The Use of Case Studies in an Undergraduate Biochemistry Course

ARTICLE *in* JOURNAL OF CHEMICAL EDUCATION · MARCH 1998

Impact Factor: 1.11 · DOI: 10.1021/ed075p475

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Use of Case Studies in an Undergraduate Biochemistry Course

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The case-study method of instruction is increasing in popularity. In an article in the *Journal of College Science Teaching*, Clyde Freeman Herreid notes that, unlike instructors of business or law, instructors of science have rarely used the case-study method (*1*). Fortunately, that is changing and instructors of various scientific disciplines are adapting this method to their courses. Articles have appeared in which instructors describe how they use the case study method in their courses to solve "real-life" problems in environmental chemistry (*2*), general chemistry (*3*), molecular modeling and computational chemistry (*4*), scientific inquiry courses (*5*), and nonmajors science courses (*6*).

For years, medical schools have used the case-study method during the clinical portion of instruction, but only recently have case studies been used in the preclinical portion of the medical curriculum (e.g., in the first-year biochemistry course). Preclinical problem-based curricula have been established at Harvard University (*7*), Michigan State University (*8*), University of New Mexico (*9*), the Chicago College of Osteopathic Medicine (*10*), Rush Medical College in Chicago (*11*), Dalhousie University in Canada (*12*), and many others. In some institutions, the problem-solving method is used throughout the entire curriculum; at others, case-study exercises are held in conjunction with introductory lectures. In any case, in the medical school environment, use of the problem-solving method is faculty intensive. The case-study exercises are structured so that medical school faculty act as facilitators for groups of 5–6 students. The facilitator meets with the group throughout the semester and guides it in problem-solving efforts.

For instructors of biochemistry who wish to adapt this type of problem-solving exercise to their undergraduate courses, this type of arrangement is not possible. At liberal arts colleges, chemistry department faculties are small and usually include only one biochemist. Even at midsize schools, the number of biochemists on the chemistry department faculty is likely to be small. Therefore, several modifications must be made in using this type of teaching method. The lack of sufficient faculty to act as facilitators for student groups means that the instructor plays the role of consultant rather than facilitator. The student groups must also of necessity work more independently than their counterparts at medical schools. The case-study exercises themselves must be fairly structured.

The exercise described here was developed at Providence College to assist students in learning the biochemical pathways of the cell. While students appeared to master individual pathways fairly easily, they seemed to have greater difficulty making connections among pathways. The assignment was designed to help students make these connections, with the hope that at the same time, retention of basic biochemical facts would improve and students would rely less on rote memorization of facts and more on understanding the basic principles. Clinical cases were chosen because the majority of students who take biochemistry at Providence College are interested in attending medical school or are interested in scientific disciplines related to medicine.

Benefits of the Case-Study Exercise

The outcomes of problem-based learning in medical schools have been extensively reviewed (*13*). The authors note that both students and faculty found the experience more enjoyable, and that the students performed as well as or better than their conventionally trained counterparts on clinical examinations. From educators of undergraduate students, evidence that case-study exercises are beneficial is mainly anecdotal. Instructors who have used the case-study method have noted that the exercise is an "engaging vehicle" for learning the terminology and methodology of the discipline (*6*) and that it allows students to develop flexibility in their thinking processes (*2*). The hands-on approach of the case-study method of problem solving allows students to learn by doing instead of by reading a textbook or listening to a lecture. In the process of solving the case, students develop higher-order skills of analysis and application, which is the goal of most science courses. The use of a realistic situation also illustrates the relevance of basic science course work to society (*1*).

Description of Assignment

Providence College offers a one-semester biochemistry course that covers structure and function of macromolecules, intermediary metabolism, and a short introduction to molecular biology. Students undertake the case study after the intermediary metabolism portion of the course has been completed. The class is divided into groups of 3–5 students. The groups are randomly assigned a case, and each group receives a different case. The case describes a patient who is suffering from an inherited metabolic disease. In most cases, the disease is an "inborn error of metabolism"—that is, a particular enzyme in a metabolic pathway is deficient or nonfunctional. The patient's symptoms are described. Sample laboratory data are provided along with normal values, so that students can discern deviations from the norm. The description of the case is followed by a series of questions in which students are asked to determine the identity of the missing enzyme, and then to explain why the missing enzyme leads to the observed symptoms. In some cases, students might be asked to prescribe a course of treatment (excluding gene therapy) and are required to explain why the proposed treatment would be effective in relieving the patient's symptoms.

The student groups meet outside of class and solve the case in the best manner they see fit. They use their course textbook and are encouraged to use outside resources, including the campus library and even local health professionals with whom they may be acquainted. Students are invited to consult with the instructor regarding their cases, especially if they are not sure they are on the right track, but they are not required to do so. They then write a short (3–5 page) paper that describes the solution of their case-study problem. During the final week of the semester, each group is allotted 15 minutes to deliver an oral presentation of their case to the class. The team receives a single grade for their oral and written work, and each member of the team receives the same grade.

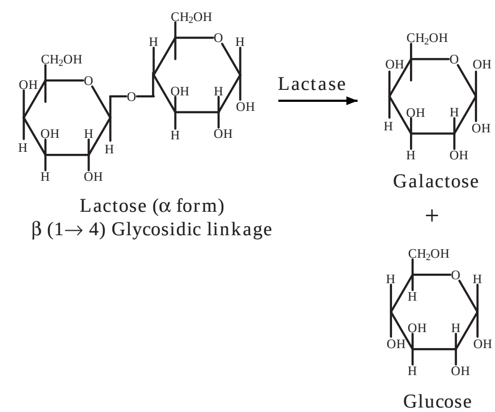
A Typical Case

The patient is a seven-day old baby boy who has failed to thrive since birth. He was born with cataracts. Vomiting and diarrhea began within the first few days of milk ingestion. Galactosemia and galactosuria were also noted. An assay of galactose-1-phosphate in erythrocytes showed a level of 400 mg/g of hemoglobin (the normal concentration is 0–50 mg/g). The galactosuria disappeared within three or four days of intravenous glucose feeding.

1. Why does the infant boy have galactosemia and galactosuria following milk ingestion? Why do these symptoms disappear when glucose is administered intravenously?
2. What enzyme is the infant lacking? Explain your answer.
3. The physician decides to treat the patient by dietary galactose restriction. On the galactose-free diet, all of the infant's symptoms disappear—he gains weight, nausea and vomiting cease, and the cataracts regress. Should she instruct the parents to give the infant soybean milk? (Hint: Soybean milk contains raffinose and stachyose.)
4. You are concerned that the galactose-free diet might be harmful to the infant. After all, galactolipids are necessary for myelin formation in the developing neonate. The physician assures you that the diet is not harmful. How will the infant synthesize the necessary galactolipids on a galactose-free diet?
5. In diabetics, cataracts form because the high concentration of glucose in the lens allows some of it to be converted to sorbitol. Sorbitol, a sugar alcohol, changes the osmolarity of the lens, which leads to the aggregation and denaturation of lens proteins. Similarly, in the patient described here, cataracts form because of the conversion of galactose to galactitol. Describe this pathway in more detail.

Case Solution

The sequence of reactions involved in the metabolism of galactose is shown in Scheme 1. The accumulation of galactose-1-phosphate indicates that the infant lacks the enzyme galactose-1-phosphate uridyl transferase. Lactase is present to hydrolyze the lactose in milk to glucose and galactose, so the infant doesn't suffer from lactose intolerance. Galactokinase is also present to phosphorylate the galactose to galactose-1-phosphate. At this point, the missing transferase results in galactose-1-phosphate accumulation. The transferase enzyme is necessary to convert galactose-1-phosphate to glucose-1-phosphate, which can enter glycolysis. Galactose accumulates as well, causing galactosemia and galactosuria.



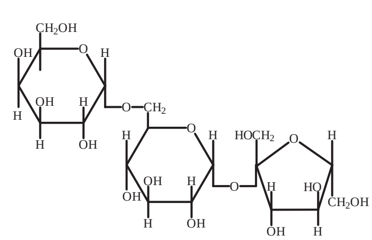
Galactose + ATP $\xrightarrow{\text{galactokinase}}$ Galactose-1-phosphate

Galactose-1-phosphate + UDP-glucose $\xrightarrow{\text{galactose-1-P}_i\text{ uridyltransferase}}$ Glucose-1-phosphate + UDP galactose

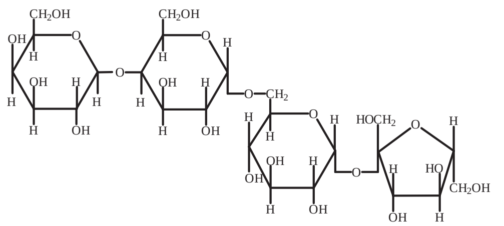
UDP-galactose $\xrightarrow{\text{epimerase}}$ UDP-glucose

Scheme I

On a galactose-free diet, the symptoms that are caused by accumulation of galactose-1-phosphate disappear. Since breast milk contains lactose, which is metabolized to galactose, it is not recommended as a food source for the infant. At first glance, it appears that soy milk would also be inappropriate, since the sugars raffinose (1) and stachyose (2) also contain galactose, as can be seen in the structures below. However, enzymes are not available to metabolize raffinose and stachyose to free galactose, so soy milk is a perfectly acceptable food source for the infant.

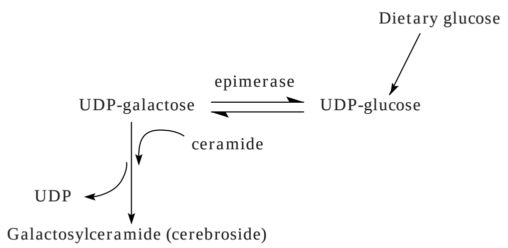


raffinose (**1**)



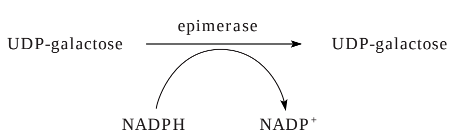
stachyose (**2**)

Galactolipids can still be synthesized from a galactose-free diet because the epimerase reaction is reversible, as shown in Scheme II. Dietary glucose is converted to UDP-glucose. The epimerase reaction then converts the UDP-glucose to UDP-galactose, which can be used to synthesize galactosylceramide, a cerebroside.



Scheme II: the reversible epimerase reaction

The patient suffers from cataracts because galactose is converted to galactitol, which causes aggregation and denaturation of lens proteins. The aldose reductase enzyme catalyzes the reduction of galactose to galactitol with concomitant oxidation of NADPH, as shown by the following reaction scheme:



Resources

The above case was constructed using several articles that appeared in the *Journal of Pediatrics* in the early 1960s (*14, 15*). Similar cases have been written using material found in this journal as well as the *Journal of Clinical Investigation*, the *New England Journal of Medicine*, and others, including the following cases:

1. An 11-month-old boy with a mild case of ornithine transcarbamylase deficiency who suffered from irritability, lethargy, and failure to thrive. The infant's blood ammonia levels and urine glutamine levels were high. Successful treatment involved a low-protein diet (*16*).
2. A 19-month-old boy with poor appetite and vomiting, metabolic acidosis, jaundice, and a slightly enlarged liver due to fat storage. Treatment with intravenous glucose relieved his symptoms. Glucose-6-phosphatase activity was normal. Further investigation revealed that the defective enzyme was PEPCK (*17*).
3. A patient with an erythrocyte pyruvate kinase deficiency with low hemoglobin levels, which the patient tolerates fairly well owing to increased production of 2,3-bisphosphoglycerate (*18*).

Because writing new cases using the original literature can be time consuming, I have found it helpful to obtain ideas for new cases by consulting the most recent edition of Stanbury's classic textbook *The Metabolic Basis of Inherited Disease* (*19*). Biochemical explanations and clinical symptoms are summarized for a variety of diseases resulting from inborn errors of metabolism. Each chapter includes literally hundreds of references, so it is a simple matter to consult the original papers for any of the diseases discussed in the text. There are also several textbooks devoted to the case-oriented approach, which can be adopted for use in a biochemistry course (*20, 21*) and several resources are available that can be used to supplement a traditional biochemistry textbook (*22–24*).

Student Responses

Student responses to the case-study exercise have been positive. In an evaluation at the end of the semester, students were presented with a series of 30 statements concerning the course and were requested to answer whether they agreed, strongly agreed, disagreed, strongly disagreed, or were neutral about the statement. In response to the statement "The case study was a valuable exercise", 45% of the 51 students in the class strongly agreed, 31% agreed, 18% were neutral, and 6% disagreed. In contrast, in response to the statement "The homework assignments were a valuable exercise" 18% of the students strongly agreed, 45% agreed, 23% were neutral and 14% disagreed. Thus the case study exercise has the effect of involving students who would not otherwise be engaged. A representative sample of unsolicited comments regarding the case study exercise is shown below.

> I really liked the final case study. It wasn't until I was talking with my group and we were all contributing equally that I realized how much I had really learned!
>
> I especially enjoyed doing the case study…[it] made us apply all that we had learned through the semester.
>
> It was very interesting; you applied what was taught in class to "real life" situations.
>
> I would suggest that we do more than one case study. I found that I was learning more by reviewing all the metabolic processes. It was a good way to relearn, or look at in greater depth, what I had learned in class.

Discussion

For students who are accustomed to working independently on assignments, the case-study exercise provides the opportunity to work collaboratively with their peers. To successfully solve the case, the students need to be actively engaged in proposing solutions to the problem. In a course such as biochemistry, where it is all too common for students to feel completely overwhelmed by the sheer volume of the material, an exercise like the one described here allows the students to sort through the large amount of data and begin to make important connections between topics. The exercise requires the students to articulate, both verbally and in writing, the solution to the problem and they must present compelling evidence to support their solution. I have found in using this method that most groups of students perform quite capably, even students who typically do not earn the highest grades.

As successful as I have found this method to be, I have also found that there are a few minor problems associated with it. Because the biochemistry course at Providence College is a one-semester terminal course, the discussion of intermediary metabolism is completed in the last few weeks, which doesn't give students as much time to work on their projects as they would like. I have tried to solve this problem by writing cases involving carbohydrate metabolism, which is covered earlier in the course. Instructors of full-year biochemistry courses may find that a case-study exercise like the one described here would work well in the middle of the second semester of the yearlong course, after students have become comfortable with integrating various metabolic pathways. Another anticipated criticism is that this exercise is written for students who are interested in attending medical school. Students at Providence College have not criticized the exercise in this regard, mainly because the vast majority of them are interested in medicine or other health-related careers, and students who are not so inclined still seem to have a natural fascination with how the human body works. Thus, the clinical case method employed here is appropriate for my audience; but instructors at other institutions who wish to adopt this method might consider writing cases in the areas of agriculture, nutrition, or environmental studies.

In summary, the use of case studies in a biochemistry course encourages students to actively participate in the learning of biochemistry rather than serving as passive recipients of large amounts of factual data. For students who have difficulty seeing the connections between their courses and their career aspirations, the case-study exercise allows them to see that knowledge of biochemical concepts and analytical problem-solving skills are essential to the solution of a clinical problem.

Acknowledgments

I would like to thank David Moss, Paul Czech, and the reviewers for their helpful comments as I was preparing this manuscript.

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