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THE SIREN SONG OF ERADICATION

Lilly Lecture

Donald A. Henderson, M.D., M.P.H.

University Distinguished Service Professor

The Johns Hopkins University School of Hygiene and Public Health
Baltimore, Maryland 21205

Address: Hampton House
Baltimore MD 21205
Tel: 410-955-1624
Fax: 410-889-6514
eMail <dhenders@jhsph.edu>

Over recent years there have been increasing numbers of scientists who have advocated that programs of disease eradication and elimination be undertaken and that large sums of money be appropriated specifically for such efforts. Regrettably few of these initiatives have been carefully considered as to their scientific feasibility and even fewer have been subjected to practical field demonstrations.

Caution is warranted in launching such programs. So far this century, seven global eradication campaigns have been launched, only one of which, for smallpox, has succeeded. Four programs have been abandoned and two are in progress with, as yet, an uncertain outcome in prospect. History has shown that eradication programs are not only costly of themselves but that when they have failed, they have left behind a legacy of distrust and rancor..

In the world of infectious diseases today, it is increasingly difficult to discover those who advocate simply the effective control of a disease as a practical objective. Rather, "eradication" has become the popular lure with its implicit promise of permanency and ultimate achievement. All manner of diseases have been and are being proposed as subjects for eradication by would-be eradicators. When the scientific feasibility of that goal is challenged, advocates customarily respond that even if success is not achieved, it is unimportant because with additional funds made available for eradication, the worst that can happen is that the disease will be better controlled. The argument is a seductive one but one fraught with serious risk as I shall elaborate.

In instances in which "eradication" is considered too patently beyond scientific reason, enthusiasts often propose "elimination of disease x as a public health problem", whatever this may mean. At least ten diseases have already been so targeted by one group or another. The exercise in discovering conditions to eradicate or eliminate seems now to be spreading from infectious disease specialists to those concerned with nutritional deficiencies and I'm sure it is only a matter of time before those concerned with the chronic illnesses will be afflicted. In fact, based on recent trends in extravagant goal setting, it is possible that we may eventually have programs with eradication or elimination goals of some sort for most illnesses and conditions. This could leave us with the potentially embarrassing dilemma of identifying some few conditions which we would not try to eliminate so that there might be some cause of death to affix to a death certificate.

The increasingly cavalier use of terms such as eradication and elimination should concern us all for these terms implicitly state policies and promises. When expectations are not met, as in practice most cannot, the credibility of medical and public health professionals is and will be called into question. And this in the past has had serious repercussions.

The epidemic of what I would call evangelistic goal setting began in May 1980. It followed shortly after the declaration by the World Health Assembly that smallpox had been eradicated (1). This was, of course, the first occasion on which a disease

had been vanquished but many forget that it was not the first serious effort to do so but the fifth. Four large scale multi-national eradication programs preceded it -- campaigns against malaria, yaws, yellow fever and hookworm. All had failed and had left little to show for a very large investment.

In 1980, within a month after the announcement of smallpox eradication, an international meeting was convened at the U.S. National Institutes of Health to explore the question of what diseases next should be eradicated (2). This was but the first of a series of eradication conferences. At that first meeting, a surprising list of diseases and conditions was nominated ranging from urban rabies to periodontal disease to leprosy. Some spoke of eradication, others of elimination. A tumultuous discussion eventually culminated in the decision that measles, polio and yaws were clearly suitable for at least regional eradication but that there were many other possible candidates.

One skeptical note was struck at the symposium and that was by the two keynote speakers -- Dr. Frank Fenner from Australia and myself (3,4). We reflected on the broader applicability of disease eradication from our vantage point of nearly 15 years in the just concluded smallpox eradication campaign. Our basic conclusion was that there was at that time no other suitable candidate for eradication. As we pointed out, smallpox had a large number of highly favorable clinical and epidemiological characteristics which facilitated eradication. In addition, we had, as a tool, a highly heat stable vaccine which protected with a single dose. No other disease came close to matching these advantages. Despite this, smallpox eradication was achieved by only the narrowest of margins. Its progress in many parts of the world and at different times, wavered between success and disaster, often to be decided by quixotic circumstance or extraordinary performances by field staff. Nor was support for the program generous, whatever the favorable cost-benefit ratios may have been. A number of endemic countries were themselves persuaded only with difficulty to participate in the program; the industrialized countries were reluctant contributors; and, UNICEF, so helpful to the previous malaria eradication campaign, decided that it wanted nothing to do with another eradication program and

stated that it would make no contributions(1). Several countries made donations of vaccine and a West African program funded by the U.S. government was important. Cash contributions to WHO during the first seven years of the smallpox program, 1967-73, amounted to exactly \$79 500 (5). That is not per year but *in toto* for the entire period. The pall cast by the failed malaria eradication effort was profound.

Given these considerations, it seemed in 1980 to be little more than an interesting academic exercise to debate what next to eradicate (6) and somewhat facetiously, I offered the proposal that we simply eradicate the word "eradication" so as not to be distracted by costly and unproductive quests for an unattainable Holy Grail. This was not a welcome proposal.

The four eradication programs which had preceded that for smallpox each had important lessons to convey but few took the time to examine them. The first of the programs had been directed against hookworm (7). It had been launched by Rockefeller philanthropy in 1909 and eventually extended to 52 countries on 6 continents and to 29 island groups. Through systematic screening and treatment of residents and the provision of sanitary facilities, it was believed that hookworm could readily be eliminated. Not until some 13 years after the program began were field studies conducted to determine whether the objective was in fact being achieved in fact (8). It was not. The worm burden was somewhat diminished but that was all and thus some 15 years after launch, the effort was abandoned.

The second campaign, against yellow fever, began in 1915, again a Rockefeller initiative(9). Its aim was to eradicate yellow fever from the Americas within five years; eradication in Africa was expected soon thereafter. The objective was to control the urban mosquito vector, *Aedes aegypti*, thereby interrupting yellow fever virus transmission. Epidemic yellow fever quickly disappeared but then began to recur in 1928. Only then were mechanisms put in place to detect and investigate all human cases. Four years later, endemic jungle yellow fever was discovered, dooming the program just 17 years after it began.

The third of the eradication campaigns was against yaws. Its launch in 1955 was precipitated by the availability of inexpensive injectable penicillin for the single

dose treatment of cases of yaws. In all, more than 160 million persons were screened and more than 50 million treated in 61 countries. Clinical cases rapidly diminished. Only after some 10 years were field studies conducted to assess progress. It was soon discovered that there were many subclinical infections and these were fully capable of sustaining transmission(10). The program lapsed some 12 years after beginning.

Each of these programs can be seen, in retrospect, to have had three important and fatal flaws. First was the decision to embark upon each of them without first validating, with some degree of certainty, that disease transmission could be interrupted over some large geographical area given the tools then available. The impracticability of hookworm and yaws eradication could have been discovered quickly and a jungle yellow fever reservoir would have become apparent with even a modest surveillance and case investigation effort. Second, none of these programs provided for an on-going program for the monitoring of cases. Thus, in each instance, the programs proceeded for more than a decade before the fact was revealed that not only was the program progressing unsatisfactorily but that eradication was impossible given the available technology. Third, none of the three supported a research program. The assumption was made that the tools were in hand and that all that was required was to administer them effectively.

Finally, there was the malaria program, launched in 1955, about the same time as the one for yaws. The strategy was based primarily on application of the insecticide DDT to the walls of houses. This killed mosquitoes when they rested on the walls after feeding thereby preventing further transmission of the parasite. The malaria program was, by far, the largest of all the campaigns. During its 15 years of existence, it accounted for more than one-third of WHO's total expenditures and its 500 person WHO staff dwarfed all other programs. More than two billion dollars was expended in this effort (11).

The malaria campaign, during its existence, dominated the international health agenda (12,13,14) It was a costly program which in the many countries which were engaged in Latin America and South Asia, consumed a substantial proportion of

national health expenditures as well as major inputs from WHO and international donors. The program failed but lessons derived from malaria eradication proved to be central in shaping the smallpox eradication strategy. Three operating principles were of particular importance. First was the relationship of the program itself to the health services. It was a tenet of the malaria eradication directorate that the program could not be successful unless it had full support from the highest level of government. This translated into a demand that the director of the program in each country report directly to the head of government and that the malaria service function as an independent, autonomous entity with its own personnel and its own pay scales. Involvement of the community at large or of persons at the community level was not part of the overall strategy.

Second, all malaria programs were obliged to adhere rigidly to a highly detailed, standard manual of operations. It mandated, for example, identical job descriptions in every country and even prescribed specific charts to be displayed on each office wall at each administrative level. The program was conceived of and executed as a military operation to be conducted in an identical manner whatever the battlefield. Third, the premise of the program, like the other eradication efforts, was that the needed technology was available and that success depended solely on meticulous attention to administrative detail in implementing the effort. Research was suspended from the very beginning of the program.

Not surprisingly, malaria eradication, like its predecessor eradication campaigns left little as a legacy when ultimately it collapsed.

The smallpox eradication campaign had to function differently. Segregating it as an autonomous entity reporting to the head of state was neither politically acceptable nor financially feasible. With a program budget of only \$2.4 million per year, there was no hope of underwriting more than a small proportion of personnel and program costs. The program necessarily had to function within existing health service structures and had to take advantage of available resources. This proved advantageous, as contrary to common belief, under-utilized health personnel were abundant in most countries. With motivation and direction, most performed well. It

was also discovered that those in the community such as teachers, religious leaders and village elders, could and did make invaluable contributions. Secondly, rigid manuals of operations intuitively made little sense given the diverse nature of national health structures and so broad goals with provision for flexibility in achieving them became the accepted mode.

Finally, research initiatives were encouraged at every level. This occurred despite the opposition of senior WHO leadership who insisted that the tools were in hand, that the epidemiology was sufficiently well understood and that better management was all that was necessary to eradicate smallpox. Research initiatives included the development of new vaccination devices to replace traditional lancets; field studies which revealed the epidemiology of the disease to be far different from that described in the textbooks and, in consequence, the need for basic operations to be modified; the discovery that the duration of vaccine efficacy was far longer than that normally stated making revaccination much less important; and studies which demonstrated conclusively that there was no animal reservoir. Indeed, without the fruits of research, it is highly unlikely that eradication would have succeeded. Even as the last cases were being discovered, a joint Dutch-Indonesian study of a new tissue culture vaccine was just being completed (15,16).

Finally, we sought from the beginning of the program to strengthen the reporting of cases and to use the surveillance data as a quality control measure in assessing progress and in guiding strategy and operations.

These principles, all of which were a departure from past eradication programs, remain remarkably valid today and, as applied in Guinea worm eradication (17) and in polio eradication in the Americas (18) and western Asia, they have proved eminently successful.

One might imagine that the subject of which diseases might next be eradicated would have been a primary topic of conversation among the large and talented group of epidemiologists who, through the late 1970s, were engaged in eradicating smallpox. In fact, I can't recall the question ever having been seriously raised or discussed. Indeed, the question didn't seem especially relevant. This is not to say

that we regarded the eradication of smallpox as an end in itself. Far from it.

At the time the smallpox eradication program began, only two vaccines - BCG and smallpox - were at all widely used throughout the developing world. Few countries had organized national vaccination programs and those that did seldom extended much beyond the larger urban areas; substandard and/or poorly preserved vaccine were in common use; information about disease incidence was woefully inadequate; and effective supervision was generally poor to nil.

Conceptually, as we envisaged it, an effective campaign required the development of a management structure extending from the capital city to the furthest villages; it required that mechanisms be established to assure that fully potent and stable vaccine was used; that plans be implemented within the health service structure to assure its distribution to at least 80% of the inhabitants. It demanded that a national surveillance system be established, then an unknown entity in most of the world; and it required that planning be done and goals established to reach a finite end point within a given period. It seemed to us that a successful program would provide valuable training and experience but, most important, that it would create a skeleton framework permitting other activities to be added. Additional vaccines were obviously a logical further step.

In some countries, the simultaneous vaccination with two antigens began soon after the beginning of the program. In western and central Africa, all countries administered smallpox and measles vaccines; in a number of countries of eastern Africa, BCG and vaccinia began to be given at the same time; and in some countries, yellow fever vaccine was also added. Few developing countries, however, provided DPT, measles or polio vaccine.

With expansion of the immunization program in mind, we in WHO organized, in 1970, an international meeting to review the status of vaccination internationally and to recommend model programs (17). In 1974, this expanded program of immunization was approved by the World Health Assembly; in 1977, program leadership was strengthened and the program began to grow (18).

From the eradication of smallpox in 31 endemic countries to the

implementation of immunization programs for six diseases in more than 100 countries represented an enormous increase in program complexity. Nevertheless, remarkable progress was made in expanding and intensifying immunization activities throughout the world. In 1990, this culminated in the World's Summit for Children and the nominal achievement of the goal of vaccinating 80% of the world's children against six major diseases.

One component of that program which lagged significantly was surveillance. Not all of the EPI diseases lend themselves readily to national programs of disease reporting and surveillance but such appeared feasible, at least for neonatal tetanus, polio and measles. However, persuading governments and health workers, whether national or international, that surveillance is as vital for disease control as for eradication proved to be a formidable task. In fact, until 1985, little progress was made.

At that time, de Quadros, director of the immunization program for the Americas, visualized an approach to spur the development of national surveillance programs (19). The vehicle was the eradication of polio. With polio eradication having been determined to be technically feasible and, in the Americas, practicable as well, the countries of PAHO endorsed the eradication goal and, in so doing, committed themselves to the development of a hemisphere-wide surveillance effort. Sites reporting suspect cases each week increased from some 500 to more than 20 000. Reporting for acute flaccid paralysis was soon extended to include neonatal tetanus, measles and cholera.

During the course of polio eradication in the Americas, new paradigms for community involvement in public health emerged as well as approaches for bringing together public and private sector agencies; national immunization days were demonstrated to be a practicable, often more efficient means for vaccine delivery; new approaches evolved for the planning and integration of international assistance; a hemisphere-wide laboratory network was created; and new mechanisms for vaccine purchase, utilizing PAHO and UNICEF administrative channels, were established. Polio eradication was the visible target of the program but the agenda was far broader

than this and the accomplishments likewise.

With this further background of experience, what now are the lessons for the future? We need first to bear in mind that there are two diseases and only two diseases which the World Health Assembly has committed itself to eradicate - Guinea worm and polio. Guinea worm eradication with Donald Hopkins as its brilliant and persuasive advocate and strategist, has been conducted with all due attention to surveillance, to community participation, to political commitment and to research in shaping an evolving agenda(20). Despite this, it lags behind scheduled targets and it is clear that its successful conclusion will require a high degree of commitment and political skill. The outcome is not a foregone conclusion but I believe it can and will succeed.

Polio programs have only begun in those areas of Africa and south Asia which all but thwarted global smallpox eradication. Thus, the most difficult and problematical areas are still ahead with program implementation notably hampered by its reliance on a heat-labile vaccine whose efficacy leaves much to be desired. While there are expectations that the program can succeed, there is much yet to learn and to be applied before success can be assured.

However, an international commitment has been made and high priority must be given to meeting these goals. A failure, especially in achieving polio eradication, could as certainly call into question the credibility of medical and public health leadership as did the collapse of the disastrous malaria eradication effort 30 years ago.

As we contemplate the future, is it necessary or even desirable to focus on the narrow question of what disease or diseases next should be eradicated or eliminated? Through implementation of the smallpox, polio and Guinea worm programs, innovative breakthroughs have been made in organizing large-scale nationwide campaigns; in devising new methods for approaching and mobilizing communities; in developing effective national surveillance networks and in using the data in evolving better strategies; in fostering effective and relevant research programs to facilitate disease control; and in mobilizing support at international,

national and local levels.

These approaches are revolutionizing and revitalizing public health. Implicit in these new approaches is the setting of measurable goals and a willingness to look at all alternative methods for achieving them. Once it was implicitly assumed that every intervention, every vaccine, every drug had to somehow be directed through or dispensed by some sort of primary health center. Certainly, health centers continue to play an important role but we know that when such as vaccines, micro nutrients and family planning services are taken into the community, when community leaders and volunteers are mobilized, extraordinary results can be obtained. Who would have imagined, for example, that India's health services could mobilize to vaccinate more than 100 million children in a single day?

The new initiatives and new approaches are of special relevance as we endeavor to deal with tuberculosis, leprosy, and micro nutrient deficiencies. Likewise, use of albendazol, ivermectin and praziquantel on a strategically targeted community-wide basis could have a profound effect on many types of symptomatic parasitic disease (21). None of these are conditions to be eradicated in our lifetimes but they are diseases in which far more substantial progress could be made than we are now making while relying primarily on one-on-one traditional curative treatment. As time progresses, it may become apparent that certain of these diseases might warrant an eradication effort or might warrant one if better tools could be made available. However, it is abundantly clear that as of today, there is no disease beyond the two already targeted which are serious candidates for either eradication or elimination.

Thus, in looking to the future, I believe it is critical that we remember the past, that we critically and scientifically analyse our policy options and that we not be blinded to the range of new public health program possibilities by staring fixedly at the blazing beacon of a few eradication or elimination dreams built on a foundation of sand.

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