Michael Mao
Assistant Professor
Mao.michael@mayo.edu
Disclosures

**Relevant Financial Relationship**

None

**Off-Label/Investigational Uses**

None
Case 1
Presentation

• A 59 yoF with COPD, HTN, T2DM, and CKD Stage III (baseline creatinine of 1.6 checked yesterday) is admitted due to pneumonia with fever, shortness of breath, and productive cough. Associated symptoms include nausea, poor appetite, and fatigue. Medications include lisinopril, amlodipine, metformin, and albuterol PRN.

• Laboratory studies:

\[
\begin{array}{c}
11.0 \\
14.3 \\
154 \\
5.1 \\
20 \\
1.9 \\
141 \\
111 \\
52 \\
165
\end{array}
\]
Case 1, Q1: What is the appropriate diagnosis of her creatinine change?

A. “CKD Stage 3”
B. “Elevated Creatinine” and “CKD Stage 3”
C. Acute on chronic renal failure
D. “AKI, AKIN stage I” and “CKD Stage 3”
E. “AKI, AKIN stage 2” and “CKD Stage 3”
Case 1
Answer

• Choice D
Case 1
Explanation: Documentation

• Chronic kidney disease/failure:
  • State cause, stage of CKD and if on dialysis, and link consequences
  • “CKD Stage IV, due to HTN with chronic anemia”

• Acute Kidney Injury
  • State cause, state lesion/pathology, and list CKD as a separate diagnosis
  • “AKI due to septic shock on CKD stage 3, due to hypertension”
Case 1
Explanation: Documentation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pneumonia</th>
<th>Pneumonia with AKI</th>
<th>Pneumonia with AKI due to ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS-DRG Assignment</td>
<td>195-Pneumonia without CC/MCC</td>
<td>194- Pneumonia with CC</td>
<td>193-Pneumonia with MCC</td>
</tr>
<tr>
<td>Geometric Mean Length of Stay (GMLOS)</td>
<td>2.9</td>
<td>3.8</td>
<td>4.9</td>
</tr>
<tr>
<td>2014 Hospital Medicare Reimbursement</td>
<td>$6,044</td>
<td>$8,143</td>
<td>$11,955</td>
</tr>
</tbody>
</table>

Borrowed from Chris McCoy, M.D..
**Case 1**

**Explanation and Pearls**

**RIFLE** ➔ **AKIN**

**KDIGO**

<table>
<thead>
<tr>
<th>AKI</th>
<th>Creatinine</th>
<th>UOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKIN/KDIGO Stage 1</td>
<td>Increase in Cr of 0.3 mg/dL or &gt; 50%</td>
<td>UOP &lt; 0.5 mL/kg/hr for &gt; 6 hours</td>
</tr>
<tr>
<td>AKIN/KDIGO Stage 2</td>
<td>Increase in Cr &gt; 100%</td>
<td>UOP &lt; 0.5 mL/kg/hr for &gt; 12 hours</td>
</tr>
<tr>
<td>AKIN/KDIGO Stage 3</td>
<td>Increase in Cr &gt; 200%</td>
<td>UOP &lt; 0.3 mL/kg/hr for ≥ 24 hrs or ≥ anuria 12 hours</td>
</tr>
</tbody>
</table>

*Absolute serum Cr change is within 48 hours, the % change in serum Cr within 7 days.*

Case 1
Explanation and Pearls

- AKI can be diagnosed with an absolute creatinine change of 0.3 mg/dL in 48 hours or a 50% percentage increase over seven days.

- Correct diagnosis is important from both a documentation and clinical perspective.
Case 2
Presentation

• A 36 yoM with bipolar disorder, panic attacks, and history of polysubstance use presents to the ED with sudden shortness of breath, chest discomfort, lightheadedness and a sensation of impending doom. Medications include lithium, ibuprofen, and quetiapine. Vitals: Temp 37.0°C, P 115/min, BP 110/74 mmHg, RR 30, O₂ sat 96% on RA. EKG: Normal sinus rhythm.

• Laboratory studies show:

ABG: pH 7.49, pO₂ 80, pCO₂ 25, HCO₃ 18.
Case 2

Question

What is the acid-base disturbance?

ABG: pH 7.49, pO\textsubscript{2} 88, pCO\textsubscript{2} 25, HCO\textsubscript{3} 18.

A. Metabolic acidosis with compensatory respiratory alkalosis.
B. Metabolic alkalosis with compensatory respiratory acidosis
C. Acute respiratory acidosis with metabolic alkalosis.
D. Acute respiratory alkalosis with metabolic acidosis
E. Chronic respiratory alkalosis with appropriate compensation.
F. I sense no disturbance (… in the force).
Case 2, Q2: What is the acid-base disturbance?

A. Metabolic acidosis with compensatory respiratory alkalosis.
B. Metabolic alkalosis with compensatory respiratory acidosis
C. Acute respiratory acidosis with metabolic alkalosis.
D. Acute respiratory alkalosis with metabolic acidosis
E. Chronic respiratory alkalosis with appropriate compensation.
F. I sense no disturbance (… in the force).
Case 2
Answer
• Choice D
Case 2
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 2
Presentation with Highlights

• A 36 yoM with bipolar disorder, panic attacks, and history of polysubstance use presents to the ED with sudden shortness of breath, chest discomfort, lightheadedness and a sensation of impending doom. Medications include lithium, ibuprofen, and quetiapine. Vitals: Temp 37.0°C, P 115/min, BP 110/74 mmHg, RR 30, O₂ sat 96% on RA. EKG: Normal sinus rhythm.

• Laboratory studies show:

ABG: pH 7.49, pO₂ 80, pCO₂ 25, HCO₃⁻ 18.
Case 2
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 2
Explanation: 6 step approach to acid-base

3. Acidemia or Alkalemia?
   • Normal pH = 7.35 – 7.45

Case 2
Explanation: 6 step approach to acid-base

4. Respiratory, Metabolic, or Mixed
   • “ROME”: look at pH and pCO$_2$
     • Respiratory Opposite
     • Metabolic Equal

ABG: pH 7.49, pO$_2$ 88, pCO$_2$ 25, HCO$_3$ 18.
Case 2
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Expected Bicarbonate Compensation for Respiratory Acidosis/Respiratory Alkalosis

For every 10 mmHg ↑ in pCO2: HCO₃ should ↑ by 1 (Acute) or 3 (Chronic) Respiratory Acidosis

For every 10 mmHg ↓ in pCO2: HCO₃ should ↓ by 2 (Acute) or 5 (Chronic) Respiratory Alkalosis
Case 2
Compensation

ABG: pH 7.49, pO₂ 88, pCO₂ 25, HCO₃ 18.

1) Alkalemia with acute respiratory alkalosis, so check renal compensation
   • $\Delta$ pCO₂ = 15
   • Expected $\Delta$ HCO₃ (acute) = 3
   • Expected HCO₃ = 24 - 3 = 21

2) Concurrent metabolic acidosis
Case 2
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap

Anion Gap = Na − (Cl + HCO₃) ± 2
Case 2
Compensation

ABG: pH 7.49, pO₂ 88, pCO₂ 25, HCO₃ 18.

1) Alkalemia with respiratory alkalosis, so check renal compensation
   • $\Delta$ pCO₂ = 15
   • Expected $\Delta$ HCO₃ (acute) = 3
   • Expected HCO₃ = 24 - 3 = 21

2) Concurrent metabolic acidosis

3) AG: 12 = normal. Therefore:
   Combined acute respiratory alkalosis with normal anion gap metabolic acidosis.
Case 2

Pearls

• In acid-base disturbances, do a quick check of compensation to ensure no occult secondary disorders
Case 3
Presentation

• A 53 yoF with fibromyalgia, GERD, HTN, and arthritis was admitted to ICU for somnolence, hypotension, and intractable nausea and vomiting for the past 6 hours. She was initially agitated but became progressively somnolent prior to presentation. Associated symptoms include tinnitus. She is a “naturalist.”

• Medications include oil of wintergreen, “Pepto-Bismol,” and calcium carbonate PRN.

• Vitals: Temp 38.1°C, P 110/min, RR 30/min, BP 90/40 mmHg.
Case 3
Presentation

ABG: pH 7.35, pO$_2$ 110, pCO$_2$ 22, HCO$_3$ 15.

- EKG: sinus tachycardia. CXR: Bilateral infiltrates without focal consolidation. No pleural effusions or cardiomegaly.
Case 3

Question

Which of these statements would be most correct?

A. There is no acid-base disorder.
B. Respiratory acidosis with metabolic alkalosis
C. Respiratory acidosis.
D. Metabolic acidosis.
E. Metabolic acidosis with respiratory acidosis.
F. Metabolic acidosis with respiratory alkalosis.
G. None of the above.

ABG: pH 7.35, pO$_2$ 110, pCO$_2$ 22, HCO$_3$ 15.
Case 3, Q1: Which of these statements would be most correct?

A. There is no acid-base disorder.
B. Respiratory acidosis with metabolic alkalosis
C. Respiratory acidosis.
D. Metabolic acidosis.
E. Metabolic acidosis with respiratory acidosis.
F. Metabolic acidosis with respiratory alkalosis.
G. None of the above.
Case 3, Q1

Answer

- Choice F
Case 3
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 3
Presentation Highlights

• A 53 yoF with fibromyalgia, GERD, HTN, and arthritis was admitted to ICU for somnolence, hypotension, and intractable nausea and vomiting for the past 6 hours. She was initially agitated but became progressively somnolent prior to presentation. Associated symptoms include tinnitus. She is a “naturalist.”

• Medications include oil of wintergreen, “Pepto-Bismol,” and calcium carbonate PRN.

• Vitals: Temp 38.1°C, P 110/min, RR 30/min, BP 90/40 mmHg.
Case 3
Presentation

ABG: pH 7.35, pO₂ 110, pCO₂ 22, HCO₃ 15.

- EKG: sinus tachycardia. CXR: Bilateral infiltrates without focal consolidation. No pleural effusions or cardiomegaly.
Case 3
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 3
Explanation: 6 step approach to acid-base

3. Acidemia or Alkalemia?
   • Normal pH = 7.35 – 7.45

   ABG: pH 7.35, pO₂ 110, pCO₂ 22, HCO₃⁻ 15.
Case 3
Explanation: 6 step approach to acid-base

4. Respiratory, Metabolic, or Mixed
   • “ROME”: look at pH and $pCO_2$
     • Respiratory Opposite
     • Metabolic Equal

ABG: pH 7.35, $pO_2$ 110, $pCO_2$ 22, $HCO_3^-$ 15.
Case 3

Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Expected Compensation for Metabolic Acidosis

• **Winter’s Formula:**
  • \( pCO_2 = [(1.5 \times HCO_3) + 8] \pm 2 \)

• **Rule of 15:**
  • \( pCO_2 \approx HCO_3 + 15 \)

• **Thumb rule:**
  • \( pCO_2 \approx \text{last two digits of pH} \)
Case 3
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap

\[
\text{Anion Gap} = \text{Na} - (\text{Cl} + \text{HCO}_3) \pm 2
\]
Case 3
Compensation

ABG: pH 7.35, pO$_2$ 110, pCO$_2$ 22, HCO$_3^-$ 15.

1) Acidemia with metabolic acidosis, so check respiratory compensation
   • Expected pCO$_2$ = (1.5 * 17) + 8 = 33.5
2) Concurrent respiratory alkalosis
3) AG: 28 = elevated. Therefore:
   Combined anion-gap metabolic acidosis with respiratory alkalosis.
Case 3, Q2: What is the diagnosis?

A. I know the answer
B. I don’t know the answer, but I like pushing buttons.
“GOLD MARK”
Etiologies for Anion-Gap Metabolic Acidosis

G: Glycols (ethylene and propylene)
O: Oxoproline
L: L-lactate
D: D-lactate
M: Methanol
A: Aspirin
R: Renal failure
K: Ketoacidosis

Case 3
Salicylate toxicity

• In overdose, $t_{1/2}$ as long as 30 hours.

• Pathophysiology:
  • Irreversible inhibition of COX-1 & 2.
  • Stimulation of medulla chemoreceptor trigger zone $\rightarrow$ nausea/vomiting
  • Activation of medulla respiratory center $\rightarrow$ hyperventilation and respiratory alkalosis.
Case 3
Salicylate toxicity

• Clinical suspicion with …

• Confirmation: Serum salicylate concentrations
  • Therapeutic 10-30 mg/dL
  • >40 = toxicity
  • Warning bells: ingestion of 10-30 g ASA by adults or 3 g by children

• Chronic salicylate poisoning – sign/symptoms may be milder or absent!
Case 3

Pearls

• *Always* calculate the anion gap.

• GOLD MARK for differential dx of an anion gap.
Case 4
Presentation

- A 66 yoF with HTN, T2DM, irritable bowel syndrome, and depression is admitted for pneumonia with fever, productive cough, shortness of breath and nausea. No recent weight changes. Review of systems negative otherwise. Medications include amlodipine, fluoxetine, and polyethylene glycol.

- Vitals: Temp 37.6°C, P 86/min, RR 18/min, BP 136/66 mmHg, SpO₂ 88%. Weight 60 kg. Physical exam shows moist mucous membranes, regular heart rate, left lower lung rales, and mild 1+ bilateral lower extremity edema.

Serum Osmolality: 260 mOsm/kg [275-290]

Urine:
- \( U_{Na} \): 124 mEq/L
- \( U_{Osm} \): 600 mOsm/kg
Case 4, Q1: What is the most likely cause of her hyponatremia?

A. Dehydration
B. Syndrome of inappropriate antidiuretic hormone
C. Malnutrition
D. Congestive heart failure
E. Hypothyroidism
F. Pseudohyponatremia

17% 17% 17% 17% 17% 17%

©2016 MFMER | 3543652-47
Case 4, Q1
Answer

• Choice B
Hyponatremia severity

<table>
<thead>
<tr>
<th>Mild to Severe Hyponatremia</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>130-135 mEq/L</td>
</tr>
<tr>
<td>Moderate</td>
<td>120-129 mEq/L</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 120 mEq/L</td>
</tr>
</tbody>
</table>

Acute: < 48 hours

Chronic: ≥ 48 hours
Case 4, Q2: The kidneys maintain a constant plasma osmolality by regulating the excretion of which of the following?

A. Glucose  
B. Sodium  
C. Creatinine  
D. Water  
E. Potassium
Case 4, Q2
Answer

- Choice D
Case 4
Explanation: Water Regulation

- The kidneys regulate effective circulating volume (ECV) and osmolality through regulation of GFR, sodium, and water.

- Sodium and water balance is handled “separately” by the kidneys.*
  - Water: Tonicity, antidiuretic hormone (ADH) & urine osmolality.
  - Sodium: intravascular volume & urine sodium.

- Hyponatremia is a problem usually associated with a disproportionate increase in “water”.

- Terminology: Osmolality versus tonicity.
  - “Tonicity” describes the solute effect (oncotic force) and its importance on cell size.

*This is a severe simplification for the scope of this discussion.
Case 4
Explanation: Causes of Hyponatremia

- **Impaired water excretion** (the usual cause)
  - Diminished delivery of water to nephron
    - Low ECV
    - Low GFR
  - Impaired dilution of tubular fluid
    - Diuretics
    - Dysfunctional tubules from acute or chronic kidney disease
  - Excessive ADH effect
    - Volume contraction
    - Medication
    - Syndrome of Inappropriate ADH

- **Excessive water ingestion**

- **Conditions associated with normal or elevated osmolality**, such as hyperglycemia
How good are we at clinically assessing volume status?

- Study examined the sensitivity and specificity of clinical assessment of volume status in 58 non-edematous hyponatremic patients ([Na] < 130 mEq/L)

- Clinical assessment correctly identified only 47% of hypovolemic patients and 48% of normovolemic patients

- The concentration of a spot urine sample clearly separated hypovolemic (mean $\text{U}_{\text{Na}} = 18.4$) from normovolemic (mean $\text{U}_{\text{Na}} = 72$)

One imperfect algorithm for Hyponatremia

Hyponatremia

Serum Osmolality

Isotonic Hyponatremia

1. Pseudohyponatremia:
   a) Hyperproteinemia
   b) Hyperlipidemia
2. Glycine, sorbitol

Hypotonic Hyponatremia

1. Hyperglycemia
2. Mannitol, sucrose or maltose (e.g. IVIG)

Hypertonic Hyponatremia

Can correct for hyperglycemia:

\[ [\text{Na}] \downarrow \text{ by 1.6} = \text{every 100 mg/dL rise in serum glu.} \]

One imperfect algorithm for Hyponatremia

- **Hyponatremia**
  - Serum Osmolality
    - Isotonic Hyponatremia
      - Hypovolemic
        - $U_{Na} < 20$ mEq/L
        - $U_{osm} >$ high
        1. Dehydration
        2. Extrarenal loss
    - Hypotonic Hyponatremia
      - Evuolemic
        - $U_{Na} > 20$ mEq/L
        - $U_{osm} >$ high
        1. Diuretics
        2. Mineralocorticoid deficiency
        3. Cerebral salt wasting
    - Hypertonic Hyponatremia
      - Hypervolemic

*FENa should not be utilized unless there is AKI with oliguria. This is not a comprehensive algorithm for diagnosis or etiologies.*

One imperfect algorithm for Hyponatremia

**Hyponatremia**

- **Serum Osmolality**
  - **Isotonic Hyponatremia**
    - **Hypovolemic**
      - $U_{Na}$ Variable
        - $U_{osm}$ High
          - 1. SIADH (usually low BUN and uric)
          - 2. Hypothyroidism
          - 3. Adrenal insufficiency
          - 4. Reset osmostat
          - 5. Diuretics (e.g. HCTZ)
    - **Euvolemic**
      - $U_{Na}$ Variable
        - $U_{osm}$ low
          - 1. Psychogenic polydipsia
          - 2. Beer potomania
          - 3. Malnutrition
  - **Hypotonic Hyponatremia**
  - **Hypertonic Hyponatremia**

*FENa should not be utilized unless there is AKI with oliguria. This is not a comprehensive algorithm for diagnosis or etiologies.*


One imperfect algorithm for Hyponatremia

Hyponatremia

Serum Osmolality

Isotonic Hyponatremia

Hypotonic Hyponatremia

Hypertonic Hyponatremia

Volume Status

Hypovolemic

Euvolemic

Hypervolemic

$U_{Na} < 20 \text{ mEq/L}$

1. CHF
2. Cirrhosis
3. Nephrotic Syndrome

$U_{Na} > 20 \text{ mEq/L}$

1. Renal failure

*FENa should not be utilized unless there is AKI with oliguria. This is not a comprehensive algorithm for diagnosis or etiologies

Case 4
Pearls

- Check serum osmolality if clinical suspicion.

- Algorithms exist but understanding their limitations, the pathophysiology, and a love for urine (studies) may aid evaluation and management of hyponatremia.
Case 5
Case Presentation

• A 77 yoM with history of obesity, osteoarthritis, T2DM, hyperlipidemia, fibromyalgia and depression is admitted following a right total hip arthroplasty. The operation was uncomplicated. Post-operatively he has difficult to control pain and then complains of nausea and vomiting from oral analgesics. On post-operative day 2, he is progressively more lethargic and on afternoon rounds he no longer responds. Nurse feels he’s just being difficult because he does not want oral pain medications, and she has not been giving him IV pain medications. Medications include citalopram, atorvastatin, acetaminophen, naproxen, and oxycodone.

• Vitals: Temp 37.6°C, P 70/min, RR 18/min, BP 142/66 mmHg, SpO₂ 90%. Physical exam shows an obese man, mildly dry mucous membranes, skin turgor normal, regular heart rate, clear lungs, right sided LE edema with a clean/dry/intact dressing.
Case 5

Case Presentation

• Morning and repeat stat studies show:

Serum Osmolality: 258 mOsm/kg [275-290]

Urine:
- $U_{Na}$: 200 mEq/L
- $U_K$: 100 mEq/L
- $U_{Osm}$: 550 mOsm/kg

ABG: pH 7.42, $pO_2$ 70, $pCO_2$ 46, $HCO_3$ 22.

EKG: no acute changes.

Troponin: pending.
Case 5, Q1: What is the best next step in management?

A. Administer naloxone
B. Administer lorazepam and call neurology.
C. Administer 1 liter of normal saline
D. Administer 1 liter of half normal saline with 20 mEq K
E. Administer 50-100 mL of 3% saline
F. Initiate free water restriction ± loop diuretics or NaCl tablets.
G. Consult nephrology for dialysis
Case 5, Q1
Answer

- Choice E
Table 2. Patients With Hyponatremic Seizures, Coma, or Cerebral Edema Treated With Hypertonic Saline (Serum Sodium Level at < 4 Hours)

<table>
<thead>
<tr>
<th>Study</th>
<th>Etiology</th>
<th>Age/ Sex</th>
<th>Seizure</th>
<th>Cerebral Edema</th>
<th>Initial Sodium Level, mmol/L</th>
<th>Post-Treatment Sodium Level, mmol/L</th>
<th>Time Between Laboratory Values, h</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worthley and Thomas [94]</td>
<td>Postoperative</td>
<td>65 M</td>
<td>Yes</td>
<td>Unknown</td>
<td>109</td>
<td>116</td>
<td>0.5</td>
<td>Recovered</td>
</tr>
<tr>
<td>Worthley and Thomas [94]</td>
<td>Postoperative</td>
<td>47 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>109</td>
<td>117</td>
<td>0.5</td>
<td>Disabled*</td>
</tr>
<tr>
<td>Worthley and Thomas [94]</td>
<td>Postoperative</td>
<td>28 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>100</td>
<td>109</td>
<td>0.5</td>
<td>Recovered</td>
</tr>
<tr>
<td>Worthley and Thomas [94]</td>
<td>Burns</td>
<td>45 M</td>
<td>Yes</td>
<td>Unknown</td>
<td>106</td>
<td>112</td>
<td>0.5</td>
<td>Recovered</td>
</tr>
<tr>
<td>Worthley and Thomas [94]</td>
<td>Psychosis/polypidipsia</td>
<td>67 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>99</td>
<td>106</td>
<td>0.5</td>
<td>Recovered</td>
</tr>
<tr>
<td>Drescher et al [95]</td>
<td>Psychosis/polypidipsia</td>
<td>63 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>100</td>
<td>108</td>
<td>1</td>
<td>Recovered</td>
</tr>
<tr>
<td>Snell and Bartley [96]</td>
<td>Hypoadrenal/polypidipsia</td>
<td>25 M</td>
<td>Yes</td>
<td>No</td>
<td>111</td>
<td>117</td>
<td>3.6</td>
<td>ODS/recovered†</td>
</tr>
<tr>
<td>Goudie et al [98]</td>
<td>Runner</td>
<td>31 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>116</td>
<td>121</td>
<td>2</td>
<td>Recovered</td>
</tr>
<tr>
<td>Hew-Butler et al [100]</td>
<td>Psychosis/polypidipsia</td>
<td>47 M</td>
<td>Yes</td>
<td>Unknown</td>
<td>112</td>
<td>116</td>
<td>1</td>
<td>Recovered</td>
</tr>
<tr>
<td>Rae [99]</td>
<td>Psychosis/polypidipsia</td>
<td>53 F</td>
<td>Yes</td>
<td>Unknown</td>
<td>112</td>
<td>124</td>
<td>2</td>
<td>Recovered</td>
</tr>
<tr>
<td>Schreiber et al [102]</td>
<td>Postoperative/DDAVP</td>
<td>50 F</td>
<td>No</td>
<td>Yes</td>
<td>111</td>
<td>116</td>
<td>4</td>
<td>Recovered</td>
</tr>
<tr>
<td>Speedy et al [96]</td>
<td>Runner</td>
<td>35 M</td>
<td>Yes</td>
<td>No</td>
<td>116</td>
<td>122</td>
<td>4</td>
<td>Recovered</td>
</tr>
<tr>
<td>Fisher et al [100]</td>
<td>SSRI</td>
<td>92 F</td>
<td>Yes</td>
<td>Yes</td>
<td>109</td>
<td>112</td>
<td>4</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

Abbreviations: ODS, osmotic demyelination syndrome; DDAVP, desmopressin; SSRI, selective serotonin reuptake inhibitor.
*Given additional 90-ml bolus of 29.2% saline after resolution of seizures; 31-mmol/L increase in serum sodium level over 8 hours.
†Water diuresis after adrenal replacement; 28-mmol/L increase in serum sodium level in 42 hours.
Treatment of **symptomatic** hyponatremia

- Target a 4 – 6 mmol/L increase in serum sodium concentration in the first few hours

- Goal change in 24 hours should be the same if unknown chronicity!

- Administer a 50 ml bolus of 3% NaCl over 10 minutes
  - Can repeat 50-100 ml’s 3% NaCl two to three times if persistent symptoms or [Na] does not improve

- Obtain frequent sodium values to guide therapy
Indications for the treatment of symptomatic hyponatremia

- Patients with severe symptoms due to hyponatremia
- Patients with acute hyponatremia who have symptoms, even if symptoms are mild
- Patients with hyperacute hyponatremia due too self-induced water intoxication, even if there are no symptoms
- Symptomatic patients who have acute postoperative hyponatremia or hyponatremia associated with intracranial pathology

Case 5, Q2: After administration of 3% saline, his sodium improves to 126 and his symptoms resolve. What is your next step in medical management aside from following his laboratory studies?

A. Administer 1 liter of normal saline
B. Administer normal saline at 150 mL/hr for the next 24 hours.
C. Administer 1 liter of half normal saline with 20 mEq K
D. Administer 50-100 mL of 3% saline
E. Initiate free water restriction ± loop diuretics or NaCl tablets.
F. Consult nephrology for dialysis
Case 5, Q2

Answer

• Choice E
Case 5, Q3: Your student is tasked to follow the labs. She asks when she should definitely call you for concern.

A. If the [Na\(^+\)] does not further improve further.
B. If the [Na\(^+\)] is back in the normal physiologic range [135-145].
C. If the [Na\(^+\)] is nearing 130 mEq/L.
D. If the [Na\(^+\)] is greater than 145 mEq/L.
E. Don’t call me (unless you have my coffee).
Case 5, Q3

Answer

• Choice C
Correction of chronic hyponatremia

- Whenever duration of hyponatremia is unclear, assume chronic!

- No therapeutic limit is absolutely safe.

- Goal therapeutic limits of correction:
  - 10 mmol/L in 24 hours
  - 18 mmol/L in 48 hours

- Therapeutic goal is to avoid serious complications of hyponatremia while avoiding iatrogenic injury:
  - 6 – 8 mmol/L in 24 hours
  - 12 – 14 mmol/L in 48 hours
Estimating Sodium after Intervention

• Androgué-Madias Formula

\[ \Delta Serum\ Na = \frac{(Infusate\ Na - Serum\ Na)}{TBW + 1} \]

Adrogué and Madias. JASN. 2012.
Be wary of estimating equations

Figure 2. Ratio of actual to expected increase in sodium as calculated using the Adrogue-Madias formula. A value of 1 indicates that the observed increase in serum sodium concentration after hypertonic saline (actual Δ serum [Na+] equals the increase in serum sodium predicted by the formula (expected Δ serum [Na+]). Values greater than 1 indicate that the actual increase exceeded the predicted increase in most patients. Data from Mohmand et al.
A tool for predicting response to free H$_2$O restriction

- Check urine sodium and potassium. If

\[
\frac{Urine \ Na+K}{Serum \ Na} < 0.5 \quad \text{Electrolyte-free water = hyponatremia will improve}
\]

\[
\frac{Urine \ Na+K}{Serum \ Na} > 1 \quad \text{No electrolyte-free water = hyponatremia will be refractory unless further intervention}
\]
<table>
<thead>
<tr>
<th>$[\text{Na}^+ + \text{K}^+]_u$</th>
<th>$[\text{Na}^+]_s$</th>
<th>U/S electrolyte ratio</th>
<th>Impact on $[\text{Na}^+]_s$</th>
<th>Estimated change in $[\text{Na}^+]_s$ per liter of urine</th>
<th>Clinical examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>120 mEq/L</td>
<td>120 mEq/L</td>
<td>1.0</td>
<td>$\leftrightarrow$</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>180</td>
<td>120</td>
<td>1.5</td>
<td>$\downarrow$</td>
<td>$-1.6$</td>
<td>$-2.5$</td>
</tr>
<tr>
<td>60</td>
<td>120</td>
<td>0.5</td>
<td>$\uparrow$</td>
<td>1.6</td>
<td>2.5</td>
</tr>
<tr>
<td>20</td>
<td>120</td>
<td>0.17</td>
<td>$\uparrow\uparrow$</td>
<td>2.7</td>
<td>4.2</td>
</tr>
</tbody>
</table>

70-kg man 50-kg woman

Thiazide treatment

SIAD

Furosemide administration in heart failure

Withholding water in primary polydipsia
Treatment of “asymptomatic” SIADH hyponatremia

- Treat underlying cause

- Fluid restriction in patients with ADH secretion

- Consider NaCl tablets (1 g = 17 mEq) or furosemide
  - Tailor therapy depending on total body volume and ECV

- Consider hypertonic saline 15 – 30 ml/h until serum [Na] increased by 4 – 6 mmol/L or water diuresis starts

- Check chemistries at least every 4 hours during infusion therapy and monitor urine output closely
  - *Don’t rely just on formulas

Sterns et al Seminars in Nephrology, 2009
Case 5
Brief explanation on why intravenous isotonic fluids will worsen hyponatremia in SIADH

If time allows…
Initial: $[\text{Na}] = 124 \text{ mEq/L}$, urine $[\text{Na}] 30 \text{ mEq/L}$, plasma osmolality 265 mOsm/kg, urine osmolality 600 mOsm/kg. Weight 60 kg.

- If you give 1 liter of normal saline

1 Liter of NS

$\text{Na} 154 \text{ mEq} + \text{Cl} 154 \text{ mEq} = 308 \text{ mEq/mOsm}$

Patient’s urine is concentrated to 600 mOsm/kg

- $[\text{Na}] = 124 \text{ mEq/L}$, TBW 30 kg
Initial: \([\text{Na}] = 124\ \text{mEq/L},\ \text{urine}\ [\text{Na}] = 30\ \text{mEq/L},\ \text{plasma osmolality}\ 265\ \text{mOsm/kg},\ \text{urine osmolality}\ 600\ \text{mOsm/kg}.

- The kidneys excrete all of the NaCl because there is no stimulus to retain sodium \(\rightarrow\) resulting in free water retention.

\[ [\text{Na}] = 122\ \text{mEq/L},\ \text{TBW}\ 30.5\ \text{kg} = \] Decrease in [Na] by -2 mEq/L!
Using urinary cation’s (sodium + potassium) is more accurate because it avoids confounding osmolytes

- If you give 1 liter of normal saline

1 Liter of NS

Na 154 mEq = 154 mEq

Patient’s urine is concentrated to Na + K = 300 mEq/L

• [Na] = 124 mEq/L, TBW 30 kg
Estimating Sodium after Intervention

• Androguie-Madias Formula

\[
\Delta \text{Serum Na} = \frac{(\text{Infusate Na} - \text{Serum Na})}{TBW + 1}
\]

\[
\Delta \text{Serum Na} = \frac{(\text{Infusate Na} + \text{Infusate K}) - \text{Serum Na}}{TBW + 1}
\]

• Edelman Formula

\[
\text{Na in plasma water} = \frac{1.11*(\text{Nae} + \text{Ke})}{TBW - 25.6}
\]

\( \text{Na}_e = \) Total exchangeable sodium
\( \text{K}_e = \) Total exchangeable potassium
Simplified Edelman Equation

\[ \text{plasma } [Na] = \frac{\text{Total body } N_a + K_e}{\text{Total body } H_2O} \]

Hashim et al. CJASN. 2007.
Case 5

Pearls

• In chronic hyponatremia correction:
  • Therapeutic **limits**:  
    • 10 mmol/L in 24 hours
  • Therapeutic **goal**:  
    • 6 – 8 mmol/L in 24 hours

• Do not give intravenous normal saline in SIADH.

• Prediction correction equations are a **TOOL** but there is **no** replacement for rechecking labs.
Case 6
Case Presentation

• A 61 yoF with history of depression, prior sinusitis, and sensorineural hearing loss with vertigo symptoms was admitted for worsening vertigo, nausea, vomiting, hematemesis (x1 day) and renal failure. She has been followed by ENT for the past 3 months for treatment of possible Meniere’s disease with BPPV. Home medications include venlafaxine and valium (for vertigo). Associated symptoms include fatigue and anorexia. She denies any dysuria or other voiding symptoms. No recent NSAID use. No history of kidney stones. She has not noticed any changes in urine color or consistency. She does not regularly see a physician.

• Vitals: Temp 36.4°C, P 98/min, RR 18/min, BP 152/78 mmHg, SpO₂ 90%. Physical exam shows an obese female with bilateral lower extremity edema 1-2+, regular heart rate, clear lungs, and no asterixis.

• An EGD subsequently showed a gastroesophagael ulcer that was clipped. She received blood transfusions.
Case 6
Case Presentation

Calcium: 7.6
Phosphorus: 7.6
LFT’s: normal.
Albumin: 3.2
Serum Osmolality: 298
LDH: 158.

$U_{Na}$: 60
$U_{Cr}$: 42

**Urinalysis**

<table>
<thead>
<tr>
<th>Source</th>
<th>Void</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Normal</td>
</tr>
<tr>
<td>Osmolality</td>
<td>296</td>
</tr>
<tr>
<td>pH [4.5-8.0]</td>
<td>5.3</td>
</tr>
<tr>
<td>Glucose [0-15]</td>
<td>12</td>
</tr>
<tr>
<td>Protein [ &lt;22 mg/dL]</td>
<td>77</td>
</tr>
<tr>
<td>Protein/Osmolality [&lt;0.27]</td>
<td>2.6</td>
</tr>
<tr>
<td>Predicted 24 h Protein [mg/24h]</td>
<td>1594</td>
</tr>
<tr>
<td>Hemoglobin, QL</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Urine Microscopy**

<table>
<thead>
<tr>
<th>Microscopy</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>11-20</td>
</tr>
<tr>
<td>WBC</td>
<td>1-3</td>
</tr>
<tr>
<td>Casts, Hyaline</td>
<td>3</td>
</tr>
<tr>
<td>Squamous Epithelial Cells</td>
<td>4-10</td>
</tr>
<tr>
<td>Bacteria</td>
<td>-</td>
</tr>
<tr>
<td>Yeast</td>
<td>-</td>
</tr>
<tr>
<td>Crystals</td>
<td>-</td>
</tr>
<tr>
<td>Dysmorphic RBC’s [&lt;=25]</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>
Case 6, Q1: What is the most likely etiology of her renal failure?

A. Pre-renal injury
B. Acute tubular necrosis (ATN)
C. Acute interstitial nephritis
D. Nephritic Syndrome
E. Nephrotic syndrome
F. Obstructive Uropathy
Case 6, Q2: What is the best initial next step in evaluation / management?

A. Start a diuretic and schedule an outpatient evaluation for newly diagnosed chronic kidney disease

B. Place a PICC line and administer 2-4 liters of normal saline over the next 24 hours.

C. Obtain a non-contrast renal CT

D. Obtain a functional imaging study (e.g. MAG-3)

E. Obtain complement levels, anti-GBM, ANCA, ANA with reflex.

F. Obtain a SPEP, UPEP, and free light chain levels.

G. Placement of a temporary dialysis line for initiation of hemodialysis.
Case 6, Q1
Answer

• Choice D
Case 6, Q2

Answer

• Choice E
Case 6
General indications for hemodialysis

- A: Acidemia (pH < 7.1)
- E: Electrolytes
- I: Intoxications
- O: Overload
- U: Uremia
Case 6
Nephritic versus Nephrotic Syndrome

• Nephritic:
  • Proteinuria (usually < 3 g/day)
  • Hematuria (dysmorphic RBCs or red cell casts)
  • Renal failure (sometimes oliguria)
  • Hypertension
  • Edema

• Nephrotic:
  • Proteinuria (usually > 3.5 g/day)
  • Hypoalbuminemia < 3 g/dL
  • Edema
  • Hypercholesterolemia
  • Lipiduria
  • (Associated with thrombotic disease)
Case 6
Case Presentation

• A 61 yoF with history of depression, prior sinusitis, and sensorineural hearing loss with vertigo symptoms was admitted for worsening vertigo, nausea, vomiting, hematemesis (x1 day) and renal failure. She has been followed by ENT for the past 3 months for treatment of possible Meniere’s disease with BPPV. Home medications include venlafaxine and valium (for vertigo). Associated symptoms include fatigue and anorexia. She denies any dysuria or other voiding symptoms. No recent NSAID use. No history of kidney stones. She has not noticed any changes in urine color or consistency. She does not regularly see a physician.

• Vitals: Temp 36.4°C, P 98/min, RR 18/min, BP 152/78 mmHg, SpO₂ 90%. Physical exam shows an obese female with bilateral lower extremity edema 1-2+, regular heart rate, clear lungs, and no asterixis.

• An EGD subsequently showed a gastroesophageal ulcer that was clipped. She received blood transfusions.
Case 6
Case Presentation

<table>
<thead>
<tr>
<th>Urinalysis</th>
<th>Urine Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Void</td>
</tr>
<tr>
<td>Appearance</td>
<td>Normal</td>
</tr>
<tr>
<td>Osmolality</td>
<td>296</td>
</tr>
<tr>
<td>pH [4.5-8.0]</td>
<td>5.3</td>
</tr>
<tr>
<td>Glucose [0-15]</td>
<td>12</td>
</tr>
<tr>
<td>Protein [ &lt;22 mg/dL]</td>
<td>77</td>
</tr>
<tr>
<td>Protein/Osmolality [&lt;0.27]</td>
<td>2.6</td>
</tr>
<tr>
<td>Predicted 24 h Protein [mg/24h]</td>
<td>1594</td>
</tr>
<tr>
<td>Hemoglobin, QL</td>
<td>Negative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Microscopy</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>11-20</td>
</tr>
<tr>
<td>WBC</td>
<td>1-3</td>
</tr>
<tr>
<td>Casts, Hyaline</td>
<td>3</td>
</tr>
<tr>
<td>Squamous Epithelial Cells</td>
<td>4-10</td>
</tr>
<tr>
<td>Bacteria</td>
<td>-</td>
</tr>
<tr>
<td>Yeast</td>
<td>-</td>
</tr>
<tr>
<td>Crystals</td>
<td>-</td>
</tr>
<tr>
<td>Dysmorphic RBC’s [&lt;=25]</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>

Calcium: 7.6
Phosphorus: 7.6
LFT’s: normal.
Albumin: 3.2
Serum Osmolality: 298
LDH: 158.
U<sub>Na</sub>: 60
U<sub>Cr</sub>: 42
Case 6
Common noninvasive GN tests*:

- Common tests**:
  - *Urinalysis with microscopy*, calcium, phosphorus, magnesium, uric acid, 24-hr creatinine clearance, 24-hr urine protein.

- Nephritic:
  - HIV, C3, C4, total complement, anti-dsDNA and ANA with reflex CTD, Anti-GBM, ANCA (PR3, MPO)

- Nephrotic:
  - HIV, Hep B and C, anti-dsDNA and ANA with reflex CTD, SPEP/UPEP and FLC’s, lipid screen, (anti-PLA2R)

*There is significant overlap (e.g. HIV can be associated with a nephritic or nephrotic syndrome or AIN)
** Do not obtain urine eosinophils.
Case 6
GN can present as clinical spectrum

The spectrum of glomerular diseases

SLE
IgA nephropathy

Minimal change nephropathy
FSGS
Diabetic nephropathy
Membranous nephropathy
Amyloidosis
MCGN
Post-streptococcal glomerulonephritis
Small vessel vasculitis
Anti-GBM disease

Nephrotic
Mechanism
- Injury to podocytes
- Changed architecture:
  - Scarring
  - Deposition of matrix or other elements

Haematuria
Proteinuria

Nephritic
Mechanism
- Inflammation
- Reactive cell proliferation
- Breaks in GBM
- Crescent formation

From Public Domain
Case 6
PICC Lines associated with venous stenosis

---

Table 2. Logistic Regression Analysis of Lack of Functioning AVF in Patients With History of PICC

<table>
<thead>
<tr>
<th>Adjustment</th>
<th>PICC Anytime</th>
<th>PICC Before AVF or ESRD</th>
<th>PICC Before ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>3.21 (1.91-5.50)</td>
<td>3.29 (1.78-6.29)</td>
<td>4.18 (2.04-9.14)</td>
</tr>
<tr>
<td>Adjusted for sex</td>
<td>3.24 (1.89-5.59)</td>
<td>3.32 (1.77-6.41)</td>
<td>3.93 (1.89-8.67)</td>
</tr>
<tr>
<td>Adjusted for vein size&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.32 (1.79-6.28)</td>
<td>3.00 (1.49-6.23)</td>
<td>3.54 (1.53-8.72)</td>
</tr>
<tr>
<td>Adjusted for artery size&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.80 (1.54-5.17)</td>
<td>2.70 (1.35-5.56)</td>
<td>3.46 (1.50-8.55)</td>
</tr>
<tr>
<td>Adjusted for tunneled dialysis catheter</td>
<td>2.52 (1.43-4.54)</td>
<td>2.28 (1.18-4.55)</td>
<td>3.39 (1.55-8.03)</td>
</tr>
<tr>
<td>Adjusted for any CVC</td>
<td>2.70 (1.55-4.79)</td>
<td>2.64 (1.38-5.23)</td>
<td>3.80 (1.76-8.93)</td>
</tr>
<tr>
<td>Adjusted for sex, vein/artery size, and any CVC</td>
<td>2.79 (1.45-5.50)</td>
<td>2.49 (1.19-5.43)</td>
<td>3.08 (1.26-8.20)</td>
</tr>
</tbody>
</table>

<sup>a</sup>n = 222.
<sup>b</sup>n = 220.

Note: Values given as odds ratio (95% confidence interval).
Abbreviations: AVF, arteriovenous fistula; CVC, central venous catheter; ESRD, end-stage renal disease; PICC, peripherally inserted central catheter.
Case 6
Urine eosinophils a poor diagnostic test
Case 6
Pearls

• Always obtain urinalyses for acute kidney injury.

• Avoid PICC lines in patients who may require dialysis in the future.

• Urine eosinophils offer little benefit.
A Few More Challenging Cases
Case 7
Presentation

• A 56 year old male with history of hypertension, T2DM with neuropathy, and depression is admitted due to abdominal pain, nausea, weakness and lethargy for the past week. He is a poor historian and unable to provide additional history. Abdominal x-ray shows significant stool with no evidence of obstruction or perforation. Medications include amlodipine and metformin.

• Vitals: Temp 37.1°C, P 108/min, RR 16/min, BP 154/98 mmHg, SpO₂ 94%. Physical exam shows a male with in mild distress, non-oriented, regular heart rate, clear lungs, mildly decreased skin turgor, no asterixis.
Case 7
Case Presentation

Calcium: 12
Phosphorus: 5.5
LFT’s: normal.
Albumin: 2.1
TSH: normal.

**Urinalysis**

<table>
<thead>
<tr>
<th>Source</th>
<th>Void</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Normal</td>
</tr>
<tr>
<td>Osmolality</td>
<td>130</td>
</tr>
<tr>
<td>pH [4.5-8.0]</td>
<td>5.3</td>
</tr>
<tr>
<td>Glucose [0-15]</td>
<td>10</td>
</tr>
<tr>
<td>Protein [ &lt;22 mg/dL]</td>
<td>176</td>
</tr>
<tr>
<td>Protein/Osmolality [&lt;0.27]</td>
<td>-</td>
</tr>
<tr>
<td>Predicted 24 h Protein [mg/24h]</td>
<td>6100</td>
</tr>
<tr>
<td>Hemoglobin, QL</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Urine Microscopy**

<table>
<thead>
<tr>
<th>Microscopy</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>0</td>
</tr>
<tr>
<td>WBC</td>
<td>1-3</td>
</tr>
<tr>
<td>Casts, Hyaline</td>
<td>3-10</td>
</tr>
<tr>
<td>Fatty Casts</td>
<td>3-10</td>
</tr>
<tr>
<td>Bacteria</td>
<td>-</td>
</tr>
<tr>
<td>Yeast</td>
<td>-</td>
</tr>
<tr>
<td>Crystals</td>
<td>-</td>
</tr>
<tr>
<td>Dysmorphic RBC’s [&lt;=25]</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>
Case 7, Q1: A repeat total calcium level is 12.4. What is the best next step in diagnosis of the etiology of his symptoms?

A. Obtain ionized calcium
B. Obtain serum PTH
C. Obtain 24 hour urine calcium
D. Obtain 1,25- and 25-vitamin D levels
E. Obtain imaging of parathyroid glands
F. Obtain CT chest/abdomen/pelvis
Case 7, Q1
Answer
• Choice B
One approach for Hypercalcemia

Hypercalcemia

- Recheck calcium (total or ionized)

Hypercalcemia

PTH (intact)

- Low
  - Workup for 1’ hyperparathyroidism

- Inappropriately normal
  - Consider FHH: 24 hr urine calcium

- High
  - 25- “vitamin D”
  - 1,25- “vitamin D”
  - PTHrP
  - Negative studies
    - SPEP, UPEP, FLCs
Case 7

Pearls

• The first diagnostic step for hypercalcemia after a history and exam is to obtain a parathyroid hormone level (PTH).
Case 8
Presentation

A 36 yoF with depression, anxiety, and history of alcohol abuse is admitted to the ICU after being found unresponsive and groaning on the floor by her husband. She was at her baseline state of health the prior night.

Home medications: Ibuprofen, fluoxetine, and trazodone.

No empty drug bottles or missing drugs. During transfer to the ED, she developed seizures. On arrival, she was intubated. Lorazepam and fosphenytoin were initiated.

Vital signs: Temp 34.8°C, P 111, BP 100/70. SpO₂ 97% on ventilator. She was unresponsive, had occasional muscle twitches, lung fields clear, bowel sounds diminished and no skin rash.
Case 8
Presentation

ABG: pH < 6.8, pO₂ 195, pCO₂ 32, HCO₃ 5.

Pregnancy: negative
Ethanol: negative
Prescription drug screen: negative

Lactate: 6.94
Measured serum osmolality: 461

CT head: no hemorrhage, edema, or acute findings
Case 8, Q1: What is the most likely etiology for her overall presentation?

A. Acetaminophen overdose
B. Methanol toxicity
C. Isopropyl alcohol toxicity
D. Lactic acidosis
E. Starvation ketoacidosis
Case 8, Q1

Answer

• Choice B
Case 8
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 8
Presentation

A 36 yoF with depression, anxiety, and history of alcohol abuse is admitted to the ICU after being found unresponsive and groaning on the floor by her husband. She was at her baseline state of health the prior night.

Home medications: Ibuprofen, fluoxetine, and trazodone.

No empty drug bottles or missing drugs. During transfer to the ED, she developed seizures. On arrival, she was intubated. Lorazepam and fosphenytoin were initiated.

Vital signs: Temp 34.8°C, P 111, BP 100/70. SpO\textsubscript{2} 97% on ventilator. She was unresponsive, had occasional muscle twitches, lung fields clear, bowel sounds diminished and no skin rash.
Case 8
Presentation

ABG: pH < 6.8, pO₂ 195, pCO₂ 32, HCO₃ 5

Pregnancy: negative
Ethanol: negative
Prescription drug screen: negative

Lactate: 6.94
Measured serum osmolality: 461

CT head: no hemorrhage, edema, or acute findings
Case 8
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Case 8
Explanation: 6 step approach to acid-base

3. Acidemia or Alkalemia?
   • Normal pH = 7.35 – 7.45

   ABG: pH < 6.8, pO$_2$ 195, pCO$_2$ 32, HCO$_3$ 5
Case 8
Explanation: 6 step approach to acid-base

4. Respiratory, Metabolic, or Mixed
   • “ROME”: look at pH and pCO$_2$
     • Respiratory Opposite
     • Metabolic Equal

ABG: pH < 6.8, pO$_2$ 195, pCO$_2$ 32, HCO$_3$ 5
Case 8
Explanation: 6 step approach to acid-base

1. History
2. Labs
3. Acidemia or Alkalemia?
4. Respiratory, Metabolic, or Mixed
5. Compensation
6. Anion Gap
Expected Compensation for Metabolic Acidosis

• Winter’s Formula:
  \[ p\text{CO}_2 = \left(1.5 \times HCO_3\right) + 8 \pm 2 \]

• Rule of 15:
  \[ p\text{CO}_2 = \left(1.5 \times HCO_3\right) + 8 \pm 2 \]

• Thumb rule:
  \[ p\text{CO}_2 = \text{value} \cong \text{last two digits of pH} \]
Case 8
Compensation

ABG: pH < 6.8, pO₂ 195, pCO₂ 32, HCO₃ 5.

1) Acidemia with metabolic acidosis, so check respiratory compensation
   • Expected pCO₂ = (1.5 * 5) + 8 = 15.5
2) Concurrent respiratory acidosis
3) AG: 28 = elevated. Therefore:
   Combined anion-gap metabolic acidosis with respiratory alkalosis.

*ΔΔ Gap: For every AG acid, except 1 HCO₃ compensation
ΔAG: 18 → Expected HCO₃ ~6 → No NAGMA

* May be beyond the scope of this discussion
Calculated Serum Osmolality

\[ 2 \times \text{Na} + \text{Glucose} + \text{BUN} + \text{ETOH} \]

\[
\begin{array}{ccc}
18 & 2.8 & 4.6 \\
\end{array}
\]

Osmolar Gap:
Measured - Calculated Osmolality: > 10

Osmolar Gap = Measured sOsm – Calculated sOsm
Calc Osm: (2 x[Na]) + [glucose (mg/dL)]/18 + [BUN (mg/dL)]/2.8
Osmolar gap = 461 – 312 = 149 (!!!) → differentials for OG
Differential Diagnosis of Increased Osmolar Gap

- Increased Serum Osmolality Gap
  - Methanol
  - Ethanol
  - Diethylene glycol
    - Diuretic (Mannitol)
    - Isopropyl alcohol (rubbing alcohol)
    - Ethylene glycol
  - Propylene glycol
“GOLD MARK”
Etiologies for Anion-Gap Metabolic Acidosis

G: Glycols (ethylene and propylene)
O: Oxoproline
L: L-lactate
D: D-lactate
M: Methanol
A: Aspirin
R: Renal failure
K: Ketoacidosis

Case 8
Pearls

• Calculate osmolar gap always in suspected toxic ingestion

• Isopropyl alcohol causes an osmolar gap but not an anion gap.
Case 9
Presentation

A 22 yoF presents to the ED due to progressive nausea, weakness, and headaches for the past week. ROS is only significant for diarrhea. She has been eating normally. She denies any drug use. Medications include ibuprofen, rhubarb root, and caster oil.

Vitals: Temp 37, HR 62, RR 18, BP 110/70, Wt 50 kg, BMI 18. Physical exam is unremarkable. Labs: Na 122, K 2.4, Cl 93, HCO$_3$ 19, BUN 10, Cr 0.6. Osmolality 255. An initial urine shows U$_{osm}$ 296 mOsm/kg. Urine pregnancy test negative.

She is given a bolus of 1 liter of normal saline with improvement of her sodium to 126 mEq/L in 6 hours and nursing notes “good” urine output with two urinary counts so far. She receives acetaminophen and ondansetron and all of her symptoms has resolved. She is tolerating her normal oral diet so a total of 160 mEq of potassium is orally supplemented. Further IV fluids are stopped.

The next day, her laboratory studies show:
Na 141, K 3.8, HCO$_3$ 21, BUN 10, Cr 0.6.
Case 9, Q1: Which of the following likely led to the overcorrection of her hyponatremia?

A. Potassium supplementation
B. Surreptitious laxative use
C. Polydipsia
D. Surreptitious hydrochlorothiazide use
E. Acute kidney injury
F. The student forgot to turn off the IV fluids

A. 17%
B. 17%
C. 17%
D. 17%
E. 17%
F. 17%
Case 9, Q1
Answer

• Choice A
Potential Pearls/Pitfalls

- K supplementation can lead to too rapid of Na correction

Intracellular Space
- Primarily contains [K]

Extracellular Space
- Primarily contains [Na]

\[ \text{[Na]} \uparrow \]
Complications of Hyponatremia: Osmotic Demyelination Syndrome (ODS)

• Terminology - ODS includes:
  • Central pontine myelinolysis
  • Extrapontine myelinolysis

• Biphasic pattern: Occurs 1 – 7 days after treatment

• Clinical diagnosis, but MRI (or autopsy) reveals pontine and extrapontine myelinolysis after ~ 2 weeks

• Risk factors: alcoholism, liver disease, and malnutrition

Complications of Hyponatremia: Osmotic Demyelination Syndrome (ODS)

- Symptoms include:
  - Pseudobulbar palsy and quadriplegia
  - Movement disorders
  - Behavior disorders
  - Seizures
  - “Locked-in” syndrome
  - Vegetative state
Therapeutic re-lowering of [Na] for prevention and treatment of ODS

• Performed within 12-24 hours after rapid correction of hyponatremia

• Use D5W to match urinary loss

• Consider desmopressin

• May be reversible
Case 9

Pearls

• Potassium supplementation can inadvertently cause over-correction of hyponatremia and potentially lead to osmotic demyelination syndrome (ODS).
Case 10
Presentation

A 39 yoM with history of long-standing EtOH dependence and associated withdrawal seizures presents to the ED with confusion. Her daily intake is 15 – 20 beer cans per day.

Physical exam reveals a somnolent male with slurred speech. Oriented x3 but difficulty with short-term memory. Diagnostic work-up shows no findings suggestive of cirrhosis or CHF. Labs: Na 100, K 3.0, BUN 5, Cr 0.7. Osmolality 210.

Vitals: temp: 37.3, HR 84, RR 14, BP 140/84. The patient was initiated on 1 L of normal saline containing magnesium and thiamine.

On arrival to the floor, he was making 500 ml/h of urine. D5W was initiated with the subsequent changes noted. On day 7 he developed decreased alertness and day 9 MRI brain showed findings of pontine and extrapontine myelinolysis

Sanghavi et al. AJKD. 2007
Case 10
Presentation: Serum sodium over time
Case 10, Q1: What is the most likely contributing cause of her hyponatremia?

A. Pseudohyponatremia
B. Congestive heart failure
C. Low solute intake
D. Cirrhosis
E. SIADH

A. 20%
B. 20%
C. 20%
D. 20%
E. 20%
Case 10, Q1
Answer

• Choice C
Beer potomania

- Typical Western diet 600 – 900 mOsm/day

- If maximum urinary dilution capability is 50 mOsm/L, you can excrete > 20 L of urine/day!

- However, in beer potomania, patients often have very low solute intake of ~ 250 mOsm/day

- What does this mean for the creation and correction of hyponatremia? What is the ADH level?
### Table 1. Treatment and Limits of Correction of Severe Hyponatremia

<table>
<thead>
<tr>
<th>Duration</th>
<th>Related Behavior or Condition</th>
<th>Clinical Features</th>
<th>Initial Therapeutic Goal</th>
<th>Limit of Correction and Management of Overcorrection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Several hours</td>
<td>Self-induced water intoxication associated with psychosis, running in marathons, use of 3,4-methylenedioxy-methamphetamine (MDMA, or “ecstasy”)</td>
<td>Headache, delirium, vomiting, seizures, coma, neurogenic pulmonary edema, brain swelling with risk of fatal herniation</td>
<td>100-ml bolus of 3% saline three times as needed for severe symptoms; increase plasma sodium concentration by 4–6 mmol/liter in first 6 hr</td>
<td>Excessive correction not known to be harmful</td>
</tr>
<tr>
<td>1–2 days</td>
<td>Postoperative hyponatremia, especially in women and children; hyponatremia associated with intracranial disease</td>
<td>Headache, delirium, vomiting, seizures, coma, neurogenic pulmonary edema, brain swelling with risk of fatal herniation</td>
<td>100-ml bolus of 3% saline three times as needed for severe symptoms; increase plasma sodium concentration by 4–6 mmol/liter in first 6 hr</td>
<td>Avoid increasing plasma sodium concentration by &gt;10 mmol/liter/day</td>
</tr>
<tr>
<td>Unknown or ≥2 days</td>
<td>Conditions associated with high risk of the osmotic demyelination syndrome (plasma sodium concentration, 105 mmol/liter or less; hypokalemia, alcoholism, malnutrition, liver disease) †</td>
<td>Malaise, fatigue, confusion, cramps, falls, 10% incidence of seizures with plasma sodium concentration &lt;110 mmol/liter, minimal brain swelling, and no risk of herniation</td>
<td>Extra caution indicated for conditions associated with high risk of osmotic demyelination syndrome; 100-ml bolus of 3% saline if needed for seizures; increase plasma sodium concentration by 4–6 mmol/liter in first 24 hr</td>
<td>Avoid increasing plasma sodium concentration by &gt;8 mmol/liter/day; consider lowering again if limit is exceeded, especially in patients with high risk of the osmotic demyelination syndrome</td>
</tr>
</tbody>
</table>

* Severe hyponatremia is defined as a plasma sodium concentration below 120 mmol per liter. In the absence of urinary loss of water, 1 ml of 3% saline per kilogram of body weight will increase the plasma sodium concentration by approximately 1 mmol per liter.

† The osmotic demyelination syndrome may develop when the plasma sodium concentration is increased rapidly in outpatients who became hyponatremic while drinking normal amounts of water and in hospitalized patients who became hyponatremic over 2 or more days.
Case 10

Pearls

• Maintain a high index of suspicion for beer potomania and “treat” appropriately to avoid complications.
Thank you for your attention
Questions & Discussion