Case-based learning of blood oxygen transport

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LEARNING THE DYNAMICS of oxygen transport by the blood is a demanding task for the undergraduate student of physiology. He/she must piece together how oxygen distributes itself among the alveolar airspace, plasma, and red blood cells as blood flows through the lungs and how blood unloads oxygen as it flows through the tissues. The student must make sense of the dynamic aspects of these processes in view of the partial pressures of oxygen (PO2) reported in different locations in the body and the relation between PO2 and oxygen content of the blood illustrated by the oxygen-hemoglobin (Hb) dissociation curve. It is no wonder that mastering the dynamics of oxygen transport is one of the more challenging activities facing students as they strive to understand respiratory physiology.

It would certainly make it easier if students arrived at a physiology course with a familiarity with the necessary background chemistry. However, classroom research has shown that, despite the exposure to solution chemistry and the chemistry of equilibria gained from previous coursework, students frequently have difficulty creating meaningful models of how oxygen is transported by the blood, and this adversely affects their ability to comprehend respiratory physiology.

This article reports on the student analysis of a case study designed to enhance the understanding of oxygen transport by the blood (1). Case-based learning offers an active alternative to traditional instruction by lecture or textbook reading (3). Students test their conceptions of oxygen transport by exploring the pathophysiology of a real world problem: carbon monoxide (CO) poisoning. They reexamine their comprehension of the chemistry of oxygen-Hb binding as they investigate the degree to which CO poisoning reduces the amount of oxygen carried to body tissues. They strengthen their understanding of the role that Hb plays in external respiration by localizing where CO acts to disrupt oxygen transport. As students provide answers to the case study questions, they open a window into their conceptions of the dynamics of oxygen transport by the blood. The present study tracked the answers provided by students and interpreted them in light of the mental models that students may have built about oxygen transport. The companion study (4) describes the impact of this type of case-based learning on the remediation of the Sa/PO2 misconception.

METHODS

Case Study and Learning Issues

This article contains the case study given to the students and provides learning issues and teaching notes helpful for instructors who want to use it in class. The case and a more extensive set of teaching notes are available on the internet (2). The case study is reprinted here courtesy of the National Center for Case Study Teaching in Science (http://ublib.buffalo.edu/libraries/projects/cases/case.html) and the Journal of College Science Teaching (1).

When Charles returned to his apartment at 5 PM in the evening, he turned on his old kerosene-fueled space heater. It had been a cold day in late spring and his third floor apartment was chilly. After spending an hour fixing dinner, he ate while watching the evening news. He noticed that his vision became progressively blurred. When he got up to go to the kitchen he...
felt lightheaded and unsteady. Upon reaching the kitchen he became very disoriented and passed out. The next thing he remembers was waking up in the intensive care unit of the hospital. His friends stopped by about 7 PM and found Charles unconscious on the kitchen floor. By ambulance he was rushed unconscious to the hospital.

An arterial blood sample drawn when he first arrived at the hospital shows the following values:

<table>
<thead>
<tr>
<th>Gas</th>
<th>Partial Pressure</th>
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<tbody>
<tr>
<td>N₂</td>
<td>573 mmHg</td>
</tr>
<tr>
<td>O₂</td>
<td>95 mmHg</td>
</tr>
<tr>
<td>CO₂</td>
<td>40 mmHg</td>
</tr>
<tr>
<td>CO</td>
<td>0.4 mmHg</td>
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</table>

**Question 1.** The blood gas measurements show abnormalities in the partial pressure(s) of what gas(es)?
A. N₂, O₂, and CO
B. CO and CO₂
C. CO alone
D. N₂ and CO
E. O₂ and CO

**KEY LEARNING ISSUES.** Students need to know the normal arterial partial pressures of the major blood gases as a point of comparison. Students should realize that trace amounts of CO are normally found in the blood but at partial pressures considerably below the value reported for the patient.

A measurement of Charles’ blood reveals that Hb is 50% saturated with CO (50% HbCO).

The oxygen-Hb saturation curve in Charles’ blood (50% HbCO) and that under normal conditions (2% HbCO) is shown in Fig. 1. CO₂ binding to Hb is normal in both cases.

**Question 2.** What is the approximate percent saturation of Hb by O₂ in normal arterial blood?
A. 100%
B. 97%
C. 75%
D. 50%
E. 35%

**ADDITIONAL TEACHING NOTES.** Instructors need to point out that the axis showing the percent oxygen saturation represents the percentage of the total Hb-binding sites potentially available to oxygen that are actually occupied by oxygen. CO does not reduce the total binding sites but makes them unavailable for oxygen binding.

**Question 3.** What is the maximum amount of O₂ (ml/100 ml blood) that can be carried in Charles’ arterial blood?
A. 2 ml/100 ml
B. 5 ml/100 ml
C. 10 ml/100 ml
D. 15 ml/100 ml
E. 20 ml/100 ml

**KEY LEARNING ISSUES.** Students need to know that the ml/100 ml value is the measure of the oxygen-carrying capacity of Hb in blood. Students must be able to use the graph to derive the ml/100 ml value of CO-poisoned arterial blood as a function of its PO₂. Question 3 affords an opportunity for the instructor to assess student conceptions about how CO caused a reduction in the oxygen-carrying capacity of the blood.

**Question 4.** CO enhances the Bohr effect. This means that CO will cause a more pronounced shift of the Hb-oxygen saturation curve to the:
A. right.
B. left.

**ADDITIONAL TEACHING NOTES.** Instructors may want to address the fact that CO enhances the fixed acid Bohr effect and that the direction and extent of the shift depends on whether the blood is in the lungs or in the tissues.

**Question 5.** If the PO₂ in the body tissues is 20 mmHg, what is the best estimate of the amount of O₂ (ml/100 ml) that can be released from Charles’ blood as it circulates in his systemic capillaries?
A. <1 ml/100 ml
B. 1 ml/100 ml
C. 2.5 ml/100 ml
D. 5 ml/100 ml
E. 10 ml/100 ml

**KEY LEARNING ISSUES.** Students need to recognize that the amount of oxygen delivered to the tissues is the difference between the amount in the blood that enters from the arteries and the amount that leaves after the blood equilibrates with the tissues at the capillaries. Question 5 affords an opportunity for the instructor to assess whether students understand that the oxygen-Hb dissociation curve can be used to determine differences in the oxygen content of blood found at different locations in the body.

**ADDITIONAL TEACHING NOTES.** It is likely that the PO₂ in body tissues will be reduced to a much greater extent than 20 mmHg during CO poisoning since tissue PO₂ is not fixed but rather is a dependent variable of tissue oxygen extraction. Instructors should address the issue of whether oxygen consumption in the tissues of a CO-poisoned individual would be expected to be reduced to the extent implied by the answer to the question. Instructors may want to alter question 5 by posing a signifi-

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1 Instructors may alter the question by posing a significantly lower tissue PO₂ or they may ask students to determine the PO₂ in the tissue fluids of a CO-poisoned individual under the condition where the tissue oxygen consumption has remained normal.

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**Fig. 1.** The oxygen-hemoglobin (Hb) saturation curve in Charles’ blood (50% HbCO) and that under normal conditions (2% HbCO).
cantly lower tissue PO₂ or they may want to ask students to determine the PO₂ in tissue fluids of a CO-poisoned individual under the condition where the tissue oxygen consumption has remained normal.

Question 6. In Charles’ blood, the partial pressure of CO in the blood is far lower than the Po₂, yet the percent saturation of Hb by each gas is equal. This result indicates that the affinity of Hb for CO is approximately how many times greater compared with O₂?
A. 38
B. 100
C. 238
D. 708
E. 1,783

Key Learning Issues. Students must realize that CO competes with oxygen for binding to Hb. Students must understand that affinity is a measure of the tendency of a molecule (ligand) to bind to its target (receptor) and that it can be expressed as the percent occupancy of the target at a known concentration of the ligand. Students need to know that the percent saturation is a measure of the percent occupancy and that Po₂ is a measure of ligand concentration. The students need to realize that when two competing ligands show equivalent percent occupancies, then the ratio of the concentrations (or partial pressures) of the two different ligands reflects the inverse ratio of their relative affinities. The instructor has an opportunity to assess the extent of student understanding of oxygen transport by blood as a process of reversible, specific binding to Hb.

Question 7. Would you expect Charles’ disorder to be accompanied by chemoreceptor-mediated hyperventilation?
A. Yes, because the percent oxygen saturation of Hb in his blood is decreased.
B. Yes, because CO acts as a central nervous system neurotransmitter and central chemoreceptors are located in the brain.
C. Yes, because an elevated partial pressure of CO is detected by peripheral chemoreceptors in carotid and aortic bodies.
D. No, because the Po₂ in his blood is normal.
E. No, because CO is unable to diffuse across the blood-brain barrier.

Key Learning Issues. Students need understand that the respiratory control system regulates ventilation by selectively monitoring the PO₂ in the arterial blood. Question 7 affords an opportunity for the instructor to assess how students understand the physiological relation between the monitoring of blood oxygen and the delivery of oxygen from the lungs to tissues.

Additional Teaching Notes. Instructors may want to include the added dimension that arises from the metabolic acidosis induced by the prolonged oxygen starvation and ask students to explain its impact on the regulation of ventilation in a CO-poisoned individual.

Question 8. Fundamentally, Charles’ condition is a problem of:
A. pulmonary ventilation.
B. diffusion across the respiratory membrane between the alveolar airspace and alveolar capillaries.
C. transport of gases between the alveolar capillaries and capillary beds in other tissues.
D. exchange of dissolved gases between the blood and interstitial fluid in peripheral tissues.
E. absorption of oxygen and release of CO₂ by cells in the peripheral tissues.

Key Learning Issues. Students need to know the individual steps and sequence of events in the transport of oxygen from the lungs to cells. Question 8 provides an opportunity to assess the extent to which students understand how and where Hb functions in external respiration.

Additional Teaching Notes. The problem of inadequate oxygen transport extends beyond the specific step in external respiration impaired by CO poisoning. The instructor may want to challenge students to explain the secondary consequences of CO poisoning on each of the subsequent events in external respiration.

Question 9. With regard to the physiology of external respiration, Charles’ disorder is most analogous to:
A. barbiturate-induced hypoventilation.
B. altitude sickness.
C. emphysema.
D. acute hemorrhagic anemia.

Key Learning Issues. Students need information about how each disorder alters the oxygen chemistry of the blood. Question 9 affords another opportunity for students to demonstrate that they understand how Hb functions in external respiration by identifying the pathophysiological disorder whose effect best corresponds with the inhibitory action of CO on Hb in the blood.

Additional Teaching Notes. Matching by analogy requires careful reasoning. Instructors may want to ask students to explain the extent to which CO poisoning is or is not analogous to each of the disorders described.

Question 10. Which of the following is NOT an appropriate component of an aggressive treatment plan for Charles’ disorder?
A. Administration of a breathing gas mixture with a high percentage of oxygen.
B. Alkalization of the blood (increase the pH).
C. Partial blood replacement with normal, compatible whole blood.
D. Administration of a breathing gas mixture with elevated levels of CO₂.

Key Learning Issues. Students need to know the effect of concentration on competitive inhibition, the effect of pH changes on the uptake and release of oxygen by Hb, the effect of dilution on the action of an inhibitory molecule, and the effect of an elevated blood partial pressure of CO₂ on the rates of ventilation and excretion of volatile substances from the body. This multifaceted question gives students the opportunity to trace out the cause-and-effect relations that lead to the changes in external respiration induced by each of these treatments. This analysis enables students to determine whether or not each treatment would enhance of the ability of the blood to deliver oxygen to the tissues by counteracting the effect of CO poisoning.

Student Analysis of the Case

A detailed presentation of the case study and its use in teaching human physiology has been published (1). The case was designed for undergraduates majoring in biology, nursing,
and education who have had instruction in first-year college-level sciences and who are enrolled in the second semester of an introductory course in human anatomy and physiology. These students are typically sophomores who have successfully passed a year of general chemistry or a one-semester survey of chemistry for nonmajors. The description provided here situates student work on the case study in relation to the sequence of other learning activities in the course. Students were given the case story and questions before any instruction in respiratory physiology had taken place. They solved the case study outside of regular class time and were allowed to work individually or in groups. Students submitted their machine-scoreable answers after all instruction on respiratory physiology had been completed and before the in-class review of the case. Multiple-choice answers were compiled and tabulated. For more information about additional assessment activities administered during student work on the case, see the companion study (4).

RESULTS AND DISCUSSION

Analysis of Student Answers

A record of the answers to the case questions provided by the class of 42 students is shown in Table 1. A large majority of the students (80% or higher) correctly answered questions 1, 2, 3, 4, 6, and 7. However, only 24% of the students provided the correct answer for question 5. The majority of the wrong answers (27 of 32) reflected imprecise use of the oxygen-Hb dissociation curve to determine the amount of oxygen in the venous blood leaving the capillaries. This was evident by the fact that most of the students correctly determined the amount of arterial oxygen entering the capillaries, as shown by their answer to question 3. The imprecision revealed by the majority of the wrong answers to question 5 suggests that greater emphasis ought to be placed on helping students in the graphical analysis of the oxygen-Hb saturation curve to make more exacting determinations of the oxygen content for a particular PO2 of the blood.

A comparison between student answers to questions 1, 6, and 7 on the case study and the prevalence of the Sa/PO2 misconception after instruction in respiratory physiology (3) yielded an intriguing disparity. The student answers to question 1 indicated that 93% of students determined that the arterial PO2 of the individual was normal. Presumably, students recognized this as a result of their examination of the blood gas values provided by the case study. They also used this observation to make proper determination of the relative affinity of Hb for CO in question 6 (see Table 1). Furthermore, by their response to question 7 on the case study, 36 of 42 students acknowledged that the PO2 in the blood of the CO-poisoned individual was normal. Thus, by their answers to these three questions on the case study, most students indicated that they judged that CO poisoning did not alter PO2.

Nevertheless, the analysis of student answers to the postinstructional conceptual diagnostic question about Sa/PO2 misconception yielded a different picture (4). Here, 56% of the students predicted that poisoning of Hb by CO would cause a decrease in PO2. What might account for this disparity? How could a substantial percentage of students have indicated that the PO2 of a CO-poisoned individual was normal based on their analysis of the case, yet predict that CO poisoning would reduce PO2 on the postinstructional query? These results highlight the transience and fragility of student conceptualizations of the relation between free and bound oxygen in the blood over the course of instruction.

It may be relatively easy to affirm that information presented in a case study indicates that the PO2 in a CO-poisoned individual is normal. It appears to require a more robust understanding of the mass action of the oxygen-Hb reaction to make a correct prediction about the effect of CO poisoning on PO2 of the blood in response to a conceptual diagnostic question. The disparity points out the difficulty that students apparently experienced in applying the comprehension of partial pressure, percent saturation, and equilibrium chemistry of the oxygen-Hb reaction gained from case analysis to successfully answering the conceptual diagnostic question designed to evaluate their understanding of these same concepts.

The disparity also begs the question of whether the student responses to questions 1 and 7 from the case study were useful diagnostics for student understanding of the dynamics of oxygen-Hb binding in the blood. The student response to question 8 may tell us otherwise. This question asked students to associate CO poisoning with the different physiological components of external respiration. Only 21% of the students answered this question correctly (see Table 1); 61% of the erroneous answers identified the problem as gas diffusion across the respiratory membrane (see Table 1, question 8, answer B). Thus, a majority of the students apparently situated the CO problem at the entry step of oxygen uptake into the blood.

Furthermore, the student answers to question 9 indicated the high degree of assurance that these students had in this placement. All of the students (20 of 20) who had located the problem in the lungs on question 8 (answer B) also identified emphysema as the pathology that was analogous to CO poisoning (question 9, answer C). This disease is specific to the respiratory membrane and is associated with impaired gas diffusion. The fact that 100% of these students chose this disease shows that they were careful in their selection of the analogous pathology based on the respiratory locus they had chosen. Thus, the student responses to questions 8 and 9 tells us that the high frequency of correct answers to questions 1 and 7 may be unreliable indicators of the extent of student understanding of the mass action of oxygen entry into the blood and binding to Hb.

Moreover, this misunderstanding of the location of CO poisoning was remarkably persistent. Two weeks after students

Table 1. Student answers to the case study questions

<table>
<thead>
<tr>
<th>Question</th>
<th>A</th>
<th>B</th>
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<td>10</td>
<td>1</td>
<td>12</td>
<td>1</td>
<td>27</td>
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</table>
had received the correct explanation to question 8, they were asked on an in-class exam to choose the phrase that best completed the statement “CO poisoning is fundamentally a problem of...” Only 55% of the students answered this question correctly with the choice “transport of O₂ by red blood cells.” Although the distribution of individual answers on the exam was not recorded and could not be matched with the student answers from the case study, it may be presumed that a large fraction of the incorrect answers could be correlated with the original response to question 8 on the case study: “diffusion across the respiratory membrane between the alveolar airspace and alveolar capillaries.” What might explain the persistence of this response?

The rationalization provided by a student during the in-class case study review may clarify our understanding. This student suggested that, because oxygen was “not getting into the blood” (i.e., to Hb), the problem must have resided at the entry step. While the reasoning behind this explanation is apparent, it reflects an underlying misconception about what constitutes oxygen entry into the blood and how it would be observed. The student failed to recognize that the uptake of oxygen into the blood is a two-stage, sequential process involving three distinct compartments: alveolar air, plasma, and red blood cells. In this way of thinking, a reduction in the percent saturation of Hb in the blood cells indicated there was a difficulty with the entry of oxygen into the blood. The significance of PO₂ as a measure of oxygen uptake into the plasma was apparently discounted.

If this type of faulty reasoning underlies the oral explanation, then it is clear that the student overlooked the evidence manifest in the patient’s PO₂: that oxygen did normally enter the plasma. In effect, the student ignored the first stage of oxygen uptake into the blood and, as a result, made a direct association between changes in diffusion across the respiratory membrane and changes in the percent saturation of Hb. This finding is consistent with the interpretation of the Sa/PO₂ misconception provided by Michael et al. (6). It would be interesting to confirm that other students who placed the location of the CO problem at the respiratory membrane reasoned in this way. If this explanation is typical of student thinking, an exploration of this question may help to illuminate why some students retain the Sa/PO₂ misconception in spite of instruction in respiratory physiology.

Of the nine students who answered question 8 correctly, i.e., they indicated that the fundamental problem in CO poisoning involved the transport of oxygen between the lungs and tissue (see Table 1), six students also made the correct prediction about the change in PO₂ on the postinstructional conceptual diagnostic question about Sa/PO₂ misconception (3). These six students represented 43% of the all students who showed repair of the Sa/PO₂ misconception over the course of instruction in respiratory physiology. Moreover, nearly all of the students who answered question 8 correctly also answered question 9 correctly as well (7 of 9 students). These results show that this group of students demonstrated a cohesive understanding of both the problem’s locus and its analogy.

On the other hand, none of these nine students made correct predictions about PO₂ in response to the conceptual diagnostic questions probing the Sa/PO₂ misconception prior to instruction or at the time when students handed in their case analysis (4). Thus, although a correct response on the case study about the location of CO poisoning was not correlated with remediation of the Sa/PO₂ misconception at the time that students handed in the answers to the case questions, it did appear to predispose the students toward correcting their misconceptions by the time of the postinstructional query. These results suggest that learning activities that help students obtain a clearer conception of the locus of the problem of CO poisoning may play an important role in helping students eventually overcome the Sa/PO₂ misconception.

Only a minority of students correctly answered question 10 about the treatment of CO poisoning. Presumably, this reflects the difficulties that many students have in using their comprehension of the chemistry and physiology of the problem to delineate a single, correct answer. However, few students incorrectly chose answers A or C, suggesting that there was widespread understanding that CO poisoning represents a preferential competition with oxygen for Hb binding. This left most students with a choice between “alkalization of the blood” and “breathing elevated CO₂.” Why did so many students decide incorrectly between these two choices? Students may have overestimated the benefits of a pH-dependent, leftward shift in the oxygen-Hb dissociation curve on oxygen uptake at the lungs and underestimated or neglected the detrimental effects of a leftward shift on oxygen release at the tissues. With regard to “breathing elevated CO₂,” students could have put too much emphasis on the detrimental effects of elevated CO₂ on body function compared with the value of CO₂-induced hyperperpnea for increasing the excretion of CO. In either circumstance, the distribution of the student answers suggests that students have a rudimentary ability to reason beyond their limited understanding of the dynamics of oxygen-Hb binding and chemoreceptor activation. It is likely that a more indepth exploration of the physiological benefits and pathophysiological deterrents due to alkalization of the blood or breathing elevated CO₂ will help students arrive at a more robust understanding of blood oxygen transport and chemoreceptor-mediated regulation of external respiration.

Implications for Teaching and Learning

The analysis of student answers to the case questions suggests that work on the case study can help students to overcome the difficulties they experience in using the oxygen-Hb dissociation curve to inform their understanding of how oxygen is carried in the blood. A high percentage of students could correctly use the oxygen-Hb dissociation curve to make realistic estimates of the amount of oxygen transferred from the lungs to tissues. This is not surprising because the case study emphasized the practical importance of indicators of blood oxygen chemistry (PO₂, percent saturation, and volume of O₂ per 100 ml blood) for estimating the amount of oxygen that can be taken up and released by the blood. The case also challenged the students to think more deeply about the role that Hb plays in oxygen transport by asking them to situate its function in the process of external respiration. Furthermore, as documented in the companion study (4), student work on the case study was associated with a selective 36% reduction in the frequency of the Sa/PO₂ misconception over the course of instruction in respiratory physiology. Thus, the case study showed practical utility in helping the students learn important concepts in blood oxygen transport.
Despite the success indicated by the high percentage of students who correctly use the oxygen-Hb dissociation curve, student answers to questions 8 and 9 indicated that many students failed to build an accurate and sturdy model of how oxygen moves from the alveoli to the blood and how it is partitioned between the plasma and red blood cells. In particular, these students do not appear to distinguish the plasma from the red blood cell in their analysis of oxygen uptake into the blood. These results suggest that students would benefit from additional learning activities designed to enhance their understanding of the dynamics of how oxygen is partitioned between these three physiological compartments. For example, students could be required to create two-dimensional oxygen maps that represent oxygen transport from the lungs to blood under relevant physiological conditions (5) or to analyze visual representations of the oxygen partitioning between plasma and red blood cells when blood is subject to different PO2s (7). In conjunction with case analysis, these instructional activities should help a greater number of students to surmount the Sa/Po2 misconception and arrive at a more comprehensive understanding of oxygen transport by the blood.

REFERENCES