EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

STRATEGIES FOR THE 21ST CENTURY:

CONTROL OR ERADICATION

D.A. HENDERSON, M.D., M.P.H.

Associate Director for Life Sciences

Centennial Symposium on Tropical Medicine
University of Texas Medical Branch at Galveston

Galveston, Texas

May 31, 1991

STRATEGIES FOR THE 21ST CENTURY -- CONTROL OR ERADICATION

In the field of tropical medicine, it is now especially critical that we look ahead to the next century. As we have heard during this centennial symposium, recent advances in biomedical sciences offer undreamed of vistas for prevention, diagnosis and treatment of that incredible array of tropical diseases which plague the third world. Once, not so long ago, those who specialized in the communicable diseases, were regarded as occupying a niche in a medical backwater. Today, research on the immune system, if not yet on all the pathogens which assault it, is at the cutting edge of biomedical science. A magnificent future beckons which should not be distracted by all too futile policy debates about eradication and control or by evangelists who preach a gospel of eradication without comprehending it. Let me try to offer a perspective on future strategies and some directions for the future.

Eradication, as the ultimate objective for a disease control program, is not a recent development. The concept that it might be possible to eradicate a disease, at least regionally, dates back just a century -- to 1884.[1] That year Congress created a Bureau of Animal Industries whose sole, stated objective was to eradicate a disease of cows -- bovine contagious pleuropneumonia -- which had been imported from Europe 40 years before and had spread across the country. The Bureau was given a 5 year target and, surprisingly, it succeeded. Soon, other animal diseases and vectors began to be targeted.[2] By and large, the programs relied on isolation or slaughter of infected herds -- an approach not well-suited for dealing with human disease.

These experiences generated the belief that there might be a substantial number of microorganisms or vectors which clung so tenuously to an ecological niche that simple measures, thoroughly applied, could upset the balance of nature. Disease eradication programs soon became a familiar concept to the veterinary community.

Eradication programs for human diseases, however, were not discussed until early this century. This is somewhat surprising because smallpox then was a major concern; vaccination was widely employed, at least in Europe and North American; and quarantine measures were widely applied to keep the disease out os smallpox-free areas. But no one spoke of smallpox eradication as a concept or objective until the 1950s. Meanwhile the first eradication programs were launched, respectively, for hookworm in 1907 and yellow fever in 1910.[3,4] The basis for these campaigns was more firmly based in visionary belief than in scientific understanding of the diseases and their ecology. Both were products of the philanthropy of John D. Rockefeller.

The magnitude of the efforts were extraordinary, even by contemporary standards. Hookworm programs eventually extended over 52 countries on 6 continents; yellow fever programs and laboratories were developed throughout the Americas and some African countries. The programs were highly centralized and quasi-military in nature. Progress was measured by inputs -- for hookworm, it was the numbers of treatments administered and the number of privies constructed; for yellow fever, it was the number of dwellings inspected and treated to destroy Aedes aegypti mosquitoes. Neither program sought to measure the numbers of cases of the disease in question and their decline in incidence -- or lack thereof. Neither had a

program for research. The belief quite simply, was that the tools were available. The problem was solely an administrative one -- to apply them.

Not until 10 years after the hookworm campaign began was an effort made to assess the impact.[5] When this was done, it was discovered that, even with an optimum program, the prevalence of infection was unchanged. However, those infected did have fewer worms, on average, and thus fewer symptoms. For the yellow fever program, more than 15 years were to elapse before the jungle reservoir of the disease was detected.[6] When it was, the target was shifted from yellow fever eradication to Aedes aegypti eradication with little consideration given to either the cost or practicability of hemisphere wise extermination of a mosquito species.[7] That program in various guises extended for another 30 years before finally being abandoned as impractical.

With the discovery of DDT, malaria eradication became the next campaign to emerge -- in 1955 -- and this was not a regional but a global commitment.[8] Its genesis rested more on evangelistic commitment than upon sound science. In fact, although billed as global in scope, it was recognized that existing methods then offered no hope for the whole of sub-Saharan Africa.[9] Nevertheless, a research program was not high on anyone's agenda. Conversely, many existing research centers were closed in the conviction that the necessary tools were available. All that was thought to be required were sound administration, national commitment and money. Jeffery, a senior statesman, ruefully pointed out: "The science of malaria control . . . was almost overnight converted to the rather simplistic technology of

malaria eradication, which basically required that one know how to deliver 2 grams of something to every square meter of a sometime elusive wall."[10] McGregor lamented the diminishing number of "malariologists" and the proliferation of "eradicationists."[11]

The same quasi-military, highly structured methods were used as with yellow fever eradication. Seventeen years later and after an expenditure of more than $2 billion, it was apparent that eradication was nowhere in sight. And the program gradually began to be phased down. Efforts began to be made to reconstruct a once-robust research activity but there was little left to build upon.

In 1965, about the time it was becoming apparent that malaria eradication was not a viable concept, Rene Dubos published his book, Man Adapting. In the book, he reflected the views of many in the science community when he wrote: "Public health administrators, like social planners, have to compromise with the limitations of human nature. For this reason, and many others, eradication programs will eventually become a curiosity item on library shelves, just as have all social utopias."[12]

Clearly, there was widespread disillusionment with eradication programs as public health policy. The year of my arrival in Geneva -- 1966 -- was not an auspicious time for a neophyte eradicator to assume direction of a budding smallpox eradication effort. It was discouraging but not surprising to find that antipathy towards smallpox eradication extended from the Director General throughout the Organization and indeed to many national health administrators as well. Even the initial WHO smallpox budget of $2.4 million had been controversial. That budget

provided just $50,000 per year for each country where a program was needed but it passed by only 2 votes with 12 nations abstaining.[13] No WHO budget, before or since, has proved to be so divisive as that one. Contributions were sparse. During the first seven years of the program, the combined cash contribution of all donors amounted to less that $200,000 per year. UNICEF, a major supporter of malaria eradication refused to support the program as did many bilateral contributors. Indeed, smallpox eradication, as other categorical program, was considered suspect and derisively labelled a "vertical" program to be discouraged if not abandoned. I will not further dwell on the issue and the manifestations. The important point is to appreciate how damaging unrealistic eradication programs had been to public health credibility.

Two features, in particular, distinguished smallpox eradication from previous eradication efforts. These proved critical to its success: surveillance and research. The goal, as we saw it, was a simple and specific one -- zero cases of smallpox. To measure progress we needed a reporting system and this was given priority. Systems were established to assure weekly reporting of cases from all health units in all infested countries. Through the data which flowed in, we learned that the distribution of smallpox and its manner of spread was quite different from our original planning assumptions. We learned that vaccine immunity was far more durable than any had believed and we discovered that little of the vaccine in use met acceptable standards. With this information, program strategy continually evolved in an on-going effort to bring to bear the maximum of resources where the problems were greatest.

A plea for research funds was initially denied by WHO on the grounds that a good vaccine was available; that the epidemiology of smallpox had been thoroughly studied; and that the sole problem was an administrative one -- to vaccinate everyone. After a year, a $40,000 research budget was reluctantly agreed upon and with this, we were able to leverage a broad scale cooperative research program. This resulted in changes in the smallpox vaccine strain, in the methods of vaccine production, in the basic vaccination instrument, in the discovery and characterization of monkeypox and, finally, in the sequencing of the virus -- a development which resolved some very contentious issues related to possible animal reservoirs.

Neither disease surveillance nor research were important components of earlier eradication efforts. Those programs were driven more by evangelism than by science, by emotion more than reason, by the belief that answers lay primarily in diligent administration, by the belief that it was better to try and fail than not to try at all. By the time smallpox eradication was decided upon, the most feasible of all programs, public credibility was at a low ebb. We have now recaptured some of that credibility.

Today, proposals are regularly being advanced to undertake a host of new eradication campaigns -- measles, poliomyelitis, even tuberculosis, leprosy, yaws, urban rabies, hunger and many others.[14] [15] [16] However, as public health professionals, our credibility simply cannot tolerate another debacle comparable to those of the past with all the attendant repercussions.

Have we learned from these experiences of the past? With notable exceptions, the answer has to be -- not well. The clarion cry to eradication is regularly sounded by some as an attention-getting, fund-raising initiative albeit with little expectation of achievement of the objective. The stated rationale is that it is better to try and fail than not to try at all. Such scientific charlatans are to be deplored. Regrettably often they continue to receive an undeserved hearing and respect.

There are three specific programs, however, which deserve comment -- two are stated global objectives -- for Guinea worm and polio; one, for measles, is widely regarded as perhaps the next target. The Guinea worm campaign, whose champion and guiding spirit is Don Hopkins, is proceeding exceptionally well. When it began, it readily passed the primary acid test of having already been demonstrably effective in some developing countries. Adequate methods were available to interrupt transmission and, through research, these have been steadily improved. Surveillance, conducted primarily by area-wide search, has proven its worth and is steadily improving. And, finally, its strategy has steadily evolved based on empirical experience. If adequate resources and national commitment can be sustained, it should be successful. The biggest problem is that it is a disease of the rural poor, a group not high on the priority list of governments or donors.

The experience with measles has been quite the converse. Many have argued -- and passionately -- that global eradication is vitally important because of the severity of the disease. None can argue with this premise but because eradication is desirable doesn't mean it is feasible. To be noted is the fact that no industrialized

country, let alone a developing one, has yet succeeded in stopping transmission for more than a matter of a few months. A more antigenic vaccine, one which could be given at or near birth, conceivably could provide the necessary opening to eradication -- and there are lines of research which might open the way to such a vaccine. However, few are being explored and those in a more casual than deliberate effort.

The saga of global polio eradication is more encouraging but only so in its launching. A brief recapitulation of events illustrates the problem. In 1985, the Director of PAHO called together a small group to advise on the feasibility of a regional eradication effort.[17] WHO's expanded program on immunization had been operative for a decade and polio incidence in the Americas had fallen dramatically even in the tropical areas where the oral vaccine was known to be generally less effective. After due deliberation, we concluded that eradication was a conceivable objective with the caveat that due attention be paid to the development of surveillance and to research. Funds were promised from UNICEF, AID, the IADB and Rotary. A major stumbling block, however, was that none saw the need for research and only one agreed to make such funds available -- and then only with great reluctance.

The director of that program, Dr. Ciro deQuadros, has proved to be an impresario of uncommon skill. Within a year after the program began, surveillance revealed distressingly large numbers of type III cases among well-immunized children. Field studies were immediately undertaken which showed the need to double the type III component of the vaccine, the first modification of the vaccine in 20 years. Quite

promptly, the type III problem disappeared. The surveillance program called for reporting of all cases of acute flaccid paralysis in young children, once considered to be all but pathognomonic of polio. To everyone's surprise, acute flaccid paralysis in young children, even in polio free areas, was far more prevalent than any had expected. Rates of 1 to 2 cases per 100,000 children under 15 years of age were common. A range of clinical studies were needed to help refine diagnostic criteria. A network of laboratories was established and stool specimens were collected. With support from program funds, Kew and his CDC colleagues sequenced the virus strains which were isolated and discovered distinct regional variations in strains. He showed also that the variations were sustained over time. This suggested that polio did not spread easily or frequently over long distances. Surveillance data complemented this observation in showing that the epidemiology of the disease most closely resembled smallpox, i.e., it was widely prevalent over a country during peak seasons but retreated to crowded urban settings during the interseasonal low. DeQuadros utilized these findings to develop a strategy which called for intensive house-to-house vaccination campaigns in lower socio-economic areas during interseasonal periods. Polio incidence dropped precipitously. In brief, the program rapidly changed and adapted in response to a good surveillance and research program. Today, a network of 10,000 health posts report cases of acute flaccid paralysis every week, 80% of which are detected within 2 weeks of onset and from 80% of them, stool specimens are obtained.

In 1988, WHO decided that the progress in the Americas justified launching a global eradication program.[18] In candor, its feasibility had to be questioned if for no

other reason than that the vaccine is so heat sensitive as to require refrigeration up to the point of administration is of such poor antigenicity in tropical areas that seroconversion cannot be assured with as many as 5 doses. It is, at best, marginally satisfactory for Latin America. For Africa and must of Asia, a far less developed infrastructure of services makes it a doubtful commodity indeed. Those who expressed reservations about a global program were assured by WHO that a research program would be vigorously pursued. Three years have elapsed, few funds have been found for needed research and little progress has been made. Surveillance programs are still vestigial; reporting is more often monthly than weekly; and most countries depend on information from only a few sentinel sites. The dominant theme which reaches through all discussions is that we have a protective vaccine; and that the problem is basically an administrative one.

Polio eradication is inevitably a far more difficult proposition than smallpox eradication, given the problems of surveillance and accurate diagnosis. Even with a vaccine which is thermostable at ambient temperatures for a month or more and which is fully protective with one or at most two doses, the task will be difficult. We must recall that smallpox eradication succeeded but by only the narrowest of margins and that the basic infrastructure of services in many developing countries has changed very little over the past 15 years.

Eradication of a disease is a difficult, complex task for which we need far sharper tools than we now have. Thus you will understand my gloomy appraisal that, on entry into the 21st century, I foresee, at present, little prospect of even being able

to contemplate global disease eradication except possibly for Guinea worm. The current problems in eradication exemplify to me a far more basic and serious problem which pertains to all tropical diseases. That, quite simply, is the lack of resources for research. This derives, in part, from limited understanding on the part of program managers of the potential created by progress in biomedical research especially over the past decade and, at the same time, the lack of comprehension by so many who are doing basic research as to the practical needs of those in the field. The case for research is simply not being made and development agencies, in consequence, are funding precious little. A schism has been permitted to grow -- and perhaps has been encouraged -- between administrators of health programs and those in the research laboratories. In part, the fault lies with a generally traditional administrative cadre who are most comfortable with what they know than with the unknown and uncertain. In part, the fault lies with those in basic research, the majority of whom reside in industrialized countries far removed from the tropics and assert little interest in the application of what they discover or in learning about diseases and their manifestations under natural settings.

It seems to me that one fundamental approach to begin to cope with this problem rests in the development of a network of multidisciplinary centers firmly anchored in the countries which daily must cope with tropical infections. Where better to decide priorities, where better to link presently insoluble disease problems with the biomedical research which might provide the answers.

Much has been written and said by the development community over recent years regarding the need for capacity building both of institutions and people. So far, there has been little but rhetoric in the health field. There are those who would argue that one philanthropy has been extended quite far enough and that unless such a program could be defined in terms of a national interest, it is a non-starter. Happily, Lederberg, Morse and their colleagues are now providing an all too obvious raison d'etre in calling attention to the potentially devastating problems posed by new and emerging viruses and other microbial agents.[19,20] As they have pointed out, if we are to have any hope of dealing with a newly emergent microorganism, an HIV-like infection, for example, a contemporary swine flu or who knows what other agents, early detection and an accelerated research agenda are the only possible answers. To achieve this, there is absolutely no choice but to have effective sentinel centers in countries around the world, especially in the tropics and near densely populated lower socio-economic areas of third world countries. It is in our own interests as well as theirs. In fact, our very survival could be at stake. It would seem to me that this is a rationale for an investment worthy of as much attention as, for example, a super-conducting supercollider.

Let me conclude by suggesting that debates over what or whether we eradicate or contain are idle exercises. Without far better tools and a far better understanding of diseases in the tropics, satisfactory disease control, let alone eradication, is simply not in the cards. Rather the thrust of one policy should be to staff and support a research infrastructure working in optimal locations to ask the right questions.

1. Hinman, E.H., World Eradication of Infectious Diseases, Springfield, Thomas, 1966.

2. Hagan, W.A., The control and eradication of animal diseases in the United States. Ann. Rev. of Microbiol., 12:127-144, 1958.

3. Fosdick, R.B., The Story of the Rockefeller Foundation, New York, Harper and Brothers, 1952.

4. Strode, G.K., ed. Yellow Fever, New York, McGraw-Hill, 1951.

5. Smillie, W.G., The results of hookworm disease prophylaxis in Brazil, Amer. J. Hyg. 2:77-95, 1922.

6. Soper, F.L., Jungle yellow fever: new epidemiological entity in South America. Revista de higiene e saude publica, 10:107-144, 1936.

7. Duffy, J., ed. Ventures in World Health. The Memoirs of Fred Lowe Soper, Washington, Pan American Health Organization, 1977.

8. Pampana, E.J., A Textbook of Malaria Eradication, London, Oxford University Press, 1963.

9. Downs, W.G., A new look at yellow fever and malaria. Amer. J. Trop. Med. and Hyg., 30:516-522, 1981.

10. Jeffery, G.M., Malaria control in the twentieth century. Amer. J. Trop. Med. and Hyg., 25:361-371, 1976.

11. McGregor, I., Malaria-recollections and observations. Transactions of the Royal Soc. Trop. Med. and Hyg., 78:1-8, 1984.

12. Dubos, R., Man Adapting, New Haven, Yale University Press, 1965.

13. Fenner, F., Henderson, D.A., Arita, I., Jezek, Z., Ladnyi, I., Smallpox and Its Eradication, Geneva, World Health Organization, 1988.

14. Stetten, D., Jr., Eradication. Science, 210:1203, 1980.

15. Hopkins, D.R., Hinman, A.R., Koplan, J.P., Lane, J.M., The case for global measles eradication. Lancet 1:1396-1398, 1982.

16. Hopkins, D.R., After smallpox eradication: yaws? Amer. J. Trop. Med. and Hyg., 25:860-865, 1976.

17. deQuadros, C., Polio eradication: fulfilling the first EPI promise, Protecting the World's Children: An Agenda for the 1990s, Task Force for Child Survival, pp. 79-102, Atlanta, 1990.

18. World Health Organization Global Eradication of Poliomyelitis in the year 2000. Geneva, World Health Organization (Resolution WHA 41.28)

19. Lederberg, J. Medical science, infectious disease and the unity of humankind, JAMA 260:684-685, 1990.

20. Morse, S.S., and Schlenderberg, A. Emerging viruses: the evolution of viruses and viral diseases, J. Inf. Dis. 162:1-7, 1990.