

Acid Base Abnormalities

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ABSTRACT

This Approach To article provides an overview on acid-base imbalance, with a particular focus on metabolic acidosis. It provides a general step-wise approach on how to determine what acid-base imbalance is occurring and some of the potential underlying causes for each.



KEYWORDS

Acid-Base Disturbances, Acidemia, Alkalemia

1 | QUESTION

A 23-year-old male is brought to the Emergency Department by his mother. She reports that he has been acting strangely and is unable to answer her questions coherently. She adds that this all started after he was found sitting in the corner of the bathroom with his hands covering his ears, next to an empty bottle and blood-tinged vomit on the floor. On the way to the hospital, the patient reported nausea and severe abdominal pain. His mother notes that she has been feeling worried about her son given that he lost his job during the COVID-19 pandemic and has been severely depressed for several

weeks.

You observe the following on examination:

General appearance: Diaphoretic

Neurologic: Not responding coherently to questions, complains of ringing in his ear

GI: Had another blood-tinged episode of vomiting, abdomen soft but has mild diffuse tenderness

Vital Signs: Temp: 37.7°C, HR: 122, BP: 144/96, RR: 28, Sat: 95% on RA

Labs: Na⁺: 137 mEq/L (N: 135-145), Cl⁻: 90 mEq/L (N: 98-107), K⁺: 4.8 mEq/L (N: 3.5-5.1), BUN: 5 (N: 2.1-8.0), Glu: 7, Osmolality: 305 (N: 275-295)

Arterial Blood Gas: pH: 7.53 (N: 7.38-7.46), PaCO₂: 18

mmHg (N: 32-45), PO_2 : 85 mm Hg (N: 83- 116), HCO_3^- : 7 mEq (N: 22-27)

Normal Values as per the Medical Council of Canada indicated in brackets ¹

Which of the following is the most likely cause of the patient's condition and blood gas findings?

- A. Salicylate intoxication
- B. Opioid overdose
- C. Diabetic ketoacidosis (DKA)
- D. Alcohol overdose
- E. Acetaminophen intoxication

2 | ANSWER

The patient in this case is mostly likely experiencing salicylate toxicity (A). Salicylate toxicity is characterized by a mixed acid-base disturbance presentation, in which the patient exhibits respiratory alkalosis (*salicylate directly stimulates the cerebral respiratory drive, leading to ↑ respiratory drive and consequent ↓ in CO_2*) and anion gap metabolic acidosis (*due to ↑ lactic acid, ketoacids and salicylic acid*).^{2,12} Respiratory alkalosis can be identified with ↑ pH > 7.45 and ↓ PaCO_2 < 32-35. Metabolic acidosis can be identified by an anion gap of 40 (*Anion Gap* = $\text{Na} - [\text{Cl} + \text{HCO}_3^-]$; N: 10-12) indicating the presence of unbuffered acids. Early clinical features of salicylate toxicity include tinnitus (ringing of the ears) and irritation of the GI tract which can lead to nausea, vomiting and abdominal pain and tachypnea.² Later signs include agitation, delirium and seizures.^{2,12}

3 | INITIAL APPROACH

Normal serum pH is tightly controlled within a range of 7.38-7.46¹ (Note: These values can vary between institutions; many books will use 7.35 as the lower limit). Maintenance within this range is essential for normal protein and enzymatic activity. Alterations of the serum pH can lead to disruption of cellular functions required for survival. Metabolism in the body produces large amounts of volatile and non-volatile acids. Volatile acids include CO_2 derived from the breakdown of carbohydrates and

fats, which can bind with water to form carbonic acid. CO_2 levels are controlled by alveolar ventilation. Non-volatile acids are derived from a few sources, including protein metabolism. These acids are eliminated in a 2-step process: 1) Acids combine with buffers such as extracellular bicarbonate (HCO_3^-), intracellular phosphate (HPO_4^{2-}) and carbonate in bones and 2) Kidneys excrete surplus of H^+ and reabsorbs HCO_3^{3-} .

Using these concepts, it is possible to approach acid-base disturbances using a step wise approach. This article will explore the approach that can be used to determine whether a patient is presenting with a simple or mixed acid-base disturbance.

Stepwise Approach to Acid-Base Disorders

Step 1: Establish the primary diagnosis^{4,5}

- Look at the pH and determine whether there is an acidemia or alkalemia present:
 - Acidemia: pH < 7.35 (~7.38 per MCC)¹
 - Alkalemia: pH > 7.45
- Look at the PaCO_2 and determine if the disturbance is respiratory or metabolic:
 - If PaCO_2 moves in the opposite direction of pH → Respiratory Process
 - If PaCO_2 moves in the same direction as pH → Metabolic Process

Step 2: Assess the degree of compensation^{4,5}

Use the ratios listed in Table 1 to determine whether there is adequate compensation. If there is insufficient compensation, there is a greater chance that more than one acid-base disorder is present.

Step 3: Measure the following values (*especially important in metabolic acidosis*)^{4,5}

The **Anion gap**. Normally, anions are present in our bodies and act as buffers for the cations that are present; mainly Na^+ . These anions include proteins, circulating phosphates and sulphates, and albumin. It is important to note that some anions, such as pathological proteins, cannot be measured by routine labs.⁶ When an excess of acids are present due to any pathologic condition, a gap forms between the number of acids present and the number of anions available to buffer them. In other words, an insufficient number of anions are present to

act as buffers.

- The formula for the anion gap is ($AG = [Na^+] - ([Cl^-] + [HCO_3^-])$)
- The normal value for the anion gap is 12 mEq/L ^{4,5,6}

If the anion gap is elevated, the **osmolal gap** must be calculated to determine if the underlying cause of elevated acid levels can be attributed to excess alcohol present in the body. The exact alcohols will be specified later in this article.

- The formula for the osmolal gap is (**Measured Osmolality on lab**) – (**Calculated Osmolality**).
- The formula for the **calculated osmolality** = $2[Na^+] + [Glucose] + [Urea]$.
- The normal value for osmolal gap is <10.4

If the anion gap is elevated, the **Delta anion gap/delta HCO_3^- ratio** can be calculated to compare the change in anion gap to the change in $[HCO_3^-]$. An increase in acid content, reflected by a high anion gap, will cause the $[HCO_3^-]$ to decrease as it will act as a buffer for the excess acids. Therefore, the increase in acid levels is normally proportional to the decrease in $[HCO_3^-]$, rendering the delta anion gap/delta HCO_3^- ratio to be usually 1:1 or between 1 to 2. ^{4,7}

- The formula used to calculate delta anion gap/delta HCO_3^- is
$$\frac{|(\text{NormalAGvalue}) - (\text{MeasuredAG})|}{|(\text{NormalHCO}_3^-\text{value}) - (\text{MeasuredHCO}_3^-\text{value})|}$$
- If the ratio <1, this implies that there is a greater loss in HCO_3^- than expected via compensation. Therefore, a concurrent non-anion gap metabolic acidosis process is present. ⁴ For instance, a patient presenting with DKA and profuse diarrhea will exhibit a ratio <1.
- If the ratio is >2, this implies that $[HCO_3^-]$ value has not decreased as expected, and there is a concurrent metabolic alkalosis or an elevated HCO_3^- at baseline as a result of chronic respiratory acidosis. ^{4,7} For instance, this can be seen in a patient presenting with DKA and profuse vomiting of acidic gastric content.

Step 4: Establish the final diagnosis & determine underlying causes

While Table 2 is not an exhaustive list, it highlights some of the key causes for these disturbances.

4 | BEYOND THE INITIAL APPROACH

4.1 | Metabolic Acidosis

Metabolic acidosis is more complex than the other acid-base disturbances because it is further subdivided into two categories: 1) **High anion gap metabolic acidosis (AGMA)** and 2) **Non-anion gap metabolic acidosis (NAGMA)**. As explained earlier, the increase in the anion gap occurs due to the presence of excess acids. Many etiologies can account for this increase in acid content, and these etiologies can be remembered using the commonly used acronym “**MUDPILES**” (see Table 2). The following text expands on these etiologies.

Methanol, Propylene, Ethylene glycol intoxication

Ingested toxic alcohols such as methanol, propylene glycol and ethylene glycol are metabolized into organic acids that have significant side effects on the body, which can include causing metabolic acidosis. ⁹

Uremia (reflecting renal failure)

In renal failure, a reduction in normal phosphate secretion increases hydrogen retention. ¹⁰ This process is further aggravated by impaired excretion of other substances such as organic anions and sulphates. ⁸

Diabetic ketoacidosis

Ketoacidosis is a metabolic state in which there is a lack of glucose or an inability to use the glucose present, causing the body to break down fatty acids for fuel production. ¹¹ This forms a high amount of ketone bodies, particularly acetone, acetoacetate, and beta-hydroxybutyric acid. This is commonly seen in: 1) diabetic ketoacidosis, 2) starvation and 3) excessive alcohol ingestion. ^{8,9,11}

Lactic acidosis

Lactic acidosis commonly occurs as a result of hypoperfusion to the tissues. This decrease in perfusion can be due to various causes, such as systemic hypotension secondary to shock. ⁹

Salicylate overdose

Lastly, salicylate overdose is characterized by a mixed acid-base disturbance presentation. The patient will

have respiratory alkalosis because salicylates directly stimulate the cerebral respiratory drive, resulting in increased respiratory drive and consequent decrease in CO_2 . There will also be an anion gap metabolic acidosis due to cumulative accumulation of lactic acid, ketoacids and salicylic acid.¹²

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5 | TABLES & FIGURES

Disorder	Primary Change	Compensatory Response
Respiratory Acidosis pH <7.35	↑ in CO ₂ due to ↓ in ventilation	<u>Acute Response:</u> • Rapid ↑ in [HCO₃⁻] to buffer CO₂ • Compensation: ↑ 1 mEq/L HCO₃⁻ per 10 mmHg ↑ in PaCO₂ <u>Chronic response (requires 3-5 days to complete):</u> • Kidney reabsorbs ↑ [HCO₃⁻] in PCT and excretes more H⁺ • Compensation: ↑ 3.5-4 mEq/L HCO₃⁻ per 10 mmHg ↑ in PaCO₂
Respiratory Alkalosis pH >7.35	↓ in CO ₂ due to ↑ ventilation	<u>Acute Response:</u> • Rapid ↓ in [HCO₃⁻] to decrease buffering • Compensation: ↓ 2 mEq/L HCO₃⁻ per every 10 mmHg-change in PaCO₂ baseline <u>Chronic response (requires 3-5 days to complete):</u> • Kidney produces less and excretes more HCO₃⁻ in resp. disorder lasting > mins-hours • Compensation: ↓ 4-5 mEq/L HCO₃⁻ per every 10 mmHg-change in PaCO₂ baseline
Metabolic Acidosis pH <7.35	↑ in acid content <u>or</u> ↓ in [HCO ₃ ⁻]	<u>Acute Response (begins within 30 min & completed within 12-24 hrs):</u> • Hyperventilate (increased tidal volume or resp. rate) to expel CO₂ and decrease PaCO₂ • Compensation: ↓ 1.2 mmHg PaCO₂ per every 1 mEq/L ↓ HCO₃⁻
Metabolic Alkalosis pH >7.45	↓ in acid content <u>or</u> ↑ in [HCO ₃ ⁻]	<u>Acute Response:</u> • Hypoventilate to retain CO₂ and ↑ PaCO₂ • Compensation: ↑ 0.6-0.7 mmHg PaCO₂ per 1 mEq/L ↓ HCO₃⁻

TABLE 1 Different types of acid-base disorders, the associated primary change involved and the expected normal compensatory mechanism

Adapted from Table 5.2 in (Rennke & Denker, 2014)³ using information from (Emmett & Palmer, 2020)⁵

Common etiologies ⁸	
Respiratory Acidosis	Respiratory Alkalosis
• Primary pulmonary disease (e.g., COPD) • Drug Induced Hypoventilation (e.g., narcotics, sedatives, etc.) • Neuromuscular disorders (e.g., Myasthenia Gravis) • Respiratory Muscle fatigue (prolonged hyperventilation)	• Anxiety • Pulmonary Embolism • Pneumonia • Sepsis • Hypoxia • Mechanical ventilation • Pregnancy • Medication (e.g., Salicylate Toxicity)
Metabolic Acidosis	Metabolic Alkalosis
See "Beyond the Initial Approach" section below	
High Anion Gap Metabolic Acidosis: TRICK: MUDPILES • Methanol intoxication • Uremia (reflecting renal failure) • Diabetic ketoacidosis • Propylene glycol Intoxication • Isoniazid & Iron • Lactic Acidosis • Ethylene glycol intoxication • Salicylate overdose Non-Anion Gap Metabolic Acidosis • GI loss of HCO₃⁻* - Diarrhea (most common cause) - Pancreatic Fistula • Renal loss of HCO₃⁻* - Proximal tubular acidosis aka Type 2 RTA (↓ reabsorption) - Distal tubular Acidosis aka Type 1 RTA (↓ production) - Carbonic anhydrase inhibitors <i>*differentiated using Urine AG</i>	Associated with volume loss*- Loss of HCO₃⁻ and/or RAAS activation • Gastric drainage • Vomiting acidic gastric content • Diuretics Associated with volume expansion*- • Adrenal disorders (Primary hyperaldosteronism) Others causes: • Severe hypokalemia • Impaired renal function • Iatrogenic (administration of bicarbonate) <i>*differentiated using urine chloride</i>

TABLE 2 List of etiologies causing various types of acid-base disturbances

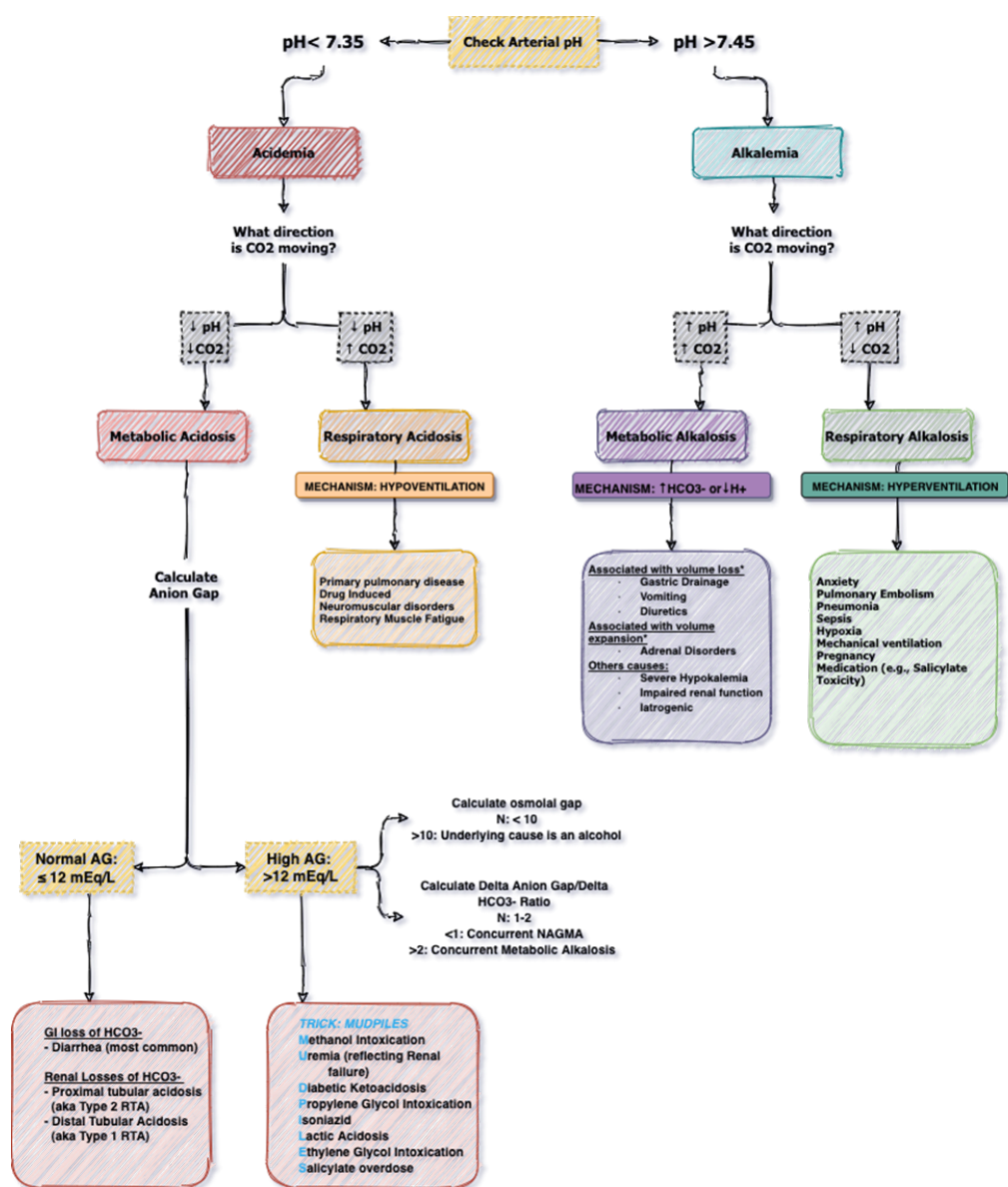


FIGURE 1 Summary of steps that can be used for acid-base disturbances.
Inspired by Acidosis and Alkalosis Flowchart (Le et al., 2021)¹³