

2006 Association of American Physicians Presidential Address

The US's changing competitiveness in the biomedical sciences

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ellow AAP members, friends, and guests, it's been a true pleasure serving the Association for the past 11 years, first as a Council member, then as an Officer, and this year as President. The entire 11 years has been a real honor and privilege, and also a thoroughly enjoyable experience. I'm glad to report that the organization is strong, financially stable, and moving forward, and I think this year's meeting has been an excellent one, at least to this point. And this of course, brings me to the annual ritual of the Presidential Address.

In approaching the Presidential address and selecting potential topics to cover, it has become a virtual catechism for past Presidents to review a large number of previous Presidential Addresses. These are all published in the Transactions of the AAP up to 1993, and since then, in the JCI. Being a traditionalist, I have followed this well worn and highly rewarding path, and what began as a task quickly turned into a labor of love. Reading these previous addresses was stimulating and illuminating, and I highly recommend this exercise to anyone interested in trends in academic medicine, the evolving history of the physician/scientist, and the demographics of scientific meetings. I guarantee that anyone who starts this process will be entertained and enlightened by numerous great ideas, humor, prescient hypotheses, words of wisdom, and analyses of a number of recurrent themes.

Figure 1 lists the topics which have been most frequently, and appropriately, touched upon over the last several years: 1) the history of the AAP, its mission, goals, current status and what the future holds;

MAJOR THEMES OF PAST ADDRESSES

- 1. HISTORY OF THE AAP
- 2. THE CLINICAL INVESTIGATOR
- 3. THE PHYSICIAN/SCIENTIST
- 4. THE ANNUAL MEETING
- 5. MEETING ATTENDANCE
- 6. ROLE MODELS AND MENTORING

Figure 1

2) next we have the clinical investigator – how difficult it is to become one, the paucity thereof, the importance thereof, and how to produce more thereof; 3) closely related is the theme of the physician/scientist, again, the importance thereof, the paucity thereof, and how to produce more and make them successful; 4) this meeting and all its incarnations and permutations since the last Atlantic City meeting of the Tri Societies in 1976; 5) Meeting attendance, which declined for many years, but has now stabilized and increased in the past 5 years; and 6) the importance of role models and academic heroes and mentoring of physician scientists.

Of course, a number of other topics have been addressed, but these are the general subjects with the most frequent refrains, and it is of great interest to trace the ideas of these themes and how they have evolved, retreated, and progressed throughout these meetings and throughout these past Presidential Addresses.

Since all of these themes have been covered so well, and rather recently, I have elected not to revisit them this year, but instead will talk about a subject which has become increasingly popularized over the past one or two years, and which has become a side hobby of mine. This involves the declining role of the US as the world's leader in science and technologic innova-

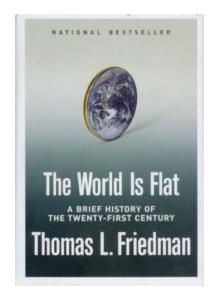


Figure 2

tion. This subject has recently had high visibility with respect to the physical and informational sciences, but I would like to focus most of my attention on the biomedical sciences.

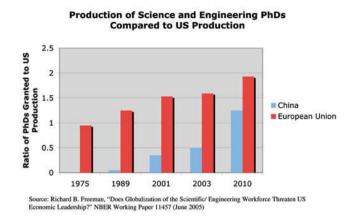
The idea that the US has lost, or is losing, its technical edge to the rest of the world in the fields of engineering, the physical sciences, computer sciences and information technology is currently a topical subject in economic, technical,

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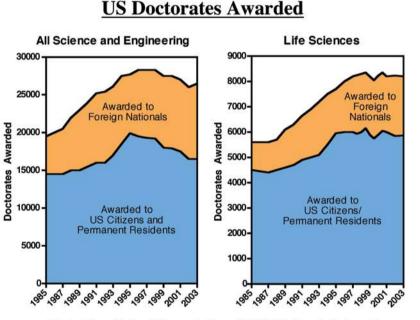
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Adapted from National Research Council. 2005. Bridges to Independence. Fig TS-1c National Academy Press: Washington, D.C.

Figure 4

PUBLICATIONS AND CITATIONS FROM THE US AND EU IN 2002

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	United States	European Union
Publications	1,265,608	1,347,985
Citations	10,850,549	8,628,152

Source: G. Dosi, P. Llerena, and M.S. Labini. 2005.

Figure 5

and political circuits. There are several recent popular books on this subject, including the recently published book "The World is Flat" by New York Times columnist Thomas Friedman (Figure 2). Although a significant component of this book relates to economic and business interests, exploring how manufacturing, labor forces, and supply networks are evolving in other parts of the world while flattening or receding in the US, much of the book, and many other articles and reports, are devoted to science and technology. Some of the basic themes surrounding this issue are that our education system is producing fewer and fewer engineers, computer scientists and life scientists who are US citizens, at the same time that other countries have geared up their educational institutions to produce more. Coupled with this, as the world has become more globalized, and the Internet more pervasive throughout business and scientific affairs, more and more of the work and innovation in high-technology areas is being conducted in other countries. This involves outsourcing, offshoring and other descriptors of the basic fact that the essential work in these areas, and the innovations in these areas, are increasingly coming from the non-US part of the world.

The recent spate of books, articles and National Academy of Sciences reports on this subject, focus largely on the disciplines of engineering, computer sciences, physics, mathematics and information technology centered fields, and for purposes of today's discussion, I will refer to all these fields in aggregate as the Physical Sciences.

China, India, and Eastern Europe are the main emerging forces behind these trends, and this is supported by some rather astounding facts. As just a couple of many examples, the proportion of American students who receive undergraduate degrees in science has fallen to 20th in the world. Science and Engineering degrees represent 60% of all BS degrees in China, 43% in North Korea, 41% in Taiwan, and only 31% in the US. In Engineering, it's 5% in the US, compared to 25% in Russia, and 46% in China. In computer sciences, mathematics, and other related fields, we are similarly outpaced. The US is not being overwhelmed simply in terms of sheer numbers, but a strong argument is made that these other countries are also gaining on us in terms of measures of quality such as innovation, creativity, numbers of patents, etc.

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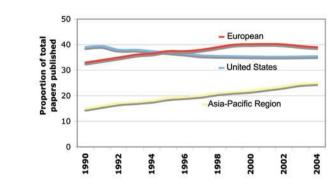
In Figure 3, the total US doctorate production is normalized to 1, and you can see that in 1989 the EU exceeded America in the production of science and engineering doctorates, and continues to gain, and by 2010, China will also produce more doctorates than the US. In aggregate, the US share of the world's science doctorates will be 15% in 2010, down from 58% in 1970. This is a 75% decline, and buried in these numbers is the fact that, ~1/3 of US doctorates are conferred to non-US citizens.

This trend also holds for the life sciences, which follows a very similar pattern as total science and engineering degrees (Figure 4). Production of new doctorates who are US citizens or permanent residents, has been flat since the mid nineties, and any small increase in total US life science doctorates has been in the non citizen category. Due to this stagnation in new US graduates, the overall science labor force in the US is aging. The only reason that the number of US workers in the Science and Engineering fields has increased is because of the influx of foreign-born scientists. For example, between 1990 and 2000, the proportion of foreign-born PhDs in the labor force, rose from 24-38% and the numbers are approaching 50% today. As just one example, at Johns Hopkins University, 60% of all graduate students in all the sciences are foreign students, according to Bill Brody, the President of the University.

I would like to emphasize that this is not just a matter of numbers, since many assessments of quality show the same trends. This is evidenced by the dramatic fall in the US share of publications in first line physics, engineering, and information technology journals, the fall in the US share of patents in these areas, and the increasing proportion of high-level innovation and creativity that originates outside the US. This has been going on for a decade or more.

As an example, for many years the US has dominated the entire world in terms of scientific output in all fields, and the output of the US was greater than the rest of the world combined. This has changed. Now the output of the US is still greater than any other single country, but much less than the entire world. There are many published graphs and statistics to document this, but I'll just use 2 simple figures to make the point. In Figure 5, we see that by 2002 the EU exceeded the US in terms of total papers and is catching up in terms of citations, and this doesn't include Japan, Canada,

Publication of Scientific Papers



Source: Thomson National Science Indicators. Nature 430:311-316, 2003.

Figure 6

Australia, India or China. Looking at trend lines, the world's scientific publications have increased by 40% since 1992, while the scientific papers written by Americans has fallen by 10%. This is depicted in Figure 6, which, in addition to the US and the EU, also includes the Asia-Pacific region. If this trend continues, demographers forecast that Asia-Pacific publications will exceed the US in 6-8 years.

Highly respected, adequately compensated jobs are becoming more available in these other countries, and workers trained within these countries, as well as those trained overseas, are increasingly finding rewarding in-country science careers centered in their own cultural and societal norms. In this sense, the rich tradition of America as an immigrant nation for scientists is experiencing a changing demographic, in which US academic institutions increasingly serve as short-term training sites, after which skilled high-tech scientists return to their native countries. In addition, internally we train fewer and fewer scientists with US citizenship, and, as shown in the earlier Figure, these trends are in sharp contrast to the greatly expanded production of these workers in other countries.

No matter where engineers and scientists are trained, the country they choose to work in is where they will have their impact, and there are several evolving issues related to the migration or location of this kind of intellectual capital. An equation was proposed some years ago to analyze the distribution of scientific productivity, called "Lotka's Law". The details aren't important, but the general concept makes practical sense. The equation would predict that for every 100 scientists, 75 will have a degree of productiv-

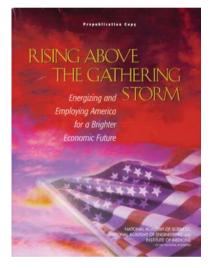


Figure 7

ity and creativity equaled to one unit. 24 will have 3 units of productivity and 1 will have 10 units. In other words, it's a pyramid, and most of the creativity, publications, productivity and patents come from the top tier. This is important because in past years, it was this top tier of engineers and scientists who often immigrated from India, China, and other countries to the US. This dynamic, while it still exists, is now changing. Increasingly, there is repatriation of top scientists back to their home countries and more and more are trained in country and don't leave, except for brief periods of overseas training. In the physical sciences, this is exemplified by the many high-tech global corporations that have established major R&D centers in India and China.

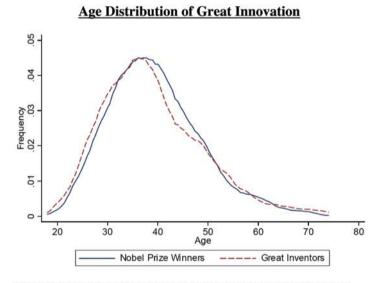
As this directional shift in the brain drain continues, it is likely that shortages



PERCENT NON-US PUBLICATIONS

	<u>1981</u>	<u>1991</u>	<u>2005</u>
NEJM	16%	30%	47%
JCI	10%	28%	47%
JBC	14%	34%	54%
Science	11%	16%	48%

Figure 8



Source: Benjamin Jones. 2005. Age and Great Innovation (Working Paper 11359). Cambridge MA: National Bureau of Economic Research.

Figure 9

in scientific personnel in the US and other developed countries will increase. In order for the US to meet its projected goals of new researchers in the work force, we will have to increasingly draw on foreign-born researchers, at a time when greater incentives are being put in place to keep the best of these scientists in their own countries. In the physical sciences, this is exemplified by the many high-tech global corporations that have established major R&D centers in India and China.

This subject has become reasonably topical, drawing the attention of many journalists, popular writers, and academics. It was a central subject of a recent National Academy of Sciences report "Rising Above the Gathering Storm" (Figure 7), which is filled with graphs, tables, recommendations and other factual information on the subject. Recently, this subject has also gotten some political traction in both Houses of the Congress and even received special mention at President Bush's last State of the Union Address, in which a promise was made to increase funding for education and research support in mathematics and the physical sciences. Hopefully, this high level of attention will actually lead to some action.

All of this has been widely talked about in the past couple of years and many of these major themes are probably familiar to most of you. However, what I would like to do is to extend this conversation to the idea that in the broad field of science, these trends and dynamics are not isolated to the Physical Sciences, but are happening in the biological and clinical sciences as well.

Like most of you, I frequently visit different medical schools and research institutions, and over the past few years, when I meet with the people working in the laboratories, I've been increasingly struck with the fact that a larger and larger proportion of them are not US citizens. In fact, current data show that ~60% of all postdoctoral fellows in the US are non-US citizens. In another capacity, I am one of the Editors of a broad-based scientific journal, the Journal of Biological Chemistry, and over the past several years, I've had the impression that most of the submitted papers do not come from the United States. To do an "evidence-based medicine" test on some of these impressions, I decided to collect some facts.

Figure 8 shows data I collected related to four of the major US-based journals in the biomedical sciences, the NEJM, the JCI, the JBC, and Science, and the data are remarkably consistent across these 4 journals. If we look at the year 1981, we can see that for all these journals, the US dominance in publications is pretty obvious, with 84-90% of all papers originating from US labs. If one looks at 1991 and then 2005, the trend is clear, with the US publication rate clearly losing its edge, so that now it's about a 50:50 split between US and non-US papers. These trends are mostly reflective of an increased proportion of papers coming from non-US labs, rather than a major decrease in the absolute numbers of US papers.

In this analysis, I assigned papers to countries based on the communicating authors. In other words, it's based on the laboratory of origin of the work, and not based on the nationality of all the authors. Obviously, almost all the papers have multiple authors, and for the US-based papers, the great majority of them contain co-authors from other countries, most of whom are probably foreign-born trainees working in the US. For the papers originating outside the US, it is less common to find co-authors who are not from that country.

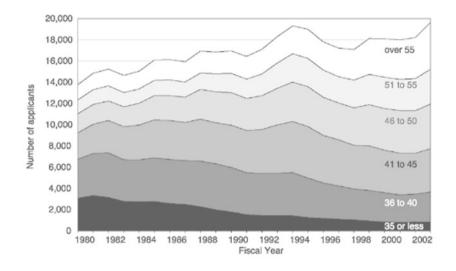
With respect to the nationality of scientists working in US biomedical laboratories, my numbers are less statistically sound and somewhat anecdotal. What I did was poll 25 colleagues and friends who supervise laboratories with 10 or more people. These unaudited, self-reported numbers indicate that in these 25 labora-

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tories, 68% of all laboratory scientists were non-US nationals. This compares well to the national average which is ~60%.

I have spoken with a number of scientists and research administrators in other countries about these issues. One common theme I hear is that in past years a frequent part of any successful biomedical career involved a period of training in the US. This rule no longer holds. More and more, graduate students, postdoctoral fellows, and early career physician-scientists are either training within their home countries, or seek additional training in Europe, Japan, Australia, or other non-US ports of call. Students are still leaving countries such as China and India, but there is now significant international competition for the best students. These countries are also creating the necessary infrastructure to develop attractive jobs so that students leave for a brief period of training and then return to the home country for their careers. This does not mean that the absolute number of trainees coming to the US is less. Quite the opposite, these numbers continue to rise, as evidenced by the observation that an increasing number of graduate students in the US are foreign-born and that so many of our major research laboratories are populated by postdoctoral fellows and other scientists from other countries. The fact is that the number of trainees seeking careers in biomedical sciences from developing countries has increased, so that while the US share may not declining in absolute numbers, a greater proportion of these trainees are being accommodated elsewhere. These trends are well established, and the numbers are so large that it is hard to see how substantial changes can be made at the macro level. What needs to be determined is how we are doing on receiving the best and the brightest. Are we losing them? It's not known at this time, but maintaining our flow of the very top non-US trainees is where we could best focus our attention.

A factor related to this trend, and which may be somewhat unique to the US, involves age. Many studies have been done relating age to the innate capacity of professional scientists for innovation and creativity (Figure 9). I'm sure all the senior folks in this room will assume that they are an exception to these averages, but the peak years for innate creativity and innovation are between 30 and 50, on average. If we accept this as a general biological principle, albeit with many individual



Source: National Research Council. 2005. Bridges to Independence. National Academy Press.: Washington, D.C.

Figure 10

K-12 EDUCATION RECOMMENDATIONS

- Identify, train, motivate and compensate high quality K-12 science teachers.
- 2. Incentivize students, particularly minorities and women to complete K-12 science course work.
- 3. Provide innovative curricula, infrastructure (computers, etc.) and modern teaching methods for K-12 science education.

Figure 11

HIGHER EDUCATION RECOMMENDATIONS

- 1. Increase the number and proportion of US citizens holding BS degrees in the biomedical area to be on a par with other leading countries.
- 2. Increase the number of US MD and PhD graduate students in biomedical sciences.
- 3. Enhance faculty skills as educators and role models.

Figure 12

exceptions, then it doesn't play well with the current demographic trends in the biological sciences. We all know that training periods are increasing in length. PhDs and MDs choosing careers in the biological sciences often do protracted and sometimes multiple postdoctoral fellowships and the average age that an applicant receives his or her first NIH grant has moved from 34 years in 1981 to 42 today. In 1981, 55% of all R01 grants went to PIs under the age of 40. By 2003, only 17% of awards went to PIs under 40, and that's a huge change. One reason for this is that the younger PIs are not applying (Figure 10). Since 1980, there has been a steady decline in NIH grant applications from the younger age groups, while applications by more senior



Research Support and Work Force Recommendations

- 1. Increase Federal support for biomedical research.
- 2. Revise tax policies to favor private investments in research.
- 3. Stimulate interest of young people in biomedical science careers.
- Encourage more MDs to seek careers as physician/scientists and provide the resources and infrastructure to sustain them.
- Create a national strategy to attract and retain the best and brightest of international students and trainees to enter the US biomedical science enterprise.

Figure 13

PIs dominate. Thus, the funding and resources to conduct research are becoming increasingly offset with the peak years of creativity and innovation. By the time you become well-funded, most of your best years are behind you.

This must also be viewed against another statistic which pervades most, and probably all, US medical schools and biomedical research institutions. The average age of tenured faculty has increased substantially, and a greater and greater proportion of faculty are professors or senior scientists and the overwhelming majority of NIH and other federal grants are held by this senior, aging cadre.

From these numbers, we see that, currently, the US still clearly exceeds any other single country in terms of scientific productivity, but with respect to the totality of the rest of the world, we are losing ground and will continue to do so. This has obvious repercussions for our economy, as well as our social and cultural future. These trends are due to many factors, including inadequate federal support for biomedical research, increased investments in this sector by other countries, and a decreased number of US citizens seeking careers in science.

As these trends increase, our unique UScentric position as the dominant force in biomedical sciences will continue to decline, and more and more biomedical research and innovation will take place in other countries. Insofar as there is a close connection between knowledge creation and economic and societal success, this may be a problem for America, but, overall, it might not be such a bad thing for the world. The less dependent the world becomes on the US engine for advancing biomedical sciences, the less impact downturns in the US biomedical enterprise will have on the rest of the world. In other words, restrictions in federal support for biomedical research, particularly NIH budget crunches, such as the current one, will be felt largely within the US with lesser impact worldwide. In the past, any decline in research productivity in the US meant that the world's knowledge production in biomedical sciences fell. As more and more of the knowledge creation takes place outside the US, the ebb and flow of NIH and other federal biomedical research budgets will have a smaller impact on the rest of the world. But don't get me wrong: This is still not a good thing for America.

These trends towards a diminishing role of the US in the overall biomedical enterprise has certainly hit the biopharmaceutical world. The major pharmaceutical companies are now global corporations with facilities all over the world. For the same reasons that Microsoft, Intel, GE, and many other hightech companies have developed substantial facilities in developing countries, particularly in India and China, so to has this happened in the biopharmaceutical world. As an example, Indian and Chinese medicinal chemists are excellent and well-trained, and we have seen a number of biopharmaceutical companies outsource these functions to these countries where the work can be done at much lower cost and frequently more quickly. This kind of thinking began some years ago on the clinical development side, where large-scale clinical trials can be done at reduced costs and more quickly, because of the availability of large patient populations in these countries and the lower wages of healthcare workers.

What can be done to change these patterns? My purpose here was largely to point out that these trends and patterns which are so well documented in the Physical Sciences have now begun and continue to be ongoing in the biomedical sciences. My goal was not to dwell on a long list of potential solutions, since these have already been well documented in reports on this issue related to the Physical Sciences. The solutions in the biomedical sciences are largely those that have already been proposed for the physical sciences. Therefore, I'll be very brief about recommendations, since the possible remedies are outlined in great detail in the National Academy of Sciences report I mentioned earlier.

Clearly, this begins with major changes in our education system and expanded government funding for research infrastructure and support, and these general recommendations are summarized in the next couple of figures.

In the K-12 area (Figure 11), one of the major needs is to train, motivate and compensate more high-quality science teachers. We also need to incentivize students and improve our curriculums, and a number of very specific plans are contained under each of these general recommendations in the National Academy of Sciences report for those of you who might be interested.

At the higher education level (Figure 12), the ideas are fairly similar, with specific recommendations for increasing the number of US citizens with BS and graduate degrees in the Biomedical Sciences and improvements in our educational system.

For research support and infrastructure (Figure 13), most of the recommendations are fairly obvious and involve various ways to increase federal investment in physician/scientists and PhDs, particularly the younger ones, and to enhance research support. This can be done through federal funds as well as through the private sector by creating more favorable tax policies for research investment. It's not just a matter of throwing money at the problem, but rather specific, targeted investments and programs, the details of which I don't have the time to elaborate.

Of particular interest are these last items in Figure 13 which indicate that to remain competitive with the rest of the world for foreign trainees, we need to generate a national strategy to make certain that we continue to attract, and in many cases retain, the best and brightest of international students. Since we are so dependent on foreign nationals for our science work force, and will be so for many years to come, it would be in our interest to have policies, which increase the stay rates of the very best of these trainees. Many other countries are already addressing this by creating programs which produce an



easier path to citizenship. In the US, we need to address the hurdles for obtaining visas, and the difficulties in obtaining permanent resident or citizenship status for foreign scientists.

The aim of my thesis is to demonstrate that what has happened in the Physical Sciences has already begun in the biomedical sciences and that the early warning signs and demographic trends are already behind us and continuing. These changes in economic, societal and cultural trends are not amenable to quick fixes. The next generation of biomedical scientists, and the infrastructure to support them, will take a long time to come to fruition, even if we start tomorrow. Thus, the current trends are likely to continue for years, even with active efforts to reverse them starting now. However, if we don't start soon, these developments will inevitably continue and will be more and more difficult to affect as years go by. From a purely pragmatic point of view, as the economic world becomes more globalized and flatter, the US could be at an increasing disadvantage. The US economic future, as has been documented by many experts, will increasingly be in innovation, creativity and high-end jobs. We have been losing the game in these very areas in the Physical Sciences, and we have begun the same trends in the broad swath of biomedical sciences. The horse is not out of the barn yet, but it's getting there, so I hope that as a nation we don't wait as long in the biomedical sciences as we have in the Physical Sciences to take corrective actions.

Once again, let me thank the members and the Association for providing me the opportunity to serve as this year's President. It has been a true privilege.

Thank you.