# POLIO ERADICATION - REFLECTIONS

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I very much appreciate the opportunity to join with you in this Colloquium, albeit, considering the time and the day, I wondered if there might not be a greater interest in the eradication of the speaker than in the eradication of poliomyelitis. Your persistence and forbearance are appreciated, however.

At the outset, let me state that I believe the global eradication of poliomyelitis to be a feasible goal. The critical question is when, and this I will return to later. Given my previous association with smallpox eradication, many of you might assume that I would be an unabashed enthusiast of eradication programs of whatever stripe. However, it is precisely because of my long association with the smallpox campaign that I have been and continue to be reticent about another eradication goal - and for a very simple reason. Smallpox, by virtue of its clinical and epidemiological characteristics, offered, by far, the most susceptible target. A ten year goal was established - and achieved - the last case occurring on 26 October 1977 some nine months after the target date. The course of the campaign, however, was anything but a smooth one, and the outcome anything but foreordained as late as six months before the last case. Adequate funding was an ever-present problem and, despite the fact that smallpox was a concern

to every country and that all countries were engaged in costly vaccination and quarantine programs, only $8 million on average per year was contributed. On more occasions then I care to count, success hung by the most slender of threads - dependant on events outside of our control, be it a change in government, the cessation of a civil war or the occurrence (or non-occurrence) of natural disasters such as floods or famine. Indeed, programs during the last 12 months of the campaign were conducted in the face of open warfare between Ethiopia and Somalia, extensive famine throughout the infected areas of both countries, unprecedented floods in the most infected areas of Somalia and constantly moving, infected refugees and nomads. I would suggest that the situation today is better in some areas but worse in others, albeit more substantial funding is available for the polio program than it was for smallpox - at least for the moment.

The eradication of smallpox relied heavily on what we termed surveillance-containment. Reporting networks and active searches identified cases; surveillance teams then isolated patients and systematically vaccinated all contacts. Infected patients capable of transmitting infection all exhibited a characteristic rash which was recognizable by villagers and staff alike. Thus, we could discover at any point in time where infection was present and, because 70% bore residual scars, we could ascertain the past history of disease in an area. These were formidable advantages in devising strategy and tactics. And indeed it proved possible in some areas to interrupt transmission when as few as 50% had been

vaccinated. While the disease and its epidemiology offered other favorable characteristics, these were the most important.

Poliomyelitis infection, in contrast, is difficult to track given the fact that only 1 in 50 or 1 in 100 or perhaps fewer infected persons exhibit paralytic symptoms. There is great difficulty in determining where the virus is and whether a given focus has been eliminated. Moreover, surveillance requires a far more elaborate laboratory support structure and more finely honed clinical skills in differential diagnosis of the paralytic cases which do occur.

Given the intrinsic problems of polio surveillance and recognizing the narrow margin by which smallpox eradication was achieved, it is evident that to succeed we will require every advantage we can muster and the most critical is a highly antigenic, thermostable vaccine. The existing vaccine, essentially unchanged in 25 years, requires constant refrigeration essentially up to the point of administration thus, a 'cold chain' is needed which is all but impossible to sustain reliably in primitive tropical countries. Contrast this with smallpox vaccine which could withstand temperatures of 37° C. for one to six months. Moreover, the present polio vaccine, when used in tropical countries, induces seroconversions in only 60 to 80% of recipients after the administration of three doses - and reaching populations of very young children once, let alone three times in a year, is a formidable challenge in many countries. Again, this is in marked contrast with smallpox vaccine which confers immunity in close to

100% of children with one dose.

It is unconscionable that so few resources have been made available for improving the present quarter-century old vaccine, but such have been our priorities. A number are now endeavoring to redress this situation albeit still with far less financial support than needed - and time is of concern.

Why do I say this? If history is a reasonable barometer, we can predict fatiguing interest both among national governments and the international donor community within a period of a decade, perhaps less. Such is the history of health programs. Given the decision in 1988 by the World Health Assembly to embark upon a global polio eradication program, one can anticipate the beginning of a fading interest perhaps as soon as five years out. Thus, my concern for deliberate haste in our research efforts, an urgency regrettably not as yet responded to by potential funders.

Given these problems, the not illogical question to ask is - why polio eradication, why not pursue more modest goals of polio control? Let me answer this by tracing the history of the effort beginning with perceptions at the time of introduction of oral polio vaccine which, as you know, contains the Sabin strains.

Knowing Albert Sabin, as so many of us do, one might have anticipated him to issue a clarion call for polio eradication soon after the vaccine was licensed, but he did not. In his 1965 Lasker Award lecture, he was asked to discuss the prospects for polio eradication. He said, "...we now have the knowledge and the means with which to eradicate poliomyelitis in many parts of the world

and quickly to control epidemics where the disease cannot, for various reasons, be eradicated..."[1] His caution, in part, may well have reflected the then prevalent belief that paralytic poliomyelitis was not yet a significant problem in the developing world. Payne[2] and Paul,[3] in the mid-1950's, had argued that clinical poliomyelitis tended to increase only when infant mortality rates declined below 75 per 1,000 live births and most developing countries were then above this level.

The belief that polio was not a significant problem in developing countries persisted into the 1970's. Indeed, the first proposed immunization programs for developing countries, in 1971, recommended polio vaccine for general use only in selected countries or areas.[4]

The possibility that polio might be a more serious problem than we had thought was suggested to me by American orthopedic surgeons working in Jordan in the late 1960's. They commented on the remarkable frequency of polio-induced contractures which they were finding. We had a chance to explore this as a by-product of the smallpox eradication campaign. Staff were exploring a variety of problems through survey methods and so we proposed a study of polio occurrence to be measured by a survey of the prevalence of flaccid paralysis among young children. The belief was that few conditions other than polio induced persistent flaccid paralysis. By assessing the prevalance of such conditions, an estimate of polio incidence could be obtained. Such studies in Indonesia and Bangladesh, and later, other countries, revealed a far higher

incidence than any had suspected. Whether or not the Payne and Paul correlation of low polio rates with high infant mortality resulted from artifacts of under-reporting or were no longer valid observations, has not been clarified. Whatever, polio was clearly a problem of greater magnitude in all countries then had been thought and it was added to the list of vaccines recommended by the 1974 World Health Assembly for WHO's expanded program on immunization.

Meanwhile, poliomyelitis incidence in the United States fell to very low levels [**SLIDE 1**]. Note that this is a log scale. Indeed, after 1972, virtually all cases were vaccine-associated or represented importations - primarily from Mexico or, in one instance, a 15 case outbreak among the Amish, imported from the Netherlands via Canada. Canada's experience was similar [**SLIDE 2**]. If one excludes the 11 cases occurring among Amish groups in 1978-79, it is apparent that wild virus transmission probably ceased in Canada sometime in the early 1970's.

That transmission may have been interrupted in the early 1970's was not appreciated, however, by those at CDC or those in Canada. As recently as 1987, CDC staff wrote about "the <u>virtual</u> elimination of disease caused by wild polio virus," - but not about the interruption of virus transmission. Other industrialized countries likewise ceased to find cases caused by the wild virus and, in retrospect, concluded that transmission had been interrupted. Neither in North America nor in Europe as a whole, was there an organized program of surveillance which endeavored to

document currently all suspect patients with paralytic illness. In fact, it can be argued that there was no pressing need to do so. As we shall see, however, the launching of an eradication program throughout Latin America required the building de novo of a base of experience regarding the surveillance of paralytic illness and the epidemiological behavior of polio. There were a number of surprises.

What led to the decision to undertake a polio eradication program? As I had noted earlier, the 1974 World Health Assembly decided on a global immunization program designed to provide antigens against six diseases: polio, measles, diphtheria, pertussis, tetanus and tuberculosis. Estimates at that time suggested that not more than 2 to 5% of children were being vaccinated with these well-established antigens. The program gradually grew in scope but resources were never plentiful. Finally, in 1983, Robert MacNamara, through Jonas Salk's intervention, took a personal interest in the program and proposed that the Rockefeller Foundation convene a meeting in Bellagio (March 1984) to acquaint major donors with the needs and opportunities. Subsequently, UNICEF and AID, among others, substantially increased their contributions. Meanwhile, Sabin interested Rotary International in the polio activities and Rotary subsequently raised nearly $250 million in support. Immunization coverage steadily increased.

The next important event was precipitated by Brazil's experience in polio control [**SLIDE 3**]. Dr. Ciro de Quadros of the

Pan American Health Organization convened a meeting to discuss the feasibility of polio eradication throughout the Western Hemisphere. Reporting was acknowledged to be deficient but it was clear that the reporting system which previously had reported hundreds of cases per week was now reporting very few. Most of the cases during the 1970's had been reported from tropical areas of the Northeast, areas where various studies had shown that seroconversion rates seldom exceeded 60 to 80% after three doses of vaccine. National Vaccination Days, conducted twice each year, and offered to all children from zero to five years was clearly having a surprising impact even in the tropical Northeast. Similar experiences were documented in other Latin countries. Shown here are Bolivia [**SLIDE 3B**] and Columbia [**SLIDE 3B, SLIDE 3D**]. An eradication program throughout the Western Hemisphere with a target date of December 1990 was recommended and subsequently approved by the Directing Council of PAHO.

The program embraced two new components which inexplicably had been lacking in the decade-old global immunization program - surveillance and research. For surveillance, a reporting network was created calling for weekly reports from all hospitals, rehabilitation centers and clinics apt to see cases of paralysis. Today, there are more than 7,000 reporting sites. Each site reports all cases of acute onset flaccid paralysis among children less than 15 years of age. Trained surveillance officers are expected to visit each case within 48 hours and if a specific diagnosis other than poliomyelitis cannot be made, it is labeled as

"possible poliomyelitis" and specimens are obtained. Reporting of 'acute flaccid paralysis' rather than polio was decided upon, when it was found that some pediatricians, confronted with flaccid paralysis in a vaccinated child, diagnosed the illness as Guillaine-Barre disease. Possible vaccine failure was seldom considered. Guillaine-Barre syndrome, however, was thought to be extremely rare in children. I say 'thought' because the literature provided us little guidance as to incidence and consultant pediatricians could offer only informed clinical judgment, without data. Polio control experiences in North America and Europe were of no help as no attempt had been made at a central level to gather data on the occurrence of flaccid paralysis.

The surveillance system quickly divulged two important findings. The first was that most cases were type III polio, customarily much less common than type I polio, and that many were in vaccinated patients. Studies of serological responses to the OPV formulation then in use showed a satisfactory serological response among less than 40%. Additional studies revealed that if the type III titer were doubled a response was obtained which was comparable to monovalent type III vaccine. The vaccine formulation for the Americas was promptly changed (for the first time in 25 years, I might add) and type III cases quickly dropped. The second discovery was that cases of acute flaccid paralysis, even in areas where no polio virus could be found, were far more common than we had believed. Rates of one to two cases per 100,000 children were usual. Most cases appeared to be Guillaine-Barre disease, but to

be more certain of the diagnoses, qualified neurologists had to be incorporated into the surveillance teams. And such is now the practice in all countries.

A laboratory network was established, now embracing ten laboratories. This was done through careful selection of the best of the Latin American laboratories already employing tissue cultures. A standard manual of procedures was developed, training courses were held and all were provided with identical equipment and reagents. Their task was maximally simplified to the extent that the laboratories were expected only to identify and type polio viruses. Other pathogenic enteroviruses were not characterized. Unknown panels of specimens are distributed every six months as a quality control check. Simple, straightforward - yes, <u>but</u> results from the first panel of unknowns looked as though diagnoses had been made by casting darts at a dart board. Another year of intensive training and no end of problems with laboratory contaminants, changing personnel and a host of other problems were to ensue before prompt, reliable results could be obtained. Meanwhile, analyses of serological specimens revealed them to be of little help. And this indeed had been our experience in the United States during the 1960's. Accordingly, serological testing was stopped.

Surveillance for wild polio virus in the Americas now depends on isolation of polio virus from two stool specimens, desirably collected within 14 days of onset. We believe this should identify at least 95% of infections but studies are needed to confirm this.

Again, past experience in other countries has been of no help - this measure of sensitivity has never been assessed! **SLIDE 3** shows that specimens are now being obtained from 80% of cases and within 14 days.

Meanwhile, Olin Kew at CDC, with PAHO support, began to sequence wild polio viruses [**SLIDE 4**] and discovered that all strains within defined geographic areas and, indeed, over a period of many years were highly related and could be readily differentiated from strains prevalent in other areas. This was a startling discovery - although perhaps one which we might have anticipated - as it implied that the virus did not readily spread from endemic areas to distant ones. It seemed reasonable to conclude that if a substantial geographic area became free of polio, it was likely to remain so. With this information, it was possible to deploy resources more effectively.

The vaccination strategy came to consist of three parts [**SLIDE 5**]. The so-called 'mopping up' component may be subdivided into two. The first is prompt and intensive vaccination of <u>all</u> children under five years whenever a possible case is discovered. This is done on the assumption that cases are most likely to be found in areas of poorest coverage and that the populace is most receptive to vaccination when there is a suspect case in the area. A second component consists of a special house-by-house vaccination in slum areas during the inter-seasonal low in incidence. This followed on the discovery that cases tended to be most prevalent in urban slums and, reasoning from our smallpox studies, this would be

the area which would sustain transmission between peaks in occurrence of disease.

So what has happened? **SLIDE 6** shows the expected rising incidence of reported cases of acute flaccid paralysis as surveillance improved but, at the same time, a declining incidence of confirmed cases. Isolates of wild polio virus for 1987 are shown in **SLIDE 7**; for 1988 in **SLIDE 8**; and for 1989 in **SLIDE 9**. During 1990, four isolates of wild polio virus have been obtained:

in Ecuador in March

in Peru in April

in Mexico in February and June.

The last known case experienced onset in Mexico on 8 June, four months ago. There may or may not be others but hope runs high that the last case will occur before the end of the year.

The next vexing problem is to prove to our own satisfaction and to others that transmission has been interrupted - and proving a negative in science, as you all know, is difficult. As one approach, studies are now in progress to assess the potential application of the PCR technique to detect wild polio virus in sewage specimens. The results, so far, are cautiously encouraging.

The dramatic progress in the Americas was noted by other countries and, with only a limited understanding of the difficulties in executing this program, the 1988 World Health Assembly decided on the goal of global polio eradication by the year 2000 - an action reaffirmed in September of this year at the World Summit for Children.

My own views were solicited at the time, and I am happy to reiterate them here as later experiences in the Americas have not altered the conclusions. Taking into account the existing state of health services and the infrastructure of roads and communications in different countries, I would foresee the possibility of transmission being interrupted fairly soon throughout Europe, including that part of the USSR in Asia, throughout North Africa and in such industrialized countries as Japan, Korea, Australia and Taiwan. Success in China might also occur but problems with the quality of its vaccine make this an uncertain proposition.

South Asia and sub-Saharan Africa are the most difficult challenges, as they were during smallpox eradication. Health services are weak and poorly supervised, laboratory facilities are sparse and transport is difficult. For neither of these areas do I have much hope for interruption of polio transmission without simpler, more foolproof diagnostic methods and a far more heat stable vaccine which confers upwards of 95% protection after no more than two doses. Appeals for research funds to abet this effort have been made to both national and international organizations but, as yet, few resources have been made available.

However, in consequences of these initiatives, a meeting of international and bilateral agencies was convened in September at which it was decided that substantial additional funds should be provided in support of research to produce new vaccines and new methods of vaccine presentation so as to protect children at or soon after birth against a broader array of diseases, using multi-

component antigens administered by mouth, if possible. Proposed budgets ranged from $150 to $1,000 million dollars over the next decade. It was agreed that an inter-organizational task force should be established to set priorities and to orchestrate the effort.

The next chapters remain to be written.

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