Beyond Blood Gases: Making Use of Additional Oxygenation Parameters and Plasma Electrolytes in the Emergency Room*

Abstract: When provided with an emergency blood gas or electrolyte readout, clinicians must identify the critical parameters that require immediate intervention. This article provides concepts in oxygenation and electrolyte evaluation to help fine-tune the initial treatment and monitoring orders for emergency patients.

Oxygenation Parameters

PaO₂/FIO₂ Ratio
Normal reference values for the alveolar–arterial (A–a) gradient can vary up to 100 mm Hg in animals receiving oxygen supplementation with a fraction of inspired oxygen (FIO₂) >0.21. Therefore, when arterial blood gases for animals receiving oxygen supplementation are assessed, the ratio of the arterial partial pressure of oxygen (PaO₂) to the FIO₂ (PaO₂/FIO₂ or P/F ratio) allows objective estimation of oxygenation at different concentrations of inspired oxygen. A healthy small animal breathing room air (FIO₂ = 0.21) should have a measured PaO₂ approximating 100 mm Hg and a P/F ratio of around 500. Supplemented with 100% oxygen (FIO₂ = 1.0), this same patient should have a measured PaO₂ approximating 500 mm Hg and a similar P/F ratio. A P/F ratio >400 suggests that pulmonary function is normal. As respiratory function progressively decreases, the ratio decreases and approaches 200. In humans, a P/F ratio <200 meets the criteria for acute respiratory distress syndrome. In essence, the P/F ratio can help identify the adequacy of the patient’s response to oxygen therapy. PaO₂ is measured as part of the arterial blood gas analysis, whereas FIO₂ can be measured with a handheld oximeter or estimated (TABLE 1).

Arterial Oxygen Saturation
PaO₂ serves as the driving force to push dissolved oxygen into hemoglobin molecules. Saturated hemoglobin is then responsible for carrying approximately 98% of the total blood oxygen content to tissue. The oxygen–hemoglobin dissociation curve depicts the relationship between PaO₂ and arterial oxygen saturation (SaO₂; FIGURE 1). A patient with a PaO₂ of 60 mm Hg has an SaO₂ of approximately 91%. This corresponds to a level of hypoxemia below which therapeutic intervention may be warranted. Further PaO₂ reduction from 60 mm Hg causes stress to the patient, and even minor additional decreases in PaO₂ are associated with significant oxygen dissociation from the hemoglobin molecules, as demonstrated by the steep portion of the curve.

Arterial Oxygen Content
SaO₂ provides no information about blood oxygen content because a patient can have a very low hemoglobin concentration (i.e., severe anemia) but still be fully saturated (SaO₂ of 99% to 100%). The arterial oxygen content (CaO₂) equation indicates how much oxygen is available to the tissues. It incorporates hemoglobin saturation (SaO₂) and hemoglobin concentration (Hb) as well as the relatively minor contribution...
of unbound or freely dissolved oxygen \( (P_aO_2) \). The normal range of \( CaO_2 \) is 16 to 20 mL oxygen/dL of blood. The following formula is used to calculate \( CaO_2 \):\[ CaO_2 = (Hb \times 1.34 \times SaO_2) + (P_aO_2 \times 0.003) \]

\[ 98\% \text{ Bound} + 2\% \text{ Dissolved} = \% \text{ Oxygen content} \]

[Hb] can be estimated by multiplying the measured hematocrit by one-third or can be measured with a hemoglobinometer; the normal [Hb] is 15 mg/dL. The constant 1.34 is the amount of oxygen (in mL) that each gram of hemoglobin can bind when fully saturated. \( SaO_2 \) is the actual percentage of oxygen saturation, and 0.003 is the solubility constant for dissolved (unbound) oxygen in plasma at body temperature.

This calculation is useful in anemic patients, which can have \( P_aO_2 \) and \( SaO_2 \) within normal limits while \( CaO_2 \) remains markedly reduced until [Hb] is increased with a transfusion of blood or hemoglobin-based oxygen carrier.

**Electrolytes**

**The Anion Gap**

The anion gap (AGap) is an adjunct to blood gas evaluation that helps differentiate causes of metabolic acidosis. It is calculated as the difference between the measured plasma concentrations of the major positively charged ions (cations) and the major negatively charged ions (anions). In reality, the body always attempts to maintain electoneutrality, so the concentration of serum cations equals that of anions.

**FIGURE 2** shows the approximate plasma concentrations of cations and anions in healthy dogs and cats. The charge contributions of cations and anions must balance each other to maintain electrochemical neutrality.

The AGap exists because standard electrolyte panels do not measure all the anions present in serum; thus, in general, the AGap represents the unmeasured anions (proteins, organic acids, and inorganic acids). In a healthy dog or cat, plasma proteins account for most of the AGap. As shown in **FIGURE 3**, the AGap is calculated from four measured chemistry values: sodium (Na\(^+\)), potassium (K\(^+\)), chloride (Cl\(^-\)), and bicarbonate (HCO\(_3^-\)) ion concentrations. The serum total carbon dioxide (TCO\(_2\)) concentration can be used in place of the HCO\(_3^-\) concentration.

Metabolic acidosis, a very common acid–base disturbance in critically ill small animal patients, causes a reduction in HCO\(_3^-\) concentration. When there is an increase in unmeasured anions or in the Cl\(^-\) concentration, the HCO\(_3^-\) concentration decreases to maintain electrochemical bal-

**TABLE 1** Methods of Oxygen Supplementation and Approximate \( FiO_2 \) Achieved

<table>
<thead>
<tr>
<th>Administration Technique</th>
<th>Recommended Oxygen Flow Rate (L/min)</th>
<th>Mean ( FiO_2 ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face mask, loose fit</td>
<td>2–5</td>
<td>40–50</td>
</tr>
<tr>
<td>Flow-by</td>
<td>2–5</td>
<td>25–40</td>
</tr>
<tr>
<td>Elizabethan collar canopy</td>
<td>1–5</td>
<td>30–50</td>
</tr>
<tr>
<td>Nasal catheter (unilateral)</td>
<td>≤2</td>
<td>40–50</td>
</tr>
<tr>
<td>Nasal catheter (bilateral)</td>
<td>≤2 for each</td>
<td>40–50</td>
</tr>
<tr>
<td>Intratracheal catheter</td>
<td>1</td>
<td>40–60</td>
</tr>
<tr>
<td>Oxygen cage</td>
<td>As needed to maintain ( FiO_2 ) at 40%–60%</td>
<td>21–60</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1–2</td>
<td>100</td>
</tr>
</tbody>
</table>

The oxygen dissociation curve showing \( P_aO_2 \) versus \( SaO_2 \). The shaded portion represents the steep part of the curve (i.e., \( P_aO_2 \leq 60 \text{ mm Hg and } SaO_2 < 91\% \)). With \( P_aO_2 \) in the 100 to 500 mm Hg range, \( SaO_2 \) remains fully saturated at 98% to 99%; this corresponds to the upper, flat portion of the curve. \( P_aO_2 \) = arterial partial pressure of oxygen, \( SaO_2 \) = arterial oxygen saturation.
Increased AGap acidosis arises when excess acid containing unmeasured anions (i.e., anions other than Cl−) accumulates in the blood. Examples include lactic acidosis, ketoacidosis, uremic acidosis (phosphate and sulfate acidosis), ethylene glycol (antifreeze) poisoning, and salicylic acid (aspirin) poisoning. These excess anions titrate the HCO3− concentration downward, thus preserving electrochemical balance.13

Metabolic acidosis characterized by a normal AGap arises when chloride, which is routinely measured, is added to the blood (e.g., dilutional acidosis with aggressive sodium chloride fluid administration) or when HCO3− loss from the body (e.g., associated with diarrhea) is replaced with chloride to maintain electrochemical balance.15 Again, the excess Cl− titrates the HCO3−, thereby preserving the electrochemical balance.

The first step in incorporating the AGap into the acid–base evaluation is to identify metabolically acidosis from the pH and the base excess of the extracellular fluid (or HCO3−) value. If metabolic acidosis is present, the adequacy of the normal physiologic compensatory reaction (i.e., decreased PCO2) should be determined. If the compensation is adequate, a simple acid–base disorder is present.3 The AGap should then be evaluated for the presence of high or normal AGap acidosis. If the AGap is normal, hyperchloremic metabolic acidosis is most likely present, although the AGap may be falsely normal in patients with low serum proteins (see Hypoalbuminemia section below). If the AGap is increased, high AGap acidosis is present and the bicarbonate gap should be calculated to help identify possible concurrent mixed metabolic disorders.

The Bicarbonate Gap

The bicarbonate gap is defined as the increase in the AGap from the midpoint of its reference range (∆AGap) minus the change in HCO3− concentration from the midpoint of their respective reference ranges (∆HCO3− or ∆TCO2; FIGURE 4).14 It serves to identify non-parallel changes in HCO3− concurrent with high AGap acidosis.14 If AGap acidosis is the only acid–base abnormality, there should be a 1:1 correlation between the rise in AGap and the fall in HCO3−, and the bicarbonate gap should be zero. For example, if the AGap goes up by 10 mEq/L, indicating high AGap metabolic acidosis, then the HCO3− or serum TCO2 should go down by 10 mEq/L. A bicarbonate gap other than zero suggests a mixed metabolic disorder.14 If the bicarbonate gap is positive, mixed AGap acidosis and concurrent metabolic alkalosis should be suspected. If the bicarbonate gap is negative, mixed AGap and hyperchloremic acidosis should be suspected.

A positive bicarbonate gap suggests that the HCO3− value is higher than expected for a given concentration of unmeasured anions, which would develop, for example, in a vomiting patient with concurrent lactic acidosis from impaired tissue perfusion and hypochloremia from loss of hydrochloric acid in the vomitus. In this case, the AGap would be increased but the HCO3− level would not be equally decreased because of the concurrent Cl− loss (FIGURE 5). This mixed meta-
Approximate plasma concentrations of commonly measured electrolytes in dogs and cats. These are used to calculate the AGap. The AGap represents the unmeasured serum anions (proteins, organic acids, and inorganic acids). Sodium (Na⁺), potassium (K⁺), chloride (Cl⁻), and bicarbonate (HCO₃⁻) concentrations are measured in mEq/L. The serum TCO₂ concentration can be used as a replacement for the HCO₃⁻ concentration.

An example of a positive bicarbonate gap in a vomiting patient with lactic acidosis. The decreases in HCO₃⁻ concentration are less than expected (small arrow) for a simple AGap acidosis. This is an example of mixed AGap acidosis and metabolic alkalosis. These two disorders have opposing (neutralizing) effects on the blood’s pH.

The bicarbonate gap serves to identify nonparallel changes in bicarbonate concurrent with high AGap acidosis. If the AGap acidosis is the only acid–base abnormality, then the bicarbonate gap should be zero. If the bicarbonate gap is positive, a mixed AGap acidosis and a concurrent metabolic alkalosis should be suspected. If the bicarbonate gap is negative, a mixed AGap and hyperchloremic acidosis should be suspected.

Approximate plasma concentrations of commonly measured electrolytes in dogs and cats. These are used to calculate the AGap. The AGap represents the unmeasured serum anions (proteins, organic acids, and inorganic acids). Sodium (Na⁺), potassium (K⁺), chloride (Cl⁻), and bicarbonate (HCO₃⁻) concentrations are measured in mEq/L. The serum TCO₂ concentration can be used as a replacement for the HCO₃⁻ concentration.

An example of a negative bicarbonate gap in a patient with diabetic ketoacidosis treated with 0.9% NaCl replacement fluid. The decreases in HCO₃⁻ concentration are in excess (double arrow) of those expected for a simple AGap acidosis. This is an example of concurrent mixed AGap acidosis and hyperchloremic metabolic acidosis. These two disorders have additive effects on the blood’s pH.

The metabolic acidosis in this case could be severe because of the two concurrent sources of bicarbonate loss. The low blood pH may prompt the use of more alkalinizing IV fluid crystalloids.

Hypoalbuminemia
Because the AGap in healthy dogs and cats is mostly a result of the negative charge of serum proteins, hypoalbuminemia can lead to underestimation of high AGap metabolic acidosis. Patients with high levels of unmeasured anions (e.g., increased lactic acid due to hypotension) and concurrent hypoalbuminemia may have normal AGap measurements because the low albumin concentration causes the AGap to decrease, perhaps back to the reference range. In dogs, for each 1 g/dL decrease in albumin, there is a corresponding 4.1 mEq/L decrease in the AGap. The following formula can be used to correct the AGap for changes in albumin concentration and reveal an increased AGap acidosis:

\[(\text{AGap}_{\text{measured}} + 4.2) \times (3.77 - [\text{albumin}_{\text{measured}}]) = \text{AGap}_{\text{corrected}}\]
References