

Renal Tubular Acidosis

Key Points:

1. Think of RTA when you have a non-gap acidosis and diarrhea is not the cause.
2. Look at the serum bicarbonate and urine pH: a very low HCO_3^- level and high urine pH suggest Type I RTA.
3. Consider underlying causes, especially multiple myeloma for Type II and autoimmune diseases for Type I.

A little review of kidney physiology...

Bicarbonate: 90% of HCO_3^- reabsorption occurs in the proximal tubule via the Na-H pump. The other 10% gets reabsorbed in the distal tubule through the H-ATPase pump which secretes a proton. Normally, there is virtually no bicarbonate in the urine and normal urine pH is around 4.5-5.0

Acid: The distal tubule does acid secretion. Acids are derived daily from metabolism of sulfur-containing amino acids. Were we not to have a buffering system in place, urine pH would be less than 2.5!

What buffers all that acid in the blood and urine?

Ammonia and phosphate! The kidney produces ammonia in response to intracellular acidosis which in the distal tubule combines with hydrogen to make ammonium. So acidosis results when there is a defect in either ammonia or hydrogen secretion. Type I RTA has a problem with hydrogen ion secretion and Type IV RTA struggles with ammoniogenesis.

Going from proximal to distal...

Type II RTA (proximal): caused by a reduction in bicarbonate reabsorptive capacity.

Causes of Type II?

In adults think **multiple myeloma or certain drugs**. The light chains in multiple myeloma are resistant to degradation in the proximal tubular cells and accumulate there to cause impairment. Other things to consider are: **Primary:** Familial disorders (cystinosis, Wilson's, glycogen storage disease type I, and other metabolic disorders), idiopathic

Secondary: multiple myeloma, amyloidosis, drugs (ifosfamide, carbonic anhydrase inhibitors), heavy metals (lead, mercury, copper), Vit D deficiency, PNH, renal transplant

What about serum bicarbonate levels? Serum bicarb will drop initially but then will be maintained in the **12-20 meq/L** range because the bicarb will be reabsorbed distally.

What does the urine look like? Urine pH is variable but **usually less than 5.3**. It will be greater than 5.3 if bicarbonate reabsorptive capacity is surpassed, such as with administration of alkali therapy.

What's Fanconi's syndrome?

A general proximal tubular dysfunction which can result in glucosuria, phosphaturia, uricosuria, aminoaciduria, and tubular proteinuria. Most Type II RTAs are also Fanconi's syndrome unless they have an isolated tubular defect of acid secretion.

Type I RTA (distal): due to an impaired capacity of hydrogen ion secretion (and therefore ammonium secretion) in the collecting tubules.

What's the pathophysiology of the impairment?

This can be from decreased H-ATPase activity, increased luminal membrane permeability with leaking of hydrogen ions, or diminished tubular sodium reabsorption which reduces the electrical gradient for hydrogen excretion (sickle cell or obstructive uropathy).

What are the causes of Type I RTA?

Think **autoimmune disorders** such as Sjogren's, RA, SLE. Consider drugs (ifosfamide, amphotericin B, lithium), sickle cell anemia, hypercalciuria, hyperglobulinemia, cirrhosis, obstructive uropathy, or renal transplant. Of course, there's still the idiopathic and familial types.

What about serum bicarb levels?

Can drop **quite low** (ie below 10meq/L) because there is no way to excrete the acid load.

And the urine pH? Symptoms too?

Greater than 5.5. These patients can develop kidney stones and nephrocalcinosis because chronic acidosis causes bone resorption and renal tubular resorption of calcium.

Type IV RTA (hyporenin/hypoaldo)

The pathophysiology?

Due to either aldosterone deficiency (ie diabetic nephropathy) or tubular resistance to the action of aldosterone (chronic tubulointerstitial disease or potassium-sparing diuretics).

What happens to serum electrolytes?

Hyperkalemia is the most common disturbance. Acidosis is mild with bicarbonate levels above 17meq/L, likely due to suppression of ammonia excretion due to the hyperkalemia.

And the urine pH?

Generally acidic at <5.3 because hydrogen is being excreted in place of potassium.

*What happened to **Type III RTA?***

There actually is a Type III RTA which is a rare autosomal recessive syndrome due to carbonic anhydrase II deficiency which is in essence a combination of both Type I and Type II. These children have mental retardation, cerebral calcification, and osteopetrosis.

How do I treat these disorders?

Luckily this is pretty simple! Certainly you should search for potential underlying causes.

For Types I and II you can administer oral bicarbonate. Type II disease (proximal) often requires high levels of bicarb. Treatment of mild acidosis (bicarb 22meq/L or greater) may not be necessary in adults, but children should be treated due to acidemia causing impaired growth.

For Type IV disease, potassium restriction and diuretics (non-potassium sparing of course!) are usually enough. In severe cases, fludrocortisone may help in reducing serum potassium levels.

What about chronic renal failure?

Most patients with chronic renal failure have a bit of a gap acidosis due to retention of phosphate, urate, sulfate, and other anions. But the mechanism is actually similar to that of Type I RTAs in that there is impaired ammonium secretion. To distinguish the two, look at the creatinine and the urine pH...(high creatinine and normal urine pH in renal failure).

Characteristics of the Different Types of Renal Tubular Acidosis			
	Type 1 RTA	Type 2 RTA	Type 4 RTA
Primary defect	Impaired distal acidification	Reduced proximal bicarbonate reabsorption	Decreased aldosterone secretion or effect
Plasma bicarbonate	Variable, may be below 10 meq/L	Usually 12 to 20 meq/L	Greater than 17 meq/L
Urine pH	Greater than 5.3	Variable, greater than 5.3 if above bicarbonate reabsorptive threshold	Usually less than 5.3
Plasma potassium	Usually reduced but hyperkalemic forms exist; hypokalemia largely corrects with alkali therapy	Reduced, made worse by bicarbonaturia induced by alkali therapy	Increased

References:

Renal texts, UpToDate 10.3