Renal Tubular Acidosis

Recall…
- a metabolic acidosis is either AG (i.e. "MUDPILERS") or non-AG
- a non-AG acidosis is either renal (i.e. renal failure, RTAs) or non-renal bicarb wasting; recall the non-AG acidosis differential "DURHAM“:
  - diarrhea/ileus/fistula/villous adenoma (GI causes)
  - urinary tract diversions
  - renal tubular acidosis/renal failure
  - hypercapnia (transiently after chronic hypercapnia)
  - acid administration (hyperchloremic acid: dilutional/NaCl, NH3Cl, TPN, cholestyramine)
  - medications (e.g. carbonic anhydrase inhibitors)

To differentiate between renal and non-renal causes of a non-AG acidosis, measure urine lytes to calculate the urine anion gap (UAG) (urine sodium + urine potassium - urine chloride). The UAG is normally a bit negative since the major unmeasured cation in the urine is NH4+, usually excreted with Cl-.

If UAG is negative (esp if < -10), the problem is non-renal…
If there is too much acid around, the kidney’s normal response is to make more ammonia & dump more NH4+ into the urine -> higher amt of Cl- & unmeasured cations in the urine.

If UAG is positive (esp if >10), the problem is renal*…
If there’s a defect in renal acidification of urine, excretion of NH4+ is impaired -> less Cl- and less unmeasured cations in the urine.

*Before jumping to diagnose an RTA, remember that renal failure is a much more common cause of renal acidosis than RTA in the hospital. Acidosis (incr in proportion to decr CrCl) in early renal failure / CKD is caused by a decr in nephron number leading to decr ammonia production & decr medullary trapping of NH4+ (impaired ammonia secretion, as in Type I RTA except Cr high & urine pH normal). As CKD progresses, kidney loses ability to excrete anions (phos, sulfate, urate, etc.) & acidosis goes from non-AG to AG.

Type II RTA (proximal)
Causes: primary (familial disorders, e.g. wilisons) or secondary (myeloma**, amyloid, drugs, heavy metals, vit D defic, PNH, renal transplant) **in myeloma, light chains accumulate in prox tubule cells
Manifestations: bicarb initially drops then maintained 12-20 range as reabsorbed distally, urine pH usually <5.3 w/o alkali tx; often Fanconi’s syndrome (glucosuria, phosphaturia, uricosuria, aminoaciduria, tubular proteinuria); often see K+ wasting & hypoK+; phosphate wasting can lead to osteomalacia

Type I RTA (distal)
Causes: impaired H+ secretion from decr H-ATPase activity, incr luminal membrane permeability & H+ leakage, or decr tubular Na+ reabsorb which decreases gradient for H+ secretion (sickle or obstructive uropathy); primary (familial or idiopathic types) or secondary (autoimmune dz [sjogren’s, RA, SLE], drugs [ampho B, lithium], sickle cell, hyperCa++, hyperpt, cirrhosis, obstructive uropathy, renal tsplnt)
Manifestations: very low bicarb (b/c no way to get rid of acid load), urine pH >5.5, chronic acidosis can cause bone resorption & renal tubular resorption of Ca++ leading to renal stones & nephrocalcinosis

Type IV RTA (distal)
Causes: aldo defic (DM nephropathy) or tubular resistance to aldo (chronic tubulointerstitial dz or K-sparing diuretics)
Manifestations: hyperK+ is main problem, not acidosis (bicarb usually >17, likely d/t suppression of ammonia d/t hyperK+), urine pH<5.3 and typically acidic b/c H+ gets excreted instead of K+

Management
Bicarb for Type II (usually need a lot) or Type I. For Type IV, restrict K+ & give non-K+ sparing diuretics, fludrocortisone in severe cases.

<table>
<thead>
<tr>
<th>Type II</th>
<th>Type I</th>
<th>Type IV</th>
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<tbody>
<tr>
<td>Causes</td>
<td>Primary, myeloma, amyloid, acetazolamide, heavy metals, Fanconi</td>
<td>Primary, ampho B, autoimmune dz [sjogren’s, RA, SLE], myeloma, marked vol depletion</td>
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<tr>
<td>Location/Defect</td>
<td>Proximal problem with HCO3 resorption (UAG less applicable)</td>
<td>Distal acidification defect</td>
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<tr>
<td>Urine Ph</td>
<td>&gt; 5.3 (or &gt;6.0)</td>
<td>Normal or low (made better by alkali therapy)</td>
</tr>
<tr>
<td>Serum K</td>
<td>Normal or low (made worse by alkali therapy)</td>
<td>Variable (may be &lt; 10 mEq/L)</td>
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<tr>
<td>Serum HCO3</td>
<td>Moderately low (12-20)</td>
<td>Variable (may be &lt; 10 mEq/L)</td>
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