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Commentary

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Rethinking Premedical and Health Professional Curricula in Light of MCAT 2015

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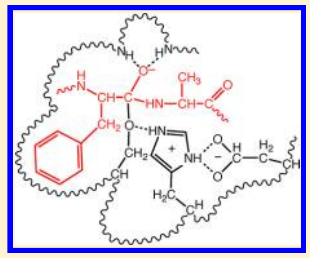
ABSTRACT: The 2015 redesign of the Medical College Admissions Test (MCAT) is a disruptive event that has stimulated a great deal of discussion in undergraduate educational circles. These discussions include figuring out who will teach biochemistry, whether nonmajor chemistry courses should be changed, whether the psychosocial material to be tested constitutes academic behavioral science or the sensibilities that come from exposure to different cultures, and determining whether resources need to shift. The 2015 MCAT has also begun to alter admissions requirements and curricula in medical, pharmacy, and dental schools. Though many medical schools are taking the position that biochemistry will already have been covered as an undergraduate requirement and seem to be deemphasizing molecular science in the first-year curriculum, at least one college of dentistry has embraced the better prepared first-year student in order to offer advanced biochemistry and genomics that will build on undergraduate biochemistry.



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A FEW WORDS OF DEFINITION

This commentary deals with two different stages of education, both of which are termed undergraduate by the faculty who do the teaching. Baccalaureate biology, chemistry, and biochemistry are taught to college and university undergraduates and to postbaccalaureate students who intend to apply to health professional schools. However, medical school is also termed undergraduate in contradistinction to internship, residency, and fellowship programs, which are termed graduate medical education. Here, undergraduate refers to the former constituency.

THE U.S. PREMEDICAL PIPELINE

The pipeline that begins with first-year college students and produces U.S. medical doctors is exceedingly leaky. The sum of first-year students in two- and four-year colleges in the United States is 3,000,000.[1] Textbook publishers estimate the number of students who annually take general and organic chemistry to be 500,000 and 165,000, respectively. In 2008, 42,200 students applied to U.S. medical schools and 18,000 matriculated. These schools produced 17,300 medical doctors (M.D.s) in 2012.[2] Thus, for every 100 general chemistry students, we produce 33 organic chemistry students, 8 medical school applicants, and three physicians.

Because so many more students begin college as premeds than enter medical school, it must be appreciated that what we teach to students indicating a premedical interest will greatly influence the training of a wide swath of learners. Indeed, few students enroll in college with an understanding of chemical, biological, and biomedical research—future researchers are frequently recruited from the ranks of students with premedical interests. For this reason, the coursework for premedical students should not just be sufficient for MCAT preparation. Curricular redesign should be geared to build scientific literacy, to educate students to make future discoveries in molecular sciences, and to practice molecular medicine. These aims are not in conflict.

UTILITY OF THE MCAT

Though the MCAT is widely used as a medical school admissions standard, its use is not universal. Indeed, the Humanities and Medicine (HuMed) Program at Mt. Sinai School of Medicine, admission to which does not require MCAT, organic chemistry, or physics, has performed well, though not identically to the traditional program at Mt. Sinai. In post hoc analysis, HuMed produced more students who performed well in psychiatry clerkships. However, their Step 1 United States Medical Licensing Examination scores were lower, and the fraction of HuMed students who took a nonscholarly leave of absence was higher than those of traditional Mt. Sinai students.[3] The HuMed approach, which admits students after only two or three years of college, remains the exception rather than the rule, though it is being expanded at Mt. Sinai.[4] Because the average medical school applicant submits 14 applications,[2] students tend to homogenize their course selections to those required by the vast majority of medical schools. The data indicate that those students with higher MCAT scores experience higher rates of unimpeded progress toward the M.D. and that the MCAT score is a better predictor of unimpeded progress than undergraduate grades.[5]

MCAT 2015: WHY THE CHANGE?

The last MCAT exam redesign occurred in 1991. Two years before the rollout of the 2015 MCAT exam redesign, it is useful

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to think about how far molecular medicine has evolved in the last quarter-century. In 1991, a skilled molecular biologist with an ample supply budget and a well-equipped laboratory could perform assays for mutations in four human genes: those encoding hypoxanthine-guanine phosphoribosyltransferase, glycophorin A, human leukocyte antigen A, and hemoglobin.[6] Today, any person can obtain a "spit kit" from a direct-to-consumer genetic testing company such as 23andMe and obtain genotypic data from interrogation of 1.2 million single nucleotide polymorphisms at the cost of $99.[7] Consumers are thereby availed of personalized risk assessments for complex diseases, many of which are still not understood mechanistically.

Going forward, it is clear that physicians will use many more genetic and metabolomic tests and will be expected to provide insights into conditions whose underlying mechanisms are at or beyond the cutting edge of knowledge. To be sure, drug companies will take advantage of the data and attempt to recommend specific treatments for specific genotypes and patterns of metabolites. For example, whereas statins are often prescribed to reduce levels of low density lipoprotein cholesterol,[8] how many different treatments will be recommended on the basis of the levels of 600 different plasma lipid species that can now be measured?[9] Clearly, the physicians practicing in 2020 and beyond will require more molecular knowledge than those in the 1990s.

■ MCAT CHANGES

The 2015 MCAT will consist of three sections—the writing section will be eliminated. In the natural sciences section, 75% of the material will be similar to that in the current MCAT, while 25% will be new. The new questions will test biochemistry, integration of natural sciences knowledge, and will also require students to use data analysis. In a new section, the MCAT will aim to test concepts foundational for understanding behavioral and social determinants of health. The critical analysis and reasoning subtest will be based on readings from the social sciences and humanities.[10]

■ THE EXPERIENCE AT IOWA

As the chair of a college of medicine biochemistry department, who teaches undergraduate biochemistry nonmajors and majors, and whose department also teaches biochemistry to graduate, medical, physician assistant, dental, and pharmacy students, I have multiple perspectives on MCAT 2015 as a disruptive event. MCAT 2015 will not only reshape undergraduate and medical education. It is also potentially a catalyst to alter the flow of resources to academic units. Dagmar Ringe and I spoke to key stakeholders locally and nationally before developing the American Society for Biochemistry and Molecular Biology (ASBMB) premedical curriculum recommendations.[11] Here I review the state of change and conversation at my own institution in the hopes that our discussions enable other institutions to make informed choices.

Conversations at Iowa have been convened in parallel by the College of Liberal Arts and Sciences (CLAS), which educates most undergraduate premedical students and works closely with the academic advising center, and by the Carver College of Medicine (CCOM). CLAS's goal is to align all of the departments that educate premedical students with a sensible plan for students. CLAS consulted CCOM to ensure that Iowa undergraduates will be well prepared CCOM applicants. However, CLAS premedical students need to be prepared to apply to medical school anywhere and CCOM cannot confine its required courses to those particular to Iowa.

In earlier decades, it was common for first-year biology to be a descriptive course that dwelled on morphology of plants and animals. For this reason, we recommended that the year of biology allow students to achieve competencies in molecular genetics and biological information transfer.[11] At Iowa, undergraduate biology has recently been redesigned with a strongly genetic orientation. CCOM formerly allowed a great deal of flexibility in the biology requirement, such that botany and zoology could have sufficed. Because the biology department had already updated its course, undergraduate advising at Iowa did not change its recommendation for a year of biology. CCOM tightened its language regarding biology coursework so that botany no longer counts. Various stakeholders at Iowa have argued that an advanced genetics course should be recommended to premedical students. Though this has not been adopted by undergraduate advising at Iowa, there is little doubt that individual faculty members (including this one) will recommend that students take more than the minimum amount of biology and genetics.

Chemistry is the foundational discipline for molecular medicine. Moreover, chemistry departments are of key importance in educating premedical students and in filtering out those students who are insufficiently disciplined or intellectually inclined to grasp the scientific basis for medicine. Chemistry departments teach large numbers of nonmajors, yet there is relatively little differentiation between the general and organic chemistry curricula for majors and nonmajors. To be sure, not all chemistry nonmajors are biomedical—some are preparing for chemical engineering or physics. However, the proportion of chemistry nonmajors that are biomedically oriented is very large. For these reasons, Dagmar Ringe and I recommended a new, two-semester, life-oriented organic chemistry course that will emphasize functional group reactivity, deemphasize organohalides and synthesis, and specifically prepare students to understand the chemistry of reactions such as Michael additions, alkaline hydrolysis, and aldol condensations, which occur at enzyme active sites.[11]

Though there is not a commonly used book that teaches organic chemistry this way, there is considerable interest in such an approach among educators and book publishers. I predict that as chemistry educators see that the premedical students in organic chemistry are all bound for biochemistry, they will aim to spend more time on functional groups and less time on nonderivatized alkanes, alkenes, and alkynes. Importantly, the ASBMB recommendation is for a two-semester organic chemistry course, not a blended organic chemistry–biochemistry course that would focus on protein structure and metabolic pathways.[11,12] For example, I envisage that when a life-oriented chemistry class compares alkaline hydrolysis of an amide or ester to the chymotrypsin reaction mechanism, students will learn that the enzyme is a large molecule in which the oxyanion hole and catalytic triad exert concerted effects that can be understood geometrically and electronically. This grounding in enzyme *chemistry* will prepare them to learn in a *subsequent biochemistry course* how the chymotrypsinogen mRNA is translated and folds into a proenzyme, how related enzymes work, and how chymotrypsin functions in digestive pathways.

If chemistry departments want the chemistry major to be an attractive one for premedical students, it makes sense to develop life-oriented organic chemistry as a course that will also satisfy the major requirement. However, at the end of a year of life-oriented organic chemistry, students will be more prepared to understand biochemical reactivity but less prepared to do synthesis. Chemistry majors who have taken life-oriented chemistry might be encouraged or required to take a course in methods in chemical biology.

Earlier, I pointed out that the premedical pipeline is a leaky one and that students who do not make it into medical school need to succeed in other paths. Thus, the general chemistry coursework that precedes a life-oriented chemistry course should ideally be the same general chemistry that a major would take. At Iowa, there is every indication that a course in life-oriented chemistry will satisfy the organic chemistry requirement of biology, biochemistry, microbiology, and human physiology majors.

We have suggested that a 1:2:1 curriculum[13] is an attractive way to organize traditional chemistry and premedical students, because they could all take the same semester of general chemistry prior to taking a different organic chemistry course. At Iowa, there is not yet a new chemistry course for biomedically oriented students. However, biochemistry and biomedical engineering plan jointly to develop a new computational biochemistry course.

In the MCAT revision process, medical school faculty identified biochemistry as the most important discipline for mastery of future medical school curricula.[14] University of Iowa stakeholders agreed, though they did not agree with a formal recommendation of a two-semester biochemistry course.[11,12] Thus, Iowa premedical students will be recommended to take a one-semester biochemistry course developed for nonmajors. CCOM admissions will also require one semester of biochemistry—our department offers a one-semester biochemistry course live and online, such that it should be possible for students at smaller colleges to take biochemistry from us if it is not offered at their home institutions.

Despite the reticence of Iowa stakeholders to recommend the majors course, taking the two-semester course will have multiple advantages for those who elect it. First, it covers material in more depth than the nonmajors course. Second, it covers material more slowly than the nonmajors course. Third, as a Lehninger-based course, it requires and is built atop organic chemistry.[15] The one-semester course uses an abbreviated Stryer text that does not assume prior organic chemistry.[16]

University of Iowa stakeholders have not decided whether specific psychology or sociology courses should be required, and thus far, the CCOM has not required new coursework in behavioral science. In the opinion of this educator, who is admittedly not a behavioral scientist, coursework might be developed by theater or other departments that would effectively sensitize undergraduates to behavioral and social determinants of health.

■ PATHWAY ISSUES FOR BETTER—AND FOR LESSER—PREPARED STUDENTS

Most chemistry educators to whom I have spoken agree that one semester of college general chemistry can suffice to prepare students for the chemistry of carbon. However, student preparedness varies markedly between institutions and among students at the same institution. At institutions where most students have taken advanced placement chemistry, it is not unreasonable for such students to take a semester of general chemistry as first-semester, first-year students and progress to an organic chemistry course in the spring semester of their first year. However, students who have not taken chemistry since the 10th or 11th grade in high school are not likely to be prepared for such a course—there are many such students at the University of Iowa. These students will potentially need a year of general chemistry before organic.

■ RESOURCE ISSUES AT SMALLER INSTITUTIONS

Small colleges have two major issues to face. First, if they develop life-oriented organic chemistry for premedical students, will they be able to continue to offer conventional organic chemistry? Second, who will teach biochemistry? Assuming that the biochemistry course is a one-semester one and there is no department of biochemistry, there are essentially two approaches to teaching this course. If the course is to be taught in biology, then a survey using a short-course text is a viable approach. If a one-semester course is to be taught in chemistry, I would suggest a chemically oriented text such as Lehninger.[15] However, faculty should realize there is no way to cover the entirety of a book such as this in one semester. The key material premedical students need from their biochemistry course is macromolecular structure, enzyme function, and central carbon metabolism. Thus, a chemistry-taught semester of biochemistry can set out to teach select chapters of a rigorous textbook and work with the biology department to ensure that the molecular genetics material in biology effectively covers mechanisms of information transfer and gene regulation.

■ RESOURCE ISSUES AT LARGER INSTITUTIONS

Larger undergraduate institutions that separately teach organic chemistry for majors and for nonmajors should be able to redirect faculty effort from the nonmajor course to teach life-oriented organic chemistry.[12]

Many institutions are experiencing changes in course enrollment that could be further altered by what the undergraduate premedical advisers decide to recommend. For example, if the premedical advisers decide that one or more sociology courses should be taken by students to prepare for MCAT, enrollment will increase and departments will request additional faculty and teaching assistant (TA) effort to satisfy this demand. Such requests will come to deans and provosts precisely when Shirley Tilghman's report on the size of the Ph.D. workforce is on their desks.[17] This report makes the case that we are training too many Ph.D.s in proportion to the available research funding. Thus, if a chair of biochemistry or sociology were to request more TA lines to help teach undergraduate courses, the dean is likely to ask for assurance that more Ph.D. students not be admitted to these departments. Simply put, while the demand for help with undergraduate teaching is directly related to undergraduate course size, the demand for future Ph.D.s in a field is not well correlated to the service needs of departments. Accordingly, it is far from assured that an increasing teaching load will result in significantly increased departmental resources. Increased class sizes are to be expected. Support for TA or instructional effort may follow but it may not be measured in TA lines.

As a department chair, I would offer that the best way to be responsive to the workforce needs of a particular field is to adjust the number of first-year graduate student positions to the amount of research funding in the department. With an all-

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funds budget, if anticipated research support of the faculty is projected to decline, there will be fewer funds available for first-year graduate student packages and there will be fewer faculty mentors with whom students can match. In times of limited research funding, which is the new normal, I view the need to provide TAs for undergraduate classes as unrelated to the optimal size of the graduate program. Because our graduate students are paid 100% from research grants, their fractional teaching effort in the semester in which they have a TA assignment must be paid by the department, but this is a small fraction of the cost of an annual TAship. In point of fact, if faculty effort is freed up by loss of research grants, more faculty effort is available for teaching.

■ A DENTAL CURRICULUM AGAINST THE TIDE

Medical curriculum renewal is occurring at a large number of allopathic medical schools with the goal of accelerating the preclinical years from 2 to 1 or 1.5 and, in some cases, to accelerate the medical degree from a four-year program to a three-year program.[18] New curricula emphasize clinical skills,[19] team-based care,[20] and other aspects of healthcare delivery. Whereas the first-year curriculum was once built around courses run by the traditional five basic science departments (anatomy, biochemistry, microbiology, pharmacology, and physiology), new curricula are centrally run by divisions of medical education, which aim to integrate and streamline basic science content, focusing on material deemed to be clinically relevant.[21] In these curricula, basic science material is sometimes fractionated into organ systems or mechanisms of health and disease.[22] For example, in an organ system-based curriculum, students are taught the anatomy, biochemistry, microbiology, pharmacology, and physiology of the liver and then the musculoskeletal system, brain, and so on. In some of these curricula, a small amount of foundational biochemistry is taught on students' arrival in the fall of the M1 year. However, the instructional time in foundational biochemistry has been cut drastically at many institutions.[23]

Many colleges of pharmacy are also following suit. Because Pharm.D. graduates increasingly function in chain-store dispensaries with electronic systems that attempt to identify contraindications, process payments, and deal with government regulations, pharmacy school may focus more on clinical practice and less on drug action.[24]

Because the 2015 MCAT will test biochemistry,[10] the PCAT already tests biochemistry,[25] and increasingly, dental schools require biochemistry, some architects of curricular changes in health professional schools have claimed that entering students will have already been taught much of the foundational science that underlies their clinical practices. However, one or two semesters of undergraduate biochemistry provide little more than the *vocabulary* of medical, pharmaceutical, and dental biochemistry. For example, undergraduate biochemistry students will learn that acetyl-coA is the central mediator of mitochondrial fuel utilization and they may learn how ketone bodies can be transported from liver to brain in a process that relieves high mitochondrial Ac-coA. However, they will not have learned how diabetes dysregulates the process of ketogenesis.

MCAT 2015 was, in large part, launched by a joint report from the American Association of Medical Colleges and the Howard Hughes Medical Institute on the scientific foundations for future physicians.[26] It was clearly not the intent of the authors of that report to reduce the amount of medical biochemistry taught. Robert Alpern and colleagues wrote:[27]

> *If students are better prepared, medical school curricula can focus on more advanced aspects of the biomedical sciences. It is also hoped that medical schools will use this opportunity to address the teaching of the biomedical sciences, again placing a greater emphasis on the physical sciences and their relevance to the biological sciences and medicine.*

The ASBMB Education Committee, which consists of Daniel Raben, Bettie Sue Masters, Judith Bond, Peter Kennelly, Edward Dennis, and me, has been unable to find any new medical school curriculum in the United States that is teaching biochemistry at a higher level, or placing a greater emphasis on physical sciences, or both. Typically, when an entire semester of medical biochemistry is eliminated, it is replaced with an 8- or 10-week block that integrates molecular, cellular, and tissue-based concepts. We are greatly concerned that graduates of medical school in 2020 will be ill prepared for the new era of molecular medicine.[23]

One professional school of which we are aware is bucking the trend. At the University of Iowa College of Dentistry, educational leaders have reserved the first-year fall semester for an advanced biochemistry and genomics course to be taught by the department of biochemistry. At least initially, this course will be taught jointly to first-year students in the College of Pharmacy. The course will be pitched to students who have taken undergraduate biochemistry and will consist of lectures on Mondays and Wednesdays, and clinically oriented discussions on Fridays.

The course will differ somewhat from a medical biochemistry course because dentists and pharmacists are less likely to need to diagnose problems in nitrogen metabolism than pediatricians. Given the epidemics of obesity and diabetes, we decided to emphasize carbohydrate and fat metabolism to the exclusion of protein and nucleotide metabolism. Though the course is expected to evolve in coming years, it will initially be organized around 15 weekly topics, all of which will build on the vocabulary built in undergraduate biochemistry. It is our hope that when the pendulum swings back to demand a more advanced medical biochemistry curriculum, this course can serve as a model. The planned topics and clinical discussions are the following:

1. The Human Genome: Organization and Variation. Discussion: How sequence information is used in the clinic.
2. Gene Expression: Focus on RNA. Discussion: Dysregulated transcription factors in cancer.
3. Protein Synthesis and Structure. Discussion: Structure-based drug development.
4. Enzymes. Discussion: Drug targets in virology.
5. Signaling. Discussion: Nitric oxide signaling in vasodilation.
6. Carbohydrate Metabolism. Discussion: Galactosemia and lactose intolerance.
7. Respiration, Energy Generation and Thermogenesis. Discussion: Mitochondrial diseases.
8. Lipogenesis. Discussion: Drug dosing as a function of body mass and composition.
9. Lipoproteins and Lipolysis. Discussion: Cholesterol management.
10. Regulation of Metabolism. Discussion: Insulin, glucagon, and ketogenic diets.

11. Obesity and Diabetes. Discussion: Medical management of obesity.
12. Drug Metabolism and Action. Discussion: Coumadin and genotype.
13. The Microbiome. Discussion: Complications of antibiotic therapy.
14. Biochemistry of Taste and Pain. Discussion: Nonsteroidal anti-inflammatory drugs.
15. Biochemistry of Infection and Inflammation. Discussion: Inflammatory bowel disease.

■ CONCLUSIONS

Though undergraduate advising and medical school admissions offices are preoccupied with revising the minimally required courses, educators should not lose sight that students ask us for our opinions on *optimal preparation* for their career and life interests. I advise all of my students to read literature, and study creative works, history, politics, and language. I advise all biomedical students to take courses in genetics, immunology, bioinformatics, and computational science in addition to their required core science courses. Not being in a chemistry department, I can only advocate for a new life-oriented organic chemistry course to emerge as a rigorous alternative to the synthetic organic course. Whether chemistry departments take a mostly revolutionary or mostly evolutionary approach, I am confident that colleagues in chemistry will move existing courses in a bioorganic direction. Finally, educators can be confident that students who take a year of biochemistry in college and are able to build upon that base a semester of clinically oriented biochemistry in health professional schools will be much more prepared to practice in the era of personalized medicine than students who take just enough biochemistry for the MCAT and have little to no biochemical reinforcement as first-year professional students.

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Notes

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