WORKBOOK TO ACCOMPANY

CLINICAL APPLICATION OF BLOOD GASES

FIFTH EDITION

PAUL MATHEWS

BARBARA LUDWIG

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Clinical Application of Blood Gases

Fifth Edition

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Dedication

The authors wish to dedicate this workbook to Donald F. Egan, M.D., and Hugh S. Mathewson, M.D.: Mentors, Colleagues and Friends.

Learning is not a destination — it is a journey with stops and detours along the way to examine things off the beaten track, smell the flowers, meet new friends and visit with old friends. - PJM

Life is a bowl of cherries that includes both the pits and the stems. - BAL

Acknowledgements

The authors would like to acknowledge the support of our families (Micky, Heather, Amy and Tim - PJM; Margey - BAL) and our colleagues JAM, BLG and TSD. Deserving of special gratitude for their help and patience are Erica Luper, our secretary, and the editorial staff at Mosby — Jim Shanahan and Jennifer Roche.

We would especially like to acknowledge Barry A. Shapiro, M.D., for his guidance in this endeavor.

Introduction

Arterial blood gases are among the most valuable diagnostic tools available to practitioners of critical care medicine. They are also among the least understood of these tools. The study of acid-base and blood gas physiology is an important facet to the understanding and mastery of pulmonary physiology and pathophysiology.

This workbook is designed to aid in mastery of these topics. While keyed to the first ten chapters of Shapiro's *Clinical Application of Blood Gases*, this workbook can also serve as a stand-alone review text on acid-base and blood gas physiology. The question of why this workbook covers only the first ten chapters of Shapiro has been raised by colleagues and reviewers. The answer is simple: Chapters 1-6 cover the scientific and physiologic basis of ABG and acid-base studies. The remaining chapters (7-10) deal with the appropriate application of acid-base and blood gas data to acute clinical situations. These are the areas which generally cause the new learner studying arterial blood gases the most problems, and these are the areas on which we decided to concentrate.

In large part, the remainder of Shapiro's text (Chapters 11-27) deals with measuring and analytical systems, equipment and techniques of sampling, and quality assurance issues. Additionally, sample case studies are presented in those chapters which allow application of the content of the text.

The workbook is designed to present the concepts, facts and theories covered in Shapiro in several different ways in order to provide a learning tool applicable to varied learning styles. Thus, a content area is often presented using several approaches. We feel that any redundancy is valuable if it allows for fuller comprehension of this difficult subject matter.

Any factual or interpretive errors in this workbook are the fault of the authors and should not and do not reflect on the accuracy of Dr. Shapiro's text. As we end this introduction, we would like to take this opportunity to thank Barry Shapiro, M.D., for his support and trust in this project. Thanks, Barry.

How to use this workbook

The workbook is specifically structured to provide a balance between the attainment of new knowledge and the application of that knowledge. Each chapter has a similar framework designed to lead the learner into a full understanding of Shapiro's text. Generally, the content of each chapter is presented in the following order and format:

Objectives - This section provides learning objectives keyed to the chapter content from both the text and the workbook.

Definitions - This section presents new and/or important words, phrases, and symbols and their meanings.

Introduction - This portion of the chapter summarizes the content of the text chapter, adding some interpretation to the more difficult concepts.

Key Points - This section provides a detailed list of Shapiro's most important statements in the text chapter. These points provide a focus for review and self-assessment.

Tables and Figures - Each chapter of the workbook contains several tables and/or figures, some from the text and some designed especially for the workbook. These tables and figures summarize important information and should be consulted to clarify concepts and information.

Formulas - All formulas presented in the text are duplicated in the workbook. We have also included other useful formulas in the appropriate chapters.

Problems - Each chapter of the workbook contains problems to use as a self-review. We recommend that you treat these questions as a test; do not look at the answers until you complete the practice problems.

Answers to Problems - The answer to each problem in the previous section is provided along with the rationale for that selection.

Application Exercises/Case Studies - This portion of the workbook chapter gives you a chance to test your knowledge with case studies, problem situations and other activities. We have provided solutions for the application exercises/case studies in Chapters 1-3 and Chapter 6. These are not necessarily the only answers but give some insight into our problem solving approach. Chapters 4-5 and 7-10 do not have answers so that the course instructor can apply his or her own methods to the application exercise problems.

Suggested Additional Readings - Each chapter includes a bibliography of additional sources relevant to the topic covered in that chapter. These readings either expand upon the content in Shapiro and this workbook or present the topic in a slightly different way. We urge the reader to consult these excellent sources.

Review Questions - At the end of the workbook there is a self-test which consists of questions from each of the ten chapters of the workbook. These questions are comprehensive and should provide the reader with a challenge. The answers to the review questions are provided in a key following the questions but without explanation.

We suggest that persons utilizing this workbook for review do so in the order that material is presented. Instructors may wish to have their students begin by reviewing the objectives and definitions, followed by the introduction and key points. The tables, figures and formulas will help explain lecture material. Problems and application exercises will be most helpful when used to supplement lecture topics. The review questions provide a comprehensive test bank for the instructor's use.

Contents

CHAPTER 1

Metabolic Acid-Base Balance

Objectives

After reading Chapter 1 and successfully completing this chapter of the workbook the student will be able to:

1. Given the appropriate data, identify the acid-base status of a series of patients.
2. Discuss the concept of ionic dissociation.
3. Define and give examples of dissociation.
4. Define and provide examples of the process of buffering.
5. Write and discuss the chemical equation relating H_2CO_3 production to metabolic end products.
6. Define and compare weak acids and weak bases.
7. Differentiate between volatile and nonvolatile compounds.
8. Define the term *end product*.
9. Write the Henderson-Hasselbalch Equation.
10. Explain the significance of the Henderson-Hasselbalch Equation.
11. Assuming the appropriate data, use the Henderson-Hasselbalch Equation to calculate pH.
12. Discuss why water has a pH of 7.00 in terms of pK_w and the dissociation of H^+ and OH^-.
13. Given the appropriate data, calculate anion gap values.
14. State the pK for human plasma.
15. State the solubility coefficient for CO_2.
16. Define the standard bicarbonate and compare it with CO_2 combining power.
17. Define the following terms/symbols:

acidemia	metabolic alkalosis
alkalemia	metabolite
anion	pH
anion gap acidosis	red cell mass
anion gap anhydrase	respiratory acidosis
carbonic anhydrase	respiratory alkalosis
cation	uncalculated anion
ion	uncalculated cation
metabolic acidosis	[ ]

18. List three therapeutic interventions which may result in increased uncalculated cations.
19. Name three sources of nonvolatile acid metabolites which may cause anion gap acidosis.
20. Name two major sources of hyperchloremic acidosis.

Definitions

acid A substance which will donate hydrogen (H^+) ions to a solution (strong acids donate many H^+ ions; weak acids donate few H^+ ions to the solution).

acidemia pH is more acidic (lower) than normal, below 7.35 (determined by H^+ levels).

acidic solution [H^+] ions outnumber [OH^-] ions. Kw still = 1×10^{-14}.

acidosis More acid than bases in the solution (determined by HCO_3^- plasma levels; pH may be within normal range).

aerobic With oxygen or oxygen utilizing.

alkalemia pH is more basic (higher) than normal, above 7.45 (determined by H^+ levels).

alkalosis More base than acid in the solution (determined by HCO_3^- plasma levels; pH may be within normal range).

anaerobic Without oxygen.

anion Negatively (–) charged ions (H^+ acceptors).

anion gap The mathematical difference between the measured cations and the measured anions in the blood plasma.

base A substance which will accept hydrogen (H^+) ions from a solution (strong bases accept many H^+ ions; weak bases accept few H^+ ions from the solution).

base excess/deficit The deviation from the "normal" buffer status. May be either deficit (–) or excess (+).

basic solution [OH^-] ions outnumber [H^+] ions. Kw still = 1×10^{-14}.

bicarbonate The HCO_3^- ion, a "weak" base.

buffered A biochemical process through which the effects of strong acids or bases are mediated resulting in a relatively stable and moderate physiologic pH.

[ ] Symbol for "concentration," the amount of solute per unit of solvent.

carbonic acid H_2CO_3, a "weak" acid.

carbonic anhydrase An enzyme which increases the rate of carbonic acid formation by hydrating (adding H^+) and dehydrating (reducing H^+) CO_2.

catalyst A substance which affects the rate of a chemical reaction or changes that reaction's outcomes but is itself not changed or consumed by that reaction.

cation Positively (+) charged ion (H^+ donors).

CO_2 combining power Measured using an anaerobic plasma sample exposed to an equilibrated endtidal air sample.

dissociation The tendency or ability of a substance to break into its constituent elements or into intermediate compounds. Dissociation usually occurs in liquid environments or solutions.

extracellular Outside the cell.

Henderson-Hasselbalch (HH) Equation Mathematical expression of the physiologic acid-base relationship.

homeostasis The tendency of the body to maintain the stability of its chemical, physical and electromechanical systems in a state of dynamic balance. It involves a continuous process of adaptation and change in response to internal and external environmental factors.

hydroxyl ion The OH^- ion.

intercellular Between cells.

intercellular metabolism The physiologic processes of energy production and use within the cells.

intracellular Within the cell.

ion An electrically charged atom or compound. May be either negative (–) or positive (+).

Ka Dissociation constant of an acid (a).

ketoacidosis Increased H^+ due to reduced cellular glucose. Usually secondary to insulin deficiency. Also called diabetic acidosis.

Kw Dissociation constant of H_2O (1×10^{-14}).

logarithm The power to which 10 must be raised to equal a given number.

metabolites (end products) The biochemical elements or compounds which remain after the production of energy through metabolic processes.

mole/L 1 gram equivalent weight of a solute in each liter of solute.

neutral solution A solution whose $[H^+]$ and $[OH^-]$ are nearly equal. pH $\simeq$ 7.00.

nonvolatile substance A substance which does not change state easily (stable).

pathogenic metabolites Metabolic end products which produce effects resulting in a disruption of the body's homeostatic balance.

pH Shorthand notation which describes the **hydrogen ion (H^+) activity** or hydrogen ion concentration in a solution. pH is usually expressed to the second decimal point; e.g., 7.12.

pK pH point at which the solute is 50% dissociated (i.e., the point of maximum buffering capacity).

plasma bicarbonate A HCO_3^- value calculated from plasma pH and PCO_2.

red blood cell mass The total amount of red blood cells in the body.

sodium (Na) pump A biophysical mechanism that redistributes sodium across cell membranes into the extracellular spaces.

solubility coefficient A mathematical constant that reflects the relative ability of a solute to break into its constituent ions in a solvent (to form an ionic solution).

standard bicarbonate Bicarbonate (HCO_3^-) measured in fully oxygenated blood exposed to CO_2 at 40 mmHg pressure at 37° C.

uncalculated cations/anions Electrolytes (ions) measured or unmeasured which are not included in the anion gap calculation.

volatile substance A substance which can change its state or composition.

volatility The relative rate of change of state or composition.

Introduction

In Chapter 1 Shapiro discusses the important concepts of metabolic acid-base balance. In the course of this discussion he not only explains the basics of metabolic acidosis and alkalosis but also covers the following related ideas, mechanisms and equations:

pH – definition and calculation
metabolites – metabolic end products
the carbonic acid cycle
volatile vs. non-volatile acids
buffer systems
Henderson-Hasselbalch Equation – derivation and use
anion gap – function and calculation

Shapiro provides a logical and concise progression of equations detailing the derivation of the Henderson-Hasselbalch (HH) Equation. He first discusses the dissociation constant of water (Kw). Then he derives the HH Equation and its clinical modifications, pointing out its clinical implications. He next discusses the renal compensation (buffering) mechanisms. He describes three methods by which the kid-

ney eliminates H^+ ions. The filtration and carbonic anhydrase production functions of the kidney are also introduced in this chapter. Renal response to acid-base status changes is the next issue considered. Shapiro presents metabolic and respiratory acidosis and alkalosis states, describing the mechanisms by which the kidneys work to mediate acid-base disorders and maintain a dynamic homeostasis. These range from phosphate and ammonia buffer systems in metabolic acidosis to increased H^+ elimination and/or increased HCO_3^- introduction into the blood.

In terms of alkalotic states, HCO_3^- reclamation from the urine is an important defense against metabolic alkalosis. Hypokalemia (decreased plasma K^+) and hyponatremia (reduced plasma Na^+), however, reduce the efficiency of HCO_3^- reclamation from the urine. In respiratory alkalosis, decreased PCO_2 results in a decrease in H^+ production through carbonic anhydrase activity and therefore decreases HCO_3^- retention and reduces H^+ excretion.

The effects of abnormal electrolytes on the renal buffer systems and the hemoglobin buffers can be profound. Potassium (K^+) ions are moved to the extracellular spaces because of the Na^+ pump mechanism. Hemoglobin (Hb) thus exists as a weak acid in equilibrium with its weak K^+ salt (KHb). The K^+ ions can be exchanged for H^+ ions in the distal renal tubules. Reduced Na^+ requires renal reabsorption, thereby deferring HCO_3^- reclamation and H^+ ion excretion. Chloride (Cl^-) ion depletion reduces renal tubule cation exchange in preference to anions such as HCO_3^-.

Shapiro next discusses the concept of anion gap. Anion gap is a calculated value which describes the (charge) inequality between the major cations (K^+, Ca^+, Mg^+) and the major anions (Na^-, Cl^-, HCO_3^-). The "normal" anion gap equals 8-16 mMol/L. He also defines some common sources of anion gap disturbance. These include lactic acidosis, ketoacidosis, acidosis of renal failure and toxic anion gap acidosis. (See Chapter 13 of the text for more details.) Additionally, Shapiro discusses nonanion gap acidosis. This typically occurs with increased Cl^- plasma levels which replace reduced plasma HCO_3^- as in renal tubular acidosis or acute massive diarrhea or chronic diarrhea.

Metabolic acid-base disturbances are indicated by plasma HCO_3^- levels outside of the normal range. Remember that HCO_3^- is part of the Henderson-Hasselbalch Equation. Therefore HCO_3^- can be calculated from measured pH and PCO_2 values obtained through blood gas analysis. Determination of the status of buffering capacity of the blood can be carried out through calculation of the base excess or base deficit. These can be calculated independently of the compensating PCO_2 changes.

Lastly, Shapiro points out the differences between the terms *acidosis* and *alkalosis* and *acidemia* and *alkalemia*.

Key Points

- Life processes require a narrow range of pH.
- Normal metabolism results in the production of end products (metabolites) which form acids in aqueous (water) solutions.
- The major acid-forming metabolite is carbon dioxide (CO_2). 98% of normal metabolite end products are CO_2.
- CO_2 reacts with water (H_2O) to form carbonic acid (H_2CO_3), a volatile acid.
- H_2CO_3 can easily be reconverted to H_2O and CO_2 gas which can be exhaled ($H_2CO_3 \longleftrightarrow H_2O + CO_2$).
- Nonvolatile acids (1-2% of normal metabolites) are buffered.
- Strong acids donate many H^+ ions to the solution; weak acids donate relatively few H^+ ions to the solution.
- Strong bases accept many H^+ ions from the solution; weak bases accept relatively few H^+ ions from the solution.
- H^+ ion concentration ($[H^+]$) is referred to as pH.
- pH ranges from 0 to 14. The pH of pure water is 7.00.
- The ionization constant of water (Kw) is 1×10^{-7}.
- Water dissociates weakly to form H^+ and OH^- ions.
- The $[H^+] = 1 \times 10^{-7}$ ions and $[OH^-] = 1 \times 10^{-7}$ ions.
- Since $[H^+] = [OH^-]$ the solution is considered to be neutral.
- $H^+ + HCO_3^- \longleftrightarrow H_2CO_3 \longleftrightarrow H_2O + CO_2$; the H_2CO_3 cycle can be bi-directional.
- The Henderson-Hasselbalch Equation states:

$$pH = pK + \log \frac{[HCO_3^-]}{[H_2CO_3]} \simeq pH = pK + \log \frac{[HCO_3^-]}{PCO_2}$$

- pH is a ratio of $[HCO_3^-]$ to $[H_2CO_3]$ or $[HCO_3^-]$ to PCO_2.
- pK is 6.1 for human blood.
- The solubility coefficient for CO_2 is 0.0301.
- Normally renal blood flow should lose H^+ ions and gain HCO_3^- ions.
- pH is regulated by the kidney through two mechanisms: active exchange of H^+ and Na^+ ions in the renal glomerular tubules and the production of carbonic anhydrase by renal epithelial cells.
- Carbonic anhydrase is an enzyme (catalyst) which enhances the hydration and dehydration of CO_2.
- The kidney uses three methods to excrete H^+: reabsorption of filtered HCO_3^-, phosphorylation and ammonia formation. All of these cause HCO_3^- and Na^+ to enter the blood while H^+ is eliminated.

- The kidney controls both H^+ excretion in the urine and HCO_3^- reabsorption from the urine.
- Metabolic acid-base balance is dependent on the total amount of H^+ excreted.
- In order for phosphate and ammonia buffers to work in metabolic acidosis, adequate plasma sodium and phosphate levels must be present.
- Due to intercellular K^+ availability, hemoglobin (Hb) exists as a weak acid in equilibrium with the potassium salt (KHb).
- K^+ can be exchanged for H^+ in the distal renal tubule.
- In **respiratory acidosis** rising PCO_2 in the tubular cells causes increased intercellular $[H^+]$ which increases H^+ removal and HCO_3^- addition to the blood.
- Prevention of **metabolic alkalosis** requires normal Na^+ and K^+ plasma levels to reduce HCO_3^- reclamation and thus reduce plasma H^+ levels.
- **Respiratory alkalosis** is characterized by reduced PCO_2 which inhibits the carbonic anhydrase system's ability to both eliminate H^+ through and reclaim HCO_3^- from the urine.
- K^+ ions are primarily distributed to the intercellular spaces by the sodium pump mechanism which forces Na^+ into the extracellular compartment displacing the K^+ ions.
- If the sum of the serum cations (positively charged ions) is subtracted from the sum of the serum anions (negatively charged ions), the remainder is the anion gap. (K^+ is often not included in the calculation.)
- Normal anion gap is 8-16 mMol/L (12-20 mMol/L adding K^+).
- Decreased anion gap is commonly associated with decreased uncalculated anions or, less commonly, with increased uncalculated cations.
- Increased uncalculated cations may occur with Polymyxin-B, calcium or magnesium administration.
- Increases in uncalculated anions will cause anion gap acidosis and may occur secondary to metabolic acidosis, excessive organic salt therapy (Ringer's Lactate, etc.), dehydration or renal failure.
- Decreases in uncalculated cations may also result in anion gap acidosis.
- Anaerobic metabolism causes increased lactic acid and eventual lactic acidosis. This can be reversed by returning to aerobic metabolism.
- Some anaerobic metabolism is normal (in red and white blood cells, the brain and skeletal muscles). (See Chapter 13 of the text for more details.)
- Inability to utilize or produce glucose leads to ketoacidosis and is most often found in diabetics who don't produce insulin. (See Chapter 13 of the text for more details.)
- Renal failure results in retention of both organic and inorganic acids.
- Ingestion of toxic substances can cause anion gap acidosis. Examples include methanol, ethylene glycol and acetic acid.
- Increased plasma Cl^- occurs secondary to loss of plasma HCO_3^- and may be due to diarrhea or renal wasting.
- A key factor in determining metabolic acid-base status is the normality of the plasma HCO_3^-. This can be calculated from the pH and PCO_2.
- CO_2 combining power is measured using an anaerobic plasma sample exposed to an equilibrated endtidal gas sample.
- Standard CO_2 is measured in blood at 100% O_2 and 40 mmHg CO_2 at 37° C.
- Buffering capacity is defined in terms of base excess or base deficit.
- Acidosis and alkalosis refer to whether the acids or the bases are dominant in the plasma.
- Acidemia and alkalemia refer to the pH of the blood.

Tables and Figures

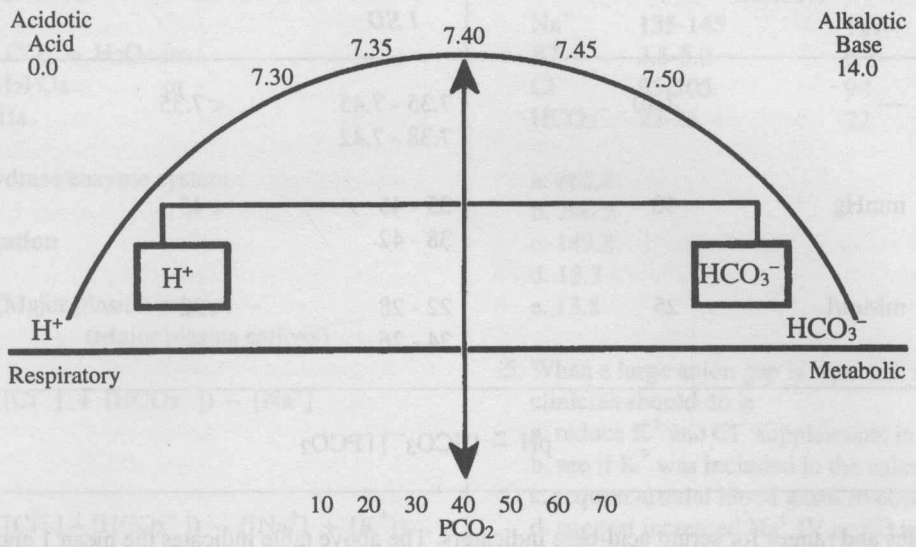

Figure 1: Graphic illustration of an acid-base balance model. As the PCO_2 (H^+ ion concentration) increases, the pH decreases (becomes more acidic). These changes can be balanced by increasing HCO_3^-. Note that normal arterial pH is slightly on the alkalotic side.

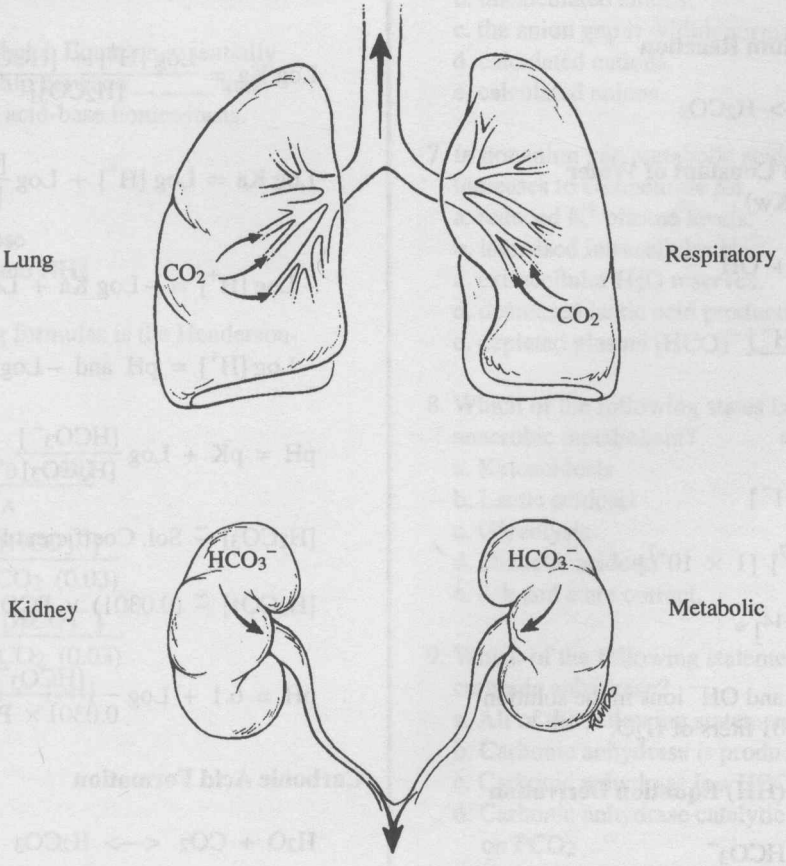

Figure 2: Illustration of the primary functions of the lungs and kidneys in acid-base balance. Note: The kidneys are responsible for metabolic components and the lungs for respiratory components of acid-base balance.

	Units	*Mean*	*Normal* *2 SD* *1 SD*	*Acidotic*	*Alkalotic*
pH	—	7.40	7.35 - 7.45 7.38 - 7.42	< 7.35	> 7.45
PCO_2	mmHg	40	35 - 45 38 - 42	< 45	> 35
HCO_3^-	mMol/L	25	22 - 28 24 - 26	< 22	> 28
$pH \simeq [HCO_3^-] \mid PCO_2$					

Table 1: Normal values and ranges for serum acid-base indicators. The above table indicates the mean 1 and 2 standard deviation ranges and the decision points for the three main clinical indicators of acid-base status.

Formulas

Carbonic Acid Equilibrium Reaction

$$H_2O + CO_2 \longleftrightarrow H_2CO_3$$

Ionization (Dissociation) Constant of Water (K_{H2O} or Kw)

$$H_2O \longleftrightarrow H^+ + OH^-$$

$$Kw = \frac{[H^+]\,[OH^-]}{H_2O}$$

Modified Kw formula

$$Kw = [H^+]\,[OH^-]$$

$$Kw = [1 \times 10^{-7}]\,[1 \times 10^{-7}]$$

$$Kw = [1 \times 10^{-14}]\ *$$

* The total number of H^+ and OH^- ions in the solution equals 0.00000000000001 liters of H_2O.

Henderson-Hasselbalch (HH) Equation Derivation

$$H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

$$Ka = \frac{[H^+] + [HCO_3^-]}{[H_2CO_3]} \text{ but:}$$

$$\text{Log Ka} = \frac{\text{Log}\,[H^+] + [HCO_3^-]}{[H_2CO_3]}$$

$$\text{Log Ka} = \text{Log}\,[H^+] + \text{Log}\,\frac{[HCO_3^-]}{[H_2CO_3]}$$

$$-\text{Log}\,[H^+] = -\text{Log Ka} + \text{Log}\,\frac{[HCO_3^-]}{[H_2CO_3]} \text{ but:}$$

$-\text{Log}\,[H^+] = pH$ and $-\text{Log Ka} = pK = 6.1$; thus:

$$pH = pK + \text{Log}\,\frac{[HCO_3^-]}{[H_2CO_3]}$$

$[H_2CO_3] \simeq$ Sol. Coefficient PCO_2 (0.0301) $\times$ PCO_2

$[H_2CO_3] \simeq (0.0301) \times PCO_2$; thus:

$$pH = 6.1 + \text{Log}\,\frac{[HCO_3^-]}{0.0301 \times PCO_2}$$

Carbonic Acid Formation

$$H_2O + CO_2 \longleftrightarrow H_2CO_3 \overset{CA*}{\longleftrightarrow} HCO_3^- + H^+$$

* carbonic anhydrase enzyme system

Renal pH Buffering Systems

$PCO_2 \longrightarrow CO_2 + H_2O \longrightarrow^{*} HCO_3^- + H^+ +$

a. $HCO_3^- \longrightarrow CO_2 + H_2O$ or
b. $HPO_4 \longrightarrow H_2PO_4$– or
c. $NH_3 \longrightarrow NH_4$–

* carbonic anhydrase enzyme system

Anion Gap Calculation

Anion Gap = (Major plasma anions) – (Major plasma cations)

Anion Gap = $([Cl^-] + [HCO_3^-]) - [Na^+]$

or

Anion Gap = $([Cl^-] + [HCO_3^-]) - ([Na^+] + [K^+])$

Problems

Select and mark the best answer.

1. The Henderson-Hasselbalch Equation essentially quantifies the relationship between _____ and _____ in maintaining acid-base homeostasis.
   a. pH and $[Cl^-]$
   b. kidneys and lungs
   c. pH and P_B
   d. lactic acid and glucose
   e. carbonic anhydrase and NH_3

2. Which of the following formulas is the Henderson-Hasselbalch Equation?
   a. $F_ACO_2 = \frac{V_{CO_2}}{\dot{V}_A}$
   b. $P_ACO_2 = \frac{V_{CO_2}\,(P_B - 40)}{\dot{V}_A}$
   c. $pH = pK - \text{Log}\frac{[HCO_3^-]}{PCO_2\ (0.03)}$
   d. $pH = pK + \text{Log}\frac{[HCO_3^-]}{PCO_2\ (0.03)}$
   e. $[HCO_3^-] - [PCO_2] = [pH]$

3. The pK of plasma is
   a. 7.45.
   b. 6.1.
   c. 7.38.
   d. 6.4.
   e. 1×10^{-7}.

4. Given the following data, calculate the anion gap:

	Normal	Measured
	mMol/L	
Na^+	135-145	127
K^+	3.5-5.0	6.8
Cl^-	95-105	98
HCO_3^-	22-26	22

   a. 265.8
   b. 200.2
   c. 149.8
   d. 15.2
   e. 13.8

5. When a large anion gap is reported, the first thing the clinician should do is
   a. reduce K^+ and Cl^- supplements in the patient's diet.
   b. see if K^+ was included in the calculation.
   c. request arterial blood gases to check arterial pH.
   d. suggest increased Na^+ IV or PO intake.
   e. check for increased plasma albumin levels.

6. The anion gap in question 4 is due to
   a. uncalculated cations.
   b. uncalculated anions.
   c. the anion gap is within normal range.
   d. calculated cations.
   e. calculated anions.

7. In nonanion gap metabolic acidosis, chloride [Cl] increases to compensate for
   a. reduced K^+ plasma levels.
   b. increased intracellular Na^+.
   c. extracellular H_2O reserves.
   d. decreased lactic acid production.
   e. depleted plasma $[HCO_3^-]$.

8. Which of the following states is not the result of anaerobic metabolism?
   a. Ketoacidosis
   b. Lactic acidosis
   c. Glycolysis
   d. Diabetic acidosis
   e. a, b and c are correct.

9. Which of the following statements is true regarding carbonic anhydrase?
   a. All of the following statements are correct.
   b. Carbonic anhydrase is produced in the kidneys.
   c. Carbonic anhydrase is a HCO_3^- catalyst.
   d. Carbonic anhydrase catalytic activity partly depends on PCO_2.
   e. Carbonic anhydrase helps conserve plasma bicarbonate and reduce plasma H^+.

10. Which of the following set of values will result in an acidotic pH if used in the HH equation?

	PCO_2	HCO_3^-
a.	47	32
b.	40	26
c.	32	24
d.	43	20
e.	38	23

For questions 11-15 use the paired PCO_2 and HCO_3^- values given to calculate the pH using the Henderson-Hasselbalch Equation (see log table in the appendix of the text).

11. PCO_2 40 mmHg; HCO_3^- 24 mMol/L; pH _____

12. PCO_2 35 mmHg; HCO_3^- 30 mMol/L; pH _____

13. PCO_2 50 mmHg; HCO_3^- 24 mMol/L; pH _____

14. PCO_2 14 mmHg; HCO_3^- 8.4 mMol/L; pH _____

15. PCO_2 65 mmHg; HCO_3^- 38 mMol/L; pH _____

Answers to Problems

1. b: [HCO_3^-] quantifies kidney function and PCO_2 quantifies lung function.

2. d: The Henderson-Hasselbalch Equation allows calculation of pH by examining the logarithmic function of the ratio of [HCO_3^-] and PCO_2. This must yield a positive number and account for the pKa of plasma. Thus, the positive log must be added to the pK.

3. b: The dissociation constant for human blood plasma is 6.1, the pH at which both the H^+ and HCO_3^- ions are 50% dissociated. pK is sometimes referred to as the plasma acid dissociation constant (pKa).

4. a: Anion gap represents the difference between the cations (positively charged ions) and the anions (negatively charged ions). The normal range of the ion gap is 12-20 mMol/L if potassium (K^+) is included or 8-16 mMol/L if K^+ is omitted from the equation.

5. e: Although K^+ may or may not be included in the anion gap calculation, its inclusion should be a matter of policy within the institution. Additionally, this value accounts for only a small portion of the anion gap. Plasma albumin, on the other hand, accounts for up to 50% of the anion gap.

6. c: Normal anion gap ranges from 8-16 mMol/L if K^+ is excluded to 12-20 mMol/L if K^+ is included in the calculation.

7. e: Because there is a direct trade of Cl^- for HCO_3^- (note the signs are the same), the anion gap will remain within normal limits; but because the HCO_3^- is the offsetting buffer for H^+ ions and Cl^-, it is not a good mediator of pH. pH will be shifted toward the acidic range.

8. c: Each of the other choices lists a condition or conditions caused by oxygen free metabolism. Answers a and d are synonyms for the same condition. Answer b refers to the end product of cellular anaerobic metabolism.

9. a: Each of the statements describes a true function or characteristic of carbonic anhydrase, an important renal enzyme (catalyst) for the maintenance of acid-base balance through the elimination of H^+ ions and the conservation of HCO_3^-.

10. d: In order for pH to be acidotic, the PCO_2 must be higher than the normal range (35-45) and the HCO_3^- must be equal to or lower than its normal range (22-28 mMol/L). That is, the ratio of HCO_3^- to ($PCO_2 \times 0.03$) must be greater than 20:1.

11. pH = 7.40: This is a "normal" set of PCO_2 and HCO_3^- values resulting in a "normal" pH. The ratio of HCO_3^- to ($PCO_2 \times 0.03$) is $24/(40 \times 0.03) = 24/1.2 = 20/1$ or 20. The Log of 20 = 1.30.

    pH = pK + 1.3; pH = 6.1 + 1.3; pH = 7.40

12. pH = 7.56: This is an example of an alkalotic pH. The ratio of HCO_3^- to ($PCO_2 \times 0.03$) is $30/(35 \times 0.03) = 30/1.05$; reduced this equals a ratio of $\simeq$ 28.6 / 1. The Log of 28.6 = 1.4564.

    pH = pK + 1.4564; pH = 6.1 + 1.4564; pH = 7.5564; pH $\simeq$ 7.56

13. pH = 7.30: This is an example of an acidotic condition. The ratio of HCO_3^- to ($PCO_2 \times 0.03$) is $24/(50 \times 0.03) = 24/1.5$; reduced this equals 16/1. The Log of 16.0 = 1.2041.

    pH = pK + 1.2041; pH = 6.1 + 1.2041; pH = 7.3041; pH $\simeq$ 7.30

14. pH = 7.40: Even though there are serious abnormalities in the HCO_3^- and PCO_2 as reported, the ratio of HCO_3^- to ($PCO_2 \times 0.03$) is $8.4/(14 \times 0.03) = 8.4/0.42$. This approximates 20/1, resulting in a "normal" pH. The Log of 20 = 1. 3010.

    pH = pK + 1.3010; pH = 6.1 + 1.3010; pH = 7.4010; pH $\simeq$ 7.40

15. pH = 7.39: Again we see a case where severely abnormal [HCO_3^-] and PCO_2 result in a "normal" pH. The

reason is the same; the ratio of [HCO_3^-] and (PCO_2 × 0.03) remains at about 20/1. 38/(65 × 0.03) = 38/1.95. Reduced this equals 19.48/1. The Log of 19.48 ≃ 1.2900.

pH = pK + 1.2900; pH = 6.1 + 1.2900; pH = 7.3900; pH ≃ 7.39

Case Study

Chief Complaint: Mary Timmons, a 67-year-old black female, presented to the ER today with a chief complaint of nausea, vomiting and diarrhea of three days' duration.

Clinical Course: Three days prior to admission the patient attended a regional church meeting that included a pot luck picnic.

Pre-admission day 2: She awoke in the middle of the night with a headache, stomach cramps, nausea, vomiting and diarrhea. She woke her husband, who stated she had fever and chills at that time; her temperature was 102.5° F by oral thermometer. Assuming she would recuperate over the course of the day, she remained in bed and drank fluids and broth.

Pre-admission day 1: The symptoms remained unchanged. To combat the headache and the aches and pains she self-administered 2 (60 gr) buffered ASA tablets Q3-Q4° through the next day. She continued to run a temp (99.4-101.3° F). She would vomit and have attacks of diarrhea every 4-5 hours. She continued to push fluids and continued bed rest.

Admission day: The patient was transported to the ER by her husband, who gave the above history. The patient was admitted to the ER at 1:30 A.M. via wheelchair.

Past Medical History: The patient is a married mother of 3 (ABO 1) with no significant neuro, orthopedic, ob or gyn problems or Hx. Six years ago she was diagnosed as having "mild to moderate" COPD secondary to smoking. No previous history of GI or cardiac problems was elicited during the history taking. EENT: no history except for the need for glasses since age 35.

Social History: 20-year smoking history of 1-1.5 ppd. The patient states she stopped smoking at age forty concurrently with the birth of her first grandchild. The patient denies use of ETOH or nonprescribed drugs. Children and spouse L&W, 5 grandchildren L&W. The patient is a cytotechnology supervisor at this institution and is a civic and church leader.

Physical Exam:

Subjective:

The patient is a slim, febrile and mildly disoriented black female. She is hunched over, clutching her stomach, moaning and grimacing in pain. She appears to be short of breath and breathes in short, shallow, rapid respirations. She is responsive but vague in her answers to questions.

Objective:

Abdomen: Bowel sounds are hyperactive; no rebound tenderness although patient states "the muscles hurt when I vomit."
AP scar noted.

Chest: Slight increase in AP diameter. HS normal with slight tachycardia (98-108 bpm). Decreased expiratory sounds in the bases with a slight expiratory wheeze noted. No rhonchi or rales present. Respiratory rate increased, depth decreased.

HEENT: Neck supple, PERRLA, mouth dry and inflamed

Neuro: non-contributory except as noted

GU: deferred

Vital signs: T = 99.5° F oral
P = 99 beats per minute
R = 28 breaths per minute, shallow
BP = 132/90

Laboratory: Among other tests, ABGs were drawn to assess her current status relative to her pre-existing COPD. Additionally, bloods for serum electrolytes were drawn simultaneously. A GI motility test was ordered but deferred as the patient was unable to comply with the conditions for the test. Chest x-rays and an EKG were done.

EKG: Mild tachycardia with U waves and flat T waves noted. Rate is increased, rhythm is WNL, no indications of prior cardiac disease. IMP: mild tachycardia, hypokalemia.

CXR: Air bronchogram is noted, decreased aeration in bases, occasional patchy infiltrates noted in periphery. Diaphragm is mildly flattened, AP diameter is increased. IMP: mild to moderate COPD, ? pneumonic process/aspiration.

ABGs

	Norm	Obs
pH	7.35-7.45	7.52
PCO_2	35-45 mmHg	38
PO_2	80-100 mmHg	82
O_2	sat ≥ 95%	90

Chemistry

	Norm	Obs
Na^+	135-145 mMol/L	105
K^+	3.5-5.0 mMol/L	2.8
Ca^+	5.0-10.0 mMol/L	4.0
Cl^-	95-105 mMol/L	110
HCO_3^-	22.0-26.0 mMol/L	30.0
Glucose	0.5-1.5 gm/dL	0.6

Hematology		
	Norm	Obs
Hb	12-18 gm/dL	16 gm/dL
Hct	37-52%	60%
RBC	4-6 million/mm3	4-6 million/mm3
WBC	6-10 thousand/mm3	18 thousand/mm3
Osmolality	285-295 mOsm/L	288 mOsm/L

1. What is the probable diagnosis for Mrs. Timmons?

2. What is Mrs. Timmons' acid-base balance status?

3. Explain the effects of Mrs. Timmons' symptoms on her acid-base values.

4. Why are her Hb and Hct elevated? What should be done to rectify this? What might you expect to happen to her "lytes" and acid-base balance due to the treatment of her elevated Hb and "crit"?

5. What is Mrs. Timmons' anion gap? Why is this condition present? What additional treatment is indicated to correct the anion gap?

6. What effect did Mrs. Timmons' COPD have on her current problem? How do you think her admission pH and PCO_2 compare with her usual "normal" pH and PCO_2?

7. Should oxygen be given to treat the tachycardia and low PO_2?

8. What respiratory monitoring or evaluation procedures should be ordered?

9. What effect will Mrs. Timmons' temperature have on CO_2 and production of metabolites?

Answers to Case Study Questions

1. Bacteremia, secondary to food poisoning from contaminated food at the church picnic. The vomiting and diarrhea has compromised an already delicately balanced acid-base status.

2. Mixed metabolic and respiratory alkalosis.

3. The metabolic alkalosis is secondary to "acid dumping" caused by the vomiting and diarrhea which result in the loss of metabolic acids (H^+ donors). The respiratory component is due to the tachypnea (because she is a COPD patient we would expect an elevated P_aCO_2).

4. The nausea, vomiting and diarrhea result in decreased absorption and retention of fluids, thus reducing circulating fluid volumes. As a result of the lower volume of fluid, the solute concentrations increase, although the total amount of solute may decrease or remain the same. The increased temperature (pyrexia) will also promote increased insensible water loss further concentrating the solutes (Hb, Hct and electrolytes).

5. Anion Gap = $([Cl^-] + [HCO_3^-]) - ([Na^+] + [K^+]) =$
$([110] + [30.0]) - ([105] + [2.8]) =$
$(140) - (107.8) = 32.2$

   IV administration of a balanced electrolyte solution and reduction /control of nausea, vomiting and diarrhea are the treatments of choice in Mrs. Timmons' care.

6. Given her COPD, Mrs. Timmons' admission pH and P_aCO_2 were probably radically different from her "normal" pH and P_aCO_2. A COPD patient would have elevated CO_2 levels and a normal or low (more acid) pH. As Mrs. Timmons becomes more fatigued, her respiratory efficiency will decrease and her work of breathing (WOB) will increase, resulting in more CO_2 production. The elevated temperature suggests not only an infective process but also increased metabolic rate. The increased metabolic rate will increase O_2 consumption while concurrently increasing CO_2 and metabolite production.

7. No, Mrs. Timmons' PO_2 is in the low normal range. Additional O_2 is not needed and may increase her risk of respiratory distress as her CO_2 levels are below the hypercapnic response levels. Also, her tachycardia is at the high end of the normal range and will decrease as her temperature decreases. Resolution of the pneumonia, tachypnea and hyperventilation should help address the acid-base and PCO_2 problems.

8. Pulse oximetry and endtidal CO_2 should be monitored, as should ECG and cardiac rate. The first two monitors will reduce the need to perform arterial puncture to obtain arterial blood gases. Additionally, aerosolized bronchodilators and steroids in conjunction with high volume aerosols will liquify and decrease the viscosity of secretions which can then be mobilized by using assisted cough and airway clearance techniques.

9. Increased temperature indicates an increase in metabolic rate. As metabolism increases, to produce energy needed to combat infection, so do its end products (CO_2, heat and other metabolites). The result is an increase in temperature and an increase in PCO_2. The increased temperature (pyrexia) will also promote increased insensible water loss, further concentrating the solutes (Hb, Hct and electrolytes).

   Note: Only Chapters 1-3 and 6 will include answers to the Application Exercises/Case Studies. The remaining Applications Exercises/Case Studies will be used by the instructor to augment, lead to or enhance Socratic or discovery method dialogue with the students.