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Research --A voyage of Discovery

I thank you for the invitation to be with you on this very important evening and the honor of having the opportunity to speak with so many Rochester alumni and friends in so many places. We who were students here shared an intellectual experience that changed our lives, my own included, and provided us an approach to the world of medicine that I later came to realize was different from that offered in most institutions. It relates to research and, on this evening, my charge, on the eve on the occasion of the ceremonial opening of a magnificent new laboratory science facility is to elaborate briefly on the theme of research.

At this time in history, it is not difficult to wax lyrical about the subject of biomedical research what with the all but unbelievable advances that have taken place over recent years. Whole new fields of endeavor have opened. Typical is the experience of a decade ago, for example, of being able to meet around a dinner table with most of the researchers in one's special area of investigation, only to find today that one is attending a formal meeting of several thousand with several simultaneous sessions. Progress has been that fast. It is difficult to convey to you the diversity of new opportunities, the excitement, the promise ---and to accomplish this in just 20 minutes.

During my years as a science adviser to President George Herbert Walker Bush, Dr. Alan Bromley, a physicist, and the President's chief science adviser, observed that, as he saw it, the last half of the 20th century was the era during which the physical sciences predominated on the research stage -- the era of the atom, of nuclear fission, of rocketry and space travel. For the 21st century, he foresaw the biological sciences assuming that role. He has been proved right. There is no question but that there have continued to be important developments in the world of the physical sciences but they pale in comparison with our efforts

in biology to probe and understand the genetic makeup of ourselves as well as life on earth; to define how the world of living entities grow, respond to challenge and develop.

During these remarkable changes, Rochester has continued as one of the world's premier academic medical centers, contributing its share to our accumulating knowledge of health and medicine. For me, and I know to many of its graduates, it has played an additional, important, and in many ways unique but less well-recognized role in the molding of its graduates. Let me illustrate by noting a personal voyage of discovery.

George Whipple was still the Dean when I enrolled as a medical student. It was clear that he and the faculty at that time placed a special emphasis on a research experience as part of one's medical education. Some took off a year off for a special laboratory experience; some for shorter periods. I was not one of those strongly attracted to the laboratory. However, events conspired, namely a shortage of funds, so that I spent a summer working with Dr. William McCann, then Chairman of Medicine, in a laboratory working on mechanisms of magnesium metabolism. My competence in chemistry is best summarized by noting that I barely succeeded in passing college organic chemistry. I can't say that much progress was made during my tenure in understanding the metabolism of magnesium and certainly no thanks to me. But, in retrospect, I now recognize that, for me, this was my introduction to the excitement of being part of a team that was exploring ideas and concepts -- exploring a terrain where none had ever trod before. It was a different world from poring over books and memorizing facts; it was a different world from learning techniques of surgery or medicine; one was probing areas and ideas for which there was no blue print, no certain path and no promised outcome. Amidst what superficially might have appeared to be a

great deal of dull laboratory work, there was a pervasive excitement in wondering what each day would bring.

A second part of my Rochester experience as a medical student related to the offer of a prize that had been created -- the George Corner Prize -- for the best historical treatise in medical history. The prize was $200. I can't say I was terribly interested in the history of medicine but $200 for a young medical student and his wife was serious money. A book, then current, called "Grandfather Tales" documented a fascinating series of events during the 18th century in upper New York State. One chapter offered a brief account of epidemic cholera in 1833. That became the subject of my paper and the cause for endless hours in the library reviewing newspapers of the time, trying to reconstruct the evolution of the epidemic and the nature of a community's response to it. It proved to be my introduction to epidemiology and public health. And, yes, I did receive the prize and "no" there were no other contenders for it.

Thus, my introduction to the excitement inherent in research and in public health--to explore where none had ever been before. Twelve years after graduation, I was confronted with the challenge of directing a global program whose goal was the eradication of a disease. No disease had previously been eradicated and, indeed, none has been eradicated since. The program itself could be said to be an experiment on a global scale. The challenge -- to implement programs of smallpox eradication in some 50 countries with a population of about 1.5 billion persons. A disease that afflicted some 10 to 15 million persons in 1967 and claimed 2 million lives was expected to be reduced to "0" in just 10 years. For this purpose, we were given $2.4 million per year and could use whatever else we could persuade countries to donate. Over the first 6 years of the program, cash contributions amounted to just $70,000. There wasn't a great deal of confidence in the world that eradication was achievable.

It seemed to me that it would be prudent to use part of our allotted funds to undertake a research program. I didn't really know enough about the challenges or the disease to identify what research was needed, only the conviction that there would be questions that needed to be explored and that we should be prepared to respond. My request for a research fund was severely frowned upon and, when finally agreed, amounted to only $40,000. The leadership at the World Health Organization argued that because the disease had been around for centuries and had been so thoroughly studied, there was little of significance that could yet be learned. Smallpox eradication, as they viewed it, was a straightforward administrative exercise. Vaccinate everyone in the world and smallpox will vanish. The task, quite simply, was to obtain sufficient vaccine, to distribute it appropriately and persuade the governments to vaccinate. This was 1967.

Twelve years before, in 1955, an earlier global eradication program had been mounted by WHO--one designed to eradicate malaria. DDT was a comparatively new product then and had proved to be an exceptional insecticide. Its use was the key technical innovation to accomplish malaria eradication. So confident was the international leadership that all ongoing research efforts were stopped; laboratories were closed; scientists moved on to other fields. As the program continued into the 1960s, problems began to be identified -- DDT resistance was growing; the parasite was developing resistance to anti-malarial drugs; tropical Africa was proving to be an impossible challenge. By then, there was no where to turn. As one malariologist expressed it: "We didn't eradicate malaria but we virtually eradicated the malariologists".

This was a lesson not to be ignored. And, indeed, research eventually proved to be so essential that one eventually could say, with confidence, that the eradication of smallpox would not have been achieved without it. We were to learn that much of what was written in the textbooks was wrong. It was said that

the disease spread like wild fire and could be found all over a country. In fact, smallpox usually spread slowly, moving from village to village, from one area of a city to the next and one could stop its spread by concentrating on a vaccination program where the cases were found --"ring vaccination" --we called it. It was said that vaccination every 3 to 5 years was necessary. We quickly discovered that in the endemic countries, vaccine protection extended for 20 years or more. All efforts quickly shifted to getting a vaccination scar on every arm. Revaccination was deemphasized. Research on vaccine strains revealed two strains of the many then available to be especially suitable for use and gradually most laboratories around the world adopted one of these two strains. Industrial research revealed a number of approaches that would increase production and decrease the chance of contamination. These were widely shared. A new device, invented by industry, called the bifurcated needle, proved to be far simpler to use than the lancets then being used in most countries. Most villagers could be trained to use the bifurcated needles within 10 to 15 minutes; successful vaccinations rose to almost 100%; only one-fourth as much vaccine was needed. A vial that could be used to vaccinate only 25 persons could now vaccinate 100. The last case of smallpox occurred on 26 October 1977 -- the last case in a continuing chain of human to human transmission extending back at least 3500 years. The end of a disease that, in the 20th century alone had killed 300 million persons. We continued the research program to the last and, as the last cases were occurring, were completing field studies of a new tissue cell culture vaccine.

The secret of success was a close working relationship between those endeavoring to implement the program and those in industry and academia who had a great many answers if only we could enunciate the questions.

In 1980, the World Health Assembly declared that smallpox had been eradicated. I had thought that we had written the final chapter on this disease but

now, as you know, the threat of smallpox has arisen once again. In fact, of all the potential agents that might be used as a biological weapon, this is the one we fear the most but it is not the only one.

It has become apparent that we, in this country, have enjoyed a false complacency -- the belief that the infectious diseases, at least in a modern industrial state, were primarily of historical interest and that we could diminish our research investments and resources in favor of dealing with the chronic conditions. The discovery of HIV-AIDS in 1983 was an alarming discovery but confidence was expressed at that time that a vaccine would be found within 2 years and that this would solve the problem. Nearly 20 years later and with a global pandemic in progress, we have neither a vaccine nor a curative drug despite spending over $2 billion a year in a research effort. There are other infections which have appeared in recent years, some new, some migrating from distant areas -- mad cow disease, West Nile encephalitis, dengue fever. There will be more in an increasingly crowded globe with a host of organisms constantly mutating and seeking a foothold. Couple that with the increasing availability of techniques for growing and manipulating microorganisms, as well as disseminating them.

The threat of bioterrorism has catalyzed the Executive, the Congress and the nation. The budget for which my office has responsibility was $300 million last year. On January 10, the President signed the Appropriations legislation providing us with $3 billion for this year for what promises to be a greatly heghtened public health and emergency response to deal with potentially catastrophic epidemic disease -- whether man-made or naturally occurring. The president in his next year's budget has asked for a further 50% increase, primarily for research. Rochester is already playing an important role. The County, with University support, is one of three national demonstration and development

programs for bioterrorism preparedness. It is one of the designated national vaccine evaluation centers. A special program to aid rapid diagnosis of rash diseases is a pioneer effort in the Department of Dermatology and there are a number of other now burgeoning initiatives.

Rochester's role as educator, catalyst, bridge and advocate could not be more important to the new frontiers of biology. There are exciting days and exciting adventures ahead.