The Albert B. Sabin Lecture: The Eradication of Poliomyelitis

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The understanding and ultimate conquest of poliomyelitis was Albert Sabin's life-long preoccupation, beginning with his earliest work in 1936 (Sabin and Olitsky 1936; Sabin 1965). The magnitude of that effort was aptly summarized by Paul (1971) in his landmark history of polio: "No man has ever contributed so much effective information—and so continuously over so many years—to so many aspects of poliomyelitis." Thus, appropriately, this inaugural Sabin lecture deals with poliomyelitis and its eradication.

POLIO VACCINE DEVELOPMENT AND ITS INTRODUCTION

In the quest for polio control and, ultimately, eradication, several landmarks deserve special mention. At the outset, progress was contingent on the development of a vaccine, and the production of a vaccine, in turn, necessitated the discovery of new methods to grow large quantities of virus. The breakthrough occurred in 1949 when Enders and his colleagues showed that large quantities of poliovirus could be grown in a variety of human cell tissue cultures and that the virus could be quantitatively assayed by its cytopathic effect (Enders et al. 1949).

Preparation of an inactivated vaccine was, in principle, a comparatively straightforward process. In brief, large quantities of virus were grown, inactivated with formalin, and bottled. Assurance that the virus had been inactivated could be demonstrated by growth in tissue culture. Within 5 years of the Enders report, large-scale field trials were already under way, and in 1955 the inactivated, so-called Salk vaccine was licensed for use.

To many scientists, however, including Sabin, a living, attenuated poliovirus vaccine was far more attractive as a preventive agent. They believed that the immunity conferred by an infection would more closely mimic naturally occurring poliomyelitis and was thus more likely to offer lifetime protection. Furthermore, by inducing intestinal immunity, which the Salk vaccine did not, the live vaccine should inhibit the spread of circulating wild viruses and this, in turn, should result in diminished virus spread in the community.

The development of an attenuated live polio vaccine posed a formidable challenge. How poliovirus strains could be attenuated was little understood at the time, and there was only limited empirical experience with attenuation of other viruses. Equally as problematic were questions of how to demonstrate with certainty that a candidate vaccine strain was, in fact, attenuated and that it would not become virulent during growth in the human host. The very limited animal host range of naturally occurring polio

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strains—chimpanzees and monkeys—made the task especially difficult. Many struggled with these problems, but none with greater or more single-minded dedication than Sabin himself. He describes in his history of polio vaccine development a 2-year period when he first began to administer vaccine to adult volunteers (Sabin 1985). In all, during those 2 years, he fed vaccine to some 133 subjects but, to ascertain the degree of attenuation of the strains both before feeding and after recovery from stools, he inoculated 9000 monkeys and 150 chimpanzees. The required intraspinal and intrathalamic inoculations were difficult to perform and to interpret. Most were performed by Sabin himself.

Eventually, he selected three candidate strains, plaque-purified them, and repeatedly tested them for virulence in monkeys and chimpanzees. Small-scale trials in humans proved successful, but to assess adequately both efficacy and safety, large-scale trials involving hundreds of thousands of human subjects were needed. Neither the United States nor most of western Europe provided suitable sites. The Salk vaccine was, by then, in widespread use, and unvaccinated susceptible children were comparatively few. Developing countries were unsatisfactory because of the widespread prevalence of natural infection at very early ages. Eastern Europe, however, offered a fortuitous opportunity and, in 1956, Sabin began a productive collaboration with academician Mikhail Chumokov, the director of a new Institute for Poliomyelitis Research in Moscow. It was a collaboration which, uniquely for the era, transcended the Iron Curtain. By the end of 1959, more than 15 million persons in the USSR had received vaccine in field trials (Agol and Drozdov 1993). It proved to be both effective and safe. On the basis primarily of these Russian data, the vaccine was licensed for use in the United States in 1962.

A vaccine which could be given orally—the first such vaccine ever to be licensed—opened new possibilities for large-scale immunization. Throughout the 1950s, there had been opposition, both in the United States and in other countries, to mass campaigns using the Salk polio vaccine. The medical community insisted on inoculations being administered personally by qualified physicians or under their close supervision, and there simply were not enough physicians or interest to permit an intensive large-scale effort. Oral vaccine totally altered the calculations. Little professional expertise was required to ensure that two drops of vaccine were placed on a sugar cube and the cube placed in a child's mouth. The cost of the vaccine was literally pennies per dose, and if the child received more doses than were called for, so much the better. The way was paved for mass application of the vaccine.

Sabin argued for community-wide administration of vaccine in the United States on the grounds that rapid, widespread dispersion of the vaccine virus would displace other enteroviruses and perhaps eliminate circulating wild poliovirus. Initially, he was rebuffed in his efforts, but undaunted, he took the case to the Board of Trustees of the American Medical Association and gained its endorsement (Sabin 1985). Thereafter, and often under the aegis of county medical societies, campaigns were conducted in many parts of America that were labeled "S.O.S.," or "Sabin on Sunday." Many service clubs and voluntary organizations, as well as vaccine producers and public health agencies, participated in that effort. The S.O.S. programs continued from 1962 through 1964. In all, an estimated 100 million Americans were vaccinated with the three monovalent strains then in use. Reported cases of paralytic polio in the United States fell from 988 in 1961 to 106, 3 years later.

These landmarks in the saga of oral polio vaccine are a reminder that there was not one, but many, challenges to be surmounted in realizing the promise of the oral polio vaccine. These ranged from problems of attenuation to methods for quality control to new approaches for field use. Many individuals contributed to the solutions, but it was the ever impatient and determined Albert Sabin who seemed to be simultaneously everywhere, able and prepared to play the role of scientist, advocate, politician, clinician, and epidemiologist in transforming a concept into practical reality.

THE GLOBAL CHALLENGE

The widespread use of oral polio vaccine in the primarily tropical developing countries posed the ultimate challenge. It should be recalled that, until the 1970s, polio was generally thought to be an inconsequential problem for the developing world (Sabin 1981). Most such countries recorded few cases. In part, deficient reporting was responsible, but epidemiologists postulated also that in these countries almost all children became infected so early in life that virtually all developed immunity without paralysis. Polio immunization was thus not considered to be a high priority, and indeed, as of 1975, less than 5% of children in the developing world were receiving polio vaccine. During the early 1970s, however, "lameness surveys" began to be conducted, first in Indonesia and Ghana and later in other countries. These surveys of school children measured the prevalence of leg weakness characteristic of residual polio paralysis. Surprisingly, the surveys, wherever conducted, revealed rates which were as high as in the industrialized countries before vaccine became available (Nicholas et al. 1977). The complacency with which polio had been viewed in the developing countries was shattered.

Because of these findings, oral polio vaccine was one of six antigens selected in 1974 by the World Health Organization (WHO) to be incorporated in a new global program for immunization. There were many, however, who expressed skepticism about the possibilities for effective polio control in the developing countries. There were two reasons for this. First, the vaccine was very susceptible to inactivation by heat. Thus, an elaborate network of freezers, refrigerators, and insulated ice chests ("the cold chain") had to be established and maintained to assure that the vaccine reached children in viable form. The cold chain was costly and difficult to maintain. Second, in tropical areas, serological conversion rates following administration of polio vaccine were often surprisingly poor. The rates varied widely, but some rates as low as 40–50% were observed after three doses of vaccine. In comparison, rates above 95% are expected in industrialized countries. The most plausible explanation for this poor response was the high prevalence in the tropics of competing enteroviruses which block infection with the live polio vaccine.

Sabin (1980) argued the need for large-scale vaccination programs in tropical areas, citing two particular experiences. The first was the field studies of oral vaccine in Toluca, Mexico, which he had carried out with Ramos-Alvarez in 1960 (Sabin et al. 1960). These studies showed that a single dose of trivalent oral vaccine given to 85% of children resulted in a marked, immediate suppression of other enteric viruses. Sabin and Ramos-Alvarez believed that it was reasonable to infer that wild poliovirus would likewise be displaced. Sabin also cited Cuba's experience (Rodriguez Cruz 1984). Beginning in 1962, Cuba had conducted two vaccination weeks each year in which all young children were vaccinated irrespective of their immunization status. Vaccination was performed house to house utilizing some 82,000 Committees for the Defense of the Revolution. Between 1962 and 1980, only seven cases of polio were detected, where once thousands of cases had occurred annually. Most health officials in the Americas applauded the effort but saw little hope for mounting a similar type of campaign in a nontotalitarian state.

Could a nationwide campaign be conducted in a country other than Cuba, and if so, what effect might it have? Brazil soon provided an answer. As of 1980, Brazil's routine vaccination program was attaining levels of coverage of less than 50%, despite widespread programs designed to educate and motivate the population about the need for vaccination. In frustration, the Brazilian health staff reverted to a mass campaign strategy, one which they had perfected during the smallpox eradication campaign. They

decided to organize two national immunization days each year (Risi 1984). In 1980, more than 300,000 community volunteers, utilizing 90,000 vaccination posts, vaccinated some 20 million children under 5 years of age on each of two national immunization days. This represented about 90% of children in this age group. This has been the practice every year since. The results were dramatic. Reported cases promptly dropped from more than 2000 per year to 100 or less, and most of southern Brazil became polio-free.

Meanwhile, with leadership from the Pan American Health Organization (PAHO), programs for immunization throughout the Americas had progressively improved. Polio incidence fell steadily and, in 1985, the countries agreed that a hemisphere-wide eradication effort should be undertaken with the objective of interrupting poliovirus transmission by December 1990 (de Quadros et al. 1991). This program broke new ground in public health in its use of epidemiology to guide strategy and tactics, in its involvement of community leadership, and in its planned coordination of the efforts of national and international agencies, as well as Rotary Clubs, across the continent. The use of national immunization days was an important feature in the strategy, but there were other components of comparable importance, as described below.

Six years later, in August 1991, the last known case of poliomyelitis occurred, and it was from this case that the last native wild poliovirus was isolated in the Western Hemisphere. This was less than 8 months beyond the target date which had been established in 1985. Subsequently, wild poliovirus was imported into Alberta, Canada, in 1993, from Holland, infecting a religious sect which refused vaccination. However, no cases occurred and no transmission beyond the religious group itself was found. In fact, a hemisphere-wide investigation of all other related religious groups was undertaken, but it turned up no cases and no other isolates.

Meanwhile, in 1990, an International Commission on the Certification of Poliomyelitis Eradication (ICCPE), chaired by Dr. Fred Robbins, had been convened to decide on criteria it would require before certifying that the circulation of wild poliovirus had been interrupted in the Americas (PAHO 1993) and to offer advice to the organization on its efforts. Pursuant to its recommendations, independent national commissions were constituted for each country 3 years after the occurrence of the last known case of poliomyelitis. Each was charged to undertake a critical review of a national program and to report its findings to the International Commission. On September 29, 1994, the International Commission, after further deliberation, reported finally to the Ministers of Health of the Pan American Health Conference: "Based on the impressive evidence submitted, the ICCPE concludes that wild poliovirus transmission has been interrupted in the Americas."

STRATEGY AND TACTICS IN POLIO ERADICATION

The first requirement for an eradication program is a commitment by all the countries concerned both to undertake needed efforts in their own countries and to cooperate with others in coordinated hemisphere-wide activities. This commitment was made in September, 1985 by the nations of the Americas at the Pan American Directing Council (PAHO 1993).

In designing strategy and tactics, the experiences gained during the smallpox campaign proved invaluable. The underlying strategic principles were the same: establishment of a surveillance system for rapid case detection, investigation, and outbreak control, as well as intensification of the vaccination program to heighten immunity. However, the differences between the two diseases, smallpox and poliomyelitis, dictated very different tactics (de Quadros and Henderson 1993).

Surveillance

Surveillance was the most critical component. Effective execution of any disease eradication or control program requires that program directors have current information regarding the occurrence of cases and their epidemiological pattern of spread. Until 1985, information about cases of polio had been provided by fewer than 500 of the larger medical centers in Latin America and the Caribbean. Reports were provided sporadically and were more often monthly than weekly. Nevertheless, the system, incomplete though it was, recorded ever fewer cases as national immunization programs were strengthened.

It was decided to expand the number of reporting sites, first to all hospitals and rehabilitation centers where cases might be seen, and later to all hospitals and clinics. A weekly report was requested irrespective of whether cases had been seen, and plans were made to assure that each case would be investigated by a trained epidemiologist. The number of reporting sites steadily increased from fewer than 500 in 1985 to more than 20,000 by 1993, with more than 90% reporting promptly each week.

What should be reported as a case; how could one monitor the disease epidemiologically? These were more difficult questions than it might seem. The three types of poliovirus are each capable of inducing infection and, in developing countries, virtually all children will have been infected by all three strains by age 4 or 5 years. Most of those infected have few or no symptoms whatsoever; only 1% experience paralysis. The paralytic cases, therefore, represent only a marker indicating the presence of poliovirus infections. Thus, it was especially important that all possible paralytic cases be identified.

To ensure that all possible cases of paralytic polio in a country are duly reported is itself a formidable challenge. However, in surveillance programs in the United States, another factor was found to mitigate against full reporting. It was discovered that many physicians, seeing a paralyzed patient with a history of prior vaccination, often dismissed the possibility of polio and suggested an alternative diagnosis. That the history of vaccination might have been in error or vaccine failure might have occurred was often ignored. Because of this experience, it was decided to request that all patients presenting with flaccid paralysis of acute onset (AFP) be reported, recognizing that this would inevitably identify some cases which were not polio. Reporting of cases was restricted to those under 15 years of age because essentially all cases of polio in Latin America were in children. All such cases were termed "suspected polio." An epidemiologist evaluated each case within 48 hours and discarded the case only if an alternative definitive diagnosis could be made. All remaining cases were labeled "probable polio," specimens were collected, and a follow-up visit was made at 60 days to determine the paralytic status of the patient.

In theory, the system appeared workable. Aside from poliomyelitis, only two other conditions were thought likely to account for small numbers of acute paralytic illnesses—the Guillain-Barre syndrome and paralysis caused by other enteroviruses. The Guillain-Barre syndrome, however, was then considered to be uncommon in young children; moreover, experience had shown that paralysis caused by other enterovirus infections was also uncommon and almost never resulted in paralysis lasting beyond 60 days. Thus, it was expected that essentially all illnesses with residual flaccid paralysis would be poliomyelitis. Experience proved otherwise. It was soon discovered that Guillain-Barre syndrome was far more prevalent than had been expected, that it was often difficult to differentiate clinically from polio, and that there were other undefined causes of AFP. Indeed, in every country, cases of non-polio AFP occurred at an annual rate of 1–2 cases per 100,000 children. Some wondered if this unexpectedly large number of paralytic cases might be a phenomenon unique to the tropics but, surprisingly, when the United Kingdom undertook a similar type of surveillance, an identical rate was

found (D. Salisbury, pers. comm.). Hoping to sort out this morass clinically, special diagnostic teams were established consisting of a neurologist, a pediatrician, and an epidemiologist. These teams proved helpful, but despite their best efforts, many cases of uncertain cause remained on the list as "possible cases."

Virological examination of stool specimens, collected soon after onset, offers important information and, from the beginning, intensive efforts were made to establish a reliable network of laboratories. By 1989, the network was fully operative. However, despite best efforts there still remained a residual number of patients who were reported too late for specimens to be taken or who were lost to follow-up.

These several factors made it difficult to obtain a clear picture of the evolving epidemiology of poliomyelitis in Latin America. Cases from which a wild poliovirus strain was isolated and those in epidemic clusters provided a minimum estimate of incidence and geographic spread, but it was recognized that there were other polio cases mixed in with the much larger number of AFP cases of unknown etiology.

In 1990, with virologically confirmed cases approaching nil, it was decided to alter the tactics and to focus on the detection and patterns of occurrence of isolates of poliovirus, however recovered. Efforts were intensified to obtain many more specimens—a minimum of two stool specimens from every suspect case, as well as five stools from family and neighborhood contacts. From 1990 through 1994, 36,250 stool specimens were collected from countries throughout Latin America and the Caribbean. Wild poliovirus, all type I strains, were isolated from 27 cases in 1989, 18 in 1990, and 9 in 1991, but none was isolated after August of that year.

Although the surveillance data were often difficult to interpret, there were early observations which proved of inestimable value. Brazil's central laboratory (the Oswaldo Cruz Institute) was one of the first to become fully operational and in 1986 began to isolate type III strains from patients, many of whom had received three or more doses of OPV. Since type III polio vaccine virus was known to be the least antigenic of the strains, the question arose as to whether there might be insufficient type III vaccine virus in the vaccine mixture. Special field studies were promptly undertaken which indicated that a much better serological response could be obtained by doubling the quantity of type III virus in the vaccine (PAHO 1986). This was done, and type III polio rapidly vanished.

Efforts to Improve Immunity

Three special efforts were made to improve immunity. Experiences in Brazil and Cuba had demonstrated that national immunization days could have a significant effect in displacing wild poliovirus, but few countries were prepared, initially, to undertake such an effort. Some were simply reluctant to mount such a campaign, having had little previous experience in so doing, and some saw little need. Chile and Panama, for example, had detected no poliomyelitis for a decade or more, and others countries, such as Argentina and Uruguay, were at virtually nil incidence. Inadequate surveillance systems undoubtedly conveyed a falsely optimistic picture but, even so, it was clear in many countries that polio cases were not occurring in sufficient numbers to engender heroic special efforts.

A more difficult issue was that large-scale immunization programs, for whatever purpose, were an anathema to traditional health service staff in many countries. It was taken as an article of faith that such programs could not be sustained and that they were too costly. Brazil's program, however, continued successfully year after year and at a cost shown to be less than half that required for routine vaccination at clinics and hospitals (Creese 1984). With support and encouragement by PAHO staff, increasing num-

bers of countries began to adopt the strategy of national immunization days, usually offering several vaccine antigens in addition to polio. Eventually, national immunization days were conducted in 15 countries with a total population of 380 million persons—80% of the total population of Latin America.

A second approach toward improving immunization coverage was adapted from the containment strategy of the smallpox program. Plans called for the rapid administration of polio vaccine to all children under 5 years of age within an extended geographic area near the residence of a "probable polio case." It was recognized that this action was unlikely to contain the spread of wild poliovirus, given the large proportion of subclinical infections and the likelihood that, by the time a case was discovered, the virus would already have spread. The reason for outbreak vaccination was based on the smallpox experience, in which it had been found that the occurrence of a smallpox case frequently served as a marker of generally low vaccination coverage in a community. Moreover, under the threat posed by a case, most residents eagerly sought to be vaccinated. The emergency vaccination campaigns also dramatized to the public the fact that health authorities took the reporting of cases seriously, thereby encouraging improved reporting.

A third strategy, unquestionably the most important, was the so-called "mopping-up" program. This consisted of delineating specific high-risk areas in every country. These were primarily densely populated and less well vaccinated urban slums. At the low point in the polio season, two house-by-house campaigns one month apart were conducted to vaccinate all children under 5 years of age. This strategy had an epidemiological rationale, deriving as well from the smallpox experience. Although attempts to characterize the epidemiology of polio in Latin America had proved problematical, intuitively it seemed that smallpox and polio should share similarities in disease transmission patterns. Both are person-to-person contact-spread diseases, and the infected individual in both cases is able to transmit infection for a period of only a few weeks before developing immunity.

In the case of smallpox, epidemiological studies had revealed, at the height of seasonal occurrence, many cases and many outbreaks, widely spread. However, after the seasonal peak, cases and outbreaks decreased rapidly, so that eventually there would be perhaps as few as 3–5 discrete outbreaks, where earlier in the year there had been hundreds. At the low point in the season almost all such outbreaks were in poor, urban areas. A house-to-house vaccination campaign in the high-risk urban areas at the low point of the season was intended to eliminate the remaining chains of transmission. The oral polio vaccine was especially well suited for this purpose, since an infected vaccinee spread infection to all, or almost all, susceptibles in his household.

The mopping-up program was launched in 1989 and reached some 7 million children in 10 countries—not more than 10% of the population—but it appeared to be the right 10%. Polio cases dropped by 60%—from 315 cases in 1988 to 115 cases in 1989. The program continued in 1990 with a further reduction in cases of more than 80%—to only 18 cases. Finally, 9 cases were detected in 1991, the last case in the Americas occurring in August of that year.

The comparative efficacy of the several tactics is impossible to assess, because all were introduced more or less simultaneously. We suspect, however, that the targeted vaccination of high-risk areas was the most important.

The Global Program

As early as 1988, it was apparent that PAHO's goal to interrupt transmission in the Western Hemisphere by 1990 might well be achieved, and this stimulated interest in a

global effort. It was recognized that polio eradication in the Americas was more feasible than on most other continents because of the generally better developed infrastructure and greater health resources. Still, there are substantial areas in Latin America which are comparable to parts of Africa and Asia. Success was becoming apparent there as well, despite the problems in developing effective surveillance systems and in accurately diagnosing cases as well as the inherent problems of the vaccine itself—its thermolability and its deficiencies in antigenicity in tropical areas.

In 1988 the World Health Assembly agreed to undertake a global effort, and programs began on all continents, utilizing the manuals and methodologies essentially as they were developed in the Americas. A WHO Global Consultative Group assigned special priority to the program in WHO's Western Pacific region, i.e., East Asia. The countries of that region were strongly committed to such a program and several, including China, had already greatly intensified their efforts. Fully 30% of the world's population resides in this region. The Consultative Group reasoned that if transmission could be interrupted over a very different but large and populous area, it would offer encouragement to all countries across the world.

Progress in the Western Pacific has been dramatic, although this is still little known outside Asia. As of 1993, the number of reported cases fell to a record low of 1100 and continued to fall during 1994 despite far more sensitive surveillance systems than even 2 years previously. Of special interest is China itself. During early 1993, province-wide immunization days were conducted in those provinces experiencing the highest polio incidence, and targeted vaccination in high-risk areas also began. During 1993, there was for the first time no evident seasonal increase in polio. Then in December 1993 and in January 1994, China undertook to conduct national immunization days intended to reach all children under 4 years of age. Nearly 90 million children were vaccinated on each of these days in the single largest immunization effort ever conducted.

China's surveillance system now embraces a national diagnostic laboratory network, and its focus has shifted to surveillance for wild polio viruses, much as the Americas did during the final months prior to the interruption of poliovirus transmission. During 1992, wild poliovirus was detected in half of China's 30 provinces. In 1993, wild virus isolates were found in only 7 provinces, all but one of these being located in the southeast. Through August 1994, only one isolate has been found, and that in previously endemic areas in southeast China.

The goal in the Western Pacific region is to interrupt transmission by the end of 1995. In China, this appears attainable. The Philippines have detected no wild polioviruses since May 1993. Only three countries still record cases—Vietnam, Laos, and Cambodia—but programs in all three countries are progressing well and the number of cases is falling rapidly.

THE FUTURE

Certification of polio eradication in the Americas with prospects for the imminent interruption of wild virus transmission throughout Eastern Asia, coupled with steadily intensifying programs in Africa and elsewhere in Asia, provide encouragement that global eradication could be a reality, perhaps by the end of the century or soon thereafter.

This is still a possibility, but not a certainty. There are many obstacles yet to be surmounted. Resources are a constraint; political commitment in a number of countries is yet inadequate; conducting programs during civil strife is difficult and sometimes impossible for periods of time. Note, however, that all of these problems were likewise faced and successfully surmounted during smallpox eradication. In practice, experience showed that as it became increasingly apparent that eradication was achievable and im-

minent, needed resources and unique approaches could be found to deal with previously insoluble difficulties.

Which will be the most problematic areas? Many suggest Africa, but we believe not. We believe the most difficult challenge will be north India, Pakistan, and Bangladesh. The reasons are epidemiological and, again, smallpox is a model. Like smallpox, to sustain itself the poliovirus must be continually passed from one human to another in an unbroken chain of transmission. Children who are infected with a wild polio strain will excrete the virus for perhaps 5 to 6 weeks, but at the end of that time, they will have an immunity that will block subsequent virus acquisition. In developing countries, virus infection occurs early in life; at present virtually all adults and older children are immune. Thus, the critical links in the chain of transmission are children under 5 years of age and, indeed, primarily those under 3 years of age. For poliovirus to move from one village to another or from one country to another thus requires that a young infected child be transported from one site to another. In most countries and under most circumstances, few young children are transported from place to place.

Even in the case of smallpox in which adults accounted for 20% or more of cases, smallpox did not usually spread rapidly or over long distances. Cases were seldom transported across national borders on any continent, and most of those transporting infection from one area to another were young men and adults—not infants. When transmission was interrupted in one geographic area, it usually remained free from disease even when infection was widely prevalent in adjacent areas. This pattern has been seen with polio in Latin America.

How difficult was smallpox eradication in Africa? In all sub-Saharan countries of Africa, it was apparent that the disease died out rapidly even with modest levels of immunization, say 70–80%, and usually before effective measures could be mounted to detect and contain outbreaks. Indeed, smallpox virus transmission was effectively interrupted across almost the whole of Africa in less than 5 years. This can be explained by the problems of sustaining chains of infection on a comparatively sparsely populated continent with limited transportation facilities and with population centers that are relatively isolated from each other. To date, available polio data from Africa indicate that even with the modest efforts so far made, surprisingly large areas may already be polio-free, including much of southern Africa, as well as large areas of north Africa. However, improved surveillance is needed to confirm this.

In contrast to Africa, the transportation infrastructure of the south Asian countries of India, Pakistan, and Bangladesh is extensive and very inexpensive for the traveler. Buses, trains, and boats transport tens of millions of people annually, including families, to and from urban areas as well as to large fairs and religious gatherings. Smallpox proved to be extremely difficult to control in such settings, even with effective surveillance and containment measures. Whether the targeted mopping-up vaccination campaigns in high-risk areas can achieve the interruption of transmission remains to be evaluated. Other tactics may be required.

CONCLUSION

It now appears that the concluding battles of the polio eradication campaign will eventually be joined across three of the most populous countries of south Asia. Whatever can be done to improve the prospects for success must be pursued. A more stable and more antigenic polio vaccine could substantially improve the prospects for success, as could more rapid, precise measures for identifying poliovirus in the laboratory.

The next 5 years will be challenging indeed. The remarkable success of the Amer-

icas offers a beacon of hope, soon to be echoed by a second beacon in east Asia. As in the Americas, we can foresee as by-products greatly strengthened programs of immunization, of surveillance, and of laboratory diagnosis applicable to the control of other diseases. Albert Sabin would be pleased, I know, but predictably his comment would be, "See, I told you so!"

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