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Voyages for the 21st Century --Johns Hopkins School of Medicine --23 May 2002

It is, for me, a privilege and an honor to have been asked this year to be your convocation speaker and to offer some few words of reflection to those of you graduating from a School so rich in history --and, today, as it has been historically, at the cutting edge of medicine. I join in congratulations to you today as you receive degrees that are recognized internationally as representing a paragon of excellence.

As Dean Miller has illustrated in his very generous introduction, I have found it difficult to hold any job for very long. And as my wife has reminded me over the past, 8 months, I am in the process of failing retirement for the fifth time but more dramatically than ever before. One surprise for me has been the sudden tidal wave of interest in smallpox. Just over 20 years ago we completed our archival history entitled "Smallpox and its Eradication" (a regrettably unimaginative title). In 1700 pages, it tells you more than you really want to know about the disease. The World Health Organization had printed some 5000 copies but within a couple of years were wondering if they could sell them as door stops. Meanwhile, I had assumed that I had lectured on the subject for probably the last time. Then came September 11. Anthrax could clearly be seen as a serious threat but smallpox, were it to occur, could result in an international catastrophe. The book is now out of print; the National Library of Medicine has put it on a web-site; and, so I am told, it is selling on ebay for \$800 a copy. Now, I am routinely asked what was the most important lesson the global campaign had taught me. The most obvious is that one should choose one's specialty with care. After 11 years, I had achieved the distinction of being an international expert on the disease of smallpox, only suddenly to discover there was no disease. Having no disease and no marketable skills, the only solution was to become a Dean.

I want to reflect with you today on a new world that the events of September 11 have brought into focus. It is not that the world itself has been suddenly transformed. It hasn't. What changed was our perception of the world as we know it today and what the future may bring. First, it is certain that the directions of biology in the 21st century will govern, in a major way, the future of mankind. The biological sciences offer increasingly the possibility of a

cornucopia of products that can make life better, more productive and more secure. There is, as well, a dark side -- the possibility of new classes of weapons -- more powerful than any hitherto used and accessible even to small groups and to those with limited resources. Second is the recognition that the ecological relationships between man and microbe are changing more rapidly than ever in history, bringing with them, a range of new or newly emergent organisms --HIV, mad cow disease, Hanta virus pulmonary disease, and others. Third is a recognition that there is a potential now to transform the quality of life for peoples around the world with vaccines and drugs, an endeavor that must enlist the best efforts of those in biological research and those in medicine and public health ..

Seven years ago, new counter-terrorism programs were launched by the President who, in 1995, issued a Directive asking that all Departments take special measures in planning and development to deal with bioterrorism. Impetus for these efforts was provided by the devastating sarin gas attack in the Tokyo subway by an apocalyptic terrorist group and the later discovery that they had endeavored to spread anthrax and botulinum toxin as aerosols throughout Tokyo. If a hitherto unknown religious sect could undertake such actions, who was to say there were not other groups similarly motivated? The concerns were heightened as it became apparent that the Soviet Union, unbeknownst to the West, had developed a biological weapons program that rivaled their nuclear program in size and sophistication. Whether work was still continuing could not be discerned. Meanwhile, many scientists from the Soviet laboratories had migrated to other countries around the world. And, finally, it became apparent that year that Iraq's program was an elaborate one with considerable capacity. How many other countries might have bioweapons programs still undetected? Detection of such activity was close to impossible, --so little space, money and manpower being needed.

Initially, in this country, efforts and resources were devoted to strengthening the capacity of "first responders" to deal with explosive events or a chemical weapons attack-- specifically police, fire and emergency rescue personnel who, with sirens and flashing lights, would decontaminate and

evacuate those afflicted. The naïve assumption was that biological events would be treated in the same manner. What was not understood was that the release of a biological agent would be surreptitious, undetected, silent and that casualties would only begin to show up in emergency rooms days to weeks later. It would be an epidemic.

Gradually, Congress and the Executive began to understand that the problem was very different from that which they had perceived -- that biological weapons posed a threat substantially greater than that of either chemical or nuclear weapons. The budget for the Department of Health and Human Services gradually rose from just \$8 million in 1998 to \$300 million last year and to \$3 billion this year.

Is this a "problem of the year" funding effort that will quickly be forgotten? All of us who are concerned with this problem would be delighted if we could foresee that day when we would no longer need to worry about biological weapons. I am afraid that is a futile wish. Recall that only some 10 grams of a high grade anthrax powder was used in the anthrax attack. Some one, some group made that preparation and there is no question but that they must have made much more. It takes practice and a number of attempts to produce a product comparable to that which was used. Unquestionably, there is more such material out there somewhere. Note that the Soviet bioweapons program kept 30 metric tons of dried spores in storage at all times as well as tons of smallpox virus..

For the 21st Century, our concerns extend beyond the release of new organisms by man. The potential threat of new and emerging infections has likewise changed. There is a constantly mutating diverse microbiota throughout the world, regularly throwing off new variants into a now more densely populated world -- many persons now living in densely crowded tropical cities with poor nutrition and sanitation. A fertile ground for breeding new agents. Will there be another agent like HIV with a long incubation period -- becoming epidemic before we recognize it? Will there be a new influenza variant behaving as did the 1918 Swine Flu? Prospects for the emergence of new diseases are greater than at

any time in history and growing. To cope with this challenge requires the same public health-medical infrastructure that we need to cope with biological weapons.

And finally, there are growing numbers of laboratories throughout the world that are now able to manipulate microorganisms through the use of microbial genetics and recombinant technologies to create all manner of new and interesting organisms. -- organisms and products that could offer barriers of prevention and new methods for treating some of our most deadly diseases. Those laboratories do have the potential for creating, quite unknowingly, chimeras that could escape the laboratory and be as devastating as any new weapon.

In brief, we are dealing with a new world of biology which, in the 21st century promises to be different by orders of magnitude from that to which we have become accustomed.

But, for all the problems that are posed, there are equally cogent reasons to believe that we are now poised to take on the challenge of dealing effectively with some of the most significant problems of the developing world -- of AIDS, of tuberculosis, of malaria, of dengue, of the hemorrhagic fevers.

Over the past 30 years, there have been dramatic changes in infectious disease morbidity and mortality, changes that are not fully appreciated. In the course of these programs, new approaches to disease control have been developed that have given those of us in the public health community confidence that much more is possible if we have the right tools..

For example, as we began the smallpox eradication program in 1967, we worked with different African countries to map out mass vaccination programs. Based on earlier efforts by colonial health services, we estimated that it would take not less than 3 years to vaccinate throughout each of the countries. With difficult road and communication systems and understaffed and inexperienced health staff, even 36 months looked optimistic. However, as systems developed and experience accumulated, it soon became apparent that two years was ample and, based on more recent experiences, I would warrant that, if one had a

vaccine that one wanted to administer continent-wide, at least 80% could be vaccinated in 9 months.

At the beginning of the smallpox program, we came to the startling realization that except for a not very effective tuberculosis vaccine, little in the way of vaccination was being provided to children in the developing world. It seemed logical to try to give more than one vaccine and so, four years into the program, we proposed what inelegantly we called "the Expanded Program on Immunization" to make available, as well, diphtheria, pertussis, tetanus, measles and polio vaccines. We really should have come up with a sexier name --like "Operation Protective Shield" or some such (perhaps I have been spending too much time with the Office of Homeland Security). Whatever, that effort gradually gained momentum and by 1990, 80% of all children were receiving those vaccines and, in some countries, Hepatitis B, h. influenzae and yellow fever vaccines were being added.

Smallpox deaths dropped from 2 million a year to "0". In Latin America, childhood mortality rates dropped at a faster rate than ever in history. Inevitably, concern was expressed that population growth would explode causing more problems than ever. But, as was discovered, fertility rates began dropping as precipitously as the childhood death rates. In brief, it translated into fewer, healthier children.

Amelia
Meanwhile, those in the Brazilian program tried a new approach in vaccination -- called National Immunization Day. The idea was, on a single day, to vaccinate all children throughout the country. Ninety percent got vaccinated. Rates of polio fell precipitously. Other countries began to do the same and, in 1985, the countries with leadership from the Pan American Health Organization, decided to eradicate polio from the hemisphere. The last case occurred just over five years later. National Immunization Days have extended throughout the world -- indeed to China and then to India where, in each country, more than 100 million vaccinations were performed on a single day.

Now, with over a billion dollars in support from the Gates Foundation and with generous contributions from governments and others, large scale efforts

have been launched to introduce more vaccines to developing countries throughout the world and to move aggressively to develop new vaccines for many of the major killers. What a sea change has taken place over just a 30 year period. The potential is there for accomplishing as much and more in the next 30 years.

Working in public health offers one quite different dimensions and opportunities than does clinical medicine. For example, I have yet to have someone come up and thank me for their not having had smallpox or polio. However, one cannot help but remember the faces of agony as one rounded on a smallpox ward or dealt with a room full of polio patients breathing with the assistance of a respirator -- and to recognize that those wards are no more..

On the occasion of our celebration of the 100th Anniversary of the Johns Hopkins Hospital, Dean Richard Ross said to me; "You know, I suspect that at the School of Public Health, you are probably responsible for saving more lives in a year than we have saved at the Johns Hopkins Hospital in its entire history.." I told him that I thought he was right but I think it misses the point that medicine and public health make an excellent and necessary complementary team. In the 21st century world of the biological sciences, we have a task greater than both of us. Josh Lederberg pointed this out when he said: "Man's only contender for dominion of the planet are the viruses -- and the outcome is, by no means a foregone conclusion."

I welcome you all to participation in a great adventure.