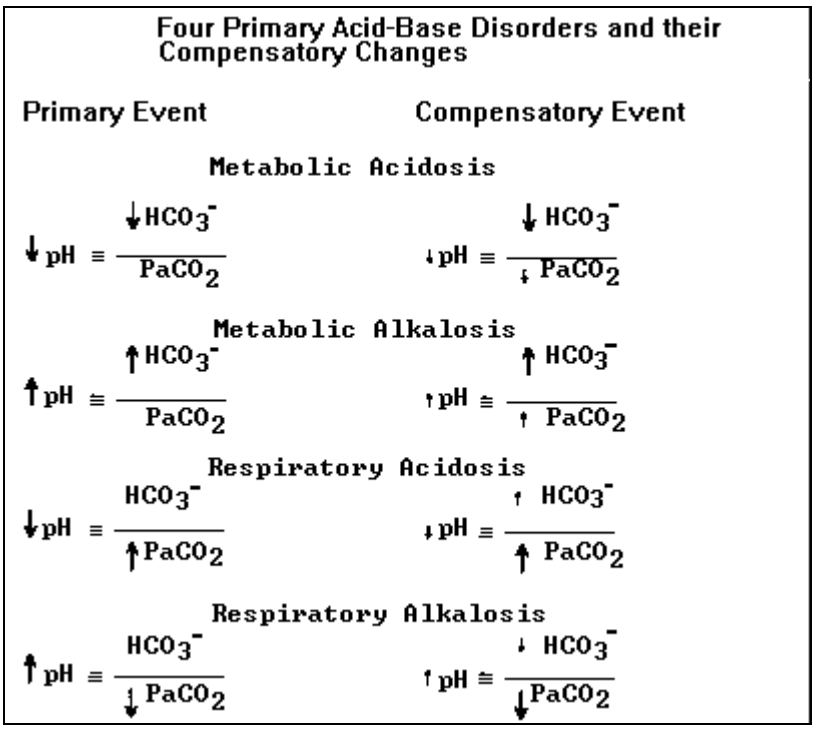
Evaluation of Acid-Base Disorders

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 $PaCO_2$ range: 38 – 42 mmHg (40 mmHg)
Normal serum CO_2 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 CO_2, it *represents* the bicarbonate moiety (HCO_3) that is buffered by organic acids.

Remember, $pH = - \log [H^+] = 6.10 + \log ([HCO_3] / [0.03 * PaCO_2]) \approx (HCO_3/PaCO_2)$



RESPIRATORY ACIDOSIS

Characteristics: elevated $PaCO_2$, decreased extracellular pH
(CO_2 production at tissue level exceeds 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 HCO_3 increases by 1 mEq/L per 10 mmHg increase in $PaCO_2$ (up to a $PaCO_2$ of 70)
CHRONIC: pH drops by 0.03 units and HCO_3 increases by 3-4 mEq/L per 10 mmHg increase in $PaCO_2$ (up to a $PaCO_2$ of 70)
Renal compensation (HCO_3 retention) generally at its maximum by 4 days, is never complete (i.e., pH is never normalized).

Consider: In general, if the HCO_3 is above 30, look for a second process (chronic respiratory acidosis, concomitant metabolic alkalosis).

RESPIRATORY ALKALOSIS

Characteristics: decreased $PaCO_2$, increased extracellular pH
(implies that the increase in alveolar ventilation and consequent decrease in $PaCO_2$ 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 HCO_3 decreases by 2 mEq/L per 10 mmHg decrease in $PaCO_2$ (down to a $PaCO_2$ of 20)

CHRONIC: pH increases by 0.03 units and HCO_3 decreases by 5 mEq/L per 10 mmHg decrease in $PaCO_2$ (down to a $PaCO_2$ of 20)

Renal compensation via suppression of renal acid secretion and subsequent consumption and decrease in serum HCO_3. In contrast to respiratory acidosis, however, the compensation for a long-standing process may eventually become complete (i.e., pH normal).

Consider: If the HCO_3 has dropped by more than 2-4, consider a superimposed metabolic acidosis, ASA, sepsis, or chronic hyperventilation.

METABOLIC ACIDOSIS

Characteristics: decreased serum HCO_3, decreased extracellular pH

Causes: divide into INCREASED versus NORMAL ANION GAP causes.

Anion Gap (AG) = $Na - [Cl + HCO_3] = 12$ (10-14)
{best 'normal' AG is from recent electrolytes measured when the patient had a normal acid-base balance}
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 HCO_3; renal tubular acidosis, carbonic anhydrase inhibitor use (e.g., acetazolamide); renal compensation for respiratory alkalosis; drugs (cyclosporine, amphoB, cholesyramine); 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 $PaCO_2 = (1.5 \times \text{serum } HCO_3) + (8 \pm 2)$; a shortcut to this formula is that the Expected $PaCO_2$ is approximately equal to the last two digits of the pH ± 2.

Using the "rule of 15" you can predict the $PaCO_2$ and pH from the serum HCO_3: measured HCO_3 + 15 = predicted $PaCO_2$ and the last two digits of the pH. As the HCO_3 drops below 10 and approaches 5 mEq/L, the $PaCO_2$ should go to 15.

If the $PaCO_2$ is lower than expected, there is also a concomitant primary respiratory alkalosis (this is NOT just better respiratory compensation).

If the $PaCO_2$ is higher than expected, then there is a concomitant primary respiratory acidosis.

Also: Check the Δ/Δ: This is the $\Delta AG/\Delta HCO_3$ [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 ($\Delta AG - \Delta HCO_3$), and should equal zero. In other words, the ΔAG plus the measured HCO_3 should equal a normal HCO_3 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 HCO_3 in the extracellular compartment.

If the ΔAG is smaller than the ΔHCO_3 by at least 4 (HCO_3 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 HCO_3 (non-gap metabolic acidosis and/or bicarbonate excretion as compensation for respiratory alkalosis).

If the ΔAG is greater than the ΔHCO_3 by at least 4 (HCO_3 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 HCO_3, 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 HCO_3, increased extracellular pH (may see mild increase in $PaCO_2$ 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 $NaHCO_3$.

Compensation: is highly variable, and in some cases there may be no or minimal compensation. In chronic metabolic alkalosis, the $PaCO_2$ should increase by roughly 5 mmHg for every 10 mEq/L increase in serum HCO_3.

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: $PaCO_2$ > 40 mmHg
   Metabolic acidosis: serum HCO_3 < 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 $PaCO_2$ and serum HCO_3 in metabolic acidosis
     Winter's formula: expected $PaCO_2$ = [1.5 x (serum HCO_3)] + [8±2]
     if $PaCO_2$ lower, there is a concomitant primary respiratory alkalosis
     if $PaCO_2$ 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 $PaCO_2$, but the $PaCO_2$ rarely rises to levels above 50 mmHg
     - a subnormal $PaCO_2$ clearly indicates a concomitant primary respiratory alkalosis
     - if the $PaCO_2$ is $\geq$ 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 HCO_3 = delta gap + measured serum HCO_3
   delta gap = calculated anion gap – 12 (normal anion gap)
   if the corrected HCO_3 is greater than the expected 24 mEq/L, there is a concomitant primary metabolic alkalosis
   if the corrected HCO_3 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:

M.L. Morganroth (1990) An analytic approach to diagnosing acid-base disorders. J. Crit. Illness 5(2):138-150.