MGH/HMS Internal Medicine Comprehensive Review and Update
Renal Cases - June 2022

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Disclosures

- UpToDate (Royalties) – not relevant to this presentation.
- Teladoc – Advance Medical – providing expert opinions.

Case # 1

- 92 yo woman with HTN and asthma
- 1 week history of cough, malaise, fatigue, not improved on oral antibiotics (Cephalexin)
- BP medications: Lisinopril 40 mg po daily; Hydralazine 50 mg po BID (recently added);
- Normal baseline renal function
- No NSAIDS or recent renal insults
- Exam: Afebrile; BP 178/97, Pulse 70 reg, RR 18

  Lungs right sided crackles; C&V RRR, no murmurs or gallops; No edema, no rashes.

Case # 1 (cont.)

- Labs: Na 132, K 5.1, CO2 21, AG 14, **BUN 83**, **Creatinine 4.79**; Alb 3.1, Hgb 8.1, Gluc 107
- U/A: **2 + blood, 2 + protein, >100 RBCs, WBC casts, RBC casts** and muddy brown casts present

Question

The most likely etiology for the patient's acute kidney injury is:

- A. Acute interstitial nephritis from the Cephalexin
- B. Acute tubular necrosis
- C. Rapidly progressive glomerulonephritis
- D. Post-infectious acute glomerulonephritis
- E. Malignant hypertension

Question

The most likely etiology for the patient's acute kidney injury is:

- A. Acute interstitial nephritis from the antibiotic – RBC cast very atypical
- B. Acute tubular necrosis – RBC cast atypical
- **C. Rapidly progressive glomerulonephritis**
- D. Post-infectious acute glomerulonephritis -

  wrong time frame, but check C3 and C4
- E. Malignant hypertension – data doesn't support

Case # 1 (cont.)

- P-ANCA (MPO-ANCA) titers:
- On admission – 14,336 (abnormal > 2.8)
- 1 month later – 1,153
- 3 months later – 2,406

Follow-up

- Developed pulmonary hemorrhage as well
- Required hemodialysis
- Treatment: 1. Plasmapheresis x 7
  2. Pulse steroids x 3, then oral prednisone
  3. Low dose oral cyclophosphamide
  4. Rituximab 1 gm x 2, then q 4 months

Follow-up (cont.)

- Renal function slowly improved, and hemodialysis stopped after 6 months

  Serum creatinine stabilized at 1.6 mg/dl

  Prednisone gradually tapered off; cyclophosphamide stopped after 6 months

  No further pulmonary hemorrhage

  Doing well clinically 24 months later, age 94

Teaching Points

- Hydralazine can cause a pauci-immune p-ANCA positive vasculitis with RPGN
- May involve organs other than the kidney
- P-ANCA (MGPO-ANCA) titers are often very high (tip-off)
- First : STOP the drug; Second: +/- immuno-suppression
- Treatable condition

Babar F et al J of Comm Hosp Int Med Persp 2016

Case # 2

- 37 yo woman admitted with 1 week history of watery, non-bloody diarrhea
- No vomiting
- Poor oral intake
- Normal baseline renal function

Case # 2 (cont.)

- History of migraine headaches, on topiramate 100 mg po BID (Topamax)
- Type 2 myotonic dystrophy
- Anxiety disorder
- Distant gastric bypass surgery for obesity
- Chronic pain, on prn Alleve and/or Advil, denies excessive use

(continued)

- Physical Examination on admission notable for mild volume depletion, no fever, otherwise unremarkable
- Received several liters of intravenous normal saline in the ED
- Initial laboratory evaluation reveals:

Laboratory values on admission

- Na 136, K 3.6, Cl 104, **CO2 12**, **AG 20**
- BUN 6, Creatinine 0.33, Glucose 114
- Albumin 3.7
- Urine analysis relevant for pH 5.0;

  2+ ketones; rest is unremarkable
- ABG on room air: **pH 7.24/pCO2 19**/pO2 81/HCO3 13 (calculated)

Question 1

- This patient has a combined AG and non-AG metabolic acidosis
- A. True
- B. False

Question 2

The etiology for her metabolic acidosis is/are:

- A. Loss of bicarbonate (or equivalents) via diarrhea.
- B. Loss of bicarbonate (or equivalents) via diarrhea plus a starvation ketoacidosis.
- C. Starvation ketoacidosis.
- D. Lactic Acidosis.
- E. Both A and D.

Correct Answer is: B

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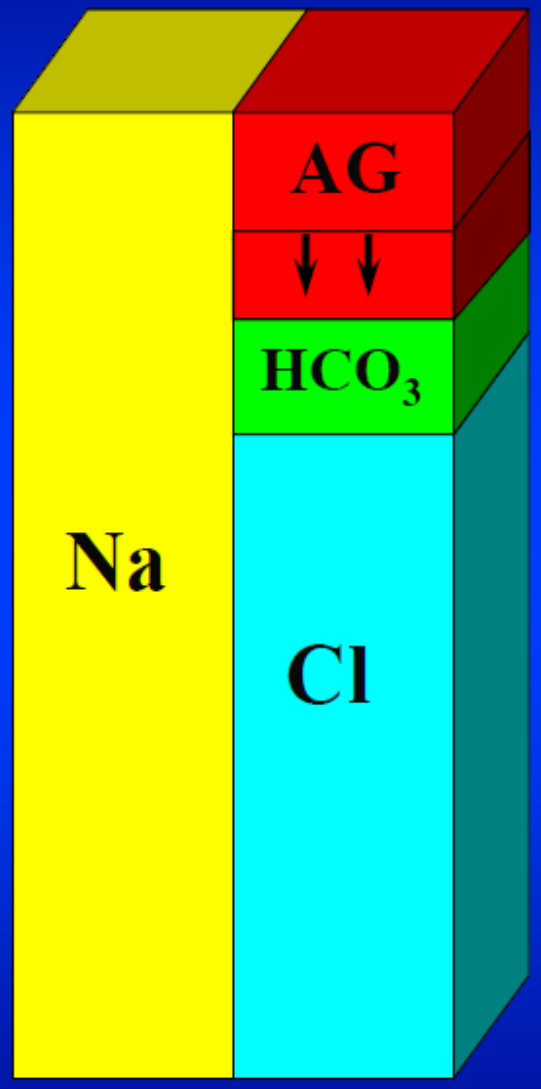
ANION GAP METABOLIC ACIDOSIS



Glycols – ethylene, propylene & diethylene

Oxoproline(5-) (Pyroglutamic Acid)

L – Lactic Acid

D – Lactic Acid

Methanol – Formic Acid

Aspirin – Multiple Organic Acids

Renal failure (Uremia) – Multiple organic & inorganic acids

Ketoacidosis – β-OH-Butyric & Acetoacetic Acid

Mehta A, Emmett M, Emmett J

The Lancet Volume 372 2008

Case 2 Followup:

- 3 days later, the patient feels much improved
- Follow-up labs reveal the following:
- Na 139, K 4.1, Cl 111, **CO2 16, AG 12**, Creatinine 0.52, BUN 10, Glucose 77.
- **Urine ph is now 8.0**; rest of the U/A is normal.
- A renal consult is requested regarding the ongoing non-AG metabolic acidosis.
- The diarrhea has resolved.

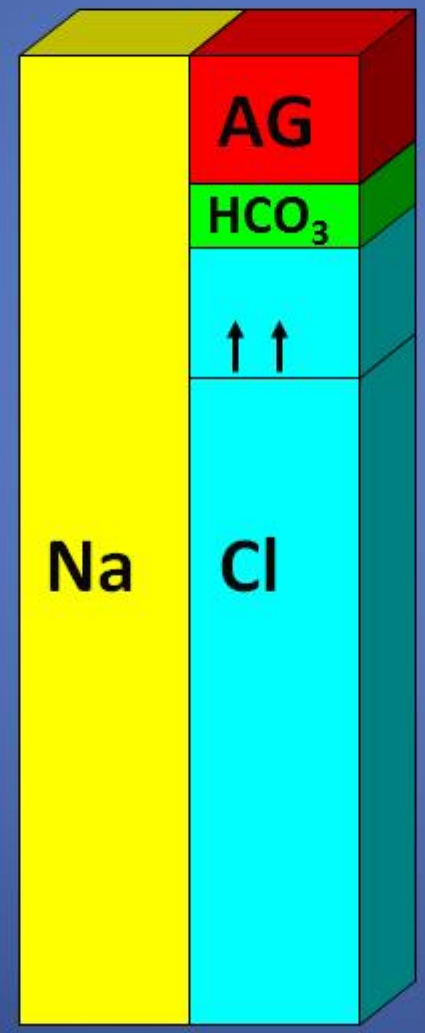
Question 3

- The most likely cause for this non-AG metabolic acidosis is:
- A. An inherited Type 2 (proximal) RTA.
- B. A Type 1 (distal) RTA.
- C. A Type 4 RTA.
- D. Topiramate (Topamax).
- E. Alleve and/or other NSAID use by the patient.

Metabolic Acidosis

- Divided into two categories:
- 1. Anion gap metabolic acidosis.
- 2. Non-anion gap metabolic acidosis or hyperchloremic metabolic acidosis.

HYPERCHLOREMIC METABOLIC ACIDOSIS



CAUSES:

1. Add HCl, or Potential HCl, to ECF

$$HCl + HCO_3^- \rightarrow Cl^- + H_2CO_3$$

2. Lose $NaHCO_3$, or Potential $NaHCO_3$, from ECF

Topiramate in Clinical Use

- 1. Anticonvulsant
- 2. Prevention of Migraines
- 3. Weight loss (in combination with phentermine)

Physiologic Effects of Topiramate

- Dose-dependent inhibition of voltage-gated sodium and calcium channels.
- Augmentation of GABA-induced chloride flux.
- Inhibition of glutamate-related excitatory neurotransmission.
- **Inhibition of carbonic anhydrase**.

  This last effect is dose-dependent, and long-term may predispose to the formation of kidney stones as well.

The frequency and severity of metabolic acidosis related to topiramate. Ture H, et al 2016. Journal of International Med Research

Case # 3

- 57 year old man with CLL, usual WBC around 200,000
- Type 2 DM, hyperlipidemia
- Suffered an unwitnessed fall
- Altered, hypotensive, tachycardic in the field
- ED evaluation reveals bacterial meningitis

Case # 3 (continued)

- Admit labs: **WBC 330,680**, Hgb 7.1, Hct 21.4, plts 78,000
- **Na 167**, **K 8.1**, **Cl 126**, CO2 26, **BUN 53**,

Creatinine 3.63, Albumin 3.0, Ca 7.3, Glucose 258.

- Repeat **K is 10.1**.
- Emergent renal consult called for critical hyperkalemia.

Question

Don’t Panic, your first order is:

- A. Order repeat stat K in routine plasma.
- B. Order repeat stat K in serum
- C. Stat 12 lead EKG
- D. Give CaCl IV push
- E. Give oral Kayexalate 30 gms stat

Pseudohyperkalemia

- CLL. Usually WBC above 120,000. In either plasma or serum.
- Thrombocytosis
- Plasma versus serum
- Blood sent for blood gas analysis

Pseudohyperkalemia

- Suggested Reference

Lee HK, Brough TJ, Curtis MB, and Polito FA. Pseudohyperkalemia-is serum or whole blood better?

Clinica Chimica Acta 2008.

Case # 3 Followup:

- Patient treated for the “hyperkalemia”
- Repeat K was 2.6 using an arterial blood sample
- Surgery finally accepted our diagnosis

Case # 4

- 74 year old man with HTN, Type 2 DM, GERD, esophageal cancer, on chemotherapy
- Baseline serum creatinine 1.2 mg/dl
- Routine clinic follow-up: creatinine **3.4**,

  BUN 38, HCO3 18, **Mg 1.4**, Ca 8.3, Albumin 3.2.
- Urine with **WBCs**; positive for **eosinophils**.
- Admitted. 2 days later, serum creatinine is **5.1**.

Case # 4 (continued)

- Medications: Pravastatin, Omeprazole, Senna
- Last chemotherapy several weeks ago with Carboplatinum and Taxol
- Renal sonogram: normal size kidneys with increased echogenicity bilaterally
- All cultures negative
- A renal biopsy is performed

Question 1

- The cause of the patient’s AKI is:
- A. Post chemotherapy ATN
- B. Pre-renal cause
- C. Acute proliferative GN
- D. Allergic interstitial nephritis
- E. Obstructive Uropathy

Question 2

Cause of the patient’s hypomagnesemia is:

- A. Acute Tubular Necrosis
- B. Pre-renal cause
- C. Omeprazole
- D. Pravastatin
- E. Taxol

Allergic Interstitial Nephritis

- How good are urinary eosinophils?
- How good is the classic triad: fever, rash, eosinophilia?
- What is the most common drug causing this entity today?
- How do you treat?

PPIs and Hypomagnesemia

- Chronic use of omeprazole (> 1 year), and other PPIs.
- Reversible
- Impaired absorption of Mg by the intestinal epithelial cells caused by PPI-induced inhibition of **transient receptor potential melastatin-6** (TRPM6) and TRPM7
- More pronounced when NSAIDs are consumed at the same time

Case # 4 (follow-up):

- Patient treated with Solumedrol for 3 days, followed by Prednisone 60 mg daily
- Improved over several weeks, but had weight gain, LE edema, and higher BPs
- Serum creatinine 1.62 mg/dl one month later
- What if we did not treat with steroids?

Case # 5

- 73 year old woman with severe COPD, pulmonary hypertension, on home oxygen, admitted for worsening dyspnea.
- Type 2 Diabetes Mellitus, CAD, CHF, Stage 3 CKD, baseline serum creatinine of 1.8, prior uroepithelial carcinoma (chemotherapy in the past).
- Recent weight gain of 7 lbs.
- Recent cystoscopy as a day surgery patient.
- Admitted to the CCU: concern for UTI, pulmonary edema, ? early cardiogenic shock, AKI, chronic respiratory failure.

Case # 5 (continued).

- Relevant home medications: Metformin 500 mg BID, metoprolol 25 mg daily, Protonix 40 mg daily, Dapagliflozin 10 mg daily, Pravastatin40 mg daily, spironolactone 50 mg BID, many inhalers, Acetaminophen 650 mg as needed for pain.

Case # 5(continued).

- Physical Examination: No fever, BP 120/80, Pulse 86, RR 24; on BIPAP.
- Notable for: lung exam - diminished breath sounds, bibasilar crackles
- C&V exam – distant S1 and S2, no gallops, no rubs, + JVD
- Extremities – 2 plus LE pitting edema
- Chest X-ray – pulmonary edema
- ECG – chronic RBBB, no acute ischemia

Case # 5 (continued).

- Labs: BUN **90**, Creatinine **3.34**, Glucose 192; Na 137, K 4.6, Cl 93, HCO3 **31**. Thus, Anion Gap of 13.
- ABG: on 10 L oxygen: pH 7.22**/pCO2 82**/pO2 85/CO2 33 – usual pCO2 is 60.
- What is the suspected acid-base disturbance here?

a. A compensated chronic respiratory acidosis.

b. A poorly compensated respiratory acidosis

c. A compensated chronic respiratory acidosis, and a metabolic acidosis of the non-AG type due to AKI/CKD.

The Answer Is:

- c. a compensated chronic metabolic acidosis (hence the bicarbonate level of 31, elevated, but not 35), and a metabolic acidosis of the non-AG variety (? Surprised – this is actually very common in AKI/CKD).

Case # 5 (continued).

- Labs. 24 hours later:
- Na 143, K 4.0, Cl 94, HCO3 **17**, hence AG **32**. Glucose **177**
- BUN 93, Creatinine 3.17; ABG **pH 7.13**/pCO2 73/pO2 121
- Lactate 1.1 mmol/L.
- What is happening here??!

THE ANSWER IS:

- We checked a Beta Hydroxybutyrate level:
- 9.5 mmol/L, markedly elevated.
- THE DISAGNOSIS IS: Euglycemic Diabetic Ketoacidosis.
- So -
- Patient treated with insulin IV.
- 24 hours later, the AG was down to 15. Glucose was 181.
- Blood pH much improved at 7.29.

The SGLT2 Inhibitors are Amazing

BUT ….

Notable Adverse Effects of SGLT2 Inhibitors

- Genito-urinary tract infections – including fungal UTIs
- Hypotension
- Acute kidney injury
- Euglycemic diabetic ketoacidosis (Glucose less than 250)
- Extremity amputations

Thank you for your attention.

- Questions??

HUMAN ALBUMIN

− >> +

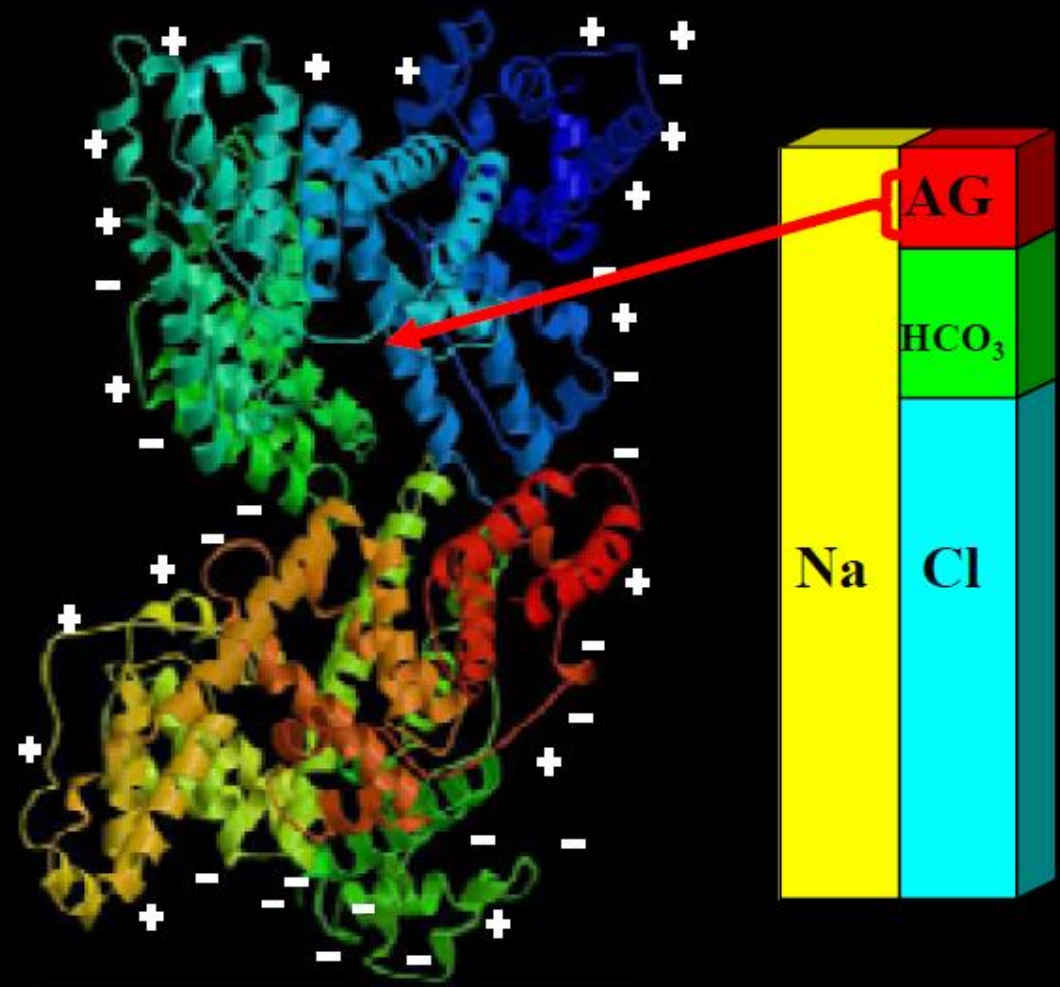
Net Na-Albumin

At pH = 7.4
about net 16 negative charges

MW = 66,500 mg/mm
1 gm% = 0.154 mm/l
∴ 1 gm% = ~2.5-3 mEq/l

For each 1 gm% fall in
albumin the AG falls
~ 2.5 - 3 mEq/l

AG adjusted =
AG + 3 (4.5-observed Alb)



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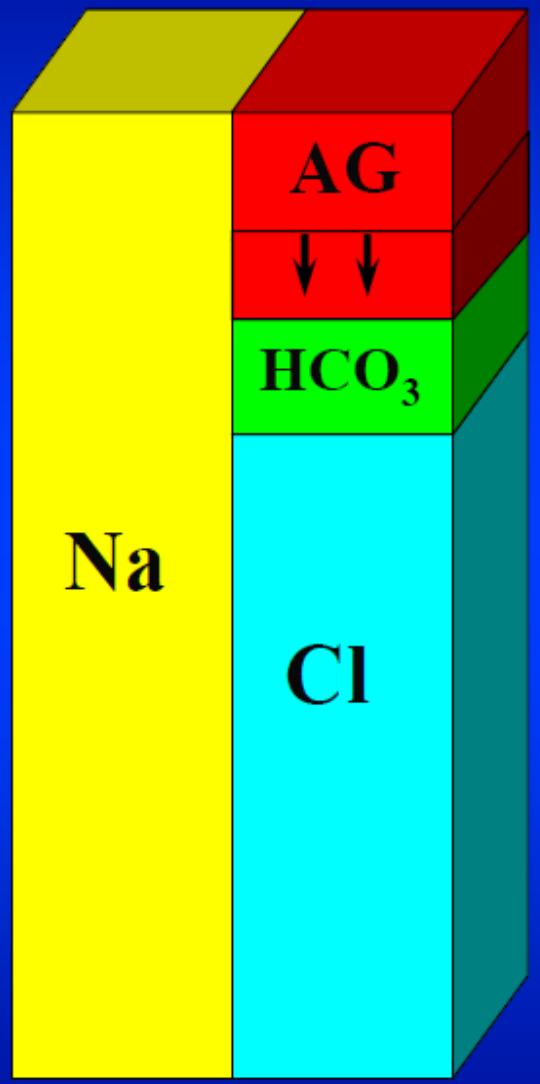

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