

Dawn of a New Era for Infectious Disease Challenges

D. A. Henderson, Taipei, Taiwan, July 5, 2013

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Minister Chiu, Distinguished Delegates, Ladies and Gentlemen,

I greatly appreciate your thoughtful invitation for me to participate in this APEC Conference on Emergency Response Systems. It is most timely. What with another corona-like virus lurking, the memories of the 2003 SARS epidemic are all too fresh in our minds. I well recall the fears and apprehension we felt 10 years ago as alarming reports flowed in steadily from China, Hong Kong, Taiwan, Vietnam, Singapore, and Canada—the explosive outbreaks, the numbers of doctors, nurses, laboratory staff, and other caregivers who became acutely ill, some fatally. It was difficult from the array of fragmented reports to understand how and why the virus sometimes spread as rapidly as it did; how even very stringent respiratory isolation procedures sometimes seemed to fail. Enormous efforts were made to screen passengers at airports in order to prevent entry of the virus but, as usual, airport quarantine measures proved to be of little value.

Much has since been learned about the SARS virus. An unprecedented array of cooperative international studies has provided valuable information about the virus and the disease. It appears now that bats are an important reservoir and can spread the virus to other animals and subsequently to man. However, we do not yet have a vaccine or antiviral agents for prevention or treatment. Meanwhile, this year we have learned of another coronavirus, called MERS, which has caused similar illnesses. And then 2 new influenza viruses emerged whose pandemic capabilities are still not certain. What is now a certainty, however, is that new or emergent biological agents will continue to challenge mankind with a frequency that we have not seen before. Improved preparedness and response programs in all countries are thus far more critical than they have ever been.

For those of us with national responsibilities for health security, the appearance of SARS was an alarming experience. Only a year before the SARS reports, I had been requested to return to government service on an emergency basis. I was asked to serve as Director of a new Office for Public Health Emergency Preparedness. The office reported directly to the US Secretary of Health and Human Services. This office was created in December 2001, just a few weeks after the September destruction of the World Trade Towers and distribution through the mail of anthrax organisms by an unknown terrorist. The country was in turmoil. There was fear that there would be other attacks. The anthrax in the envelopes had been in a powder form. People began noticing white powder everywhere—samples of white powdered sugar on donuts and even samples from sugar bowls were sent to laboratories to be tested for the possible presence of anthrax spores. Within weeks, tens of thousands of samples had been submitted, but we had only 5 laboratories in the entire country that were equipped to test for anthrax. In some instances when a white powder was found, all the workers in the building were evacuated. Some so-called “first responder” teams put the workers through showers just as they would after a chemical attack. It was entirely uncalled for but, at that time, emergency teams had received little or no training in how to deal with a biological incident.

It was a shock to the country. It was clear that every town and city was at risk. All had to be prepared to deal with an outbreak, possibly an epidemic of anthrax or possibly smallpox—little more than a year later SARS made its appearance. Our state and local health departments were understaffed; laboratories were small and equipped to deal with only a few types of organisms. Our CDC laboratory staff was technically skilled and responding as best they could. However, it was impossible to meet the demands of an uninformed public. CDC epidemiologists were available but limited in what they could achieve given the inadequacies of our existing emergency communications systems and the lack of local public health

resources. A stockpile of antibiotics had been created, but there was no plan for their distribution. This was the status little more than 10 years ago in the US.

Our country, as well as others, had become complacent about the possible threat posed by new or emerging infectious diseases. There were local teams prepared for emergency rescue of victims and evacuation of the injured following accidents. In areas prone to forest fires, there were experienced local fire fighters. For dealing with a surprise infectious disease epidemic, such as SARS or pandemic influenza, local public health resources were poorly equipped to handle even modest-sized epidemics of well-known pathogens. Emergency assignment of a handful of health staff was a band-aid when confronted with a potentially widespread biological threat. Nor could the country depend on the national guard or army reserve, however willing they might be. Informed and prepared leadership at the national level was important, but the threat and response was at the local level.

Our Congress acted within months after the anthrax attacks to provide \$3 billion in emergency funds to strengthen our national efforts for preparedness and response. The appropriation provided for the development of emergency communication and control centers, for epidemiologists, for laboratory expansion, for research to identify effective vaccines and drugs as countermeasures, for the development of educational materials, and for hospital planning for dealing with large numbers of casualties. There was a lot that needed to be done. Most important was the fact that one-third of all funds were specifically directed to the development of services at the state and local levels and to hospitals to prepare to receive unexpectedly large numbers of infected patients.

The SARS experience demonstrated that Mother Nature, if you will, could potentially be more dangerous and destructive than a terrorist. With the emergence of SARS, it was clear that we had to be much more conscious and concerned about infectious diseases wherever they might be found. With the pace and extent of modern travel, what was happening in Mexico or Australia or Saudi Arabia or the Congo today could well be echoing across countries in any continent within days or weeks. Improved and sustained rapid communication with WHO and other countries was critical. There was a need, as never before, for up-to-date national and international communication and cooperation, and—more than ever—for planning, for research, and for training.

Indeed, there was a broad overlap in resources needed to counter the challenges posed by new or epidemic diseases by terrorists using biological weapons and by threats posed by emerging infections, floods, earthquakes, or tornados.

The SARS epidemic reinforced the need and the motivation of those at all levels. Years would be required to build needed competence but there was a new spirit. However, as time has passed, so have memories of SARS and of the anthrax cases. Hopefully, the recent threats posed by MERS as well as H5N1 and H7N9 influenza strains will serve to remind everyone of timely preparedness. Our leaders must understand that if there is a large fire spreading rapidly through a town, it is too late to decide whether or not buy a fire engine.

An Earlier Day

The SARS experience was an important event in altering our attitudes toward the necessity for public health resources. I decided today that it might be helpful to remind you of an even earlier time when our own country and a number of others as well became mistakenly overconfident in our ability to deal with infectious diseases. It was a period beginning around 1960 and extending over the next 30 years. During this period I was deeply engaged in infectious disease programs at CDC, in directing the global WHO's smallpox eradication campaign, and as Dean at Johns Hopkins. From my earliest years at CDC, it had seemed to me that, the infectious diseases posed continuing, major national health problems throughout the world and that they deserved a far higher priority and more attention than they were receiving. From a global perspective, it was apparent that much more could and should be done with preventive measures and feasible programs that were available but not being funded. At that time, the industrialized countries were becoming increasingly preoccupied with chronic diseases. There was no question but that these presented pressing problems in our aging populations. Many argued for sharply curtailing infectious disease programs in favor of chronic disease initiatives. To me, it seemed

that there was so much more that remained to be done in the infectious disease field—so much more that could be done inexpensively—that I decided that my focus should continue in the field of infectious diseases.

It may be difficult for those of a younger generation to appreciate that, during this period I am referring to, there were many in the industrialized countries who were supremely complacent about infectious diseases. MacFarlane Burnett, Australian scientist and Nobel Laureate, publicly argued in the 1960s that we were reaching the end of an era—the demise of the infectious diseases. This he attributed to ever more effective antibiotics and new vaccines. Robert Petersdorf, President of the Association of American Medical Colleges stated at a 1985 national meeting that we had so many infectious disease specialists in training that they soon would have little to do but culture each other. The reason being that the remaining problems were marginal and that attention should now turn to the chronic diseases. Indeed, during the 1980s, Departments of Infectious Diseases in a number of medical schools were merged into other departments. When I became Dean at Johns Hopkins, I was stunned to discover that our infectious disease faculty in epidemiology consisted of only one person.

It was during this era of disinterest in infectious diseases that the 1966 World Health Assembly decided to undertake smallpox eradication. A smallpox eradication program had long been advocated by the Soviet Union and a number of developing countries, but there were strong objections by others to undertaking the program. Massive decade-long global malaria eradication programs were collapsing at that time. Most scientists doubted the potential for the eradication of any disease. International travel was far less extensive than today, and patients with so-called "tropical diseases" were few in number. A resolution in the World Health Assembly to undertake smallpox eradication was opposed by almost half of the countries as well as WHO's Director-General. The decision to go ahead passed by only 2 votes.

The program started under a dark cloud and with few resources. However, it made surprising progress. Five laboratory directors agreed on a protocol for producing a stable freeze-dried vaccine and helped laboratories in the developing countries to test and manufacture it. More than 250 million doses annually were the product. A new vaccination instrument was invented and a new technique for vaccination became universal; field epidemiology led us to continually modify traditional strategies to meet real problems; human monkeypox cases were found that superficially resembled smallpox, but that disease proved to be no problem; WHO's smallpox staff never numbered more than 150 and, at one time or another, citizens of 73 different countries served in the program. A considerable number were young, creative, tireless, and dedicated. National leadership and their staffs were energized. During the concluding years, as many as 150,000 national staff became involved at key points in the program. Much to the surprise of everyone, smallpox eradication succeeded. It missed its 10-year target but by only 9 months. The last case occurred in October 1977. The numbers of smallpox cases *each year* decreased from 10 million to zero; an annual toll of 2 million deaths was averted. It was a remarkable campaign that required all countries to participate and, under WHO auspices, it had succeeded. The program proved to be surprisingly inexpensive and was well received, even in areas where vaccination itself had previously been unknown.

We advocated that the program be broadened, and this was approved by the World Health Assembly in 1974. It began by including vaccines for measles, polio, diphtheria, tetanus, and whooping cough. It was named the "Expanded Program on Immunization." Other vaccines are now being incorporated and new vaccines are under development.

A New, Grim Reality is Recognized: Emerging Viruses

In 1982, only 2 years after smallpox eradication had been confirmed, it was announced that a new virus had been recovered from a mysterious, deadly disease that was only beginning to be characterized. It was HIV, the human immuno-deficiency virus, the cause of what we now call AIDS. The disease spread steadily across the world. Enormous sums of money supported studies in many of the world's finest laboratories with the best scientists. The immediate goal and need was for a preventative vaccine and for curative antiviral drugs that would eliminate the virus. So far, both efforts have failed. Costly new drug therapies administered daily can keep the virus at bay but, to date, there is no cure. Programs to deter virus spread by behavioral changes have

proved partly successful, but the epidemic continues. Some 35 million people are now infected and the count is steadily increasing. It is the fourth leading cause of death in the world today. It was a virus unknown to the world community before 1982.

Soon after the virus was characterized, critical questions arose. Where did the virus come from and how long has it been around? Are there other viruses which could perhaps pose an even more serious threat to the future of mankind? The African tropical rain forest was undoubtedly the geographic source of this virus. Similar viruses had been isolated from monkeys in this area. In the tropical forest areas, human populations are sparse and healthcare facilities are scattered. Thus, it is possible that human cases could have been occurring and spreading for decades before being detected. Its startling occurrence emphasized the point that we all dwell within One World; as new organisms grow and spread, they could be of importance to all, and even better methods for detection and more open communications are needed as never before.

As the 21st century progresses, it is apparent that citizens in all countries are increasingly being exposed to a stream of different organisms as population density increases and mega cities grow. Meanwhile, the organisms themselves are continually mutating, continually changing as they multiply. With increasing numbers of travelers, and many who are exploring biologically rich and diverse tropical areas, we can expect to see many more organisms over the years ahead.

In 1989, at the instigation of the distinguished Nobel Laureate Joshua Lederberg, a special symposium of some 40 leading infectious disease experts was convened by the Rockefeller Foundation and the National Institutes of Health. They were asked to examine seriously the possibility of the "emergence of new infectious agents as threats to human existence." Seven years had passed since HIV had been discovered, and little progress had been made in prevention or control. Confidence had been shaken in the capabilities of our ever more sophisticated research laboratories to cope with such new microbes.

A 2-day meeting explored the questions in considerable detail. As a last item, Lederberg posed the question: "Is it possible that some day we might have to cope with a newly emergent virus infection that produced few or no acute symptoms, like AIDS, that was difficult to detect; that spread widely; and that could produce a rapidly fatal disease. In brief, might this be a pandemic disease which would provide too little time for the development and production of new drugs or vaccines." There was a long pause, and then a quiet response by one of the most distinguished of the virologists who said, simply: "Yes, I'm afraid that is possible." Lederberg concluded by pointing out that "mankind's only competitors for dominion of the world are the viruses ... and the ultimate outcome is not foreordained." I personally was stunned. I had never thought of the threat in such terms.

Surveillance: A Primary Building Block for Preparedness

A primary factor for coping with this threat is a surveillance system to detect a new organism—to provide an alert that there are a number of serious cases, possibly an outbreak, of an unfamiliar disease that should be investigated and response measures taken. For smallpox eradication, the pattern was for each health center to report suspect cases weekly. In response, a small team was to go to the site, confirm the diagnosis, identify other cases, and vaccinate contacts. Smallpox, with its distinctive rash, was reasonably easily identified. But, as we were to discover, fewer than 1 in 20 cases actually were known to national authorities. As reporting rapidly improved, local health staff realized that there would be a response to reports, providing assistance for control. They were not simply being filed away somewhere. In some countries, we found that there was notification of other kinds of serious outbreaks, motivated by the hope that a team might come to provide help. Except for smallpox, a team seldom came.

To date, the current emphasis for surveillance in many countries is the detection of severe influenza-like respiratory diseases—primarily pneumonias—and the development of laboratories capable of making definitive identification of agents. This is understandable. The need for early detection of SARS, MERS, and pandemic influenza outbreaks is unquestionably critical. However, at present, there seems to be a primary emphasis on

harvesting ever larger quantities of data from whatever source so as to feed it into ever more competent computers in order to generate all manner of graphs, spot maps, epidemic curves, etc.

However, there are a number of important newly emergent infections which are not associated with severe respiratory disease. Some have a potential to cause outbreaks and perhaps widespread epidemics. As forecast in the original 1989 meeting on emerging viruses, they are increasing in number. They include viruses such as Ebola and Marburg; monkeypox; encephalitis-causing viruses; the Nipah and Hendra viruses found in Australia and South Asia. Large-scale data collection systems could not be expected to detect outbreaks of these diseases at an early stage and they haven't. How were they discovered? In most instances, it has been one or a few astute physicians who were concerned about the patients; interested and responsive government officials who received the reports; and qualified health staff who went to investigate. Specimens were obtained and laboratory studies followed.

It seems to me that what is most critically needed is a sensitive system whose central core is a designated national surveillance unit, perhaps with subunits at state or local levels, with responsibility to be in close touch with those in the field and in major hospitals where serious cases might be admitted. Provided there was frequent contact with those in the field, early detection and investigation of significant outbreaks should be possible.

International Communication

If SARS taught us nothing else, it demonstrated the essential importance of prompt and continuing communication among countries and through WHO. This has been facilitated by the 2007 International Health Regulations which call for countries to report within 24 hours anything that "may constitute a public health emergency of international importance." The regulations also allow for WHO to follow up on informal reports about diseases.

In the past, countries sometimes did not report cases, fearing that trade sanctions might be imposed or that tourist trade would be damaged. During smallpox eradication, there were 2 such instances, once in Africa and once in the Middle East, when reports of cases were denied for considerable periods by countries, albeit they worked on their own in endeavoring to control outbreaks. In both instances, we at WHO were well aware of the cases, but the countries denied the reports. They used inferior vaccine and inadequate control measures. This resulted in a persistence of spread and, in each country, more than 1000 cases of smallpox and more than a year for special control measures. The countries' prestige were likewise seriously compromised. Neighboring countries even publicly lectured officials responsible for the negligence. This should not be allowed to happen again.

It is impossible to know what future challenges must be faced, but we know now that there will be more frequent challenges than in the past. SARS was a startling new disease that fortunately was able to be stopped. Without the continuing communications that took place, without an up-to-date flow of information as to the nature of the disease, information about control procedures, therapies, laboratory studies—what seemed to be working and what did not—there could readily have been not 8000 cases but 1000 or more times that number.

I look forward to what promises to be an interesting and informative meeting.