

Clinical Case Conference: Acid-base disorders

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I. David Weiner, M.D.  
Professor of Medicine and Physiology

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How do you “measure” renal new bicarbonate generation?

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- Two things increase new bicarbonate generation, titratable acids and ammonia
- One thing decreases new bicarbonate generation, failure to reabsorb luminal bicarbonate
- Net acid excretion (NAE) = urinary titratable acids + urinary ammonia – urinary bicarbonate
  - $NAE = U_{TA}V + U_{Amm}V - U_{HCO_3^-}V$

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Case 1

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- A patient presents with metabolic acidosis with a pH 7.20,  $HCO_3^-$  12 and  $pCO_2$  32 mmHg.
- How can you tell if this is results from:
  - Renal failure to generate “new” bicarbonate, or
  - Bicarbonate losses from diarrhea?

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**Case 1 – Answer**

- Major component of NAE (new bicarbonate formation) is:
  - Ammonia metabolism and excretion.
- Glutamine metabolism:
  - With urinary ammonia excretion
    - 1 mmol new  $\text{HCO}_3^-$  per mmol of ammonia excreted
  - Without urinary ammonia excretion
    - Glutamine converted to urea



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**Case 1 – answer**

- How do you measure urinary ammonia?
  - Lab can, but won't
- Bad news ...
  - Urine doesn't cause lightning
  - Urinary cations = urinary anions
- Trick,
  - Urinary cations –  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{NH}_4^+$
  - Urinary anions –  $\text{Cl}^-$  and  $\text{HCO}_3^-$ 
    - If urine pH  $\leq 6.5$ , urinary  $\text{HCO}_3^-$  inconsequential
  - Lab will measure urinary  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Cl}^-$
  - If urinary  $\text{Na}^+ + \text{K}^+ \approx \text{Cl}^-$ , then minimal  $\text{NH}_4^+$ 
    - Renal tubular acidosis
  - If urinary  $\text{Na}^+ + \text{K}^+ \gg \text{Cl}^-$ , then substantial  $\text{NH}_4^+$ 
    - Diarrhea



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**Case 2**

- A 4 year-old child presents for “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and  $\text{K}^+$  is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
- What is the diagnosis?
  - Proximal RTA (renal tubular acidosis)



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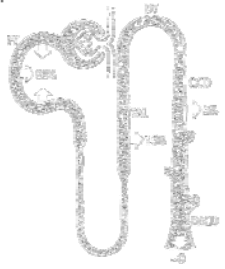
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### Proximal renal tubular acidosis (Type II)

- Proximal tubule unable to reabsorb normal amounts of filtered bicarbonate
- At normal serum bicarbonate, TAL and collecting duct unable to reabsorb all the bicarbonate that “escapes” the proximal tubule
- Alkaline urine and progressive urinary bicarbonate losses
- Eventually serum bicarbonate levels decrease, which decreases filtered bicarbonate



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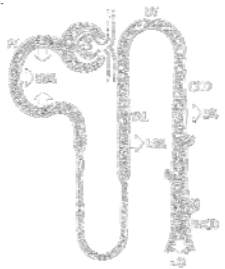
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### Proximal renal tubular acidosis (Type II)

- With decreased filtered bicarbonate, proximal tubule able to reabsorb “enough” bicarbonate
- When bicarbonate delivered to TAL and collecting duct normal the collecting duct is able to acidify the urine
- Key features:
  - Alkaline urine pH when serum bicarbonate normal
  - Acid urine pH when serum bicarbonate low



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### Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and  $K^+$  is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
- What is the diagnosis?
  - Proximal RTA
- Why is he not growing normally?



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### Metabolic acidosis and the skeleton

- Substantial alkali load in skeleton as alkali salts
- Metabolic acidosis
  - Stimulates osteoclast bone resorption
  - Inhibits osteoblast bone formation



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### Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and  $K^+$  is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
  - What is the diagnosis?
  - Why is he not growing normally?
  - Why is his serum  $K^+$  low?



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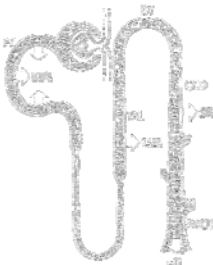
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### Proximal RTA and potassium

- Bicarbonate excreted in urine must be balanced by cation
  - $Na^+$  or  $K^+$
  - Initially both lost
  - With  $Na^+$  depletion comes intravascular volume depletion
    - Stimulation of aldosterone release
    - Stimulation of principal cell-mediated  $Na^+$  reabsorption and  $K^+$  secretion
  - Eventually substantial total body  $K^+$  losses, and hypokalemia



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### Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and  $K^+$  is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
  - What is the diagnosis?
  - Why is he not growing normally?
  - Why is his serum  $K^+$  low?
  - What will happen to his urine pH if you give him oral alkali therapy?



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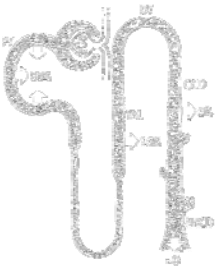
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### Therapy of proximal RTA

- Alkali therapy raises serum bicarbonate
  - Raises filtered bicarbonate
    - Above level that proximal tubule can transport
    - Excessive bicarbonate delivery to TAL and collecting duct
    - Urinary bicarbonate losses
    - Alkaline urine



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### Case 2

- A 4 year-old child has “failure-to-thrive.” His serum bicarbonate is 12 mmol/L and  $K^+$  is 2.8 mmol/L. His urine pH is 6.1, and the urine does not contain glucose or amino acids.
  - What is the diagnosis?
  - Why is he not growing normally?
  - Why is his serum  $K^+$  low?
  - What will happen to his urine pH if you give him oral alkali therapy?
  - Will he/she need a little (~1 mmol/kg/d) or lot (10-15 mmol/kg/d) of oral alkali therapy?



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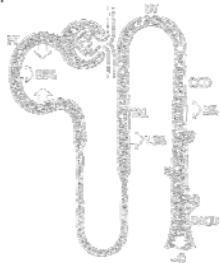
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### Therapy of proximal RTA

- As serum bicarbonate increases, urinary bicarbonate losses increase
- Need 10-15 mmol/kg/d
  - Replace bicarbonate deficit
  - Replace ongoing, and worsening, urinary bicarbonate losses
  - 50% as Na<sup>+</sup> salt and 50% as K<sup>+</sup> salt



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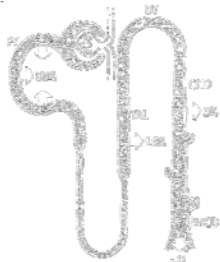
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### Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- [HCO<sub>3</sub><sup>-</sup>] is 4 mmol/L, [K<sup>+</sup>] is 2.1 mmol/L, and urine pH is 7.5
- What is the diagnosis?



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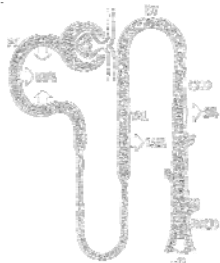
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### Case 3

- Key data: acidemic with metabolic acidosis but alkaline urine
- Where does urine pH decrease?
- Collecting duct
  - Distal renal tubular acidosis (type I)



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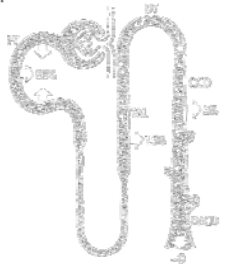
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# Renal Physiology

## Acid-base clinical case conference

**Case 3**

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- $[HCO_3^-]$  is 4 mmol/L,  $[K^+]$  is 2.1 mmol/L, and urine pH is 7.5
- Why is the acidosis so much worse than the last case?



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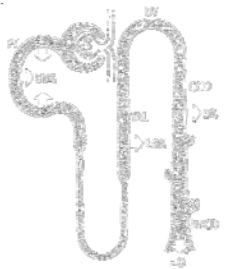
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**Case 3**

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- Why is the acidosis so much worse than the last case?
  - Ongoing renal  $HCO_3^-$  losses, plus inability to generate titratable acids and to excrete ammonia



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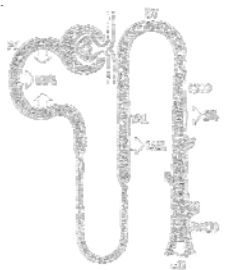
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**Case 3**

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Laboratory studies show acidemia with primary metabolic acidosis
- Why is  $K^+$  low?
  - Ongoing renal  $HCO_3^-$  losses need to be balanced by cation excretion



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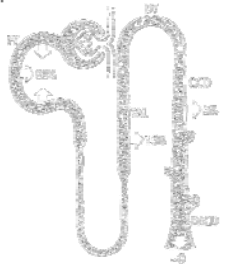
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### Case 3

- 23 yo ♂ presents with chief complaint of "I keep having kidney stones and they hurt!!!!"
- Diagnosis: Distal RTA
- Distal RTA causes kidney stones, but proximal RTA does not. Why?
  - Both cause  $\text{Ca}^{+2}$  salt resorption from bone, excreted in urine
  - $\text{Ca-PO}_4$  solubility is pH-dependent,
    - ↓ when  $\text{U}_{\text{pH}}$  is high
    - ↑ when  $\text{U}_{\text{pH}}$  is low




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### Case 4

- 64 year old with diabetes mellitus, chronic kidney disease is acidemic with a primary metabolic acidosis
  - The patient has osteoporosis, so you are worried
  - Evaluation shows the serum  $[\text{K}^+]$  is 6.1 mmol/L (normal is 4-5.5)
  - Urine pH is 5.8
- Why does your patient have metabolic acidosis and what should you do to treat him/her?




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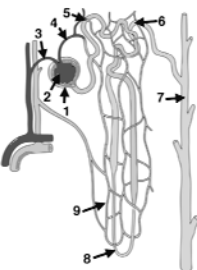
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### Case 4 - answer

- Serum  $\text{K}^+$  regulates renal ammonia metabolism
- Why?
  - Long-term serum  $\text{K}^+$  is regulated by renal  $\text{K}^+$  excretion
  - Occurs in collecting duct
  - How does the collecting duct "know" what the serum  $\text{K}^+$  is?




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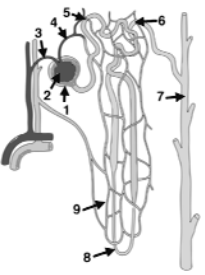


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**Case 4 - answer**

- Serum  $K^+$  regulates renal ammonia metabolism
- Hypokalemia:
  - Increases proximal tubule ammonia production
  - Increases ammonia reabsorption in TAL
- Ammonia regulates collecting duct  $K^+$  transport
  - Inhibits  $K^+$  secretion
  - Stimulates  $H^+-K^+$ -ATPase


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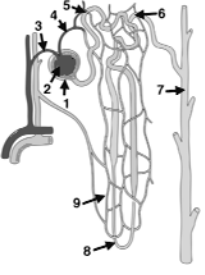


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**Case 4 - answer**

- Serum  $K^+$  regulates renal ammonia metabolism
- Hyperkalemia
  - Inhibits renal ammonia metabolism
  - Decreases ammonia-mediated "new" bicarbonate generation
  - Causes metabolic acidosis


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**Case 4**

- 64 year old with diabetes mellitus, chronic kidney disease is acidemic with a primary metabolic acidosis
  - The patient has osteoporosis, so you are worried
  - Evaluation shows the serum  $[K^+]$  is 6.1 mmol/L (normal is 4-5.5)
  - Urine pH is 5.8
- Why does your patient have metabolic acidosis?
  - Hyperkalemia, resulting from diabetes mellitus and chronic kidney disease
    - Decreases renal ammonia excretion
    - Decreases net acid excretion
    - Results in chronic metabolic acidosis
- What should you do to treat him/her?
  - Treat the hyperkalemia
    - Diuretics as first-line therapy


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