

## Voyages for the 21<sup>st</sup> Century

MinnAndersonLecture03Voyages

Gaylord Anderson Lecture

University of Minnesota School of Public Health

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It is, for me, a special honor to be asked to present the Gaylord Anderson lecture. As one who spent only 14 years as a Dean, I have reverence for one served Dean for 32 years! As I was entering the field of public health in 1955, Dr. Anderson was unquestionably one of the most prominent of the international leaders in the field – a statesman, a diplomat and a scientist. The most serious public health crisis at that time was the occurrence of some 200 cases of paralytic polio following administration of the new inactivated polio vaccine -- which, as it turned out, was not fully inactivated. There was a real crisis of confidence among the public and scientists alike. A small group of the most knowledgeable and respected public health authorities were convened to deliberate a future course of action. Dr. Gaylord Anderson was one of that group – a thoughtful, reflective personage, it was clear that his views carried great weight. The problems were sorted out and a concerned public reassured as polio vaccination resumed. At this time, I only wish we had a Gaylord Anderson to help us generate needed confidence in smallpox vaccination.

As Dean Becker has illustrated in his very generous introduction, I have found it difficult to hold any job for very long. And as my wife regularly reminded me over the past 2 years, I am in the process of failing retirement for the fifth time. One surprise, during the past few years has been the tidal wave of interest in smallpox. As you know, we haven't had a case for more than 25 years. And just over 15 years ago we completed our archival history entitled "Smallpox and its Eradication" (with a bit more imagination, we could have come up with a livelier title – e.g. Smallpox, sex and the single virus, but didn't). In 1700 pages, it tells you more than you really want to know about the disease. The World Health Organization printed some 5000 copies but after several years and still with a thousand or so copies remaining, the WHO Publications staff was beginning to wonder what to do with them. Since they weighed fully 2 pounds each we proposed selling them as door stops. Then came

September 11. Anthrax was clearly recognized as a serious threat but smallpox, were it to occur, could result in an international catastrophe. To make a long story short: the book is now out of print; the National Library of Medicine has put it on a web-site; a CD Rom is available, and, so I am told, it is selling on ebay for \$800 a copy. Would that I had stashed a few copies away.

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. Sudden transformation – no—but steady change, increasing logarithmically. What has changed most dramatically is our perception of the microbial world and what the future may have in store. It is certain that the directions of biology in the 21<sup>st</sup> century will govern, in a major way, the future of mankind. Dr. Alan Bromley, Chief Science Adviser to George H.W. Bush when I was in the White House, firmly believed that, over the past half century, physics had been the premier cutting edge science but, for the 21<sup>st</sup> Century, it would give way to biology. 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, the dark side which we once innocently ignored. First, 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, SARS and now, an outbreak of monkeypox centered in Wisconsin, of all places. However, there is now a new recognition that there is a potential to transform the quality of life for peoples around the world with vaccines and drugs.

Eight years ago, new counter-terrorism programs were launched by President Clinton who, in 1995, issued a Presidential Decision Directive. He asked that all Departments take special measures in planning and development to deal with terrorism. Impetus for these efforts was provided by the devastating sarin gas attack in the Tokyo subway by an apocalyptic terrorist group. It was later discovered 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 in the early 1990s 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, as the Cold War wound down, many scientists from Russian laboratories began to migrate to other countries around the world. And, finally, in 1995, Iraq, in a written submission to the UN, acknowledged having a program far more sophisticated than UNSCOM teams had suspected, let alone identified. It raised the question as to how many other countries might have bioweapons programs still unknown? Detection of such programs was close to impossible, --so little space, money and manpower being needed to produce quantities of the most potent weapons.

Beginning in 1995 in this country, efforts and resources were devoted to strengthening the capacity of "first responders" to deal with an attack using a bomb or a chemical weapon -- 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 could 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 once perceived. It was clear that biological weapons were unique and posed a threat substantially greater than that of either chemical or nuclear weapons. And here, I pause to pay special tribute to your own Mike Osterholm who has been one of the best of the educators. Gradually, the budget for the Department of Health and Human Services rose from just \$8 million in 1998 to \$300 million in 2002 and to \$4.5 billion this year.

Is this is a "problem of the year" funding effort that will quickly be forgotten? All of us who are concerned about bioterrorism 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 also 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 21<sup>st</sup> 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. It regularly throws off new variants into a much more populous world – a world now with more than 30 cities with populations of 7.5 million or more—densely crowded, many in tropical areas with poor nutrition and sanitation. A fertile ground for breeding new agents. After AIDS, we speculated as to whether there would ever be an agent like it – a highly fatal disease with a long, silent incubation period – and becoming epidemic before we recognized it? And, lo and behold, mad cow disease (TSE) emerged. We have wondered for a long time whether there could possibly be a new influenza variant behaving as did the 1918 Swine Flu. We have had several alarms, including indeed a swine flu strain, but none has yet proved to be anywhere near as virulent or capable of spreading. Much to everyone's surprise we are now dealing with a new respiratory infection of a type not seen before in man – SARS – with a potential for explosive spread and a case-fatality rate of some 10 to 15% among those with clinical disease. What the autumn may bring is cause for real concern as there is no effective therapy and it is difficult to imagine a vaccine in less than 2 to 3 years however great the priority assigned. The new microbial world cannot be taken lightly.

Some have speculated that we are, perhaps, only identifying a number of disease entities that we have simply overlooked in the past. Not so. Population pressures; greatly expanded tourism and to remote areas; internationalization and industrialization of our food supply have together conspired to create a biological threat potential that is unique in history and that serves to greatly increase the probability of emergence of many more new or previously latent diseases. The contributing factors are continuing to make these ever more likely. However, whether our problems derive inadvertently through Nature or are the product of a terrorist, the challenge and the needs for public health and medicine will be the same.

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 and products. These could offer barriers of prevention and new methods for treating some of our most deadly diseases. Such laboratories also have the potential for creating, perhaps unknowingly, chimeras and genetically altered organisms that could escape the laboratory and be as devastating as any new weapon. For example, what happens if one takes a gene from Ebola virus and puts it in the human immunodeficiency virus or in a hepatitis virus. Yes, both of those experiments have been performed.

We are dealing with a new world of biology which, in the 21<sup>st</sup> century promises to be different by orders of magnitude from that to which we have become accustomed. We are beginning to prepare for agents of bioterrorism but we are beginning to recognize now that Mother Nature herself has quite as much potential to create and to destroy.

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 confronting effectively 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 experience, I would be confident 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, in 1967, we came to the startling realization that little in the way of vaccination was being provided to children in the developing world except for a not very effective tuberculosis vaccine. It seemed logical to try to give more than just smallpox 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, rubella, 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, albeit with a lag in time. In brief, it translated into fewer, healthier children.

Meanwhile, those in the Brazilian program tried a new approach to vaccination. They were having difficulty obtaining coverage rates of more than 60% despite all manner of efforts to have the vaccine distributed in clinics, hospitals and through private care-givers. They decided to try a National Immunization Day. The idea was, on a single day, to vaccinate all children under 5 years throughout the country. On each of the first two days, 90% were vaccinated. Polio rates fell precipitously. Health policy gurus in Geneva solemnly assured everyone that such a program could not be sustained. The Brazilians persisted and Immunization Days continued every year. As one Brazilian health official said to me: "We have Carnival every year and no one seems to get tired of it. Why not Immunization Days every year?" Other countries began to do the same and, in 1985, the Latin American 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 now 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, large scale efforts have been launched to develop new vaccines for many of the major killers – malaria, AIDS, tuberculosis and dengue. Mechanisms are being explored to make such vaccines more affordable to the countries needing them and to introduce more vaccines to the developing countries in particular. The Gates Foundation has invested more than a billion dollars in support of these efforts and there are increasingly generous contributions from national governments and non-governmental organizations throughout the world. Thirty years ago an international conference on vaccination would draw perhaps 500 persons. Today, there would be several times that number in a conference dealing with respiratory diseases alone. What a sea change has taken place over just a 30 year period. There is both the potential and the need to effect a change of similar magnitude over the next 30 years.

Working in public health offers one quite different dimensions and opportunities than does clinical medicine. 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..

The task before us is a substantial one as Josh Lederberg pointed out when he said: "Man's only contenders for dominion of the planet are the viruses -- and the outcome is, by no means a foregone conclusion."