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THE ALBERT B. SABIN LECTURE

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In this inaugural lecture, it would be unconscionable not to deal with poliomyelitis and its eradication. As we all know, Albert's formidable intellect and skills in persuasion pervaded a broad agenda. However, as he himself noted, the understanding and ultimate conquest of poliomyelitis was a life-long preoccupation, beginning with his earliest work in 1931.[1,2] The sheer magnitude of that effort was aptly summarized by Dr. John Paul 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."[3]

It is important to recall a few highlights. The decisive years were the 1950s and 1960s. New vistas had been opened by Enders, Weller and Robbins who showed that poliovirus could be grown in a variety of human cell tissue cultures and that the virus could be quantitatively assayed by its cytopathic effect.[4] The growth of large quantities of poliovirus opened the way to the development of a polio vaccine. Preparation of an inactivated vaccine was, in principle, a comparatively straightforward process. In brief, large quantities of virus were grown, then purified, inactivated with formalin and bottled. Assurance that the virus had been inactivated could be demonstrated by growth in tissue culture. Within five years after the Ender's report, the large-scale Francis field trials were underway and in 1955 the inactivated, so-called Salk vaccine was licensed.

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 active infection more closely replicated naturally-occurring poliomyelitis and was thus more likely to offer lifetime protection. Furthermore, by inducing intestinal immunity, which the Salk vaccine did not, the spread of circulating wild viruses would be inhibited, 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 other virus vaccines. 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 strains — chimpanzees and monkeys — only made the task more difficult. Many struggled with these problems but none with greater or more single-minded dedication than Sabin himself. He describes in his history of poliovaccine development a two-year period when he first began to administer vaccine to adult volunteers.[5] In all, during that time 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 9,000 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 tested them repeatedly 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 were 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 millions persons in the USSR had received vaccine in field trials.[6] It proved to be both effective and safe. Based primarily on these Russian data, the vaccine was licensed for use in the U.S. 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 U.S. and in other countries, to mass campaigns using the Salk polio vaccine. The medical community insisted on inoculations being administered personally by a qualified physician or under his close supervision and there simply were not enough physicians or interest to permit an intensive large-scale effort. Oral vaccine totally altered the calculus. Little professional expertise was required to assure 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 vaccine.

Sabin argued for community-wide administration of vaccine in the U.S. 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 eventually took the case to the Board of Trustees of the American Medical Association and gained its endorsement.[5] Thereafter and often under the aegis of county medical societies, campaigns were conducted in many parts of America which were labelled "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 through 1964. In all, an estimated 100 million Americans were vaccinated with the three monovalent strains then in use. Reported cases of paralytic polio fell from 988 in 1961 to 106, three years later.

I briefly call attention to certain of these landmarks in the saga of oral polio vaccine as 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 and some, indeed, are here tonight. 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 poliovaccine 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.[7] Most such countries recorded few cases. Poor reporting was responsible, in part, but epidemiologists postulated that in countries with poor sanitation, children became infected early in life and developed immunity without paralysis. For these countries, polio immunization was not a high priority. Indeed, as of 1975, less than 5 percent of children in the developing world were receiving poliovaccine. During the 1970s, however, "lameness surveys" began to be conducted, first in Indonesia and Ghana and later in other areas. These measured in school children the prevalence of leg weakness characteristic of residual polio paralysis. The surveys, wherever conducted, revealed astonishingly high rates[8] — rates which were as high as in the industrialized countries before vaccine became available. The complacency with which polio had been viewed was shattered.

Not surprisingly, oral poliovaccine was one of the six antigens[9] selected by the World Health Organization (WHO) to be incorporated in the new expanded global program for immunization. But there were many who expressed skepticism about the potential

efficacy of polio control in the developing countries. There were two reasons for this. First, the vaccine was very susceptible to inactivation by heat. 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, as foreseen, it proved difficult to maintain. Second, in tropical areas, serological conversion rates following administration of vaccine were often surprisingly poor. The rates varied widely but some rates as low as 40 to 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 poliovaccine.

Sabin argued the need for large-scale vaccination programs[10] in tropical areas, citing two particular experiences. The first were the field studies of oral vaccine in Toluca, Mexico, which he had carried out with Ramos-Alvarez in 1960.[11] They found that a single dose of trivalent oral vaccine given to 85% of children resulted in a marked, immediate suppression of other enteric viruses. It was reasonable to infer that wild poliovirus would likewise be displaced. Sabin also cited Cuba's experience.[12] Beginning in 1962, Cuba 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 were not impressed, seeing little prospect for a similar type campaign in a non-totalitarian state.

Could a nationwide campaign be conducted in a country other than Cuba and, if so, what effect might it have? Brazil soon provided the answer. During its smallpox eradication program, Brazilian staff had developed exceptional skills in organizing mass campaigns and, following smallpox eradication, Brazil also employed mass campaigns to combat meningococcal epidemics. As of 1980, Brazil's routine vaccination programs were attaining levels of coverage of less than 50% and so health staff turned to the mass campaign which had served them so well in the past. They decided to organize two national immunization days each year.[13] More than 300,000 community volunteers, utilizing 90,000 vaccination posts, vaccinated some 20 million children under 5 years on each of two National Immunization Days. This represented about 90% of children in this age group. And this has been the practice every year since. The results were dramatic. Reported cases dropped from more than 2000 per year to 100 or less. Most of southern Brazil became polio-free, although transmission continued, especially in poverty-stricken areas of the Northeast.

Meanwhile, with leadership from the Pan American Health Organization, programs for immunization in the Americas had steadily 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 transmission by December 1990.[14] Since

1985, I have been privileged to serve as chair of the Technical Advisory Group for the effort. The program, directed by Dr. Ciro de Quadros, marks a major advance in public health in its creative use of epidemiology in designing strategy and tactics, in its imaginative involvement of community leadership and in its effective orchestration 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, at least as important, which I shall describe.

After 1985, polio incidence in the Americas continued to fall dramatically and, in 1988, the World Health Assembly decided on a target of global eradication by the year 2000. Albert's single-minded dedication to his beliefs had finally materialized as a major global effort.

In the Western Hemisphere the last known case of poliovirus occurred in August 1991 and, indeed, it was from this case that the last native wild poliovirus was isolated. This was less than 8 months beyond the target which had been established six years before. Subsequently, wild poliovirus was imported into Alberta, Canada, in 1993, from Holland infecting a religious sect which refused vaccination. But 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 an International Commission on the Certification of Poliomyelitis Eradication (ICCPE), chaired by Dr. Fred Robbins, was convened in 1990 to decide on criteria it would require before certifying that the circulation of wild poliovirus had been interrupted.[15] Over the past four years the Commission has closely followed progress in the program and has offered helpful advice. Independent National Commissions in every country have critically reviewed all data and, in August, reported their data to the International Commission. Seven days ago, the Commission reported 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

Let me return to 1985 and the launch of the eradication effort in order to explore with you the strategy and tactics employed. As I noted, the impetus for launching the polio eradication program in the Americas had been the rapid decrease in reported poliomyelitis coincident with improved immunization coverage and, especially, the remarkable results reported by Brazil. Could a hemisphere-wide effort succeed, an effort necessarily involving countries at all stages of economic development? It was clear that it would require an unprecedented level of cooperation and effort by every country. In September 1985 at the Pan American Directing Council[16] the nations of the Americas made the decision to begin.

Experiences gained during the smallpox campaign proved invaluable. The underlying strategic principles were the same — establishment of a surveillance system for rapid case detection and investigation and intensification of the vaccination program to heighten immunity. However, the differences between the two diseases, smallpox and poliomyelitis, dictated very different tactics.[17]

Surveillance

Surveillance was the critical component. Effective execution of any disease control program requires that program directors have current information regarding the occurrence of cases and their pattern of spread. In 1985 as eradication in the Americas began, information about cases of polio was provided primarily by a limited number of the larger medical centers — less than 500 in all, throughout Latin America and the Caribbean. Reports were provided sporadically and were more often monthly than weekly. Nevertheless, the system, incomplete though it was, recorded fewer cases than ever before.

There was a need 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 or not and plans were made to assure that all cases would be investigated by a trained epidemiologist. A standard form was designed to be completed for each case. The number of reporting sites

increased from less than 500 in 1985 to more than 20,000 by 1993. More than 90% reported promptly every week.

But what should be reported as a case? Experience with polio surveillance in the U.S. had revealed that physicians, seeing a paralyzed patient with a history of having been vaccinated, often dismissed the possibility of polio and suggested an alternative diagnosis. That the history of vaccination may have been in error or vaccine failure may have occurred was often ignored. We believed it to be critical that cases not be missed. If anything, we felt it better to err on the side of overreporting and so we decided to request that all patients presenting with flaccid paralysis of acute onset (AFP) be reported. Reporting of such cases was restricted to those under 15 years because essentially all cases of polio in Latin America were in children. Such cases were termed "suspect polio." The epidemiologist evaluated the cases within 48 hours. The case was discarded only if there was another definitive diagnosis. Otherwise, the case was labelled "probable polio," specimens were collected and a follow-up visit made at 60 days to determine the paralytic status of the patient.

In theory, the system appeared workable. Guillain-Barre disease, another cause of flaccid paralysis, was then thought to be very uncommon in young children and, thus, we believed that the great majority of cases of AFP in children would be caused by polio. Moreover, experience had shown that cases with paralysis caused by other enterovirus infections normally recovered fully by 60 days. Thus, it was anticipated that essentially all

cases with residual flaccid paralysis would be poliomyelitis. Experience proved us wrong. It was soon discovered that Guillain-Barre syndrome was far more prevalent than had been expected, that it was often difficult clinically to differentiate 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 to 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 Britain undertook a similar type of surveillance,[18] an identical rate was found. 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, too 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 remained a residual number of patients who were reported too late for specimens to be taken or who were lost to follow-up.

Because of these many factors, it proved difficult to obtain a clear picture of the 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 there were unquestionably 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 wild isolates of polio, however recovered. Efforts were redoubled to assure the collection 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; 18 in 1990, 9 in 1991 but none after August of that year.

Although the surveillance data were difficult to interpret, there were other 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, very early in the eradication effort began to isolate Type III strains from patients, many of whom had received three or more doses of OPV. Knowing that Type III poliovaccine virus was the least antigenic of the strains, the question rose as to whether there might be deficient amounts of type III vaccine virus in the mixture. Special field studies were promptly undertaken which indicated that a far better serological response could be obtained by doubling the quantity of type III virus in the vaccine.[19] 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 (NID) could have a significant effect in displacing wild poliovirus but initially few countries were prepared 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; others 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 was not occurring in sufficient numbers to engender 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 as well as in WHO. 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 shows to be less than half that required for routine vaccination at clinics and hospitals.[20] With support and encouragement by PAHO staff, increasing numbers of countries began to adopt the strategy, usually offering several vaccine antigens in addition to polio. Eventually, NID 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 OPV to all children under 5 years within an extended geographic area near the residence of a "probable polio case." We recognized that this action was unlikely to contain the spread of wild poliovirus given the very large proportion of subclinical infections. We assumed that by the time a case was discovered, the virus would already have spread. The reason for outbreak vaccination was based on our smallpox experience in which it had been found that the occurrence of a smallpox case signalled low vaccination coverage in a community and, under the threat posed by a case, most residents eagerly sought to be vaccinated. Moreover, an immediate vaccination campaign dramatized the fact that health authorities took the reporting of cases seriously.

A third strategy, unquestionably the most important, was the so-called "mopping up" program. This consisted of delineating in every country, specific high risk areas. 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. As I noted, attempts to characterize the epidemiology of polio in Latin America had proved problematical. Intuitively, however, it seemed that smallpox and polio should share similarities in disease transmission patterns. Both are person-to-person contact

spread diseases, the infected individual being able to transmit infection for a period of only a few weeks before developing immunity. At the height of the smallpox season, there had been many cases and outbreaks and they were widely spread. However, after a seasonal peak, the numbers of cases and outbreaks decreased rapidly, eventually reaching the point where there would be perhaps as few as 3 to 5 discrete outbreak areas where earlier in the year there had been hundreds. Almost all such outbreaks at the low point in the season were in poor, urban areas. The house-to-house polio vaccination campaign in these high-risk urban areas at the low point of the season was intended to eliminate the remaining chains of transmission. The oral poliovaccine was especially well-suited for this purpose given the fact that 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 7.0 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 in the Americas occurring in August of that year.

The comparative efficacy of the several tactics is impossible to assess, given the fact that all were introduced more or less simultaneously. We believe, however, that targeted vaccination of high risk areas was especially critical. Indeed, in retrospect, it seems

probable that fewer and less intensive efforts might have successfully interrupted transmission in the Americas. If so, this could have important implications to the success of eradication efforts, especially in Africa and Asia.

The Global Program

As early as 1988, it was apparent that PAHO's goal to interrupt transmission 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 given 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.

The World Health Assembly in 1988 agreed to undertake the 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 countries across the world.

Progress in the Western Pacific has been dramatic although, as yet, this is little known outside of Asia. As of 1993, the number of reported cases had fallen to a record low of 1100 and is continuing to fall this year despite far better surveillance than even 2 or 3 years ago. Of special interest is China itself. During early 1993, province-wide immunization days were conducted in those provinces experiencing the highest polio incidence and the so-called mopping up activities 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 what is the single largest immunization effort ever conducted.

A national surveillance system has been greatly strengthened and a diagnostic laboratory network is now in place. China has reached the point where 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 only 7 provinces had wild virus isolates, all but one of these being located in the Southeast. Through August 1994, only two

isolates have been found, one in far western China, believed related to outbreaks in Pakistan, and the second in southeast China.

The goal in the Western Pacific Region is to interrupt transmission by the end of next year. In China, this appears attainable. The Philippines have now 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 numbers of cases are falling rapidly.

The Future

Certification of polio eradication in the Americas with prospects now 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, however, 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

imminent, 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 I think not. I believe the most difficult challenge will be north India, Pakistan and Bangladesh.

The reasons are epidemiological and, again, I will draw on smallpox as a model. Like smallpox, the poliovirus, to sustain itself, must be continually passed from one human to another in an unbroken chain of transmission. A child who is infected with a wild polio strain will excrete the virus for perhaps five to six weeks but, at the end of that time, he will have an immunity which 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. 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 widely or rapidly. 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 of 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 to 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 which 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. Improved surveillance is needed to confirm this, of course.

In contrast to Africa, the transportation infrastructure of the south Asian countries of India, Pakistan and Bangladesh is extensive and very inexpensive for the traveller. 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 targetted "mopping up" vaccination campaigns in high

risk areas can achieve the interruption of transmission remains to be evaluated. Other tactics may be required.

Thus, it seems likely that the concluding battles of the polio eradication campaign will 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, more antigenic poliovaccine could substantially improve the prospects for success as could more rapid, precise measures for identifying poliovirus in the laboratory.

The next five years will be challenging ones indeed. The remarkable success of the Americas offers a beacon of hope, soon to be strengthened by a second beacon in east Asia. And, 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 would be pleased, I know, but predictably his comment would be — "See, I told you so!"

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