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"The Deliberate Extinction of a Species"

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

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

and recommended that:

(2)
- "Smallpox vaccination should be discontinued in every country, except for investigators at special risk" and
- "No country should now require vaccination certificates from international travelers."

More than two and a half years had elapsed since October, 1977, when (3) 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 more than 10,000 years. So concluded a chapter in medical history - the first successful deliberate extinction of a species - smallpox.

Even today, however, there are some who remain skeptical that this ancient disease has actually been eliminated. Understandably most skeptical are those who have lived or worked in Asia or in Africa and who appreciate well the immense geographical expanse of these areas and their still primitive state.

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, therefore, recall briefly the history of smallpox and its impact on mankind, before describing the development of the global campaign and, finally, the evidence upon which the World Health Assembly reached its decision that smallpox has been eradicated.

Smallpox had 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 concentration of population to permit a chain of infection to be sustained. Most likely it began as a mutant of one of the large family of animal poxviruses. The earliest evidence of its presence dates back more than 3,000 years. (4) The mummy of Ramses V, who died in 1160 B.C. bears unmistakable, characteristic lesions of smallpox.

Throughout history, few diseases have proved so devastating. Death rates of 20% to 40% were normal. Most who survived were permanently scarred, and some were blind. The disease could spread in any climate, in any area. Like measles, essentially everyone contracted the disease. There was and is no treatment. So feared was smallpox that deities consecrated to this disease are known in many cultures. (5) Throughout India, there were temples to Shitala mata. Shitala was believed to possess the power to ward off smallpox. In other cultures, there were other deities such as (6) Shapona in Western Africa, and (7) Omulu in Brazil.

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. (8) In the 17th 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." Nor was Royalty ~~was not~~ 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 precipitated the collapse of both the Incan and Aztec civilizations, and settlers in the New World experienced surprisingly few problems, quite simply because so few Indians remained after smallpox had taken its toll.

Edward Jenner's demonstration in 1796 that an infection induced with cowpox virus could prevent smallpox was hailed as one of history's most important advances. Folklore of the 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, Sarah Nelms, and inoculated it into the arm of 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 person. 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. However, such vaccine, after harvest, became inactive in days. With increasing 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 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."

During the 1940s, vaccination programs in Europe and North America finally eliminated smallpox, but for the tropical areas, heat stable vaccines were essential. Finally, in the 1950s, a freeze-dried vaccine was developed which remained potent for a month or longer at temperatures of 98°F.

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

In 1959, the World Health Organization began a global eradication campaign. Mass vaccination programs were begun in many countries, but few 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 be working. In some areas of India, a larger number of vaccinations were reported than there were people - but still smallpox persisted.

With an increasing sense of frustration, 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 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 any 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 before been eradicated.

The program commenced on January 1, 1967. Thirty-four countries were then endemic, and 9 others experienced importations, ~~that year~~. There were estimated to be 10 to 15 million cases that year.

The belief that eradication of smallpox could be achieved was based on a unique group of characteristics of the disease. Of principal importance is the fact that man was the only host for the virus. A person with smallpox could transmit infection only from the time when the rash first appeared, until the last scabs separated. Following recovery he was immune. 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 spread through face-to-face contact in a continuing chain of infection. By tracing the source of infection of the victim, and by identifying his contacts, other cases in the chain could be identified and outbreaks contained. Moreover, smallpox, when introduced into remote villages, soon depleted the susceptible population, and often died out even if nothing was done. This occurred even over extensive, sparsely populated areas. In Brazil, for example, the smallpox program initially concentrated on heavily populated coastal areas. When teams moved through the Amazon, no cases were found. Finally, the heat-stable vaccine conferred long-lasting protection, at levels of more than 90% for twenty years or longer.

For vaccination, we needed more than 250 million doses of vaccine each year. Donations from the Soviet Union and the United States provided most of this 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 and they, in turn, contributed vaccine to others.

(13)

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.

(14)

WHO staff working in Pakistan designed a unique needle holder. Sterilized needles were dispensed from one holder and used needles placed in a second. At the end of the day the plastic holders could be dropped in boiling water, removed after 20 minutes, shaken once and the vaccinator was prepared for the next day.

Vaccination was further simplified when it was found that an alcohol saturated cotton sponge did little more than rearrange bacteria on the skin surface. Vaccinators were thus instructed only to wipe away caked dirt if present. (15) 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 1969 programs began in most infected countries, and by 1971, all were in operation. The strategy initially called for nationwide, systematic vaccination programs to be completed over two to three years. It was expected that by then an effective reporting system would detect the remaining outbreaks, which could quickly be eliminated by isolating the patient, and vaccinating his contacts. ~~However~~, We quickly found that even in poorly vaccinated areas, case detection systems could rapidly be developed and outbreaks eliminated. The program strategy was therefore changed to give priority to "surveillance-containment," rather than to mass vaccination. In Africa

and South America, a surveillance team of only 2 to 3 persons could control smallpox in an area inhabited by a population of 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 persons 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.[16] By 1970, the number of endemic countries had decreased from 33 to 17.[17] By 1973, smallpox was confined to the Indian subcontinent, to Ethiopia whose program did not begin until 1971, 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. Train and bus service facilitated extensive travel. 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 not be achieved. We wondered if they might not be right.

During the summer of 1973, 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 thousands of vehicles, as well as tens of thousands of bicycles, boats and rickshaws.

The first search took place in October. The results were depressing. In the northern Indian State of Uttar Pradesh, 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 ~~began to be~~ 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. Vaccination teams lived in each infected village, to search and vaccinate in a wide radius around the village. As cases decreased, a reward ~~began to be~~ 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 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 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 is 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. Insurrection and fighting were widespread. Smallpox staff were periodically kidnapped and fired upon; one of our helicopters was destroyed by a hand grenade, and others damaged by bullets. Health staff were few in number and less than 100 could be employed for the program. In 1971, during the program's first year, 26,000 cases were recorded, probably one-tenth the actual number. Gradually an intrepid team which included volunteers from the United States, 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 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, the 23-year-old cook in Morka, 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 have a comparable level of confidence, sufficient to permit them to stop vaccination?

As pointed out, smallpox, to persist, must continue to spread from person to person. Evidence of persistent transmission thus should be increasingly evident with time, either through detection of one of an ever increasing number of cases or through detection of facial scars. We believed that two years of surveillance should detect cases if present. Experience supported this presumption. Following the occurrence of the last cases, we publicized that a reward would be given to anyone who reported a case which could be confirmed as smallpox. The announcement of a reward brought a veritable flood of persons with rash. Special teams conducted repeated house to house searches over vast areas. Many other measures were employed as well, but 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. For the commissions, knowledgeable individuals from many different countries were selected whom it was felt would be especially critical in their judgment. Before the commission's visit, each country prepared detailed reports of its program. After reviewing the reports, commission members themselves decided on the areas in each country which they wished to visit to verify the work.

In all, 10 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 ever more widely known.

Finally, in 1978, the Director-General appointed a WHO Global Commission comprised of 21 persons from 19 countries and charged them with the responsibility to satisfy themselves personally that global eradication had been achieved.[27] After two years' work, the Chairman was able to report to the WHO 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 three laboratories in the world.

The possibility that there might be a natural reservoir of the virus had been a persistant 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 detected in smallpox-free areas since the program began were able to be specifically 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.

The recurrence of smallpox due to deliberate release of the virus as an act of terrorism cannot be ruled out.[28] However, the potential hazard of such an act should not be exaggerated. Smallpox does not spread rapidly, as does measles or influenza, and between each generation of cases, there is an interval of two weeks or more. Intensive vaccinaton programs thus should readily be able to contain a terrorist-propagated outbreak within a four to six week period. Unhappily, it should also be noted that if a group decided to employ biological weapons, there are other agents for which there are no effective vaccines and whose characteristics are more destructive even than those of smallpox.

LIGHTS

However, as insurance against presently unforeseen events, the WHO has establisted vaccine storage reserves containing some 200 million doses of vaccine.

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

Savings to be realized annually because of the cessation of vaccination are estimated to be $1 to $2 billion dollars. In comparison, international assistance to the program amounted to an average of only $8 million per year.

Many have proposed that, now, another disease should be targeted for eradication. Unfortunately, there is no other disease which possesses so many characteristics favorable to an eradication effort or for which we have simple, effective measures. Although smallpox eradication may now seem to have been comparatively straightforward, I recall well innumerable instances in which the program balanced on a knife edge between success and disaster, decided by such as an unexpected change in government, a cessation of hostilities or an heroic exhibition of dedication, and courage by field staff. There were a multitude of miraculous and timely events. To relate them all will require a book. Even with these, eradication just barely succeeded.

The smallpox eradication program illustrates how inexpensive and effective prevention can be. For developing countries, prevention based on immunization is especially applicable. And indeed, WHO has begun a global Programme of Immunization to protect the 100 million newborns each year against six major infectious diseases.

More than 700 international staff from 69 countries served in the field during the smallpox program. More than 150,000 national staff were also engaged. It is they whom the Lasker Foundation honored with this citation:

> "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."

A first step has been taken in a long and difficult journey but in taking that step, we all have obtained renewed confidence that other successes are possible.