Basic science, the hope of progress

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In a recent contribution to the "Bridges" series the physicist Sheldon Glashow commented on the importance of basic science and of serendipity for technological development and for the benefit of mankind. He gave examples from physical science and described their impact on engineering. I have made similar arguments in relation to biomedical science and its impact on human health. I would like to begin today with biomedical science and extend the discussion along several lines, including the following: the underlying reason and the indispensable nature of basic research; the meaning and the mechanism of serendipity; the relationship of basic science to industry, government and society; the relationship of science and religion; and the implications for cultural accommodation between peoples and for peace. I must emphasize at the outset that my expertise lies in a limited area of chemical and biomedical science. I am not a social scientist, and my opinions on social matters are entirely personal. They may be of interest, perhaps even provocative, but they carry no more weight than those of any member of this audience.

History of medical science

It may surprise you to know that medical science is only 100 years old. Whereas physics and chemistry began centuries before, human biology was neglected. Human disease was attributed to an imbalance of humors, and the treatments were bleeding and violent purgatives. Doctors were scarcely educated men. With the first stirrings of medical science then president of Harvard Charles Eliot proposed its addition to the curriculum at the medical school, to which a noted surgeon on the faculty objected that this would be impossible, because few of the students could read or write.

Today medical science stands as a triumph of the intellect and the greatest frontier for intellectual activity of the future. If the 20th century was the age of physics, then the 21st century is the age of biology, especially human biology. This is not to diminish the ongoing importance of the physical sciences. Quite the contrary. The boundaries between disciplines have largely disappeared. We have a near continuum of science from the atomic level to that of the whole organism. We will one day understand every aspect of human life in chemical and physical terms. With that understanding will come control over disease, over behavior including intolerance and aggression, even control over aging and the future of the human race.

The past affords clear guidelines for fulfilling this great promise. If I were to ask what were the major advances in medical science of the past century, most of you would make a similar list: X-rays for both diagnosis and treatment; antibiotics which have largely eradicated bacterial disease; noninvasive imaging, especially magnetic resonance imaging, or MRI, for early detection of cancer and other conditions; genetic engineering, the basis of most new medicines; the list could go on. These medical advances have one thing in common: They were all discoveries made in the pursuit of knowledge for its own sake, with no notion of any application, no idea of curing disease. The lesson of the past is counterintuitive: to solve a difficult problem in medical science, don't study it directly, but rather pursue a curiosity about nature and the rest will follow. Do basic research.

It is instructive to examine a couple of these examples, X-rays and antibiotics, in more detail. X-rays were discovered by Wilhelm Roentgen, the only child of a textile merchant in the Netherlands. At age 18 he was permanently expelled from school for refusing to inform on a classmate who had drawn a caricature of a teacher. He nevertheless went on to an academic career, and while holding the chair in physics at the University of Wurzburg in 1895 he investigated the effects of electrical discharge in a cathode ray tube. He happened to notice a faint light on a fluorescent screen nearby in the laboratory, even when the cathode ray tube was completely covered in black cardboard. He referred to the radiation emanating from the cathode ray tube as X-rays. Soon after, while holding materials in front of the tube to test their ability to block the rays, he saw the skeleton of his own hand on the fluorescent screen. Within a year or two

X-rays found application in medicine, and in 1901 Roentgen was awarded the first Nobel Prize in Physics.

Turning to antibiotics many of you have doubtlessly heard the famous story of Alexander Fleming and the discovery of penicillin. You may not know, however, that it was a previous chance finding that formed the basis for the discovery, and moreover that Fleming did not pursue the medical application of penicillin. Fleming was a Professor of Bacteriology at St. Mary's Hospital in London and was growing bacteria that caused disease in a dish when in 1922 a drop from his nose fell into the dish and killed the bacteria. Fleming traced the effect to a human protein, an enzyme called lysozyme. While proteins were generally unsuitable for medical use, the possibility of a natural anti-bacterial agent was raised. This hope was realized in 1928 when Fleming noticed that a mold growing in one of his dishes had killed the bacteria. He named the active agent penicillin, but he could not isolate it, wrote a paper describing his findings and gave up on any medical use.

A decade later at Oxford Howard Florey and Ernst Chain were investigating lysozyme and its target, the bacterial cell wall. Florey, son of a shoemaker in Australia, had come to England on a Rhodes Scholarship and had risen through the ranks to Director of the Sir William Dunn School of Pathology. Chain, a refugee from Nazi Germany and musical as well as scientific genius, was Florey's first hire at Oxford. The two decided to broaden their study to include other natural anti-bacterial agents, which they presumed to be other lysozymes. Chain recalled Fleming's publication on penicillin and set about its isolation. He overcame the problem of instability and soon discovered both the uniqueness of penicillin and its extraordinary potential for medical use. There remained the problem of obtaining sufficient quantities, which eventually entailed a collaboration of dozens of institutions including universities, government agencies, research foundations and pharmaceutical companies. The result was the virtual eradication of bacterial disease. For this achievement Fleming, Florey, and Chain shared the 1945 Nobel Prize in Physiology or Medicine.

The nature of discovery

These brief accounts of X-rays and antibiotics serve both to reinforce the crucial role of basic research and to illuminate the process of discovery. The work is invariably done by individuals, free to explore and to follow the scientific path wherever it may lead. All such paths lead ultimately to underlying principles, to the fundamental truths of nature. And it is from this knowledge, from deep understanding, that all practical benefit derives. Discovery is the engine of progress. Discovery and its offspring, technology, are all that separate us from our original primitive condition. Discovery is the hope for advancement in the future.

The importance of discovery for medical, economic, even military benefit has not been lost on central planners. The problem is that discoveries, by their very nature, cannot be planned. They arise from untargeted research. They arise by serendipity, as in the work of Roentgen, Fleming and others. The only way to assure they will arise is by the support of talented individuals in the unfettered pursuit of knowledge.

This important fact, well established by the experience of the past century, is often forgotten by people in government and industry who desire greater, more immediate benefit. I recall words of the American president Lyndon Johnson to the effect of "life-saving discoveries locked up in the laboratory". This serious sentiment was mistaken. Application of existing knowledge is not the limiting factor. The knowledge itself is limiting.

It has been remarked that we know 1% of everything about the human body. A small fraction of a percent would probably be more accurate. But consider how enormous have been the benefits to our health and to economies from what little we know now. Imagine how great would be the benefits of knowing the remaining 99%!

The roles of government and industry

Another lesson from the past relates to the support of basic research. This has come from government rather than from industry. And for good reason. The timeline is very long – fundamental problems take decades to solve. Only the public, with a long range interest in bettering the human condition, will support such an undertaking. Industry, with a short term interest in the bottom line, can hardly be expected to do so. What CEO could report to his or her board that a major investment has been made in research that may or may not become profitable in ten or twenty years or longer? Let me give you a concrete, almost frightening example. Pharmaceutical companies developing anti-cancer therapies are regularly forced to choose between a drug that cures cancer with a single dose and one that must be administered weekly and which only prolongs life by a year or two. Management invariably makes the right decision on behalf of shareholders and pursues the less effective drug. This is not an isolated or rare occurrence. It occurs on a weekly basis in the best companies. Government clearly has a special responsibility and a unique role to play.

The return on investment by government in basic research has been huge. The eradication of polio, the cure of childhood leukemia and many other diseases, have saved vast amounts in treatment and productivity as well as human suffering. Not only has the investment been repaid many times over, but it was small to begin with. The annual budget for cancer research in the United States today is only $5 billion, less than 10% of the annual expenditure on soft drinks, less than a week of the war in Iraq.

You may ask why not wait for a large country like the United States and its rich government to fund basic research and publish new knowledge. Why should not a smaller country like Malaysia or Thailand concentrate on applications of particular economic, military or other value? The answer is not only the importance of knowledge, but also of intellectual infrastructure, of investing in people. Consider high tech and biotech. Both began next door to the universities in the San Francisco Bay Area where the fundamental discoveries were made. Others around the world have also joined in the rewards, but the leaders have been vastly more successful - not only in the past, but also in the future. This applies particularly to the people involved, the talent that drives the enterprise. The best and the brightest come to train in the San Francisco Bay Area and remain, or they are attracted after training elsewhere. It is important for other places, other countries to compete, to retain their native talent and to recruit as well. A marketplace for talent is in the best interests of all.

A market for the employment of young scientists is crucial not only to retain their talent, but also to encourage them to do science at all. The choice of a career in science represents a great sacrifice. A passion for science must be weighed against a long period of training - ten or more years of postgraduate study at low wages - and the possibility of no career at the end. The importance of young scientists cannot be overstated. Progress in science and discovery in particular, is the work of young minds.

The marketplace for talent to which I have alluded is both academic and industrial. Indeed by emphasizing the crucial role of government in the support of science, I do not mean to diminish the importance of industry. I have already noted the vital contribution made by pharmaceutical companies in the development of penicillin. This is not an isolated or rare example, but rather an illustration of a time-honored process. Industry has been and will remain primarily responsible for translating discoveries made in academic laboratories into commercially viable technologies. The time scale for industrial development may be small, but the financial scale is not. A pharmaceutical company will invest hundreds of millions of dollars in the improvement and testing of a single drug to gain regulatory approval.

Science and society

Basic science may be a panacea for practical problems, but what possible relevance does it have to social questions of human rights, international peace and other pressing issues? On one level the practice of science, as it has evolved over the past century, is an example of international cooperation. A majority of the young scientists in my own laboratory over the years have come from Europe and Israel, from Asia, from Central and South America, and my laboratory is no exception. The findings made by these young scientists, and indeed by all others, are published in a worldwide scientific literature, available to be read, criticized and eventually to be exploited by all.

It is sometimes said that education is an antidote to hatred, intolerance and other afflictions of society. Education is indeed important, but education alone will not suffice. The most learned society - that of twentieth century Germany - perpetrated the worst offense against humanity, the Holocaust. More than half of those who planned the mass murder of the Jews at the Wannsee Conference in 1941 held doctoral degrees. The product of scholarship, including science, will not protect us from such atrocities in the future.

Rather it is the nature of science that may serve as a paradigm for addressing societal problems. Science seeks fundamental principles and proceeds from objective, verifiable truths. In an analogous fashion societies are sustained by the rule of law, whose application depends on an unbiased judiciary. In a world beset by irrational forces science represents the light of reason. The rule of law has been viewed since ancient times in a similar way. Sandra Day O'Connor, a former Associate Justice of the US Supreme Court, has quoted the belief of Aristotle that the Rule of Law is "nothing less than the rule of reason, balanced by considerations of equity so that just results may be achieved in particular cases".

Science and religion

The pursuit of truth underlying the human condition is older than Aristotle. Both Eastern and Western religion are founded on fundamental principles, for example the precepts of Buddhism or the Ten Commandments of Judaism. Beyond a foundation on principle both science and religion seek to explain the fundamental mysteries of our existence and of the universe. What is remarkable is that we seek knowledge at all, that we feel impelled to do so. We will expend enormous effort to do so. We will take mortal risks and endure great suffering to do so. An obvious example is the exploration of earthly and outer space; the creation of art and literature is another. An urge to explore is a part of our nature. It was a major factor in the evolution of our species.

The urge to understand has been encouraged by our amazing success in doing so. As others have commented, no human capability is more remarkable than that of unraveling the mysteries of our existence including our capabilities themselves. The question is how far these capabilities will extend. Already our explanations have gone beyond simple reason. Cosmology, chemistry, biology can only be understood in terms of abstract ideas. These are the great abstractions of energy, of scale and of time. The behavior of matter at high energy is treated in terms of relativity. The nature of matter on the atomic scale is described in term of quantum mechanics. And the evolution of the species is a reflection of geologic time.

I can illustrate the nature of these great abstractions with an example of evolution from my own research. I have studied genetic information. As you know, genes perform a dual role: They are a repository of information, passed from parents to offspring, and they are at the same time a source of information for use by every generation. The first step in the use of the information is reading it, which is accomplished by a giant protein. My colleagues and I have obtained an image of this protein in the very act of reading genetic information. The image reveals the 30,000 individual atoms involved. What we observe is a minute machine, with moving parts such as clamp, jaws, rudder, lid, trigger and so forth. It is a marvel of natural engineering. Its intricacy and efficiency present a problem for understanding in terms of evolution. And yet it did arise by evolution, over a period of time we can scarcely imagine.

It may be thought that understanding fundamental processes in this way and grasping the power of geologic time may somehow diminish the wonders of nature. On the contrary, we are awestruck by the beauty and grandeur of it all. This sense of awe can evoke a spiritual response. Einstein once wrote:

> The most beautiful emotion we can experience is the mysterious. It is the fundamental emotion that stands at the cradle of all true art and science. He to whom this emotion is a stranger, who can no longer wonder and stand rapt in awe, is as good as dead, a snuffed-out candle. To sense that behind anything that can be experienced there is something that our minds cannot grasp, whose beauty and sublimity reaches us only indirectly: This is religiousness. In this sense, and in this sense only, I am a religious man.

The same sense of awe can engender a belief in the power of reason. Many of us engaged in work such as I have described share the conviction that all mysteries of nature will ultimately succumb to explanation in chemical and physical terms. Of course, we cannot know this is so. It is rather an article of faith which will continue to be tested for as long as we endure.

In all its aspects, of the quest for larger meaning, of passion in the pursuit and of faith in ultimate success, science resembles religion. At the deepest level both science and religion are expressions of the human spirit. Where science departs from religion is in its foundation upon objective, verifiable truth. That is its greatest appeal and what it offers to society.

Bridges

To summarize, basic science is a literal bridge to understanding nature and to the practical benefits and the personal fulfillment that follow. Basic science is at the same time a figurative bridge to the solution of societal problems, through the example it sets of rationality and impartiality. Science leads directly to technological progress. The culture of science may lead, albeit indirectly, to progress towards peace and understanding.