measure pH in 0.5 increments and only if >5.5
- > urine Cl is hard to do without all labs can do it

**Alkali Replacement:**
- > Total body bicarb deficit (mEq)= (desired - actual) x 0.6 x wt
- > Baking soda contains 12 mEq bicarb/g and ~270 mg Na+/g
- > K-citrate & Na-citrate (Dicitrate) contain 1mEq bicarb/mL (+ 1mEq K+ or Na+ per mL)
- > NaBicarb tablets contain 325mg NaBicarb (=4 mEq bicarb + 90 mg Na+ per tablet)

**Type 2 RTA (proximal RTA, pRTA)?**
- decreased bicarb resorption in proximal tubule (threshold >15)
- Don’t forget about NH3 synthesis/transfer defect:
  - Features: urine pH<5.5, normokalemic

**Type 1 RTA (distal RTA, dRTA)?**
- permeability defect
- "back-diiffusion of H+ out of tubule
- NH3 synthesis 
- Ability to acidify urine...
- "transcytosis"
- "rate limited defect"
- \(-\)defective H+ pump

**Type 4 RTA!**
- Hyperkalemia causes 1
  - NH3 synthesis \(-\) ability to acidify urine...
- "hypokalemic" urine pH<5.5 when acidic

**Renal Tubular Acidosis Comparison Table**

<table>
<thead>
<tr>
<th>Type</th>
<th>Metabolic acidosis?</th>
<th>Anion gap</th>
<th>Serum Cl(\uparrow)</th>
<th>Serum K(\uparrow)</th>
<th>UAG**</th>
<th>Urine pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>pRTA (Type 2)</td>
<td>✓</td>
<td>Normal</td>
<td>↑</td>
<td>Normal</td>
<td>NEG</td>
<td>&lt;5.5 when acidic</td>
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<tr>
<td>dRTA (Type 1)</td>
<td>-NH(3) synth / transport defect</td>
<td>✓</td>
<td>Normal</td>
<td>↑</td>
<td>Normal</td>
<td>POS</td>
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<td>-secretory defect</td>
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<td>↑</td>
<td>↓ in 30-50% of cases</td>
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**Non-drug causes:**
- Primary, hereditary, sporadic, decreased carbonic anhydrase activity/CA deficiency, genetic diseases
- Fanconi syndrome, tyrosinemia, Wilson’s disease
- glycogen storage disease, galactosemia, ARC Syndrome, Alport syndrome, multiple myeloma, amyloidosis, nephrotic syndrome, hypocalcemia, vit.D deficiency / resistance, Sjogren’s syndrome, renal vein thrombosis, renal transplant rejection, lead / cadmium / mercury toxicity, hyperparathyroidism, medullary cystic kidney disease

**Therapy if primary, drug can’t be stopped or short-term therapy needed:**
- Often none
- High dose oral alkali (4-20 mEq/kg/d bicarb), (see bottom left for quantities)
- +/- thiazide diuretic + low Na diet
- K+ supp may be needed

**Non-drug causes:**
- Primary (sporadic [eg. sepsis], hereditary, a.k.a "incomplete RTA")
- Genetic (Mastai’s syndrome, sickle-cell disease, elliptocytosis, medullary cystic disease, Fabry’s disease, Wilson’s disease, Ehlers-Danlos syndrome, osteopetrosis)
- Autoimmune (Sjogren’s syndrome, SLE, RA, vasculitis, hyperparagammaglobulinemia, chronic active hepatitis, primary biliary cirrhosis, thyroiditis, fibrosing alveolitis)
- Calcium problems (idiopathic hypercalcuria, hyperparathyroidism, medullary sponge kidney)
- Chronic pyelonephritis, renal transplant, hepatic cirrhosis, amyloidosis, vanadate

**Therapy if primary, drug can’t be stopped or short-term therapy needed:**
- Initially to correct acidosis: calculate bicarb required based on total body bicarb deficit and give 1/3-1/2 IV over 4-8 hours. Give remainder over >24 hours (eg. infusion at ~2 mEq/kg/d as Na-bicarb or K-bicarb)
- Chronic therapy: PO bicarb 0.5-2 mEq/kg/d in 2-4 doses as baking soda (mixed in water or diet soda) or Na or K ctitrate solution (Dicitrate). (see bottom left for quantities)
- Supplement K+ if hypokalemic (K-bicarb or K-citrate) use furosemide if volume overload or renal insufficiency is a problem

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†currently thought to be due to overactive CI-/HCO3- exchange pump in distal tubule (in Type1) [Pediatr Nephrol 2006;21:206-211]
*when corrected for acidosis (eg. pH Δ 0.1 + K+ Δ 0.6 mmol/L)
**UAG = urine (Na + K) – Cl

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