CASE 1
Eradicating Smallpox

Geographic Area: Worldwide

Health Condition: In 1966, there were approximately 10 million to 15 million cases of smallpox in more than 50 countries, and 1.5 million to 2 million people died from the disease each year.

Global Importance of the Health Condition Today: Smallpox has been eradicated from the globe, with no new cases reported since 1978. However, the threat of bioterrorism keeps the danger of smallpox alive, and debate continues over whether strains of the disease should be retained in specified laboratories.

Intervention or Program: In 1965, international efforts to eradicate smallpox were revitalized with the establishment of the Smallpox Eradication Unit at the WHO and a pledge for more technical and financial support from the campaign's largest donor, the United States. Endemic countries were supplied with vaccines and kits for collecting and sending specimens, and the bifurcated needle made vaccination easier. An intensified effort was led in the five remaining countries in 1973, with concentrated surveillance and containment of outbreaks.

Cost and Cost-Effectiveness: The annual cost of the smallpox campaign between 1967–79 was $23 million. In total, international donors provided $98 million, while $200 million came from the endemic countries. The United States saves the total of all its contributions every 26 days because it does not have to vaccinate or treat the disease.

Impact: By 1977, the last endemic case of smallpox was recorded in Somalia. In May 1980, after two years of surveillance and searching, the World Health Assembly declared that smallpox was the first disease in history to have been eradicated.

The eradication of smallpox—the complete extermination of a notorious scourge—has been heralded as one of the greatest achievements of humankind. Inspiring a generation of public health professionals, it gave impetus to subsequent vaccination campaigns and strengthened routine immunization programs in developing countries. It continues to be a touchstone for political commitment to a health goal—particularly pertinent in light of the United Nations' Millennium Development Goals (MDGs).

But the smallpox experience is far from an uncomplicated story of a grand accomplishment that should (or could) be replicated. While the story shows how great global ambitions can be realized with leadership and resources, it also illustrates the complexities and unpredictable nature of international cooperation.

The first draft of this case was prepared by Jane Seymour.

The Disease

Smallpox was caused by a variola virus and was transmitted between people through the air. It was usually spread by face-to-face contact with an infected person and to a lesser extent through contaminated clothes and bedding.

Once a person contracted the disease, he or she remained apparently healthy and noninfectious for

up to 17 days. But the onset of flu-like symptoms heralded the infectious stage, leading after two or three days to a reduction in fever but to the appearance of the characteristic rash—first on the face, then on the hands, forearms, and trunk. Ulcerating lesions formed in the nose and mouth, releasing large amounts of virus into the throat.

Nearly one-third of those who contracted the major form died from it, and most of those who survived—up to 80 percent—were left with deep-pitted marks, especially on the face. Many were left blind. In 18th century Europe one-third of all cases of blindness were attributed to smallpox (WHO 2001).

Possible Eradication?

In 1798, Edward Jenner announced success in vaccinating people against the disease and went on to claim that his vaccine was capable of eradicating it (Fenner et al. 1988). With the development in the 1920s of an improved vaccine, mass vaccination programs became theoretically viable. Subsequently, national programs—including the Soviet Union's experience in the 1930s—showed that eradication was possible. However, it wasn't until the early 1950s that eradication became a practical goal, with the development of a vaccine that did not require cold storage and could be produced as a consistently potent product in large quantities.

In its earliest form, the idea of a global effort to eradicate smallpox was far from popular. In 1953, the World Health Assembly (WHA)—the highest governing body of the WHO—rejected the notion that smallpox should be selected for eradication. In 1958, however, the deputy health minister of the Soviet Union and delegate to the WHA, Professor Viktor Zhdanov, proposed a 10-year campaign to eradicate the disease worldwide, based on compulsory vaccination and revaccination—and he promised that the Soviet Union would donate 25 million vaccine doses to initiate the program. A year later, a WHO report on the proposal suggested that eradication could be achieved by vaccinating or revaccinating 80 percent of the people in endemic areas within "four to five years." The Russian proposal was passed in 1959.

Smallpox was a suitable candidate for eradication for several reasons. The disease was passed directly between people, without an intervening vector, so there were no reservoirs. Its distinctive rash made it relatively straightforward to diagnose, and survivors gained lifetime immunity. The relatively long time between contracting it and becoming infectious meant that an epidemic took a while to take hold—and because sufferers were likely to take to their beds as they became infectious, due to the severity of the symptoms, they tended to infect few others. Good vaccination coverage, it was reasoned, would disrupt transmission entirely; where an outbreak occurred, these factors gave health workers time to isolate victims, trace contacts, and vaccinate the local population.

The vaccine itself has characteristics that also gave reason for optimism. The freeze-dried version produced in the early 1950s eliminated reliance on a cold chain; if stored properly, the vaccine maintains its strength for many years. A single vaccination can prevent infection from smallpox for at least a decade, while some studies have suggested that some protection is present even 30 years after vaccination. Even where vaccination failed to prevent infection, the resulting disease tended to be milder and have a lower fatality rate (WHO 2001).

Burden of Smallpox at the Start of the Eradication Effort

In 1959, 63 countries reported a total of 77,555 cases of smallpox (Fenner et al. 1988). Acknowledged at the time to be an underestimate, it was revised to closer to 100,000, although it later became clear that as few as 1 in 100 cases was reported. Despite well-developed health systems, some countries only reported cases that surfaced in major urban hospitals, while others failed to report at all. Information was also lacking from countries that were not WHO members then, such as China.

It has subsequently been estimated that in 1959 smallpox remained endemic in 59 countries containing about 60 percent of the world's population (Fenner et al. 1988). In the early 1950s there were probably around 50 million new cases each year (WHO 2001). However, several countries were on the verge of disrupting transmission of the disease, including China, Iraq, Thailand, and Algeria.

A Slow Start

In the early stages the WHO plan relied on national campaigns for which prime responsibility in cost and human resources would rest with national governments. The WHO saw itself in the role of providing technical assistance where called for and helping out by ensuring the production of the vaccine.

In fact, in its earliest days, the smallpox eradication program was a minor concern of the WHO. The reliance on national activities and vaccine donations, and pressures of a campaign against malaria (given the go-ahead four years before smallpox), gave the WHO little incentive to allot significant funds to smallpox eradication.

At the start of the campaign, around 977 million people were estimated to live in endemic areas; to vaccinate them was estimated to cost 10 cents per person, a total of $97.7 million. However, the actual amount spent in the first half of the 1960s was around $0.5 million a year, 0.2 percent of the WHO's regular budget. For several years, a medical officer and secretary were the only full-time employees working on the program at the WHO's headquarters in Geneva, and until 1966 only five full-time employees were assigned to field programs.

Each year the WHO's director-general told the WHA that eradication wasn't going as well as hoped because of lack of funds for vehicles, supplies, and equipment. And each year the WHA pressed for more funds to be made available. But they were not.

Political and financial support was in short supply in all quarters. The smallpox effort relied heavily on the donation of vaccines, so there was little to be done when supplies ran short. The problems were illustrated in India in 1963, where the WHO's encouragement led to the announcement of a mass vaccination campaign, only to see the campaign run into trouble when it failed to generate sufficient donations of freeze-dried vaccine.

More fundamentally, the WHO approach of relying on national campaigns and providing only limited leadership gave those who doubted the feasibility of eradication every reason to withhold funds and political support. An expert committee set up in 1964 realized that case reporting was running at not more than 5 percent of actual cases—indeed, it was later realized to be closer to 1 percent. This discrepancy meant that no one could tell where progress was being made or where there was a problem. Paradoxically, because the successes in some countries were not tracked with good monitoring systems, progress that was made could not be presented as evidence to bolster support.

The campaign mode was showing its limits in some settings. India, for example, saw vaccination programs that concentrated on the easiest targets to achieve 90 percent coverage in some districts. But outbreaks were still occurring in remote villages and slums, among traveling workers, and even in the heavily vaccinated areas, mainly because of bureaucratic reporting systems and quota-driven campaign efforts. For example, schoolchildren were often revaccinated many times to fulfill quotas for numbers of vaccinations performed, while those not attending school were not vaccinated at all. Thus, in 1964, the WHO recommended that the entire population be vaccinated to achieve eradication.

At the same time, the recognition that the malaria campaign was running into difficulties exacerbated the smallpox situation, and the malaria campaign's shortcomings were threatening to undermine the WHO's credibility. Overall, in the first half of the 1960s, the smallpox eradication effort hardly looked like the global success it would eventually prove to be.

Momentum Builds

The program's fortunes then took a turn for the better. New appointments to WHO in 1964 revived the conviction that smallpox was beatable and created the impetus to set up a separate Smallpox Eradication Unit, which provided focused leadership for international efforts. This coincided with the development of a better method of delivering the vaccine. And in 1965, the US government, the WHO's largest contributor, promised more technical and material support to the campaign.

The US decision to provide more support—a key factor in the program's development—came about through a combination of serendipitous circumstances, which started with then President Lyndon B. Johnson's search for an initiative to mark "International Cooperation Year" in 1965. A com-

bined measles control and smallpox eradication program in western and central Africa was the favored candidate. However, some in the US Communicable Disease Center (now the US Centers for Disease Control and Prevention, or CDC), especially Dr. D. A. Henderson, who later led the WHO's intensified smallpox program**,** doubted the sustainability of such an effort, due to the high cost of the measles vaccine (at that time more than $1 per dose), which made it unaffordable to many developing countries. An alternative smallpox eradication plan for the region was proposed. Although this wasn't immediately accepted, it started discussions that led to smallpox eradication being put on the US agenda for western and central Africa and finally, US support for the global effort.

Growing political and financial support from the United States, combined with the long-standing campaign from the Soviet Union, compelled the WHO's director-general, Dr. M. G. Candau, to reenergize the eradication plans. In 1965, at the WHA's prompting, Dr. Candau set out the current understanding of the global spread of smallpox and what would be needed to eradicate it. The WHA resolved that smallpox eradication was one of WHO's "major objectives."

Several elements figured prominently in the director-general's proposals. First, the budget was divided so that one part remained in the main WHO budget and the other in a dedicated fund. This maneuver allowed countries' commitment to smallpox eradication to be gauged, while at the same time safeguarding the WHO's core budget. Second, the general approach was designed to learn from the problems with the malaria program. For example, rather than setting out a strict set of rules, the program articulated "principles" to allow for flexibility. Indeed, the WHO handbook for the program was written as a "draft," leaving headquarters and national staff to infer that it was not the final word and could be updated. Third, the case reporting system was to be developed right at the start of the program to guide its progress; and fourth, research was encouraged. The proposals also made it clear that all WHO member countries would be required to participate, and their efforts would need to be coordinated.

In 1966, the WHA finally agreed to back the objective adopted the previous year for the Intensified Smallpox Eradication Programme, which started on January 1, 1967. The budget allocation was $2.4 million, which, if divided among the roughly 50 countries where programs were needed, amounted to about $50,000 per country.

At that point, there were between 10 million and 15 million cases worldwide. It was estimated that 1.5 million to 2 million people died of smallpox each year, and those who survived were disfigured; some were left blind or with other disabilities. The 31 endemic countries included many in sub-Saharan Africa, six in Asia, and three in South America. And some of those countries remained divided by war and famine.

A Full Effort

The Smallpox Eradication Unit set to work, with minimal staff and Dr. Henderson as the chief medical officer. For most of the campaign, the staff consisted of four medical officers, one administrator, a technical officer, and four secretaries. With strong support from the US CDC, the team produced an epidemiological report every two to four weeks, produced training materials, and dealt with the media.

Vaccine jet injectors, kits for collecting and sending specimens, and training aids were stored in Geneva and sent out on request. The effort also supplied a new breakthrough: the bifurcated needle. The needle was a marvel of simple technology that reduced costs (1,000 needles for only $5) and made vaccinating easier. Each needle could be boiled or flamed and reused literally hundreds of times, and one vial provided enough vaccine for four times as many people due to the smaller amount of vaccine required. Plus, they were very easy to use. A villager could be instructed and trained in its use in 15 minutes.

The quality of the international staff was important to the program, but recruitment wasn't easy. In 1967, few infectious disease control epidemiologists were familiar with smallpox, and the WHO was not organized to provide specialized training for new recruits.

Despite the limits of personnel, progress was noticeable—initially in western and central Africa, where quick detection and containment of outbreaks

took effect. Within two years, 17 of the 21 countries in the region were free of smallpox, despite their overall levels of poverty. Brazil also made spectacular progress, enabling the Western Hemisphere to be declared free of endemic smallpox in April 1971. Provision of enough quality freeze-dried vaccine and the introduction of the bifurcated needle started taking effect, especially in eastern and southern Africa.

New Methods

The following year saw major disruption to the program's successful trajectory, as Bangladesh lost its smallpox-free status to the refugees fleeing the civil war that led to independence. Botswana was faced with an epidemic, and it became clear that Iran and Iraq were both endemic again. Thanks to focused campaigns, however, all except Bangladesh were clear of the disease by the end of 1973. In September of that year, intensified campaigns began in the five remaining endemic countries: Bangladesh, India, Nepal, Pakistan, and Ethiopia.

The momentum was regained as new methods and extra resources were mobilized to cope with the large numbers of refugees from both natural and human-made disasters. With the WHO's persuasion, there was a move away from concentrating on general vaccination campaigns to focusing on actively seeking out cases and containing outbreaks with quarantine and vaccination of local people. Using the surveillance and containment strategy, teams were equipped with Jeeps and motorbikes to search villages, markets, and even houses for cases.

The approach appeared increasingly military, as motorized teams sped to an area as soon as an active case was announced. Massive efforts were then made to isolate cases and vaccinate everyone in the area, whether or not they had been vaccinated before. WHO staff on short-term contracts supplemented the ranks of local health workers.

The military-like approach succeeded even in the most difficult of circumstances. By the end of 1976, tens of thousands of health staff in search and containment programs stopped smallpox transmission in Ethiopia, a country embroiled in civil war and suffering with poverty and little infrastructure. In this final stage, large numbers of volunteers and helicopters were used to respond to outbreaks. As smallpox was contained in Ethiopia, war and the resulting refugees took the disease back into Somalia, but campaign coordinators could see there really was an end in sight, and experienced staff and money from many countries were marshaled to contain the outbreak.

In October 1977—10 years, 9 months, and 26 days after the start of the intensified campaign—the last endemic case of smallpox was recorded in Somalia. National staff and WHO officials embarked on an intense program of tracing contacts, quarantine, and vaccination. In May 1980, after two years of surveillance and searching, the WHA declared that smallpox finally had been eradicated.

Costs of Eradication

The costs of smallpox eradication have been estimated, although the underlying data are limited. In 1967 the main program cost was associated with vaccine, personnel, and transport. For the developing countries, this amounted to about 10 cents per vaccination. Estimating that about a fifth of the 2.5 billion people living in developing countries were vaccinated each year suggests that $50 million a year was spent on vaccination. However, the actual expenditure was much less, approximately $10 million per year by the endemic countries (Fenner et al. 1988).

India is the only developing country that has estimated the economic loss due to smallpox. In 1976, it was estimated that the cost of caring for someone in India with smallpox was $2.85 a patient, so the annual total cost of patient care for India alone would be $12 million (Ramaiah 1976a, 1976b). Based on the proportion of the global smallpox cases that India reported, these figures suggest that caring for people with smallpox cost developing countries more than $20 million in 1967. Estimating a person's economic productivity during his or her lifetime, it has also been calculated that India lost about $700 million due to diminished economic performance each year. Assuming 1.5 million deaths due to smallpox occurred in 1967, it is reasonable to estimate that smallpox was costing developing countries as a whole at least $1 billion each year at the start of the intensified eradication campaign (Fenner et al. 1988).

Industrialized countries, on the other hand, incurred the cost of vaccination programs to prevent the reintroduction of the disease. In the United States, the bill for 5.6 million primary vaccinations and 8.6 million revaccinations in 1968 alone was $92.8 million, about $6.50 a vaccination. Of those vaccinated, 8,024 people had complications requiring medical attention, 238 were hospitalized, nine died, and four were permanently disabled. With other indirect costs of the vaccination program, such as absences from work, the cost for 1968 was 75 cents per person. Even assuming that other developed countries had lower costs, this puts the annual cost for these countries around $350 million, based on their total population. Overall, the suggested global cost, both direct and indirect, of smallpox in the late 1960s was more than $1.35 billion (Fenner et al. 1988).

The ultimate expenditures of the intensified eradication program were around $23 million per year over 1967–79, including $98 million from international contributions and $200 million from the endemic countries (Fenner et al. 1988). It has since been calculated that the largest donor, the United States, saves the total of all its contributions every 26 days, making smallpox prevention through vaccination one of the most cost-beneficial health interventions of the time (Brilliant 1985).

Lessons Learned

Observers attribute much of the program's success to political commitment and leadership, in this case from WHO and its partner at the US CDC, along with specific funds, staff, and a unit with overall accountability and responsibility for the program. The initial dismal phase of the eradication program in the first half of the 1960s showed how lack of that commitment and organization undermined the efforts.

For national programs, it is generally agreed that success hinged on having someone who was responsible, preferably solely, for smallpox eradication. This individual was the main contact in the country and could be held accountable. Best results were obtained where WHO staff, or supervisory people, went into the field frequently to review activities and resolve problems. Their work showed that relatively few highly committed and knowledgeable people could motivate large numbers of staff successfully, even in unstable areas and the poorest of countries.

No two national campaigns were alike, which points to one of the significant lessons that can be learned from smallpox eradication: the need for a flexible approach. Vaccination programs had to be adapted to different administrative, sociocultural, and geographical situations, and ways of assessing the work had to be devised. Indeed, it was important that funds raised did not come with conditions that prevented their use for different activities in different areas.

Using existing healthcare systems for the program both took advantage of established ways of working in some countries and forced other countries to bring their services up to standard. This helped develop immunization services more generally—health staff helping with the campaign received training in vaccination and search and containment. This training was especially important for hospital-based health systems that had no experience in setting up preventive campaigns. The knowledge gained this way then went into other campaigns, offsetting the cost of the initial campaign. This work outside hospitals also reinforced how important it was to seek the support of community leaders and thus the participation of their communities. These lessons have provided a strategy for many community-based projects, including the trachoma control program (case 9) and the guinea worm campaign (case 10).

It was also discovered during the campaign that more than one vaccination could be given at a time, an idea now taken for granted. In 1970, the Smallpox Eradication Unit proposed an Expanded Programme on Immunization to increase the number of vaccinations administered during a single patient interaction. The proposal sought to add diphtheria, tetanus, pertussis, polio, and measles vaccines to the routine smallpox and BCG (to prevent tuberculosis) vaccines. In 1974, the WHA agreed, and the United Nations Children's Fund (UNICEF) became a major supporter of the Expanded Programme on Immunization in the 1980s.

Routine immunization in the developing world under the program may prove in the end to be the smallpox eradication effort's greatest contribution: By 1990, 80 percent of the children throughout the

developing world were receiving vaccines against six childhood killers, compared with only 5 percent when the program started.

The importance of monitoring results is another transferable lesson. In the early 1960s, several countries relied on measuring activity as an indicator of success—and duly reported that they had vaccinated a large number of people. Yet the number of new cases remained high. Clearly, there was a problem with the surveillance and program evaluation, but because the monitoring indicator was within an acceptable range, nothing changed. From 1974, standards were established for surveillance and containment as well as for vaccination coverage.

Good reporting ensures that success can be measured, but publicity of that success is essential. The message that the smallpox eradication campaign was working really spread among donors only in 1974, when just five endemic countries remained, thus triggering large donations and more funds.

Impact of Eradication

The eradication of smallpox continues to inspire and highlights the importance of cooperation, national commitment, leadership, reliable epidemiologic information, and appropriate technology. The particular features of smallpox, both in terms of the disease and the vaccine, which made the disease a prime candidate for eradication, may not be found in other diseases. And recent events have highlighted the potential of an eradicated disease becoming a bioweapon (see box 1.1).

Box 1.1 The eradication debate

Smallpox was one of only a handful of diseases that are good candidates for elimination or eradication. ("Elimination" refers to reducing the number of new infections to zero in a defined geographical area, with continued interventions required to prevent reestablishment of transmission. "Eradication" means permanently reducing the number of new infections worldwide to zero, with interventions no longer needed.) Few human ailments meet the six preconditions for disease eradication (IOM 2002):

- no animal reservoir for the virus is known or suspected;
- sensitive and specific tools are available for diagnosis and surveillance;
- transmission from one individual to another can be interrupted;
- nonlethal infection or vaccination confers life-long immunity;
- the burden of disease is important to international public health; and
- political commitment to eradication efforts exists.

During the 20th century, global efforts were made to eradicate seven diseases: hookworm, yellow fever, malaria, yaws, smallpox, guinea worm, and polio (Henderson 1999). Smallpox was eradicated in 1977. Today, worldwide campaigns against polio continue, with the hope that it will become the second disease to be eradicated. Interventions against guinea worm continue in sub-Saharan Africa, the only remaining endemic area.

Benefits of Elimination and Eradication

The most obvious benefits of disease eradication are that no illness or death from that disease will ever occur again (Dowdle 1999). Control programs are no longer needed, and this allows resources, both monetary and

(Box continues on next page)

Box 1.1 The eradication debate *(continued)*

otherwise, to be redirected. These benefits result from the two basic objectives of eradication programs: to eradicate the disease and to strengthen and further develop the health system (Goodvan et al. 1998).

The monetary benefits of elimination and eradication can be substantial. One study estimated that if measles were eradicated by 2010, and vaccination could be discontinued, the United States could save $500 million to $4.5 billion (Miller et al. 1998). Another study estimated that seven industrialized countries (Canada, Denmark, Finland, the Netherlands, Spain, Sweden, and the United Kingdom) would save between $10 million and $623 million if measles were eradicated, even assuming that measles vaccination would continue (Carabin and Edmunds 2003).

Other benefits of elimination and eradication relate to the campaigns themselves. Surveillance, logistics, and administrative support are invigorated to achieve a higher standard of performance. If designed with system strengthening in mind, elimination and eradication programs that benefit from high political visibility and financial support can improve the quantity and quality of health workers, bolster health infrastructure, foster coordination among donors, and contribute to other improvements in the backbone of public health.

Potential Pitfalls of Elimination and Eradication Campaigns

Efforts to eliminate or eradicate disease also can inadvertently cause major problems. The near-term risk is that the focused efforts to deal with one ailment detract from a health system's ability to deal with many other causes of human suffering. Particularly in global eradication programs, where large outlays may be required to reach populations in which the disease in question is of relatively small importance (compared with other illnesses), the diversion of resources can be detrimental; local political commitment can waver in the face of pressures to address higher-priority health concerns. This risk can be—but is not always—countered by explicit attention to how the eradication campaigns can strengthen the basic functions of the health system, such as surveillance, human resource development, management, and others.

The longer-term risk is that it may be impossible to obtain all the promised benefits because vaccination (or other preventive actions) must continue, even if the program is successful in reducing to zero the incidence of a disease. As the US Institute of Medicine Forum on Emerging Infections puts it in a 2002 report, "Even in developed countries where infections have been eradicated or near-eradicated, mass vaccinations will probably have to be maintained at very high levels for an extended time in order to protect against reintroduction from areas where poverty, civil unrest, or lack of political will impede high vaccination coverage and sustain endemicity" (Institute of Medicine 2002). In fact, without continued preventive measures, eradication can put the world's population at risk if there are changes in the natural history of the disease, or the scientific community is wrong about the effectiveness of immunization or other preventive measures, or if bioterrorism is a threat.

Being prepared for outbreaks of long-gone diseases comes at a price. In 1997, for example, the US Department of Defense contracted with BioReliance to deliver 300,000 doses of an improved smallpox vaccine for $22.4 million (about $70 per dose), and in 2000, the US Centers for Disease Control and Prevention (CDC) contracted OraVax to manufacture 40 million doses of smallpox vaccine beginning in 2004 and continuing through 2020 at a cost of $8 per dose, though this schedule was altered after the 2002 anthrax outbreak. By the end of 2002, the Bush administration had set aside $500 million to procure 300 million doses of smallpox vaccine (Koplow 2003). As of January 31, 2003, 291,400 doses were released by the CDC to vaccinate first responders in the United States against smallpox, and $42 million was appropriated to establish the Smallpox Vaccine Injury Compensation Program, even though smallpox was eradicated almost 30 years ago (CDC 2004).

However, the lessons learned from the campaign can be adapted to other circumstances. The lasting legacy to public health of the smallpox eradication campaign is the demonstration of how the combination of good science, outstanding organization, focused monitoring, and international commitment can make a substantial difference to global health, saving generations from disability and premature death.

References

Brilliant, L. B. 1985. *The Management of Smallpox Eradication in India: A Case Study and Analysis.* Ann Arbor, MI: University of Michigan Press.

Carabin, H., and Edmunds J. 2003. Future Savings from Measles Eradication in Industrialized Countries. *Journal of Infectious Diseases* 187, supplement 1: S29–S35.

CDC (US Centers for Disease Control and Prevention). 2004. Smallpox Vaccination Program: Vaccine Doses Shipped and Released for Use. Atlanta, GA: Centers for Disease Control and Prevention. www.cdc.gov/od/oc/media/smallpox.htm (accessed February 20, 2004).

Dowdle, Walter R. 1999. The Principles of Disease Elimination and Eradication. *Morbidity and Mortality Weekly Report* 48, SU01: 2307. Atlanta, GA: US Centers for Disease Control and Prevention.

Fenner, F., D. A. Henderson, I. Arita, Z. Jezek, and I. D. Ladnyi. 1988. *Smallpox and Its Eradication.* Geneva: World Health Organization. www.who.int/emc/diseases/smallpox/Smallpoxeradication.html (accessed August 6, 2004).

Goodvan, R. A., K. L. Foster, F. L. Trowbridge, and J. R. Fgueroa. 1998. Summary. *Bulletin of the World Health Organization* 76, supplement 2: 9–11.

Henderson, D. A. 1999. Lessons from the Eradication Campaigns. *Vaccine* 17, supplement 3: S53–S55.

Institute of Medicine, Forum on Emerging Infections. 2002. *Considerations for Viral Disease Eradication: Lessons Learned and Future Struggles.* Washington: National Academy of Sciences.

Koplow, D. A. 2003. *Smallpox: The Right to Eradicate a Global Scourge.* Berkeley, CA: University of California Press.

Miller, M. A., S. Redd, S. Hadler, and A. Hinman. 1998. A Model to Estimate the Potential Economic Benefits of Measles Eradication for the United States. *Vaccine* 20: 1917–22.

Ramaiah, T. J. 1976a. Cost-Benefit Analysis of the Intensified Campaign Against Smallpox in India. *National Institutes of Health Administration and Education Bulletin* 9: 169–203.

Ramaiah, T. J. 1976b. Cost-Effectiveness Analysis of the Intensified Campaign Against Smallpox in India. *National Institutes of Health Administration and Education Bulletin* 9: 205–19.

WHO (World Health Organization). 2001. *WHO Fact Sheet on Smallpox.* Geneva: World Health Organization. www.who.int/emc/diseases/smallpox/factsheet.html (accessed August 6, 2004).