

# **HIGH ANION GAP METABOLIC ACIDOSIS**

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# INTRODUCTION

- High Anion Gap Metabolic Acidosis (**HAGMA**) is a medical condition characterized by acidemia and an increased **anion gap**, which occurs when the body accumulates "unmeasured" **acidic anions** that consume bicarbonate.

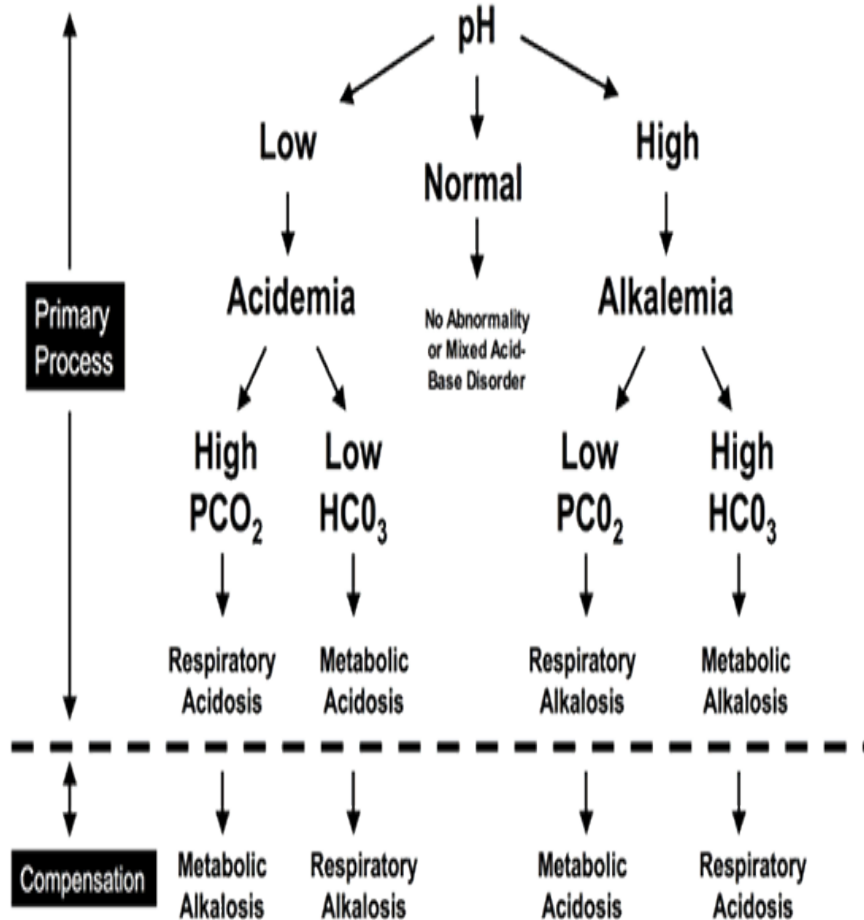
- **Formula:**

$$AG = Na - (Cl + HCO_3)$$

- **Normal Range:** Typically **8 to 12 mEq/L**.
- **Significance:** A high anion gap (usually **>12 mEq/L**) indicates that unmeasured organic acids—such as lactate or ketones—are present.

# BASICS

Figure 2: Primary And Compensatory Processes



## Normal Arterial Blood Gas Values\*

pH	7.35 - 7.45
PaCO <sub>2</sub>	35 - 45 mm Hg
PaO <sub>2</sub>	70 - 100 mm Hg **
SaO <sub>2</sub>	93 - 98%
HCO <sub>3</sub> <sup>-</sup>	22 - 26 mEq/L
%MetHb	< 2.0%
%COHb	< 3.0%
Base excess	-2.0 to 2.0 mEq/L
CaO <sub>2</sub>	16 - 22 ml O <sub>2</sub> /dl

\* At sea level, breathing ambient air

\*\* Ana-dependent



# TERMINOLOGIES

- **Corrected Anion Gap:** An adjustment for **hypoalbuminemia** (low protein), which can mask a high anion gap.  
**Calculation:** For every 1 g/dL decrease in albumin below 4.0 g/dL, the anion gap falls by about 2.5 mEq/L.
- **Osmolar Gap (OG):** The difference between measured and calculated serum osmolality. A gap **>10 mOsm/kg** suggests the presence of unmeasured toxic alcohols like methanol or ethylene glycol.

# TERMINOLOGIES

- **Delta Gap (Delta-Delta):**
- A ratio comparing the increase in the anion gap to the decrease in bicarbonate.
- It identifies **mixed acid-base disorders**.

$$\text{DELTA RATIO} = \frac{\Delta \text{ anion gap}}{\Delta \text{ HCO}_3^-} = \frac{[\text{AG} - 12]}{[24 - \text{HCO}_3^-]}$$

< 0.4	Hyperchloraemic non-anion gap metabolic acidosis
0.4 - 0.8	HAGMA + NAGMA [may be isolated renal failure]
1 - 2	uncomplicated HAGMA
> 2	Metabolic acidosis w/ pre-existing elevated HCO <sub>3</sub> <sup>-</sup> [metabolic alkalosis or respiratory acidosis]

# CAUSES OF HAGMA

## High Anion Gap Metabolic Acidosis (HAGMA)

- |                                       |  |
|---------------------------------------|--|
| <b>M:</b> methanol                    | <b>G:</b> glycols (propylene glycol and ethylene glycol)   |
| <b>U:</b> uremia                      | <b>O:</b> 5-oxoproline (associated with acetaminophen use) |
| <b>D:</b> diabetic ketoacidosis (DKA) | <b>L:</b> L-lactate  |
| <b>P:</b> phenformin, paraldehyde     | <b>D:</b> D-lactate (short bowel syndrome)                 |
| <b>I:</b> INH, iron                   | <b>M:</b> methanol   |
| <b>L:</b> lactic acid                 | <b>A:</b> aspirin  |
| <b>E:</b> ethanol, ethylene glycol    | <b>R:</b> renal failure                                    |
| <b>S:</b> salicylates                 | <b>K:</b> ketoacidosis (diabetic/alcohol/starvation)       |

## CAUSES OF NORMAL/LOW AG ACIDOSIS

**Table 29.5** Most common causes of normal AG metabolic acidosis

Cause	Mechanism
Diarrhea	Loss of $\text{HCO}_3^-$ in stool
Ureterosigmoidostomy, ileal conduit	Loss of $\text{HCO}_3^-$ in stool
Carbonic anhydrase inhibitors	Loss of $\text{HCO}_3^-$ in urine
Recovery phase of ketoacidosis	Less $\text{HCO}_3^-$ synthesis from decreased availability of ketones
Chronic kidney diseases (stages G4–G5)	Decrease in $\text{NH}_3$ excretion
Proximal renal tubular acidosis (type 2)	Loss of $\text{HCO}_3^-$ in urine
Distal renal tubular acidosis (type 1)	Decreased renal acid secretion
Distal renal tubular acidosis (type 4)	Decreased acid secretion and low $\text{NH}_3$ production
Dilutional acidosis	Increased $\text{Cl}^-$ due to normal saline administration
Cholestyramine	Release of $\text{Cl}^-$ in exchange for $\text{HCO}_3^-$

**Table 29.6** Most common causes of low AG metabolic acidosis

Cause	Mechanism
Hypoalbuminemia	Decreased number of anions
IgG myeloma	Increased number of cations
*Bromide intoxication	Bromide measured as chloride
Salicylate overdose	Salicylate measured as chloride
Hypercalcemia	Increased number of cations
Hypermagnesemia	Increased number of cations
Lithium toxicity	Increased number of cations
Hypertriglyceridemia	Different laboratory analysis

\*Negative AG

# Approach to diagnosis of metabolic pH abnormalities

Calculate anion gap =  $\text{Na} - \text{Bicarb} - \text{Cl}$

Anion Gap < 12 mM  
(normal anion gap)

Bicarb < 22 mM

Non-AG gap  
metabolic  
acidosis  
(pure NAGMA)

Bicarb  
22-28 mM

Normal

Bicarb  
> 28 mM

Metabolic  
alkalosis

Anion Gap > 12 mM  
(elevated anion gap)

Compare:

$\Delta \text{Anion Gap} = \text{Anion Gap} - 10 = \text{elevation of anion gap}$

$\Delta \text{Bicarb} = 24 - \text{Bicarb} = \text{reduction in bicarbonate}$

$\Delta \text{AG} \ll \Delta \text{Bicarb}$

AG metabolic acidosis  
PLUS non-AG  
metabolic acidosis  
(AGMA + NAGMA)

$\Delta \text{AG} \sim \Delta \text{Bic}$

AG metabolic  
acidosis  
(pure AGMA)

$\Delta \text{AG} \gg \Delta \text{Bicarb}$

AG metabolic  
acidosis PLUS  
metabolic  
alkalosis



# Algorithm recommended for etiological diagnosis of metabolic acidosis

