

An Easy Approach to Understanding Acid-Base Balance in a Blood Buffer System

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ABSTRACT

Understanding acid-base disorders using weak-acid concepts learned in general chemistry class is challenging for pre-nursing and pre-professional biology students enrolled in anatomy/physiology and biochemistry classes. We utilized a graphic seesaw model of carbonic acid-bicarbonate equilibrium using the Henderson-Hasselbalch (H-H) equation of a weak acid. We then used real-world clinical case studies for students to identify acid-base disorders and the appropriate compensatory responses of the lungs and kidneys. Students developed a working knowledge of how the bicarbonate blood buffer system maintains a physiological pH of 7.4 using a “seesaw” with metabolic $[HCO_3^-]$ on one side, and respiratory PCO_2 on the other at a ratio of 20:1 in the H-H equation. When the dysfunction of either the kidneys or lungs causes the seesaw to tip, homeostasis pH is disrupted, causing an acid-base disorder classified as metabolic or respiratory acidosis or alkalosis. The functioning organ can “level the seesaw” by compensating for the dysfunction of the opposite organ to regain homeostasis. Unlike traditional ways of explaining acid-base disorders, this graphic seesaw method is a simple and easy way to achieve understanding.

Key Words: acidosis; alkalosis; bicarbonate; blood buffer; compensation; Henderson-Hasselbalch equation; homeostasis; kidneys; lungs; metabolic; respiratory; seesaw; weak acid.

○ Introduction

Although undergraduate health science students are first exposed to acid-base concepts in general chemistry courses, they seldom apply weak-acid equilibria concepts to biological systems. As a result, students may erroneously use strong acid/base equations to describe weak acid buffers. A buffer system is formed when a weak acid is paired with its corresponding salt. The tendency for a weak acid to retain its proton is defined as the pKa, a dissociation constant unique to each weak acid. Weak acids with a higher pKa have a stronger tendency to retain their acidic hydrogen, thereby decreasing hydrogen ions in solution. In an ideal buffer, the weak-acid affinity for protons acts as a “backup reservoir” supplying protons as needed within the buffer range defined as $pK_a \pm 1$ pH unit. This helps to keep the H^+ concentration stable, and thus the pH of the

solution within the buffering capacity when protons are added or removed from solution.

Maintaining physiological human blood pH (7.35–7.45) is vital for normal cell function. Blood pH that is too acidic or too alkaline can denature vital proteins and enzymes needed for normal cell processes (Rosival, 2011). Acute cases of acidosis or alkalosis where pH is outside of buffering capacity can result in sudden coma and potentially death if timely intervention does not occur. Therefore, early detection, diagnosis, and compensation are critical factors in determining patient outcome. The major buffer system responsible for stabilizing pH of the blood and extracellular fluids is the carbonic acid-bicarbonate conjugate pair (Figure 1).



Figure 1. Carbonic acid-bicarbonate equilibrium equation.

The H-H equation defines the relationship between pH and the ratio of salt (bicarbonate) and weak acid (carbonic acid):



The weak acid of the bicarbonate buffer system, carbonic acid, has a pKa of 6.1 (Pratt & Cornely, 2018). It is important to note that the pKa of carbonic acid is constant, and therefore pH is directly dependent on the ratio of bicarbonate to carbonic acid in the H-H

(A) H-H Equation

$$pH = pK_a + \log \frac{[Salt]}{[Acid]}$$

(B) H-H Equation for Carbonic Acid

$$pH \text{ of blood plasma} = 6.1 + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

$$pH = 6.1 + \log \frac{20}{1}$$

$$7.4 = 6.1 + 1.3$$

Figure 2. (A) Henderson-Hasselbalch equation for buffer systems; pH is a function of the pKa of applied weak acid (HA) and the logarithmic ratio of conjugate base (A^-) to weak acid concentration. **(B)** Henderson-Hasselbalch equation for the carbonic acid conjugate base buffer system; pH = 7.4 when the ratio of bicarbonate to carbonic acid is 20:1.

equation. The only mathematical way to satisfy the H-H equation with pH = 7.4 is for the overall ratio of bicarbonate to carbonic acid to be 20:1 (Figure 2).

○ Instructional Methods: Use of Visual Seesaw Model of Henderson-Hasselbalch Equation (H-H) in Clinical Case Studies of Acid-Base Disorders

Visual models are a powerful teaching tool that can be used to familiarize students with the dynamics of complex systems (Bobek & Tversky, 2016). Using a fun and easy seesaw method of the H-H equation, students can effectively identify acid-base disorders and compensatory functions of the lungs (carbonic acid) and kidneys (bicarbonate). One student even stated: “I got this nailed so clear.”

○ Materials

Introductory anatomy/physiology and biochemistry learning objectives pertaining to the bicarbonate-buffer system’s role in maintaining blood pH homeostasis can effectively be met using a simple seesaw method derived from the H-H equation. Under normal conditions (Figure 3), the seesaw is level when pH is 7.4, and the ratio of bicarbonate to carbonic acid is the ideal 20:1 ratio. This visual model emphasizes the respective roles of the lungs and kidneys in regulating PCO_2 and $[\text{HCO}_3^-]$ in maintaining a physiological blood pH and allows for quick recognition of imbalance and compensatory responses.

Classification of Acid-Base Disorders

There are two organs responsible for regulating carbonic acid and bicarbonate concentrations: the lungs via respiratory function, and kidneys via metabolic function (Figure 4). The lungs facilitate a fast-acting response to fluctuations in blood pH by triggering a change in respiration that quickly removes/retains CO_2 in the blood, thereby decreasing/increasing carbonic acid in the blood. The kidneys regulate carbonic acid when filtering blood by retaining or excreting H^+ or $[\text{HCO}_3^-]$ ions in the urine. Dysfunction of either the kidneys or lungs may affect their regulatory ability of respective blood buffer components. If the acid-base imbalance is induced by renal

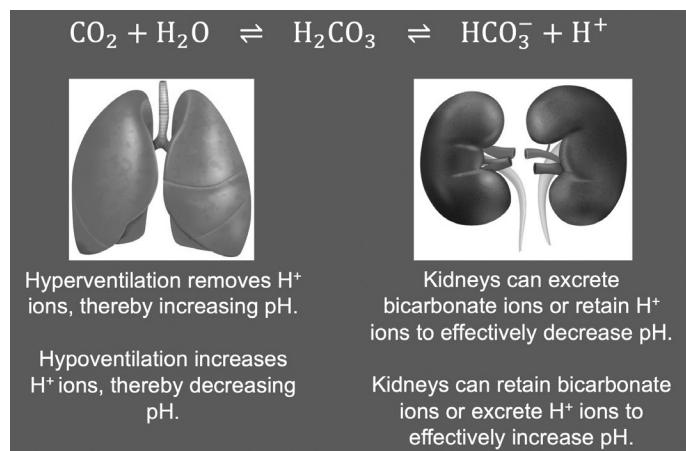


Figure 4. Overview of the roles and mechanisms of the lungs and kidneys in maintaining blood pH equilibrium.

dysfunction, the disorder is considered to be metabolic in origin. If the acid-base imbalance is induced by pulmonary dysfunction, the disorder is considered to be respiratory in origin. This brings about the possible diagnoses of either respiratory or metabolic acidosis or alkalosis.

Applying H-H Equation to Analyze Clinical Diagnostic Data

An arterial blood gas (ABG) test is a diagnostic tool used by health professionals to measure oxygen and carbon dioxide exchange in patients (Raffin, 1986). Routine ABG tests provide valuable information for making accurate diagnoses and management plans for acid-base disorders. We used realistic ABG test data so that students could reinforce the buffer concepts taught in lecture through real-world practical applications. Six data points are quantified in an ABG test: pH, PCO_2 , PO_2 , $[\text{HCO}_3^-]$, O_2 saturation, and base excess. However, the H-H equation only requires PCO_2 , and $[\text{HCO}_3^-]$ to determine overall system pH. This allows for a simple model to illustrate the balance between blood buffer components contributing to system pH.

There are three distinct steps in the interpretation of an ABG test: (1) determine status of overall system pH, (2) identify the abnormal buffer component, and (3) determine the appropriate compensatory response (Figures 4 and 9). The normal values for each of these three measurements must be provided and/or known (Figure 5).

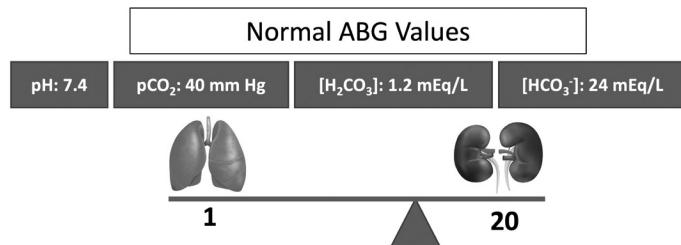


Figure 3. Carbonic acid-bicarbonate equilibrium illustrated as a level seesaw. The component on the lefthand side of the seesaw is $[\text{H}_2\text{CO}_3]$ obtained by converting from the ABG PCO_2 value. The component on the righthand side of the seesaw is $[\text{HCO}_3^-]$ and is obtained directly from the ABG results. Note how the fulcrum is off-center toward $[\text{HCO}_3^-]$ because the ratio of bicarbonate to carbonic acid is 20:1.

Normal ABG Results	
pH	<7.35 (acidic) 7.35-7.45 (normal) >7.45 (alkaline)
PCO_2 Respiratory Component	35-45 mm Hg
$[\text{HCO}_3^-]$ Metabolic Component	22-26 mEq/L

Figure 5. Table of normal ABG test result values relevant to the diagnosis and management of acid-base disorders.

Students must first establish whether the ABG blood plasma is normal, acidic, or alkaline. If the ABG pH value is outside the normal range, students can easily identify acidemia or alkalemia by the comparison of normal values (Figure 5). If the pH status of the blood plasma is identified as either acidic or alkaline, the second step is to determine which component in the buffer ratio is abnormal. Students can now identify the ratio of these components in the H-H equation. Here, students are asked to draw a seesaw as shown in Figure 7. The tilt of the seesaw aids in identifying the disorder and also determines which organ is causing the pH imbalance. Students can now easily see how the functional organ will compensate to reestablish a normal pH.

An ABG machine measures PCO_2 and converts to $[\text{H}_2\text{CO}_3]$ rather than directly measuring $[\text{H}_2\text{CO}_3]$ (Figure 6). This conversion can easily be carried out by multiplying PCO_2 by the solubility constant of carbonic acid in human blood (0.03 mmol/L). This provides a simple 20:1 ratio of $[\text{HCO}_3^-]$: PCO_2 in the H-H equation, resulting in normal blood pH 7.4 (refer back to Figure 2).

While the H-H equation is very helpful when working with buffer systems, this quantitative approach to the bicarbonate-buffer system is sometimes difficult to relate to physiological concepts. However, the proposed seesaw model is an excellent way to both visually and functionally relate weak acid buffer concepts to biological regulatory mechanisms.

(A) Normal ABG Values	(B) Metabolic Acidosis ABG Values
$\text{pH} = 6.1 + \log \frac{[24 \text{ mEq/L}]}{[0.03(40 \text{ mm Hg})]}$	$\text{pH} = 6.1 + \log \frac{[17 \text{ mEq/L}]}{[0.03(40 \text{ mm Hg})]}$
$\text{pH} = 6.1 + \log \frac{[24 \text{ mEq/L}]}{[1.2 \text{ mEq/L}]}$	$\text{pH} = 6.1 + \log \frac{[17 \text{ mEq/L}]}{[1.2 \text{ mEq/L}]}$
$\text{pH} = 6.1 + \log \frac{[20]}{[1]}$	$\text{pH} = 6.1 + \log \frac{[17]}{[1.2]}$
$7.4 = 6.1 + \log (20)$	$7.25 = 6.1 + \log (14)$

Figure 6. **(A)** Median normal values for $[\text{HCO}_3^-]$ and PCO_2 are used to demonstrate the calculation of pH using the Henderson-Hasselbalch equation. **(B)** Example of $[\text{HCO}_3^-]$ and PCO_2 values from a patient with an acid-base disorder. Since $[\text{HCO}_3^-]$ is <22, PCO_2 is normal, and pH is <7.35, this is a case of metabolic acidosis.

Recall from Figure 2, the ratio of salt to weak acid in the H-H equation must be 20:1 for a normal blood pH 7.4 (represented as a level seesaw in Figure 7A). If the pH is greater than 7.45, then the ratio of buffer components is >20:1, and the scale tips to the right denoting alkalemia. Alkalemia can be induced by increased renal $[\text{HCO}_3^-]$ retention in the blood resulting in metabolic alkalosis (Figure 7B) or decreased PCO_2 in the blood by the lungs resulting in respiratory alkalosis (Figure 7C). If the pH is less than 7.35, then

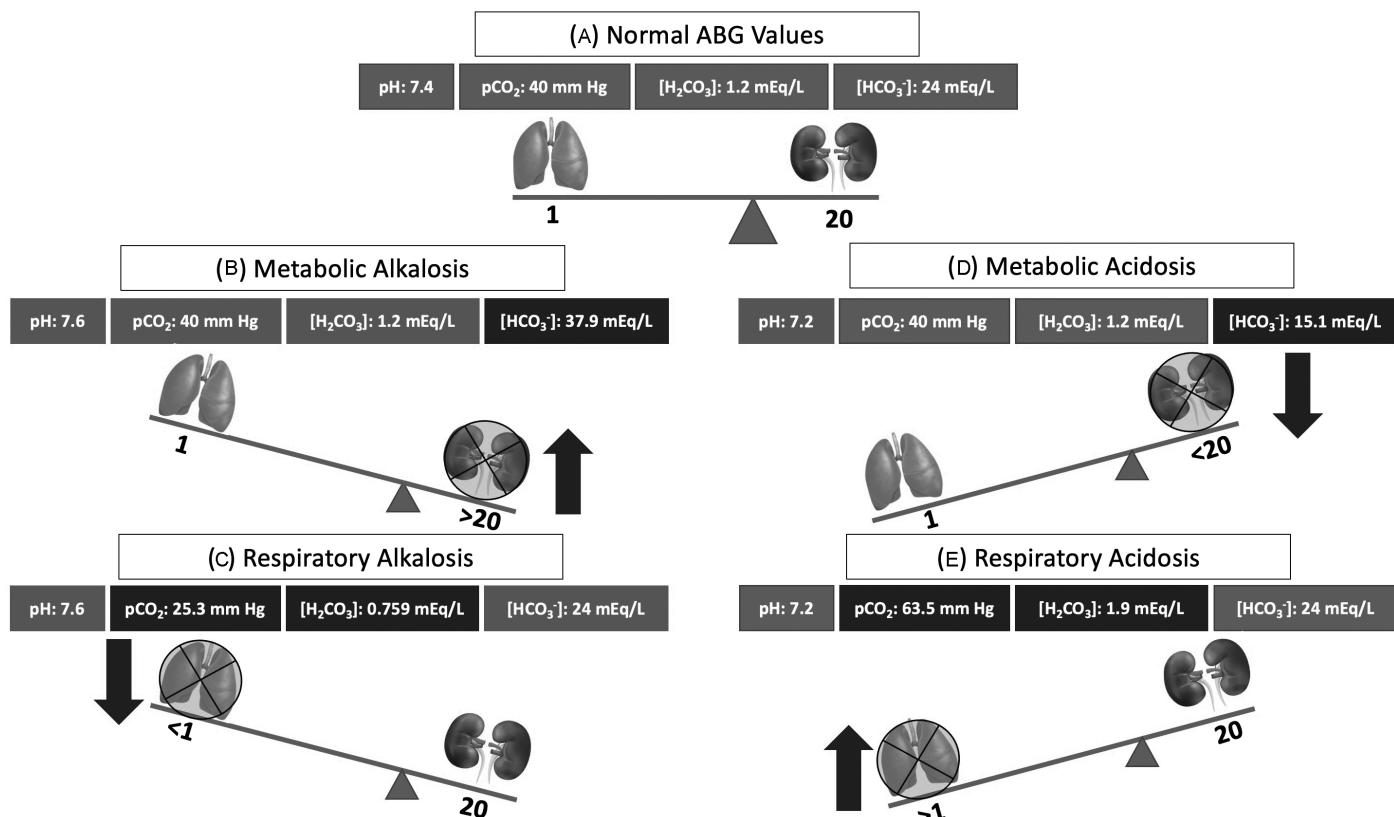


Figure 7. The dysfunctional organ as indicated by the abnormal buffer component is denoted by a circular "X" in parts B–E, along with an adjacent arrow indicating directionality of deviation from normal ABG values. **(A)** pH = 7.4 (normal), PCO_2 / $[\text{HCO}_3]$ is a straight line (20:1 ratio). **(B)** pH = 7.6, PCO_2 (normal), $[\text{HCO}_3]$ = 37.9 mEq/L (high; metabolic), the scale tilts toward $[\text{HCO}_3]$. **(C)** pH = 7.6, PCO_2 = 25.3 mm Hg (low, respiratory), $[\text{HCO}_3]$ (normal), the scale tilts toward $[\text{HCO}_3]$. **(D)** pH = 7.2, PCO_2 (normal), $[\text{HCO}_3]$ = 15.1 mEq/L (low; metabolic), the scale tilts toward PCO_2 . **(E)** pH = 7.2, PCO_2 = 63.5 mm Hg (high, respiratory), $[\text{HCO}_3]$ (normal), the scale tilts toward PCO_2 . Figure adapted from Pollak et al., 2018.

the ratio of buffer components is <20:1, and the scale tips to the left denoting acidosis. Acidemia can be induced by decreased renal $[HCO_3^-]$ retention in the blood resulting in metabolic acidosis (Figure 7D) or increased PCO_2 in the blood by the dysfunctional lungs resulting in respiratory acidosis (Figure 7E). Students can see the practical use of this diagnostic seesaw in Figures 9 and 10.

The seesaw gives students a concrete way to visualize abstract variables while retaining functionality for the purposes of ABG interpretation. A tipped seesaw reveals an evident imbalance, which allows for quick identification of the abnormal buffer component while also alluding to the correct compensatory response. The seesaw illustration of acid-base balance (Figure 7) in conjunction with an explanation of physiological regulatory mechanisms (Figure 4) sufficiently addresses the learning objectives related to blood pH homeostasis in anatomy/physiology and biochemistry while remaining interesting and easy to follow for students. This model provides students a simple, effective, and fun way to visualize the dynamics of the bicarbonate blood buffer system.

In the case of an uncompensated acid-base disorder, the individual buffer component that causes a disruption in the homeostatic 20:1 ratio is considered “dysfunctional,” and the buffer component involved in the corrective response is deemed “functional.” The key objective of a compensatory response is to restore a 20:1 ratio and therefore a pH of 7.4. The functional organ must

independently act to compensate for the dysfunction of the other to restore a 20:1 ratio (Pratt & Cornely, 2018). As shown in Figure 8, metabolic alkalosis can be compensated by increasing PCO_2 through hypoventilation restoring a 20:1 ratio and an equilibrium pH (Figure 8B). Metabolic acidosis can be compensated by decreasing PCO_2 through hyperventilation restoring a 20:1 ratio and an equilibrium pH (Figure 8D). The same principle can be applied in cases of respiratory dysfunction. For example, respiratory alkalosis can be compensated by the kidneys through excretion of $[\text{HCO}_3^-]$ in urine or increasing H^+ ions through retention in the blood (Figure 8C). Lastly, respiratory acidosis can be compensated by the kidneys through retention of $[\text{HCO}_3^-]$ in the blood or excretion of H^+ in the urine (Figure 8E).

Student Case Study & Survey Responses

After a preliminary lecture, Gordon State College students enrolled in anatomy/physiology and biochemistry classes were assigned a problem set of real-world acid-base disorder cases. The case studies outlined both the qualitative and quantitative approach to the bicarbonate-buffer system previously discussed; however, emphasis was placed on the visual seesaw shown in Figure 7 and maintaining a 20:1 ratio of buffer components in the H-H equation. Each case in the problem set presented a brief synopsis of the patient's symptoms and included data obtained from an ABG test (see Figure 9). Using

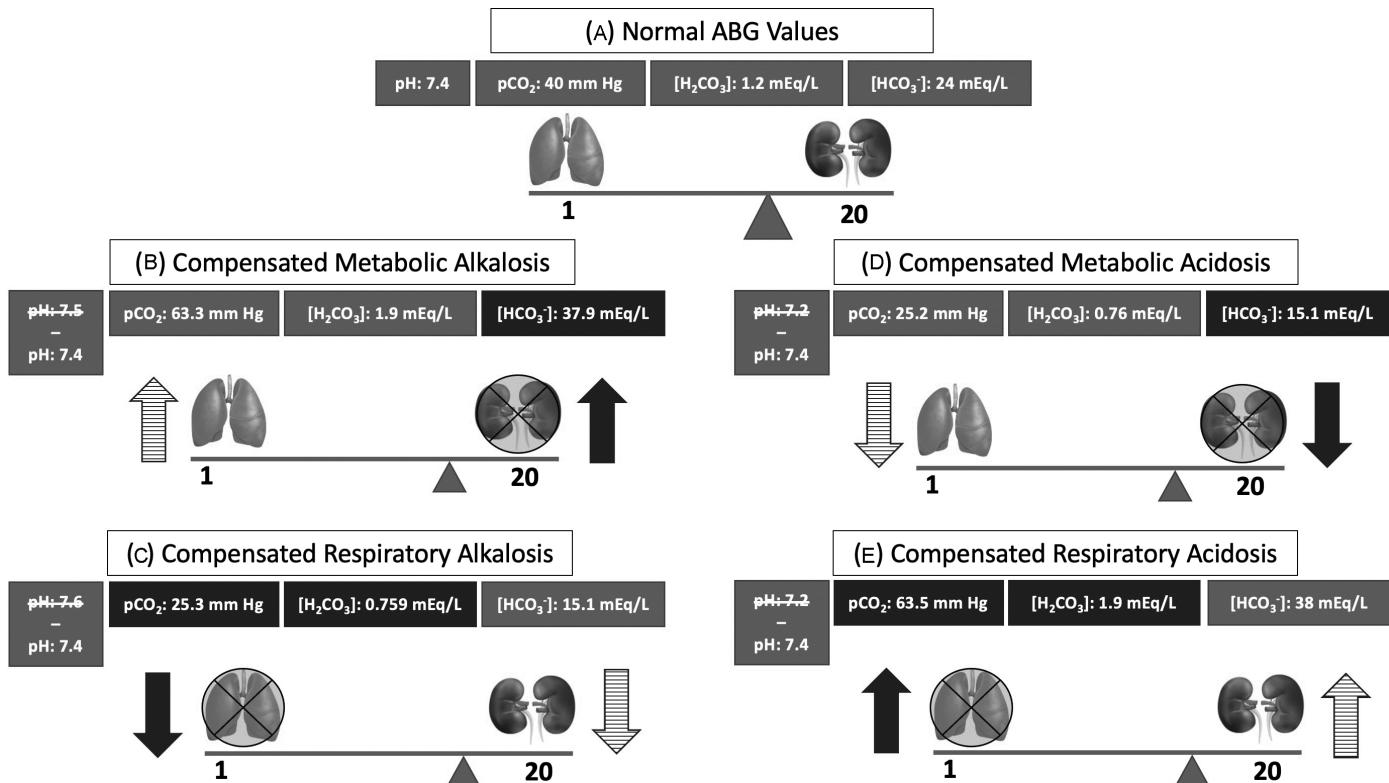


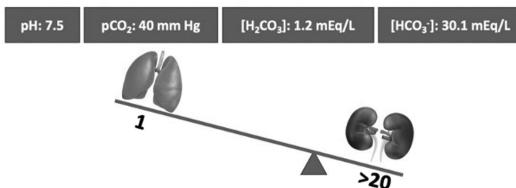
Figure 8. Abnormal pH is crossed out to emphasize before-and-after results of pH of compensation. The dysfunctional organ, as indicated by an abnormal ABG buffer component value, is denoted by a circular "X" in parts **B–E** because they cannot contribute to the compensatory response. An adjacent solid arrow indicates directionality of buffer component abnormality coupled with a dashed arrow indicating directionality of compensatory response. **(A)** Normal reference figure, pH = 7.4 (normal), $\text{PCO}_2/\text{[HCO}_3^-]$ is a straight line (20:1 ratio). **(B)** Metabolic alkalosis compensated by increased PCO_2 by the lungs to restore pH 7.4. **(C)** Respiratory alkalosis compensated by decreased $[\text{HCO}_3^-]$ by the kidneys to restore pH 7.4. **(D)** Metabolic acidosis compensated by decreased PCO_2 by the lungs to restore pH 7.4. **(E)** Respiratory acidosis compensated by increased $[\text{HCO}_3^-]$ by the kidneys to restore pH 7.4.

A 72-year-old male has been suffering with acute acid reflux and took half a bottle of antacid tablets to help alleviate his heartburn. A few hours later, he fell ill and was rushed to the hospital. The ABG indicated that the patients' blood pH was 7.5, his PCO_2 was 38, and his $[\text{HCO}_3^-]$ concentration was 29. Use this information to answer the following questions.

a) Which blood gas values are out of the normal range based on the ABG report? Explain what this could indicate.

His pH is 7.5 which indicates that he is in a state of alkalosis likely caused by the abundance of antacid tablets ingested. His pCO_2 , and therefore $[\text{H}_2\text{CO}_3]$ are well within the normal range (38 mm Hg, 1.14 mEq/L). However, his $[\text{HCO}_3^-]$ is too high indicating a **metabolic cause** of the disorder.

b) Illustrate this scenario by drawing a seesaw to visualize where the imbalance lies. (See Figure 8 for reference).



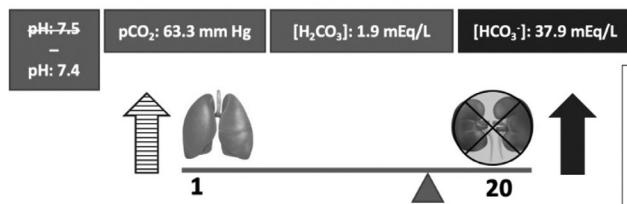
As shown in the figure, $[\text{HCO}_3^-] = 30.1 \text{ mEq/L}$ is greater than the normal range of values (22-26 mEq/L). $[\text{HCO}_3^-]$ is the metabolic component which is regulated by the kidneys which suggests renal dysfunction. Since $[\text{HCO}_3^-]$ is high and pCO_2 is normal, the scale will tip towards the 'heavy' renal component.

Figure 9. Case-study sample question (part 1 of 2) requiring students to identify the pH status of blood and recognize the abnormal buffer component.

c) What is the appropriate diagnosis for this patient based on the ABG test results and the known symptoms?

Metabolic Alkalosis

d) Based on what you know about the buffer system, which organ will be responsible for compensating to re-establish a physiological pH? (See Figure 9 for reference)



In this case, the kidneys are not functioning normally. Therefore, the $[\text{HCO}_3^-]$ value cannot change, and the compensatory response must be initiated by a respiratory pathway.

Since the kidneys are not functioning normally, the renal component $[\text{HCO}_3^-]$ cannot initiate the compensatory response. Instead, the lungs can compensate by slowing the respiratory rate which increases pCO_2 . While neither pCO_2 nor $[\text{HCO}_3^-]$ are normal, the temporary compensation by the respiratory component allows for $\text{pH} = 7.4$ while the metabolic issue is addressed.

Figure 10. Case-study sample question (part 2 of 2) requiring students to properly identify diagnosis and the appropriate compensatory response.

this information, students were asked to identify the correct disorder, identify the abnormal buffer component organ, and predict the compensatory response needed to restore a 20:1 ratio.

The seesaw model proved to be an effective tool for students when completing case-study problems similar to what can be seen in Figures 8 and 9. Of the students in both classes that were offered bonus surveys following the problem set, 21 of 24 (88%) from biochemistry and 32 of 32 (100%) from anatomy/physiology II elected to participate. Students from both sections demonstrated a clear understanding and ability to accurately diagnose acid-base disorders using ABG test results within the context of patient symptoms.

Most importantly, the students demonstrated the ability to think critically by applying the concepts of the H-H equation.

○ Discussion

Acid-base equilibrium is a fundamental biochemistry and physiology topic that has clinical implications for students entering careers in health care. This concept is especially important to understand in the wake of the COVID-19 pandemic due to the associated effects on lung function. While the H-H equation is ideal for describing the

bicarbonate-buffer system, the abstract variables can be difficult to conceptualize. Illustrating the H-H equation as a seesaw gives students a visual frame of reference to contextualize both the biological and chemical concepts needed to understand blood acid-base disorders. Student survey responses suggest that these methods effectively increased confidence and students' ability to recognize and identify acid-base disorders along with respective compensatory responses. Our students found the seesaw method to be a simple, yet effective, visual tool when applied to complex acid-base concepts.

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