Impact Through Discovery: A Global Challenge
Presidential Address at the American Heart Association 2011 Scientific Sessions

Gordon F. Tomaselli

“He who has health has hope; and he who has hope has everything.”

—Arabic proverb

Good afternoon; on behalf of the American Heart Association and American Stroke Association, welcome, colleagues and friends from around the globe, to Scientific Sessions 2011. Whether you are in clinical care, research, or education, I thank you for joining us. It is truly an honor to be in the company of those engaged in the noblest of endeavors, the improvement of human health. I would like to take a moment to personally thank those of you joining us from around the world. Approximately 100 nations are represented at Sessions this year. That is only fitting because global prevention of cardiovascular disease and stroke is a major focus of our meeting. To succeed in global prevention, we must all be part of a united front.

I am going to discuss how our research world reaches far beyond the laboratory and the clinical setting. We will explore the crucial differences it makes in human health, in addition to how vital biomedical research is to economies and societies around the world. And we will discover some of the perils we will face globally if we do not find ways to fund more research.

The community of cardiovascular practitioners and researchers has much to be proud of. The trends in mortality from cardiovascular disease and stroke having increased over the first half of the past century have significantly declined since the 1960s. Much of the decline is in the reduction in mortality from coronary heart disease. The decline is attributed to dramatic advances in the acute and chronic treatment of atherosclerotic coronary artery disease. The recognition of the importance of control of risk factors such as tobacco use, blood pressure, cholesterol and glucose control, diet, and exercise have resulted in improvements in both primary and secondary prevention of coronary artery disease. Despite these advances, heart disease and stroke remain the number one and number four killers of Americans and the leading discharge diagnosis from hospitals in the United States.

Moreover, awareness and management of risk factors are low, particularly in the young and minorities who are disproportionately affected by adverse health factors, have less access to care, and are less aware and thus less likely to be treated. We have an obligation to our patients, our countries, and to ourselves to discover new ways to promote and improve health, reduce health care costs, and fight the leading cause of death in the world, cardiovascular diseases. The discoveries we need for this fight are most likely to come from a broad range of scientific research.

Some nations recognize the importance of this more than others. In this country, I am very concerned about the decrease in research support in general—and the declining share of publically funded research across science disciplines. This is extremely troubling for future innovation. If the history of science and medicine has taught us anything, it is the difficulty of predicting the next breakthrough or paradigm-shifting discovery.

The contemporary era of investment in biomedical research has produced a number of breakthroughs that have fundamentally changed the way we treat patients with cardiovascular disease and stroke. Many of these breakthroughs were made possible by complementary public and private funding. What is notable about many of these research milestones such as cardiac transplantation, anticoagulant and antithrombotic therapy, cardiopulmonary bypass, and the links between dietary fat, cholesterol, and atherosclerosis (Table) is that nearly all are derived from a basic science finding that was translated to the bedside.

My home institution’s history features a significant number of important advances. Many Johns Hopkins investigators were funded by the American Heart Association and the federal government, including Peter Agre, the discoverer of...
cardiac arrest (SCA), research from around the world, includ-
ing work from our own laboratory, has provided insights into
the fundamental nature of excitability of the heart. It also
provided the foundation for another important step, the
pharmacological treatment of cardiac arrhythmias, which are
the primary cause of sudden cardiac death in most cases.
Detailed clinical investigation over decades highlighted not
only the important benefits but also the limitations of drug
therapy for the prevention and treatment of sudden cardiac
death.

The confluence of research in physiology and the genetic
revolution have contributed enormously to our understanding
of the molecular basis of inherited and acquired cardiac
arrhythmias. An intriguing example comes from our own
laboratory. We were evaluating a patient with syncope whose
abnormal electrocardiogram (ECG) suggested he was at risk
for a serious heart rhythm problem. We diagnosed Brugada
syndrome with a type 1 ECG and a mutation in the cardiac
sodium channel gene, SCN5A. The mutation caught our
attention because it was in a region of the channel that is
involved in regulating channel function in response to stress-
sors. Some of these stressors may be triggers for lethal
arrhythmias. We created DNA vectors containing SCN5A
carrying the disease-causing mutation. We expressed and
isolated the mutated channel peptide. Unlike the wild-type
peptide, the mutated channel peptide could no longer be
modified by protein kinase A, one of the main enzymes that
is activated by the sympathetic nervous system. We then
expressed the channels in tissue culture cells and recorded
currents using patch clamping. We found that under basal
conditions, the mutant currents were the same as currents
through wild-type channels. But with stress, wild-type chan-
nels exhibit a robust increase in the current that may be
protective against arrhythmias and is not present in the
mutant channel. This is consistent with the clinical situation
in this patient, and in others with this syndrome. Arrhythmias
are typically triggered in patients with Brugada syndrome
when there is stress of various kinds, prominently fever.

It is now possible to take fibroblasts from such patients and
reprogram them to become heart cells. These are called
induced pluripotent stem cells. Reprogramming is a very
powerful technique that allows us to study the effects of a
human mutation in its native context. Induced pluripotent
stem cells are a platform for drug testing in a human cellular
model and may, in the future, be a method applied to
regenerative medicine. This is just one example of the
enormous potential of research that ranges from the clinic to
the bench and back.

But why is it that this young man had syncope and an
abnormal ECG while his sister and mother who carried
the same mutation were completely without symptoms or the
ECG signature of the syndrome? This question reinforces the
concept that even the most straightforward disease mecha-
nism is an incredibly complex systems biology problem. The
reasons are the enormous dynamic range of the expressed
genome and the incredible connectivity of apparently diver-
gent pathways in the human body. Appropriately, a major
effort in the postgenome era is applying systems biology
methods to understanding the clinical implications of rare and
common variations in the human genome.
and since then it has actually been shrinking (Figure). In the National Institutes of Health (NIH) budget-doubling period, this spending was only 0.23% of the gross domestic product. Importantly, in recent years, biomedical research sector, serving as an example to other developed nations. However, in the United States, research spending has not kept pace. Importantly, in recent years, research spending by the U.S. government has decreased. The correlation between those death rates and federally funded research is profound. Manton estimated the economic impact of NIH funding on tax revenues by considering mortality reduction and the decline in disability rates resulting in a larger number of taxpayers. The total gain in tax revenue alone is estimated to be $885 billion over 10 years. These savings alone would nearly be enough to triple the NIH budget over the same 10 years. Estimating the additional economic value of healthier workers to the gross domestic product is difficult, and then there is still the direct economic benefit of the research work itself and Medicare savings. Adding it all together, an economic benefit of more than $1 trillion to the U.S. economy seems conservative.

The economic benefit of funding of research is clear and far reaching. Direct NIH funding produced approximately a half a million U.S. jobs in 2010. Sixteen states added more than 10,000 jobs. That means jobs and revenue to workers and their families, more tax revenue, and less cost to states to support the unemployed. This analysis does not even consider the economic impact. Manton estimated the economic impact of NIH funding to tax revenues. He did this by considering the research-associated decline in mortality and disability rates resulting in a larger number of taxpayers. The total gain in tax revenue alone is estimated to be $885 billion over 10 years. These savings alone would nearly be enough to triple the NIH budget over the same 10 years. Estimating the additional economic value of healthier workers to the gross domestic product is difficult, and then there is still the direct economic benefit of the research work itself and Medicare savings. Adding it all together, an economic benefit of more than $1 trillion to the U.S. economy seems conservative.

The economic benefit of funding of research is clear and far reaching. Direct NIH funding produced approximately a half a million U.S. jobs in 2010. Sixteen states added more than 10,000 jobs. That means jobs and revenue to workers and their families, more tax revenue, and less cost to states to support the unemployed. This analysis does not even consider the economic impact of the research work itself. A recent report by United for Medical Research considered the relative benefits of investment in research in the context of the current fiscal deficit. The deficit feedback effect of government spending describes the potentially deleterious effect of growing the deficit on private sector investment. However, there is good evidence that investment in basic research by the NIH, rather than shrinking private investment, serves as a catalyst for such investment by contributing to the intellectual and physical infrastructure that supports innovation. The spending on research is an investment, and not simple spending without return. This fact was recognized by a study of the bipartisan congressional Joint Economy Committee, which concluded in a report published in 2000, that federal and private investments in biomedical research are
complementary. An independent analysis by the National Bureau of Economic Research in 2009 concluded the each dollar of NIH research support led to a 32-cent increase in privately funded medical research emphasizing the same point.

The long-term benefit of federal research funding is clearly seen in the NIH’s impact on the medical and biotech sectors of the economy. Nearly a million U.S. citizens work in this wide-ranging sector, producing $84 billion in wages in 2008. In 2010, this sector exported $90 billion worth of various goods and services, including pharmaceuticals, medical equipment, and supplies. Investment in research leads to additional basic and important societal benefits, but these can be easy to overlook. This investment supports education and training—vital components in any society’s ability to thrive. Government investment enables new technologies and new economic sectors. The Internet, genetic engineering, and biotechnology are just a few examples.

There is room for debate about the magnitude of the economic benefit of investment in biomedical research, but in the final analysis investment in research not only is good for human health but also is a boon for national economies. A failure to invest, however, will have unfortunate consequences and economic benefits can easily disappear. Education would suffer because research supports and enhances technologies used directly in education and training. Research underwrites some of the cost of running universities and creates a highly trained and affordable workforce. From a science standpoint, large gaps in the knowledge base will remain and probably will grow. When funding becomes difficult, risk-taking in research and translation is stymied. And this slows the development of new diagnostics, treatments, and cures. A lack of funding means a loss of young investigators to other careers. Important opportunities are lost.

How can we, as clinicians, researchers, and educators, ensure this investment happens? We need to make ourselves more available as role models in science and medicine. This will enable us to find and develop the next generation of leaders in science and medicine. We must provide the motivational message that I think is at the core for most of us: science and medicine are remarkably fulfilling careers, and they enable us to positively impact humanity.

The American Heart Association clearly understands the importance of investing in research, and in fact has been the largest funder of research in cardiovascular diseases and stroke outside the federal government. We have a very rich history in this area, having funded 12 Nobel Prize winners. At the American Heart Association, we continually work to grow the research portfolio and increase financial support for investigators and supported more than $3.3 billion in cardiovascular and stroke research. Although the specific programs have changed since the first research committee was convened and led by Dr Louis Katz in 1949, the fundamental tenets remain consistent, to support the individual investigator, to recognize the importance of a wide spectrum of scientific disciplines, to promote collaboration, and to invest in young scientists. Indeed, within 15 years of the beginning of the American Heart Association research program, there was at least one funded American Heart Association investigator in every medical school in the United States and many outside the United States.

We must maximize our communication sources, including meetings such as Scientific Sessions, scientific journals, the Emerging Science Series, and social networking. The American Heart Association also has a role in accelerating translation of discoveries into clinical solutions. This can help us convince the public and policymakers about the importance of fundamental science. Our new Science Accelerator program can bring science and business together in an effort to more quickly turn research findings into clinical solutions. It will be collaborative, not competitive, with other programs such as the NIH National Center for Advancing Translational Sciences and other translational research programs at universities and in private sectors around the globe.

Perhaps most importantly, as a community we must become more vocal. We need to overcome our reticence to talk about the importance of our work. We tend to be analytic and reserved, but we must remember our larger obligation. We have to change the tenor of the conversation. We must make our elected officials understand that this investment builds healthy lives and healthy economies. We must all advocate for research support.

I believe science and professional organizations need to redouble our efforts to advocate for more government funding. I urge everyone here to get involved. Become a member of the American Heart Association and the American Heart Association’s “You’re the Cure” network. Or join another specialty science, medical, or professional society around the world. No matter where you are from, make sure your government knows how important this is. Get out there and be heard.

Moreover, both individuals and organizations have to think and work outside the traditional advocacy lines. A few years ago, Alan Leshner, chief executive officer of American Association for the Advancement of Science, proposed what he called a “glocal” science advocacy approach to complement and enhance traditional methods. Perhaps most importantly, as a community we must be heard.

I think the sentiment is correct, although there are many glocal approaches. In essence, the approach is to take a global issue and make it meaningful to a community or society at a local level. Operationally, scientists, physicians, and advocates recruit nonscience and medicine community members to promote and lobby elected representatives and other decision-makers, such as city councils, school boards, and other community groups. The approach is grass-roots advocacy and complements less frequent but regularly more massive advocacy efforts inside the Washington beltway. This will require a major engagement of the science and medicine communities in advocacy, education, and communication outside of the university, hospital, and laboratory. Indeed, all physicians and scientists need to recognize that advocating and educating the public about the work that they do is part of the job. This needs to be recognized and supported by leaders of schools, institutes, departments, and divisions, as well as peers.

Despite the enormity of this challenge, I have faith in the community where I have made my professional life and I
remain optimistic. I come by that optimism and that faith in medicine honestly. You see, I am a physician and a researcher, but I also have benefitted personally from scientific discovery. Nearly 30 years ago, my mother, at age 49, needed a new heart. She was suffering from dilated cardiomyopathy complicated by sudden cardiac arrest. She waited 19 days, and it was a very tense time for our family; fortunately, she finally got a new heart. I remember her miraculous transformation; one day she was breathless from the simplest tasks like bathing, and a few days later she was riding an exercise bike. From there, Patricia Tomaselli went on to live a rich full life. She watched her children get married; she welcomed her grandchildren into the world. She saw those grandchildren graduate and even saw some get married. The extension of my mother’s life was to my family a true miracle. And it was possible because of science, discovery, and translation into practice. So you can see why I remain optimistic about the future of cardiovascular research despite the obstacles we face. I have personally experienced how research can save and improve lives.

References

Impact Through Discovery: A Global Challenge: Presidential Address at the American Heart Association 2011 Scientific Sessions
Gordon F. Tomaselli

Circ Res. 2012;110:12-16
doi: 10.1161/RES.0b013e3182455714

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/110/1/12

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/