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JAPAN PRIZE LECTURE

The Eradication of Smallpox

(Full Text)

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In 1966, the World Health Assembly voted to commit US \$2.4 million to intensify the program of smallpox eradication. This program began in January 1967. Although hope was expressed that the goal could be achieved in 10 years, most delegates were, in fact, skeptical of the prospects for its success. Their doubts were understandable. An important underlying concern was the fact that no disease had ever before been eradicated. Many believed that, through evolution, man and his microbial environment were so related and interdependent that eradication of an organism could not be achieved however many resources were made available. Smallpox at that time was then endemic in more than 30 countries with a population of more than 1,000 million persons (slide 1). Many of these countries were among the world's poorest and most densely populated. In all, there were between 10 and 15 million cases occurring each year. To imagine that all countries which were endemic for smallpox, as well as adjacent ones, could work cooperatively and effectively together to achieve any common objective seemed most unlikely. Even with universal goodwill, the problems of war and civil

strife, as well as natural disasters would inevitably have to be overcome. The obstacles were formidable and the resources available were few indeed.

We began the program with a two-fold strategy. First was to vaccinate 80% of the population in all endemic countries with smallpox vaccine of assured potency. The second was to establish a comprehensive reporting system which would detect cases of smallpox when they occurred and to investigate and to contain outbreaks by isolation of the patient and vaccination of his contacts.

The strategy was different from that which had been employed before 1967. Until 1967, progress in smallpox control had been measured in terms of millions of persons vaccinated. Little had been done to assure that the vaccine in use was potent or that the numbers of vaccinations being reported were accurate. Nothing had been done to improve the reporting of cases and, indeed, as studies later revealed, only one case in 100 was actually being reported at that time.

We estimated a need for more than 250 million doses of vaccine each year. If purchased, this would have exceeded the entire budget available to us. And so, we sought donations while, at the same time, we worked with laboratories in the developing countries to help them produce their own vaccine. Two laboratories, one in Canada and one in the Netherlands, agreed to test batches of vaccine intended for use in the program. This was the first international quality control system ever to be established for a biological product, but all countries

cooperated fully in the effort. Initially, most of the vaccine was donated by the U.S.S.R. and U.S.A. but within six years, 80% of the vaccine was able to be produced in the developing countries themselves.

In 1968, we field tested a remarkable new invention developed by Wyeth Laboratories in the U.S.A. - the bifurcated needle (slide 2). The needle was dipped into the vaccine. By capillarity, vaccine was held between the tines and 15 rapid strokes implanted sufficient vaccine virus to assure successful vaccination. Only one-fourth as much vaccine was required as had been required with older techniques. Vaccinators could be trained in 10 to 15 minutes. The needles were inexpensive and could be sterilized and reused many times.

During vaccination campaigns, we organized teams which visited a sample of the areas which had been vaccinated to verify that at least 80% had been vaccinated and that the vaccinations were successful. This approach was a revolutionary idea for many countries and often accepted only with reluctance because to national health officials, it seemed wasteful to assign valuable staff only to check the work of others. This, of course, represented nothing more nor less than "quality control," much as is practiced in industry, and wherever assessment was implemented, the performance of the vaccination teams improved.

The most important component of strategy in the campaign, however, was the addition of surveillance for smallpox cases. "Surveillance" incorporated a number of different activities designed to improve the detection and reporting of smallpox cases. Our target was "0" cases of smallpox (slide 4). To measure progress, we had to know how many cases

were occurring. By continually determining which groups of individuals were developing smallpox, we were able to alter our strategy to assure vaccination of those who were most frequently afflicted and to stop outbreaks by isolating patients and vaccinating their contacts. Roving teams visited health centers and hospitals to ask that they report cases each week. They visited schools and markets to show the WHO Recognition Card (slide 5) and to ask if anyone had seen cases of smallpox. When cases were reported, the teams promptly investigated them and contained the outbreaks. In Africa and South America, we found that a surveillance team of only two to three persons could control smallpox in an area inhabited by two to five million persons.

Between 1967 and 1969, programs began in most infected countries and by 1971, all were in operation. Progress in most of Africa and the Americas was rapid (slides 5 and 6). By 1970, the number of endemic countries had decreased from 33 to 17 (slide 7). By 1973, smallpox was confined to the Indian subcontinent, to Ethiopia whose program had just begun and to Botswana which became free of smallpox later that year.

The Indian subcontinent, however, proved to be a formidable challenge. Efforts such as we had made in Africa had little impact. In the endemic Asian areas, nearly 700 million people lived in the most densely populated regions on earth. They traveled frequently and for long distances by trains and buses. Many smallpox patients, infected in cities, returned to their villages to recover or to die. The disease spread rapidly and widely. There were many then who knowingly assured us that in Asia, the traditional, ancient home of smallpox, eradication

could never be achieved. More than once we wondered if they might not be right.

During the summer of 1983, a special campaign was planned. All health workers, during one week each month, would visit every village in India - later every house - in search of cases. When cases were discovered, special teams moved in to contain the outbreaks. The logistics were formidable - 120,000 workers were assigned to visit over 100 million households. Assessment teams visited a 10% sample to verify the work. Additional teams searched for cases at markets and schools. More than 8 tons of forms were needed for each search, and hundreds of vehicles, as well as tens of thousands of bicycles, boats and rickshaws.

The first search took place in October. The results were appalling. In the northern Indian State of Uttar Pradesh, whose population was 100,000,000, two years of intensive work had already been devoted to improve the reporting system (slide 8). Several hundred cases were then being reported each week. During the first one-week search, nearly 7,000 unreported cases were found. However, with the search program, more outbreaks were found, and more rapidly. Once found, they could be contained. The quality of the searches steadily improved. More rigid control measures were used. House guards were posted at each infected house on a 24-hour schedule to prevent patients from leaving, and to vaccinate all visitors (slide 9). As cases decreased, a reward was offered to the villager who reported each new case. Techniques employed in India were soon adapted for use in Pakistan, Nepal and Bangladesh.

By the summer of 1974, we knew that eradication in Asia could be achieved. In October 1974, the last case occurred in Pakistan; in May 1975, in Nepal; in June 1975, in India; and, finally, on 16 October, 1975, in Bangladesh (slide 10). This three-year-old girl, Rahima Banu, became the last victim of smallpox in Asia.

Only Ethiopia remained to be conquered (slide 11). Ethiopia, however, was a challenge unto itself. It was a country of 25 million people scattered across desert and highland plateau in an area three times larger than Japan. It is a country where half the population lives more than a day's walk from any accessible road (slides 12 and 13). Health staff were few; we had less than 100 for the entire country. Insurrection and fighting were widespread. Our smallpox staff were periodically kidnapped and fired upon; one of our helicopters was destroyed by a hand grenade and others damaged by bullets. In 1971, during the program's first year, 26,000 cases were recorded, probably one-tenth the actual number. Gradually an intrepid team, including volunteers from Japan, the U.S.A. and Austria, eliminated the disease from the northern highland areas. Smallpox remained only among nomads of the vast Ogaden desert. Here, it was difficult even to find the nomads, who often traveled 20 or 30 miles in a night. To solve that problem, we hired and trained the nomads themselves as vaccinators and searchers. In August 1976, the last outbreak was contained.

There was, however, one last chapter. Somali guerrillas, then fighting Ethiopian forces, brought the disease back to Somalia. The first cases were reported in September 1976. For yet another year a smallpox campaign was waged throughout Somalia. But, at last, the final chains

of transmission were severed (slide 14). Ali Maalin, a cook from Merka, Somalia, proved to be the last case in a continuing chain of infection extending back at least 3,000 years. The 10-year time target had been missed, but only by 9 months and 26 days.

Two questions remained: (1) How could we be certain that eradication had been achieved; and (2) even if we were confident, how could national authorities also be sufficiently confident to permit them to stop vaccination?

Smallpox, to persist, had to continue to spread from person to person. Thus, evidence of persistent transmission would be increasingly apparent with time, either through detection of one of an increasing number of cases or through detection of facial scars. We believed that two years of surveillance would detect cases if present. After the last cases occurred in a country, we publicized a reward to be given to anyone who reported a case which could be confirmed as smallpox. The reward brought a flood of reports of persons with diseases of all types. In addition, special teams conducted repeated house to house searches over vast areas. No cases were found.

To provide assurance to others that eradication had been achieved, international commissions were appointed to visit each previously infected country after at least two years had elapsed since the last case. The commissions reviewed detailed reports of the programs and verified these through visits in the field.

In all, 14 different International Commissions visited 48 different countries. Special visits were made by WHO staff and consultants to an additional 28 countries. Because numerous respected scientists from many different countries participated in these Commissions, knowledge of the program and the rigorous evidence required to certify eradication became widely known.

Finally, in 1978, the Director-General of WHO appointed a Global Commission to satisfy themselves personally that global eradication had been achieved. After two years' work, the Chairman was able to report to the World Health Assembly that there was adequate evidence. Vaccination has now been stopped and international vaccination certificates are no longer needed.

Variola virus is now confined to glass vials in just two laboratories.

The possibility that there might be a natural reservoir of the virus had been a continuing concern to us. Wide-ranging studies were undertaken to try to discover such a reservoir. None was found. The best evidence that there is no reservoir comes from epidemiological observations. All smallpox outbreaks which were detected in smallpox-free areas since the program began were able to be traced to other known human cases. If there were an animal reservoir or if the virus could persist in nature in scabs or other material, apparently "spontaneous" outbreaks should have been discovered. None were identified.



Thus, barring improbable circumstances, a human case of smallpox will never again be seen.

The savings to be realized because of the cessation of vaccination and quarantine measures are estimated to be U.S. \$2,000 million dollars each year. In comparison, international assistance to the program amounted to an average of only U.S. \$8 million per year.

The program illustrates how inexpensive and effective prevention can be and how applicable it is for developing countries. Smallpox eradication was achieved primarily by national health staff. At WHO headquarters, we never had more than six professionals and never more than 100 in the field at any given time. Prevention based on immunization is especially applicable. Indeed, WHO has built on the smallpox program to begin a global Program of Immunization to protect the 100 million newborns each year against six major infectious diseases.

Smallpox eradication may now seem to have been comparatively straightforward but there were innumerable times in which the program balanced on a knife edge between success and disaster, decided by an unexpected change of government, a cessation of hostilities, or an heroic exhibition of dedication and courage by field staff.

A small but important step has been taken in a long and difficult journey toward better health but in taking that step, we have renewed confidence that other successes in prevention and public health are possible.

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