Chapter **62**

Control and Eradication

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The Controversy: Control or Eradication?

We cannot refrain altogether from examining the roots of this controversy if only because the extreme views for and against eradication have exerted and are still exerting a . . . highly detrimental influence on public health practice.
—P. Yekutiel, *Eradication of Infectious Diseases: A Critical Study*

Eradication of an infectious disease is an extraordinary goal. Its possibility became apparent as soon as Edward Jenner demonstrated an ability to provide immunity to smallpox. Writing in 1801, Jenner observed that, through broad application of vaccination, "it now becomes too manifest to admit of controversy that the annihilation of the Small Pox, the most dreadful scourge of the human species, must be the result of this practice" (Jenner 1801). Louis Pasteur claimed that it was "within the power of man to eradicate infection from the earth" (Dubos and Dubos 1953). And yet, by and large, public health has proceeded with more modest goals of local and regional disease control. Notable successes have occurred. Indeed, some diseases now thought of as "tropical" were previously endemic in temperate climates. Systematic application of hygiene, sanitation, environmental modification, vector control, and vaccines have led, in many countries, to the interruption of transmission of microbes causing such diseases as cholera, malaria, and yellow fever.

Intensive efforts to eliminate breeding sites of the yellow fever mosquito vector, *Aedes aegypti,* interrupted transmission of this disease in Havana in 1901 and throughout Cuba soon thereafter. Subsequently, yellow fever and malaria were able to be controlled in Panama, thus permitting construction of the Panama Canal. In 1915, the Rockefeller Foundation launched an effort to eradicate the disease worldwide. Transmission appeared to have ceased in the Americas by 1928, but then cases reappeared, and by 1932, it became clear that a nonhuman endemic focus was serving to reinfect areas otherwise free of yellow fever. In the 1930s, F. L. Soper set out to eradicate the *Aedes aegypti* vector from the Americas. By 1961, Soper reported that he had largely succeeded except for the United States, where the program received little support. By the 1980s, *Aedes aegypti* had become reestablished in Central and South America.

In 1953, Brock Chisholm, the first director-general of the World Health Organization (WHO), tried to persuade the World Health Assembly (WHA) to undertake smallpox eradication, but a number of countries objected on the grounds that eradication was not technically feasible. Instead, in 1955, under the leadership of his successor, Marcolino Candau, WHO began a global effort to eradicate malaria primarily by means of household spraying of DDT. The relatively sophisticated science of malaria control was abandoned in favor of this simplistic technology (Jeffrey 1976). Despite an expenditure of more than US$2 billion, the effort failed.

Even while the malaria eradication effort was under way, the Soviet Union, in 1958, proposed to the WHA that smallpox be eradicated. A resolution to this effect was offered in 1959 and passed unanimously. However, the resolution provided little international funding or support. Over the next seven years, disease transmission was interrupted in some 30 countries in Africa, Asia, and South America, but endemic smallpox persisted in the Indian subcontinent, Indonesia, most of Sub-Saharan Africa, and Brazil. WHO launched an intensified effort in 1967 to eradicate the disease within a decade. This new

resolution included an annual budget of US$2.4 million, to be paid according to the WHO scale of assessments. The resolution passed by the narrowest of margins, but a reinvigorated effort was soon under way and paved the way for a historic public health achievement (Henderson 1988). Following an extraordinary worldwide effort, the last case of smallpox was isolated in October 1977, and the disease was certified as being eradicated in 1979, 170 years after Edward Jenner first dreamed of that possibility. Understanding how and why smallpox eradication succeeded is essential to the study of control and eradication.

The smallpox success was inspirational, even though the leaders of WHO's smallpox eradication effort cautioned that, among all the diseases that might be considered candidates for eradication, smallpox was unique (Fenner and others 1988) and that they foresaw no other disease as a candidate for eradication (Henderson 1982). At a meeting convened by the Fogarty International Center of the National Institutes of Health in 1980, scientists, public health officials, and policy makers discussed the merits of eradicating other diseases, with schistosomiasis, dracunculiasis, poliomyelitis, and measles identified as possible candidates (Henderson 1998a). However, no consensus was reached at that time on moving forward with any of those diseases.

Poliomyelitis became the next principal target when mass vaccination campaigns, proposed by Albert Sabin (1991), proved remarkably successfully in Cuba and Brazil. In 1985, an American Health Organization coordinated campaign was launched to interrupt poliovirus transmission in the Americas by 1991, and this effort succeeded. Some believed that global eradication might be possible, although others were concerned that the far less developed infrastructure of health, transportation, and communications services in many parts of Asia and Africa would make it an unachievable task. In 1988, the WHA adopted a resolution to eradicate polio, but at that time, a longer-term strategy for ending polio vaccination was neither formulated nor agreed on by the public health and scientific community.

The WHA has adopted only one other resolution to eradicate a disease—guinea worm, or dracunculiasis. The eradication of this disease can be achieved by applying simple technologies for providing water that is free of the vector copepod and parasite and for treatment of patients with the disease. This eradication program has made steady progress but has been hampered in part by civil and political unrest and lack of program priority because of low mortality and low incidence in some remaining endemic areas. However, given the environmental restriction of the parasite to rural tropical areas and its relatively low transmissibility, eventual global eradication seems within reach.

One other case—that of measles—is worth noting. A number of public health authorities have raised the possibility of eradicating that disease. In the Americas, spurred on by the success of regional cessation of transmission of wild poliovirus, eventual consensus was reached to intensify measles control efforts, primarily through surveillance and periodic pulse application of measles vaccine in national campaigns. As a consequence, transmission of measles virus was temporarily interrupted in the Americas on several occasions but reestablished again by importations (CDC 1998a). Although the U.S. Centers for Disease Control and Prevention (CDC) and WHO have advocated extending measles "elimination" through vaccination campaigns and second-dose opportunities to other regions (Biellik and others 2002; CDC 1998a, 1998b, 1999a, 1999b, 2003d, 2004b, 2004d, 2004f), the intensive control efforts required to break transmission of this highly infectious agent make global eradication unlikely at this time.

DEFINITIONS

Yekutiel (1980, 5–8) provides an excellent treatise on the concept of *eradication,* which includes a summary of the multiple definitions that have been formulated (Andrews and Langmuir 1963; Cockburn 1961, 1963; Payne 1963a, 1963b; Spînu and Biberi-Moroianu 1969). A conference devoted to eradication held in Dahlem, Germany, in 1997 (Dowdle and Hopkins 1998) set out to provide precise definitions for *control, elimination*, *eradication*, and *extinction* in a biological, economic, and political context (Dowdle 1998, 1999; Ottesen and others 1998); however, a number of eminent public health officials (Cochi and others 1998; de Quadros 2001; Goodman and others 1998b; Henderson 1998b; Salisbury 1998) challenged these definitions at two subsequent meetings at the CDC (Goodman and others 1998a, 1998b) and the U.S. Institute of Medicine (Knobler, Lederberg, and Pray 2001).

Unfortunately, broadly accepted, standard definitions for key concepts pertaining to disease control and eradication do not exist in the literature. Making matters more confusing, certain of the concepts have been given names that are part of our everyday language and so are easily misinterpreted by nonspecialists as meaning something different from the meanings understood by those who are preoccupied with eradication programs. Most unfortunate is the all too casual use of the words *elimination* and *eradication* to promote programs that cannot reasonably be expected to achieve the promise implicit in these words. Moreover, the two words themselves are commonly used interchangeably.

Control

Two concepts are central to this chapter: control and eradication. By *control,* we mean a public policy intervention that restricts the circulation of an infectious agent beyond the level that would result from spontaneous, individual behaviors to protect against infection (Barrett 2004).

Although control is a range rather then a level, a particular level of control may be an aim of policy. Because every choice entails consequences, choice of the "optimal" level of control requires economic analysis. *Optimal* here is defined in relation to the model that gives rise to the result. Control is local and so needs to be looked at from the local perspective. Because one country's (or region's) control may affect other countries (regions), a global perspective exists as well. The level of control that is optimal for one country (region) may not be optimal from the perspective of the world as a whole. Thus, a need exists to distinguish between, say, a locally optimal level of control and one that is globally optimal.

Finally, control requires ongoing intervention. Sustaining a given level of control requires an annual expenditure.

Eradication

Eradication differs from control in that it is global. The term denotes the certified total absence of human cases, the absence of a reservoir for the organism in nature, and absolute containment of any infectious source. Eradication permits control interventions to stop or at least to be curtailed significantly. Finally, eradication is binary. Control levels can vary, but a disease is either certified as eradicated or not.

Every disease can be controlled, even if only by using simple measures, such as quarantine. The ultimate achievement of control is eradication. But not every disease that can be controlled can be eradicated. Very few diseases, in fact, are potential candidates for eradication. The criteria for the feasibility for eradication as a preference over control are discussed in the section titled "Economic Considerations."

Elimination

Control and eradication are the essential concepts, but two other terms bear mention. The first is *elimination.* Some who are concerned with eradication programs have explicitly defined this term to denote the cessation of transmission of an organism throughout a country or region. In contrast, *eradication* is defined as a global achievement. Like control, elimination is location-specific and would require ongoing interventions to be sustained in order to prevent reemergence of the disease from microbe importations.

Two problems exist with the term *elimination.* First, it has been used to describe different phenomena, not just that described in the definition given above. For example, some public health officials have promoted programs aimed at "eliminating a disease as a public health threat," which is interpreted to mean reducing incidence to an "acceptable" level but not necessarily to zero. This usage is very different from the one outlined above and is almost certain to be misunderstood. Second, the definition of the word *elimination* in common use, as applied to disease control, is indistinguishable from eradication. The 1993 edition of the *New Shorter Oxford English Dictionary,* for example, defines *eliminate* as to "remove, get rid of, do away with, cause to exist no longer." This same dictionary defines *eradicate* as "pull up or out by the roots, uproot, remove or destroy completely, extirpate, get rid of." This ambiguity invites misunderstanding among those not intimately involved in an eradication effort. For purposes of clarity, we seldom use the term *elimination* in this chapter and then only to signify control measures sufficient to interrupt microbe transmission in a specified area.

Extinction

Finally, the literature sometimes refers to *extinction* as a possible policy goal. In the context of infectious disease control, the concept is problematic for two reasons. First, proving that an organism has become extinct is impossible. To do so would require demonstrating not only that the organism no longer exists in nature but also that it no longer exists in any controlled environment—a practical impossibility. Second, de novo synthesis of viral agents from published genomes (Cello, Paul, and Wimmer 2002) now put the concept in peril, although much research remains to be done in this area. Extinction, in the context of infectious diseases, may no longer be irreversible.

Clearly, policy making will be improved by stating the goal of any particular intervention in precise language.

FRAMEWORKS FOR ERADICATION

Numerous issues need to be considered in planning expanded control measures that lead, possibly, to regional cessation of transmission or global eradication of disease. These complex issues will be further examined in the chapter.

Scientific Considerations

Scientific considerations include the nature of potential reservoirs for disease-causing microbes or their vectors, technologies available for interrupting disease transmission, changes in host capabilities to deter infections and disease, and satisfactory containment of organisms in laboratories.

Geographic and Environmental Controls. The limit of endemicity for microbes and their associated diseases is determined in part by their ability to exist in nature outside the human host. Both geographic and temporal variations determine the ecological niche of microbes, resulting in variable annual incidence rates throughout the world. This niche limitation is further extended to intermediary vectors and hosts in complex biological systems. Natural environmental barriers also may isolate the habitats of helminths. Infectious agents that are not limited to an environmentally restricted intermediary

host or those that have longer latent periods, thereby allowing translocation, may have a global pattern of distribution. Examples include the highly transmissible viral agents such as measles, rubella, influenza, and varicella. Although these agents are not geographically constrained, their transmission patterns are directly and indirectly influenced by seasonal environmental factors and population-based immunity.

Potential Reservoirs. A microbe and associated disease can not be eradicated if the microbe is capable of persisting and multiplying in a reservoir. Microbes that thrive in nonhuman species may reemerge if control efforts cease, thus leaving human populations susceptible. Similarly, if the infectiousness of a human is long lived or could lead to potential recrudescence, surveillance efforts would have to continue as long as the last individual remained potentially capable of transmitting infection, as would be the case with tuberculosis or hepatitis B infection.

Transmissibility. The inherent rate of a microbe's ability to cause secondary infections is defined by an organism's reproductive rate in a fully susceptible (R_0) and partially susceptible (R) population. The reproductive rate of organisms that infect individuals only once because of durable immunity is inversely proportional to the average age of infection in an endemic area. Agents that cause childhood infections, such as viral respiratory agents, are far more transmissible than helminths and subsequently require more intensive control efforts to interrupt transmission.

Natural Resistance to Reinfection. Many natural infections induce long-lived immunity to reinfection. Although the most commonly used vaccines have been available for fewer than 50 years—less than the lifetime of an individual—they, too, are assumed to offer long-lasting immunity. Because eradication depends on reducing susceptible populations in potentially endemic areas, long-lived protection through immunization or natural disease is important to successful programs.

Laboratory Containment. Laboratory specimens containing the organism targeted for eradication could serve as reservoirs. Considerable effort may be necessary to ensure their maximum security. That these microbes may be inconspicuous in specimens collected for other purposes poses special challenges. This situation is especially true for the poliomyelitis virus, which may be found in many stool specimens collected for studies completely unrelated to current poliomyelitis eradication efforts.

Operational Considerations

Optimization of control requires a fundamental appreciation of the biological systems that govern the ecology of microbes and their intermediary and human hosts. The reproductive rate, R, is influenced by many local factors, including population density (of vectors, intermediary hosts, and humans) and other environmentally determined conditions, all highly variable throughout the world. For a disease to be controlled to stop transmission, the intervention-altered reproductive rate must be maintained below 1.0. At the same time, all reservoirs of the responsible microbe must be controlled.

Three main components of possible eradication programs are

- surveillance, including environmental sampling where appropriate and clinical testing
- interventions, including vaccination and chemotherapy or chemoprophylaxis or both
- environmental controls and certification of eradication.

Each of these components must be undertaken at local, community, national, regional, and global levels. Eradication differs from control in that it is expected to be permanent. Success depends on having adequate surveillance to identify potentially infectious persons and on stopping transmission before infection of a new cohort of susceptible persons arises as a result of births, migration, or the waning effectiveness of prophylactic measures.

Disease Surveillance. Effective surveillance requires a sensitive system to detect the presence of microbes within the environment, intermediary hosts, and clinical cases. Surveillance and response systems need to be more efficient than the rate of transmission of the targeted agent. As eradication progresses, the sensitivity of detection systems must be steadily enhanced to detect all existing foci. Nonclinical or latent infections pose formidable barriers to eradication efforts. Operationally, the need for near-perfect sensitivity comes at the expense of lower specificity. Thousands of skin lesions from suspected smallpox patients were tested in reference laboratories during confirmation of smallpox eradication, and tens of thousands of stool specimens are being examined for poliovirus. Highly sensitive systems used to detect measles cases in the Americas began to identify a greater proportion of rubella and parvovirus infections because of the nonspecific surveillance of rash illness. Such findings are important because the identification of other diseases that mimic the targeted disease can lead to a misdirection of resources. However, the ability to detect such similar clinical cases can serve as a proxy measure for the adequacy of surveillance. For example, identification of a minimum incidence of cases of acute flaccid paralysis that is not related to polio has served as an indicator of adequate efforts of case finding for polio.

Interventions. Interventions to block transmission of the targeted infectious agent should be easy to deploy and adaptable

to diverse conditions, given the global goal of eradication. Cost considerations and local acceptance of the required sacrifices (both short and long term) are crucial for success. Interventions may be designed for environmental control of microbes, isolation (quarantine) of clinically infectious individuals to limit their contacts with susceptible persons, treatment of clinical cases to limit the duration of infectiousness, or reduction in the infected pool of individuals through immuno- or chemoprophylaxis.

Certification. The last tool for eradication is a certification process whereby independent, respected parties certify the absence of disease transmission or the existence of any specific microbe in an uncontrolled reservoir, including laboratories (Breman and Arita 1980). Although certification can be implemented on a regional basis, it must ultimately be done globally. Certification is one of the greatest challenges in any eradication effort, given the exceedingly great difficulty of verifying a negative finding in a reasonably short period of time. When certification is completed, curtailment of control measures should be possible.

Strengthening control efforts sufficiently to achieve eradication is a difficult and expensive task. It requires that scaling up of such efforts occur over a wide area—at the community, national, regional, and global levels. Its efficacy depends heavily on the adequacy of local financial and human resources, as well as on a broad range of logistical factors.

Economic Considerations

Control and eradication programs have many economic dimensions: private versus social net benefits, short-term versus long-term net benefits, and local versus international net benefits. Such interventions also have implications for existing public health programs.

Private versus Social Net Benefits. Individuals have private incentives to protect themselves from disease—by means of vaccination, for example. But when individuals protect themselves—when they elect to be vaccinated—they offer a measure of protection to others by helping limit the spread of infection. In brief, the social benefit of vaccination is greater than the private benefit alone. As more people become vaccinated, the *marginal* private and social benefit of vaccination—that is, the benefit of vaccinating an additional susceptible person—declines. The marginal private benefit is likely to fall because, as more people are vaccinated, the probability of a susceptible person becoming infected falls. The marginal social benefit is likely to fall for the same reason and for one other: as more people become protected, the total number of susceptible persons falls. The marginal social benefit of vaccination falls sharply at the *critical* level of immunization—the level at which *herd immunity* is conferred on all susceptible persons. When a population is immunized to this level, a disease ceases to be endemic, and imported infections cannot spark an epidemic.

This level is determined by the epidemiology of a disease, but whether it pays to vaccinate to this level depends on the economics, and the economics depend in turn on the social costs and not only the social benefits of vaccination. These costs consist of the direct costs of producing, distributing, and administering a vaccine. The economics depend also on the costs borne by the individuals who are vaccinated, such as those incurred by individuals who experience vaccine complications. The proportionate costs of reaching people who live in remote areas and those who are at special risk, such as migrants and the homeless, increase as the fraction of the population vaccinated increases.

The economics of varying levels of disease control depend on the relationship between the marginal social benefits and the marginal social costs of vaccination. As vaccination levels increase, the marginal social benefits of vaccination fall, whereas the marginal social costs rise. Social welfare is maximized where these two relations intersect, which might be called the "optimal" level of vaccination—a level that may or may not achieve cessation of transmission or eradication.

Short-Term versus Long-Term Net Benefits. Control programs require ongoing intervention. Sustaining a given level of protection requires that, over time, a certain proportion of new susceptible persons be vaccinated. Eradication differs from control in being permanent. The economics of eradication must therefore take account of long-term benefits as well as short-term costs.

The long-term benefits of eradication consist of avoided future infections and vaccination costs—a dividend. To calculate this benefit, one projects future infection and vaccination levels in the absence of eradication, attaches values to these, and discounts them. If this sum exceeds the costs of eradication, then eradication enhances social well-being, and it therefore should be undertaken.

In deciding on the benefits of eradication, the cost of future infections and vaccination should ideally be compared with the best alternative to eradication: the level of optimal control (Barrett and Hoel 2003).

The costs of eradication must also take into account ongoing surveillance requirements, laboratory containment, and perhaps the maintenance of stockpiles of vaccine in the chance event of disease reemergence. From an economic perspective, attractive candidates for eradication are those diseases that some countries have themselves targeted for interruption of transmission nationally or regionally.

Local versus International Net Benefits. Control differs from eradication in another important way. Control refers to

location-specific interventions. Eradication, by contrast, is global. In economic terms, eradication is a global public good. No country can be excluded from the benefit of eradication, and no country's consumption of that benefit diminishes the amounts available to other countries. Control, by contrast, supplies only a local public good.

Eradication requires a global effort. A disease can be eradicated only if microbe transmission ceases everywhere. This spatial dimension to eradication is of fundamental importance because no world government can implement an eradication policy; the WHA can declare its support for eradication, but WHO does not have the power to enforce the execution of a national program in support of that goal. The outcome experienced by any country depends not only on whether the country itself eliminates the disease within its borders but also on whether all other countries do so. Indeed, eradication is a weakest-link public good.

Whether eradication is achieved depends on the level of control adopted by the country that undertakes the least control. In practical terms, any country in which disease is endemic can prevent eradication from being achieved. In 2004, the global polio eradication initiative, after investing more than US$3 billion and involving some 20 million volunteers over a period of 16 years, was placed at risk of failure by the actions of one local administration. In the Kano state of Nigeria, local leaders claimed that the polio vaccine was tainted with the AIDS virus and sterility drugs and declined to participate in a national immunization day program. The European Union then declined to pay for the national program in Nigeria, believing the money would be wasted (Roberts 2004). One consequence was the subsequent spread of polio to nine formerly polio-free countries. Concerted efforts by WHO later persuaded local leaders in Nigeria to rejoin global efforts, but special vaccination programs had to be launched over a population area of more than 300 million persons. This situation dramatically illustrated the vulnerabilities inherent in a weakest-link public good.

What are the incentives for states to participate in an eradication effort? To begin, assume that countries are symmetric, meaning that all countries have the same benefits and costs of control. Assume as well that eradication is feasible. Four possible situations then exist (Barrett 2003):

- First, the global net benefit of eradication may be negative—the cumulative programmatic costs outweigh the net present value of the cumulative benefits. In this case, elimination would also yield a negative net benefit to every country, and so no country would eliminate the disease.
- Second, the global net benefit of eradication may be so large that each country would choose to eliminate the disease even if others did not. In this case, all countries would eliminate the disease, and the disease would therefore be eradicated. In these two cases, no need exists for an international policy.
- Third, each country may have an incentive to eliminate a disease only if all other countries have eliminated it. In this case, achieving global eradication requires coordination. Here a role exists for international policy, but all that is required is for each country to be assured that all others will eliminate the disease.
- Finally, and noting that the "last" country to eliminate a disease would get just a fraction of the global dividend from eradication, under some circumstances no incentive may exists for this country to eliminate the disease—even if all other countries have done so and even if the entire world would be better off if it did. This case is the most worrisome, because implementation of the efficient outcome would likely require enforcement.

All this hypothesizing assumes that countries are symmetric, and of course they are not. Some countries gain less from control and would gain less from eradication than others. Some are unable to implement an elimination program, even if they would very much like it to succeed. In these situations, achieving an eradication goal will require international financing and technical assistance, with the countries that benefit most from eradication compensating the other countries for the costs of eradicating the disease. National and international reproach are often expressed if a country lags in its eradication efforts. International financing has been a key element in all eradication programs.

We have thus far looked at eradication from the perspective of only the self-interests of states. But eradication also has implications for development. In particular, eradication has two advantages over control programs. The first is that the rich countries may gain directly if the goal is achieved, giving them a vested interest in ensuring that the goal is achieved. The second is that eradication is permanent, making an investment in eradication financially sustainable. This second advantage is important because financial sustainability has proved to be a key problem for disease control programs in developing countries (Kremer and Miguel 2004).

Vertical versus Horizontal Programs. Control and eradication programs cannot be viewed in isolation. All programs have implications for the delivery of comprehensive primary care services. An important question is whether targeted, or so-called vertical, programs draw critical resources away from other health care programs or whether they serve instead to augment competence and capacity. The evidence is mixed.

Evidence suggests that disease-specific systems can serve to expand polyvalent services (Aylward and others 1998). Smallpox eradication, for example, gave many national governments the confidence to introduce the Expanded Program on

Immunization, with the ability to deliver vaccines and micronutrients in routine schedules and through national campaigns. However, other evidence suggests that some vaccination programs have adversely affected primary health services (Steinglass 2001; Taylor, Cutts, and Taylor 1997) and may have even increased costs. Implementation of international initiatives can also expose conflicts of priorities. The polio eradication initiative, for example, has successfully vaccinated children in the poorest of countries against this disease, but in some of these countries it has failed to timely include the coadministration of measles and other common childhood vaccines, which would have had a much greater effect on child mortality.

DISEASE-SPECIFIC CASE STUDIES

In this section, we apply the reasoning developed previously to provide an empirical analysis of the three most recent eradication programs—smallpox and the two ongoing programs, poliomyelitis and dracunculiasis.

Smallpox

As noted before, smallpox eradication was achieved in October 1977, 11 years after the intensified program began. Following implementation of a rigorous certification procedure, the WHA declared smallpox eradicated in 1980.

Fenner and others (1988) have estimated the annual benefits of smallpox eradication to developing and industrial countries (see table 62.1). These aggregate estimates, obtained by prorating estimates of the benefits of eradication for India and the United States to all developing and industrial countries, respectively, suggest that developing countries benefited more from smallpox eradication than industrial countries. Qualitatively, a consistent picture emerges: smallpox eradication was not only an extraordinary investment for the world; it was also an investment that benefited every country, rich and poor alike.

Table 62.1 Benefits and Costs of Smallpox Eradication
(Millions of U.S. dollars)

	Annual amount
Beneficiary	
India	722
United States	150
All developing countries	1,070
All industrial countries	350
Total annual benefit	1,420
Expenditure	
Total international, on eradication	98
Total national, by endemic countries	200
Combined total, on eradication	298
Benefit-cost ratio	
International expenditure	483:1
Combined total expenditure	159:1

Source: Adapted from Fenner and others 1988.

When the eradication effort began, smallpox was no longer endemic in most industrial countries. Nonetheless, these countries needed to maintain populationwide immunity under the threat of possible imported cases from endemic countries. They would gain from eradication not only through the cessation of vaccination and its associated costs but also by being able to decrease the number of quarantine inspectors at ports of entry and by averting costs of care related to the adverse events from this live vaccine.

The still-endemic countries would also save vaccination costs, although most were vaccinating only a comparatively small proportion of their populations. The greater benefit to them was the avoided cost of disease, including the extraordinary death toll. A number of developing countries had accorded smallpox prevention a high priority, as was evidenced by the number that succeeded in interrupting transmission without international assistance. This list includes China, which was not a member of WHO at the time the eradication effort commenced.

Indeed, and as shown in table 62.1, the still-endemic countries contributed an estimated two-thirds of the US$298 million cost of eradication. International sources funded the balance. If the latter cost is interpreted as the incremental cost of achieving eradication, the benefit-cost ratio of global smallpox eradication was over 450:1, a singularly high figure. Even including the expenditure by endemic countries, the benefit of eradication exceeded the cost by an unusually large amount.

Brilliant (1985) calculated the annual costs of the smallpox eradication campaign for India to be about US$17 million per year, including indirect costs (lost productivity caused by adverse reactions to vaccination) and opportunity costs (health workers being diverted from other programs). These costs were only a fraction of the annual benefits of eradication to India, which, by Brilliant's calculations, were US$150 million. The benefit estimates by Fenner and others (1988) are much larger, and those of Ramaiah (1976) are smaller, but all three studies draw the same (qualitative) conclusion: smallpox eradication was a good investment for India. Basu, Ježek, and Ward (1979, 312) present estimates identical to those in Ramaiah (1976), but without giving attribution.

Originally, India had decided to undertake a smallpox program just one month after the WHA voted to eradicate the disease globally in 1959. The attempt failed, however, largely for administrative reasons (Basu, Ježek, and Ward 1979; Brilliant

1985; Fenner and others 1988). Essentially, India had an economic incentive to control smallpox on its own (Brilliant 1985, 33) but lacked organizational capacity and an effective strategy for achieving this goal. Note, however, that India had other health priorities, including family planning. According to Brilliant (1985, 33), "for India's health planners, occupied then by emergencies and competing political demands on scarce resources, the long-term benefits from disease eradication were not a great motivation. Health planners are sensitive to immediate political realities, and the benefits of smallpox eradication would be realized only at some future time when the $3 million annual expenditures for smallpox could be applied to other health problems. In the meantime, however, the cost of putting so many scarce resources into one program rather than into many health needs was high."

Table 62.2 provides estimates of the benefits of smallpox eradication to the United States. The total benefit of eradication to the United States is about the same order of magnitude as India's, but the breakdown is different. Whereas India benefited mainly from avoided infections, the United States benefited mainly from avoided vaccinations. By the time the eradication program was launched, the United States had already interrupted smallpox transmission, but vaccination was costly, both in economic and human health terms (a small number of people died every year from infections arising from the live vaccine). Defending the nation from imported infections imposed additional costs.

In health terms, smallpox eradication saved millions of lives; in economic terms, it yielded a benefit many times greater than the cost. Identifying another investment that has yielded comparable returns and has benefited every country is difficult. One reason that the economics of smallpox eradication were so favorable is that all countries had strong incentives to join in the eradication of the disease. A huge organizational effort, but only a relatively small incremental cost, was needed to achieve eradication. The specter of global terrorism has recently caused some countries to prepare themselves for a possible smallpox attack by stockpiling vaccine. Although such actions reduce the benefits of eradication, the economics remain favorable.

Table 62.2 Benefits of Smallpox Eradication to the United States, 1968
(Millions of U.S. dollars)

	Amount
Direct costs for medical services	
Vaccination	92.8
Treatment of complications	0.7
Indirect costs, loss of productivity	
Work losses attributable to vaccination and reactions	41.7
Permanent disability attributable to complications	0.4
Premature death	0.1
Cost of international traffic surveillance and delays in clearance of vessels	14.5
Total	150.2

Source: Sencer and Axnick 1973; see also Fenner and others 1988, table 31.2.

Smallpox, however, was a special case. Many attributes of the disease and the vaccine favored eradication. The vaccine was heat stable and required only a single dose to protect a person for a period of at least 5 to 10 years. Vaccination was easily performed and protected immediately on application. Every individual who became infected exhibited a typical, easily recognized rash, thus permitting accurate surveillance without recourse to laboratory diagnosis. The disease spread slowly so that transmission could readily be stopped by isolating the patient and vaccinating contacts within the area.

Poliomyelitis

The polio eradication program, launched by the WHA in 1988, has made substantial progress (CDC 2003a, 2003b, 2003c, 2004a, 2004c, 2004e, 2004g, 2005). The incidence of paralytic poliomyelitis in children fell by more than 99 percent, from an estimated 1,000 cases per day worldwide in 1988 to fewer than 4 cases per day in 2003. The number of poliomyelitis-endemic countries also fell, from 125 in 1988 to just 6 by 2003 (Afghanistan, the Arab Republic of Egypt, India, Niger, Nigeria, and Pakistan). This laudable reduction was the result of repetitive vaccination campaigns with easily administered oral polio vaccine to whole regions, to nations, and to large subpopulations.

During 2004, however, polio immunization activities in northern Nigeria were halted for an extended period for fear of tainted vaccines, and this permitted the development of epidemics extending throughout the country. The disease spread as well to 10 other African countries and to Saudi Arabia, Yemen, and Indonesia. Transmission has again been reestablished in several African countries (Burkina Faso, Central African Republic, Chad, Côte d'Ivoire, and Sudan). Heroic efforts are being made to control these outbreaks by large-scale immunization, but in countries such as these, where health services are stressed and the health, communication, and transportation infrastructures are weak, disease transmission is difficult to interrupt. Meanwhile, other countries throughout the world that appear to be polio free are continuing their vaccination programs but finding it increasingly difficult to maintain a momentum of interest, effort, and financing.

The difficulties of maintaining credible surveillance systems throughout the developing countries were vividly demonstrated by the discovery of polio in Sudan in May 2004, more than three years after the last case had been reported (CDC 2005). In the interim, specimens from 75 to 90 percent of such

cases were processed in the laboratory, and measures of surveillance for acute flaccid paralysis cases were reported to have been entirely satisfactory. At first, the Sudanese cases were considered to have resulted from importations from Nigeria, and, indeed, some cases were. However, from more detailed laboratory studies, it was determined that type 1 wild virus had been circulating undetected for more than three years and type 3 virus for nearly five years.

Clearly, stopping the continuing transmission of wild poliovirus is itself a formidable challenge, the success of which is by no means certain. A problematic discovery since the global eradication program began was the finding that individuals with particular immunologic disorders shed polio vaccine virus for many months to years, thus serving as a reservoir for this virus. The virus, in turn, can revert to a neurovirulent form, which is capable of causing outbreaks of disease (Bellmunt and others 1999). Such individuals may be wholly without symptoms and impossible to identify except through fecal cultures. Moreover, no treatment is known to stop them from shedding virus. They pose an all but insurmountable challenge to the current poliomyelitis eradication effort.

The program is further hampered by the tool that has provided so much success—oral poliovirus vaccine (OPV). In resource-poor environments, poliomyelitis is best controlled with the inexpensive, live, and easily administered oral vaccine. The live vaccine is excreted and can infect other susceptible contacts. The ability of OPV to immunize others indirectly makes it an ideal vaccine for achieving high levels of population-based immunity, especially in lower socioeconomic populations that are the most difficult to reach. However, the excreted virus occasionally reverts to a pathologic state, causing not only cases but outbreaks of vaccine-associated paralytic polio, which may not emerge until months or even years after the vaccine has been administered (Kew and others 2004). Unfortunately, the alternative inactivated polio vaccine (IPV) is not immediately an option in many nations, not least because global manufacturing capacity could not begin to meet demand. Other problems include the current cost differential between OPV and IPV, the increased difficulty of administering the vaccine by syringe and needle, and the need to achieve higher coverage rates with IPV because it does not spread from person to person as does OPV.

Tragically, if OPV use were discontinued, in the absence of alternative immunity, polioviruses would likely circulate silently (Eichner and Dietz 1996) and reemerge. Preliminary results from a model presented by WHO indicate a greater than 60 percent chance of an outbreak within two years of the possible global cessation of OPV (WHO 2004) because of continuous circulation of undetected live vaccine viruses that can revert. Outbreaks have already been observed in several regions where decreasing use of live vaccine has left pockets of susceptible persons who eventually have been exposed to vaccine-derived pathogenic viruses (Kew and others 2002). Such an outbreak could occur with disastrous speed because the polio virus is far more contagious than that of smallpox. In developing countries, virtually all cases of polio occurred among those under five years of age, older persons having been protected by the natural immunity of earlier infection. Within five years after vaccination ceased, therefore, the population immunity level in the developing countries would be no better than it was before vaccination was introduced. With this is mind, it seems questionable as to whether all health ministers could be persuaded to call for a country-wide cessation of poliomyelitis vaccination itself, given the uncertainties of virus detection in so many remote and inaccessible areas of the world.

By definition, eradication implies certifying cessation of virus transmission and the absence of reservoirs so that control interventions can cease. As noted earlier in this chapter, it is only for this reason that eradication yields a dividend. Although the interruption of wild poliomyelitis virus transmission is theoretically feasible, the obstacles to achieving and maintaining this goal are formidable. At this time, it is difficult to foresee a future that does not envisage a continuing vaccination program, perhaps with IPV use in countries that can afford the substantial additional costs entailed and with OPV use in all other countries.

The polio eradication initiative, like that for smallpox, has had to rely primarily on voluntary donations provided both to WHO and bilaterally. Playing an especially important role have been the Rotary International Foundation and the Bill & Melinda Gates Foundation. From 1988 to 2004, more than US$3 billion was spent on the effort (WHO 2003).

What are the economics of polio eradication? Bart, Foulds, and Patriarca (1996) developed the first global cost-benefit analysis of polio eradication, beginning with the costs incurred since 1986, the year that the Pan American Health Organization launched a regional eradication effort, and extending to 2040. They assumed that eradication would be achieved in 2005, using OPV, and that vaccination would cease after eradication had been certified. Benefits (like costs, discounted at 6 percent) reflect the avoided costs of acute care and avoided vaccination costs after certification. Their analysis showed that the initiative would break even by 2007 and yield a net benefit to the world of more than US$13 billion by 2040—an encouraging result, but it was based on the assumption that all vaccination would stop abruptly in 2005.

Khan and Ehreth (2003) developed a similar analysis but provided regional detail. They estimated the costs and medical costs avoided of polio immunization and eradication over the period 1970 to 2050, assuming that vaccination could cease after 2010. As table 62.3 shows, Khan and Ehreth estimated that polio immunization and eradication would entail a negative net cost overall, with Europe and the Americas saving the most and with other regions incurring a positive net cost. Compared

Table 62.3 Net Costs of Polio Immunization and Eradication
(Millions of U.S. dollars)

WHO region	Medical care cost savings	Immunization costs	Net costs	Cost/DALY saved
Africa	1,100	3,942	2,842	442
Americas	76,900	25,460	−51,440	−4,983
Eastern Mediterranean	1,930	3,512	1,582	426
Europe	38,250	17,249	−21,001	−2,780
Southeast Asia	1,270	6,519	5,249	1,041
Western Pacific	8,670	10,327	1,657	356
World	128,120	67,009	−61,111	−1,457

Source: Khan and Ehreth 2003.
Note: Cost savings, immunization costs, and net costs are present values for 2000 in millions of U.S. dollars, calculated for the period 1970–2050 and discounted at 5 percent. These estimates assume that immunization by OPV can cease after 2010.

Table 62.4 Postpolio Eradication Costs
(Millions of U.S. dollars)

	Continue OPV	Stop OPV	Universal IPV
Low-income countries	1,364	487	4,418
Middle-income countries	12,196	12,196	12,196
High-income countries	6,409	6,409	6,409
Subtotal	19,969	19,092	23,023
Global response capacity	1,120	1,320	1,120
Total	21,089	20,412	24,143

Source: Sangrujee, Cáceres, and Cochi 2004.
Note: Costs are expressed in present value terms, calculated over the period 2005 to 2020, and discounted at 3 percent.

with other health interventions, this cost to developing countries may still be comparatively cost-effective. However, Khan and Ehreth comment that the cost per disability-adjusted life year (DALY) saved is high for developing countries (see table 62.3). As they explain (Khan and Ehreth 2003, 705), "This implies that without the financial support from developed countries of the world many developing countries would not have opted for polio interventions for implementation. From the developed countries' point of view, providing support for the polio program is not simply helping the poor and the disadvantaged, it actually represents a good economic investment."

Unfortunately, both of these cost-benefit studies have substantial limitations. First, both show that eradication is economically attractive if one incorporates all costs and benefits from the inception of this program. Because eradication has not yet been achieved, this approach mixes retrospective evaluation and prospective analysis (historical expenditures and benefits are sunk and so are irrelevant to the current situation). Second, benefits and costs are calculated in both studies relative to a world without immunization. A better approach would be to calculate the net benefits of eradication compared with the alternative of an optimal control program. The choice is not between doing nothing and eradication. It is between an optimal level of control and eradication. Finally, both studies assume that vaccination can cease in 2005 or 2010. As explained previously, this possibility is highly unlikely.

A more recent analysis by Sangrujee, Cáceres, and Cochi (2004) calculates the costs for 15 years following the goal of certification of eradication in 2005 for three different scenarios: continued use of OPV, OPV cessation with optional use of the killed or inactivated polio vaccine, and OPV cessation with universal IPV. Table 62.4 shows their results.

The respective cost to middle- and high-income countries is the same for all three scenarios, reflecting the assumption that the high-income countries will switch to IPV by 2005 and middle-income countries will do so between 2006 and 2008. The scenarios differ only for the low-income countries. In the first scenario, these countries are expected to continue routine immunization using OPV; in the second, immunization ceases in 2011, followed by a system of surveillance and response. In the third scenario, the low-income countries join the others in switching to IPV between 2008 and 2010. Of these three scenarios, the second comes closest to the 2005 post-eradication strategy now advocated by the polio eradication program leadership.

Unfortunately, this analysis is also deficient. First, interruption of transmission will not occur before 2006, and certification will take an additional three years. Hence, analysis of post-eradication costs should begin in 2009 at the earliest, with the costs of continuing immunization needing to be borne up until that time. Second, the analysis assumes a capacity to supply IPV that exceeds current estimates. It is not obvious that this scenario is feasible or, if it were, if the costs of scaling up production are adequately reflected in the calculations. Third, and most importantly, table 62.4 indicates that only low-income countries would benefit from polio eradication over this 15-year time scale—and yet the table does not include any estimate of the risk these countries would bear of a possible outbreak.

Although this analysis suggests that the discontinued use of OPV promises the greatest return to eradication, this assumes that circulating vaccine-derived polioviruses could be contained if and when they emerged. However, preparing for this possibility would require a far more effective global surveillance system than now exists, maintenance of a laboratory infrastructure, and stockpiles of OPV. In addition, controlling outbreaks with OPV without the risk of viruses reverting to virulence will be exceedingly difficult in the setting of an accelerating proportion of immunologic-naive individuals. The use of OPV in this scenario could very well cause poliomyelitis to

again become endemic. In any case, the estimated cost of any of the strategies exceeds $20 billion.

The economics of polio eradication are thus not as favorable as concluded by either Bart, Foulds, and Patriarca (1996) or Khan and Ehreth (2003). Both studies assume that vaccination can cease without IPV being used as a substitute anywhere, both exclude the costs of maintaining a response capacity, and neither accounts for the real threat of reemergence. Sangrujee, Cáceres, and Cochi (2004) take account of two of these considerations, but their analysis calculates only the costs for 15 years, ignoring both the risk of reemergence and the benefits of eradication. Hence, each study provides only a partial glimpse of the economics of polio eradication and does not adequately address the fundamental difficulty (inability) of stopping vaccination and maintaining eradication.

In conclusion, although the economics of polio eradication may have been thought to be favorable by some (Aylward and others 2003), they are far less favorable than were the economics of smallpox eradication, even assuming that polio vaccination could cease.

Dracunculiasis

Dracunculiasis, or guinea worm disease, is a nematode infection, which is controlled not by vaccination but by education of the affected population, provision of nematode-free water through wells or filtration, and treatment of cases. It is not a global disease but found only in the rural areas of a few very poor tropical countries. This last difference is especially important from an economics perspective. It means that international financing of a guinea worm eradication program needs to rely more heavily on development assistance rather than on the self-interest of donor countries.

Thus far, the eradication program has been successful in reducing the number of cases of guinea worm 99 percent from the 1986 level (Carter Center 2004). The geographic range of the disease has also been reduced from 20 to just 12 countries. Although this achievement is important, eradication remains elusive many years beyond 1995, the year that the WHA set for eradication in 1991 (Cairncross, Muller, and Zagaria 2002, 232).

Only one cost-benefit study of the guinea worm eradication program has been published (Kim, Tandon, and Ruiz-Tiben 1997), and it is unfortunately flawed in a number of respects. First, as indicated previously, eradication costs should be compared with those associated with an alternative optimal control program. Second, the cost-benefit analysis applies to the period 1987 to 1998 and thus is backward looking. The analysis can reveal whether the money spent previously yielded a benefit in excess of the cost (it did), but it cannot reveal whether eradication was worth pursuing at the time that this study was undertaken. Finally, it takes no account of the investment decision of eradication—the main reason for pursuing the eradication goal in the first place.

This last omission is especially relevant to the study's analysis of the eradication program in Sudan. The study projected that, by 1998, infections would cease everywhere except Sudan. (Plainly, this prediction was wrong, although Sudan is the largest problem for the program, mainly because of the ongoing civil war, which has limited accessibility to endemic areas; see Hopkins and others 2002.) It then calculates the net present value of eliminating the disease there. The results are not promising. They show that eradication is attractive only if the disease can be eliminated in Sudan within five years. However, this analysis ignores the dividend that eradication would earn Sudan. It also disregards the most important feature of eradication—that if the disease were certified to have been eliminated from its last stronghold, it would yield a benefit to *all* potentially vulnerable countries. Thus, the economics of eliminating dracunculiasis from Sudan, if that is where the disease makes its last stand, will be much more attractive than suggested by this analysis.

CONCLUSIONS

Of the several attempts to eradicate diseases, all but one has failed. Even the exception, smallpox, barely succeeded despite the many factors favorable to eradication. Whether any eradication effort will ultimately succeed or fail cannot be known with certainty at the time it is launched. Eradication entails risk. Money spent on eradication may not ultimately pay a dividend. Health risks may also exist. If eradication fails and vaccination levels drop after the eradication goal is abandoned, susceptible persons who were previously shielded from infection may become infected at a later age, when the disease can cause greater harm. The risk also exists that, even if eradication succeeds, the disease may be reintroduced by accidental or deliberate release.

The reasons for potential failure of an eradication effort are many. A nonhuman host may not be discovered until the number of infected humans drops to a very low level (as happened with yellow fever). The tools of eradication may be vulnerable to resistance (insecticides and drugs in the case of malaria). Political problems and civil strife may prevent an eradication program from being executed in critical areas where the disease makes its last stand (a problem today for guinea worm). Termination of vaccination may leave populations vulnerable to microbe reintroduction from an unforeseen reservoir or vaccine strain reversion (a risk now facing the poliomyelitis initiative). Another potential reason for failure is the inability to raise the financial resources needed to complete programs that extend beyond expected targets. All eradication programs have experienced serious financial stringencies during the course of their execution.

Most eradication programs to date have been launched as visionary, far-reaching efforts but with vastly incomplete

information. Basic epidemiological information and knowledge of the effectiveness and operational constraints of interventions and costs in different settings are often inadequate, and the required monitoring, evaluation, training, and research components of the program may be absent. If a program's administrators lack a careful, probing analysis of the epidemiology of the various candidate diseases or of the technologies available, and if their comprehension of the potential costs and who would bear them is limited, a program is likely to founder, causing a dispirited staff, confused beneficiaries, and donor fatigue and ambivalence. It is crucial that the eradication methodologies and assumptions in those regions of the world that would be most likely to pose the most significant problems be tested and addressed before launching an eradication program and that evaluation and research continue during the program.

Proposals for disease eradication have seldom been brought to the WHA with specific plans, costs, and uncertainties fully laid out. Nor have the expected sources of fiscal support and needed country support been addressed with specific commitments requested of the members. The WHA has only a limited deliberative capacity, and too much cannot be expected of its members in session. However, designated special committees of the WHA can and should be appointed, consisting of both visionary eradicationists and field-experienced public health and social science personnel. The WHA should take up the question of eradication only after the subject has been thoroughly vetted and sufficiently large-scale pilot programs in the most problematic areas have clarified that an adequate understanding of the epidemiology exists and that the appropriate technologies are available.

In the past, members have not voted for a specific program for which all the uncertainties have been laid out and the benefits and costs associated with different outcomes have also been calculated. Nor, with one exception, have they voted for a resolution imposing responsibilities, including financing obligations, on individual states. The next time a proposal to eradicate a disease is presented to the WHA, it should be comprehensive. It should demonstrate why the effort is worth taking, even if the final outcome is uncertain; it should bind states, morally if not legally, to fulfill the pledges needed to see the program through to its completion; and it should prepare contingencies should the eradication effort fail.

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REFERENCES

Anderson, R. M., and R. May. 1991. *Infectious Diseases of Humans: Dynamics and Control*. Oxford, U.K.: Oxford University Press.

Andrews, J. M., and A. D. Langmuir. 1963. "The Philosophy of Disease Eradication." *American Journal of Public Health* 53: 1–6.

Aylward, R. B., A. Acharya, S. England, M. Agocs, and J. Linkins. 2003. "Polio Eradication." In *Global Public Goods for Health: Health Economic and Public Health Perspectives,* eds. R. Smith, R. Beaglehole, D. Woodward, and N. Drager, 33–53. Oxford, U.K.: Oxford University Press.

Aylward, R. B., J. M. Olive, H. F. Hull, C. A. De Quadros, and B. Melgaard. 1998. "Ensuring Common Principles Lead to Mutual Benefits: Disease Eradication Initiatives and General Health Services." In *The Eradication of Infectious Diseases,* eds. W. R. Dowdle and D. R. Hopkins. New York: John Wiley and Sons.

Barrett, S. 2003. "Global Disease Eradication." *Journal of the European Economic Association* 1: 591–600.

———. 2004. "Eradication vs. Control: The Economics of Global Infectious Disease Policy." *Bulletin of the World Health Organization* 82 (9): 683–88.

Barrett, S., and M. Hoel. 2003. "Optimal Disease Eradication." Disease Control Priorities Project Working Paper 22.

Bart, K. J., J. Foulds, and P. Patriarca. 1996. "Global Eradication of Poliomyelitis: Benefit-Cost Analysis." *Bulletin of the World Health Organization* 74 (1): 35–45.

Basu, R. N., Z. Ježek, and N. A. Ward. 1979. *The Eradication of Smallpox from India.* New Delhi: World Health Organization.

Bellmunt, A., G. May, R. Zell, P. Pring-Akerblom, W. Verhagen, and A. Heim. 1999. "Evolution of Poliovirus Type I during 5.5 Years of Prolonged Enteral Replication in an Immunodeficient Patient." *Virology* 265: 178–84.

Biellik, R., S. Madema, A. Taole, A. Kutsulukuta, E. Allies, R. Eggers, and others. 2002. "First 5 Years of Measles Elimination in Southern Africa: 1996–2000." *Lancet* 359 (9317): 1564–68.

Breman, J. G., and I. Arita. 1980. "The Confirmation and Maintenance of Smallpox Eradication." *New England Journal of Medicine* 303 (22): 1263–73.

Brilliant, L. B. 1985. *The Management of Smallpox Eradication in India.* Ann Arbor: University of Michigan Press.

Cairncross, S., R. Muller, and N. Zagaria. 2002. "Dracunculiasis (Guinea Worm Disease) and the Eradication Initiative." *Clinical Microbiology Reviews* 15 (2): 223–46.

Carter Center. 2004. "Guinea Worm Eradication: Review, June 1, 2003." Carter Center, Atlanta. http://www.cartercenter.org/printdoc.asp?docID=1785andsubmenu=news.

CDC (U.S. Centers for Disease Control and Prevention). 1998a. "Progress toward Elimination of Measles from the Americas." *Morbidity and Mortality Weekly Report* 47 (10): 189–93.

———. 1998b. "Progress toward Global Measles Control and Regional Elimination, 1990–1997." *Morbidity and Mortality Weekly Report* 47 (48): 104.

———. 1999a. "Global Measles Control and Regional Elimination, 1998–1999." *Morbidity and Mortality Weekly Report* 48 (49): 1124.

———. 1999b. "Progress toward Measles Elimination—Southern Africa, 1996–1998." *Morbidity and Mortality Weekly Report* 48 (27): 585.

———. 2003a. "Global Progress toward Certifying Polio Eradication and Laboratory Containment of Wild Polioviruses—August 2002–August 2003." *Morbidity and Mortality Weekly Report* 52 (47):1158.

———. 2003b. "Progress toward Poliomyelitis Eradication—Angola and the Democratic Republic of Congo, January 2002–June 2003." *Morbidity and Mortality Weekly Report* 52 (34): 816.

———. 2003c. "Progress toward Poliomyelitis Eradication—Southern Africa, 2001—March 2003." *Morbidity and Mortality Weekly Report* 52 (22): 521.

———. 2003d. "Update: Global Measles Control and Mortality Reduction—Worldwide, 1991–2001." *Morbidity and Mortality Weekly Report* 52 (20): 471.

———. 2004a. "Brief Report: Global Polio Eradication Initiative Strategic Plan, 2004." *Morbidity and Mortality Weekly Report* 53 (05): 107.

———. 2004b. "Measles Mortality Reduction—West Africa, 1996–2002." *Morbidity and Mortality Weekly Report* 53 (02): 28.

———. 2004c. "Progress toward Global Eradication of Poliomyelitis, January 2003–April 2004." *Morbidity and Mortality Weekly Report* 53 (24): 532.

———. 2004d. "Progress toward Measles Elimination—Region of the Americas, 2002–2003." *Morbidity and Mortality Weekly Report* 53 (14): 304.

———. 2004e. "Progress toward Poliomyelitis Eradication—Nigeria, January 2003–March 2004." *Morbidity and Mortality Weekly Report* 53 (16): 343.

———. 2004f. "Progress toward Sustainable Measles Mortality Reduction—South-East Asia Region, 1999–2002." *Morbidity and Mortality Weekly Report* 53 (25): 559.

———. 2004g. "Wild Poliovirus Importations—West and Central Africa, January 2003–March 2004." *Morbidity and Mortality Weekly Report* 53 (20): 433.

———. 2005. "Progress toward Poliomyelitis Eradication—Poliomyelitis Outbreak in Sudan, 2004." *Morbidity and Mortality Weekly Report* 54 (4): 97–99.

Cello, J., A. V. Paul, and E. Wimmer. 2002. "Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template." *Science* 297 (5583): 1016–18.

Cochi, S., C. de Quadros, W. Dowdle, R. Goodman, P. Ndumbe, D. Salisbury, and others. 1998. "Post-Conference Small Group Report." In *Global Disease Elimination and Eradication as Public Health Strategies,* eds. R. A. Goodman, K. L. Foster, F. L. Trowbridge, and J. P. Figueroa. *Bulletin of the World Health Organization* 76 (Suppl. 2): 113.

Cockburn, A. 1961. "Eradication of Infectious Diseases." *Science* 133: 1050–58.

———. 1963. *The Evolution and Eradication of Infectious Diseases.* Baltimore: Johns Hopkins University Press.

de Quadros, C. 2001. "Introduction." In *Considerations for Viral Disease Eradication Lessons Learned and Future Strategies*, eds. S. Knobler, J. Lederberg, and L. A. Pray, 22–32. Washington, DC: National Academy Press.

Dowdle, W. R. 1998. "The Principles of Disease Elimination and Eradication." *Bulletin of the World Health Organization* 76 (Suppl. 2): 22–25.

———. 1999. "The Principles of Disease Elimination and Eradication." *Morbidity and Mortality Weekly Report* 48 (Suppl.): 23–27.

Dowdle, W. R., and D. R. Hopkins, eds. 1998. *The Eradication of Infectious Diseases.* New York: John Wiley and Sons.

Dubos, R., and J. Dubos. 1953. *The White Plague: Tuberculosis, Man and Society*. London: Gollancz. Quoted in Fenner, Hall, and Dowdle 1998.

Eichner, M., and K. Dietz. 1996. "Eradication of Poliomyelitis: When Can One Be Sure That Polio Virus Transmission Has Been Terminated? *American Journal of Epidemiology* 143 (8): 816–22.

Fenner, F., A. J. Hall, and W. R. Dowdle. 1998. "What Is Eradication?" In *The Eradication of Infectious Diseases*, eds. W. R. Dowdle and D. R. Hopkins, 3–17. New York: John Wiley and Sons.

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

Goodman, R. A., K. L. Foster, F. L. Trowbridge, and J. P. Figueroa, eds. 1998a. "Comments and Discussion Following Work Group Reports." In "Global Disease Elimination and Eradication as Public Health Strategies," *Bulletin of the World Health Organization* 76 (Suppl. 2): 104–8.

———. 1998b. "Global Disease Elimination and Eradication as Public Health Strategies: Proceedings of a Conference. Atlanta, Georgia, February 23–25, 1998." *Bulletin of the World Health Organization* 76 (Suppl.) 2: 5–162.

Henderson, D. A. 1982. "The Deliberate Extinction of a Species." *Proceedings of the American Philosophical Society* 126: 461–71.

———. 1988. "Development of the Global Smallpox Eradication Programme, 1958–1966." In *Smallpox and Its Eradication*, eds. F. Fenner, D. A. Henderson, I. Arita, Z. Ježek, and I. D. Ladnyi, 365–419. Geneva: World Health Organization.

———. 1998a. "Eradication: Lessons from the Past." *Bulletin of the World Health Organization* 76 (Suppl. 2): 17–21.

———. 1998b. "The Siren Song of Eradication." *Journal of the Royal College of Physicians of London* 32 (6): 580–84.

Hopkins, D. R., E. Ruiz-Tiben, N. Diallo, P. C. Withers Jr., and J. H. Maguire. 2002. "Dracunculiasis Eradication: And Now, Sudan." *American Journal of Tropical Medicine and Hygiene* 67 (4): 415–22.

Jeffrey, G. M. 1976. "Malaria Control in the Twentieth Century." *American Journal of Tropical Medicine and Hygiene* 25: 361–71.

Jenner, E. 1801. *The Origin of Vaccine Inoculation*. London: Shury. Quoted in Fenner, Hall, and Dowdle 1998.

Kew, O. M., V. Morris-Glasgow, M. Landaverde, C. Burns, J. Shaw, Z. Garib, and others. 2002. "Outbreak of Poliomyelitis in Hispaniola Associated with Circulating Type 1 Vaccine-Derived Poliovirus." *Science* 296 (5566): 356–59.

Kew, O. M., P. F. Wright, V. I. Agol, F. Delpeyroux, H. Shimizu, N. Nathanson, and M. A. Pallansch. 2004. "Circulating Vaccine-Derived Polioviruses: Current State of Knowledge." *Bulletin of the World Health Organization* 82 (1): 16–23.

Khan, M., and J. Ehreth. 2003. "Costs and Benefits of Polio Eradication: A Long-Run Global Perspective." *Vaccine* 21: 702–5.

Kim, A., A. Tandon, and E. Ruiz-Tiben. 1997. "Cost-Benefit Analysis of the Global Dracunculiasis Eradication Campaign." Policy Research Working Paper 1835, World Bank, Washington, DC.

Knobler, S., J. Lederberg, and L. A. Pray, eds. 2001. *Considerations for Viral Disease Eradication Lessons Learned and Future Strategies*. Washington, DC: National Academy Press.

Kremer, M., and E. Miguel. 2004. "The Illusion of Sustainability." NBER Working Paper W10324, National Bureau of Economic Research, Cambridge, MA.

New Shorter Oxford English Dictionary. 1993.

Ottesen, E. A., W. R. Dowdle, F. Fenner, K. O. Habermehl, T. J. John, M. A. Koch, and others. 1998. "Group Report: How Is Eradication to Be Defined and What Are the Biological Criteria?" In *The Eradication of Infectious Diseases*, eds. W. R. Dowdle and D. R. Hopkins. New York: John Wiley and Sons.

Payne, A. M.-M. 1963a. "Basic Concepts of Eradication." *American Review of Respiratory Disease* 88: 449–55.

———. 1963b. "Disease Eradication as an Economic Factor." *American Journal of Public Health* 53: 369–75.

Ramaiah, T. J. 1976. "Cost-Benefit Analysis of the Intensified Campaign against Smallpox in India." *National Institute of Health Administration and Education Bulletin* 9 (3): 169–203.

Roberts, L. 2004. "Polio Endgame. Polio: The Final Assault?" *Science* 303 (5666): 1960–68.

Sabin, A. B. 1991. "Measles, Killer of Millions in Developing Countries: Strategy for Rapid Elimination and Continuing Control." *European Journal of Epidemiology* 7 (1): 1–22.

Salisbury, D. 1998. "Report of the Work Group on Disease Elimination/Eradication and Sustainable Health Development." In *Global Disease Elimination and Eradication as Public Health Strategies,* eds. R. A. Goodman, K. L. Foster, F. L. Trowbridge, and J. P. Figueroa. *Bulletin of the World Health Organization* 76 (Suppl. 2): 72–79.

Sangrujee, N., V. M. Cáceres, and S. L. Cochi. 2004. "Cost Analysis of Post-Polio Certification Immunization Policies." *Bulletin of the World Health Organization* 82 (1): 9–15.

Sencer, D. J., and N. W. Axnick. 1973. "Cost Benefit Analysis." In *International Symposium on Vaccination against Communicable Diseases, Monaco 1973*, 22: 37–46. Symposia Series in Immunobiological Standardization. Basel, Switzerland: Karger.

Spînu, I., and S. Biberi-Moroianu. 1969. "Theoretical and Practical Problems Concerning the Eradication of Communicable Diseases." *Archives roumaines de pathologie experimentales et de microbiologie* 28: 725–42.

Steinglass, P. 2001. *Thematic Evaluations in 2001 Eradication of Poliomyelitis.* Report by the director general, Programme Development Committee of the Executive Board Eight Meeting, December 13, 2001. Document EBPDC8/3. Geneva: World Health Organization.

Taylor, C. E., F. Cutts, and M. E. Taylor. 1997. "Ethical Dilemmas in Current Planning for Polio Eradication." *American Journal of Public Health* 87 (6): 922–25.

WHO (World Health Organization). 2003. *Global Polio Eradication Initiative: Estimated External Financial Resource Requirements 2004–2008.* Geneva: WHO.

———. 2004. *Report of the Strategic Advisory Group of Experts (SAGE).* Geneva: WHO. http://www.who.int/vaccines-documents/DocsPDF05/Sage_Report_2004.pdf.

Yekutiel, P. 1980. *Eradication of Infectious Diseases: A Critical Study.* New York: Karger.