Evaluation of Acid-Base Disorders

What you need: (1) arterial blood gas and serum electrolytes drawn at the same point in time; (2) an understanding of the patient's history; (3) a basic understanding of physiology and biochemistry; (4) common sense.

Normal arterial pH range: 7.38 – 7.42 (7.40)
Normal arterial PaCO₂ range: 38 – 42 mmHg (40 mmHg)
Normal serum CO₂ range: 22 – 26 mEq/L (24 mEq/L)

A note about terminology: the serum (venous) value that is measured in the chemistry lab is the total CO₂, it represents the bicarbonate moiety (HCO₃⁻) that is buffered by organic acids.

Remember, pH = - log [H⁺] = 6.10 + log ([HCO₃⁻] / [0.03 * PaCO₂] ) ≈ (HCO₃⁻/PaCO₂)

<table>
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<th>Four Primary Acid-Base Disorders and their Compensatory Changes</th>
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<td><strong>Primary Event</strong></td>
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<td><strong>Metabolic Acidosis</strong></td>
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<td>↓ pH = (\frac{\text{HCO}_3^-}{\text{PaCO}_2})</td>
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<td><strong>Respiratory Acidosis</strong></td>
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**Respiratory Acidosis**
Characteristics: elevated PaCO₂, decreased extracellular pH
(\(\text{CO}_2\) production at tissue level exceeds \(\text{CO}_2\) elimination by lungs)
Causes: CNS depression (sedatives, CNS disease, obesity-hypoventilation syndrome); pleural disease (large pneumothoraces and pleural effusions); lung disease (COPD, ARDS); musculoskeletal and neuromuscular disorders (kyphoscoliosis, Guillain-Barre syndrome, myasthenia gravis, polymyositis)
Compensation: ACUTE: pH drops by 0.08 units and HCO₃⁻ increases by 1 mEq/L per 10 mmHg increase in PaCO₂ (up to a PaCO₂ of 70) 
CHRONIC: pH drops by 0.03 units and HCO₃⁻ increases by 3-4 mEq/L per 10 mmHg increase in PaCO₂ (up to a PaCO₂ of 70) 
Renal compensation (HCO₃⁻ retention) generally at its maximum by 4 days, is never complete (i.e., pH is never normalized).
Consider: In general, if the HCO₃⁻ is above 30, look for a second process (chronic respiratory acidosis, concomitant metabolic alkalosis).

**Respiratory Alkalosis**
Characteristics: decreased PaCO₂, increased extracellular pH
(implies that the increase in alveolar ventilation and consequent decrease in PaCO₂ are not compensatory responses to hypoxemia)
Causes:
catastrophic CNS disorder (ICH); drugs (salicylates, progesterone); pregnancy (generally during 3rd trimester); decreased lung compliance (such as interstitial fibrosis) leading to hyperventilation and respiratory alkalosis even in the absence of hypoxemia; anxiety; cirrhosis; sepsis.

Compensation:
ACUTE: pH increases by 0.08 units and HCO₃ decreases by 2 mEq/L per 10 mmHg decrease in PaCO₂ (down to a PaCO₂ of 20)
CHRONIC: pH increases by 0.03 units and HCO₃ decreases by 5 mEq/L per 10 mmHg decrease in PaCO₂ (down to a PaCO₂ of 20)
Renal compensation via suppression of renal acid secretion and subsequent consumption and decrease in serum HCO₃. In contrast to respiratory acidosis, however, the compensation for a long-standing process may eventually become complete (i.e., pH normal).

Consider:
If the HCO₃ has dropped by more than 2-4, consider a superimposed metabolic acidosis, ASA, sepsis, or chronic hyperventilation.

METABOLIC ACIDOSIS
Characteristics: decreased serum HCO₃, decreased extracellular pH

Causes: divide into INCREASED versus NORMAL ANION GAP causes.

| Anion Gap (AG) = Na - [Cl + HCO₃] = 12 (10-14) |
| Represents difference between unmeasured anions (proteins, phosphates, sulfates, organic acids = 23 mEq/L) and unmeasured cations (K, Ca, Mg = 11 mEq/L) |
| Affected by albumin, which is most abundant unmeasured anion. If hypoalbuminemic, the ‘normal’ AG is lower (by 2.5 mEq/L for every 1 gm/dL the albumin is decreased from 4.0). If pH is >7.5, more negative charges are exposed on albumin therefore the ‘normal’ AG is increased. |

INCREASED AG: can divide into 4 main categories: renal failure; ketoacidosis (diabetes, EtOH); drugs or poisons (MeOH, ASA, paraldehyde, ethylene glycol); lactic acidosis (± hypoxemia); sepsis. Pneumonic MUDPILES: Methanol, Uremia, Diabetic/alcoholic ketoacidosis, Paraldehyde, Isoniazid/Iron, Lactic acidosis/ketoacidosis, Ethylene glycol, Salicylates
NORMAL AG (hyperchloremic): GI loss of HCO₃; renal tubular acidosis, carbonic anhydrase inhibitor use (e.g., acetazolamide); renal compensation for respiratory alkalosis; drugs (cyclosporine, amphotB, cholestyramine); VIP-producing tumors; ureteral diversions. Pneumonic HARDUP: Hyperventilation, Acids (carbonic anhydrase inhibitors, Addison’s disease, TPN), RTA, Diarrhea, Ureterosigmoidostomy (and ileal diversions), Pancreatic fistula or drainage.

Compensation: in a maximally-compensated metabolic acidosis (which takes about 12-24 hours), Winter’s formula applies: Expected PaCO₂ = (1.5 x serum HCO₃)+(8±2); a shortcut to this formula is that the Expected PaCO₂ is approximately equal to the last two digits of the pH ± 2.
Using the “rule of 15” you can predict the PaCO₂ and pH from the serum HCO₃: measured HCO₃ + 15 = predicted PaCO₂ and the last two digits of the pH. As the HCO₃ drops below 10 and approaches 5 mEq/L, the PaCO₂ should go to 15.
If the PaCO₂ is lower than expected, there is also a concomitant primary respiratory alkalosis (this is NOT just better respiratory compensation).
If the PaCO₂ is higher than expected, then there is a concomitant primary respiratory acidosis.

Also: Check the Δ/Δ: This is the ΔAG/ΔHCO₃ (i.e., (change in anion gap from 12)/(change in bicarbonate from 24)) and is based upon the concept that the increase in the anion gap should equal the fall in the bicarbonate and the Δ/Δ ratio should therefore equal 1.0. Another way of expressing this is called the bicarbonate gap, which is (ΔAG - ΔHCO₃), and should equal zero. In other words, the ΔAG plus the measured HCO₃ should equal a normal HCO₃ of 24.

For an uncomplicated high AG metabolic acidosis, the Δ/Δ ratio should be between 1.0 and 2.0.
The disparity from 1.0 is related to volume of distribution of different anions (e.g., lactate remains primarily extracellular versus hydrogen ions which move intracellularly) and degree of buffering in cells and bone versus by HCO₃ in the extracellular compartment.
If the ΔAG is smaller than the ΔHCO₃ by at least 4 (HCO₃ falls by more than ΔAG; Δ/Δ less than 1.0; negative bicarbonate gap), then there is a superimposed process which is causing a further fall in the HCO₃ (non-gap metabolic acidosis and/or bicarbonate excretion as compensation for respiratory alkalosis).
If the ΔAG is greater than the ΔHCO₃ by at least 4 (HCO₃ falls by less than the ΔAG; Δ/Δ greater than 2.0; positive bicarbonate gap), then there is a superimposed metabolic alkalosis and/or bicarbonate retention as compensation for respiratory acidosis.
Given the variations in baseline ‘normal’ AG, baseline HCO₃, and electrolyte values, there is no absolute cut-off for these values. The more abnormal the Δ/Δ (bicarbonate gap), the more likely it reflects a concomitant acid-base disorder.

**METABOLIC ALKALOSIS**

Characteristics: increased serum HCO₃, increased extracellular pH (may see mild increase in PaCO₂ as compensation)

Causes: generally either volume contraction (volume loss: GI tract, kidneys, skin, respiratory system, third-spaced fluid, bleeding) or hypokalemia. Also, excessive glucocorticoids or mineralocorticoids, Bartter's syndrome, exogenous alkalai ingestion.

Two types: Chloride responsive and Chloride resistant.

Chloride responsive: vomiting, diuretics, NG suction, diarrhea, villous adenoma. Spot urine Cl should be less than 10 (except with diuretic use) since the kidney should be conserving Cl. Treatment with 0.9NS should fix the disturbance.

Chloride resistant: distal exchange site stimulation by aldosterone resulting in increased H⁺ and K⁺ excretion in exchange for resorption of Na⁺ as NaHCO₃.

Compensation: is highly variable, and in some cases there may be no or minimal compensation. In chronic metabolic alkalosis, the PaCO₂ should increase by roughly 5 mmHg for every 10 mEq/L increase in serum HCO₃.

**SIX-STEP APPROACH TO ACID-BASE ANALYSIS**

1. Acidemic or Alkalemic? pH < 7.38 or > 7.42 on ABG?
2. Is the overriding disturbance respiratory or metabolic?
   - Respiratory acidosis: PaCO₂ > 40 mmHg
   - Metabolic acidosis: serum HCO₃ < 24 mEq/L
3. If a respiratory disturbance is present, is it acute or chronic?
4. If metabolic acidosis is present, is there an increased anion gap?
   - can have an anion gap acidosis even with a normal anion gap if hypoalbuminemic (decrease in unmeasured anions).
   - anion gap may be increased due to metabolic alkalosis, if pH > 7.5 more negative charges are exposed on the surface of albumin therefore there is an increase in unmeasured anions.
5. If a metabolic disturbance is present, is the respiratory system compensating adequately?
   - there is a linear relationship between PaCO₂ and serum HCO₃ in metabolic acidosis
     - Winter's formula: expected PaCO₂ = [1.5 x (serum HCO₃)] + [8±2]
     - if PaCO₂ lower, there is a concomitant primary respiratory alkalosis
     - if PaCO₂ higher, there is a concomitant primary respiratory acidosis
   - the normal respiratory response is more difficult to predict for a primary metabolic alkalosis.
   - appropriate compensation occurs with decreased alveolar ventilation and increased PaCO₂, but the PaCO₂ rarely rises to levels above 50 mmHg
   - a subnormal PaCO₂ clearly indicates a concomitant primary respiratory alkalosis
   - if the PaCO₂ is ≥ 50 mmHg this suggests a superimposed primary respiratory acidosis
6. Are other metabolic disturbances present in the patient with an anion-gap metabolic acidosis?
   - calculate the corrected HCO₃ = delta gap + measured serum HCO₃
   - delta gap = calculated anion gap - 12 (normal anion gap)
   - if the corrected HCO₃ is greater than the expected 24 mEq/L, there is a concomitant primary metabolic alkalosis
   - if the corrected HCO₃ is less than the expected 24 mEq/L, there is a mixed disorder with a superimposed non-anion gap metabolic acidosis
ADDITIONAL CONSIDERATIONS and CALCULATIONS:

1. Osmolar gap:
   a. Osmolarity, calculated = 2Na + (glucose/20) + (BUN/3) + (EtOH/4)
   b. Osmolal Gap = Measured osmolality – Calculated osmolarity
   c. Normal Osmolar Gap is approximately 10; if greater, consider a toxic alcohol

2. Urinary Anion Gap:
   a. [UNa + UK] – UCl
   b. an indirect assay for urinary NH4 excretion
   c. negative urinary AG implies increased renal excretion of NH4 (GI; type II RTA such as Fanconi syndrome, amyloidosis, multiple myeloma, acetazolamide; exogenous acid)
   d. positive urinary AG implies failure of kidneys to excrete NH4 (type I RTA, type IV RTA, early renal failure)

REFERENCES: