

**Eradication of Infectious Diseases:
Useful Strategy or Utopian Dream**

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The twentieth century has celebrated the effective control of a number of important infectious diseases--including smallpox, poliomyelitis, diphtheria and measles. For the industrialized countries, the great scourges of the past--yellow fever, plague and cholera--are effectively history. For the first time, a disease, smallpox, has been eradicated from the globe; a second, poliomyelitis, is effectively limited now to tropical Africa and south Asia with hopes for eradication early in the twenty-first century; and Guinea worm disease, now rapidly vanishing, infects but a few countries of tropical Africa. The world is a far healthier place than it was a century ago. In fact, in most parts of the world a child born today can expect to live to more than 70 years of age, double his expected life span when this century began.

These remarkable twentieth century achievements can be attributed primarily to comparatively simple, straightforward measures--better sanitation, safer water supplies, improved nutrition and a few simple vaccines and chemicals. Still to be exploited is the potential of advances in technology and the biomedical sciences of more recent years. Inevitably, the question is posed, "Why should we be content with mere control of the major infectious diseases? Why not eradicate them entirely?" All manner of candidates have been proposed--from tuberculosis to measles to hepatitis to urban rabies.

Will disease eradication be a principal public health theme for the twenty-first century? Or are we to heed the cautionary advice of the eminent biologist, Dr. Rene Dubos. He was convinced that man, microbial diseases and the environment are so closely interrelated as to preclude the possibility of a microbial agent ever being exterminated. He was so skeptical of eradicationists as to state, "*eradication programs will eventually become a curiosity item on library shelves, just as have all social*

utopias.” They have survived, however, as witness the fact that there are today global eradication programs for both poliomyelitis and Guinea worm, currently the only two active programs in a series of eradication efforts begun over the past 85 years. Most of these have been long forgotten--and for good reason.

(**SLIDE 1**) The first planned program to eradicate a human disease dates back to 1909 when the Rockefeller Foundation launched a hookworm eradication campaign, first in the United States, later extending to 52 countries on six continents. It was based on mass treatment and the construction of sanitary facilities. The strategy and the glowing predictions for success were based primarily on hope and on optimistic evangelism, rather than on sound science. Nearly 15 years were to elapse, however, before the program was critically evaluated and it was shown that this strategy, in fact, had not significantly reduced hookworm infection rates anywhere. The program died a quiet death.

Meanwhile, beginning in 1915, the Rockefeller Foundation launched, in the Americas, a yellow fever eradication campaign with the announced expectation of eradicating the disease within five years. They expected that similar programs in Africa would soon follow. However, the campaign proved to be far more difficult and costly than had been anticipated and so it never extended beyond the Americas. Finally, it foundered when it was discovered that the yellow fever virus had a natural jungle reservoir. The yellow fever eradication effort was then shifted to an attempt to eradicate the urban mosquito vector of yellow fever, *Aedes aegypti*. It was postulated that if this species of mosquito were totally exterminated, there would be no way for the virus to be transmitted from person to person. That may have been correct. However, eradicating a well-established mosquito vector from the whole of the western hemisphere proved to be a formidable task, far beyond the scope of the available technology and resources. Efforts gradually waned and finally stopped during the 1950s.

(**SLIDE 2**) The 1940s brought yet another eradication campaign--against yaws. National yaws programs extended over 61 countries. They sought to eliminate infection by mass screening and treatment with penicillin. After 20 years, however, that program

finally had to be abandoned when it was discovered that the yaws spirochete was successful in continuing to spread despite the best efforts of the field teams.

Finally, in 1955, the most ambitious of all eradication schemes, that for malaria, was blessed by the World Health Organization. As with each of the preceding eradication campaigns, the decision to launch the program was more heavily grounded in visionary enthusiasm than in sound science. The strategy relied on the use of a new insecticide, DDT, to be sprayed on the walls of dwellings. Mosquitoes, after biting a patient, customarily settled on adjacent walls but were killed by DDT and therefore unable to transmit infection further. Over a 20-year period, more than \$2500 million was expended. The programs proved to be far more complicated and costly than anticipated. Increasing insecticide resistance became a problem. For most of Africa, it had been known from the beginning that the insecticide strategy did not work, but no other solution was found. By the mid-1970s, yet another extensive and costly eradication effort had collapsed leaving as a legacy very little compared to the cost of the program.

By the 1960s when the question arose as to the feasibility of smallpox eradication, politicians and health professionals alike were extremely skeptical of any eradication effort. Each of the preceding eradication campaigns had been launched with fanfare and hopelessly optimistic forecasts of success. They all collapsed after some 15 to 20 years when it became apparent that the microbial ecology was different from what had been assumed; that the available technology was inadequate; and that needed resources were, in any case, far greater than estimated. Thus, when the World Health Assembly, in 1966, considered a proposal for smallpox eradication there was widespread skepticism among scientists and politicians alike. Eventually, this initiative with a ten-year goal, was approved but only by a very narrow vote. UNICEF, however, as well as several national assistance agencies made it clear at that time that they would not support the smallpox eradication program or any other eradication effort--and they did not!

Nevertheless, the smallpox campaign made excellent progress, and in 1977 the last case occurred, just nine months and 26 days beyond the targeted goal. Eradication was officially certified in 1980 and with certification, vaccination ceased throughout the world. The disease has not recurred. As the person responsible for the smallpox eradication program, I note, with feeling, that while it was successful, it succeeded only by the narrowest of margins.

(SLIDE 3) Given the stimulus of the victory over smallpox, two other global eradication programs have since been launched. Both were better grounded in sound epidemiology and the demonstration of practicability than had been earlier efforts. The polio eradication initiative began in the Americas in 1985 and as good progress was made, it was extended globally in 1988 with a target of the year 2000. The Guinea worm eradication program began in 1986 with the goal of eradication being 1995. In both campaigns, progress has been encouraging. Poliomyelitis was eradicated throughout the Western Hemisphere in 1991. Many other countries are free or virtually free of the disease, including many of those in Europe, east Asia and North Africa. Programs are progressing in most other countries. The principal endemic countries include India, Pakistan, Bangladesh, Afghanistan and Nepal in Asia, as well as the tropical sub-Saharan countries of Africa. By the end of 1996, the incidence of Guinea worm had been reduced to 150 000 cases from an estimated 3.5 million cases ten years earlier. Less than 10 000 villages remain infected in 15 countries of tropical Africa, Yemen and one state of India

Contrasting costs and benefits of disease eradication and control

While in progress, disease eradication campaigns are more costly and demanding than control programs. Such campaigns require that effective efforts extend throughout all areas of all countries which are infected or at risk of infection; more sophisticated surveillance systems are required to assure early detection, diagnosis and control of cases; and more elaborate quality assurance measures are needed to ensure that all targeted areas and populations are satisfactorily dealt with.

The added costs of an eradication program can be recouped many times over if the effort is successful and conventional control measures can be significantly reduced or stopped. For example, the total costs for smallpox eradication were \$100 million in international assistance over a 13-year period or less than \$8 million per year. When the program began in 1967, the annual cost of smallpox to the world was more than \$1000 million each year. That cost is now nil.

However, obtaining the added resources for an eradication campaign poses special problems. Not surprisingly, the most infected countries are usually those which are the poorest and least able to bear the costs. Thus, a successful program requires that the wealthier countries support the efforts of the poorer countries and they, in turn, must agree to give the program requisite political and moral support. Logic would suggest that the disease-free wealthier countries would readily support eradication campaigns at least against such diseases as smallpox and poliomyelitis to better protect their own populations from the risk of disease importation. However, experience shows that most industrialized countries have contributed to these two campaigns either reluctantly or not at all. Indeed, resources for the two existing eradication initiatives are today far less than could be effectively used.

Criteria for assessing candidate diseases for eradication

If other eradication programs are to be considered, it would be important that they be critically and objectively reviewed before international policies are decided. Had this been a systematic practice of the past, none of the many wasteful, failed efforts would have been launched. Five principal determinants are proposed as minimum criteria to be met before an eradication program is launched.

(SLIDE 4) 1. There is no natural reservoir for the organism other than man. Most infectious agents are not candidates for eradication because the responsible organism infects naturally both man and other mammalian species or may survive naturally in the

environment. Thus, knowledge of an organism's ecology is crucial and not to be ignored. This was aptly illustrated by the failed efforts against both hookworm and yellow fever.

(SLIDE 5) 2. The recovered patient ceases to harbor the organism and is immune to later reinfection. For those diseases in which the organism continues to be present in the body either in its naturally infectious form or a latent one (e.g., hepatitis B, tuberculosis, varicella), there is little hope for eradication. An eradication effort in such instances would require an effort extending over a generation or more--hardly a feasible proposition given the difficulties in sustaining international commitments to any program for more than 10 to 20 years.

Immunity to reinfection is likewise important. The recovered smallpox or poliomyelitis patient is effectively immune for life against a repeat infection. He cannot spread the disease. Contrast this situation with diseases such as malaria and influenza in which reinfections are the rule.

(SLIDE 6) 3. The preventive intervention is affordable and effective, and logistically practicable to apply. Affordability is critical given the fact that disease candidates for eradication afflict all or most of the poorest countries, where obtaining resources for vaccines which cost as little as US\$1 per dose have so far proved to be all but impossible.

The feasibility of application reflects the realities of the limited transportation, health and communications infrastructures in so much of the developing world. Smallpox vaccine exemplifies an ideal preventive agent--a highly heat-stable product, readily administered, which confers long-term protection to each recipient with a single dose. There is nothing like it. Oral polio vaccine, requiring three to five or more doses, clearly presents greater problems and long-term treatment regimens such as are needed now for tuberculosis control effectively preclude the possibility of eradicating that disease.

(SLIDE 7) 4. The disease is sufficiently important to warrant the effort. Most countries considered smallpox to be a priority and virtually all were engaged in control efforts when global eradication began. Not all countries, however, were able to provide adequate funds to transform a control effort into one of eradication, but all cooperated when international assistance was provided. In contrast, poliomyelitis, for example, compared to other disease problems, is not a priority for developing countries. It is doubtful, in fact, whether an eradication initiative would have begun had not the Expanded Program on Immunization already incorporated polio vaccine as one of six vaccines to be routinely used. Thus, polio eradication grew out of polio control efforts. Most of the added program costs are now being borne by the industrialized countries, the international organizations and by Rotary International. Even so, resources continue to be a significant constraint in this program, making the ultimate outcome anything but a certainty.

(SLIDE 8) 5. Interruption of transmission has been demonstrated to be possible in developed countries and in some developing ones. An eradication program is a costly investment whose benefits will not be realized unless eradication is achieved. Moreover, as has been apparent in almost every program, expectations in terms of strategy, cost and needed duration of effort have almost always proved to be seriously wrong when finally tested in the field. Accordingly, it would be only prudent to demonstrate empirically first on a national and then on a regional scale that the interruption of disease transmission is feasible before embarking on a hemisphere-wide or global effort.

Conclusion

Given this history and experience as background, what can be said for the future of eradication as a 21st century strategy? Most have assumed that one such as myself who has had responsibility for one successful eradication campaign would be enthusiastically embracing other eradication efforts. This is not the case. I do see one

potential application for an eradication effort which I shall mention in a moment. Meanwhile, I believe we will be fortunate indeed to complete successfully what has already been started. What do I mean? I pointed out earlier that the smallpox eradication effort barely succeeded and yet smallpox was by far the easiest of diseases to eradicate; poliomyelitis is perhaps next most difficult. But the differences between the two are enormous. Smallpox vaccine provided virtually complete protection after one dose; polio vaccine in the tropics requires perhaps five to ten doses. The smallpox vaccine could be kept at room temperature for months; polio vaccine has to be kept cold up to the time of administration--a major problem in the tropics. All countries feared smallpox, a disease which all persons eventually acquired and which caused severe illness, high fever, a nasty rash and a 20-30% death rate; polio infection carries no symptoms whatever in 99% of those affected with perhaps one in one hundred developing paralysis. It is not a priority for most of the world. The presence of smallpox virus could be readily detected since every infected individual showed a typical rash; in contrast, most persons infected with polio virus show nothing. Thus polio can and does spread widely, without detection. Controlling spread as we could do with smallpox is not possible. How to deal with polio in countries such as Zaire, Afghanistan, Somalia and Sudan, for example, is far from clear. At least two to three years of stability and access of health teams to all parts of these countries will be required at a minimum to eliminate the polio virus. And yet, in Sudan and Afghanistan, such a period has not occurred for more than two decades. And so long as polio virus infection continues, all other countries have no choice but to maintain their programs lest the virus be imported and spread. And so the potential savings from eradication cannot be realized.

There is one circumstance, an important one, in which the policy of eradication might be both feasible and financially supportable. Should a newly emergent and highly pathogenic microbe suddenly appear on the scene, an eradication effort might well be the best, if not the only satisfactory response. This would assume, of course, that there was no animal reservoir of the agent and that an effective vaccine could be made. Early

detection and early elimination before extensive geographic spread had occurred might well be the best use of resources.

In substance, the question if possible disease control strategies based on eradication can most sensibly and logically be left to academic debating societies--certainly until the two current campaigns are successfully concluded--and that under the best of circumstances is at least a decade distant and quite possibly, a great deal more.

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