Fundamentals of Arterial Blood Gas Interpretation

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Abstract
Acid-base disturbances in patients with cardiopulmonary or other disorders are common and are often misinterpreted or interpreted incompletely. Treating acid-base disorders in greater detail facilitates pathophysiologic understanding and improved therapeutic planning. Understanding the ratiometric relationship between the lungs, which excrete volatile acid as carbon dioxide, and the kidneys, which contribute to maintenance of plasma bicarbonate, allows precise identification of the dominant acid-base disturbance when more than a simple disorder is present and aids in executing a measured treatment response. Concordantly, mapping paired values of the partial pressure of carbon dioxide (PCO2) and the bicarbonate concentration ([HCO3−]) on a Cartesian coordinate system visually defines an acid-base disorder and validates the ratiometric methodology. We review and demonstrate the algebraic and logarithmic methods of arterial blood gas analysis through the example of a complex acid-base disorder, emphasizing examination of the PCO2-to-[HCO3−] ratio.

Case
A 62-year-old man with a history of chronic obstructive pulmonary disease and congestive heart failure presented to an emergency department for dyspnea. He was tachypneic and fatigued and had left elbow swelling with erythema. He reported not having any fever, chills, nausea, or vomiting and was subsequently admitted for observation. The patient had a long-standing history of chronic obstructive pulmonary disease from long-term cigarette smoking. Two weeks before admission, the patient had developed bilateral lower extremity edema and an unspecified amount of weight gain. The patient’s primary care physician prescribed a thiazide diuretic to reduce the edema. After hospitalization, the patient’s plasma electrolytes were sodium 136 mM, potassium 1.8 mM, chloride 52 mM, total carbon dioxide (TCO2) 68 mM, BUN 46 mg/dL, and creatinine 1.21 mg/dL. An initial arterial blood gas (ABG) measurement revealed a pH of 7.5, partial pressure of oxygen (PO2) of 88.5 mm Hg, partial pressure of carbon dioxide (PCO2) of 93.7 mm Hg, and calculated a bicarbonate concentration ([HCO3−]) of 73.1 mM.

Introduction
This brief treatise aims to expose the mathematical intricacies of ABG analysis for greater comprehension of acid-base disturbances. Often, ABG interpretation is required to elucidate an underlying combination of disorders and their severity fully. Proper interpretation of ABG requires an appreciation of its measurement limitations and insight into the components that constitute an ABG. Adherence to a disciplined approach to ABG interpretation should precede examination of electrolytes (i.e., plasma/serum anion gap [AG]) (1,2). Mixed acid-base disorders should first be determined by accurate interpretation of ABG.

ABG Measurement
An ABG machine measures pH, PCO2, and PO2. The [HCO3−] is calculated. Arterial pH is normally 7.35–7.45, and PCO2 is normally 35–45 mm Hg (3,4). The pH, measured amperometrically as hydrogen (H+) activity, is accurate to within 0.01 pH units, and the PCO2, measured using bicarbonate electrode chemistry, is typically accurate to within ±2 mm Hg. The normal PO2 is age dependent, and the reader is referred to the published literature for these values. After acquisition of a specimen for ABG analysis, chilling the specimen on ice before laboratory measurement has been recommended. A 0°C-chilled sample may be analyzed up to 60 minutes later. However, if the specimen is transported to the laboratory within 5 minutes, no chilling is necessary. Unchilled samples must be analyzed rapidly because PCO2 increases by 3–10 mm Hg per hour. Consequently, the pH will decline, and the PO2 will decline. Air bubbles will usually lead to overestimation of PO2, but underestimation can occur among patients mechanically ventilated with PaO2 >150 mm Hg (5). Overheparinization of the sample will dilute [HCO3−], PCO2, and PO2 (6). This procedural error is obviated by preheparinized ABG sample collection syringes. Pain, either anticipatory or real from inaccurate needle entry during specimen acquisition, may lead to acute lowering of PCO2, with consequent respiratory alkalosis.
Accordingly, less painful earlobe (heated) capillary blood may be used as a substitute for arterial blood, with excellent correlation between capillary and arterial ABG analyses for pH and PCO₂.

### pH and [H⁺] Determinations

The concept of pH was originally defined in 1909 by Sørensen as the power (potenz) of [H⁺]₀ (8). Currently, pH is defined as a function of H⁺ activity (a). Thus, pH equals −LOG aH⁺. Because the aH⁺ in physiologic fluids is 1, except in gastric fluids, pH becomes −LOG [H⁺] (nM), and [H⁺] = 10⁻ᵖᴴ. The concept of [H⁺] is easier to comprehend than logarithmic pH units and more easily manipulated because it is algebraically determined by the Henderson equation of 1908 (9,10):

$$[H^+] = 23.9 \times \left[ \frac{PCO_2}{[HCO_3^-]} \right] = 10^{(9-\text{pH})} \quad (1)$$

Conventionally, the coefficient 23.9 is rounded to 24 for ease of calculation. After determining [H⁺] from the pH and measurement of PCO₂ [HCO₃⁻] is calculated. The Henderson–Hasselbalch (H–H) equation of 1917 is a general equation that is applicable to the human bicarbonate-buffer system and is defined as Equation (2) (11,13–15):

$$dCO_2 + H_2O \rightarrow H_2CO_3 \rightarrow [H^+] + [HCO_3^-] \quad (2)$$

The H–H equation utilizes the apparent pKₐ (6.1) and the Bunsen coefficient (a, 0.0301 mmol/L.mm Hg) that defines the absorption of CO₂ gas in plasma at 37.5°C at barometric pressure 760 mm Hg (14–16).

$$pH = pK_a + \log(\left[ HCO_3^- \right]/dCO_2)$$

$$= pK_a + \log\left( [HCO_3^-] / (aPCO_2) \right) = -\log[H^+] \quad (3)$$

[H⁺] is determined to validate ABG [HCO₃⁻] internally, [H⁺] can be estimated or calculated from pH. Internal validity of the ABG is accomplished by determining the [HCO₃⁻] from the [H⁺] and PCO₂ (1,2). Arterial [H⁺] is determined from pH and [HCO₃⁻] from the Henderson equation. The Henderson equation–calculated [HCO₃⁻] should closely approximate the [HCO₃⁻] reported by the ABG machine.

Because of the near-linear relationship between pH and [H⁺] in the pH interval of 7.25–7.5, an estimated [H⁺] can be made by a “rule of 80” (Table 1) (1,2,16). Subtracting the last two digits of the pH from 80 approximates [H⁺]. Alternatively, one can successively multiply or divide [H⁺] from its normal baseline of 40 nM by 1.25 for each ΔpH of 0.1 units (Table 1). The multiplication/division method is the more accurate of these two estimation methods at pH >7.5 or <7.2 (1).

Because hand-held calculators and smartphones have logarithmic functions, [H⁺] can be rapidly computed as [H⁺] = 10⁻ᵖᴴ, in the above case, [H⁺] = 10⁻⁷⁻⁻⁷.5 or 31.6 nM. Determining [HCO₃⁻] from [H⁺] rapidly yields a value of 71.2 mM (24×93.7/31.6), equaling the calculated value of 70.6 mM and confirming internal validity of the data.

Previously, arterial [HCO₃⁻] was determined from a nomogram after acquisition of pH and PCO₂ (16–18). Because accuracy depended on the fastidiousness of the laboratory technologist, [HCO₃⁻] was occasionally misinterpreted and reported in error, and an “impossible” ABG would be reported. Although [HCO₃⁻] is now conveniently calculated by an autoanalyzer with embedded calculation of the H–H equation, the authors recommend performing a [HCO₃⁻] validation step because ABG results are often transmitted by telephone in “stat” situations and transcription errors still occur.

### Venous TCO₂ and Blood Gas Bicarbonate Concentration

ABG autoanalyzers compute [HCO₃⁻] from the H–H equation. The venous TCO₂ or CO₂ content is not a single analyte. It is composed of dissolved CO₂, erythrocyte carbamino compounds, and carbonic acid (H₂CO₃) and has historically been determined by addition of strong alkali to plasma, electrolytically, or by an enzymatic technique, which was used in the index patient (12,15,16,19). The H–H equation denominator equals dCO₂ plus short-lived carbonic acid (H₂CO₃): i.e., only H₂CO₃ per 340 molecules of CO₂ (12,15,20). Thus, dCO₂ as the anhydride of H₂CO₃ is 1.2 mmol/L at PCO₂ 40 mm Hg (1.2 = 0.0301×40) as described by the H–H equation (Equation 2).

Depending on the institution’s practices, venous serum or plasma TCO₂ concentration may be reported as “bicarbonate,” and bicarbonate represents 95% of TCO₂ (0.95 = 24/24 + 0.0301×40) (12,15,21). Substitution of the venous TCO₂ for arterial [HCO₃⁻] is a long-standing and errant practice, although espoused by some (22,23). Unless an ABG and venous sample are drawn simultaneously and processed rapidly, even correctly assayed values may differ. The practice of substituting venous TCO₂ for arterial [HCO₃⁻] practice is eschewed, particularly in critical care settings, where acid-base changes often transpire rapidly. Venous TCO₂ usually exceeds arterial [HCO₃⁻] because of higher venous PCO₂ tensions. Under clinically stable circumstances, venous TCO₂ is generally no greater than the arterial [HCO₃⁻] by 2–4 mM (12,21), the difference representing the

<table>
<thead>
<tr>
<th>pH</th>
<th>[H⁺], Rule of 80</th>
<th>[H⁺] × 1.25, 0.8</th>
<th>Actual [H⁺]</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>80</td>
<td>97.7</td>
<td>100</td>
</tr>
<tr>
<td>7.05</td>
<td>75</td>
<td>×1.25</td>
<td>89.1</td>
</tr>
<tr>
<td>7.1</td>
<td>70</td>
<td>78.1</td>
<td>79.4</td>
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<tr>
<td>7.15</td>
<td>65</td>
<td>×1.25</td>
<td>70.8</td>
</tr>
<tr>
<td>7.2</td>
<td>60</td>
<td>62.5</td>
<td>63.1</td>
</tr>
<tr>
<td>7.25</td>
<td>55</td>
<td>×1.25</td>
<td>56.2</td>
</tr>
<tr>
<td>7.3</td>
<td>50</td>
<td>50</td>
<td>50.1</td>
</tr>
<tr>
<td>7.35</td>
<td>45</td>
<td>×0.8</td>
<td>44.7</td>
</tr>
<tr>
<td>7.4</td>
<td>40</td>
<td>40</td>
<td>39.8</td>
</tr>
<tr>
<td>7.45</td>
<td>35</td>
<td>×0.8</td>
<td>35.5</td>
</tr>
<tr>
<td>7.5</td>
<td>30</td>
<td>32</td>
<td>31.6</td>
</tr>
<tr>
<td>7.55</td>
<td>25</td>
<td>×0.8</td>
<td>28.2</td>
</tr>
<tr>
<td>7.6</td>
<td>20</td>
<td>25.6</td>
<td>25.1</td>
</tr>
</tbody>
</table>

In the “Rule of 80,” the last two digits of the pH plus [H⁺] equals 80 (column 2). An approximating method (column 3) that more closely reflects actual [H⁺] (column 4) successively multiplies the baseline [H⁺] (40 nM) by 1.25 or 0.8, respectively, for each 0.1 pH unit decrement (acidemia) or increment (alkalemia). [H⁺], hydrogen ion concentration (nM) (1.2,16).
difference between venous and arterial blood and CO₂ mediated H⁺ buffering by hemoglobin, with a negligible contribution of erythrocyte carbaminoco₂ (12,15,16).

Agreement between central venous and ABG parameters have been published: venous pH+0.03=arterial pH and venous [HCO₃⁻]-arterial [HCO₃⁻]=0.5 mM (24,25). Peripheral venous blood gas (VBG) versus ABG parameters of pH, PCO₂, and [HCO₃⁻] have been examined. The VBG pH is 0.03–0.04 less than from a corresponding ABG (26–32). The VBG PCO₂ correlates with its arterial counterpart. The VBG [HCO₃⁻] averages 4.4–8.6 mm Hg greater than the ABG PCO₂ with large confidence intervals (23,26,29,31–33). The VBG [HCO₃⁻] is approximately 0.52–1.5 mM greater than the ABG [HCO₃⁻]. The aforementioned studies excluded patients in circulatory shock, and severe hemodynamic compromise where these correlations may not be applicable, and an ABG is warranted (23,26,29,30,32).

When venous TCO₂ exceeds arterial [HCO₃⁻] by >4 mM, considerations include venous CO₂ accrual from tourniquet-induced stasis or dilution of the blood gas by heparin (34). Larger discrepancies are encountered in critically ill patients with extreme pH deviations from the norm, which may be attributable to blood gas autoanalyzer calculations using a constant pKₐ of 6.1 (12,15,34). The value of pKₐ is not only ionic strength and temperature dependent but also pH dependent (12,15,16,35,36). We reanalyzed the relationship between temperature, plasma pH, and pKₐ values. We conducted regression analysis of the originally published data (15) for the temperature range 10°C–40°C and pH range 7–7.6 (Datafit; Oakdale Engineering, Oakdale, PA), pKₐ is a linear function of temperature and pH with R²=0.9944: pKₐ=6.6605−0.0044°C−0.0542 pH. This equation is concordant with that published by Kim (10) (Figure 1). For extreme pH values per se <7.10 or >7.80 or temperatures <32°C or >39°C, an adjusted pKₐ may be required to determine [HCO₃⁻] accurately:

\[ \text{Adjusted } pK_a = pH - \log([\text{TCO}_2/\alpha\text{PCO}_2]) -1 \] (4a)

A rapid calculation that determines whether the actual pKₐ has diverged from the canonical value of 6.1 is shown below (36). Measured [HCO₃⁻]=TCO₂−dCO₂.

Actual pKₐ = pH − LOG([calculated[HCO₃⁻]]/(measured[HCO₃⁻]]) (4b)

This equation is used when TCO₂ is significantly less than arterial [HCO₃⁻]. Venous plasma TCO₂ is determined by an enzymatic and spectrophotometric method and not by ABG machines. Thus, discrepancies can be a result of a number of reasons. In the index case, the patient’s temperature was normal, and the pH was 7.5. No pKₐ adjustments were made. Notably, the calculated [HCO₃⁻] was greater than venous TCO₂ by 5 mM. The possibility of an endogenous interferent of the TCO₂ assay was considered, but this abnormality did not persist (34). A spurious loss of CO₂ gas from plasma attributable to underfilling of a vacuum collection tube or during specimen processing may have also produced this atypical directional bias (34). More commonly, pseudohypobicarbonatemia from extremely elevated lipid levels may produce a much lower TCO₂ than [HCO₃⁻] than calculated (37). Alternatively, [HCO₃⁻] can be determined as below via the Henderson equation or following equation, using Kₐ of 794 [antilog (9−6.1)] and deriving [H⁺] from pH [Equation (1)]. An adjusted Kₐ must be calculated when pKₐ is adjusted; i.e., Kₐ=10⁻pKₐ [Equation (2)]. This adjustment is rarely required clinically (12).

\[ [\text{HCO}_3^-] = 0.0301 \times K_a \times \text{PCO}_2 /[H^+] \]

= 0.0301 × PCO₂ × 10^(pH−Adjusted pKₐ) (4c)

If variations in pKₐ and elevated PCO₂ do not provide adequate explanation for exceptionally significant differences between TCO₂ and [HCO₃⁻], troubleshooting is required.

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**Figure 1.** Temperature and pH dependency of pKₐ. Multiple regression analysis of original data from the relationship of pKₐ to pH and temperature revealed a linear equation: pKₐ=6.6605−0.0044°C−0.0542-pH; R²=0.99 (15).
Analytical measurement errors of TCO₂ should be ruled out. Errant input of patient temperature can affect the ABG analyzer pH output. Misreporting of one of the ABG results is always possible. If no consistent source of error is elucidated by these steps, an independent [HCO₃⁻] calculation using pKa of 6.1 [Equation (3)] is the last step.

**Relationships: pH, [H⁺], and RpH**

We define RpH as the ratio of PCO₂ to [HCO₃⁻], and this ratio defines a specific pH/[H⁺].

\[
RpH = \frac{PCO_2}{[HCO_3^-]} = \frac{[H^+]}{24} = \left(10^{pH}\right) / 24 \tag{5}
\]

RₚH qualitatively and quantitatively reflects the acid-base relationship between the regulation of CO₂ by the lungs: i.e., PCO₂ and the kidneys that control bicarbonate reabsorption, proton secretion, and bicarbonate regeneration as ammonium excretion. For convenience, the Henderson equation expresses the "lung" parameter (PCO₂ numerator) divided by the "kidney" parameter ([HCO₃⁻] denominator).

Consequently, RpH is determined by [H⁺] in a linear fashion (Figure 2, Table 2) but in a curvilinear fashion when related to pH (Figure 3). In Equation 6a, RpH is inserted into a modified H–H equation that emphasizes the physiologic importance of the ratio of pulmonary ventilation to renal bicarbonate balancing. Equation 6b defines a "magical" pH of 7.62 when the PCO₂ to [HCO₃⁻] ratio equals 1 (38).

\[
pH = 7.62 - \log(PCO_2/[HCO_3^-]) = 7.62 - \log(RpH) \tag{6a}
\]

\[
pH = 7.62 - \log(X/X) = 7.62 - (1) = 7.62 - 0 = 7.62 \tag{6b}
\]

The index patient’s RₚHₜ is 0.83, equaling 1.33 = 93.7/70.6. This ratio is lower than the normal Rₚ₇₄ of 1.67, or the normal ratio defined by PCO₂ 40 mm Hg and [HCO₃⁻] 24 mM. As a corollary, any condition in which the PCO₂ to [HCO₃⁻] ratio equals 1.67 will have a pH of 7.4.

Specific relationships among the parameters pH, [H⁺], and RpH deserve mention. At a pH of 7.4, [H⁺] = 40 nM and RpH = 1.67. Because of the logarithmic relationship between pH and [H⁺], when the pH is 0.3 units more acidic than normal (pH 7.1), the [H⁺] and RpH double. Moreover, when [H⁺] and RpH are halved, the plasma pH increases by 0.3 units to a severely alkaline level of pH 7.7 (Figure 4).

At any pH, a pH isopleth delineates the slope of the relationship between PCO₂ and [HCO₃⁻] (Figure 4). The pH isopleth represents the third dimension of a topological map of physiologic representations of pH, PCO₂, and [HCO₃⁻]. The figure is a remodeling of the original Davenport diagrams where pH isopleths are depicted instead of PCO₂ isobars (16). The reconfiguration designates pH domains as functions of [HCO₃⁻] and PCO₂. Each pH isopleth represents a "state" of the relationship of PCO₂ and [HCO₃⁻]: i.e., RpH.

**ABG Interpretation**

Determination of acid-base disorders requires a disciplined approach. This process involves three steps: (1)

**Table 2. Relationships among pH, [H⁺], and RpH**

<table>
<thead>
<tr>
<th>pH</th>
<th>[H⁺]</th>
<th>RpH</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>100</td>
<td>4.17</td>
</tr>
<tr>
<td>7.1</td>
<td>79</td>
<td>3.33</td>
</tr>
<tr>
<td>7.2</td>
<td>63</td>
<td>2.63</td>
</tr>
<tr>
<td>7.3</td>
<td>50</td>
<td>2.09</td>
</tr>
<tr>
<td>7.4</td>
<td>40</td>
<td>1.67</td>
</tr>
<tr>
<td>7.5</td>
<td>32</td>
<td>1.32</td>
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<tr>
<td>7.6</td>
<td>25</td>
<td>1.05</td>
</tr>
<tr>
<td>7.7</td>
<td>20</td>
<td>0.83</td>
</tr>
</tbody>
</table>

As pH increases, the [H⁺] and RpH decrease in a linear and parallel fashion. With increases or decreases of 0.3 pH units, [H⁺] and RpH are halved or doubled, respectively. Calculations are determined from the Henderson equation. [H⁺], hydrogen ion concentration (nM); RpH, ratio of PCO₂ to [HCO₃⁻] (mm Hg L/mmol) (9,10,36).
validation of the ABG; (2) delineation of primary disorders; and (3) determination of the dominant disorder. These steps can identify up to two primary disorders and should be conducted before examination of electrolytes.

After validating the ABG, identifying primary acid-base disturbances follows. There are four primary acid-base disorders: respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis (1,2). Respiratory disorders can be subcategorized as acute or chronic disorders. Because one cannot simultaneously hypo- and hyperventilate, two primary respiratory disorders cannot occur simultaneously. In healthy individuals, a primary acid-base disturbance will invoke countervailing compensation by the “other” organ. For example, in metabolic acidosis, lowered $[\text{HCO}_3^-]$ is compensated by increased “lung” ventilation (i.e., PCO$_2$). However, the respiratory compensation is incomplete, and arterial pH/$[\text{H}^+]$ is not returned to the baseline.

Simple or pure acid-base disturbances follow this rule: PCO$_2$ and $[\text{HCO}_3^-]$ are displaced in the same direction, and the resulting $[\text{H}^+]$ or pH equals that predicted by known data. Such data have been obtained empirically from dogs and humans (39–42). When the limitations of compensation formulas are exceeded, a second primary disturbance is present. Prediction rules for the six acid-base disorders are listed in Table 3. In chronic respiratory alkalosis, renal compensation is highly effective, and arterial pH may nearly normalize (2).

When compensation equations are not fulfilled in the face of a valid ABG analysis, a mixed acid-base problem is present, and the pH or the parameter that is most disproportionately displaced from its baseline value is the dominant disorder: i.e., the disorder that displaces pH most greatly. Alternatively, one may choose one of the two disorders and apply its compensation equation to determine

![Figure 3. | $[\text{H}^+]$ and $R_{\text{ph}}$ versus pH. The relationships of $[\text{H}^+]$ (left y axis, $-$) and $R_{\text{ph}}$ (right y axis, $-$), the ratio of PCO$_2$ to $[\text{HCO}_3^-]$ is logarithmically related to pH.](image)

![Figure 4. | Relationship of PCO$_2$ to $[\text{HCO}_3^-]$ at specific pH. Isopleths for pH 7.1 (---), 7.4 (--), and 7.7 (---) are plotted as functions of paired $[\text{HCO}_3^-]$ and PCO$_2$. Each isopleth slope equals the ratio of PCO$_2$ to $[\text{HCO}_3^-]$ ($R_{\text{ph}}$). As pH varies in 0.3 increments, $[\text{H}^+]$ doubles or halves in concert with $R_{\text{ph}}$. Accordingly, the respective slopes of $R_{\text{ph}}$ are 0.833, 1.67, and 3.33 at pH units of 7.7, 7.4, and 7.1. Corresponding, $[\text{H}^+]$ is a function of $R_{\text{ph}}$.](image)
what the pH (or [H⁺]) would be if there were only a single acid-base disturbance. The “distance” from pH 7.4 would indicate whether this disorder was dominant.

After an ABG has been analyzed to this point, the AG is examined. The AG may disclose a third acid-base disturbance and/or further characterize one of the disorders already identified. Electrolyte analysis detects the “triple disorder” of high AG metabolic acidosis, hyperchloremic metabolic alkalosis, and an acute or chronic respiratory disorder.

Three general rules to follow when interpreting ABG analyses are as follows. First, if the pH is normal and either PCO₂ or [HCO₃⁻] has varied from its respective baseline level (PCO₂, 40 mm Hg; [HCO₃⁻], 24 mM), there are two offsetting disorders: metabolic acidosis/alkalosis and a respiratory alkalosis/acidosis. Second, if the pH is extremely displaced from normal (i.e., <7.2 or >7.55), the probability is that two acid-base disturbances are moving [H⁺] in the same direction (i.e., two acidoses or two alkaloses). Third, when there is a mixed acid-base disorder, the degree of variation of either PCO₂ or [HCO₃⁻] from its baseline level usually indicates which disorder is dominant (i.e., a respiratory one or a metabolic one). In all cases, findings established from these general qualitative rules should be verified by quantitative analysis.

### Table 3. Linear compensation formulas for the four primary acid-base disorders

<table>
<thead>
<tr>
<th>Acid-Base Disorder</th>
<th>Compensation Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>PCO₂ = 1.54 × [HCO₃⁻] + 8.36 ± 2.2</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>PCO₂ = 0.70 × [HCO₃⁻] + 20 ± 5.5</td>
</tr>
<tr>
<td>Acute respiratory acidosis</td>
<td>[ΔHCO₃⁻]/PCO₂ = 0.12</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td>[ΔHCO₃⁻]/PCO₂ = 0.35</td>
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### Table 4. Ratiometric analysis of arterial blood gas from index case

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient Value</th>
<th>Normal Value</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.5</td>
<td>7.4</td>
<td>—</td>
</tr>
<tr>
<td>[H⁺]</td>
<td>31.62 nM</td>
<td>40</td>
<td>—</td>
</tr>
<tr>
<td>PCO₂</td>
<td>93.7 mm Hg</td>
<td>40</td>
<td>2.34</td>
</tr>
<tr>
<td>[HCO₃⁻]</td>
<td>70.58 mM</td>
<td>24</td>
<td>2.94</td>
</tr>
</tbody>
</table>

Both metabolic and primary respiratory alkalosis are present. The greater ratio for plasma [HCO₃⁻] is consistent with metabolic alkalosis as the dominant acid-base disorder. [H⁺], hydrogen ion concentration (nM); PCO₂, carbon dioxide partial pressure (mm Hg); [HCO₃⁻], bicarbonate concentration (mM).

The acid-base disorder of the index case is a mixed metabolic alkalosis with chronic respiratory acidosis. The ABG is quantitatively analyzed by a ratiometric analysis that delineates metabolic alkalosis as the dominant disorder, despite the severity of chronic respiratory acidosis. (Table 4) The R₉₃.₄ = 93.7/70.6 is lower than the normal ratio of 1.67, thereby defining an alkalolemia of pH 7.5 or [H⁺] of 31.6 nM. The ratio of current [HCO₃⁻] to normal [HCO₃⁻] = 2.94 = 70.6/24. This ratio is greater than the corresponding PCO₂ to normal [PCO₂] ratio of 2.34 = 93.7/40. The higher ratio of 2.94 exerts the greater effect of metabolic alkalosis on pH than the chronic respiratory acidosis. This ratiometric analysis of the numerator and denominator of R₉₃.₄ thus defines the respective severities of each component of a mixed acid-base disorder. The calculations are tabulated and additional examples of the ratiometric analytic approach to acid-base disorders are provided (Table 5).

### Quantitation of Parallel Mixed Acid-Base Disorders as Serial Processes

Mixed acid-base disorders that transpire in parallel can be treated as two serial disorders, virtually recapitulating prior canine experiments of mixed metabolic/respiratory acid-base disorders (43). If metabolic alkalosis were the only disorder and [HCO₃⁻] increased from 24 to 73.1 mM, the compensatory increase in PCO₂ is approximately 76.8 mm Hg (Figure 5A). The pH would increase to 7.6 = 7.62 – log(76.8/73.1) — a displacement of +0.2 pH units.

### Table 5. Mixed acid-base disturbance

<table>
<thead>
<tr>
<th>[H⁺]</th>
<th>pH</th>
<th>PCO₂</th>
<th>[HCO₃⁻]</th>
<th>Acid-Base Disorders</th>
<th>Dominant Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.8</td>
<td>7.4</td>
<td>21.6</td>
<td>13</td>
<td>Metabolic acidosis, chronic respiratory alkalosis</td>
<td>—</td>
</tr>
<tr>
<td>19.03</td>
<td>7.72</td>
<td>23.8</td>
<td>30</td>
<td>Metabolic alkalosis, acute respiratory alkalosis</td>
<td>Acute respiratory alkalosis</td>
</tr>
<tr>
<td>77.6</td>
<td>7.11</td>
<td>65</td>
<td>20</td>
<td>Metabolic acidosis, acute respiratory acidosis</td>
<td>Acute respiratory acidosis</td>
</tr>
<tr>
<td>63.1</td>
<td>7.2</td>
<td>35</td>
<td>13.3</td>
<td>Metabolic acidosis, acute respiratory acidosis</td>
<td>Metabolic acidosis</td>
</tr>
</tbody>
</table>

Each row represents a mixed acid-base disturbance comprising a metabolic disturbance and a respiratory one. Parenthetical numbers indicate the ratio of a parameter to its respective baseline. “Ideal” values: pH 7.4, PCO₂ 40 mm Hg, and [HCO₃⁻] 24 mM. The last column denotes a disturbance that altered the [H⁺]/pH to a greater degree: i.e., the dominant disorder. No inference is implied regarding the order of appearance of acid-base disturbances. These mixed acid-base disorders can be visualized on the acid-base map (Figure 5B). [H⁺], hydrogen ion concentration (nM); PCO₂, carbon dioxide partial pressure (mm Hg); [HCO₃⁻], bicarbonate concentration (mM).
Figure 5. Quantitative analysis and clinical illustration of acid-base disorders. (A) Quantitative analysis of acid-base disorder provided from index case. The arterial blood gas of the index patient: pH 7.5, PCO₂ 93.7 mm Hg, and [HCO₃] 73.1 mM. The blue filled circle corresponds to the normal PCO₂ of 40 mm Hg and plasma [HCO₃] of 24 mM at pH 7.4. The dotted lines are pH isopleths that bound pH values from 7.28 to 7.6. Conceptualization of a parallel-process, mixed acid-base disturbance developing as two distinct processes along two separate and convergent pathways: (A) metabolic alkalosis with respiratory compensation (arrow 1) followed by superimposed chronic respiratory acidosis (arrow 2) and (B) chronic respiratory acidosis with appropriate bicarbonate retention (arrow 3) followed by metabolic alkalosis (arrow 4). (B) Clinical illustration of mixed acid-base disorder provided from index case. Colored bands represent the...
from normal. The final pH of 7.5 is achieved by the addition of a chronic respiratory acidosis that increases PO2 to 93.7 mm Hg while lowering the pH by 0.1 pH units. The greater change in pH that results from metabolic alkalosis confirms that it represents the dominant acid-base disorder, with twice the effect on pH.

On the other hand, if chronic respiratory acidosis had occurred first, the increase in PO2 would have driven [HCO3−] to 42.8 mM, with a PCO2 of 93.7 mm Hg and pH of 7.28 (Figure 5A). A superimposed metabolic alkalosis that increases [HCO3−] from 42.8 to 73.1 mM, with unchanged PCO2 increases the pH by +0.22 units to 7.5. Again, the absolute difference in pH changes between the two acid-base disturbances is 0.2 pH units. On an acid-base map, we illustrate the separation of this dominant metabolic alkalosis–chronic respiratory acidosis disorder into separate pathways of two serial processes (Figure 5B).

Summary

The ABG remains the primary tool in analysis of acid-base disorders, and the following should be dealt with seriatim. Internal validation by the Henderson equation should be conducted on each blood gas, and its subsequent interpretation is conducted independently of the basic metabolic panel review. Significant differences between venous TCO2 and arterial [HCO3−] must be resolved. Appropriate quantitative blood gas analysis can reveal up to two acid-base disturbances. Subsequent ratiometric ABG analysis of [HCO3−] and PCO2 can reveal the dominant acid-base disturbances. Separation of mixed acid-base disturbances that proceed in parallel into its separately occurring serial components enhances pathophysiologic comprehension.

Disclosures

S. Frinak reports consultancy for Vasc-Alert; ownership interest in Vasc-Alert; and patents or royalties from Henry Ford Health System licensed to Vasc-Alert. J. Yee reports consultancy for AstraZeneca, Ardelyx, Bayer, EBSCO/Dynamed, Elsevier, and GLG; ownership interest in Vasc-Alert; honoraria from AlphaSights, Ardelyx, AstraZeneca, Fresenius Medical Corporation, North America, Gerson Lehman Group, and GLG; patents or royalties from Vasc-Alert; and other interests or relationships with American Journal of Nephrology (editorial board), BMC Nephrology (editorial board), EBSCO/Dynamed (editorial board), Elsevier (clinical key author and section editor), Ferri’s (clinical advisor 2022), Journal of OncoNephrology (editorial board); and Springer Heart Failure Reviews (editorial board). All remaining authors have nothing to disclose.

Acknowledgments

The authors are grateful for the artistic rendering of Figure 5B by Gerard Zasuwa.

Author Contributions

S. Frinak and J. Yee were responsible for formal analysis, software, and supervision; J. Yee was responsible for conceptualization, methodology, resources, validation, and visualization; and all authors wrote the original draft of the manuscript and reviewed and edited the manuscript.

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Received: February 2, 2022 Accepted: May 31, 2022