RTA's in a nutshell

General Comments

- Net acid excretion = [titrable acid (H^+) + NH_4^+] - urinary HCO_3^-
- NH_4^+ secretion occurs in proximal tubule, and 65-75% is resorbed in thick ascending limb (medullary recycling)
- Distal H^+ secretion occurs in a one way fashion in the medullary collecting ducts and cortical collecting duct. Most H^+ is bound by urinary buffers and NH3.
- Fractional excretion HCO_3^- less than 3% normally; 80-85% reclaimed in proximal convoluted tubule + 5-10% resorbed in proximal straight tubule and loop of Henle
- Consider Diagnosis in setting of non-anion gap metabolic acidosis

Proximal RTA (type II)

- Defect in HCO_3^- resorption
- Fanconi syndrome: Proximal tubule damage (inherited or acquired – heavy metal toxin, drugs) exhibited by phosphate, glucose, bicarbonate wasting in urine
- Acetazolamide induces Proximal RTA by blocking carbonic anhydrase
- Fractional HCO_3^- excretion of decreases as serum HCO_3^- falls below 15mmol/L (Self-limited)
- Low Urine pH, low serum K^+
- Treatment involves high doses (≥5mmol/kg) of HCO_3^- per day; may exacerbate hypokalemia

Distal RTA (type I)

- Defect in distal H^+ secretion
- Four proposed theories of defects
    - Secretory: Defective or absent proton pump
    - Voltage: Unfavorable electrical gradient for H^+ secretion (seen in dehydration with avid resorption of Na^+)
    - Permeability: Back diffusion of protons (caused by Amphotericin B)
    - NH_3: Insufficient supply of NH_3 to distal nephron
- High Urine pH, low serum K^+
- Treatment involves moderate doses (2-5mmol/kg) of HCO_3^- per day

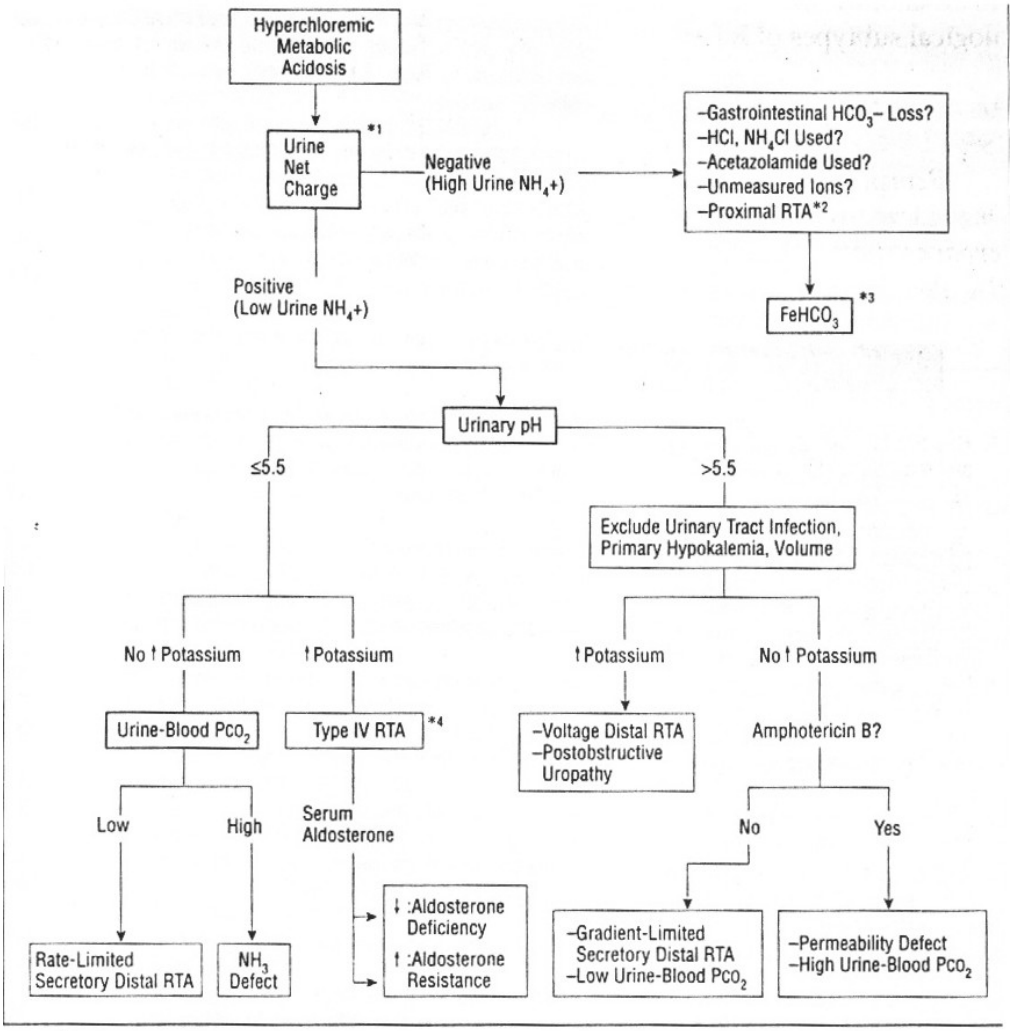
Type IV RTA (hypo-aldosterone, hypo-renin, hyperkalemic)

- Spironolactone can cause this
- Combination of secretory defect (no aldo to stimulate H^+-ATPase) and voltage defect (decreased distal sodium resorption)
- 'Lesion' is in glomerulus with absence of renin secretion triggered by JGA
    - Renin activates angiotensinogen, which converts Angiotensin 1→2
    - Angiotensin 2 stimulates aldosterone secretion (as well as ADH, ACTH)
- Associated with Diabetes Mellitus
- Low Urine pH, high serum K^+
- Treated with oral HCO_3^- or citrate; 1-2 mmol/kg

Diagnosis

- High urine pH in the face of metabolic acidosis is **Distal RTA** excluding:
    - UTI with urea splitting organisms
    - Potassium depletion
    - Volume depletion

- Urine Net charge = $Na^+ + K^+ - Cl^-$ = -[approximate NH_4^+]
  - Positive UNC = low NH_4^+ - previously thought to confirm **Distal RTA**
- Acid loading – 0.1 g oral NH4+Cl-; measure urine pH in 6-8 hours
  - Maintenance of urine pH >5.3 suggests classic **Distal RTA**
- Urine-Blood PCO2 gradient
  - Administer oral of IV HCO3- to alkalinize urine to pH>7.0
  - Normal U-B PCO2 gradient is 3.3-4.0 kPa
  - Low U-B gradient found in secretory and voltage dependent **Distal RTA**
- Fractional Bicarbonate excretion
  - Administer IV HCO_3^- to obtain plasma level of 30 mmol/L
  - Follow serial Urinary fractional HCO_3^- excretion
  - $$FE_{HCO3-} = \frac{U_{HCO3-} x P_{cr}}{P_{HCO3-} x U_{cr}} x100\%$$
  - $FE_{HCO3-} > 15\%$ diagnostic of **Proximal RTA**



Schematic diagnostic approach to renal tubular acidosis (RTA). Diagnostic tests are in bold outlined boxes. See text for explanation of asterisks with superscript numbers. FE_{HCO3-} indicates fractional bicarbonate excretion during bicarbonate loading (normal, <5% [<10% when urinary pH is very high]); urine-blood P_{CO_2}, urine-blood P_{CO_2} gradient in response to bicarbonate or neutral phosphate loading (normal, >3.3-4.0 kPa) (adapted from references 11, 27, 44, 45, 48, and 52).

Smulders YM, Frissen PH, Slaats EH, Silberbusch J. *Renal tubular acidosis. Pathophysiology and diagnosis.* Arch Intern Med. 1996 Aug 12-26;156(15):1629-36.