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 NH\(_3\).
- 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 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 \(\rightarrow\) 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 NH\(_4\)Cl; measure urine pH in 6-8 hours
  - Maintenance of urine pH > 5.3 suggests classic Distal RTA
- Urine-Blood PCO\(_2\) gradient
  - Administer oral of IV HCO\(_3^\) to alkalinize urine to pH > 7.0
  - Normal U-B PCO\(_2\) 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
  - \( FE_{HCO_3^-} = \frac{U_{HCO_3^-}xP_{cr}}{P_{HCO_3^-}xU_{cr}}x100\% \)
  - \( FE_{HCO_3^-} > 15\% \) diagnostic of Proximal RTA

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![Diagram of Renal Tubular Acidosis]

Schematic diagnostic approach to renal tubular acidosis (RTA). Diagnostic tests are in bold outlined boxes. See text for explanation of asterisks with superscript numbers. \( FE_{HCO_3^-} \) indicates fractional bicarbonate excretion during bicarbonate loading (normal, \(<5\%\) \([<10\%\] when urinary pH is very high\)); urine-blood PCO\(_2\), urine-blood PCO\(_2\) 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).