The Kidney Research Predicament

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ABSTRACT
Research funding from public and private sources has reached an all-time low. Economic conditions, sequestration, and a trend of low award success rates have created an imbalance between the supply of highly qualified research investigators and the availability of critically necessary research dollars. This grim environment continues to hinder the success of established investigators and deter potential investigators from joining the research workforce. Without action and support of innovative science, the future of the US health care system is in jeopardy, and its leadership role in medical research will decrease. This work discusses the effects of the decline in research funding, the plight of kidney research, and the impact of the American Society of Nephrology Grants Program on scientists. The ASN also calls on the entire nephrology community to rejuvenate the research environment, improve the lives of millions of people with kidney disease, and ultimately, find a cure.


The availability of research support has fallen dramatically in the United States of America. Although the National Institutes of Health (NIH) annual budget doubled from $13.7 to $26.9 billion per year between 1998 and 2003, it has failed to keep pace with inflation since 2003.1 Additionally, the across-the-board federal cuts in 2013, known as sequestration, caused a 5.5% decrease in the NIH budget in 2013.2 At the same time, funding from the philanthropic sector for multiyear high-impact programs has declined an alarming 55% since 2008, partly because of the effects of the economic downturn, such as reduced donations and fewer resources.3 With funding constraints existing in the public and private sectors, investigators now face the negative consequence of a steady decline in success rates for research funding. For example, the success rates of obtaining an NIH R01 grant—a major funding source for individual laboratories and investigators—have fallen from 58% in 1962 to 22% in 2010 and declined further to 17% in 2013.4,5 The combination of decreased resources and lower success rates has created an imbalance between the supply of highly qualified research investigators and the availability of critically necessary research dollars. Low award success rates and greater competition are reflected by the notable increase in the average age of investigators at the time of receipt of their first R01 (from 40 years old in 1991 to 45 years old in 2011). Diminishing funding prospects discourage graduate and medical students, residents, fellows, and PhD candidates from pursuing research-oriented careers.6 The long-term implications include jeopardizing the intellectual capital and research infrastructure in the United States.

THE PLIGHT OF NEPHROLOGY INVESTIGATORS

Diminished research funding has affected nephrology more than other disease-defined research communities. Historically, kidney disease research received less funding than other diseases, such as AIDS, cardiovascular disease, cancer, and diabetes.7 Despite the doubling of the NIH budget, the percentage of funding for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and kidney-related research continued to decrease, whereas the percentage of funds to other institutes, such as the National Institute of Allergy and Infectious Diseases, experienced a steady increase.8 Although investigators across all aspects of medical research face funding cuts and diminished success rates in the current funding crisis, nephrology was at a lower base level, resulting in funding reaching an all-time low. The success rate of obtaining an R01 for a kidney-related project has dropped from 23% in 2011 to 17% in 2012 (C. Ketchum, unpublished observations). Under the effects of sequestration, the 2013 NIDDK budget decreased 5.68% to $1.693

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billion, which will result in the institute funding nearly 200 fewer noncompeting research projects.9

As a result of the decline in NIH and NIDDK funding opportunities, kidney researchers are forced to seek funding from nongovernmental sources, such as foundations, voluntary health organizations, patient groups, and medical societies. The universal realities of the recession and sequestration were compounded for kidney researchers in 2012, when the National Kidney Foundation (NKF) suspended its research fellowship program that previously helped foster the careers of 1165 young investigators from 1979 to 2012. At its peak in 1981, the program awarded 44 total fellowships to researchers who were seeking to make contributions to the nephrology field. Funding from these sorts of private, nongovernmental sources can exert a significant effect on first-time investigators, particularly fellows and junior investigators interested in academic careers.10 Without support from programs like NKF’s research fellowship program, the nephrology community’s research workforce is at risk.

Unlike other disease states, kidney research lacks major nongovernmental funders, particularly voluntary health organizations and patient groups such as the Foundation for AIDS Research, the American Heart Association (AHA), the American Cancer Society, the American Diabetes Association, and the Juvenile Diabetes Research Foundation (JDRF). In fact, both AHA and JDRF fund more kidney-related research than any of the kidney-specific voluntary health organizations. Within the nephrology community, voluntary health organizations often prioritize resources to provide financial support to patients (e.g., covering transportation costs, prescription drug copayments, and kidney donor expenses), offer general health education and prevention programs, or attempt to increase the shockingly low public awareness of kidney disease.11 Although beneficial to kidney patients, the unintended consequence of this strategy is that much-needed funds are diverted from kidney research.

It is also speculated that the decreased funding and lack of public awareness have affected the way that research applications are reviewed and supported. Grant reviewers, particularly those reviewers without nephrology training, are unaware of the exponential need for funding renal research and finding a cure for this life-altering disease. Reviewers within the philanthropic sector and federal agencies are now held more accountable for public donations and federal tax dollars, which leads to more risk-adverse funding decisions. Consequently, this risk aversion is shifting funding to shorter-term translational research and reducing overall support for early stage basic research.12

THE IMPLICATIONS OF FUNDING GAPS

Without consistent support, the nephrology community continues to produce fewer clinical trials, discover fewer therapies that are approved by the Food and Drug Administration (FDA), and publish fewer original research articles than other internal medicine specialties. Between 2002 and 2012, the FDA awarded new and previously marketed products with 37 nephrology-related indications compared with 85 indications related to oncology within the same time period.10 Moreover, less than one half of these approvals are for treatments specifically for the kidney, whereas the majority is for urologic illnesses, such as bladder conditions or erectile dysfunction.13

Without active and robust clinical trials to establish accepted end points and benchmarks for kidney disease, nephrology investigators face increasing challenges in disseminating research findings. The number of published papers in nephrology is decreasing at a rapid pace. Between 1966 and 2002, “the number of randomized controlled trials (RCT) published in nephrology was fewer (2779 RCTs total) than all other specialties of internal medicine (range: 5335 in hematology to 27,109 in cardiology), and the proportion of all citations that were nephrology RCTs was the third lowest (1.15%), ahead of only neoplasms and hemic/lymphatic studies.”14 Between 2005 and 2009, the nephrology community published 96 papers in the Journal of Clinical Investigation, a well respected, high-impact multidisciplinary research peer-reviewed journal, compared with nephrology’s peak of 243 published papers from 1970 to 1974.15

Without sustained research funding and established benchmarks, nephrology investigators are unable to produce innovative research, enter patients into state-of-the-art clinical trials, or disseminate research findings in elite peer-reviewed journals. As a consequence, nephrology continues to fall behind other internal medicine specialties and struggles to develop new therapies to meet the increasing needs of patients with kidney disease.

Despite having access to more sophisticated technology within bioscience and modern tools of pharmacogenomics, kidney researchers are more discouraged than ever. Research funding cuts have forced established kidney researchers to halt studies and close their laboratories, resulting in a loss of valuable data, stunted innovation, and a declining workforce. At the same time, the next generation of investigators is choosing to pursue more inviting careers with less financial risk.6 Because the millennial generation of medical students highly value careers with a controllable lifestyle, many have opted for the emergency medicine, radiology, ophthalmology, anesthesiology, and dermatology specialties.16–18

Medical students and residents are also discouraged about pursuing careers as nephrologists and investigators for several reasons, including the perception that nephrology careers do not provide a good work–life balance, the high stress from caring for chronically ill patients, low and stagnant financial compensation, a perception that nephrology is too complex, a lack of interest in kidney pathophysiology classes, limited exposure to clinical nephrology during medical school, and a lack of mentors to positively influence nephrology career choice.6

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Compounding factors specific to the physician–scientist pathway, a vital component in applying scientific expertise to treatment innovation, include the additional debt burden incurred by extended postgraduate research training and the substantial salary differential between research-oriented and clinical care careers. The current instability in public and private funding for research has exacerbated this difficult situation. Students are more likely to pursue a research track if they had successful research experiences in medical school, residency, and fellowship. Those students who pursue MD/PhD tracks cite less debt burden, scholarships, or grants in medical school as motivating factors for their career choice. If current and future students stop entering the nephrology workforce, especially as physician–scientists, the kidney community will continue to face insufficient dialogue between the silos of cutting edge science and clinicians, resulting in a decline in innovations and treatments for the increasing number of patients.

AMERICAN SOCIETY OF NEPHROLOGY FOUNDATION FOR KIDNEY RESEARCH

In light of these disturbing trends, health professional groups, patient organizations, government, industry, and other stakeholders focused on improving kidney health must support clinical and basic researchers. If not, the kidney community must accept less progress in patient care. To administer, protect, and expand its investment in research, the American Society of Nephrology (ASN) in 2012 established the ASN Foundation for Kidney Research. Although the ASN Foundation has made progress since its inception, these efforts represent just part of the mosaic required to move from managing kidney disease to curing kidney disease.

The ASN Foundation for Kidney Research Grants Program includes the Student Scholars Grant Program, the Ben J. Lipps Research Fellowship Program, and the Career Development Grants Program. With a mission “to prevent and cure kidney disease through research and innovation,” the ASN Foundation supports investigators ranging from students eager to conduct basic nephrology research in the laboratory to new faculty seeking to establish an independent research program.

Through its Student Scholar Grant Program, the ASN Foundation encourages students to pursue basic and clinical research in nephrology. Since 2000, the program has provided more than $1.1 million in support to nearly 100 medical students to conduct full-time research in a nephrology laboratory. This program helps fuel the pipeline of the nephrology workforce by supporting and instilling passion for research in kidney disease.

As a complement to the Student Scholar Grant Program, the ASN established the Ben J. Lipps Research Fellowship Program in 2012. With a commitment to fund 10 new and 10 continuing fellows each year, the ASN is providing researchers early career support and helping to offset the low funding rates for kidney disease research.

The ASN Career Development Grants Program, the society’s first research grant program established in 1996, provides financial support to new faculty with the goal of fostering their development into independent research and successful application for NIH R01 grants or equivalent. The Career Development Program funds investigators within seven years of initial faculty appointment to complete a basic science or clinical research project that is independent of previous mentors. The 2012 ASN Career Development Grant Program consisted of the ASN-supported and partnership grants listed in Table 1.

### ASN CAREER DEVELOPMENT GRANTS PROGRAM

Since the inception of the Career Development Grants Program, the ASN has invested more than $19 million and funded more than 119 investigators to conduct original, meritorious research. The society has successfully awarded significant research funding (approximately $185,000 per recipient after adjusting for concomitant funding) to individuals who are generally earlier in their academic research careers (Instructor or Assistant Professor) and have already published numerous manuscripts in peer-reviewed journals, received funding across public and private sectors, and been promoted in academic rank.

The ASN Career Development Grant recipients are making significant contributions to disseminating nephrology research. After receiving the ASN award, 85 recipients published a total of 1108 manuscripts (review, commentary, or original research) in peer-reviewed literature (Figure 1). In addition, the average number of manuscripts published per recipient per year ranged from a high of 7.64 (2011 grant recipients) to a low of 2.3 (2007 grant recipients).

During and after the ASN award period, recipients are strongly encouraged to gain support through public and private sources to continue research. As shown in Figure 2, 85 recipients have received 37 established investigator awards (such as R awards from the NIH and merit awards from the Department of Veterans Affairs [VA]), 16 career development awards (such as K awards and VA awards), and 25 other foundation awards (from public and private foundations) after receiving funding from the ASN. The number of established investigator awards ranged from a high of nine (2006 recipients) to a low of two (2012 recipients).
In addition to disseminating research findings and successfully gaining additional funding, recipients of the ASN Career Development Grants are receiving promotions within their institutions. In fact, 44% (37 of 85) of the ASN Career Development Grant recipients have been promoted in academic rank since the ASN award (Figure 3). Among the earliest applicants in this internal program evaluation, 82% of year 2006 recipients have been promoted in academic rank and are continuing their research trajectories in academic nephrology.

Through continued research support, the ASN Career Development Grant recipients have shown tremendous productivity in terms of disseminating research findings, securing extramural research funding, and advancing in their academic research careers. The ASN Career Development Grants Program, now housed in the ASN Foundation for Kidney Research, continues to support candidates who show the most promise in leading successful careers and producing innovative research to propel the nephrology field. The program has launched successful research careers and helped investigators produce key research in nephrology.

Figure 1. Recipient productivity: publication success rate since the ASN award. The total number of manuscripts by recipients since award date is shown by the gray bars. The black bars demonstrate the average number of publications by recipients/year.

Figure 2. Recipient productivity: total grants since the ASN award. The graph shows the number and types of awards earned by recipients.

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**TIME FOR ACTION AND TIME TO REVERSE THE TRENDS**

The ASN Grants Program represents only one aspect of a multipronged strategy. The ASN has also partnered with the FDA through the Kidney Health Initiative (KHI) to create a unique opportunity for multidisciplinary specialties to advance kidney treatment, address patient safety, and develop therapies in a collaborative environment with the FDA. During its first year, KHI recruited 62 members, selected a board of directors, initiated three pilot projects, and implemented a member-driven process to identify the next round of projects. By providing a forum for scientific collaboration and encouraging open dialogue among patient groups, health care professionals, industry, and government, KHI targets issues created by funding gaps, lack of end points, fewer clinical trials, and unclear regulatory pathways in the pre- and postmarket of drugs, devices, food safety, and biologics.

Additionally, the ASN is helping address workforce challenges through several initiatives. The ASN Program for Medical Students and Residents encourages careers in nephrology by exposing trainees to innovative research, breakthroughs in the field of nephrology, and interactions with mentors (particularly nephrology fellowship program directors) at the ASN Kidney Week. The society launched a summer research and mentorship program in 2013 titled Kidney TREKS (Tutored Research and Education for Kidney Scholars) to expose first-year medical students to nephrology research and careers. In 2013, the ASN also established Kidney MAPS (Mentoring and Assessment Program for Students) to involve trainees in kidney screening programs. The ASN’s portfolio of programs...
for medical students and residents strives to improve the situation of the nephrology workforce by inspiring, guiding, and mentoring trainees throughout the educational continuum and thereby, placing them on a trajectory for a career in nephrology and hopefully, kidney research.

Although all of the ASN’s initiatives are invaluable for supporting kidney disease investigators of all career levels, these efforts alone are not enough to overcome all of the daunting challenges confronting the nephrology research community, especially the growing funding gaps in kidney research. The ASN challenges the rest of the nephrology community to protect the nephrology workforce by supporting investigators and innovative research. During his ASN President’s Address at Kidney Week 2013, Bruce A. Molitoris, MD, FASN, announced that the ASN is calling on the US Congress and President to agree to appropriate $150 million a year for 10 years in new funding for kidney research above the current funding level. This $1.5 billion total over 10 years equals 2% of the estimated federal spending each year for treating kidney disease.19 This percentage is still below the percentage for other diseases, but it is a start.7,20

Medical research and innovation are a critical component of the United States’ economic competitiveness within the global economy, and they directly feed the vitality of the country’s health care system. A vigorous research enterprise will improve the lives of millions of people with kidney disease and accomplish the ultimate goal of curing kidney disease.

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DISCLOSURES

None.

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