Ensuring the Future of Clinical and Basic Stroke Research

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The stroke field has seen tremendous progress regarding both clinical and basic research advances over the past several decades. Preclinical stroke research has identified the major components of the ischemic cascade that contribute to the death of ischemic brain tissue and the important interactions between neuronal, glial, and endothelial cells not only as they relate to acute ischemic injury but also to brain recovery. Recently, the interactions between the nervous system and other systems such as the immune and cardiovascular systems have become increasingly recognized as contributors to stroke pathophysiology. Another important basic science advance was the demonstration that processes may be deleterious at one stage after ischemic injury but recovery promoting at another phase. Many important clinical research and patient care advances have also occurred and the ones that I consider most important are provided in Table 1. A detailed report by National Institute of Neurological Disorders and Stroke’s (NINDS) Stroke Progress Review Group was presented recently. In this report, recent advances in areas including imaging, genetics, acute treatment, prevention, epidemiology, clinical trials, and health service implementation were summarized and recommendations for future research suggested. Another NINDS endeavor, a recent stroke research priorities meeting, led to a report suggesting 9 high-priority research areas outlined in Table 2 that were crosscutting along the spectrum of basic, translational, and clinical stroke research. The field of stroke has been energized by the contributions of many talented, dedicated, and innovative clinicians and basic scientists. Despite all of the successes, much work needs to be done to reduce the increasing incidence of stroke occurring in many countries, develop therapies to successfully treat ischemic and hemorrhagic stroke, and to enhance and amplify the endogenous recovery processes that occur after stroke. To meet these challenges, we will need to train and nurture the careers of a new generation of clinical and basic science researchers who will provide the talent and hard work needed to meet the many research challenges and opportunities facing the field of stroke. The increasingly difficult funding environment in the United States will make the training and nurturing of the next generation of stroke researchers difficult, and planning is needed now to ensure that inadequate funding will not derail future progress in the stroke field.

Clinical Manpower Needs

In 2012, it was determined that there was only 1115 board-certified vascular neurologists in the United States or ≈1 per 265,000 people. This does not compare favorably to other countries, because the ratio is ≈1 per 160,000 in Germany, 1 per 137,000 in Denmark, and 1 per 177,000 in Australia (personal communications from Drs Grete Andersen, Geoffrey Donnan, and Wolf Schaebetz). Only 77 vascular neurology fellowships were available in 2012, and all of them focused primarily on clinical training. In the recent past, a substantial percentage of this modest number of vascular neurology fellows then went on to train as interventionalists who after completing this additional training practice primarily as physicians who perform interventional procedures and do not frequently participate in the daily routine care of patients with stroke in most institutions. Trainees are in part attracted to become interventionalists because of the substantial salary differential between physicians who practice primarily as clinicians as compared with those who primarily perform procedures. With an annual incidence of new and recurrent strokes per year of ≈800,000 per year in the United States, the currently available supply of board-certified vascular neurologists equates to ≈720 strokes per year for each of these board-certified vascular neurologists. Although it must be acknowledged that there are some noncertified vascular neurologists and some general neurologists who have appropriate training in the management of patients with stroke to perform adequately in the day-to-day management of most patients with stroke. Many of the board-certified vascular neurologists practice at large, tertiary academic centers/hospitals. It is unclear how many are actively engaged in research, but it is highly likely that those who are engaged in research are primarily doing clinically related research of some type. The incidence of stroke in the United States is projected to increase over the next 15 years to ≈100,000 new or recurrent cases per year and the prevalence to approach 4 million. With this increased prevalence of stroke, direct medical costs are projected to more than double during that time period. Clearly, efforts will be needed to substantially increase the number of vascular neurologists to adequately care for the growing number of stroke cases and to perform research to move the field forward. In most centers, vascular neurologists are the leaders and predominant physician members of stroke teams primarily caring for patients with stroke at their institutions. It must be acknowledged that stroke teams include other physician specialties such as neurosurgeons, vascular surgeons, physiatrists, physical, occupational, and speech therapists, and most
The shortage of vascular neurologists will thus be partially compensated for by telemedicine consultations who will allow stroke specialists at large, tertiary centers to view patients at smaller remote sites and to provide input about diagnostic and therapeutic decisions.

Research Manpower Needs
Recognizing the need for more vascular neurologists to care for the growing clinical burden of stroke in the United States is a natural segue to the need for more stroke researchers. Some of those physicians who receive fellowship training in vascular neurology will be attracted to the possibility of doing research in this field as they realize the need to build on the previously mentioned advances that have improved care and the understanding of disease mechanisms. Those physicians who are attracted to an academic career in the field of stroke will need to undergo additional training beyond the 1-year vascular neurology fellowship that is primarily geared toward clinical training. Currently in the United States, the opportunities for such additional training in the various disciplines needed to perform high-quality, clinically oriented stroke research are limited. The training programs for clinical stroke research are limited by the availability of appropriate environments to perform such training and perhaps most importantly by financial constraints. The funding of additional training of vascular neurology fellows beyond the 1-year clinical fellowship is not supported by hospital funding or, to a large extent, by clinical activities. Such additional training will require specifically targeted funds for second- and third-year fellows who spend the great majority of their time receiving appropriate research training and performing research projects. The new NINDS initiative for a stroke clinical trials network does contain a modest educational component, but it is not sufficient to fund a fellow’s salary and will also need to be used for additional educational activities such as conferences and the training of center personnel. Additional funding sources will be needed to train promising vascular neurology fellows who wish to receive additional training beyond the 1-year clinical fellowship. The training of basic science-oriented individuals is also problematic. Some are currently funded as a component of grants received by their mentors, but as research grants are becoming increasingly more difficult to obtain, fewer such positions will be available. It must also be acknowledged that with the relative paucity of more senior basic stroke researchers currently active in the United States, the pool of PhD and postdoctoral positions currently available to those interested in basic stroke research is rather limited.

Funding Early Career Development
Another concern related to the development of new clinical and basic stroke researchers is their early career development after completing their training, be it a research stroke fellowship, PhD, or a postdoctoral training program. The number of active basic and translational stroke researchers in the United States is indeterminate, but it is likely that those who predominantly do stroke-related research probably number no more than a few hundreds. The opportunities for funding new basic science stroke researchers who have completed training do exist but are also limited. NINDS has early career development awards such as the K award, and the American Heart Association (AHA) also has such awards available. However, in both organizations, those interested in stroke research are competing against a much wider pool of applicants for relatively scarce resources. Some institutions do provide startup funds for junior faculty, but they are time-limited and presuppose that these funds will serve as a stepping stone toward external funding. Additional funding opportunities are needed for junior faculty who are interested in developing successful basic and clinical careers as stroke researchers.

A Proposal to Enhance the Future Supply of Vascular Specialists
How can we begin to expand the pool of well-trained clinical and basic science stroke researchers who will become the

Table 1. Select Important Clinical Research Advances During the Past 2 Decades

| Proving that stroke care units improve outcome |
| Developing advanced imaging techniques to enable tracking of stroke evolution |
| Developing acute stroke therapies: intravenous tissue-type plasminogen activator and probably soon endovascular approaches |
| Proving that prevention strategies reduce risk: antiplatelet therapy, oral anticoagulants, statins, reducing blood pressure |
| Suggestions that recovery can be enhanced: restraint therapy, drugs/stem cells (?) |

Table 2. Key Recommendations From the National Institute of Neurological Disorders and Stroke Planning Committee Report

| Accelerate the translation of preclinical stroke research into clinical studies of prevention, acute treatment, and recovery |
| Prevention of vascular cognitive impairment |
| Develop imaging biomarkers for stroke prevention |
| Expedite comparative effectiveness research |
| Expand and integrate existing stroke trials networks to accelerate translation |
| Preclinical and clinical studies to improve early reperfusion and to develop later effective/safe reperfusion |
| Preclinical and clinical studies to achieve robust brain protection with neuroprotective agents |
| Use brain–computer interfaces to potentially enhance stroke recovery |
| Develop programs of translational research that target early recovery after stroke |
next generation of physicians and scientists to lead the field of stroke? A novel mechanism would be for AHA/American Stroke Association (ASA) to assume a position of leadership by creating a new funding platform of stroke research fellowships. These AHA/ASA fellowships would fund vascular neurology fellows who have completed a 1-year vascular neurology fellowship who want to receive 1 to 2 years of additional training focused on learning how to do clinical stroke research. Basic science research fellowships would also be offered to MDs or PhDs at the postdoctoral level who wish to receive additional training in preclinical stroke research. For both the clinical and basic stroke research fellowships, a key component will be the primary mentor and other stroke faculty members and the research environment/resources where the training will be received. The awarding of the research fellowships should be by a competitive process of fellowship proposal submitted by a qualified institution/mentor with a specific candidate, which will then be reviewed and ranked by a review committee. Factors that should be considered in evaluating the strength of the submissions would include the background of the candidate, the qualifications of the mentor, the overall institutional environment available to support research training, and the research project the applicant proposes to conduct or join. The highest scoring applications will receive funding, and the total number of successful applications will be determined by the amount of funding available in this program.

The establishment of the AHA/ASA stroke research program will require the generation of substantial new amount of money that is specifically targeted for support of these fellowships. My suggested initial funding target is $10,000,000 so that a reasonable number of fellowship positions, 12 to 15 per year, can be funded each year without reducing the principal of the fund. This target may seem to be daunting, but can be achieved by AHA/ASA with the help of the stroke community by reaching out to wealthy individuals and families who have been affected by stroke, foundations that support research training, and industry. We need to think big and consider a broad range of funding sources because if only a few research fellowship positions can be funded, the impact on the field will be negligible. Another attractive approach to enhancing the impact of this new stroke research training program would be to partner with NINDS to jointly fund research training positions at the 25 stroke network centers. Such synergy would be able to have a greater impact than each of the 2 funding institutions working independently. The impact of such a large, jointly funded training program initiative could make a dramatic difference regarding the number of well-trained and highly motivated individuals who will move the field of stroke forward by becoming the core constituents of the stroke research community. A second stage for AHA/ASA support of stroke research training if fundraising for the fellowships is successful would be to raise additional funds to support the initial research projects of junior faculty as they transition from training positions to their first faculty positions. These early career development grants would be competitive and applicants not limited to individuals who have completed AHA/ASA research training fellowships.

If both the fellowship and early career development programs can be funded and then initiated, the future of stroke research in the United States will indeed be brighter. Everyone in the field of stroke should be encouraged by the great strides that have been made, but much more needs to be done to maximize stroke prevention, the care of stroke patients, and to continue to unravel the pathophysiology of brain injury in ischemic and hemorrhagic stroke. The only way to continue progress is more research across a broad spectrum of disciplines that will need to be conducted by bright, well-trained, talented, and motivated individuals. It is the responsibility of those currently in the field of stroke to ensure that more opportunities become available for the next generation of stroke researchers to receive appropriate training and then funding as they begin their careers. The hardest part in moving this vision forward of the development and nurturing of many more stroke researchers will be the generation of adequate funding to support the effort. If we work together and approach the endeavor to raise the necessary funds with vigor and innovative thinking, it can be done. We owe it to our patients and to the next generation of stroke researchers who will be the beneficiaries of the new AHA/ASA stroke research fellowships and early career development awards. I encourage all to join me and the AHA/ASA in the effort to make this a reality. I cannot think of a more important legacy to leave our future colleagues and to future stroke patients.

Acknowledgments
I dedicate this special report to the memory of Dr David Sherman, a visionary in the field of stroke, who would have shared and supported the concepts I have proposed to ensure the future of stroke research by developing and nurturing the next generation.

Disclosures
Dr Fisher receives compensation from the American Heart Association for duties as the Editor-in-Chief of Stroke.

References


**Key Words:** research ■ stroke
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Stroke. 2014;45:2493-2496; originally published online July 8, 2014;
doi: 10.1161/STROKEAHA.114.005379
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/45/8/2493

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