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GLOWING VISIONS THROUGH A DARKENED GLASS

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It is both an honor and a pleasure to be invited to present one in your series of distinguished lectures on international health. There are today regrettably few academic centers with a serious, sustained and meaningful program in the field of international health. Happily, the University of North Carolina represents one of few beacons in the field and Dr. Sagar Jain, one of the ablest of its ambassadors.

For more than 35 years, my primary interest and principal avocation has been international health. My interest germinated at the Centers for Disease Control as a result of being challenged in the field by several epidemiological adventures of multiple outbreaks of staph enterotoxin diarrhea in Puerto Rico and subsequently, outbreaks of poliomyelitis and influenza in the South Pacific, and botulinus food poisoning and smallpox in Argentina. In dealing with each of these outbreaks, it quickly became evident that application alone of epidemiology and technology were inadequate. To understand the problem and to devise a solution, one inevitably had to probe for an understanding of the health system, of the culture and of the society itself.

One quickly developed insights and a better understanding of the country and its people than one could ever do as a tourist. Indeed, for me, it ruined forever my appetite for being an ordinary tourist. I found, on return from my travels, that I dealt with domestic health problems with a keener insight and perception of options than ever before. Indeed I found I came to appreciate the potential of public health as I had not in working in the U.S. There was no question but, that I benefitted far more from the experiences than I contributed. In all of this, however, I never ceased to be impressed by how much was being accomplished by so many with far fewer resources than we had at our disposal in the U.S. At the same time, it was apparent that much more could be achieved with better strategies and even modest increments in resources.

In 1960, I returned to Atlanta from three years in training determined to expand the EIS international role from what had been an occasional, perhaps once a year international consultation. Working opportunistically with AID, Peace Corps, the Army, WHO and NIH, we succeeded in rapidly expanding the EIS international program to the point where five years later there were, simultaneously, not less than three

teams on international assignment. And coincident with this, we noted a sharp increase in retention of our two-year Public Health Service draftees -- and an institutionalization of the EIS program itself. Our young epidemiologists, like I, had come to appreciate better the challenge of public health from experience in another setting.

The challenges we faced translated into new initiatives in our research program at CDC. We embarked on studies to ascertain the possibilities for administering not one but many virus antigens simultaneously. We sought more rapid and efficacious methods for administering smallpox vaccine and better diagnostic methods. Each of these and many others translated into practical applications for Third World settings and often, indeed, changes in health practice in the U.S.

Assistance to USAID in a measles vaccination program in West Africa led to our proposing to USAID that a regional smallpox eradication -- measles control program be undertaken and, soon after this was agreed, the World Health Assembly was stimulated to call for an intensified global smallpox eradication campaign.

Quite unplanned and unexpected was the demand of the WHO's Director-General that I direct the global smallpox program and so in 1967, I assumed residence in Geneva. A recapitulation of the eradication saga is properly the subject of another lecture but certain observations during the campaign proved to be significant in future international programs. During early field operations, it quickly became apparent that, by employing a community-based vaccination strategy, upwards of 90 percent of a population could readily be vaccinated at a far faster pace and at lower cost than we had ever imagined possible. This contrasted to coverage of 40 to 60 percent when primary health centers alone were utilized. It seemed to us wasteful not to be employing other antigens as well -- at least DPT, measles and polio vaccines, then in widespread use throughout the industrialized world. In the Third World at this time, not more than 5 percent of all children were receiving these vaccines. As our earlier studies at CDC had shown, the simultaneous administration of as many as nine or ten antigens was both safe and efficacious. And so, in late 1969, we proposed an expanded program of immunization embracing six different antigens. This initiative was slow to receive financial support but eventually it materialized as the primary pillar of UNICEF's Child

Survival Revolution. Now, more than 80 percent of the world's children are being immunized with these antigens. Poliovirus transmission appears to have been interrupted throughout the Western Hemisphere and a global eradication effort is in progress. Community based interventions now extend across a number of fields. And indeed, the importance of immunization has recently begun to receive priority attention in the U.S. itself.

My Geneva years ended after 10 years when it became apparent that smallpox cases were disappearing and that smallpox experts were becoming redundant at WHO. What better task than for someone with no marketable skills than to become a Dean. Happily, it was at Hopkins, a school with long-standing international health interests. During my stay at Hopkins, our international program grew to encompass a full-time professional staff of more than 100 persons.

My intent on leaving the deanship was to return to full-time involvement in international health at what I perceived to be an especially auspicious time for undertaking new initiatives. I shall refer to these

later. However, I was unexpectedly approached and persuaded by the President's Science Advisor to incorporate my international health interests into a larger portfolio working out of an office on Pennsylvania Avenue in Washington. This proved to be a fortuitous appointment which has given me an opportunity to examine and to plan for international health activities extending across several agencies of government and with international agencies.

I apologize for this rather lengthy preamble to problems which I would like to address today but I felt it was important that you know where I come from and can anticipate certain obvious biases which I shall express.

In considering international health challenges today, it is important to appreciate what an unprecedented, staggering change has already taken place in health over a span of little more than three decades. Simple markers illustrate what I mean. In 1960, life expectancy for the world as a whole stood at 53 years; today it is 65 years, -- a 12 year gain in 30 years. In the Third World, life expectancy is now comparable to

that of the U.S. in the 1930's. In 1960, over 19 percent of children died before their fifth birthday; today, the figure is 9 percent. Most remarkable is the fact that this trend continued throughout the 1980's, a decade in which the GNP in much of the Third World stagnated or regressed. Indeed, during the 1980's mortality data for 16 lower and lower middle income countries whose per capita income actually declined show a 2.3 percent annual decrease in under 5 year old mortality rates. Smallpox has been eradicated and polio transmission throughout the whole of the Western Hemisphere appears to have been interrupted. Vaccination programs are now in place which are reaching more than 80 percent of all children by the time of their second birthday. Never in history has any government program systematically reached such a large population. Fertility has declined in virtually every country and in some dramatically. Most important, I believe, is the fact that community-based health programs have expanded successfully and rapidly. These are increasingly accepted and more such programs are planned.

Many of the advances in health in the Third World and some of the technologies which have been devised have had a direct, measurable impact on our own health care system. Smallpox vaccination has ceased with a net annual financial saving of more than \$300 million dollars. Polio has remained absent from this country despite our disastrously low vaccination coverage thanks in large part to the elimination of polio by other countries in the Western Hemisphere. Oral rehydration therapy, originally devised for the Third World, is now coming into use in this country. The concept of giving multiple viral antigens simultaneously, originally evaluated to facilitate Third World immunization programs, has become accepted practice in the U.S. Quite as significant are the techniques learned in conducting community-based programs in the Third World -- now beginning to be applied in U.S. programs. Certainly, many more examples could be offered.

As impressive as the progress has been, the potential for accelerating the pace of change has been transformed over the past decade by the revolution in biomedical research and in biotechnology. As

techniques have emerged which permit us to discern and manipulate the basic genetic structure of vectors and infectious agents, we can foresee a whole new array of vaccines, of contraceptives and of vector control technologies. We are not quite to the point of being able to design the specific tools needed for any conceptualized need but that time can be foreseen.

It is a heady time to embark upon a career in international health -- or is it? Much has been written and much said about the global village, about the emergence of a new world in a post cold war era, about the interdependence of nations and peoples what with the enormous growth in trade and travel. Despite all this, health priorities and research programs continue to divide neatly between those of the industrialized countries and those of the Third World. U.S. support for international health programs is modest indeed, perhaps reflective of a U.S. society which I perceive to be more parochial than it was 15 or 20 years ago. The NIH budget today allocates less than 2 percent of its funds for international activities. Even then, much of that flows to other industrialized countries including, for example, more than 70 percent of all international research fellowships

and more than 90 percent of all senior international fellowships. The record in other industrialized countries is not better. A number of academic centers proclaim their commitment to international health but it is uncommon to find in any, more than a handful of faculty who have engaged in more than an occasional consultation or tourist safari. No wonder that an IOM Committee convened in 1988 to examine U.S. capacity to address tropical infectious disease problems concluded that "(U.S. expertise is) insufficient to ensure U.S. ability to cope with more than occasional domestic cases of these (tropical) diseases . . . and that expertise is not being adequately renewed."

Somehow or other the U.S. must be educated to the fact that this truly is one world and to plan globally with other countries to cope with the world's health problems in its own best national interests. How can this come about?

Challenges and problems are now becoming apparent in two different arenas, each of which commands urgent attention and each of which has specific reference. Both demand approaches involving

infrastructure development, research and training. Both involve the development of component activities which bear specifically on our capacities in the broader field of international health. Many of the activities are overlapping in character. Specifically, these new or newly perceived challenges are: (1) the threat posed by new and emerging microbial agents; and, (2) increasing concerns about the possible use of biological warfare agents.

The emergence and progressive spread of the Human Immuno-deficiency Virus has proved to be a singularly humbling experience both for those engaged in research as well as for those engaged in public health. Before the epidemic emerged, I believe it is fair to say that we as a nation had grown implicitly, if not explicitly, arrogant in the belief that serious infectious disease problems were a concern of the past in our well-sanitized industrial world. The HIV epidemic shattered that confidence. But, it went further than this. It demonstrated that even with extraordinary funding to expand biomedical research efforts, effective

weapons to combat the problem were not readily forthcoming. In fact, as you know, neither a curative drug nor an effective vaccine is at hand or even imminent.

Inevitably, the question had to be asked whether this was an exceptional, aberrant phenomenon or whether we might anticipate other microbial challenges of catastrophic proportion. A meeting was convened in 1989 to survey the field of new and emergent infections and to ascertain the potential risk which such agents might pose. To me, the meeting offered a number of sobering reflections, the most pointed of which was offered by Josh Lederberg who concluded the meeting with these words: "Man's only real competition for domination of the planet remains the viruses" and "the survival of humanity is not preordained."

Subsequently, an Institute of Medicine Committee on Emerging Microbial Threats to Health was convened under the chairmanship of Lederberg and Bob Shope. The Committee's report was released this autumn. The simple fact, amply explicated in the book, is that all human pathogens are constantly mutating, constantly changing their

pathogenicity and their capability of transmission. All such organisms, whatever their origin, whether new or recently emergent, now have an increasing likelihood of survival and epidemic potential, given the factors of increasing population, crowding in ill-sanitated urban areas, and greatly heightened population mobility. The world of today, containing twice the population of a generation ago, with many times more than that now living in urban areas, offers an increasingly rich locus for transmission of microbial agents. Likewise, the potential for these agents to be disseminated widely and rapidly throughout the world is unprecedented. Indeed, such dissemination is precisely what we have witnessed -- not only with HIV but with dengue, Lassa, Ebola and Marburg viruses, Lyme disease, parvovirus, and many others. It is a certainty that over the coming years we will be challenged by many more agents for which we do not now possess adequate diagnostic methods and for which effective therapeutic and preventive measures are deficient or lacking. These conclusions and perceptions are not widely recognized.

A well-defined blueprint for response is difficult to contrive given the breadth and complexity of the challenge. The Committee, however,

has identified critical elements. I should like to refer only to a few of the most important.

Surveillance is identified as the most important of the initiatives if, indeed, new or emerging infectious diseases are to be detected in a timely manner. Globally, surveillance is woefully lacking. Even for well-recognized conditions, surveillance has been low among the priorities even of special programs. In illustration, I cite the World Health Organization's Expanded Program on Immunization which began in 1974, but which for the next 15 years, elected not to develop a surveillance program, even for the vaccine-preventable diseases included in that program.

One cannot help but wonder what might have been the history of AIDS had that disease been detected earlier. Our antennas, however, are short. Little known is the fact that, beginning in 1972 and extending through 1986, WHO supported an extensive surveillance program throughout the rain forests of northern and central Zaire to detect cases of monkeypox and to characterize them epidemiologically. This, of

course, was one of the earliest loci of emergent HIV. Mobile teams working with transponder radios were in continuing contact with an extensive network of government clinics and mission stations in an effort to detect smallpox-like monkeypox cases. More than 300 cases were identified. Given the quality of surveillance which was established -- and it was superb --, it seemed to us wasteful not to extend the scope of the team's activities to embrace other diseases. Among those of known and obvious interest were the newly recognized hemorrhagic infections, Lassa, Marburg, and Ebola virus diseases, among others. And this area, of course, as I noted, was the presumed epicenter for HIV. Our resources were limited and so we communicated with a variety of groups in WHO, USA, and Japan offering an opportunity for special studies if anyone would bear the necessary incremental costs. None expressed interest.

A global surveillance program is recommended by the IOM Committee which embraces four basic components: (1) A mechanism for detecting clinically new or unusual diseases or syndromes; (2) a supporting diagnostic laboratory; (3) a data system for reporting of cases and analysis of reports, and; (4) a response mechanism to investigate

outbreaks and to mobilize control efforts. To me, this defines well the characteristics of a needed network of tropical medicine research centers. To function effectively, such centers would have to be well versed in the expected in order to identify the new or unique.

The Committee identified a second important problem -- provision of vaccines. It recommended that mechanisms be found to support vaccine research and development as well as production. Vaccines are singled out, in particular, because of the obvious implications for prevention and the limited incentive for the private sector to assign resources for their development.

In brief, it is difficult to conceive of how we could possibly address the challenge of new and emerging microbial agents without strengthening and developing a framework well suited to a better understanding of health problems in tropical areas.

The second challenge to which I should like to refer is that posed by biological warfare agents. In contrast to open discussion of the threats

posed by nuclear and chemical weapons, comparatively little has been said about the potential of biological weapons. I suspect this can be attributed, in part, to the fact that biological weapons are not thought to have been deployed in warfare perhaps since Lord Jeffrey Amherst distributed smallpox infected blankets during the Pontiac rebellion of 1763. This has led some to suggest, hopefully, that a higher moral imperative would preclude the use of such agents. Moreover, many engaged in biomedical research understandably regard BW with such repugnance as to make the subject itself an improper one for discussion. Terrorist actions, however, are on the increase.

Many believed and hoped that the BW specter had been laid to rest when President Nixon decided in 1969 to cease research and development on offensive BW weapons. Recall, however, that in part, this decision was predicated on the availability of nuclear retaliation should any country resort to the use of BW agents. This, itself, is a chilling thought. In 1972, an international Biological Weapons Convention was adopted which prohibited the development, production, and stockpiling of biological weapons. More than 100 countries ratified the treaty, among them Iraq,

but the treaty made no provision for verification. Subsequent to 1992, government support for BW research, even for defensive purposes, came under increasing attack when not totally ignored.

Other countries at present regard BW as having a greater potential than what I sense to be the prevalent view among U.S. scientists and policy makers. Twenty years ago, there were only two countries with BW programs; today there are 10 and 20 others that are known to be seeking the technology. As we learned after Desert Storm, Iraq had been engaged in large-scale production of BW weapons with every indication that they expected to deploy them. Russia has had an extensive program which, as we have recently learned, continued in operation at least into the early part of 1992. Among its most recent projects was the development of a multi-antibiotic resistant strain of plague bacillus.

As the microbiologists here would know, BW poses special problems. Reasonably large scale production requires comparatively little space and buildings so used have no distinctive characteristics such as do production facilities for chemical and nuclear weapons. Verification of

adherence to a treaty is thus extremely difficult. Moreover, needed equipment for production has alternative and perfectly legitimate applications making it impossible to deter development of BW capability by embargo of critical production equipment. Finally, the costs of producing quantities of all manner of possible agents are affordable to even the poorest of countries. Those concerned with arms control measures label BW as potentially "the poor man's nuclear bomb." Couple these facts with a post-Cold War era now populated by a host of small, politically unstable countries, some of which espouse and practice terrorism as a legitimate weapon and it becomes apparent why there has been a sudden awakening of interest in BW.

To define a defensive strategy is quite as difficult as attempting to deter or verify the development of BW capacity in a country. Efforts to interdict possible perpetrators are unlikely to succeed given the small volumes of material needed. Thus, the key elements of defense must rely on early detection, prompt investigation and an analytic capacity to deduce the probable origin of the epidemic, perhaps through analysis of the genetic structure of the organism involved. One expert argues the

need for a global network of clinical-epidemiological centers of a character similar to that which the IOM Committee outlined as being needed to deal with new and emerging organisms.

Basic and applied research would also be vital to better understand organism pathogenicity, to identify rapid diagnostic methods and to develop and produce vaccines. Such research is, of course, wholly relevant to international disease problems.

Neither of the two challenges I have discussed have, as yet, a well-articulated strategy or, as yet, a vocal constituency either among scientists or in government. A broader public appreciation of the problems is yet to come. It is imperative, however, that the problem be addressed.

Thus, there are both justifications and opportunities to invest substantially in international health. How best to proceed? For much too long a time, we have intoned the mantra "Health for All in the Year 2000" and pretended this was some sort of program. If the phrase is to be taken literally, embracing the WHO definition of health, this goal

translates into some sort of mystical nirvana in which all disease is banished. The fact that those who invented the term did not expect to be around in the year 2000 tells you all that you need to know about this slogan as having strategic or practical meaning.

Happily, the World Bank has been engaged in an intensive year long strategic planning exercise, led by Dean Jamison now at UCLA, and in which many have participated. The document, a World Development Report to be published in June, lays out, for the first time in my view, a framework for analysis planning and development of health programs throughout the world. I would predict that it may be seen over the decades ahead as a landmark contribution, a watershed development in health throughout the world.

However, the one question which the document does not address and, in fact, cannot address is, quite simply: "Who will lead this effort?" Inevitably, those who provide development assistance play an important role in deciding. Here the world has changed dramatically over the past 30 years. You may be surprised to know that in the early 1960s, the

United States provided 95 percent of all resources for international public health in the Third World. Today, it is perhaps 10 percent. Resources for health are now provided by 18 industrial countries, the World Bank, 4 multilateral development banks, 12 U.N. agencies, 9 OPEC special funds, and between 1500 and 3000 non-governmental organizations. Many, indeed most of these entities, have little professional health expertise.

Technical leadership to help weave together the many disparate and sometimes contradictory strands should logically vest in the World Health Organization. This responsibility is clearly stated in its charter. Until recently, we were most hopeful that WHO would be able to assume that role.

However, as some of you know, the Organization's stature and leadership have eroded appreciably, especially over the past five years. As you may have read in the press, an autocratic Director-General, without vision or presence, has presided over WHO for the past five years and in January, was unexpectedly renominated by the Executive Board of the World Health Assembly to serve another five years. The United

States, joined by the European community, the Nordic countries, Canada, Australia, and the Arab League states strongly opposed his nomination and stated, in so many words, that they had no confidence in his leadership, but to no avail. A combination of special payments to Executive Board delegates and promises of WHO employment, coupled with threats of retaliation by the Director-General's sponsoring country led to a vote of 18-13, favoring his reelection. Subsequent to the vote, WHO's legal counsel informed the Chairman of the Executive Board of illegal financial transactions within WHO and, as we speak, representatives of the external auditor, the Auditor-General of the United Kingdom, are conducting a full-scale investigation. The outcome remains in doubt; the World Health Assembly votes on the nomination in May.

Multilateral agencies and donor countries alike have agonized over the question of what might be done should the Director-General be reelected. In all candor, there is no salutary answer.

We are at a point in time when we anticipate new and insightful guidelines as offered by the World Development Report; at a time when

there is real momentum in international health activities; at a time when biomedical research promises to address hitherto impossible challenges, and at a time when there are more cogent reasons for a truly international health effort than ever before. More than this, I now encounter increasing numbers of some of our alert young people who are both interested and committed to international health. Ironically, at this potential dawn of truly revolutionary development, we find that leadership in the single Organization which is so critical to the future of international health, is catastrophically inept. And through the darkened glass, I offer no solutions at this moment other than to cite the Chinese proverb: May you live in interesting times!