Acid-Base Case Study

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Patient Arrives in Emergency Room

- 22 year old female with “hyperventilation”
- Healthy female.
- No known medical problems.
- Was fine until a few days ago, when she noticed increasing urinary frequency with no pain.
- Over the past couple of days, she’s become aware of rapid, deep breathing.
Additional Information

- Patient has lost ~5 pounds over last 2 weeks, unintentionally.
- Prescription medications: oral contraceptives.
- Denies illicit drug use, except for marijuana.
- Physical examination is normal, except for
  - rapid pulse (110, normal 70)
  - deep, rapid breathing (30 /min, normal ~12 /min)
Physician’s Initial Impressions

- Anxiety reaction
- Drug abuse
- Pulmonary embolus
  - unlikely: no pain, no swelling in leg
  - but possible and could be deadly
- Urinary tract infection
  - unlikely: no pain
  - easily diagnosed and treated
Initial Tests

• Pulse oximetry: O₂ sat = 100%
• Urine dipstick testing:
  – no white blood cells, no bacteria, no blood
• Urine drug screen:
  – no drugs of abuse detected
• D-Dimer:
  – 140 (values <500 are reassuring)
  – more on this test later in course
Other Tests (1)

• co-oximetry:
  – confirm pulse oximetry $O_2$ sat
  – what if there’s an abnormal hemoglobin present?

• results:
  – 98% oxyhemoglobin ($O_2$ saturation)
  – 1% methemoglobin (normal value)
  – 3% carboxyhemoglobin (normal for Boston)

• very reassuring
Other Tests (2)

• ABGs:
  – we need to check PO$_2$
  – might as well check acid-base, too

• results
  – PO$_2$:  120 mmHg (13.3 kPa) (possible? why?)
  – PCO$_2$:  15 mmHg (2.00 kPa)
  – HCO$_3$:  6 mmol/L (acid-base status?)

as PCO$_2$ falls, PO$_2$ rises
Other Tests (2)

• results
  – \( \text{PO}_2 \): 120 mmHg (13.3 kPa)
  – \( \text{PCO}_2 \): 15 mmHg (2.00 kPa)
  – \( \text{HCO}_3^- \): 6 mmol/L (acid-base status?)

• calculate \( \text{H}^+ / \text{pH} \)
  – \( 24(15/6) = 60 \) (increase of 20 nmol/L)
  – \( \Rightarrow \) decrease of 0.20 pH units, so pH=7.20
  – \( \Rightarrow \) metabolic acidosis, with compensation
  – i.e., \( \text{HCO}_3^- \) is low, and \( \text{PCO}_2 \) is low
Summary: Acid-Base Disturbances (with compensation)

PCO$_2$ and HCO$_3^-$ always move in the same direction!
- if only one changes → acute disturbance
- if different direction → >1 disturbance!
Other Tests (3)

• With diagnosis of metabolic acidosis, we need to check anion gap status so we need ________

• Electrolytes
  – Na = 130, K = 5.2, Cl = 90, HCO₃ = 6
  – Anion Gap = 130 – (90 + 6) = 24 (normal = 11)
  – ➔ increased anion gap metabolic acidosis
Other Tests (4)

- Whoa!
- How about that Na of 130 mEq/L?
- Is it real? Could it be pseudohyponatremia?
- How can we confirm it? (2 ways)
  - non-dilutional ISE
  - measured versus calculated osmolality
Osmolality

• measurement: freezing point depression
  – not boiling point elevation (alcohols)
  – the principle underlying ice melt preparations

• calculation
  – very few substances in human serum that make significant contributions to osmolality
  – complicated by our (US) refusal to use SI units
Calculation of Osmolality: Trivial In All But Three Countries

• Osmolality is a colligative property, corresponds to
  – number of particles (millimoles)
  – not to the mass of those particles (milligrams)

(map from Wikipedia.com)
Calculated Osmolality (Na)

• normal [Na] = 140 mEq/L

• 1 mmol Na = 1 mEq Na (valence 1)

• every Na must be balanced by an anion in serum, so, for convenience, we multiply [Na] by 2 rather than adding up all the anions in serum

• typical Na (and associated anions) contribution to osmolality: 140 X 2 = 280 mosm/kg
Calculated Osmolality (Glucose)

- normal $[\text{Glucose}] = 100 \text{ mg/dL}$
- convert mg to mmol and dL to L

- $1 \text{ mmol Glucose} = 180 \text{ mg Glucose} (C_6H_{12}O_6)$
- $100 \text{ mg/dL} / 180 \text{ mg/mmol} \Rightarrow 0.556 \text{ mmol/dL}$
- $0.556 \text{ mmol/dL} \times 10 \text{ dL/L} \Rightarrow 5.56 \text{ mmol/L}$

- In general, to convert conventional units to SI units:
  - conventional units (mg/dL) / molecular weight * 10

- typical glucose contribution to osmolality:
  $100 / 180 \times 10 = 6 \text{ mosm/kg}$
Calculated Osmolality (Urea)

- normal [BUN] = 12 mg/dL
- convert mg to mmol and dL to L

- 1 mmol Urea = 60 mg Urea (NH$_2$-CO-NH$_2$)
- BUT we report Urea Nitrogen
- 1 mmol Urea = 28 mg Urea Nitrogen (2 Ns per molecule)

- Using our general formula, the typical urea contribution to osmolality is:
  \[
  \frac{12}{28} \times 10 = 4 \text{ mosm/kg}
  \]
Calculated Osmolality
(Normal & This Case)

- In serum without alcohols or drugs:
- Calculated Osmolality = \([\text{Na}] \times 2 + \left(\frac{\text{Glucose}}{18}\right) + \frac{\text{BUN}}{2.8}\)  
- Normally: \(140 \times 2 + \left(\frac{100}{18}\right) + \left(\frac{12}{2.8}\right) = 290\) mosm/kg  
- Our patient:
  - \(\text{Na} = 130\)
  - \(\text{Glucose} = 423\)
  - \(\text{BUN} = 12\)
  \(\Rightarrow 130 \times 2 + \left(\frac{423}{18}\right) + \left(\frac{12}{2.8}\right) = 260 + 24 + 4 = 288\)
  
- Measured Osmolality = 290
- This implies that the measured Na of 130 is real
- Had it been pseudohyponatremia, the calculated osmolality would have been low
This Is Not Pseudohyponatremia

• This patient has real hyponatremia
• The measurement is accurate

• It is true that the high glucose concentration is leading to the low Na concentration
• However, labs should not “correct” the [Na]
  – i.e., try to estimate what the [Na] would be if glucose were returned to normal
  – clinicians can do this themselves if they want
  – fraught with difficulties
Other Tests (5): MUDPILES

• Causes: Metabolic Acidosis with Increased Anion Gap
  – Methanol: Possible. History not suggestive.
  – Urea: Ruled out by normal BUN.
  – Diabetes: YES: very high glucose
  – Propylene Glycol: Possible. History not suggestive.
  – Isoniazid: Possible. History not suggestive.
  – Ethylene glycol: Possible. History not suggestive.
  – Salicylate: Not likely. Easily measured.

• Diagnosis = Diabetic Ketoacidosis
Alcohol Metabolism:
Why Some Alcohols Lead to Increased Anion Gap

\[
\begin{align*}
\text{CH}_3\text{-OH} & \rightarrow \text{H-C-H} \\
\text{Methanol} & \rightarrow \text{Formaldehyde} \\
\text{CH}_3\text{CH}_2\text{-OH} & \rightarrow \text{CH}_3\text{-C-H} \\
\text{Ethanol} & \rightarrow \text{Acetaldehyde} \\
\text{OH} & \text{CH}_3\text{-CH-CH}_3 \\
\text{Isopropyl Alcohol} & \rightarrow \text{Acetone} \\
\text{OH} & \text{CH}_2\text{-CH}_2 \quad \text{not an acid at all} \\
\text{Ethylene Glycol} & \rightarrow \text{H-C-C-H} \\
\text{Glyoxal} & \rightarrow \text{H-C-OH} \\
\text{Formic Acid} & \text{a strong acid} \\
\text{CH}_3\text{-C-OH} & \text{Acetic Acid} \\
\text{a weak acid} & \\
\end{align*}
\]
Metabolic Acidosis

$\text{HCO}_3^-$ Decreases from 24 to 12

Normal anion gap
Chloride has increased, replacing lost HCO3

Increased anion gap
Chloride has not changed
A new anion has replaced lost HCO3

$\text{HCO}_3 = 12$
$\text{Cl} = 112$

$\text{HCO}_3 = 12$
$\text{Cl} = 100$

$\text{?} = 12$
$\text{HCO}_3 = 12$
$\text{Cl} = 100$
So What Are Those Increased “Unmeasured” Anions?

• In diabetic ketoacidosis, several acids accumulate, two of which are among the “ketone bodies”

![The Ketone Bodies](image)

• Note: **β-hydroxybutyrate** is not a ketone
• Note: **acetone** is not an anion
  – Does not contribute to increased anion gap
  – Does contribute to osmolality
Not an Atypical Presentation of Diabetes

• Urinary frequency
  – [glucose] is beyond kidney tubules capacity for reabsorption
  – draws/keeps water in kidney tubules, causing an osmotic diuresis

• Fluid loss translates into weight loss

• As acidosis develops and intensifies
  – respiratory compensation with hyperventilation
  – can appear bizarre, as it did in this case
Topics Reviewed in this Case

- relationship between PO$_2$ and PCO$_2$ in patients
- calculation of H$^+$/pH from PCO$_2$ and HCO$_3^-$
- evaluation of acid-base disturbance
- use of anion gap in metabolic acidosis (MUDPILES)
- evaluation for pseudohyponatremia
- SI Units
- calculation of osmolality
- structures of ketone bodies
“Tests” Discussed in this Case

- pulse oximetry
- co-oximetry
- Arterial Blood Gases \((\text{PO}_2, \text{PCO}_2, \text{pH})\)
- electrolytes \((\text{Na}, \text{K}, \text{Cl}, \text{and HCO}_3^-)\)
- osmolality (as well as Glucose and BUN)
- MUDPILES
- metabolism of alcohols
- ketone bodies