Steady a disturbed equilibrium

Accurately interpret the acid-base balance of acutely ill patients.

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Derangements in acid-base homeostasis appear in a wide assortment of critical illnesses and are commonly encountered in the critical care setting. In addition to indicating a disturbance in acid-base equilibrium, these abnormalities are suggestive of other underlying disease processes. In fact, acid-base derangements may occur as a secondary phenomenon or as a result of organ damage. Accurate interpretation of acid-base balance requires simultaneous measurements of arterial pH and plasma electrolytes, as well as knowledge of compensatory physiologic mechanisms.

Critical care nurses benefit from a review of normal acid-base physiology, acid-base disturbances, and laboratory techniques and mathematical calculations used to identify the etiology of acid-base derangements. In addition, consider an overview of potential treatment modalities.
Acid-base balance

**Acid-base physiology**
Assessment of acid-base disturbances begins with evaluation of arterial pH. A normal range for arterial pH is from 7.35 to 7.45. Acidosis is defined as a pH less than 7.35 while alkalosis is defined as a pH greater than 7.45. pH is measured in terms of hydrogen (H\(^+\)) ion concentration. For example, an increase in H\(^+\) ion concentration results in changes in pH, specifically a decrease in pH. Therefore, pH and H\(^+\) ion concentration have an inverse relationship. Changes in H\(^+\) ion concentration can be stabilized through several buffering systems: bicarbonate-carbonic acid, proteins, hemoglobin, and phosphates. With this knowledge, acidosis can be better defined as a physiologic condition resulting in excess H\(^+\) ions when the body is unable to buffer the excess H\(^+\) ions. Alkalosis is a physiologic condition that results from a deficiency in H\(^+\) ion concentration. The nurse must bear in mind acidosis differs from acidemia. Acidemia refers to the condition in which arterial blood pH is less than 7.35. Likewise, alkalemia refers to the condition in which arterial blood pH is greater than 7.45.

Body acids are formed as end products of cellular metabolism. Under normal physiologic conditions, a person generates 50 to 100 mEq/day of acid from metabolism of carbohydrates, proteins, and fats. In addition, the body sustains a loss of base in the stool. To maintain acid-base homeostasis, there must be a balance of acid production with neutralization or excretion. This process of homeostasis is carried out in a complex fashion by multiple organs. Therefore, the lungs, kidneys, and bone work in concert to maintain balance. There are two forms of body acids: volatile and nonvolatile. The main volatile acid is carbonic acid (H\(_2\)CO\(_3\)). Carbonic acid is a weak acid and readily dissociates into carbon dioxide (CO\(_2\)) and water. The human body produces approximately 12,000 to 15,000 millimoles of CO\(_2\) daily, which is released via pulmonary ventilation. Nonvolatile acids are strong acids produced from the metabolism of proteins, carbohydrates, and fats. Nonvolatile acids are excreted by the renal tubules with the regulation of bicarbonate (HCO\(_3^-\)). Therefore, with the help of the physiologic buffering systems, the lungs and kidneys are the major regulators of acid-base homeostasis.

**Physiological buffering systems**
Buffering is important to acid-base balance and occurs in response to changes in acid-base status. Buffering systems exist as buffering pairs consisting of a weak acid and its conjugate base. The most important extracellular buffer systems are bicarbonate-carbonic acid and hemoglobin, whereas phosphate and protein are important in intracellular buffering. The bicarbonate-carbonic acid buffering system is unique among physiological buffering systems and can be described as follows:

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

The equation demonstrates that H\(_2\)CO\(_3\) is formed from the hydration of CO\(_2\). Therefore, the...
greater the partial pressure of carbon dioxide (CO$_2$), the more H$_2$CO$_3$ that is produced. In acidic states, the equation shifts in favor of HCO$_3^-$ and H$^+$ production, which results in excess H$_2$CO$_3$. Consequently, prevention of acidosis occurs by increased ventilation of CO$_2$ from the lungs. Increasing respiratory rate is a quick response that results in removal of CO$_2$ and retention of H$_2$O. The kidneys reabsorb HCO$_3^-$ or regenerate new HCO$_3^-$ from carbon dioxide and water; however, this mechanism is slower.

The Henderson-Hasselbalch (H-H) equation mathematically expresses the association between blood pH and the H$_2$CO$_3$ buffering system. The H-H equation expresses the pH of any buffering system as a function of the log of the concentrations of the weak acid/base forms of its components and the dissociation constant. All weak acids and bases possess a dissociation constant, thus, changes in the concentration of the acid component will result in reciprocal changes in the concentration of the base component. The application of the H-H equation can be used to approximate how much additional acid or base can be buffered by a particular buffering system to maintain a specific pH. This assumption is used in the application of the H-H equation to the bicarbonate-carbonic acid buffering system. If we know the pH of the blood, we can calculate expected changes in the CO$_2$ and HCO$_3^-$. A comparison of the expected changes versus the actual changes can give additional information about the type and nature of the acid-base disturbance/s present. Carbonic acid can be calculated by using the following equation:

$$H_2CO_3 = Paco_2 \times 0.03$$

**Hemoglobin buffering**

Intracellular blood protein buffers consist of protein buffers in the blood that are effective in maintaining acid-base homeostasis. The most important blood buffer is hemoglobin because it can buffer large amounts of H$^+$, preventing significant changes in the pH. If hemoglobin didn’t exist, venous blood would be 800 times more acidic than arterial blood, circulating at a pH of 4.5 instead of the normal venous pH of 7.37. (See Hemoglobin buffering.)

Under normal physiologic conditions, CO$_2$ is produced in tissue cells and diffuses to plasma or to the red blood cell. CO$_2$ is more soluble in the blood than oxygen, and as a result, CO$_2$ diffuses into the red blood cell easily. Carbon dioxide combines with water to form H$_2$CO$_3$, which dissociates into HCO$_3^-$ and H$^+$. Hemoglobin is an excellent buffer because of its ability to bind with H$^+$ (creating HHb) and CO$_2$ (HHbCO$_2$). Due to the increased affinity for CO$_2$, the acidic environment at the tissue level promotes the release of oxygen and diffusion of CO$_2$ to hemoglobin for transport to the lungs for removal during ventilation.

**Pulmonary compensation**

In acidotic states, the lungs are one of the first compensatory mechanisms to assist in normalizing the serum pH. Pulmonary compensation occurs in response to pH changes and involves a relationship between peripheral chemoreceptors, located in the carotid bodies, and central chemoreceptors located in the medulla oblongata. Both these receptors influence respiratory drive and can initiate changes in minute ventilation. A drop in pH stimulates the respiratory center, resulting in increased minute ventilation. This response in turn lowers the partial pressure of arterial carbon dioxide (Paco$_2$), driving the pH toward the normal range.
Conversely, an increase in pH decreases ventilatory effort, which increases Paco₂ and lowers the pH back toward normal. The chemoreceptors (central and peripheral) are involved in the manipulation of both respiratory rate and depth. Alveolar ventilation is then increased, which assists the individual to "blow off" excessive CO₂, resulting in a compensatory respiratory alkalosis.

Renal compensation
The kidneys begin to play a role in the acute compensation of acid-base disorders when other mechanisms have been ineffective. Although the respira-

Compensatory mechanisms in acid-base derangements

Changes in serum pH are dealt with by three compensatory mechanisms:

1. physiological buffers
Physiological buffers, defined as a weak acid and its salt, oppose marked changes in pH after an addition of an organic acid or a base. The human body uses three important physiological buffers to minimize surges in pH:
- the bicarbonate-carbonic acid system (primarily located in red blood cells)
- intracellular protein buffers
- phosphate buffers located within the bone.

2. lungs
Pulmonary compensation is the second compensatory system for pH changes. It involves a relationship between peripheral chemoreceptors, located in the carotid bodies, and central chemoreceptors, located in the medulla oblongata.

Both these receptors influence respiratory drive and can initiate changes in minute ventilation. A drop in pH stimulates the respiratory center, resulting in increased minute ventilation. This in turn lowers the partial pressure of arterial carbon dioxide (Paco₂), driving the pH toward the normal range.

Conversely, an increase in pH decreases ventilatory effort, which increases Paco₂ and lowers the pH back toward normal.

3. kidneys
Renal compensation occurs as the kidneys begin to play a role in the acute compensation of acid-base disorders. However, it may take more than 6 to 12 hours of sustained acidosis until an active excretion of H⁺ (predominately in the form of ammonium, NH₄⁺) with retention of bicarbonate, HCO₃⁻.

Conversely, more than 6 hours of alkemia will stimulate renal excretion of bicarbonate with retention of H⁺ in the form of organic acids, resulting in near-normalization of pH.
tory compensatory mechanisms occur almost immediately, it may take hours to days for the renal mechanisms to make a difference. It may take more than 6 to 12 hours of sustained acidosis until an active excretion of H⁺ (predominately in the form of ammonium) with retention of HCO₃⁻ begins to occur. The kidneys begin with the excretion of H⁺ ions to regenerate HCO₃⁻. Urinary buffers combine with H⁺ ions, to make hydrogen phosphate (HPO₄²⁻) and ammonium, which are then excreted within the urine. This allows H⁺ ions to be excreted, as well as for HCO₃⁻ to be recombined and added to the blood as a buffer. Conversely, more than 6 hours of alkalosis will stimulate renal excretion of bicarbonate with retention of H⁺ in the form of organic acids, resulting in near-normalization of pH. Bone may also serve as a buffer because it contains a large reservoir of bicarbonate and phosphate and can buffer a significant acute acid load. Therefore, patients with malnutrition or chronic disease, and thus low albumin and bone density, and anemic patients have an ineffective buffering capability. (See Compensatory mechanisms in acid-base derangements.)

Common acid-base derangements
Generally, derangements in acid-base homeostasis are approached by first searching for the etiology, rather than an instant attempt to normalize the pH. However, potential causes can be systematically eliminated as certain acid-base disturbances have a limited number of etiologies. Systematic analysis of arterial blood gases and identification of the acid-base disorder present can aid in the identification of the underlying etiology. (See Normal values for ABGs.) Many disorders are mild and don’t require treatment. Additionally, prompt treatment of the direct acid-base imbalance may do more harm than the actual imbalance itself. It’s critical that a full deliberation be made by the nurse as to the possible pathologic etiologies, which may need direct intervention that may benefit the patient more than normalization of the pH alone.

In addition, it is physiologically possible for a critically ill patient to demonstrate multiple acid-base derangements simultaneously. The more common acid-base derangements can be divided into four categories: metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis.

Causes of anion gap metabolic acidosis

| M | Methanol or ethanol ingestion |
| U | Uremia |
| D | Diabetic ketoacidosis, starvation, alcoholic ketoacidosis |
| P | Paraldehyde ingestion |
| I | Iron or isoniazid (INH) |
| L | Lactic acidosis (sepsis, hypotension, hypoxia, ischemia) |
| E | Ethylene glycol ingestion |
| S | Salicylate toxicity |

Metabolic acidosis
Metabolic acidosis is a disorder typified by an increase in the amount of absolute body acid, as evidenced by either an excess production of H⁺ (as with lactic acid production or ketoacid production) or an excessive loss of anion (HCO₃⁻) and accompanying loss of sodium and potassium (Na⁺, K⁺) cations. This condition indicates the presence of an underlying disease affecting the acid-base balance. There are three pathways that commonly lead to the development of acidosis. The first occurs when the kidneys fail to excrete H⁺ ions in adequate amounts to maintain a normal pH. The second pathway that leads to acidosis occurs when there is an increase in H⁺ ion production. Common conditions that generate an increase in H⁺ ions are lactic acidosis or diabetic ketoacidosis. The third mechanism leading to acidosis is a loss of HCO₃⁻, most commonly caused by severe diarrhea, or wasting of HCO₃⁻ through the gastrointestinal (GI) system or kidneys.

In general, the kidneys attempt to preserve Na⁺ by exchanging it for excreted H⁺ or K⁺. In the presence of an H⁺ load, H⁺ ions move from the ex-
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The natural response of the body to acid-base derangements is to initiate one of the compensatory mechanisms.

The tracellular fluid (ECF) into the intracellular fluid. For this process to occur, potassium moves outside the cell into the ECF to maintain electroneutrality. In severe acidosis, significant overall depletion of total body K⁺ stores can occur despite serum hyperkalemia. Clinically, this state is the rationale for initiating intravenous (I.V.) potassium in the patient with diabetic ketoacidosis early in their treatment, despite the often-elevated serum K⁺ level.⁸,⁹ External and internal potassium balances are regulated to maintain an ECF concentration of 3.5 to 5.5 mEq/L and a total body content of about 50 mEq/kg (40 mEq/kg in females).⁹ The natural response of the body to acid-base derangements is to initiate one of the compensatory mechanisms. Therefore, changes in serum pH are dealt with by one of the three compensatory mechanisms: the physiological buffers, alterations in ventilation by the lungs, or alterations in excretion of anions and cations by the kidneys.

Mind the anion gap

The causes of metabolic acidosis are divided into two categories. The first category includes those that cause an elevation of the anion gap, which is defined as the difference between the serum concentrations of cations and anions. [See Causes of anion gap metabolic acidosis.]

A non-anion gap acidosis (also known as normal anion gap acidosis) occurs as chloride [Cl⁻] replaces the loss of HCO₃⁻.¹⁰ An increased anion gap metabolic acidosis occurs when the anion replacing the HCO₃⁻ is not one that is being measured (such as albu- min, phosphate, sulfates, or lactate). Anions should always equal cations, but when the anion is not Cl then the anion gap will be elevated when calculated from routine electrolytes.¹¹ An elevated anion gap doesn’t only signify a metabolic acidosis, but can occur in alkalemia. This is because plasma proteins, when increased, influence the net anionic charge. Dehydration is a situation in which an elevated anion gap is likely to occur. In dehydration, plasma protein concentration is elevated.¹² Nevertheless, if the anion gap is greater than 20 mEq/L, a metabolic acidosis should be considered.

Non-anion gap acidosis may be present when there’s a loss of HCO₃⁻ from the kidneys or the GI tract, or when there’s a large increase of an acid containing Cl as the chief anion.¹,¹³ Other causes of non-anion gap acidosis are easily identifiable by taking a careful history and review of medications. [See Causes of non-anion gap metabolic acidosis.]
**Metabolic alkalosis**

Metabolic alkalosis is common and occurs when \( \text{HCO}_3^- \) is increased. Metabolic alkalosis is usually caused by excessive loss of metabolic acids. [See Causes of saline-responsive metabolic alkalosis and Causes of non-saline responsive metabolic alkalosis.] Remember, Paco\(_2\) increases 0.7 mm Hg for every 1 mEq/L increase of HCO\(_3^-\).

Compensation that’s inappropriate in metabolic imbalances may occur in respiratory derangements and can be identified by looking at the observed HCO\(_3^-\) and comparing it with the calculated changes in HCO\(_3^-\) for that observed in Paco\(_2\). If the observed HCO\(_3^-\) is elevated higher than the calculated HCO\(_3^-\), a chief metabolic alkalosis is mixed with the respiratory derangement. Conversely, if the observed [result from actual ABG measured in the blood] HCO\(_3^-\) is decreased more than the calculated HCO\(_3^-\) [which comes from the formula], a chief metabolic acidosis is mixed with a respiratory derangement. HCO\(_3^-\) for either respiratory (alkalosis/acidosis) can be calculated as follows:

- **Respiratory acidosis** — 1 mEq/L elevation in HCO\(_3^-\) for every rise of 10 mm Hg Paco\(_2\) (acute); 3.5 mEq/L elevation in HCO\(_3^-\) for every rise of 10 mm Hg Paco\(_2\) (chronic).

- **Respiratory alkalosis** — 2 mEq/L decrease in HCO\(_3^-\) for every decrease of 10 mm Hg Paco\(_2\) (acute); 4 mEq/L decrease in HCO\(_3^-\) for every decrease of 10 mm Hg Paco\(_2\) (chronic).

Metabolic alkalosis is categorized as either saline responsive if the urine Cl concentration is less than 15 mmol/L, or non-saline responsive if the urine Cl is greater than 25 mmol/L.\(^1\,^13\) deficit results in compensation. The mechanisms resulting in saline responsive metabolic alkalosis include GI loss, diuresis, or renal compensation from hypercapnia. Non-saline responsive metabolic alkalosis results from mineralocorticoid excess or K\(^+\) depletion.

Therefore, evaluation of ECF volume and urinary electrolytes may help to determine whether the alkalosis will be responsive to saline. Fluid administration is the foundation for treatment of saline responsive metabolic alkalosis.\(^10\) In cases of extreme alkalosis, administration of dilute hydrochloric acid may be necessary.

The management of saline-resistant alkalosis requires treatment of the underlying etiology. Treatment for non-saline responsive metabolic alkalosis requires further investigation into the patient’s medication adherence and ingestion as well as underlying renal function. Once the etiology is determined, appropriate treatment modalities can be instituted.

### Causes of saline-responsive metabolic alkalosis

- **D** Diuretics
- **A** Adenoma secretor (secretory villous adenoma of the colon)
- **M** Miscellaneous (Bartter’s syndrome, penicillin, K\(^+\) deficiency, bulimia)
- **P** Posthypercapnia
- **E** Emesis
- **N** Nasogastric tube

### Causes of non-saline responsive metabolic alkalosis

- **A** Alkali ingestion with decreased glomerular filtration rate
- **B** 11-B-hydroxylase deficiency
- **E** Exogenous steroids
- **L** Licorice ingestion
- **C** Cushing’s syndrome and disease
- **H** Hyperaldosteronism

### Respiratory acidosis

The major determinant for respiratory acidosis is the presence of a pH less than 7.35 with a concomitant increase in Paco\(_2\) above the upper limit of normal (35 to 45 mm Hg). Alveolar hyperventilation is the only mechanism that results in hypercapnia, which is an elevation of Paco\(_2\) above the upper limit of normal. The amount of alveolar ventilation necessary to maintain normal Paco\(_2\) varies depending upon CO\(_2\) produced.

The relationship between Paco\(_2\) and plasma HCO\(_3^-\) determines arterial pH. This relationship is demonstrated in the H-H equation. The acuity or chronicity of the respiratory disturbance can be determined using the equations shown in the previous section. As a general rule, acute increases in Paco\(_2\) are accompanied by only minimal changes in serum HCO\(_3^-\). However, over a period of 1 to 3 days, renal conservation of HCO\(_3^-\) results in an increase in pH.

There are several etiologies of respiratory acidosis. Primarily, chronic respiratory acidosis oc-
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Acute respiratory acidosis results from an acute change in alveolar ventilation.

Acute respiratory acidosis results from an acute change in alveolar ventilation, as is seen in chronic lung diseases such as chronic obstructive pulmonary disease (COPD). Acute respiratory acidosis results from an acute change in alveolar ventilation. Acute opioid ingestions are an important consideration in a patient with acute respiratory acidosis. The treatment for respiratory acidosis is largely supportive; however, if opioid ingestion is suspected, naloxone I.V. may be used to reverse the sedative effect and improve alveolar ventilation.

Respiratory alkalosis

Respiratory alkalosis is a common condition in the critical care setting. Respiratory alkalosis occurs when a reduction in PaCO₂ results in an increase in pH. The most common cause of respiratory alkalosis is increased alveolar ventilation. An increase in alveolar ventilation occurs in many disease states. However, it’s common with hyperventilation, mechanical overventilation, hepatic disease, pregnancy, and septicemia.

A determination of appropriate compensatory changes in HCO₃⁻ is important in determining the presence of a concomitant metabolic disorder. In chronic respiratory alkalosis, the compensatory mechanisms result in mild reduction in plasma HCO₃⁻ levels to maintain a near normal or normal pH. Therefore, the compensatory mechanisms in chronic respiratory alkalosis result in a reduction in plasma HCO₃⁻ levels. This effect results in a mixed acid-base disorder, which will be discussed later.

Treatment of respiratory alkalosis is directed at discovering the underlying etiology and correcting it. In persons hyperventilating from anxiety, breathing into a paper bag may be useful. In mechanically ventilated patients with mechanical overventilation, a reduction in minute ventilation or tidal volume will achieve an increase in PaCO₂ and a reduction in pH. Correction of respiratory alkalosis is not without risk, as a rapid reduction in chronic respiratory alkalosis (PaCO₂) may result in metabolic acidosis. For example, as the PaCO₂ returns to normal, a chronic reduction in HCO₃⁻ may result in an acute metabolic acidosis.¹⁵ (See Acid-base balance.)

<table>
<thead>
<tr>
<th>Condition</th>
<th>pH</th>
<th>PaCO₂</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure respiratory alkalosis</td>
<td>High</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Pure respiratory acidosis</td>
<td>Low</td>
<td>High</td>
<td>Normal</td>
</tr>
<tr>
<td>Pure metabolic alkalosis</td>
<td>High</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>Pure metabolic acidosis</td>
<td>Low</td>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td>Metabolic alkalosis with respiratory compensation</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Metabolic acidosis with respiratory compensation</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>
A general rule to adhere to is that the PaCO₂ can roughly be estimated or should be similar to the two last digits of pH. For example, pH 7.25, PaCO₂ should approximately be close to 25 mm Hg.²

When there’s a mixed metabolic acidosis/alkalosis disturbance, it can be identified thru the calculation of an anion gap. As mentioned, the anion gap is an approximate measure of the additional amount of acid within the body; the HCO₃⁻ should decrease by approximately an amount equaling the increase in the anion gap. If the HCO₃⁻ is higher than the calculated increase of the anion gap, a chief metabolic alkalosis is mixed with the metabolic acidosis. Conversely, if the HCO₃⁻ is lower than the increase of the anion gap, then a non-anion gap metabolic acidosis is considered to be present and is worsening the anion gap acidosis. It’s important to remember that the mortality and morbidity of patients with metabolic acidosis is closely correlated with the etiology of the underlying process that lead to the derangement and the ability to correct it.

**Mixed acid-base derangements**

Mixed acid-base derangements occur when a combination of 2 to 3 chief imbalances are present simultaneously.¹³ Frequent examples of mixed acid-base derangements include:

- presence of a respiratory disorder (alkalosis/acidosis) that shrouds a metabolic disorder (acidosis/alkalosis)
- presence of a metabolic disorder (alkalosis/acidosis) that shrouds another metabolic disorder (alkalosis/acidosis).

Combined respiratory/metabolic derangements may consist of inappropriate compensation by the respiratory system for metabolic derangements. They are identified by judging the difference between the observed PaCO₂ and the calculated changes in PaCO₂ or by the observed or expected change in HCO₃⁻.¹⁶ If observed PaCO₂ is elevated higher than the calculated PaCO₂, it is assumed that a respiratory acidosis is present with a mixed metabolic disturbance. Conversely, if the observed PaCO₂ is decreased to a lower level than the PaCO₂ was calculated to be, a respiratory alkalosis is considered to be the chief derangement mixed with a metabolic imbalance. Formula for calculation of the expected PaCO₂ for a metabolic alkalosis/acidosis is as follows:

\[
\text{Paco}_2 = 1.5 \times (\text{observed HCO}_3^-) + 8 \pm 2
\]

Paco₂ decreases 1.2 mm Hg for each 1 mEq/L decrease in HCO₃⁻.

Another useful formula is Winter’s formula, which is as follows:

\[
\text{Paco}_2 = 1.5 \times (\text{observed HCO}_3^-) + 8 \pm 2
\]

**Caring for the critically ill**

Acid-base derangements are common in the critically ill patient. Nurses in the intensive care unit benefit from a review of the basic physiology of acid-base balance, an overview of common derangement in acid-base homeostasis, pneumonics intended to help with rapid differentiation of potential etiologies, and common treatment modalities.

**REFERENCES**


At The University of Alabama at Birmingham, Susan J. Appel is an associate professor and Charles A. Downs is an instructor.