THE ERADICATION OF POLIOMYELITIS

(The Albert B. Sabin Lecture)

by

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Introduction

The understanding and ultimate conquest of poliomyelitis was Albert Sabin's life-long preoccupation, beginning with his earliest work in 1931. (Sabin and Olitsky, 1936; Sabin, 1965) The magnitude of that effort was aptly summarized by 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." (Paul, 1971) 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 1969 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, Weller and Robbins, 1969)

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 Enders' report, large-scale field trials were already underway and in 1955 the inactivated, so-called Salk vaccine was licensed for use.

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 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. (Agol and Drozdov, 1993) It proved to be both effective and safe. Based primarily on 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 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

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. (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 percent of children in the developing world were receiving poliovaccine. 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, Kratzer, Ofosu-Ammah and Belche, 1977) The complacency with which polio had been viewed in the developing countries was shattered.

Because of these findings, oral poliovaccine 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

health officials in the Americas applauded the effort but saw little hope for mounting a similar type of 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 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, 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 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 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

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)

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 assure 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 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 labelled "probable polio," specimens were collected and a follow-up visit made at 60 days to determine the paralytic status of the patient.

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 speciments — 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, 9 in 1991 but none 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

(Creese, 1984) With support and encouragement by PAHO staff, increasing numbers 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 poliovaccine to all children under 5 years 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, so encouraging improved reporting.

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

— 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 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 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.

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.

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 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 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

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 targeted "mopping up" vaccination campaigns in high

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