

2018 American Society for Clinical Investigation Presidential Address

Generations of physician-scientists

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Introduction

I feel extremely honored and humbled to have served as president of the ASCI for the past year. Most of all, I have enjoyed the collaboration and friendship of the ASCI Council members and staff, and I have been inspired by the extraordinary physician-scientists who are members of this Society.

The intellectual breadth and history of the ASCI membership connects us to a succession of accomplished investigators dating back to 1908. We all know that our work as physician-scientists is based on prior discoveries, technological developments, and theoretical frameworks. And we all strive to make contributions that will provide the scientific foundation for the next generation of researchers. The members of ASCI have engaged in these successive rounds of discovery for over a century. As we celebrate the induction of new members into our Society, the annual meeting is an opportunity to see the connections across disciplines and generations of investigators, and to recognize the accomplishments and potential of our newest members.

The meeting also focuses us on the role we play now to shape the structure of clinical investigation for future generations of physician-scientists, so they can thrive and make their own contributions. Our predecessors established the medical education, clinical training, and career tracks that we follow today. It is now our responsibility to enable the next generations of physician-scientists to be best positioned to make fundamental discoveries that will drive future changes in clinical medicine.

Generations of physician-scientists

My personal heritage as a physician-scientist is linked to this very lecture, delivered 60 years ago by the ASCI president in 1958, Richard Vincent Ebert, my grandfather

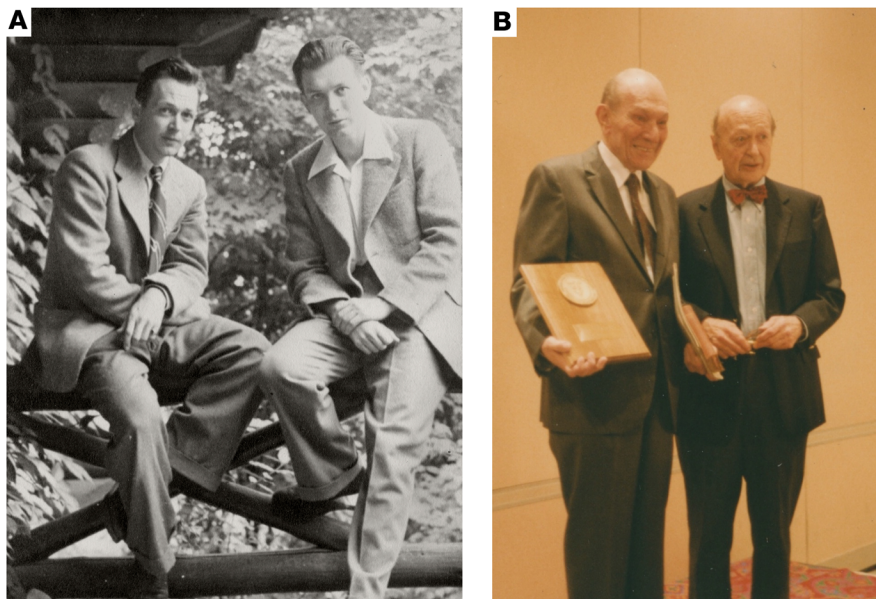


Figure 1. Richard V. Ebert and Robert H. Ebert. Richard Ebert and Robert Ebert in the 1930s (A) and in 1990 (B). Richard Ebert is on the left in both photographs.

(Figure 1). Meetings at that time were held annually in Atlantic City, New Jersey, as they were from 1911 until 1977. His talk, as relevant now as it was then, was entitled “Clinical Investigation and Medical Education” and discussed the importance that all medical students understand the scientific method and engage in primary research (1).

My grandfather’s own path to medicine began with his father, my great-grandfather. Orphaned at a young age by immigrant parents, my great-grandfather was adopted by a German farmer with the surname Ebert. He became a schoolteacher, but then used his inheritance to attend medical school and become a dermatologist, ultimately serving as Chair of Dermatology at Rush Medical College. He had two children, Richard and Robert Ebert, my grandfather and his younger brother. Both chose careers in medicine, starting with medical school at the University of Chicago. Robert Ebert

obtained additional training in scientific research, attending Oxford University as a Rhodes Scholar, where he worked with Sir Howard Florey at the Dunn School of Pathology just a few years before Florey treated the first patient with penicillin.

With the outbreak of World War II, both brothers enlisted as physicians. My grandfather served in the Harvard University Unit in the Fifth General Hospital. He was stationed in Southampton, England, before going to Normandy, landing on Omaha Beach on July 6, 1944, one month after the invasion. While deployed, he performed seminal studies on shock in the battlefield and the use of blood products, including a study on transfusion reactions to pooled plasma published in the *Journal of Clinical Investigation*, listing “European Theatre of Operations, U.S. Army,” as his institutional affiliation (2). His younger brother, Robert, joined the U.S. Navy in 1944 following an internship at Boston City Hospital. He was among the first American physicians to travel to Nagasaki after the atomic bomb explosion, where he treated victims of radiation sickness.

Reference information: *J Clin Invest.* 2018;128(10):4208–4212. <https://doi.org/10.1172/JCI124786>.

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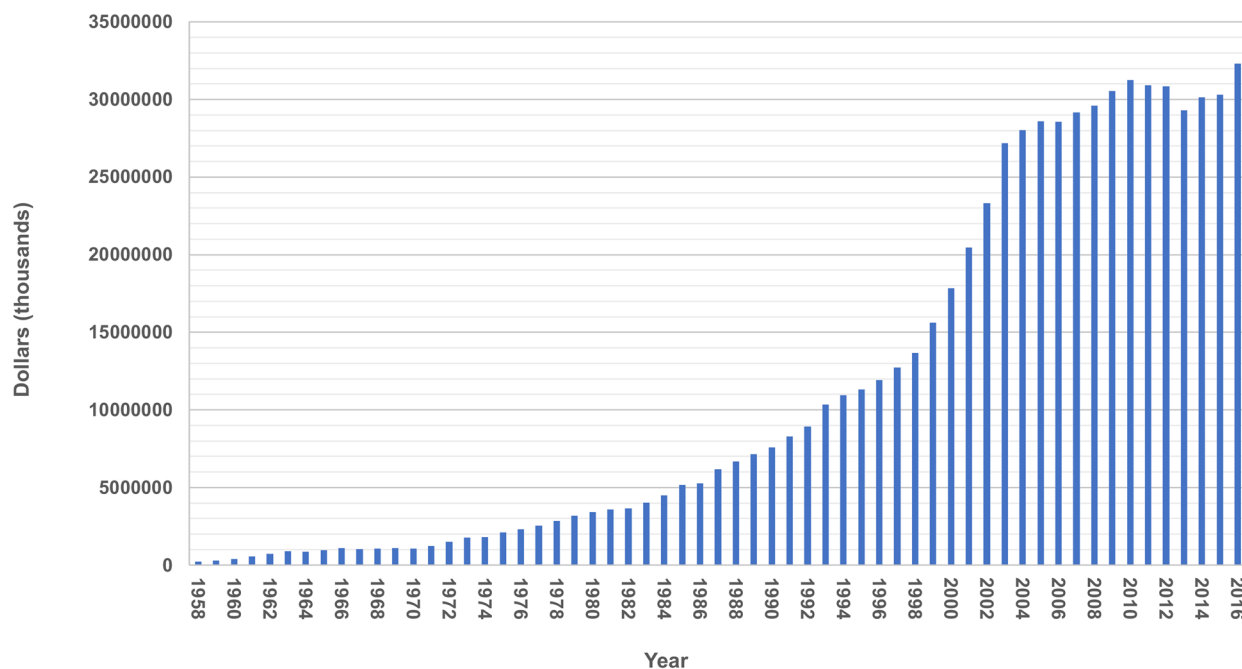


Figure 2. The NIH budget from 1959 to 2016. Source: Office of Budget, NIH.

Back in the United States, both brothers pursued careers in academic medicine. My grandfather, Richard Ebert, became Chair of Medicine at the University of Arkansas and then the University of Minnesota, and served as ASCI president from 1957 to 1958. Robert Ebert was a Professor and Chair of Medicine at Western Reserve University and ultimately served for 12 years as Dean of Harvard Medical School. The brothers maintained a close relationship throughout their careers. Both Richard and Robert Ebert had children who chose careers in medicine, including my father, Michael Ebert, who was a department chair and is currently a Professor of Psychiatry and Associate Dean at Yale School of Medicine and Chief Medical Officer of the VA Healthcare System in Connecticut. And in the following generation, both my brother and I pursued MD/PhD degrees and careers in academic medicine, the fourth generation of physicians in the family.

My professional relationship with my grandfather and his brother was limited, as both died during my first year of medical school. However, over the years, I have continued to meet their colleagues and trainees who have shared stories, whether personal or professional. One of the great features of the ASCI is the connection to

multiple generations of physician-scientists. A number of ASCI members have related anecdotes to me of working with my grandfather or great-uncle.

The generations of physician-scientists that have attended this meeting are not, of course, limited to direct familial relationships. Generations are also defined in an academic sense, describing the relationship of mentors and mentees. Our mentors, our mentors' mentors, and so on trace an academic pedigree related through an intellectual inheritance. The ASCI meeting often serves as a reunion for multiple generations of mentors and mentees.

I spent my college summers working in the research laboratory of Daryl Graner, then the MSTP Program Director at Vanderbilt, an ASCI member who is here today. After graduating from college, I went to Oxford, ambitious and naive. Through enormous good fortune, I joined the laboratory of Peter Ratcliffe, who was then a junior investigator doing groundbreaking work on the mechanisms of oxygen sensing. By a wonderful coincidence, he was selected by the American Physician Scientists Association (APSA) to give the Lasker Award Lecture immediately preceding this talk. As a postdoctoral fellow, I worked with Todd Golub at the Broad Institute; Todd is now an Association of

American Physicians (AAP) Council member and attending this meeting. And one of my trainees, Ann Mullally, an Assistant Professor of Medicine at Harvard Medical School, is in attendance and is becoming an ASCI member at this meeting. Thus, without intentional planning, multiple generations of my academic lineage are here at this meeting, and I know the same is true for many others.

Networks of friendships, mentorship, and collaboration weave the social and scientific fabric of our careers. In clear and directive ways, or subtle and unconscious ways, these relationships guide our research and career decisions. The ASCI extends these connections across the generations of physician-scientists and the breadth of disciplines.

Generational shifts and enduring themes

Academic medicine has clearly changed dramatically since my grandfather delivered his ASCI presidential address in 1958, but our motivations and the basic structure of our careers are fundamentally unchanged. Comparing the challenges and opportunities for physician-scientists across the decades highlights the shifts that have occurred in science and medicine while bringing into relief the similarities

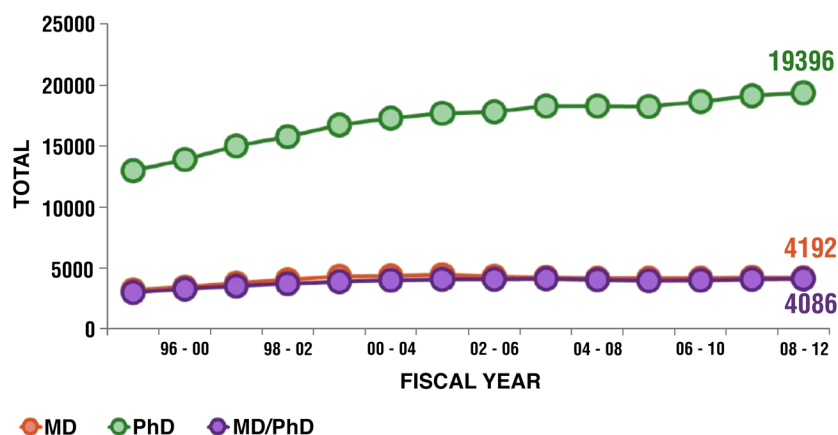


Figure 3. NIH grant awardees by graduate degrees. Historical trends are graphed for NIH individual research project grant awardees by graduate degree. Source: National Biomedical Research Workforce Dashboard, Office of Extramural Research, NIH.

in the features of a career as a physician-scientist that have held constant.

Perhaps most dramatic is the change in the size and funding of biomedical research. Research funding after World War II ushered in a rapid acceleration in medical research, with new medical schools, expansion of the Veterans Administration hospitals, and descriptions of ASCI meetings in the public press (3). The NIH reached a budget of \$210 million in 1958, an amount that likely seemed generous at the time, given the rapid rate of increase in funding (Figure 2). However, even with the relative stagnation of the NIH budget in recent years, the NIH budget has increased more than 175-fold in the past 60 years. Private sector and philanthropic support have increased by even greater margins. Biomedical research has grown into a massive enterprise with large university faculties, and the investment has yielded tremendous dividends in new therapies and improved outcomes for patients, as well as robust biotechnology and pharmaceutical industries.

In addition to the massive increases in research funding, training programs for physician-scientists have been formalized and funded by the federal government. Medical Scientist Training Programs, residency program tracks for physician-scientists, and career development awards have been established. While these programs may have contributed in some ways to the lengthened training time, the programs have yielded extraordinarily well-educated physician-scientists.

The centrifugal force of subspecialization has arguably been the most influential for the ASCI. In the 1950s, subspecialization was just beginning. The ASCI

meeting in 1958 was large and influential, a prestigious venue for delivering the first presentations of new findings. With the dramatic rise in the size of subspecialty meetings, and the increasing specialization of physicians and scientists, the size of the ASCI meeting decreased. My grandfather's career spanned this pivotal era, and he was the first to appoint division chiefs for the medical subspecialties into the Department of Medicine at the University of Minnesota when he was chair.

While these changes have transformed many aspects of biomedical research, core aspects of our careers have changed little in the past 60 years. Our core goals remain unchanged: to investigate the biological basis of human disease and the development of novel therapeutic approaches.

These more basic aspects of our careers, that have not changed over the years, are the source of the most important messages from previous generations. Ethics, codes of conduct, and the spirit of investigation have not shifted as biomedical research has been transformed. Even if not conveyed directly, I learned from my grandfather, his brother, and their generation the satisfaction and pride in a career as a physician-scientist.

I no longer use the technical methodology that I learned in the laboratories of my mentors, but I do research in the manner in which I was trained. Peter Ratcliffe, for example, taught me the rigor required for outstanding research; the focus and work ethic required for success; and the necessity of performing the best possible experiment, even if that requires learning and mastering unfamiliar techniques. Partly for this reason, apprenticeship remains a core aspect of our training as physician-scientists.

Today, as it was 60 years ago, great careers begin with strong training, mentorship, and role models. Scientific vision, creativity, and some good fortune continue to drive innovation and discovery. The experimental paths to great scientific findings enthrall the audience at today's meeting just as they did in 1958.

Training future generations of physician-scientists

The number of new members inducted into the ASCI annually has not changed nearly as much the number of physician-scientists. The number of inductees was 35 in 1958 (4). We now induct up to 80 per year. While it is difficult to equate the standards for membership, the small number attests to the ongoing challenge of being a productive physician-scientists.

One of our goals must be to do what we can to enhance the opportunities of the next generation of physician-scientists. Here, I would like to highlight the tremendous work that has been done in recent years by the Physician-Scientist Workforce Working Group, led by David Ginsburg, Sherry Mills, and Susan Shurin, a trio of leaders who will be honored with a Special Service Award later this afternoon. The task force delivered a comprehensive and detailed report in 2014, and an implementation group has since gone on to execute on each of the recommendations (5).

It is notable that the size of the physician-scientist workforce has been constant in recent decades, while funding for PhD scientists has expanded, comprising a larger percentage of grants (Figure 3). The number of physicians in the United States who report research as their primary activity has held constant at approxi-

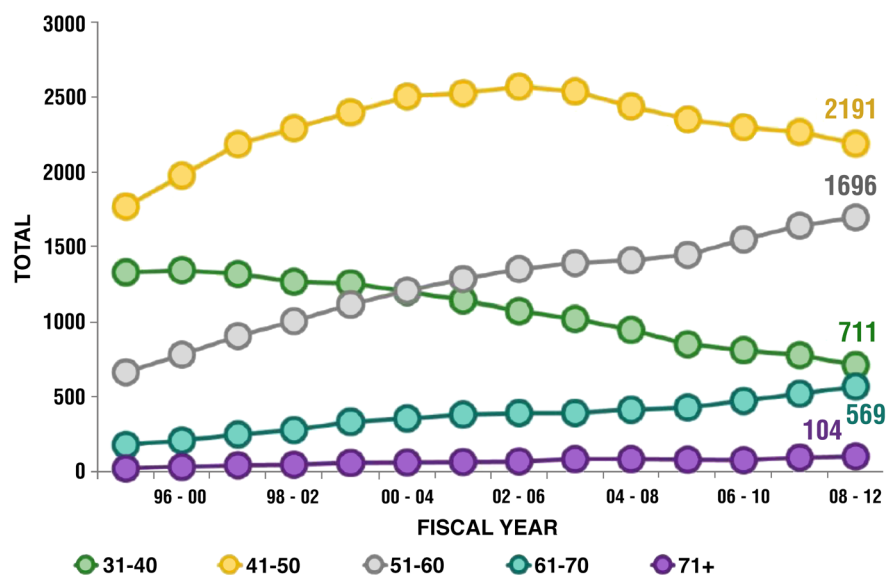


Figure 4. Age of NIH grant awardees. Historical trends are graphed for the age of NIH individual research project grant awardees with MD/PhD degrees. Source: National Biomedical Research Workforce Dashboard, Office of Extramural Research, NIH.

mately 14,000 individuals. The number of MDs or MD/PhD investigators who hold a research project grant from the National Institutes of Health has held steady at approximately 8,000 awardees, while the number of PhD scientists holding research project grants has increased steadily. The average age of physician-scientists has been increasing with prolongation of training times, later ages of retirement, and the success of senior investigators in obtaining grant funding (Figure 4).

The Physician-Scientist Workforce Working Group made a set of recommendations that was approved by the NIH Director to strengthen the number, productivity, and diversity of physician-scientists in the United States. These included strengthening support for MD/PhD training programs while increasing diversity and shortening the time of training through a series of targeted funding opportunities, career guidance, and pilot programs.

Several recommendations target the critical period as trainees transition into independent faculty members. These include new physician-scientist-specific grants, similar to the K99/R00 Program. Proposals were made to expand loan repayment programs. The task force offered ideas to leverage the existing Clinical and Translational Science Awards (CTSA) program to benefit a wider range of physician-scientists and enable their research.

The recommendations of the Physician-Scientist Workforce have the potential to influence national policy, optimize

the allocation of NIH resources, and bring together key stakeholders to bolster the pipeline and diversity of physician-scientists. In addition, the task force recognized the importance of mentorship for successful career development.

Institutional leadership that actively seeks to promote the careers and success of physician-scientists is also critical. There is great value to the careers of physician-scientists to have leaders who are themselves committed and successful physician-scientists, or those who are staunch advocates of the careers of physician-scientists. Budgetary pressures in clinical medicine and research have the potential to select leaders who focus more on clinical productivity with less emphasis on fostering the productivity of physician-scientists. The former may improve budgets in the short term, but the latter, investment in science, yields much greater returns, though sometimes over a longer time horizon.

Careers can benefit enormously from the judicious influence of an academic leader looking out for the interests of physician-scientist faculty members. Brief conversations offering guidance at a career junction, support at a tenuous moment or when opportunity is greatest, or re-allocation of clinical or administrative effort when workload impairs productivity can have major consequences for an individual investigator. Physician-scientists need sufficient administrative support to manage the regulatory requirements that have

increased in both the clinic and the laboratory. Needless to say, ASCI members populate many of the positions of leadership in academic medicine as well as industry, and this annual meeting has served to inspire me, at least, to do what I can to foster the careers of physician-scientists at my institution.

ASCI across the generations

The ASCI has become a complex organization. We own and operate two journals, the *Journal of Clinical Investigation* and *JCI Insight*, both of which are self-published, and we have a substantial staff and budget. This year, we have taken steps to formalize a number of organizational structures. The recent creation of *JCI Insight* has increased our need for oversight of our publications, and for succession plans for our editor and editorial board of the new journal. We established a Publications Committee to provide an additional level of governance, including the editors of the *JCI* and *JCI Insight*, ASCI officers, and additional members. We introduced *JCI Insight* into the ASCI bylaws, and the amendments have now been voted upon by the membership and passed.

In recognition of our growing ambitions to engage in public policy related to biomedical research and the careers of physician-scientists, we established an Advocacy Committee that has been ably led by our Vice President, Kim Rathmell. With the goal of increasing our financial resources to endow our awards and enable

new initiatives, we established a Development Committee that has been actively led by our President-Elect, Kieren Marr. We hope that these structures will stand the ASCI in good stead for years to come.

The generational cycles of the ASCI's academic leadership are particularly short, with Councilors serving for 3 years, officers serving for 4 years, and the editors in chief of *JCI* and *JCI Insight* serving for 5 years. Turnover offers the potential for frequent renewal of ideas, but threatens continuity. ASCI staff provide the primary source of continuity, institutional knowledge, and leadership that sustains the society across generations of academic leaders. Many dedicated members of the ASCI staff contribute to the Society and the publication of our journals. However, this year is a milestone that deserves particular recognition.

John Hawley, Executive Director of the ASCI, and Karen Guth, Managing Director of the ASCI, both reach their 20th year of employment this year. These two central figures have had enormous influence on the Society, and an interesting perspective on academic medicine, having shepherded 20 ASCI Councils through their annual terms.

John Hawley has an ideal leadership style for this role. He has a vast knowledge of the organization and extraordinary judgement. He guides the organization with a calm competence regardless of the circumstances. His advice is given as a gentle recommendation, highly respectful and sometimes subtle, but always accurate and extremely influential. He has guided the ASCI through countless twists and turns with great skill and dedication.

Karen Guth manages, among other responsibilities, our finances. With two journals, meetings, investments, property in Ann Arbor, and a substantial staff, our income and expenses are significant. Kar-

en manages the budget and explains the accounting to each new generation of Councilors with endless patience. The financial stability and growth of the ASCI in the face of a radically altered publishing industry owes much to Karen's deft guidance.

In addition, John and Karen are fun and engaging people with broad interests, and I have thoroughly enjoyed working with both of them. I have relied heavily on their advice throughout my term on Council and as President. The Society owes John and Karen tremendous gratitude for their leadership. On behalf of the current Council, generations of Councils over the past 20 years, and the entire ASCI membership, I would like to thank John and Karen for their service to the ASCI.

I would also like to thank the members of the ASCI Council for all of their hard work over the past year. It has been a great honor to work with each of you. Kieren Marr, who succeeds me as president, will be an outstanding leader and will leave her own indelible mark on the organization.

Congratulations to the new members of the ASCI. You are on the steep slope of your career trajectory, having already made major contributions in your fields, but still young and with enormous potential for continued productivity. I hope you enjoy and are inspired by the scientific talks and award lectures. Accomplished physician-scientists have come to this meeting to be inducted into the ASCI since 1908. They have gone on to make many of the discoveries that have transformed the practice of medicine over the past century. I have no doubt that the technologies and research opportunities available to you now will enable breakthroughs more profound and impactful for the treatment of human disease than any previous generation.

My grandfather could not have conceived of the discoveries presented at

the meeting today, but the research performed by his generation is the basis for the work we do today. The structures that his generation put in place established our training, funding, and career tracks. I have every confidence that the newest generation of ASCI members will establish the foundation for future generations of physician-scientists.

Finally, I would like to take this opportunity to thank my family. My father, the son of Richard Ebert, is here today. He, more than anyone, has been my most important role model. And I would like to thank my wife, Jane, and our children, Eliot, Iris, and Eliza, for their love and support.

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