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Incorporation of Autopsy Case-Based Learning into PhD Graduate Education: a Novel Approach to Bridging the 'Bench to Bedside' Gap

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Abstract

Given the current rapid expansion of biological knowledge and the challenges of translating that knowledge into clinical practice, finding effective methods of teaching graduate students clinical medicine concepts has become even more critical. The utility of autopsy in medical student and resident education has been well-established. Multiple studies have reported it to be a helpful means of teaching anatomy, pathophysiology, clinical problem-solving skills, and medical diagnostic techniques. While various models of training Ph.D. candidates in clinical medicine have been reported, an autopsy-based curriculum has not been previously described. For over four years, our pathology department has offered a novel semester-long autopsy-based course to educate future Cellular and Molecular Pathology (CMP) scientists about clinical medicine. Our results indicating that this 'hands-on' approach is a popular as well as effective means of teaching the pathogenesis of disease at the level of the cell, organ, and patient. The course reputation has recently led to requests to open registration to graduate students from other university programs as well as undergraduate students. Additionally, it has played an important role in our CMP program's recent receipt of a 5-year renewal National Institutes of Health funded T32 award. Overall, this course model has been successful at our own institution, and could provide a useful template for other institutions seeking to provide graduate investigators with in-depth exposure to clinical medicine.

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1. Introduction:

In the 1970's it was first reported that a shortage of clinical researchers was hindering translation of basic science advances from laboratory bench to patient bedside—the so-called 'bench to bedside gap [1].' The recent explosive growth of basic biologic knowledge in molecular genetics, genomics, cell biology, and proteomics has made it increasingly difficult for clinicians to incorporate this new information into practical medical advances and treatments, and the divide continues to grow. While combined MD-PhD programs have historically helped bridge the gap, there is concern that the number of graduating physician scientists is insufficient to meet current needs [2–3]. In the specialty of pathology, particularly, the scarcity of physician-scientists has been well-documented. A 2014 survey conducted by the Association of Pathology Chairs (APC) revealed that at least 69% of pathology residency training programs report significant difficulty in recruiting MD-PhD candidates [4]. Over the past several years, there have been decreasing numbers of physician scientists applying to pathology programs; in fact, the American Board of Pathology (ABP) recently approved a physician-scientist research pathway for pathology residents in an effort to help recruit more clinical and translational researchers into pathology [4–5]. While encouraging physicians to train as scientists represents one approach to bridging the bench to bedside gap, another less publicized option is to 'close the gap from the other side' via training PhD scientists in clinical medicine [1,6].

In 2005, the Howard Hughes Medical Institute (HHMI) introduced the "Med Into Grad" initiative proposing the integration of clinical medicine and pathobiology into PhD graduate education [7–8]. Among the obstacles previously noted to be hindering the development of effective PhD-trained clinical and translational researchers were the relatively limited clinical medicine educational options for PhD students, as well as limited opportunities for interactions with clinicians resulting in impaired ability to communicate/function in an interdisciplinary clinical research team setting [3,9]. The stated purposes of the HHMI initiative were to provide basic scientists with a strong clinical background, enabling them to better translate discoveries from bench to bedside, as well as to foster interdisciplinary research collaborations between PhD graduate and medical programs [7]. Since that time, many institutions have proposed a wide variety of models for incorporating clinical medicine rotation experiences into biomedical PhD education. While these clinical immersion/exposure experiences vary markedly in duration (e.g. hours-months) and setting (e.g. endocrine clinic, immunology clinic, heart failure clinic, cardiac catheterization lab, surgical procedure suite), the consensus appears to be that there is no substitute for clinical contact in conveying to graduate students the profound significance of bench research to patient care [3, 6, 9–11]. Such focused clinical experiences allow future PhD researchers to better understand how and why patient management decisions are made, become familiar with currently available diagnostic and therapeutic modalities, and potentially gain insight into

areas where clinical medicine falls short and research advancements are critically needed [6, 9, 11].

At the time of the last American Society for Investigative Pathology (ASIP) survey, there were 94 pathology PhD graduate training programs in the United States and Canada, of which our program was one [12]. Our pathology department sponsors a PhD training program in Cellular and Molecular Pathology (CMP) that currently hosts a total of 45 graduate students. The overall mission of our CMP program is to provide graduate students with interdisciplinary and integrated training in the pathogenesis of human diseases with an emphasis on molecular, cellular, and biochemical approaches. Given the noted success of clinical exposure experiences at other institutions, we sought to incorporate a focused graduate student clinical immersion course into our own curriculum. If possible, we wanted to provide this clinical experience from within our own department, as this approach would convey the added benefit of bringing together the clinical and research sides of our pathology department, and potentially establishing helpful future research partnerships for our CMP students.

Autopsy has long been regarded as a valuable tool in medical education; it affords medical students the opportunity to learn anatomy, trace the pathophysiology of disease, make clinicopathologic correlations, and recognize areas of medical uncertainty [13–15]. At our institution, the typical hospital autopsy case provides for discussion of a broad array of common clinical disease processes, review of a number of surgical and/or diagnostic procedures, explanation of multiple laboratory test options and interpretation of results—as well as just conveying a general understanding of how clinicians communicate and what clinical reasoning entails. Overall, the trend in medical school education has been a movement towards a case and/or problem-based learning format, and autopsy has been lauded as “the epitome of problem-based learning [16].” While autopsy has been most closely associated with medical student and pathology resident education, it has also been successfully employed to teach clinical medicine to other trainees such as nursing and physical therapy students [17–18]. In reviewing published models of targeted clinical exposure experiences for future translational biomedical researchers, however, we found no reports of a predominantly autopsy case-based clinical experience. Also, PubMed searches limited to the English language and utilizing search terms such as “autopsy PhD education” (n=1), “autopsy graduate education” (n=127), and “autopsy researcher education” (n=36) yielded no relevant articles on the subject. Thus, it seems that our predominantly autopsy case-based curriculum represents a novel approach to educating Cellular and Molecular Pathology PhD students about clinical medicine and disease pathobiology.

2. Methods:

2.1. Course Goals and Objectives

Our course goals were multiple. While we wanted our CMP students to have a formal clinical medicine curricular component that included both clinical experiential learning as well as classroom didactics, we also wanted to keep our favorable average time to PhD degree completion (currently 5.3 years). Overall, it seemed that integrating a targeted clinical medicine experience into the first year of our pre-existing graduate program

structure would be the best approach. As the disease areas in which CMP students may focus their research are unknown until later in their first year (and may even change throughout their career), we felt our course content needed to provide an overview of general clinical disease pathophysiologic concepts rather than focusing on any one particular disease entity in depth. We also wanted a targeted clinical medicine experience that would allow our students to gain familiarity with the language and culture of medicine, enabling them to effectively communicate with pathologists and other clinicians, improving their ability to form successful interdisciplinary research partnerships. Additionally, we preferred—if possible—to host this clinical experience from within our own department so as to introduce CMP students to pathology residents and faculty who might prove useful collaborators on future histologic or assay-based projects.

Given these goals, it seemed that an autopsy case-based course would provide the optimal experience. Our hospital performs approximately 500 autopsies annually, a case volume that affords ample educational opportunities. The caseload is diverse, incorporating natural as well as unnatural deaths with a broad decedent age range, and lends itself to covering a wide array of educational topics. Our premise was that by gaining an intimate understanding of how and why patients die, our students would be better equipped to understand where research advancements are critically needed to help patients live. Throughout the course, students are introduced to the pathogenesis of disease via visualization/discussion of actual autopsy patient cases over the span of a semester. Although initially conducted as an independent study section, it soon transitioned to its current format—a formal course known as ‘Histopathology for Translational Scientists’ (i.e. Pathology 802). Emphasis is placed on understanding the basic mechanisms of disease at the level of cell, organ, and body. An implicit course objective is to familiarize students with the language and culture of clinical medicine. Formally stated course objectives are to give CMP students 1) an appreciation of how disease processes directly impact patients 2) a working ability to distinguish the morphologic patterns of normal versus pathologic tissues, and 3) an understanding of the pathogenesis of selected common disease processes and how bench research could be of clinical utility in addressing these diseases.

2.2. Course Structure

Over the course of the fall semester (i.e. 15 weeks), students attend a one-hour autopsy consensus conference weekly at which pathology residents rotating on the autopsy service present a total of 1–3 recent patient cases in the morgue conference room. Presentations include a brief review of decedent medical history, projection of case photos taken at the time of autopsy, review of formalin-fixed gross organs from the case, and projection of critical correlating microscopic sections (as available). Interactive conference discussions regarding patient medical comorbidities, surgical and/or diagnostic procedures, antemortem laboratory testing results, assessment of gross/histologic pathology, and how—overall—the disease and/or injury could have precipitated death are led by three board-certified forensic pathologists.

Autopsy case-based discussions of disease pathogenesis are augmented by twice weekly didactics and periodic multi-headed microscope sessions, with the intent of furthering

students' understanding of how gross disease manifestations predict findings at the microscopic/cellular level. In general, the didactic series is structured by organ system and consists of a 1 hour presentation of normal anatomy/histology and basic physiology of a given organ system (e.g. cardiovascular system) followed by a 1 hour session focusing on high-yield pathology of that same system (e.g. ischemic heart disease). A few didactics on fundamental concepts such as cell structure, neoplasia, and inflammation/repair are also incorporated (see supplementary table for sample course syllabus).

Later in the course students are required to attend at least one autopsy prosection. This provides the opportunity for one-on-one discussion of critical gross and microscopic findings with the case pathologist, furthering a three-dimensional understanding of structure and disease. Students synthesize critical case findings into a graded 'mini autopsy report' consisting of a referenced 1–2 page clinicopathologic correlation summary comment explaining how the disease or injury precipitated death. Throughout the course of the semester, students also participate in 4 autopsy case-based exercises in which they work in teams to evaluate selected gross organs and corresponding microscopic sections in order to answer a short series of questions. Overall course grades are derived as follows: autopsy case clinicopathologic correlation (10%), 4 autopsy case-based exercises (10% each), and a final multiple-choice exam (50%).

3. Results:

3.1. Course Grading and Satisfaction

From 2012–2015, a total of 33 Cellular and Molecular Pathology students completed the course. Class sizes ranged from 7–10 students (table 1). Overall, final calculated course grades ranged from 76–98.5 (mean: 87.8). Earlier cohorts (2012–2013) tended to have slightly lower mean grades than latter (2014–2015), though this difference was not statistically significant. This trend likely reflects the fact that in earlier cohorts the final course grade was weighted much more heavily towards the final exam (80%); whereas, in later cohorts the addition of four graded case-based sessions reduced the relative contribution of this exam (50%) to the final grade. All students were surveyed for feedback on the course and individual instructors via anonymous electronic evaluations. From 2012–2014, an in-house 5 point scale survey was utilized (i.e. Learn@UW); due to its cumbersome nature and challenges inherent in extracting the data from this system, in 2015 the course transitioned to Qualtrics survey software and a 10 point scale. Students were surveyed regarding various course parameters. By both scaling systems, overall satisfaction with the course was high. On the 5 point scale system (1=very satisfied/5=very dissatisfied), students from 2012–2014 cohorts all rated the course as a 1 or 2, and the mean overall satisfaction score progressively improved from 1.5 in 2012 to 1.2 in 2014. In 2015 on a 10 point scale system (1=very dissatisfied/10=very satisfied), overall course satisfaction ranged from 7–10 with a mean of 9.29 (table 1). Free text comments were also solicited. In terms of course strengths, the general organization and utilization of autopsy material were perceived favorably:

> "I found the course to be very well-designed and valuable in gaining a broad understanding of each organ system and its histopathology. I feel more confident in

identifying disease processes and sequelae, as well as the molecular mechanisms that underpin them."

"This course was very interesting and a fantastic learning experience. It was well organized in the sequence of lectures – normal, pathologic and slide session. The autopsy viewing was a great experience and really made the course that much more interesting."

"Although I was shocked by the autopsy conference at the beginning, towards the end I was fascinated by the physiological differences visible among the gross organs…I feel better prepared to enter a translational science field having taken histopathology and been exposed to the clinical side of things. Visualizing pathological diseases at a systemic and microscopic level has motivated me to become a better scientist and translational researcher!"

"Love, love, love the autopsy portion! I wish I could attend more."

3.2. Course Improvements and Integration

Suggestions for improvements varied, but general themes included requests for more multi-headed scope sessions to reinforce didactic concepts and for quizzes to prevent so much of the course grade relying on one exam. As a result of this feedback, the number of multi-headed scope sessions was progressively increased from a few ad-hoc sessions in 2012 to a total of nine scheduled sessions in 2015. Faculty were instructed that slide sessions are primarily intended to provide the opportunity for reinforcement and application of concepts previously covered in didactics rather than introduction of new material. Four case-based exercises incorporating gross organs, histologic sections, and a short series of graded questions were added in 2014.

In terms of integrating the clinical and research sides of our department, each year graduate students receive instruction from 8–9 (mean: 8.5) pathology residents and 10–13 (mean: 11.25) pathology faculty derived from a variety of subspecialties. Such instructors represent potential future sources of academic and/or research assistance. For instance, 10 former students (10/33; 30.3%) to date have contacted the course director with requests for slide consultations (n=3), borrowing teaching slides (n=3), autopsy tissue procurement for research projects (n=2), and letters of recommendation (n=2). Anecdotally, other departmental faculty have reported being contacted by former students as well. Multiple students (from all cohorts) have continued to intermittently attend autopsy gross conference following course completion. Currently, 11 CMP students have requested to be added to the autopsy gross conference email list in which biweekly emails confirm when autopsy conferences will be held and what cases will be presented.

4. Discussion:

4.1. Utility of Autopsy-Based Education

The utility of autopsy in medical student and resident education has been well-established. Multiple quantitative studies have reported it to be a helpful educational means of teaching anatomy, pathophysiology, deductive reasoning, clinical problem-solving skills, medical

diagnostic techniques, and recognition of the inherent fallibility of medicine [13–15]. In one case-control study, medical students participating in an autopsy elective had twice as high a percent knowledge gain in pathophysiologic mechanisms as did the control group [16]. Utilization of autopsy as a teaching tool also tends to be popular with medical students, particularly if the overall experience is carefully structured and supervised [19–21].

We have found autopsy case-based learning to likewise be popular with PhD students, and moreover to represent an effective method of providing them with a solid foundation in clinical medicine. Annual anonymous student surveys have indicated a high degree of satisfaction with the Pathology 802 course overall as well as with various course parameters including the autopsy experience (table 1). In fact, course reputation has recently led to requests to open registration to graduate students from other university programs as well as undergraduate students (previously, registration has been restricted to CMP students only). In terms of course efficacy, Pathology 802 students score competitively on their final exam, which is comprised of multiple-choice questions similar in level, content, and structure to those utilized for pre-clinical year medical students. CMP students also perform well on graded case-based exercises which are modeled on those utilized in our medical school, and the didactics they receive from pathologists are in many cases similar— or even identical to — those presented to pre-clinical medical students. Although still too early to assess what impact the course ultimately may have on the clinical/translational research careers of former students, preliminary results show that our graduate students are successfully completing a semester-long course of clinical training at a level equivalent to that of pre-clinical medical students. These results are in accordance with other studies which have shown the benefits of providing targeted clinical medical experience, and teaching graduate students clinical medicine similar to the way in which medical students are taught [6, 22]. Three members of the earliest class cohort (i.e. 2012) have graduated, two of whom are completing post-doctoral degrees at academic medical centers while the third is an assistant scientist at an academic medical center. One member of 2012 cohort has been accepted into medical school and intends to matriculate following PhD degree completion this spring. Preliminarily these results would seem to suggest that CMP graduates from our program tend to be attracted to the academic patient-care setting, where they are either conducting clinical and translational research, or else have the potential to.

4.2. Caveats and Limitations

There are certain caveats to utilizing autopsy-based education. Our experience has been that such teaching requires a fair degree of both flexibility and opportunism. The average medical autopsy case entails a complex medical history filled with multiple medical acronyms, e.g. CVA, AAA, NASH, STEMI, ECMO. Presentation of the history to graduate students requires a willingness on the part of pathology residents/faculty to take the time to define the medical terminology and explain the pathophysiology–particularly in earlier sessions when students have not yet had much exposure to clinical medicine. Similarly, pathologists need to slow the pace of their average autopsy dissection and devote time to reviewing both normal and abnormal gross anatomic findings when graduate student observers are present, akin to what has been noted with medical student autopsy observations [23]. In almost every autopsy case, there are a myriad of potential diagnostic

test results, medical and therapeutic interventions, diseases and/or injuries that could potentially be discussed; pathologists must be opportunistic, selecting teaching concepts that are high-yield, and particularly those addressed in didactic sessions in order to provide concept reinforcement and maximize retention.

An inherent limitation of autopsy-based education is that it is not possible to arrange for deaths to occur of diseases in a logical sequence—our forensic pathologists have to adapt to teach the case that lies before them. While utilizing ‘man-in-a-pan’ preselected autopsy cases would represent one means of ensuring logical course organization, such a prearranged approach would also have undermined the clinical experiential learning component we were attempting to provide. Clinical medicine is inherently unpredictable—it is not possible to predetermine what disease a patient will present with, patients don’t always ‘read the textbook’ and manifest disease in the expected fashion, and patients are entitled to more than one disease process as well as ‘incidentalomas.’ In accordance with other institutions, we felt that it was particularly important for graduate students—otherwise working in a controlled laboratory environment—to be exposed to the unpredictability, variability, and inherent limitations of clinical medicine [6,11]. Another major advantage of presenting autopsy cases in real-time is that it integrally involved CMP students in the clinical reasoning process, as the disease pathogenesis and final diagnosis was not always clear-cut at the time of initial autopsy conference presentation. Students participated in generating differential diagnoses, seeing when additional testing might be indicated, and generally helping to put case findings together. In particularly complex cases, critical portions were re-presented to give follow-up once the final diagnosis was known.

Ultimately, to assist in giving the course a logical structure and ensure that all necessary topics were being covered, we felt the best approach would be to supplement the autopsy experiential component with a comprehensive series of thematically organized biweekly 1 hour didactics (see supplementary table for sample course syllabus). A broad array of pathology residents and faculty has annually volunteered to give these sessions and their dedication to graduate student education has been integral to the course’s success. Another challenge of utilizing autopsy-based education that has been alluded to in prior studies is the issue of diminishing medical autopsy case numbers [12, 15]. At our institution, we have addressed this issue by acting as an autopsy reference center for surrounding hospitals that do not have their own morgues, by accepting coroner/medical examiner cases, and by accepting private family consult cases. Our current annual volume of 500 cases provides ample educational opportunities for our graduate students, as well as medical students and pathology residents. Our Pathology 802 students are required to participate in at least one autopsy observation. A strategy we have used to circumvent the inherently unpredictable timing of deaths is to place each student ‘on-call’ for a week of autopsies. Students select their week and provide a listing of available times as well as a contact phone number; should an autopsy occur during their period of availability, morgue staff text the student with the case start time. With this system, we have consistently ensured at least one autopsy observation per student. For instance, in the 2015 cohort, students observed between 1–3 prosections each.

4.3. Conclusions

In conclusion, autopsy case-based teaching appears to represent an effective ‘hands-on’ approach to educating future translational researchers about clinical medicine. It is popular with graduate students and results in course performance at a level equivalent to that of pre-clinical medical students. It has been instrumental in ‘bridging the gap’ in our own department between the clinical and research sides, introducing CMP students to many clinical pathology faculty and residents whom students can later consult regarding research issues. Pathology 802 also played an important role in our CMP program’s recent receipt of a nearly 1 million dollar 5-year renewal NIH funded T32 award. This course has been successful at our own institution, and could provide a useful model for other departments seeking to augment graduate student clinical exposure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Pathology 802 Class Characteristics and Survey Results (2012–2015)

Cohort	2012	2013	2014	2015
Class Size	n=9	n=7	n=10	n=7
Final Calculated Grade Ranges and Means	range: 76–96 (86.5)	range: 76–94 (84.9)	range: 84–95 (88.7)	range: 84–98.5 (91)
Course Evaluation Score Ranges, Means, and Number of Respondents	5 point scale (1= very satisfied/ 5= very dissatisfied) n=4	5 point scale (1= very satisfied/ 5= very dissatisfied) n=4	5 point scale (1= very satisfied/ 5= very dissatisfied) n=10	10 point scale (1=very dissatisfied, 10=very satisfied) n=7
Course Organization	*range: 2–3 (2.3)*	*range: 1–2 (1.25)*	*range: 1–3 (1.5)*	*range: 6–10 (9.0)*
Lecture Topics	*range: 1–2 (1.3)*	*range: 1–2 (1.25)*	*range: 1–2 (1.1)*	*range: 7–10 (9.43)*
Autopsy Experience (incl. conference discussions)	*range: 1–1 (1.0)*	*range: 1–3 (1.5)*	*range: 1–3 (1.5)*	*range: 8–10 (9.43)*
Exam/Slide sessions	*range: 1–3 (1.5)*	*range: 1–3 (1.75)*	*range: 1–3 (1.6)*	*range: 0–10 (7.71)*
Grading	*range: 1–3 (1.8)*	*range: 1–3 (2.0)*	*range: 1–2 (1.2)*	*range: 7–10 (9.43)*
Overall Satisfaction	*range: 1–2 (1.5)*	*range: 1–2 (1.25)*	*range: 1–2 (1.2)*	*range: 7–10 (9.29)*
Course Resident and/or Fellow Instructors	n=8	n=8	n=9	n=9
Course Faculty Instructors	n=10	n=11	n=13	n=11
Slide Sessions	ad hoc	n=7	n=8	n=9
Case Based Exercises	n=0	n=0	n=4	n=4