Conference on Emerging Viruses

Surveillance Systems and Intergovernmental Cooperation

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The recent emergence of AIDS and dengue hemorrhagic infections, among others, are serving usefully to disturb our ill-founded complacency about infectious diseases. Such complacency has prevailed in this country throughout much of my career. Indeed, it is a matter of record that in 1968, the Surgeon General, in a speech given at Hopkins, assured his audience that in this country, we had effectively probed most frontiers of knowledge in the infectious disease field, that the remaining problems in this country, were marginal and that attention should now turn to the chronic diseases. It is evident now, as it should have been then, that mutation and change are facts of nature, that the world is increasingly interrelated and that human health and survival will be challenged *ad infinitum*, by new and mutant microbes with consequent unpredictable pathophysiological manifestations. Moreover, as we see with the Hanta viruses and others, their manifestations may be the chronic diseases. How are we to detect these at an early date so as to be able to devise appropriate preventive and therapeutic modalities? What do we look for? What types of surveillance and reporting systems can one devise?

Interestingly, some of these questions have been asked and responded to at least once before. One such time was 1950, soon after onset of the Korean War. It was perceived then that a biological warfare attack on civilian populations in this country was a realistic possibility. A number of different microbial agents were candidates and several of them could be readily dispensed in crowded centers by a lone saboteur bearing no more than an innocuous appearing briefcase. To stop such an act was seen to be all but impossible. However, early detection was vital so that measures could be taken to prevent spread, to treat and/or to decontaminate. Alex Langmuir, then head of epidemiology at CDC, proposed that a special unit be created which would be on 24-hour call to investigate immediately any unusual disease outbreaks. Thus, the Epidemic Intelligence Service came into being. Young medical officers were trained in field epidemiology and assigned to CDC, state health departments and universities. Requests for help were responded to immediately on receipt of a request. The availability of resources which could be quickly mobilized increased the reporting of outbreaks. And, in due course, the states themselves strengthened their own capacity and capability to investigate outbreaks. CDC's role in defining and characterizing a wide range of new challenges is known to you all - from AIDS to legionellosis to toxic shock syndrome to the problems of the 80/81 strain of staphylococcus. What we don't know - and fortunately so - is how rapidly and effectively a biological warfare episode would have been detected and characterized had it occurred.

To detect new or emerging viruses, the challenge we face bears some similarities to the challenge of 1950. We are uncertain as to what we

should keep under surveillance or even what we should look for. Moreover, the challenge differs in that the new or emerging viruses may not occur as outbreaks, as would be expected with biological warfare. Rather, new or emerging viruses may be manifested by scattered single cases - such as presumably happened with AIDS and as now occurs with monkeypox. Secondly, and taking a global perspective, it seems to me most probable that new infectious entities of significance are most likely to first occur either in densely populated areas where crowding and poor sanitation are prevalent or where man, monkeys and other wild mammals live closely together in tropical rain forest areas. In sharp contrast to the 1950 challenge in the U.S., such areas are minimally endowed with curative care facilities which might identify the unusual or unexpected illness. Moreover, they are all but bereft of sophisticated let alone competent microbiological expertise and equipment.

Thus, the 1950 approach in the U.S. of creating a national Epidemic Intelligence Service, while providing a partial answer to detection of new entities, would not alone provide much assurance in other countries that newly emerging viruses would be detected in a timely manner. What therefore might be proposed?

A surveillance system to detect new and emerging viruses must inevitably consist of three components, as any other surveillance system. The first consists of units, customarily clinical, which are capable of detecting unusual cases or constellations of cases. In a tropical area, this is an especially difficult task given the background level of

diverse conditions which present themselves. As was illustrated by Will Downs with respect to Lyme disease, an effective unit must link clinical and epidemiological thinking. Such units are few and far between even in the industrialized world and I need only cite the prolonged delay in identifying the Thalidomide-phocomelia connection in Europe to further dramatize this point.

The second component - Having detected an unusual case or group of cases, there must be a defined channel for reporting the occurrence and a receptive, knowledgeable unit to receive it. Health centers and hospitals throughout the world are customarily requested to provide no end of data and reports to some central unit of government. Our experience during the smallpox eradication program and more recently in the EPI program with respect to tetanus, poliomyelitis and measles, indicates that most statistical reports go to statistical offices which serve an archival function. They are little concerned as to whether reports are regularly received - only whether they have transcribed the correct numbers of reports of cases which are received. Rarely are analyses performed to assess whether there are unusual trends in incidence of any disease.

Finally, there must be some sort of capacity and responsibility at national or regional or international level which is available to respond to unusual events or requests for assistants. Indeed, the existence and responsiveness of such a unit, itself serves to strengthen reporting from the network of clinical units. This has been the strength of CDC and its EIS but such a resource, charged with

responsibility for the surveillance of a nation's health is all but unique. Many illustrations could be offered but let me cite experiences in European countries. The well-known typhoid epidemic in the Swiss ski resort of Zermatt, Switzerland, was basically sorted out by an epidemiologist from Paris' Institute Pasteur, acting outside normal channels. And the origin of the 1965 epidemic of variola minor in the United Kingdom, a laboratory-oriented outbreak, was worked out by a CDC epidemiologist sent to the U.K. as an observer. Admittedly, these events occurred some years ago but the situation today is little improved.

In summary, we are not today either well-structured or staffed on a global level to detect either new or emerging viral diseases.

To identify the needs of a sensitive surveillance system which would detect new disease entities within a reasonable time frame, I found it helpful to consider different basic epidemiological characteristics of a new disease which need to be anticipated. One manifestation of a new entity might be an outbreak form involving perhaps a hundred to several thousand clinical cases over a limited time frame and geographic area. If there were a number of associated deaths with rash and/or hemorrhagic manifestations, recent experience would suggest that even in most remote areas, they would soon come to notice and assistance in dealing with them would be sought. I would cite the experience with Ebola and Marburg virus disease in illustration. The likelihood of such outbreaks being properly investigated and characterized would depend on national governments utilizing appropriate expertise but to do so they need

assurance that competent assistance would be available to them and could respond in a timely fashion. The CDC has come to be recognized internationally as such a resource.

Could or should the WHO be in a position to discharge such a role? In principle, the answer would appear to be in the affirmative. In fact, however, WHO has pathetically few resources of its own which are not specifically committed to such as AIDS or other categorical programs. The viral diseases unit at headquarters, however defined, consists of no more than five persons. Virus disease programs in most WHO regional offices are staffed by one or two persons only. Inevitably, those who staff such units are prized more for their administrative skills in bringing experts together rather than for their own professional expertise. Another problem for WHO is its basic character as an association of fiercely independent regional offices which basically are resistant to a coordinate responsibility discharged by a central office.

I see no option but to acknowledge CDC as an international resource to fund it appropriately and to acknowledge its mandate in legislation.

Another scenario for a new or emerging virus - less dramatic and less likely to be detected - would be represented by large outbreaks with few associated deaths and/or few of the dramatic manifestations of hemorrhage or rash. Small outbreaks with high case-fatality rates and/or hemorrhage and rash would similarly be more likely to escape detection. Illustrative of such events are the jungle-related yellow fever outbreaks of the 1920s and 1930s and the variety of outbreaks

detected during the certification period of smallpox eradication. During the period of certification of smallpox eradication, we actively sought to obtain reports of possible smallpox cases. In such countries, hundreds were reported annually by health service staff, news reporters, travelers and private citizens. Most were outbreaks of measles with associated deaths, some were chickenpox involving adult populations and some were typhus. In general, they were brought to notice within a matter of a few weeks to a few months. Had the national health services not been seeking to receive outbreak reports and to investigate them, most would probably not have come to official notice. The lesson I would derive from this is that national Epidemic Intelligence Service units, developed on the CDC model, would serve to encourage outbreak reports and would serve a valuable surveillance function. In part, these could be built in conjunction with the intensified polio surveillance systems now in place throughout the Americas and which we hope will expand worldwide as the goal of global eradication is addressed. A few countries have already adopted the EIS model with encouragement and training support from CDC. It would seem logical and prudent to work with WHO in encouraging the expansion of such services, at least to the larger countries and those in the tropical rain forest.

A more difficult problem is posed by new or emerging viruses which cause only sporadic cases or comparatively few severe cases over a finite time span. Such presumably was the scenario for the emergence of HIV. This poses the most difficult problem of all. Such cases might be identified and characterized at a reasonably early date if seen in a reasonably staffed and equipped clinical center which was knowledgeable of tropical

diseases and could identify the unusual and unexpected. Unfortunately, there are few such centers anywhere in the world and, indeed, there are few persons with real expertise in tropical medicine in either the industrialized or developing countries. In our own interests, let alone the interests of populations living in the tropics, it would seem prudent to foster the development of a network of units with expertise in tropical medicine. Cost alone would necessarily curtail the number which could be established but, with time and a mandate to provide training, it should be possible to expand national capacities. Here, we have much to learn from those in the agricultural sector. Beginning with initiatives taken by the Ford and Rockefeller Foundations in the early 1960s, a network of international agricultural centers has developed, now funded by many governments and agencies. In all, there are now more than 25 and these, in turn, have stimulated the creation of a complementary network of national centers. More than 50 U.S. academic institutions have received core support to permit them to relate to and participate in the international network. For health, there is exactly one comparably supported international center and only a handful of U.S. academic centers which received from NIAID extremely modest support for a few specific programs in tropical medicine.

For purposes of improving a woefully inadequate surveillance program, I would argue for the development of a network of internationally supported health centers which, in developing countries, I would recommend be based in periurban areas of major cities in the tropics. The periurban areas are customarily where migrants and travelers from rural areas are found. A clinical facility in such an area would thus

serve to provide a window on events in surrounding rural areas. Preference, I believe, should be given to more densely populated areas and those near the tropical rain forest.

I would propose that such centers have several components: (1) a clinical inpatient and outpatient service for infectious diseases; (2) supporting diagnostic laboratories which, as needed, could serve as a locus for research studies; (3) an epidemiological unit which might serve as the national EIS resource and which would be engaged in a variety of ongoing studies in a population "laboratory" of perhaps two to five million persons. By focusing research efforts within a defined area, rapport could be developed with local leaders and an invaluable data base would gradually accrue. In the course of various studies pertaining to disease epidemiology and efficacy of interventions, observations of unusual events demanding special investigation would inevitably come to light. (4) An education-training unit for national, as well as international staff. Finally, I would propose that such centers be formally identified as part of a network with designated counterparts in the U.S. (and other countries). The network should include such as CDC, NIAID and appropriate academic centers. It would be hoped that such a network might be sponsored jointly by WHO, as well as other national governments to assure the maximum of stability and legitimacy.

In brief, if we are to have a surveillance system with reasonable prospects for the timely detection of new or emerging viruses, an investment in manpower and capital will be required. Strengthening in

mission, competence and facilities is needed at three levels - internationally, nationally and in selected cities. A beginning has been made or precedents established to address each of the components of such a system, but without a coherent vision of the whole. Thus, CDC serves now to respond to major or unusual epidemics in a number of countries. CDC has fostered the development of national EIS systems and has assisted in training of personnel. Finally, there are some centers for tropical medicine, although none wholly adequate for the purposes we are describing - in Dhaka (ICDDR,B), a number of military medical research units and some national centers (e.g., Thailand). Thus, there is precedent for formally undertaking a broader program. In the best of all possible worlds, WHO would take a lead role but, as I have noted, most would have to conclude that WHO, on its own, would not do well in developing or managing a mixed research-service network such as this. A consortium of donors, a Consultative Group on Health, could be envisioned and indeed some discussions along this line are beginning to take place.

What might this cost? Obviously, it would depend on the scope of activity and this could be infinite. Let me sketch a modest core structure as an initial goal which would begin to approach a counterpart agricultural network which is now being funded.

1. 15 broadly based tropical medicine centers of the type I have outlined - each to be funded at the level of $10 million/year. 50% of which to be provided by the U.S. Net cost $75 million.

2. Expansion and funding of CDC epidemic response to trainining facilities - say $10 million.

3. Core funding for 10 U.S. centers to participate in the netetwork of centers at say $5 million per year or a net cost of $50 miillion.

4. A special grants program of $15 million to address speecial problems.

Add all of this together and you derive a figure of $150x10^{6}. . That figure was not decided by accident. In 1969, a study performeed at CDC showed that the U.S. was spending $150 million annually in vaccccination and quarantine activities to protect itself from smallpox. TThat was considered to be affordable. Today it spends '0'. And bear in mind that those were 1969 dollars - now worth more than $300 milliomn.

Can we afford to invest in such a program? A better question is is whether we can afford not to invest in a program which could be a determminant in our own survival as a species.

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