Acid-base disturbances are common in critically ill and emergency patients, but the clinical signs associated with these disturbances are often vague. A systematic approach to blood gas analysis can yield a large amount of information in a short period of time. This lecture will cover a basic, 7 step approach to traditional blood gas analysis that can be used clinically to rapidly identify acid-base disturbances and guide treatment for emergent and critically ill patients. The following are the 7 steps:

1. Determine sample type
2. Interpret the pH
3. Evaluate the respiratory component
4. Evaluate the metabolic component
5. Determine the primary disorder(s)
6. Look for evidence of compensation
7. Evaluate oxygenation

Step 1: Determine the sample type
There are 2 basic types of blood gas samples: peripheral venous and arterial. For the purpose of acid-base analysis, any sample type can be used. When evaluating oxygenation of the sample (step 7), it is important that the type of sample is considered, as this will have a major impact on interpretation.

Step 2: Interpret the pH
The pH of the blood is the negative log of the hydrogen ion concentration and is normally between 7.35 and 7.45. If the blood pH is less than 7.35, the patient is acidemic, and if the pH is greater than 7.45, the patient is alkalemic. These terms reflect disturbances in the pH, not the underlying physiologic processes leading to the pH change, which are termed acidosis and alkalosis. It is important to remember that a patient may have a normal pH despite serious underlying acid-base disturbances, so all 7 steps must be completed even if the pH is found to be normal.

Step 3: Evaluate the respiratory component
CO₂ acts as an acid in the blood and lowers the pH. The partial pressure of CO₂ in the blood (PCO₂) is inversely proportional to minute ventilation, the product of respiratory rate and tidal volume. The higher the minute ventilation, the lower the PCO₂ in arterial and venous blood. The gradient between arterial and venous PCO₂ is usually less than 5 mmHg, so PCO₂ can be evaluated in arterial, peripheral venous, or central/mixed venous samples. Normal PCO₂ is 35-45 mmHg.

   Respiratory Acidosis: Patients with decreased minute ventilation, due to a decrease in respiratory rate, tidal volume, or both are by definition hypoventilating, leading to a respiratory acidosis from a PCO₂ of greater than 45 mmHg. Differential diagnoses for respiratory acidosis include any disease processes that compromise minute ventilation, such as upper airway obstruction, lower airway obstruction (asthma, bronchitis), pleural space disease, chest wall disease, abdominal distention, central nervous system disease, and peripheral neuropathies.

   Respiratory Alkalosis: An increased minute ventilation leads to a decrease in PCO₂ and a respiratory alkalosis. Stress, pain, fear, hyperthermia, and anxiety can all cause respiratory alkaloses. However, anemia and hypoxemia will both also lead to hyperventilation and respiratory alkalosis, and are potentially life-threatening. Therefore, it is imperative that a packed cell volume and pulse oximetry reading or arterial blood gas analysis be done in all patients with respiratory alkaloses to rule out these 2 differential diagnoses.

Step 4: Evaluate the metabolic component
Metabolic disturbances may be identified in patients by deviations in blood bicarbonate (HCO₃⁻) concentrations. Bicarbonate is the major extracellular buffer, and changes in bicarbonate reflect metabolic disturbances that can affect the blood pH. Intracellularly, other buffer systems are more important for maintaining acid-base balance, including phosphate and proteins like hemoglobin. Normal blood bicarbonate concentrations are approximately 20-25 mmol/L, and
patients with low bicarbonate have metabolic acidoses, while those with high bicarbonates have metabolic alkaloses. Although bicarbonate is the major determinant of metabolic acid-base balance and CO₂ is the major determinant of respiratory acid-base balance, the 2 exist in an equilibrium:

\[
\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+
\]

If a patient hypoventilates (has a respiratory acidosis), the CO₂ will increase and the equilibrium above will be shifted to the right, increasing the bicarbonate concentration. This has nothing to do with metabolic acid-base status, but is simply a reflection of this equilibrium. Conversely, if the patient hyperventilates (has a respiratory acidosis), the CO₂ will decrease and the equilibrium will be shifted to the left, decreasing the bicarbonate concentration.

Because the bicarbonate concentration is affected by changes in CO₂, when evaluating the metabolic component of acid-base balance, the use of the base excess (BE) may be preferable. The concept behind the BE is that if the patient’s blood sample were equilibrated to a PCO₂ of 40 mmHg (the middle of the reference range), and acid was titrated into the sample until the pH reached exactly 7.40, the amount of acid added would be the BE. Therefore, the BE represents the extra base present in the sample when the CO₂ is normalized, and is a more reliable measure of the metabolic acid-base balance of the patient. The BE normally ranges between 0 and -4 mmol/L.

**Metabolic acidosis**

Patients with a bicarbonate of less than 20 mmol/L or a BE of less than -4 mmol/L have metabolic acidoses. A metabolic acidosis can be due to two causes: (1) excess acid, or (2) loss of buffer (base). When a patient is diagnosed with a metabolic acidosis, the anion gap can help differentiate between these 2 causes. The principle behind the anion gap is that electroneutrality is always maintained in the blood, meaning that the sum of the positive charges (the cations, in the left column of the figure to the right) must be equal to the sum of all of the negative charges (the anions, in the right column). The cations consist of sodium and potassium, with a small net positive charge being contributed by the “unmeasured cations” (UC) calcium and magnesium. The anions consist mostly of chloride and bicarbonate, with a larger (compared to the UC) net negative charge contributed by the unmeasured anions (UA). In a healthy patient with no underlying acid base disturbance, the majority of the UA is comprised of albumin, which has many negatively charged groups. The anion gap (AG) is the difference between the UA and the UC (AG = UA – UC). Due to electroneutrality, this can be calculated using parameters commonly available on a blood gas using the equation:

\[\text{AG} = (\text{Na} + \text{K}) – (\text{Cl} + \text{HCO}_3^-)\]

Because acidic compounds consist of an anion with an associated hydrogen ion, patients with metabolic acidosis due to an increase in acidic compounds will have an increase in the unmeasured anions, a decrease in bicarbonate, and an increase in the anion gap. There are 4 differential diagnoses for patients with metabolic acidosis associated with an elevated anion gap, all of which are due to an increase in acidic compounds:

1. Lactic acidosis (acid = lactic acid)
2. Diabetic ketoacidosis (acid = ketoacids)
3. Uremic acidosis (acid = sulfates and phosphates)
4. Exogenous acid ingestion (examples = ethylene glycol and salicylates)

In contrast, patients may develop a metabolic acidosis due to a primary loss of buffer (bicarbonate). Bicarbonate can be lost in 2 places:

1. Small bowel diarrhea
2. Renal tubular acidosis (RTA)

Note that patients with RTA do not have elevations in BUN and creatinine, but suffer from primary renal tubular dysfunction resulting in inappropriate handling of bicarbonate and hydrogen ion. Because the primary disturbance in these diseases is loss of bicarbonate rather than increased acid, these diseases are associated with a normal anion gap. Therefore, the anion gap can be useful to prioritize these 2 groups of differential diagnoses in patients with metabolic acidoses.

**Metabolic alkalosis**

The most common cause of metabolic alkalosis in dogs and cats is vomiting, especially when it is due to an upper GI obstruction. Large amounts of chloride and hydrogen ion are lost in the vomitus. The ensuing hypovolemia stimulates reabsorption of sodium in the kidney to maintain intravascular volume and release of aldosterone. In the absence of chloride (which is lost in the vomitus), proximal tubular reabsorption of sodium is limited and the patient must reabsorb 2
as much sodium as possible in the distal tubule under the influence of aldosterone, resulting in potassium depletion. This also leads to excretion of hydrogen ions in the distal tubule and reabsorption of bicarbonate, leading to progressive metabolic alkalosis and excretion of acidic urine. The constellation of a hypochloremic metabolic alkalosis, hypokalemia, and paradoxical aciduria (called “paradoxic” because the urine would be expected to be acidic in the face of a metabolic alkalosis) is suggestive of an upper GI obstruction. Other causes of metabolic alkalosis are primarily iatrogenic, and include sodium bicarbonate administration and the use of furosemide, which blocks the sodium, potassium, 2 chloride co-transporter in the loop of Henle, leading to excessive loss of chloride and retention of bicarbonate.

**Step 5: Determine the primary disorder**

If only a single acid-base disturbance is noted in steps 3 and 4, it is the primary disorder and differential diagnoses should be considered as discussed above. If both a respiratory and metabolic disturbance is noted, and both are of the same type (i.e., both metabolic and respiratory acidosis or both metabolic and respiratory alkalosis), then both disorders are independently contributing to the abnormal pH and differential diagnoses for both disorders must be investigated. If both a respiratory and metabolic disorder are identified and they are affecting the pH in opposite ways (e.g., metabolic acidosis and respiratory alkalosis), the primary disturbance will always be consistent with the pH change. For example, if the patient is acidemic, has a metabolic acidosis and a respiratory alkalosis, the metabolic acidosis is likely the primary disturbance.

**Step 6: Look for evidence of compensation**

When an acid-base disturbance develops, in an attempt to normalize the pH, a compensatory disturbance may develop. The primary disturbance will always be consistent with the pH change. For example, if the patient is acidemic, has a metabolic acidosis and a respiratory alkalosis, the metabolic acidosis is likely the primary disturbance, and it is possible that the respiratory alkalosis is compensatory. It is possible to determine whether the degree of compensation noted on a blood gas is appropriate for the severity of the primary disorder using the following compensation equations.

<table>
<thead>
<tr>
<th>Acid-Base Disorder</th>
<th>Expected Compensation</th>
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<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>Each 1 mEq/L decrease in HCO₃⁻ will decrease PCO₂ by 0.7 mmHg.</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>Each 1 mEq/L increase in HCO₃⁻ will increase PCO₂ by 0.7 mmHg.</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>Each 1 mmHg increase in PCO₂ will increase HCO₃⁻ by 0.15 mEq/L. Each 1 mmHg increase in PCO₂ will increase HCO₃⁻ by 0.35 mEq/L.</td>
</tr>
<tr>
<td>Acute</td>
<td>Chronic</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Each 1 mmHg decrease in PCO₂ will decrease HCO₃⁻ by 0.25 mEq/L. Each 1 mmHg decrease in PCO₂ will decrease HCO₃⁻ by 0.55 mEq/L.</td>
</tr>
<tr>
<td>Acute</td>
<td>Chronic</td>
</tr>
</tbody>
</table>

It is important to note that respiratory compensation for a primary metabolic disorder will happen rapidly, within seconds to minutes of the disturbance occurring. However, metabolic compensation for a respiratory acid-base disturbance is accomplished by excretion or retention of bicarbonate in the kidney, which can take hours to start and more than a day to reach maximal efficiency. Therefore, absence of metabolic compensation for a respiratory disturbance is suggestive of an acute process, whereas evidence of compensation suggests the problem is more chronic.

**Step 7: Evaluate oxygenation**

Oxygen saturation (SO₂) or the partial pressure of oxygen dissolved in the plasma (PO₂) can provide useful information for some type of blood gases. When interpreting these values, it is important to first confirm the sample type.

*Peripheral Venous Sample:* Assessment of oxygenation for peripheral venous blood samples is rarely helpful. Because the value will be affected by local factors and the degree to which the vessel was held off to collect the sample, it yields very little information about global patient status.

*Arterial Sample:* Because blood sampled from a peripheral artery has not yet perfused a tissue bed, the oxygen content of the arterial blood can yield important information about pulmonary gas exchange. In patients breathing room air, arterial PO₂ (PₐO₂) should be between 80-100 mmHg and arterial hemoglobin saturation (S,O₂) should be 95-100%. Patients with values less than these are hypoxemic and are at risk of tissue hypoxia and organ damage. Supplemental oxygen should be provided as soon as possible in these patients until the type of respiratory disease is definitely identified and treated.
Conclusions
With practice, a full evaluation of a blood gas using this 7 step approach can be accomplished in 1-2 minutes, yielding important information about emergent or critically ill patients.