Electrolytes and Acid-Base Basics for the Boards

Division of Nephrology and Hypertension and the Kidney Institute
University of Kansas Medical Center

Outline
I. Na⁺ disorders
   - Hyper- and hyponatremia
II. K⁺ disorders
   - Hyper- and hypokalemia
III. Acid-base disorders
   - General approach
   - Metabolic acidosis & alkalosis

Financial disclosures
No conflict of interest to disclose.

Na⁺ disorders

Hypernatremia

Hypernatremia

Hypernatremia

< 800 mOsm/kg
- Renal H₂O loss
  - Diabetes insipidus
  - Osmotic diuresis
  - CDI
  - NDI

> 800 mOsm/kg
- Insensible H₂O loss
- GI H₂O loss
- Na⁺ intake

Glucose, urea, mannitol

+ Water intake
Nephrogenic diabetes insipidus
- Hypokalemia
- Hypercalcemia
- Tubulointerstitial nephropathies
  - Sickle cell disease
  - Myeloma
  - Obstructive uropathy
  - Recovery from ATN or obstruction
  - Lithium
- Chronic renal failure

Distinguishing central from nephrogenic DI
Water deprivation test
- DDAVP (desmopressin)
- ↑U_{Osm} in CDI
- No Δ in U_{Osm} in NDI

Management of hypernatremia
- Replace free water deficit (50% in first 24 hr, no more than 0.5 mM/hr)
- Replace ongoing free water losses
- Treat underlying cause
  - Desmopressin for CDI
  - No specific Rx for NDI (attempt to reduce urine output with Na restriction, thiazides or give suprathetapeutic dose of desmopressin)

Hyponatremia

Hyponatremia

Volume status
- Hyponatremia
- Hypovolemic
- Dehydration
- Addison’s disease
- Diuretics
- Edematous
- Euvolemic
- Psych. polydipsia
- SIADH
- Hypothyroid

Hypoosmolal hyponatremia

Hypoosmolal hyponatremia

Volume status
- Hypovolemic
- Dehydration
- Addison’s disease
- Diuretics
- Edematous
- Euvolemic
- Psych. polydipsia
- SIADH
- Hypothyroid

* Correct serum Na* by 1.6 for every 100 mg/dL Δ in glucose

*U_{Osm} < 100 = ADH appropriately suppressed
* U_{Na} < 20 = Extrarenal cause of ECV depletion
Rx of hyponatremia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemia</td>
<td>Isotonic saline</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Water restriction</td>
</tr>
<tr>
<td>SIADH</td>
<td>Water restriction</td>
</tr>
<tr>
<td></td>
<td>Hypertonic saline / Na tablets</td>
</tr>
<tr>
<td></td>
<td>Furosemide</td>
</tr>
<tr>
<td></td>
<td>Aquaretics (&quot;vaptans&quot;)</td>
</tr>
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</table>

Rate of correction of hyponatremia

- **Acute** (< 48 hr, usually due to hypotonic fluid intake) or severely symptomatic
  - 100 mL of 3% saline bolus to increase $S_{Na}$ by 2-3 mEq/L
- **Chronic** (> 48 hr) including SIADH and asymptomatic
  - 0.5 mEq/l per hour
- Do not exceed $\Delta 12$ mEq/L in 1st day

Osmotic demyelination syndrome

- Central and extrapontine myelinolysis
- **Risk factors:**
  - Excessive rate or amount of correction of serum Na
- Classic CPM presents with dysphagia, quadripareisis, locked-in syndrome
- Can be permanent or fatal

K+ disorders

Hyperkalemia

- Hemolysed blood sample
- Leukocytosis/thrombocytosis
  - Check EKG, whole blood potassium (e.g. blood gas analyzer)

Pseudohyperkalemia
Hyperkalemia

- ↑ Intake
- Decreased urinary K+ excretion
  - 24 hr urine K+ < 40 mEq
- Cell shift
- Metabolic acidosis
- Hyperglycemia
- β-blocker
- Digitalis
- Hyperkalemic periodic paralysis
- Cell lysis

Decreased urinary K+ excretion

- ↓ GFR
- Renal failure
- Meds
- Adrenal insufficiency
- Hyporenin hypoald
- NSAIDs
- ACE/ARB
- Heparin
- Spironolactone
- Cyclosporine
- Block Na+ channel
  - Amiloride
  - Trimethoprim
  - Pentamidine

Type IV RTA (hyporeninemic hypoaldosteronism)

- Hyperkalemia (disproportionate to level of GFR)
- Non-gap metabolic acidosis with normal urine acidifying ability
- Mild CKD
- Often underlying tubulointerstitial disease:
  - DM
  - SLE, obstruction, myeloma/amyloid, HIV etc.
  - NSAIDs

Treatment of hyperkalemia

- Stabilize membrane excitability
  - Calcium chloride or gluconate, 1 g IV
- Increase K+ entry into cells
  - Glucose 25 g and insulin 10 U
  - β2-adrenergic agonist (albuterol 10-20 mg inh)
  - NaHCO3
- Removal of excess K+
  - Cation exchange resin (Kayexalate)
  - Diuretics
  - Dialysis
- Dietary K+ restriction

Hypokalemia

DDX of hypokalemia

- Cellular shift
- GI cause
- Urinary K wasting
- Alkalemia
- Cause
- Urinary K wasting
- Insulin
- β-agost
- Hypokalemic periodic paralysis
Features suggestive of hypokalemic periodic paralysis

- +FH or Asian male with thyrotoxicosis
- Precipitated by meal or exercise
- Repetitive episodes of acute profound hypokalemia
- Recovery of serum K⁺ within hrs after each episode without repletion, either spontaneously or with propanolol
- Low urine K⁺

DDX of hypokalemia

- Cellular shift
- GI cause
- Urinary K⁺ wasting

Alkalemia
Insulin
β-agonist
Hypokalemic periodic paralysis

Diarrhea
24 hr U_k > 25 mEq

Vomiting

Hypokalemia/Renal K⁺ wasting & hypertension

Aldosterone

High
Low

Renin

High
Low

Renal artery stenosis
Primary hyperaldosteronism
Cushing’s
Liddle’s
Liquorice ingestion

Use of the urine chloride

- In the setting of metabolic alkalosis, urine Cl⁻ is a more reliable marker of hypovolemia than urine Na⁺
- Low urine Cl⁻ indicates hypovolemia due to extrarenal cause
- High urine Cl⁻ in the setting of hypovolemia/euvolemia suggests renal salt wasting
Cryptogenic hypokalemic metabolic alkalosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Volume status/BP</th>
<th>Urine Cl⁻</th>
<th>Urine diuretics</th>
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<tr>
<td>Hyperaldosteronism</td>
<td>↑</td>
<td>&gt; 40 mEq/L</td>
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</tr>
<tr>
<td>Bartter/Gitelman syndrome</td>
<td>Nl or ↓</td>
<td>&gt; 40 mEq/L</td>
<td>-</td>
</tr>
</tbody>
</table>

Acid-base disorders

General approach

1. Is there acidemia or alkalemia?

   Acidemia  pH < 7.35
   Alkalemia pH > 7.45

2. What is the primary process?

   pH = 6.1 + log \( \frac{\text{HCO}_3^-}{0.03 \times \text{PCO}_2} \)
<table>
<thead>
<tr>
<th>pH</th>
<th>PCO₂/HCO₃⁻</th>
<th>Primary disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidemia</td>
<td>↓ HCO₃⁻</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td>↑ PCO₂</td>
<td>Respiratory acidosis</td>
</tr>
<tr>
<td>Alkalemia</td>
<td>↑ HCO₃⁻</td>
<td>Metabolic alkalosis</td>
</tr>
<tr>
<td></td>
<td>↓ PCO₂</td>
<td>Respiratory alkalosis</td>
</tr>
</tbody>
</table>

3. Is there an appropriate compensatory response?

Metabolic processes

"Metabolic acidosis"

↓ HCO₃⁻

Respiratory processes

Respiratory alkalosis
down

↓ PCO₂

"Respiratory alkalosis"
down

↓ PCO₂

3. Is there an appropriate compensatory response?

Metabolic processes

Metabolic alkalosis

↑ HCO₃⁻

Respiratory processes

"Respiratory acidosis"

↑ PCO₂

3. Is there an appropriate compensatory response?

Metabolic processes

"Metabolic alkalosis"

↑ HCO₃⁻

Respiratory processes

Respiratory acidosis

↑ PCO₂

Compensatory mechanisms

- Remember the direction of compensation
- Remember that compensation is almost never complete
Metabolic acidosis

Serum anion gap

$$[\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

= Unmeasured anions - Unmeasured cations

(Normal range: 8 - 12)

High anion gap metabolic acidosis

<table>
<thead>
<tr>
<th></th>
<th>Metabolism / Metabolic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Uremia</td>
<td>Toluene abuse</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>Type B lactic acidosis</td>
</tr>
<tr>
<td>Paraldehyde</td>
<td>(metformin, NRTI)</td>
</tr>
<tr>
<td>Iron/Isoniazid</td>
<td>D-lactic acidosis</td>
</tr>
<tr>
<td>Lactic acidosis</td>
<td></td>
</tr>
<tr>
<td>Ethylene glycol &amp; ethanol</td>
<td></td>
</tr>
<tr>
<td>Salicylates</td>
<td>Propylene glycol</td>
</tr>
</tbody>
</table>

Anion and osmolal gap in diagnosis of intoxications

<table>
<thead>
<tr>
<th>Anion gap acidosis</th>
<th>Osmolal gap</th>
<th>Clues to high anion gap acidosis syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Alcoholic fetor</td>
</tr>
<tr>
<td>+</td>
<td>High</td>
<td>Papilledema</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>Osmolar gap</td>
</tr>
<tr>
<td>-</td>
<td>High</td>
<td>Undetectable serum ethanol</td>
</tr>
</tbody>
</table>

Serum osmolal gap

Osmolal gap = Measured $S_{osm}$ - Calc $S_{osm}$

Calculated $S_{osm}$:

$$2 \ [\text{Na}^+] + [\text{glucose}] / 18 + [\text{BUN}] / 2.8$$

Clues to high anion gap acidosis syndromes

- Alcoholic fetor
- Papilledema
- Osmolar gap
- Undetectable serum ethanol

Methanol intoxication
Clues to high anion gap acidosis syndromes

- No fetor
- Osmolar gap
- Calcium oxalate dihydrate (envelope-shaped) crystalluria
- Urine fluoresces under Wood's (UV) lamp

Ethylene glycol intoxication

Clues to high anion gap acidosis syndromes

- Tinnitus/deafness
- Fever, tachycardia, hyperventilation
- Associated respiratory alkalosis and metabolic alkalosis

Salicylate intoxication

Clues to high anion gap acidosis syndromes

- Normal glucose
- Serum Acetest/acetoacetate negative or borderline
- Serum β-hydroxybutyrate positive
- Serum ethanol may or may not be present

Alcoholic ketoacidosis

Clues to high anion gap acidosis syndromes

- Didanosine or stavudine use
- 2 mth - 2 yr after start of Rx
- ± concurrent tenofovir use
- Lactic acid elevated

Type B lactic acidosis 2° to NRTI

Clues to high anion gap acidosis syndromes

- Short bowel syndrome
- Episodes of ΔMS associated with AG metabolic acidosis, after CHO intake
- Spontaneous resolution if NPO
- Serum lactic acid level negative

D-lactic acidosis

Clues to high anion gap acidosis syndromes

- ICU patient sedated with high dose intravenous infusion of lorazepam
- Osmolar gap
- Elevated serum lactic acid level

Propylene glycol intoxication
DDx of a non-gap metabolic acidosis

Diarrhea

RTA

I
Classic distal

II
Proximal

IV
Hyporeninemic hypoaldosteronism

DDx of RTA

<table>
<thead>
<tr>
<th></th>
<th>Proximal</th>
<th>Classic distal</th>
<th>Hyporenin hypoaldo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum K</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Urine pH</td>
<td>Variable</td>
<td>&gt; 5.5</td>
<td>&lt; 5.5</td>
</tr>
<tr>
<td>Other features</td>
<td>Fanconi (low PO₄, glycosuria)</td>
<td>Nephrocalcinosis ± CaPO₄ stones</td>
<td></td>
</tr>
</tbody>
</table>

Causes and Rx of RTA

<table>
<thead>
<tr>
<th>Common causes</th>
<th>Proximal</th>
<th>Classic distal</th>
<th>Hyporenin hypoaldo</th>
</tr>
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<tbody>
<tr>
<td>Rrosfamide</td>
<td></td>
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<tr>
<td>NRTI (tenofovir, adefovir, cidofovir)</td>
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<tr>
<td>Myeloma</td>
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<td></td>
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<tr>
<td>Sjogren’s</td>
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<tr>
<td>SLE</td>
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<tr>
<td>Amphotericin</td>
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<td>CKD plus:</td>
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<tr>
<td>DeM</td>
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<td></td>
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<tr>
<td>Obstruction</td>
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<td>Sickle cell dz</td>
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<tr>
<td>SLE</td>
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<td>NSAIDs</td>
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<thead>
<tr>
<th>Rx</th>
<th>Bicarbonate (lots)</th>
<th>Bicarbonate (+ 1 mEq/kg/day)</th>
<th>K⁺ lowering Rx:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diuretics</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Kayexalate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low K diet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mineralocorticoid</td>
</tr>
</tbody>
</table>

Metabolic alkalosis

Induction of metabolic alkalosis

Ingestion of alkali

Antacids

Blood Tx

Loss of acid

GI loss

Vomiting

NG suction

Cellular shift

↓ K⁺

Renal loss

Diuretics

Bartter/Gitelman

Hyperaldosteronism

Maintenance of alkalosis

Requires impairment of renal excretion of excess bicarbonate:

• Volume contraction (e.g. vomiting, diuretics)
• Hypokalemia
• Renal failure
• Hyperaldosteronism
Cryptogenic hypokalemic metabolic alkalosis

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Sample board review question 1

A 26 yr-old otherwise healthy male presents with seizure.

Na 115, K 3.5, Cl 88, CO₂ 23, BUN 5, Cr 0.7

Urine: Na 30 mEq/L, Osm 45 mOsm/kg

What is the most likely diagnosis:
A. SIADH
B. Hypothyroidism
C. Psychogenic polydipsia
D. Hepatic cirrhosis
E. Adrenal insufficiency

Sample board review question 2

A 75 yr-old male with known coronary and peripheral vascular disease presents with worsening hypertension despite treatment with HCTZ, amlodipine and candesartan.

Na 141, K 3.0, Cl 108, CO₂ 29, BUN 25, Cr 1.9

Which diagnostic test is most likely to be useful?
A. Urine diuretic screen
B. Genetic test for mutations in NKCC2
C. CT scan of the adrenal glands
D. Urine metanephrines
E. Doppler ultrasound of the renal arteries

Suggested reading


Financial disclosures


No conflict of interest to disclose.