

The Great Opportunity: Cultivating Scientific Inquiry in Medical Residency

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Residency training is a profound experience that greatly influences the career trajectory of every trainee. Currently, residency programs focus heavily (or almost exclusively) on the acquisition of medical knowledge and fail to foster intellectual curiosity and introduce residents to careers in investigation. We share 3 programs embedded in residency training where this focus is shifted with an emphasis on prompting intellectual curiosity and exciting residents about careers in investigation to revitalize the physician-scientist workforce.

Keywords. physician-scientist; residency; residents; pathways; tool for human investigation.

As a medical discipline, internal medicine represents a standard-bearer for the training of physician-scientists [1, 2]. Indeed, the history of our specialty is borne from the fusion of laboratory-based investigation and clinical practice. The term “internal medicine” is derived from the German phrase *innere medizin*, which pays homage to the influence of the early German physicians. “The domain of internal medicine has by the accretion of the most various experimental disciplines reached such a scope that one man can no longer be fully authoritative in all its branches. Only the investigator is competent to critically sift the endless accumulation of detail so that the best can be offered to students and general practitioners” [3]. By the early 20th century, academic medical centers became the home for those physicians who blended scientific discovery with patient care. Yet the last 30 years has brought unprecedented forces that have challenged medical educators to remain on this path. Currently choices must be made on how to best teach “basic science” in medical schools as part of a portfolio of topics necessary for the training of the modern physician including health policy, global health, and biomedical ethics [4].

Retaining the best physicians in the field of investigation has been a source of concern for many years [5, 6]. This includes not only laboratory-based physician-scientists but also those who pursue research in epidemiology, outcomes, bioinformatics, biostatistics, and translational studies, including clinical trials. Increasingly, this pathway no longer appears to be attractive to medical students, and this directly threatens the biomedical

workforce [7, 8]. Infectious diseases and immunology continue to be areas of pivotal importance in healthcare research. Fields with broad applications in the understanding and treatment of human disease, such as immunology and molecular biology, have been a direct outgrowth of fundamental research in microbiology. Infection remains a major cause of mortality worldwide and poses serious problems of both individual and public health concern in the United States. Human immunodeficiency virus (HIV) is the most significant human pathogen in the last 40 years. Antibiotic resistance occurs at an alarming and increasing rate among all classes of mammalian pathogens. Diseases once thought to be near eradication from the developed world, including tuberculosis, cholera, and rheumatic fever, have rebounded with renewed intensity. Environmental changes and rapid movement of human populations have introduced into human communities newly discovered and emerging infectious agents, including Middle East respiratory syndrome coronavirus, Ebola virus, hantavirus, HIV, and new strains of pathogenic *Escherichia coli*. Even in developed countries, infectious diseases have undergone a resurgence: Between 1980 and 2014, age-adjusted mortality from infectious diseases in the United States increased by 64% to levels not seen since the 1940s [9, 10]. Finally, the use of sophisticated epidemiologic data and modeling inform best practices in medicine and guide health policy.

Moreover, the role of infectious agents in the etiology of diseases once believed to be noninfectious is being increasingly recognized. *Helicobacter pylori* causes peptic ulcer disease and gastric malignancy, human papillomavirus is the most important cause of invasive cervical cancer, human herpesvirus (HHV-8) causes most cases of Kaposi sarcoma, and Epstein-Barr virus causes certain lymphomas and may play a role in the genesis of Hodgkin disease. Other diseases of unknown

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cause, such as rheumatoid arthritis, sarcoidosis, or inflammatory bowel disease, may have infectious etiologies. The role of the gastrointestinal microbiome in shaping the immune system and maintaining human health is now an important area of research. Finally, understanding the rules that govern immune activation is key to achieving success in organ/cellular transplantation. Indeed, much work is yet to be done.

The next generation of physician-scientists requires rigor in both clinical and research training. Indeed, it is these 2 domains that serve as the foundation of a career as a clinician-investigator. In the United States, medical education has focused on a step-wise approach to prepare medical students for residency. Early in medical school, students are exposed to basic science principles that underlie human biology and physiology. They are taught about pathophysiology in the context of case-based discussions, but often without encountering a real patient. The last 2 years of medical school focus on the fundamentals of the practice of medicine in which known pathophysiology is emphasized and clinical decision-making matures. Residency provides an in-depth opportunity to participate materially in the care of the patient that was developed using the apprentice model. Internists skilled in clinical medicine and research led these inpatient teams and modeled outstanding patient care. Moreover, sparking intellectual curiosity about the boundless unanswered questions posed by the patients' presentations fosters excitement about a career in research-oriented academic medicine [11–15].

Recently, the practice of inpatient medicine has changed. Sicker patients now occupy inpatient beds. Multiple incentives exist to decrease inpatient length of stay. Medical advances have proceeded so rapidly that inpatient teams focus on coordinating care with subspecialists and time to reflect on pathophysiology continues to vanish. Taken together, these changes have all led to the development of inpatient medicine as a specific field of internal medicine–hospital medicine. Coupled with the need to decrease the footprint of housestaff-covered beds to focus on education within residencies, hospitalists now provide not only direct care, but have increased their presence on housestaff-led teams.

Increasingly, the conversation on rounds focuses largely on the mastery of current knowledge. Yet, the practice of clinical medicine often is mixed with patients with known pathophysiology and some in which key deficits in our understanding of the basic biology persist. What should be done about the patient who does not fit into the rubric of what is known? How do we account for unexpected responses to a treatment plan? Questions that emanate from these patients are typically not discussed in a thoughtful and investigative manner. Moreover, the intense pressure on clinical teams to manage ever-increasing clinical volume dictates that these musings about the known unknowns be relegated “for a later time.” A critical opportunity has been missed. Inquisitive residents who yearn to understand

why their patients elude diagnosis or fail to respond to current therapy are outstanding candidates for a new enriched investigative pathway to learn more about investigation. Clinical staff are also limited in their ability to foster the necessary intellectual curiosity. Due to a combination of workloads, competing demands on clinical time and often a feeling of insufficient training themselves in investigation clinical staff are often unable to serve as examples or mentors for inquisitive trainees or, worse yet, actively stifle curiosity in the name of efficiency.

Current approaches to connect investigators with trainees occur haphazardly, infrequently, and often go unattended on a busy inpatient service without any long-term consequences, leading to frustration on the part of residents and the researchers who try to engage them. Special seminars or didactic conference time are used to inject investigation into the residency experience, but are among the most poorly attended conferences. Additionally, residents are asked to seek out “mentors” from physician-scientists during their clinical training. Most of these efforts do not enjoy the level of success intended. One of the driving reasons for this failure is a lack of appreciation that residents most value learning at the bedside and focus on patients as a means to organize and give structure to their learning agendas. Indeed, the resident experience is centered on inpatient wards and ambulatory clinics. Their Brownian motion from these patient-centered areas must intersect with those whose academic spheres are normally constrained to research areas or the laboratory.

The Department of Medicine at the Massachusetts General Hospital is responsible for the education of 168 interns, junior assistant residents, and senior assistant residents. They rotate through busy inpatient general medicine units, medical intensive care units, coronary care units, oncology floors, and ambulatory clinics. Within this cauldron of typical rotations for residents, we devised 3 areas of emphasis during the clinical phase of training designed to maintain passion for research and preserve intellectual curiosity.

PATHWAYS: A NEW CLINICAL ROTATION FOCUSING ON CLINICAL INVESTIGATION

Inspired by 2 former Massachusetts General Hospital (MGH) Medicine residents, Victor Fedorov, MD, PhD, and Lauren Zeitels, MD, PhD (who died tragically in an avalanche during training), the Pathways Service at MGH is a new initiative, led by Mark Fishman, MD (former Chief of MGH Cardiology, former chief executive officer of Novartis Institute for Biomedical Research, and current faculty member of the MGH Department of Medicine) and Katrina Armstrong, MD (Chair of Medicine, MGH), to enable exploration of a single patient over a 2-week rotation with a rare and difficult-to-diagnose disease [16]. The disassembly of a patient's problems into organ systems, for the purpose of consultation and care, has missed important opportunities for understanding the unity of disease

based on fundamental mechanisms. This experience of care is reflected in medical education where trainees now spend much of their time on checklists of tasks rather than the critical thinking and diagnostic reasoning that brought them to internal medicine in the first place [17]. The Pathways Initiative is founded on the belief that curiosity driven by a single patient with a clear-cut and unexplained constellation of disorders can generate new insights into disease mechanism, creating the synergy across the missions of discovery, clinical care, and education that is fundamental to the societal value of academic medicine. Furthermore, with the technological platforms that have now arisen from molecular biology, there is a substantial opportunity to reconnect biology to the bedside by generating and testing hypotheses about potential unifying mechanisms from unexplained patients.

Two to 3 residents rotating through the Pathways service operate as a team to investigate a case referred to Pathways by developing a hypothesis about the patient's underlying mechanism of disease with both clinical and scientific outcomes. Patients with unexplained presentations/disorders are referred to the Pathways Consult Service from across the medical services. In 1 year, more than 75 inpatients have been referred to the Pathways service. The team will consult on a patient with an unexplained disorder and develop 1 or more hypotheses regarding the pathophysiology underlying the patient's disorder through meeting with the patient and care team, literature review, and meetings with relevant clinical and scientific experts at MGH and beyond. These hypotheses will be refined through an interdisciplinary conference with senior physician scientists. The rotation has several scheduled meetings with scientists, physician-scientists, and master clinicians from around the world—all focused on this single patient. Most of the rotation is self-directed research time on the case and conference presentation. A number of patients selected for the Pathways elective have relevance to immunology, inflammation, or infection including the mechanism of epithelial damage and bronchiectasis in allergic bronchopulmonary aspergillosis, potential novel infectious agents in a patient with chronic inflammation and vascular leak, and discussion of the mechanism of chronic granulomas driven by unknown antigen.

Ultimately, with the additional guidance of the director of the Pathways Clinical Faculty, the team will recommend clinical interventions and diagnostics based on their insights, as well as propose basic research questions and experiments that would help further elucidate the nature of the patient's presentation and underlying mechanism of disease. If the patient consents, there is the potential to execute the proposed experiments at MGH, or with other collaborators. In addition, Pathways residents will have an option to attend ambulatory clinics (such as genetics, infectious diseases, and immunology) chosen to enhance their understanding of the clinical manifestation of disease as well as the application of disease diagnostics.

By providing the time and resources to focus on understanding the mechanism of disease in a single patient, the goals of this program are to:

1. Promote a culture of inquiry and critical thinking with opportunities to develop unique knowledge about clinical presentations and underlying pathophysiology;
2. Advance patient care by offering unique insights into disease processes as well as clinical, diagnostic, and therapeutic recommendations;
3. Apply cutting-edge basic science techniques to advance scientific knowledge.

THE RETURN OF PHYSICIAN-SCIENTISTS AS ATTENDING PHYSICIANS ON THE INPATIENT MEDICAL SERVICE

Through the general medical service, our residents care for patients of high complexity and acuity, seeing the pathology of every organ system, and delivering the best care to a socioeconomically and geographically diverse patient population. To emphasize a team-based approach to clinical care and education, the Bigelow Service, comprised of 6 resident teams, is the core of the MGH Department of Medicine's clinical teaching experience. Each Bigelow team is comprised of 4 interns, a junior assistant resident, and 2 attending physicians who oversee the care of 16–18 patients. All interns share responsibility for all patients, and rotate through a 4-day cycle of tasks. The “call” intern admits up to 5 patients in a 24-hour call period and cross-covers all patients on the floor at night, with nighttime supervision and teaching provided by senior assistant residents. The “plan” intern leads team rounds on all previously admitted patients, creating the plan for the day and leading the daily follow-up bedside interview and examination. The “swing” intern takes the lead in communicating with consultants, coordinating and performing procedures, and managing key time-sensitive tasks that need to be completed before rounds. The junior assistant resident supervises the care provided by the team and leads discussion in work rounds. Interns and medical students experience both a wide breadth of patients and the educational opportunities of team dialogue in caring for patients when on a Bigelow team.

The opportunity to have 2 attending physicians on each Bigelow team permits pairing individuals with complementary skill sets. We have developed a robust set of core educator faculty who are national leaders in innovative medical and clinical education and provide expertise across a wide range of fields in academic medicine. During their nonclinical time, core educators teach in other educational venues, lead scholarly projects, advance research in medical education, and develop novel curricula. We have paired a number of different internists who may normally not fully engage in serving as the sole leader of an inpatient team with one of the core educators to broaden the

exposure of internal medicine to residents. Specifically, we have reengaged our physician-scientists from the Department of Medicine, including infectious diseases, to serve as a co-attending in this model. Not only do these individuals bring their subspecialty expertise, but importantly, they serve as role models for trainees and can use the interstices of their daily schedule to excite residents and students about a career in investigation by using patients on the clinical service to drive intellectual curiosity and provide a framework on how we can investigate the unknowns. The ability to carry a smaller list of patients, but also have meaningful interactions with residents, permits younger physician-scientists to engage rather than actively excluding clinical work in the early part of their careers.

In addition to the inpatient service, the leadership of the residency has active research investigators. One of the authors (J. M. V.) is the Residency Program Director as well as an active physician-scientist. His laboratory remains active and has enjoyed continuous National Institutes of Health (NIH) funding. His area of interest is in innate immunity to fungal pathogens. Many of the residency leaders are also active investigators with successful research programs. This critical mass of faculty prominently seen by the residents can have a lasting impact on their subsequent choices for careers.

EQUIPPING RESIDENTS WITH THE TOOLS FOR HUMAN INVESTIGATION

Tools of Human Investigation (THI) is a 2-week elective rotation for medicine residents that focuses on clinical investigation, analytic and presentation skills, and career development. The course director is a physician-scientist (K. E. C.) with substantial NIH funding for her research program and receives financial support as an Associate Program Director for the Residency Program. The course is offered 4–5 times throughout the academic year to retain a small-group, interactive atmosphere while ensuring that all residents participate. Residents do not have inpatient clinical responsibilities during the THI course. Residents are exposed to a broad array of investigators in the MGH community at all stages of their careers. At each session, faculty members summarize their own early career path, describe their research, and teach interpretation of the literature, presentation, writing, and research skills, exposing residents to a wide variety of research and academic careers and preparing them for leadership regardless of their chosen field. The specific aims of Tools of Human Investigation are to (1) introduce pathways for early career development; (2) provide an overview of hypothesis generation and testing using a variety of study designs; (3) provide introductory principles of clinical research, including clinical trials, genetics and genomics, epidemiology, health services research, and translational research; and (4) provide the critical thinking skills necessary to appraise the scientific literature and communicate their ideas effectively. Residents also work on existing research projects or

develop a new research question based on a clinical question from their ward experiences and then propose methods to test their hypotheses. Residents present their projects to faculty mentors and program leadership on the final day of the course. Residents are also encouraged to submit their projects to the Annual Resident Research Day sponsored by the Department of Medicine. Selected recent lectures in the THI Course include “The Genetics of Type 2 Diabetes,” “Statistics for the Basic Scientist,” and “Perspectives on Academic Career Development Seen Through the History of 50 Years of Parathyroid Hormone Research.” Ongoing analysis will measure the impact of these programs on resident career choices.

FUTURE PERSPECTIVES

There has never been a better time to be in medicine than now. The fruits of years of basic research are now being realized. Therapies for HIV and hepatitis C virus (HCV) infections have been revolutionized through a mechanistic understanding of the viral life cycle. Drugs that convert HIV from a deadly infection to a chronic disease are routinely administered. We can now cure HCV. Progress in these areas has not stopped, and we hope to witness vaccines that will prevent these infections in the near future. The lifeblood of research-oriented academic medical centers are the physician-scientists. A concerted effort to ensure a steady supply of these investigation-oriented physicians is critical to the long-term success of biomedical research. Many challenges exist in the training environment including the fractured nature of training (between clinical and research training, opportunity costs as well as the overall length of training). These issues need to be addressed directly. The federal government as well as nongovernmental organizations (including Burroughs Wellcome Fund and the Howard Hughes Medical Institute) have begun to address this critical need. Along with these initiatives, we firmly believe that it is our responsibility to instill passion for scientific inquiry and investigation as a major component of the educational mission and culture of internal medicine residency programs.

Notes

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