

TEACHERS' TOPICS

A Case-Based Toxicology Elective Course to Enhance Student Learning in Pharmacotherapy

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Objective. To assess the impact of a case-based toxicology elective course on student learning in related required courses and student performance on the Pharmacy Curriculum Outcomes Assessment (PCOA) examination.

Design. A case-based clinical toxicology elective course that contained topics from 2 required courses, Pharmacology III and Pharmacotherapy II, was offered in the spring 2009 to second- and third-year pharmacy students.

Assessment. Scores on the Toxicology subsection of the PCOA of students enrolled in the elective were higher than those of students not enrolled ($91.3\% \pm 4.1$ vs. $67.2\% \pm 5.7$). Enrollment in the elective was related to increased examination scores among Pharmacotherapy II students ($89.5\% \pm 2.0$ vs. $83.9\% \pm 1.8$). Students indicated on course survey instruments that they were satisfied with the new elective offering.

Conclusions. A toxicology elective provided a clinically relevant, active-learning experience for pharmacy students that addressed a curricular need within the college and increased examination scores.

Keywords: case-based teaching, toxicology, pharmacology, pharmacotherapy, Pharmacy Curriculum Outcomes Assessment (PCOA)

INTRODUCTION

The Accreditation Council for Pharmacy Education (APCE) standards strongly emphasize active learning and critical thinking in the pharmacy curricula, and this emphasis has recently increased with the release of Guidelines 2.0.¹ Faculty members are encouraged to adopt a “philosophy of evidence-based education,” not only to meet with the demands of recruitment posed by the addition of new colleges and schools of pharmacy but also to meet the expectations of a new generation of learners.^{2,3} While the topic of active learning sometimes polarizes faculty members, there is evidence among several branches of science that supports its acceptance and its place as a viable alternative to lectures.^{4,5} One of the key premises of active-learning strategies, including case-based teaching, is the development of process skills that enable the learner to become an effective, communicative, and independent problem solver.⁶

While the case study method enjoys a rich history in other disciplines such as business and law, it is a relatively

new educational technique in the sciences.⁷ Case-based teaching, introduced to the sciences in the late 1990s by Clyde Freeman Herreid, was proposed as a way to teach science in a manner that fosters content mastery in conjunction with analytical skills. Furthermore, this method more closely mimics behaviors used by scientific researchers by putting students into teams to confront and solve problems.^{7,8} Case studies are more effective in developing noncognitive aspects of students, such as oral communication, compared to more traditional instructor-centered teaching.⁹ Integration of case-based teaching in nursing education helped students organize clinical information better as well as increase clinical competence.¹⁰ Additionally, case-based teaching is more effective than classroom lectures in developing the skill of “distinguishing” in fields such as professional ethics.¹¹ Finally, case-study teaching also produces superior outcomes in development of students’ critical-thinking skills compared to that achieved with lecture-based teaching.⁹

Case studies have been used by some instructors in pharmacy education for many years with significant success. The University of California has used case-based teaching in pharmaceuticals for 10 years, and cites this method as an effective means to engage a large classroom

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of learners.¹² Some colleges and schools of pharmacy use case studies in medicinal chemistry to make the material more clinically relevant and to support integration of other curricular components such as pharmacology and pharmacotherapy.^{13,14} Case studies also are used as a means to deliver interdisciplinary content and to foster team relationships in an elective at Purdue University.¹⁵ Finally, case-based teaching has been used in pharmacokinetics¹⁶ and pharmacology.¹⁷ As the academy continues to push for more learner-centered instruction across professional education, case-based teaching clearly is a viable option for faculty members with a variety of expertise.^{2,18}

The Bill Gatton College of Pharmacy at East Tennessee State University admitted its first class of students in 2007, and through the process of initial assessment, the college engaged in several self-evaluation exercises, including curricular mapping. During the 2008 iteration of this exercise, Appendix B of the 2007 ACPE Accreditation Standards was used as a guideline for the curricular map.¹ Each outline point in Appendix B was assigned a code, and this coded outline was distributed to faculty members so they could report whether their individual courses addressed the standards. Consequently, the college identified several small deficiencies and one major deficiency, toxicology, in the curriculum in terms of meeting accreditation standards. Of the 6 ACPE points related to toxicology content, only 2 courses, Pharmacology I and Clinical Pharmacokinetics, professed to address toxicology, and even these only addressed 2 (a,b) of the 6 points, leaving 4 points completely neglected.¹ To address this weakness in the curriculum, a new elective, Principles of Toxicology, was created.

DESIGN

During the initial planning for the new elective offering, the number of other colleges and schools of pharmacy who offer a similar course was investigated. Using links on the American Association of Colleges of Pharmacy (AACCP) Web site, individual college and school Web sites were accessed to search their elective offerings.¹⁹ We found that approximately 30% of the schools offered an elective in toxicology. The actual number may be higher as some colleges and schools because: they did not list their electives on their Web site, they were in the early stages of developing/establishing their curriculum and did not yet offer electives, or their electives may have changed since our investigation as electives are often dynamic in nature.

The content for the new toxicology elective was based on topics covered in the course textbook, *Clinical Toxicology: Principles and Mechanisms* by Frank Barile.²⁰ This textbook covers introductory toxicology principles

as well as toxicology of therapeutic and nontherapeutic entities, including metals and biological and chemical warfare agents. Additionally, this content was mapped against the toxicology related-standards in ACPE Appendix B to ensure that all 6 points were addressed.¹ The Principles of Toxicology course was pilot tested during the spring semester 2009. The class was open to 60 students, composed of PharmD students in their second (P2) and third (P3) years of study. As a 2-hour course, the class met once a week for 2 hours. Approximately 50% of class time was used for lecture and discussion, while students spent the remaining time working in small groups to develop answers to patient cases. The cases for each week were relevant to that week's lecture and reading assignments. The groups of 2 to 4 students were organized according to the Process-Oriented Guided Inquiry Learning (POGIL) model,²¹ where every group had a manager and a recorder, and larger groups also had a reporter and a technician. The manager ensured that the group progressed throughout the activity and stayed on track, while the recorder completed the materials that were turned in for grading. The reporter communicated the group's answers to the class (orally or using a whiteboard) and the technician performed Internet searches, made calculations, and retrieved information from the textbook.

Most of the cases were inspired by reports from the literature, eg, a case report of a poisoning or accident, and then several questions were written to encourage students to fully explore each case.²² Typically, students had to decipher the offending agent in the poisoning, rationalize their finding, and make appropriate recommendations for the patient's treatment. Two sample cases are shown in Appendix 1. The cases were constructed to help the students understand and apply topics from the toxicology lectures as well as assimilate knowledge and skills from other courses, including pathophysiology, biopharmaceutics, pharmacy practice, and therapeutics.

The first class of the toxicology elective contained 14 second-year students and 46 third-year students. The P2 students also were enrolled in Pharmacology III and Pharmacotherapy II, as well as other non-elective courses. For the purposes of this project, Pharmacology III and Pharmacotherapy II are highlighted because they contained some overlapping topics with the toxicology elective. Additionally, anecdotal reports from students enrolled in Toxicology suggested that the coverage of the elective was helping them in these other courses. The extent of the content overlap is shown in Table 1.

EVALUATION AND ASSESSMENT

Although all P2 students were enrolled in Pharmacology III and Pharmacotherapy II, only 14 enrolled in the

Table 1. Content Overlap of a Toxicology Elective with Pharmacology III and Pharmacotherapy II Courses

Toxicology Elective Content	Content Overlap With:	
	Pharmacology III	Pharmacotherapy II
Introduction to toxicology and risk assessment, introduction to emergency management of toxicological emergencies		✓
Routes of toxic exposures and classification of effects (local vs. systemic, reversible vs. irreversible, etc), dose-response relationships		✓
Target organ toxicity		✓
Toxicokinetics and Toxicity testing using in vitro and in vivo models		
Principles of chemical carcinogenesis and mutagenesis		
Principles of reproductive and developmental toxicology		
Principles of radiation toxicology; historic radiation-related accidents		
Toxicity of therapeutic agents: sedative/hypnotics, anticholinergic drugs, and neuroleptic drugs	✓	✓
Toxicity of therapeutic agents: acetaminophen, salicylates, NSAIDs, and steroids		✓
Toxicity of therapeutic agents: cardiovascular drugs		✓
Toxicity of potential drugs of abuse: opioids and sympathomimetics	✓	✓
Toxicity of potential drugs of abuse: hallucinogenic agents	✓	
Toxicity of vitamins, herbs, and alcohols		✓
Toxicity of metals		✓
Agents of biological and chemical warfare		✓

Abbreviations: NSAIDs: nonsteroidal anti-inflammatory drugs

Toxicology elective course. The final examination scores from Pharmacology III were compared between the Toxicology students and those not enrolled in the elective course. Pharmacotherapy II scores for the toxicology module were compared in the same manner. To ensure that the 2 groups of students were similar, the students' grade-point averages (GPA) through the spring 2009 semester, overall undergraduate GPA, math/science undergraduate GPA, and PCAT composite scores were compared. All comparisons involved two-tailed unpaired *t* tests using GraphPad Prism (GraphPad Software, Inc, La Jolla, CA) with a significance level of $p < 0.05$.

In the Pharmacology II course, examination scores of students who completed and did not complete the elective (89.5 ± 2.0 vs. 84.0 ± 1.9 , respectively) were significantly different ($p < 0.05$; Table 2). In the Pharmacology III course, examination scores of students who did and did not complete the elective were not significantly different (88.1 ± 2.1 vs. 87.1 ± 0.9 ; Table 3).

Students' PCOA scores also were evaluated for the first semester of the toxicology course. For general college assessment purposes, 100 students (P1-P3) enrolled in spring 2009 voluntarily completed the Pharmacy Curriculum Outcomes Assessment (PCOA) examination.

Table 2. Comparison of Baseline Statistics, Mean (Standard Deviation), for Pharmacy Students Enrolled and Not Enrolled in a Toxicology Elective

Parameter	Pharmacotherapy II Cohort ^a		PCOA Cohort ^a	
	Enrolled in Elective Course (n = 14)	Not Enrolled in Elective Course (n = 59)	Enrolled in Elective Course (n = 23)	Not Enrolled in Elective Course (n = 29)
BGCOP GPA	3.4 (0.5)	3.3 (0.4)	3.5 (0.3)	3.5 (0.4)
Undergraduate GPA	3.5 (0.5)	3.4 (0.4)	3.4 (0.4)	3.4 (0.4)
Math/Science GPA	3.4 (0.5)	3.3 (0.7)	3.3 (0.4)	3.3 (0.5)
PCAT Composite	77.9 (15.1)	72.3 (11.8)	72.9 (17.4)	73.3 (11.5)

Abbreviations: GPA=grade point average; PCAT=Pharmacy College Admission Test; PCOA=Pharmacy Curriculum Outcomes Assessment; BGCOP=Bill Gatton College of Pharmacy.

^a Groups tested for significant difference using unpaired *t* test with Welch's correction ($P < 0.05$); no significant differences were found between groups.

Table 3. Comparison of Pharmacology III and Pharmacotherapy II (Toxicology Module) Scores Between Students Enrolled in a Toxicology Elective and Those Not Enrolled

	Pharmacology III		Pharmacotherapy II (Toxicology Module)	
	Enrolled in Elective Course (n = 14)	Not Enrolled in Elective Course (n = 59)	Enrolled in Elective Course (n = 14)	Not Enrolled in Elective Course (n = 59)
Final Examination Score, Mean (SEM)	88.1 (2.1)	87.1 (0.93)	89.5 (2.0)	83.9 (1.8)
P		0.69		0.048
95% confidence interval		-3.9 to 5.7		0.042 to 11.1
R square value		8.9×10^{-3}		0.10
Are means significantly different? (P < 0.05)		No		Yes

The PCOA is administered by the National Association of Boards of Pharmacy and is comprised of 4 sections (Basic Biomedical Sciences, 21%; Pharmaceutical Sciences, 29%; Social/Behavioral/Administrative Pharmacy Sciences, 15%; and Clinical Sciences, 35%).²³ Each of the 4 sections is divided into subsections. For our college, the PCOA was used as an internal assessment tool, and students' scores did not affect their progression through the program. Of the P2 and P3 students that took the PCOA, 23 were enrolled in the toxicology elective and 29 were not.

A 2-tailed unpaired *t* test ($p < 0.05$) was used to compare scores of students enrolled in the elective (P2 and P3) with those not enrolled, with the same baseline statistics compared to ensure equality between the 2 groups (Table 2). The PCOA was offered during the third week of March 2009, approximately two-thirds of the way through the spring semester. As a precaution, the scores on the 4 major sections of the PCOA were compared between the 2 groups (those who enrolled in the elective course versus those who did not) using a one-way ANOVA, Kruskal-Wallis test.

Overall PCOA scores of students who did and did not complete the elective were similar (64.70 ± 5.61 versus 64.86 ± 4.78 respectively; $p = 0.98$). The P2 and P3 students enrolled in the toxicology elective during spring 2009 administration of the PCOA scored $91.30\% \pm 4.04$ on the toxicology subsection, while students not enrolled in the elective scored $67.24\% \pm 5.7$ on this subsection. These 2 student groups were compared for pharmacy GPA, undergraduate GPA, math/science GPA, and PCAT, and were shown to be equal ($p < 0.05$).

Student satisfaction data were not quantitatively measured, but rather qualitatively evaluated using the college's Student Assessment of Instruction (SAI) tool. Fifty-two percent (31/60) of the enrolled students completed the SAI for the Toxicology elective during the pilot semester. Of the students who responded to the question "What aspects of the instruction in this course were most

effective in helping you learn?" 78% referred specifically to the use of case studies. They commented most on the use of the cases to bridge the gap between classroom and "real-life," for example, "The case studies were challenging and very interesting. They helped me see the potential real-world application of what we were learning." Another student commented "The case studies really brought the class to life and gave us a lot of real-world knowledge."

DISCUSSION

Students who completed the Toxicology elective in their second year outperformed their peers in Pharmacotherapy II, which contained some topical overlap with the elective course. Several statistical parameters for these students were compared, showing that the students who enrolled in the elective were statistically equal to those who did not take the elective (Table 2). Evidence of a positive influence from taking the elective on examination scores for Pharmacology III was less compelling. Scores of students who completed the toxicology elective were not significantly higher than scores of other students (Table 3 and Figure 1).

Performance on the toxicology subsection of the PCOA was greatly influenced by enrollment in the toxicology elective. Not only were scores of students who completed the elective course higher than those of other students taking the PCOA, but also well above national average scores on this subsection (63% for P2 students and 66% for P3 students; Table 4 and Figure 1).

While the data presented here represent only the first semester for the toxicology elective course, they suggest that enrollment in this course can help student performance in content-overlapping required courses. A weakness of these data is represented in the small sample size of P2 students enrolled in the course. Although 14 students represents only 19% of the P2 class for spring 2009, these 14 were similar to the remaining 59 in the P2 class in terms of GPA and several other factors. Pharmacy students by

Table 4. Comparison of PCOA Overall and Toxicology Subsection Scores for Pharmacy Students Enrolled and Not Enrolled in a Toxicology Elective

	PCOA Overall		PCOA Toxicology Subsection	
	Enrolled in Elective Course (n = 23)	Not Enrolled in Elective Course (n = 29)	Enrolled in Elective Course (n = 23)	Not Enrolled in Elective Course (n = 29)
Percent Score, Mean (SEM)	64.7 (5.6)	64.9 (4.8)	91.3 (4.0)	67.2 (5.7)
<i>P</i>		0.98		1.2×10^{-3}
95% confidence interval		-15.0 to 14.7		10.0 to 38.1
R square value		1.1×10^{-5}		0.20
Are means significantly different? (<i>P</i> < 0.05)		No		Yes

nature are high performers, as indicated by the GPA data and examination scores shown here, so it is often difficult to detect significant improvements in student learning as a result of curricular interventions. Therefore, while this group of students is small, seeing such a significant difference in examination scores in the therapeutics module has broader implications on the effectiveness of such a targeted elective. Furthermore, our survey of Web-posted curricula from US colleges and schools of pharmacy indicated that such an elective course is offered by only 30%; our data support the argument that a toxicology elective course is a visibly beneficial opportunity for PharmD students.

The course did have a significant impact on PCOA toxicology subscores, but unfortunately, the college has discontinued the use of PCOA as an assessment tool, so no additional data are available to see if this trend continued into subsequent semesters. The higher score of the elective course students on this subsection did not affect the overall scores compared to their peers not enrolled in the elective course because any individual subsection does not have a large impact on the overall score. The toxicology subsection is part of the Pharmaceutical Sciences section, which comprises 29% of the total examination.

CONCLUSIONS

Enrollment in a toxicology elective course during its first semester enhanced student performance on the PCOA as well as contributed to higher levels of success in a required therapeutics course. The toxicology elective course filled a curricular hole for the college and provided an active-learning, clinically relevant option that was well received by the students. Moving forward, certain modifications to the course may be considered, including Web-based cases, which have demonstrated high student satisfaction in other case-intensive pharmacy courses.²⁴ Based on the positive impact on student learning that has been demonstrated here, other colleges and schools of

pharmacy may choose to implement a similar elective to fulfill the ACPE Appendix B Curricular Standards.

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Appendix 1. Two sample cases used in a toxicology elective course.

Case 1²²

A 26-year-old woman in her third trimester of pregnancy is brought to the emergency room by her husband who describes her as “semi-responsive.” In an apparent suicide attempt, she has ingested at least 100 nonprescription analgesic tablets. On arrival to the hospital 12 hours post-ingestion, she was lethargic and complaining of abdominal pain. Blood pressure was normal, but hepatic function tests showed elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Arterial blood gasses were as follows: pH = 7.12, pCO₂ = 13 mmHg, pO₂ = 159 mmHg.

- (1) The woman’s husband brought 2 Warehouse Club bottles into the ER (1 extra-strength acetaminophen and 1 enteric coated aspirin), but based on the large number of tablets in each one, he could not tell if any were missing from either bottle. At this point, can you differentiate between possible acetaminophen poisoning and aspirin poisoning? What additional information would you like to have about this patient? Explain.

Instructor Comments. With the information given, it would be difficult for the student to distinguish between acetaminophen and aspirin poisoning. Lethargy would point more toward acetaminophen, but the blood chemistry is more suggestive of aspirin. Additional information about the patient’s temperature, complaints of tinnitus, and hyperventilation episodes should be requested by the student to further predict the offending agent. This question helps the student assimilate information from the lecture and interpret laboratory data that they would have been exposed to in previous pharmacy courses. To facilitate this point, the instructor sometimes composed a table on a whiteboard that listed characteristics of each type of poisoning and identified additional data that would be useful in making a diagnosis.

- (2) Additional laboratory work revealed a patient blood level of 225 mg/L for acetaminophen. Based on this, what therapeutic recommendation(s) will you make for the patient?

Instructor Comments. Here the student is expected to use the Rumack-Matthew Nomogram to predict the risk of hepatic damage. Based on their findings from the nomogram and the timing of the exposure, the student should recommend administration of the antidote, N-acetylcysteine.

- (3) Look up the chemical structure of the antidote. Based on this structure, would you expect this molecule to cross the placenta and give therapeutic benefit to the baby? Explain.

Instructor Comments. The structure of N-acetylcysteine (NAC) resembles an amino acid. Students must draw from their previous knowledge in medicinal chemistry and biopharmaceutics to conclude that the structure of NAC is not conducive to passive transport across the placenta, but would possibly be a substrate for amino acid transporters.

- (4) Twenty-four hours following antidote administration, the patient’s blood level of acetaminophen has dropped by 75%, but hepatic function tests show continued increase in AST and ALT levels. What prognosis do you expect for this patient?

Instructor Comments. Students should conclude at this point that the prognosis is poor, especially in regards to liver function, despite the correct identification of the toxin and the administration of the antidote. This leads to a reinforcing discussion on timely administration of antidotes and activated charcoal and the efficacy of these agents with regard to time of administration.

Case 2

You are having lunch one day in the hospital cafeteria when a young man, approximately 18-years-old, sits down and strikes up a conversation with you. He shares with you that he has been working as an assistant in the radiology department for the past 6 months in hopes of saving enough money to go to college one day. He really enjoys his job, but tells you that he has felt really “run down” lately and is complaining of difficulty swallowing. While you would prefer to just eat your lunch in peace, you feel compelled to engage the young man in further conversation. You ask him if he would mind your examining his throat, and he complies. You discover that his throat is tender to the touch and detect a small nodule from this brief physical examination.

- (1) What are your first thoughts regarding this young man’s throat problems? What organ/organ system are you concerned about?

Instructor Comments. Based on information they received in lecture, students should express concern about this patient’s thyroid health based on the nature of his job, the symptoms presented, and the location of the nodule.

- (2) Would it be useful to you to know where this man lives/has lived? Why/why not?

Instructor Comments. Certain regions of the country and certain high-risk time periods are presented in lecture. While this man is too young to be affected by these high-risk locales, this question prompts discussion about identifying high-risk age and geographically relevant groups.

- (3) What questions about his diet would be appropriate to ask? Why?

Instructor Comments. Aspects of pathophysiology are reviewed here as the students discuss goiter and the use of iodized salt.

- (4) Would you consider him radioactively contaminated? Explain.

Instructor Comments. This question gives the class an opportunity to explore the concept of radioactive “contamination,” and to discuss emergency management measures necessary for contaminated persons. This also helps transition the class into considering the role of pharmacists as first responders in a large-scale disaster.

- (5) What intervention should be conducted for this man in the short term? What about the long term?

Instructor Comments. Students should suggest administration of oral potassium iodide tablets and plan for counseling the patient on following up with his physician as well as his supervisor to ensure correct personal protective equipment is being used in the radiology department, assuming that was the source of the young man’s exposure.