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One of the best
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Intro. One thing learned

"The Death of a Virus"

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

①

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

and recommended that:

②

- 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."

③

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} ~~more than~~ 10,000 years. ~~So concluded a chapter in medical history the first successful deliberate extinction of a species - smallpox.~~

W. H. ...

Even 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 these continents, and the ~~inaccessibility of many of their ...~~

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 ~~man and history~~ ^{marked} before describing the development of the global campaign. Finally, let me ~~outline briefly~~ ^{outline} the evidence upon which the World Health Assembly concluded that smallpox had been eradicated.

→ sketch the prospects for a next chapter.

Dissect these slides



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 perhaps 10,000 years, to the time of the first agricultural settlements - to a time where there was ² sufficient concentration of 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 ^{certified} evidence of its presence dates back 3,000 years. The mummy of Ramses V, who died in 1160 B.C. bears the characteristic lesions.

Throughout history, no disease has proved so devastating. ^{over 10 million deaths} 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. Shitala was believed to possess the power to ward off smallpox. In other cultures, there were other deities such as Shapona in Western Africa.

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 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 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. ~~Settlers in North America experienced surprisingly few conflicts with Indians - quite simply because so few remained after smallpox had taken its toll.~~ And it was smallpox which during the American Revolutionary War decimated a large army intent on capturing Quebec and Montreal - so preserving Canadian independence.

¹² 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 person. In less than five years, Jenner's cowpox had been carried around the world by arm-to-arm transfer.

W.H.T.S.

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. ~~Such vaccine, however, became inactive in days unless refrigerated.~~ Gradually, industrialized countries and those in temperate areas began to control smallpox. During the 1940s, ~~vaccination programs in~~ Europe and North America finally eliminated the disease. But in the tropical areas, smallpox continued unabated. ^{Not until} ~~At last, in~~ the 1950s, ^{was} a thermolabile, freeze-dried vaccine ^{stable} developed which remained potent for a month ~~or longer~~ at temperatures of ~~98°~~ ^{99°} Celsius F.

Meanwhile, ~~imported cases of~~ smallpox continued ~~to occur and to spread~~ ^{to be imported} in smallpox-free countries. ⁽¹⁵⁾ When outbreaks occurred, the cases were as severe and fatal as in the developing ^{world.} ~~nations~~. Countries ^{consequently} protected themselves by national vaccination programs, and required vaccination certificates of all international travelers.

In 1959, the World Health Assembly decided to begin a global eradication programme. Mass vaccination ~~campaigns were~~ ^{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. ~~In some areas of India, larger numbers of vaccinations were reported than there were people — but still smallpox persisted.~~

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~~ ^{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 ~~before~~ been eradicated.

The program ⁱⁿ began on January 1, 1967 ⁽¹⁶⁾ ~~Thirty-four~~ ^{thirty-four} countries were then endemic, ⁹ others experienced importations. 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 ^{set} ~~group~~ of characteristics, ~~of the disease.~~ ⁽¹⁷⁾ Of principal importance is the fact that man was the only host for the virus. A patient 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.

12 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 program. We 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, [including generous donations from Canada.] 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.

Key materials in that effort were from the United States and the Soviet Union.

*the fishhook
device*

19 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.

15 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 were

~~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 demonstrated that an alcohol saturated cotton sponge did nothing to prevent secondary infection. ^{Accordingly,} Vaccinators were ~~thus~~ instructed only to wipe away caked dirt if present. ~~With~~ ^{With} heat stable vaccine, a vaccinator could carry in his pocket all the equipment he needed for a month's work.

Lucas

Between 1967 and 1969 programs began in most infected countries, ~~and~~ 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~~ ^{Plan} be eliminated by isolating the patient and vaccinating his contacts. We quickly found, however, that even ^{in the many of the best developed} ~~where health care facilities were sparse,~~ ^{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. ⁽²⁾ 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.

note on school children

Progress in most of Africa and in the Americas was rapid. ^{(2) (3)} By 1970, the number of endemic countries had decreased from 33 to 17. ⁽¹⁹⁾ By 1973, smallpox was confined to the Indian subcontinent, to Ethiopia - ^{had only just begun} ~~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. 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 ~~not~~^{never} be achieved. More than once 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.~~ ^{WHO Recognition Card} 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. ~~Vaccination teams lived in each infected village to search and vaccinate in a wide radius around the village.~~ 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, ~~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.

29 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, 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, 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~~ ^{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 way that} we publicized a reward to be given to anyone who reported a case which could be confirmed as smallpox. The reward brought a ~~surprising~~ flood of reports of persons with diseases of all types. In addition, special teams conducted repeated house to house searches over vast areas. ~~Many other measures were employed 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. The commissions reviewed detailed reports of the programs and verified these through visits in the field.

visit

In all, ¹⁴ 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 widely known.~~

Finally, in 1978, the Director-General appointed a WHO Global Commission, ~~comprised of 21 persons from 19 countries. He charged them with the responsibility~~ to satisfy themselves personally that global eradication had been achieved. After two years' work, the Chairman was able to report to the ^{World Health} ~~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 two laboratories.

The possibility that there might be a natural reservoir of the virus had been a ^{constant} ~~persistent~~ 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.

~~The recurrence of smallpox due to deliberate release of the virus as an act of terrorism cannot be ruled out. 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. We know that an intensive control program can readily contain such an outbreak within four to six weeks. Unhappily, it should also be noted that if a country 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.~~

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 further measures} are estimated to be \$2,000 million dollars each year. ~~In comparison, international assistance to the program amounted to an average of only \$6 million per year.~~

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

Until 1971

The United States itself was spending \$150 million / year until 1971. Vaccination ^{has} stopped and quarantine measures decreased. This country now saves the equivalent of its total contribution to the program every 42 days - and will do so forever.

But, as an aside, I ~~will~~ ^{must} note that this program could not have been achieved without WHO. The USA contribution to WHO is \$60 million - in current dollars, one-fifth of the amount it saves because of smallpox eradication. However, last year for the first time in 38 years, the U.S. ~~did~~ failed to pay its assessment and has made no provision to pay it this year. It is a time when I find it difficult ~~to~~ ^{to} meet with colleagues in other countries, to say I am proud of America.

It is a time when, as never before, we are able to respond to Mahatma Gandhi who said "I am hard-hearted enough to let the sick die if you can tell me how to prevent others from becoming sick"

This we can do and are now doing - on a scale which was unimaginable 10 years ago.

Success in the smallpox program led us to propose to the WHO that a global program be launched to provide 6 vaccines to children throughout the world DPT - polio - measles - BCG.

~~At that~~ ^{Only 10} years ago - 2% were being vaccinated / today, more than 50% are and the goal is 90% by 1990.

- It is the centerpiece of UNICEF's Child Survival and Development Revolution ^{and now an ~~expanded~~ program in countries around the world}
- Rotary International has pledged \$120 x 10⁶
- Rajiv Gandhi has stated that immunization of the children of India will be the living memorial to his mother's memory
- Today, WHO is conducting a program to eradicate polio from the

Packets of salt and sugar which can be dissolved in H₂O and given to children with diarrhea ^{has been found to} prevent death in most cases. The O R T program ^{also} began just a decade ago. UNICEF ordered 1×10^6 packets - they lasted 18 months Today - 1×10^6 packets each day are being used.

Other developments with new vaccines ^{and} with Vit A administration promise yet more. Smully's eradication was a small but important step in a long journey toward better ^{health} ~~steps~~ ^{not} ~~steps~~ ^{begin to} follow. With renewed confidence that other successes might be possible, we have ^{begin to} ~~take~~ other steps ^{in the} and the results have been ~~dramatically~~ surprising.

~~Smully's eradication was accomplished not by ^{Americans} ourselves alone. The WHO and the USSR were ^{our} the two ~~other~~ principal ^{participants} ~~participants~~. ^{part of 100 international staff from 65 countries participated} Death and disease know no boundaries and no nationalities. ^{we could it have been} ~~We need to ^{find} ~~find~~ that partnership~~ ~~let us close with a plea by the great ~~Continental~~ ~~Medical~~~~ ~~with ~~WHO~~ and the Soviet Union as well~~ ~~Get ~~going~~ together as~~ ~~There are few~~ ^{an international partnership we can ~~be~~ ~~create~~ ~~a~~ ~~great~~ ~~deal~~} ~~that partnership needs to embrace all countries - ~~which~~ ~~the~~ ~~WHO~~ ~~is~~ ~~our~~~~ And health is the least political of all activities in which we are engaged. Is it not time that we acknowledge our own debt to and support of WHO. Is it not time that we again join efforts across the Iron Curtain ~~at~~ ~~to~~ ~~accomplish~~ as we did in smallpox, far more than any one country ^{could} ~~do~~ ~~alone~~.~~