

"The Death of a Disease and the Renaissance of Prevention"

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On 8 May 1980, the 33rd World Health Assembly, in a specially convened plenary session, passed unanimously a resolution which:

- o "Declares solemnly that the world and all its peoples have won freedom from smallpox"

and recommended that:

- o "Smallpox vaccination should be discontinued in every country, except for investigators at special risk"
- o "No country should now require vaccination certificates from international travelers."

More than two and a half years had elapsed since October 26, 1977, when a 23-year-old hospital cook in Merka, Somalia, became ill with smallpox. He represented the last known case in a continuing human-to-human chain of infection extending back perhaps 10,000 years.

*** Orchestra conductor Bloomfield, like Henderson, was a native of the Cleveland OH area. He was a neighbor in Geneva for several years. Their wives shared a carpool for the children, and Henderson's daughter babysat for the younger Bloomfield children. [LAH]

Still today, however, some remain doubtful that this ancient and feared disease has actually been eliminated. Understandably most skeptical are those who have lived or worked in Asia or in Africa and who know well the immense expanse and inaccessibility of large areas of these continents.

How can we be so confident that eradication has been achieved? For a younger generation, what is so important about the disappearance of a disease of the distant tropics? Let me first recall briefly the history of smallpox and its impact on mankind before describing the development of the global campaign. Finally, let me outline briefly the evidence upon which the World Health Assembly concluded that smallpox had been eradicated.

Throughout history, no disease has proved so devastating over so many centuries as has smallpox. Death rates of 20% to 40% were usual. Most who survived were permanently scarred and some were blind. The disease could spread in any climate - in any area. Like measles, essentially everyone eventually contracted the disease. There was and is no treatment. So feared was smallpox that deities and temples consecrated to this disease are known in many cultures. Throughout India, there were temples to Shitala mata. In other cultures, there were other deities such as Shapona in Western Africa.

Smallpox has no animal reservoir and, in man, there was no human carrier state. Therefore the virus, to persist, had to infect person after person in a continuing chain of transmission. Its origins are thus

assumed to date back no more than 10,000 years, to the time of the first agricultural settlements - to a time where there was a sufficient population to permit a chain of infection to be sustained. Most likely smallpox began as a mutant of one of the large family of animal poxviruses. The earliest certain evidence of its presence dates back 3,000 years. The mummy of Ramses V, who died in 1160 B.C., bears the characteristic lesions.

From India, or perhaps Egypt, smallpox spread across Asia and Africa, becoming endemic over an ever-wider area, as population densities increased.

In the Middle Ages, it became established in increasingly populated Europe. In the 17th century Lord Macaulay 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." Nor was royalty exempt. During the 18th century alone, smallpox killed five reigning monarchs, ended the Royal House of Stuart and shifted the Hapsburg line of succession four times in as many generations.

In the Americas, smallpox was responsible for the collapse of both the Incan and Aztec civilizations. And it was smallpox which during the American Revolutionary War decimated a large army intent on capturing Quebec and Montreal - so preserving Canadian independence.

In 1796, Edward Jenner demonstrated that an infection induced with cowpox virus could prevent smallpox. Country folklore at that time attributed the celebrated unblemished complexion of dairymaids to their acquisition of cowpox. Jenner took material from a cowpox lesion on the hand of a dairymaid and inoculated it into the arm of one James Phipps. He later showed that Phipps was protected from smallpox, and that material could be taken from the pustule on his arm and successfully transferred to the arm of another. In less than five years, Jenner's cowpox had been carried around the world by arm-to-arm transfer.

Propagation of cowpox, or vaccinia as it was later called, by arm-to-arm transfer permitted only small numbers to be inoculated. Extensive vaccination was not possible until late in the 19th century when large amounts of virus were grown on the flank of a calf. Gradually, industrialized countries and those in temperate areas began to control smallpox. During the 1940s, Europe and North America finally eliminated the disease. But in the tropical areas, smallpox continued essentially unabated. Not until the 1950s was a thermostabile, freeze-dried vaccine developed which remained potent for a month at temperatures of 98° F.

Meanwhile, smallpox continued to be imported into smallpox-free countries. When outbreaks occurred, the cases were as severe and fatal as in the developing world. Countries everywhere protected themselves by national vaccination programs, and required vaccination certificates of all international travelers.

In 1959, U.S.S.R. proposed and the World Health Assembly decided to begin a global eradication programme. Mass vaccination was conducted in many countries, but few programs were successful. Countries which succeeded in stopping transmission experienced reinfection from their neighbors. Hoped-for contributions of money and vaccine were not forthcoming. Most discouraging was that the strategy of mass vaccination did not seem to work.

Although frustrated and pessimistic, delegates to the 1966 World Health Assembly decided to make one further attempt and voted to allocate \$2.5 million for an intensified effort. In perspective, this provided an average of only \$50,000 per year for the 50 countries where programs were needed. Publicly, the delegates were enthusiastic and proposed a 10-year goal for achievement. Privately, it was difficult to identify more than a few who believed eradication to be possible. The skepticism was justified, considering that the program would have to be undertaken in some of the most inhospitable parts of the world and in some of the least developed countries. Moreover, no other disease had ever been eradicated.

The program began on January 1, 1967. Thirty-one countries with a population of > one billion were then endemic, nine others experienced importations. There were estimated to be 10 to 15 million cases that year.

For vaccination, we needed more than 250 million doses of vaccine each year. The cost for purchase was greater than the entire budget of the

programme. We initially had to depend on donations - the Soviet Union and the United States provided most of the vaccine during the early years, but donations were eventually received from 26 countries. Meanwhile, we helped the developing countries to produce vaccine and, within six years, they were able to produce 80% of the needed vaccine.

In 1968, we tested a remarkable invention of Wyeth Laboratories - the bifurcated needle. The needle could be dipped into the vaccine. By capillarity, vaccine was held between the tines, and fifteen rapid strokes implanted enough vaccine to obtain a take. Only one-fourth as much vaccine was required as had been needed with older techniques. Vaccinators could be quickly trained. The needles were inexpensive and could be reused many times.

Vaccination was further simplified when it was demonstrated that an alcohol-saturated cotton sponge did nothing to prevent secondary infection. Accordingly, vaccinators were instructed only to wipe away caked dirt if present. With heat stable vaccine, a vaccinator could carry in his pocket all the equipment he needed for a month's work.

Between 1967 and 1969 programs began in most infected countries. By 1971, all were in operation. Our strategy initially called for nationwide vaccination programs to be completed over two to three years to reduce smallpox incidence. During this time, a reporting system would be developed which could detect the remaining outbreaks. These would then be eliminated by isolating the patient and vaccinating his contacts. We quickly found, however, that even in many of the least

developed countries, systems for case detection could rapidly be developed and outbreaks eliminated. The program strategy was therefore changed to give priority to surveillance and containment, rather than to mass vaccination. We found that in Africa and South America, a surveillance team of only 2 to 3 persons could control smallpox in an area inhabited by 2 to 5 million persons. Each health center and hospital was visited and asked to send a report each week as to the number of smallpox cases seen. Schools and weekly markets were visited to ask if any had seen smallpox cases. When cases were detected, 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 endemic countries had decreased from 33 to 17. By 1973, smallpox was confined to the Indian subcontinent, to Ethiopia - whose program had only 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. 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 being 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. 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. This three-year-old girl, Rahima Banu, became the last victim of smallpox in Asia.

Only Ethiopia remained to be conquered. Ethiopia, however, was a challenge unto itself. It was a country of 25 million people scattered across desert and highland plateau in an area larger in size than France, Germany and Denmark. It is a country where half the population lives more than a day's walk from any accessible road. 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 the U.S., Japan 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. 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. 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.

Finally, in 1978, the Director-General appointed a WHO 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 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 observation. 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 \$2,000 million dollars each year.

The savings to the U.S. alone amount to some $\$300 \times 10^6$. Because of eradication, we save every 42 days, the equivalent of our total contribution to this program and will do so forever.

But, in perspective, it must be borne in mind that the eradication of smallpox was but a single step in a long and difficult journey toward better health. In taking that step, however, one has heightened confidence that other successes in prevention and public health are possible.