

Smallpox Target Zero

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On October 26, 1979, victory was declared in a ten-year, worldwide effort to efface from the earth one of humankind's most ancient plagues. The author, a University alumnus, directed the campaign as chief of the World Health Organization's smallpox eradication unit.

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It was on October 22, 1977, in the southern Somalian town of Merka, that a twenty-three-year old cook, Ali Maalin, developed high fever and headache. He was hospitalized and treated for malaria, but his symptoms persisted. Four days later a rash developed. By the fifth day, it was apparent that he had smallpox. Field staff of the World Health Organization soon discovered that just nine days before he became ill, he had been exposed to two children infected with smallpox—at that time the world's only known remaining cases of this once virulent disease. Ali had exposed 161 people. All were identified, vaccinated, and kept under surveillance. None developed smallpox.

Since that date, thousands of field staff in countries that had earlier been infected searched village by village and house by house to discover other cases—in Afghanistan, Bangladesh, Ethiopia. They showed the WHO "recognition card," a picture of a person with smallpox, and asked, "Have you seen anyone with a rash like this?" "A rash on the face or on the body?"

To encourage cooperation, the World Health Organization offered a reward of \$1,000 to anyone reporting a case of smallpox. Tens of thousands of persons with rash and fever were investigated and thousands of specimens examined in WHO Reference Centers in Moscow and Atlanta. In Somalia, a visitor with even a mild case of acne could reasonably expect to be taken into custody as a suspect case.

Reports of cases came from around the world, even from villages in France, from Brussels, and from San Antonio. Two more cases occurred during 1978 following a tragic laboratory accident in Birmingham, England. But, except for these two cases, none was smallpox. International commissions visited each country to verify the results. In the fall of 1979, the last of these completed its work.

On October 26, the director-general of the World Health Organization was able to announce from Nairobi, Kenya, that "smallpox target zero" had been achieved. For the first time, a disease had been eradicated from the earth.

Variola virus, once the cause of the most feared and devastating disease known to man, is now confined to glass vials in seven laboratories under conditions of high security.

The origin of smallpox antedates written history. The great Egyptian Pharaoh Ramses V, who died 3,000 years ago, in 1160 B.C., is believed to have succumbed to smallpox, and the disease was described in 1122 B.C. in China, where it was known as "taï-tou." Indian Sanskrit texts suggest that it was known there for as long. Throughout India even today, there are temples to Sitla Mata or Sitla Devi, as she is variously known, who is believed to possess the power to ward off smallpox and to prevent death among victims of the disease. In other

cultures also there were deities consecrated to smallpox—Saponna in Western Africa, Omulu in Brazil, and others lost to history.

Deities consecrated to diseases other than smallpox are all but unknown. But few diseases anywhere were as devastating. It occurred in epidemics and killed twenty to forty percent of its victims, leaving the others permanently scarred or blinded. It could spread in any climate, in any area. As with measles, almost everyone eventually contracted the disease. There was and is no treatment.

Smallpox became established in the increasingly populated Europe of the Middle Ages. In the seventeenth century Lord Macauley wrote: "That disease was then the most terrible of the ministers of death . . . smallpox was always present filling the churchyard with corpses . . . and making the eyes and cheeks of the betrothed maiden objects of horror to the lover." Royalty was not exempt. The twenty-nine-year-old Elizabeth I of England developed severe smallpox, leaving her bald and her face permanently scarred. Smallpox fatalities included Louis XV of France, William II of Orange, Peter II of Russia, and the Emperor Joseph I of Germany.

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In 1796, Edward Jenner discovered that inoculation of cowpox material into the arm of a susceptible person prevented smallpox. Folklore of the time attributed the celebrated unblemished complexion of dairymaids to

their acquisition of cowpox, a localized infection on their hands that came from contact with cows. Jenner deliberately took material from an infection on the hand of a young dairymaid, Sarah Nelms, and inoculated it into the arm of eight-year-old James Phipps. He later showed that Phipps was protected from smallpox and that the material could be transferred to the arm of one person from a pustule on the arm of another. In less than five years, Jenner's cowpox had been carried around the world, a remarkable feat in that slower era of sailing ships and stage coaches. In 1801 Jenner wrote: "It now becomes too manifest to admit of controversy that the annihilation of the Smallpox, the most dreadful scourge of the human species, must be the result of this practice [of vaccine inoculation]." More than 175 years were to pass before his vision was realized.

Propagation of cowpox, later called vaccinia virus, by arm-to-arm transfer permitted only small numbers to be inoculated at one time. Hepatitis and syphilis were sometimes also transferred simultaneously. Extensive vaccination awaited large-scale production of vaccine. In the mid- to late 1800's, it was found that the virus could be grown in quantity on the flank of a calf. However, such vaccine, if unrefrigerated, became ineffective in a matter of days. With increasing use of refrigeration, countries in the more temperate areas began to control smallpox. Even so, as recently as 1926, a Swiss delegate to a League of Nations meeting on quarantine procedures argued: "Smallpox has, in reality, no place in an international convention. It is not a pestilential disease in the proper sense of the term; it is, in effect, a disease that occurs everywhere. There is probably not a single country of which it can be said that there are no cases of smallpox."

The United States recorded 33,000 cases that year and 10,000 cases as recently as 1939. In developing countries, the disease was all but unchecked.

During the 1940's, vaccination programs in Europe and America effectively stopped smallpox transmission in those two areas. But in the developing world, where refrigeration was virtually unknown, vaccines which could withstand warm temperatures were essential. In the early 1950's, Leslie H.



"Have you seen anyone with a rash like this?" was the constant question in the search for cases. (WHO photo by Roberts and Dale)

Collier, working at the Lister Institute in England, perfected the technique of freeze-drying vaccine, much as coffee is preserved today. Vaccine preserved in this manner remains potent for a month or longer at temperatures of 93° F.

Meanwhile, outbreaks of smallpox continued to occur in Europe as travelers brought the disease back from countries where it was still endemic. When introduced, it was as severe and as often fatal as in the developing countries. So frequent were the importations that both England and Germany maintained special smallpox hospitals that could be opened and staffed when outbreaks occurred. Vaccination certificates were required of almost all international travelers, and nationwide smallpox vaccination programs were routine in most countries, including our own.

Here was a problem of concern to all peoples. Why not a global campaign of eradication? In 1958, the World Health Assembly (the controlling body of WHO) at last decided on just such a course of action.

During the succeeding years, mass vaccination programs were begun in a number of countries, but only a few were successful. Countries which succeeded in stopping transmission of the disease within their own borders experienced reinfection from their neighbors. Hoped-for contributions of money and vaccine were not forthcoming. Most discouraging, the strategy itself did not seem to be working.

In many areas of the Indian subcontinent, more vaccinations were performed than there were people. But still smallpox persisted.

With an obviously foundering program and with an increasing sense of frustration, the 1966 World Health Assembly decided to make one further attempt. It voted to allocate \$2.5 million from its regular budget for the program. That sum is better seen in perspective when one realizes that support was required for programs in fifty countries. The \$2.5 million amounted to an average of \$50,000 per country, but it constituted almost five percent of WHO's total budget.

The program commenced on January 1, 1967. The target date for the occurrence of the last case was December 31, 1976.

In 1967, when the program began, smallpox was endemic—an indigenous ever-present illness—in thirty-four countries. Nine other countries experienced importations of the disease that year. The theory that smallpox could be eradicated was based on a number of characteristics of the disease which, taken together, are unique.

Of principal importance is the fact that humans are the only host for the virus. There is no animal reservoir as there is in yellow fever, for example. The patient can transmit infection only from the time when the rash first begins until the last scabs separate. Following recovery he is immune. There are no symptom-free carriers as there are in malaria or poliomyelitis,

for example. Thus, it was possible to know whether or not smallpox was present in an area by searching for patients with a visible rash.

The disease spreads in a continuing chain of infection as a result of face-to-face contact between a smallpox victim and a susceptible person. Usually, the patient infects no more than five other individuals. Smallpox, when introduced into a remote village, for example, will die out after only a few generations of disease, even if nothing is done. This may also occur over extensive, sparsely populated areas. In Brazil, the smallpox program concentrated on the heavily populated areas near the coast. When teams then systematically moved up the Amazon, no cases were found. Effectively the same thing happened in Nepal, making it unnecessary to conduct extensive, continuing campaigns in remote Himalayan mountain regions.

Finally, there exists a heat-stable vaccine which confers long-lasting protection. In infected areas, for example, we found that at least ninety percent of the people were protected for as long as twenty years after primary vaccination.

We estimated a need for 250 million doses of vaccine each year. An enormous quantity was already being used in these countries, but was it effective? Laboratories in Canada and the Netherlands volunteered to perform routine testing of vaccine. Less than ten percent of the vaccine met accepted standards, and some contained no detectable vaccinia virus at all.

A plea was made for donations of vaccine. During the early years, the Soviet Union volunteered 140 million doses and the United States forty million. Eventually donations came from more than twenty countries. A meeting of vaccine producers was convened and from this came a simplified, step-by-step manual describing the production process. Consultants assisted vaccine-producing laboratories in the developing countries. By 1970 all vaccine met accepted standards, and by 1972 eighty percent of it was being produced in the developing countries. Some, such as India, Iran, Kenya, Guinea, and Argentina, contributed vaccine to others. Uniquely, the program became a truly collaborative global effort rather than an assistance program of the rich giv-



Simplified techniques enabled a vaccinator to carry in his pocket a month's worth of equipment. (WHO photo by Roberts and Dale)

ing to the poor.

A new invention, the bifurcated needle, emerged from Wyeth Laboratories in 1968; immediately we tested a new technique of vaccination by multiple puncture. The needle could be dipped into the vaccine. By capillarity, sufficient vaccine was held between the tines. Fifteen rapid strokes implanted enough vaccine to obtain a take. Only one-fourth as much vaccine was required as in the older scratch technique. Vaccinators could be quickly trained. The needles were inexpensive and could be sterilized and reused many times.

A further simplification stemmed from English studies demonstrating that an alcohol- or acetone-saturated cotton swab did little more than rearrange bacteria on the skin surface. Field tests confirmed that infection rates were no different whether the skin was cleansed or not. Vaccinators were thus instructed only to wipe away caked dirt if present. Thus, with heat-stable vaccine, a vaccinator could carry in his pocket all the equipment he needed for a month's work.

Between 1967 and 1968, programs began in most of the infected countries and their neighbors, and by 1971 all were in operation. The strategy called for systematic programs of vaccination conducted throughout each nation to be completed over a two- to three-year period. Meanwhile, reporting systems were to be developed. It was expected that by the end of the three-year period, smallpox cases

would be few in number and the remaining foci could be quickly eliminated.

The program had hardly begun, however, when Dr. William H. Foegen, working in eastern Nigeria, demonstrated that even in a developing country which was poorly vaccinated a sensitive reporting system could be rapidly developed.

The program strategy was changed to give priority to "surveillance and containment." A surveillance team of only two or three persons could cover an area with a population of two to five million. Team members visited each health center and hospital and asked for weekly reports of the number of smallpox cases seen. Then they visited schools and markets to ask if any there had seen smallpox cases. When cases were reported, the surveillance teams, with local health workers, contained the outbreak.

Progress in most of Africa and in the Americas was rapid. By 1970, the number of countries where the disease persisted had decreased from thirty-three to seventeen. Programs assisted by the United States Center for Disease Control had eliminated smallpox from all but one country in west Africa. By 1973, smallpox was confined to the Indian subcontinent; to Ethiopia, where the program had not begun until 1971; and to Botswana, which became free of smallpox later that year.

The Indian subcontinent constituted a formidable problem. Efforts

such as we made in Africa appeared to have little impact. Nearly 700 million people lived in the most densely crowded areas on earth. Trains and buses traveled everywhere, many carrying smallpox patients who had been infected in the cities and who were returning to their villages to recover or to die. Many outbreaks were not reported. During the long, hot summer of 1973, a special campaign was planned with our Indian colleagues. In essence, the plan called for all health workers, during a one-week period each month, to visit every village in India, and later every house, in search of cases. When they were discovered, special surveillance teams moved in to contain the outbreaks. The logistics were formidable. The plan called for 120,000 workers to visit over 100 million households. Assessment teams visited a sample of ten percent of the households to verify the work. Special surveillance teams were organized to check the assessment teams, to contain outbreaks, and to search for cases at markets and schools during the intervening weeks. More than eight tons of forms were needed for each search, as well as tens of thousands of bicycles, boats, rickshaws, and other vehicles.

The first search took place in October. The results were worse than we had expected. The findings in the Indian state of Uttar Pradesh are illustrative. Two years of intensive work had already been done to improve the reporting system. Seven thousand cases were found in a single week; only later was it discovered that the workers had visited only half the villages. However, the outbreaks *were* being found. Once found, they could be contained. The quality of the searches steadily improved. Containment methods were made more rigid. Guards were posted around the clock at each patient's house to make sure he stayed there, and to vaccinate all his visitors. Vaccination teams, posted to each infected village, searched and vaccinated in a five-mile radius around it. As cases diminished in number, a reward was offered to the villager who reported a case and to the health worker who first investigated it. Techniques employed in India were quickly adapted for use in Pakistan, Nepal, and Bangladesh.

The number of reported cases continued to rise dramatically. In 1974, it

was the highest in fifteen years and the newspapers proclaimed "disaster." But by the summer of 1974, we knew that eradication could be achieved even in the ancient home of smallpox. In October 1974, the last case occurred in Pakistan; in May 1975, in Nepal; in June 1975, in India; and, finally, on October 16, 1975, in Bangladesh—three-year-old Rahima Banu was the final victim of smallpox in Asia.

Only Ethiopia remained to be conquered. Ethiopia, however, was a challenge unto itself: a country of twenty-five million people scattered across desert and highland plateaus in an area larger in size than France, Germany, and Denmark together; a country where half the population lives more than a day's walk from any accessible road, "road" being loosely defined; a country where then, as today, insurrection and fighting were widespread. Our staff was periodically kidnapped and fired upon; one of our helicopters was destroyed by a hand grenade and two others damaged by bullets. Here was a country where vaccination was all but unknown and, when encountered, widely distrusted; a country with only 3,000 on its health staff, only a hundred of them in the smallpox program.

The logistics were formidable: In India, the plan called for 120,000 workers to visit over 100 million households.

When the program began in 1971, 26,000 cases were recorded, but the actual number was probably ten times this figure, or about 250,000 cases. Gradually an intrepid group made up of national and WHO staff and volunteers from the United States, Japan, and Austria succeeded in eliminating the disease from the northern highland areas, leaving localized foci among nomads of the southern Ogaden desert—a scrub desert where it was difficult even to *find* the nomads—where encampments could be rapidly assembled and as rapidly dismantled and carried twenty or thirty miles in a night. Special funds permitted us to

hire and train nomads to search for cases and to vaccinate. Amazingly, these staff could walk forty miles or more a day and, seemingly by instinct alone, locate nomad bands. Whether or not there was smallpox, everybody was vaccinated. By containing the outbreaks and reducing the number of susceptible individuals, smallpox transmission was finally stopped in this sparsely populated area. The last cases were seen in August 1976 in an encampment known as Dimo.

There was still to be one last chapter, however. Somali guerrillas then fighting against Ethiopian forces in many areas of the Ogaden desert brought the disease back with them to Somalia, which had been smallpox-free. The first cases were discovered in September 1976. For yet another year, smallpox campaigns were to be waged throughout Somalia, in neighboring Kenya, and in Djibouti. More than 3,000 cases were discovered, but, at last, the disease was cornered. Ali Maalin proved to be the last case in a continuing chain of infection extending back at least 3,000 years. Eradication had been achieved, the ten-year time target missed only by nine months and twenty-six days.

More than 700 international staff members from more than fifty countries served in the field during the WHO smallpox program. Most were under forty years of age. More than 150,000 national staff were also engaged. It is they who are now providing a new impetus, renewed vigor, and a new sense of mission to an international commitment to better health for peoples throughout the world. It is they whom the Lasker Foundation honored in 1976 with a special award, presented with these words:

"We salute this historic milestone as one of the most brilliant accomplishments in medical history. We hope that it will provide an example of how, with coordinated international effort, many of the other health problems that afflict mankind can be successfully attacked."

The task has begun.