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The Global Eradication of Smallpox: Historical perspectives and future prospects*

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Introduction

In 1977, just 30 years ago, the last case of smallpox was detected and eradication of the virus was declared. This precipitated increasing interest in undertaking another eradication program and a decade later, a program to eradicate poliomyelitis was launched. For more than 20 years now, legions of health workers have struggled toward that goal but, as yet, with no certain end in sight. In frustration as they have failed to deal with this problematic challenge, some have imagined that the smallpox program was intrinsically straightforward, readily accepted and easily executed. It has been suggested that an acquiescent World Health Assembly unanimously agreed to undertake smallpox eradication; that all countries so feared the disease that all were enthusiastically supportive; that a Geneva-based Central High Command was created to direct field operations; and that armies of vaccinators simply fanned out, and smallpox vanished. The facts could not be more different.

As summarized in this paper, a program of smallpox eradication was accepted in the World Health Assembly by the narrowest of margins and only after extended debate; many health professionals, including the WHO Director-General, believed the goal to be unattainable; and twice, within the last two years of the program, it teetered on the verge of catastrophe and possible failure.

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The saga of smallpox eradication is comprised of an extraordinarily diverse array of challenges and successes punctuated by all but insurmountable setbacks, civil wars, floods, famines and refugees. Throughout most of its course, the program was provided only tepid support by some key international and national leaders, continuing scarcities of funds and vaccine, rigid bureaucracies, seriously deficient health infrastructures in many countries, and problems with both communication and transportation. Ultimately, success was finally realized, abetted by a number of notable and unexpected surprises and breakthroughs. All credit is due to imaginative and creative national and international staffs working long hours under inhospitable circumstances in a program that was anything but simple or straightforward.

There have been several historical accounts of components of the smallpox eradication program but few by those who were themselves central participants. Such accounts are needed to bring a sense of the realities of the actual implementation of this far-flung venture that involved as many as 120,000 national workers at certain times of the program, which functioned in some 50 countries but which never had more than 100 international staff in the field at any given time.

Other chapters in this series highlight events in especially important areas. Brazil was an early success and eradication there, only four years after the program began, permitted certification that the whole of the Western Hemisphere was smallpox free. It was an important impetus to the global effort. A further affirmation that the program strategy was effective was the eradication of smallpox from all of Western and Central Africa. This occurred less than five years after that program had begun and included countries that had been among the world's most highly infected and with the most limited health resources. Key to the ultimate success of smallpox eradication was India, the most populous of the endemic countries and the one that consistently recorded the largest number of cases and posed some of the most difficult operational problems. The Horn of Africa was the last stronghold of smallpox, a sparsely settled area lacking in resources and a special challenge as the program struggled to reach completion.

This paper explores several little known aspects of how the concept of eradication as a practical goal originated, first in veterinary medicine; how it later began to be applied

to human disease; and, finally, how the decision was reached to apply it to smallpox. It describes how smallpox eradication was originally agreed upon in the World Health Assembly in 1959, largely as a political gesture. Thereafter, the program languished for nearly seven years. Even when an "intensified" program was given new life at the 18th World Health Assembly in 1966, the Director General of WHO, as well as many delegates to the Assembly, doubted it could succeed and were concerned that failure would damage the credibility of the organization. Expected voluntary contributions were far less than expected, key leaders in WHO resented a targeted "vertical program" and unenthusiastically provided needed support. Eventually, even as the goal appeared to be in view, potentially fatal setbacks were narrowly avoided.

The concept of eradication

Use of the word, eradication, with respect to a disease did not arise until the latter part of the 19th century. Some have mistakenly attributed the concept of smallpox eradication to Jenner himself who, in 1800, wrote: "Cow Pox, an antidote that is capable of extirpating from the earth a disease which is every hour devouring its victims." This, of course, was little more than an optimistic hope, not a realistic expectation of a possible accomplishment. Eradication as a practical term for an operational program was first used in 1884 when, in the United States, a veterinary program was undertaken with the specific objective of eradicating bovine contagious pleuropneumonia from the country. Although due to an organism imported from Europe, it was moderately widespread. Success was achieved within five years and other zoonotic diseases were subsequently tackled in the US and Europe with the objective of achieving area-wide, regional or national interruption of disease transmission. The programs were referred to as "eradication programs".

The possibility of eradicating a human disease was first proposed in1888 by a leading public health personage of the day, Dr. Charles Chapin, Health Officer for the State of Rhode Island. He argued that preventive measures for any disease, if diligently applied, could potentially lead to eradication and, specifically, he cited tuberculosis as a worthy first objective. Nothing came of this proposal.

In the United States, public health at the turn of the century was in its infancy, responsibility devolving primarily on towns and cities. There were no national health

programs as such. The idea of undertaking a program to eradicate a human disease lay dormant until 1909 when, through the philanthropy of John D. Rockefeller, a Sanitary Commission for the Eradication of Hookworm was created and over the following decade, programs were initiated throughout the southern United States and in 52 countries on 6 continents. The strategy called for improving sanitation by the construction of privies and treating children who were found to be infected. No attempt was made to monitor the success of this effort until some 13 years after it began. At that time, it was discovered that, even where programs were well-conducted, hookworm infections persisted in the community, albeit the infections were somewhat diminished in severity. The program was abandoned but a precedent was established for other international eradication efforts.

In 1915, an international yellow fever eradication program extending throughout the countries of South and Central America was established by an International Health Commission of the Rockefeller Foundation. A program strategy had evolved from empirical observations which found that yellow fever transmission could be stopped throughout a wide area by destroying the urban breeding sites of *Aedes aegypti* mosquitoes in towns of more than 50,000 persons. In other areas, special programs were conducted only when outbreaks occurred. Progress was impressive and extensive areas of Latin America became free of yellow fever. However, in 1932, a reservoir of the virus in monkeys was discovered. Thus, eradication of the virus was impossible.

The principal driving force and strategist for the critical stages of the yellow fever eradication program had been Dr. Fred Soper, a brilliant, dominating, demanding and persuasive figure who believed passionately in the concept of eradication. As he visualized the tactics for disease eradication, success lay in "vigorous and effective action." He believed that with a tightly-managed, authoritarian administrative structure, many diseases could be eradicated. He disdained scientific research and believed that if he could obtain a national commitment to undertake an eradication campaign, available resources and strategy were of secondary concern and these could be worked out as the program progressed.

In 1947, Soper was elected Director of the Pan American Sanitary Bureau (PASB) (now Pan American Health Organization) which provided him a platform and

forum to pursue eradication on an international scale. At the XXIII Conference of the PASB (1950) and at Soper's insistence, the Directing Council (effectively, Ministers of Health of the countries of the Americas) approved regional programs for the eradication of yaws, smallpox and malaria. This was the first instance in which smallpox eradication was decided as a serious objective to be pursued on an international scale. The Bureau had only a miniscule budget and a very small staff but the decision was consonant with Soper's principle of first obtaining a commitment for the task and worrying later about strategy and funding.

Soper had had no prior interest in smallpox control or eradication. His advocacy stemmed from opportunism. In 1947, New York City had experienced an outbreak of 9 cases of smallpox resulting from an importation from Mexico. However, fear had reigned and some six million persons were vaccinated. During European visits, Soper learned of a more effective, heat stable smallpox vaccine that had been developed and sought to bring this discovery to the Americas. He believed that such a vaccine would be of special value to the U.S. and would demonstrate the value of the Bureau as an international health agency that could offer something of value even to its biggest contributor.

The Bureau's resources were sufficiently sparse that, for smallpox eradication, it could do little more than provide general encouragement to the countries and technical support to a few national laboratories for vaccine production. Expenditures for smallpox in 1953 amounted to $11,124 and averaged about $40,000 annually thereafter. Nevertheless, the countries themselves took action and, by 1966, all countries except Brazil did become smallpox-free.

A Global Commitment to Smallpox Eradication

In 1953, the first Director- General of WHO, Dr. Brock Chisholm, proposed to the World Health Assembly that a practical world program, of importance and value to every country, should be undertaken, one that would require concerted international action and would demonstrate "the importance of WHO for every Member State". He

took note of the smallpox eradication program in the Americas and proposed that a global smallpox eradication program be initiated with a 5 year budget that provided $131,000 per year. The report was not enthusiastically received. Delegates argued that smallpox was a regional or even local problem and that insufficient knowledge was available to undertake such a program which "might prove uneconomical and would not…add to the prestige of the Organization." The Assembly rejected the proposal and asked that the proposal be further studied – a routine, polite form of rejection.

Until 1958, no further interest in smallpox eradication was evinced at the Assembly. However, that year, Dr. Victor Zhdanov, Deputy Minister of Health of the Soviet Union, presented a formal lengthy report and proposed a 4 to 5 year program to eradicate smallpox throughout the world. No mention was made of the then eight year old smallpox eradication program in the Americas. The reason for his initiative, as Zhdanov later explained, stemmed from the frequency with which the Soviet Union had had to deal with imported cases and outbreaks in the Central Asian Republics resulting from importations from other Asian countries. As he reasoned, the Soviet Union, in the 1930s, had interrupted smallpox transmission nationally, including large areas with limited health services, transportation and communication. Thus, it seemed to him that all developing countries should be able to do likewise. To facilitate these efforts, the USSR pledged large quantities of vaccine.

For the Soviet Union, this was the first Assembly it had attended after a nine year absence from the United Nations organizations. In welcoming the return of Soviet participation, the delegates wanted to be responsive to its proposals. Accordingly, they asked Director-General Marcelino Candau to undertake a study of the financial, administrative and technical implications and to report back to the Assembly in 1959.

The Director General's subsequent report to the Assembly called for little in the way of additional resources. Underlying this was his personal belief, as well as that of a number of delegates, that eradication was impossible. A principal argument was that eradication would require vaccination of all peoples throughout the world. As they pointed out this was patently impossible as there were, for example, tribes in the Amazon who seldom emerged from the jungle. The Director General's plan called for the endemic countries, some 59 in all, to undertake vaccination programs using their own or

donated resources. WHO would offer technical assistance when requested and would assist in initiating vaccine production. The plan was accepted and a medical officer was recruited for WHO headquarters and, over the next six years, WHO staff members were recruited to provide assistance in five of the smallest endemic countries. Total expenditures amounted to about $150,000 per year.

Each year at the Assembly, the Soviet delegates complained bitterly that WHO was not making adequate resources available for the program, that, except for vaccine being donated by the USSR, little help was being offered and that WHO seemed to be preoccupied with malaria eradication. The fact was that global malaria eradication, begun in 1955, was proving to be far more costly and less effective than had been hoped. The US was contributing heavily to this program and fully one-third or more of the regular budget of WHO was assigned to malaria. WHO malaria staff numbered 500 to 600, a contrast to the handful working in smallpox eradication.

Other countries joined the Soviet Union in asking the Director General to provide, in his annual budget, more resources for smallpox eradication. This, however, was a problem because the industrialized countries, the major contributors, objected every year to increases in the Organization's budget, even in amounts sufficient to offset inflation. To provide more resources for smallpox eradication meant cutting budgets for other programs. The Director General temporized by arranging for an Expert Committee to be convened in 1964 to consider the situation and to provide advice. Eventually, the Committee pointed out that reporting was so poor that it was impossible to offer definitive strategic advice. The Committee did recommend that vaccination of as many as 80% of the population might not stop transmission and that, therefore, the goal must be to vaccinate 100% of the population. This only served to reconfirm the Director-General's view that eradication was impossible.

At each of the subsequent Assemblies, 1964 and 1965, increasing dismay was expressed about the lack of progress in smallpox eradication and the failure of the Director General to propose larger allocations of funds. Repeated requests were made by the Organization for voluntary contributions to the program but few were received. Meanwhile, the malaria eradication program was beginning to founder and was requiring all of the discretionary funds that could be mustered. A significant potential contributor

for the smallpox campaign was UNICEF but it had committed large resources to the malaria program and its Director bluntly stated in the Assembly that it "would be unable to participate in a world-wide mass eradication campaign against smallpox as it had against malaria".

The World Health Assembly of 1966 marked the final turning point in reaching a decision about smallpox eradication. The Director-General had been instructed to present to the Assembly that year a plan and an augmented budget for the program, utilizing funds from the regular budget of the Organization. A small WHO working group, including myself, was convened and a 10 year program plan was drawn up. It called for total expenditure of $180 million with the program beginning in 1967 and concluding in 1976. The expectation was that 75% of the cost would be borne by the endemic countries themselves with international assistance from the WHO budget and voluntary donations providing the balance. For 1967, the Director-General asked for $2.4 million for smallpox eradication. This was 35% of the estimated international assistance requirement for the first year. Voluntary donations of $4.2 million would have to be raised. This was optimistic considering that annual requests for donations during past years had seldom netted more than $200,000 to $300,000. The Director-General was reasonably confident that confronted with these fiscal realities, the Assembly would decide not to pursue smallpox eradication any more vigorously than it had in the past.

Unexpected developments in the U.S.

Meanwhile, in November 1965, President Lyndon Johnson unexpectedly announced that the U.S. would provide support for a five year program to eradicate smallpox and control measles over a contiguous block of 18 countries in West and Central Africa. It was anticipated that equipment and teams could be in place in most countries by early 1967. The decision represented the culmination of events that had begun some six years before but approval of such an extensive program was unexpected.

The chain of events began in 1961 with studies of a new measles vaccine in Upper Volta. They were conducted by staff from the U.S. National Institutes of Health and local health officials. For Africa, the possible availability of a measles vaccine was especially important as the disease was not infrequently fatal in young children. These initial studies demonstrated the vaccine to be fully satisfactory. Subsequently, at the

request of the Upper Volta government, USAID supported a national measles vaccination program for children under six years of age. One year later six West African Francophone countries successfully petitioned USAID to receive funds to support a four-year program of measles vaccination in their countries. In 1964, this offer was extended to 11 countries. Help was needed for organizing campaigns in each of the countries and USAID turned to the Communicable Disease Center for help. I was then Chief of the Surveillance Section which included a small unit dealing with measles vaccination programs.

From a public health standpoint, we thought it unwise to initiate a costly measles vaccination program which the countries could not possibly sustain. Most of the countries then had insufficient resources to buy yellow fever vaccine (less than 10 cents per dose) let alone measles vaccine costing $1.75 per dose.

At CDC, an alternative proposal was developed which called for a five year program of smallpox eradication and measles control extending over a contiguous geographic block of countries. This didn't solve the problem of sustaining a measles vaccination effort after cessation of USAID assistance. However, it could at least establish a regional smallpox eradication program that could be sustained because smallpox vaccine cost only pennies per dose. However, the effort would have to incorporate a contiguous block of countries, some Francophone and some Anglophone, because of extensive population movements across borders.

The cost of such a program was estimated to be at least five times greater than USAID had budgeted, primarily because of incorporating populous Nigeria, Ghana and Sierra Leone. USAID rejected this proposal but continued to discuss alternatives. In November 1965, however, much to everyone's surprise, word was received that President Johnson had decided to support the full 18 country program. As it was later learned, the administration had been seeking a possible U.S. initiative that could be announced as a special contribution in support of the UN International Cooperation Year. It was an unexpected impetus to the faltering WHO smallpox eradication commitment.

For the May 1966 World Health Assembly, the subject of intensifying the global eradication effort was scheduled for debate yet once again. The U.S. delegates were

instructed to pledge American support for an international program "to eradicate smallpox completely from the earth within the next decade".

The Decisive 18th World Health Assembly

The WHO budget for 1967 was the focal point of debate. The Director-General's proposed budget without smallpox eradication was $49,115,000, an increase of 12% over the preceding year, largely reflecting inflationary adjustments. If the delegates desired to provide the support that he believed necessary for smallpox eradication, a budget of $51,515,000 would be required, an overall increase of 16%. The debate was a lengthy one with many countries objecting in principle to the proposed substantial increases in budget; many questioned the feasibility of smallpox eradication itself; others expressed doubts about launching a new eradication program at a time when the flagging malaria eradication campaign needed all the resources that could be mustered. Eventually, votes were taken. A total of 58 votes was required for approval of the budget incorporating the smallpox eradication effort; 60 votes were cast in favor. The budget was approved by the narrowest margin in the history of the Assembly.

Director-General Candau, believing that the eradication of smallpox was impossible, was most unhappy that the special budget including the program had been approved. His displeasure was directed particularly at the U.S. whose advocacy for eradication, he believed, had been a critical factor in the vote. He indicated to the U.S. Surgeon General that he wanted an American to direct the program so that when the program failed, the U.S. would be seen to be a principal party at fault. He asked specifically that I be assigned.

Soon after the Assembly, the Surgeon General met with me to inform me that I was being assigned to Geneva. I declined the proposal citing, in particular, my considerable new responsibilities as Director for the recently approved African program. That program, as I pointed out, was critical in determining the feasibility of eradication. If smallpox transmission could be stopped in these African countries, then the world's most heavily infected and with the least resources, global eradication might be possible. Moreover, I shared the view of many that the prospects for global eradication were not bright given the fact that only $2.4 million would be available, about one-third as much

as was being made available by USAID for the West and Central African program alone. Voluntary contributions amounting to several times the budgeted amount were to be solicited but there had been little response to such solicitations in past years. Finally, there were WHO's well-known problems of developing and operating coherent international programs what with six very independent WHO Regional Offices that were unaccustomed to working closely together. The Surgeon General said he had no choice but to order me to assume the Directorship of the program for at least 18 months in order to get it launched. The assignment was to last 11 years.

When the program began in 1967, smallpox staff estimated that there were between 10 and 15 million cases with 2 million deaths occurring in 43 countries. Of these, 31 countries were eventually determined to have been endemic; 12 countries reported cases resulting from importations. The endemic countries included most countries in sub-Saharan Africa; the South Asian countries of India, Pakistan (which then included what is now Bangladesh), Afghanistan, Nepal and Indonesia; and Brazil. More than one billion people were living in the endemic countries.

There were some encouraging findings, however. Except for Brazil, the Western Hemisphere appeared to be free of smallpox as were countries in North Africa, the Middle East and such Asian countries as Thailand, Burma and Indochina (now Vietnam, Cambodia and Laos). China was also free of smallpox as a result of massive vaccination campaigns in the 1960s although this was not able to be confirmed until 1979.

Whatever, a serious global smallpox eradication was finally launched but as a substantially under-funded initiative and only by the narrowest of margins. The Director-General was firmly convinced it would fail as were perhaps half the delegates at the World Health Assembly and the reluctant new director of the program himself could not be characterized as optimistic.

Characteristics of Smallpox Favoring Eradication

Smallpox and smallpox vaccine have unique features that taken together made its control and eventual eradication far easier than for any other disease. Most important was that man was the only host and there was no reservoir in nature. The infection itself is of finite duration so that transmission of infection is not possible for more than two to three weeks after onset. Contrary to many medical texts of the 1960s, smallpox does not

spread easily or rapidly. The patient transmits infection only by face-to-face contact and not until he is already sufficiently ill so that he is usually bed-ridden. Following recovery, the patient is immune for life. A single vaccination provides immunity for at least 10 years and evidence of a successful vaccination can be readily determined by the presence of a pustule at the vaccination site after 7 to 10 days or, later, by the presence of a distinctive vaccination scar. The vaccine itself is sufficiently stable so that it can tolerate exposure to 37° C. for a month and its application is simple, not requiring a syringe and needle. In areas where variola major had been the prevalent form of smallpox, some 80% of those who recovered had permanent scars, permitting teams to determine both natural immunity and the history of the disease.

The Strategy

The strategy comprised a two-fold approach to be developed simultaneously. First was to diminish the number of susceptibles through vaccination using a freeze-dried vaccine of assured potency, thereby diminishing the extent and rapidity of smallpox spread. Second was to develop a surveillance system requiring weekly reports from all health centers and hospitals. Containment teams (commonly called "fire-fighting" teams) were to be created to investigate outbreaks and contain them by vaccinating patient contacts and others living in the immediate neighborhood. The process was referred to as "surveillance-containment". It recognized that smallpox persistence depended on a continuing chain of transmission of virus from case to susceptible contact and by vaccinating patient contacts, the chains of infection could be severed.

An arbitrary goal was established for each program to assure that 80% of its population was successfully vaccinated. Quality control teams were deployed to verify this in vaccination campaigns. The quality of the surveillance-containment strategy was measured in terms of the number of days between the beginning of an outbreak and its discovery and the number of days between the report of an outbreak and the date of onset of the last case.

Mistaken assumptions necessitating in changes of strategy and tactics

In the course of developing the plans for program operation, four significant assumptions had been made which soon proved to be erroneous and these required important alterations in both strategy and tactics. The four assumptions were:

1) *That there would be sufficient, high-quality vaccine available to meet the needs of the program.*
2) *That a newly developed jet gun, capable of vaccinating as many as 1000 persons per hour, would play a significant role in increasing the pace of vaccination.*
3) *That protection provided by primary vaccination was no more than 5 to 10 years and, thus, population-wide programs involving all age groups would be essential.*
4) *Rapid progress in containing outbreaks by surveillance-containment would necessitate significant improvements in population immunity.*

Availability of vaccine

It was estimated that some 300 million doses of vaccine would be required annually which, if purchased by WHO at just one cent per dose, would have exceeded the total program budget. Thus, there was no choice but to plan for all vaccine to be locally produced or donated. This did not, at first, appear to be a serious problem. As of 1967, essentially all countries were vaccinating some proportion of their population against smallpox because the disease was so greatly feared. It was, in fact, the only vaccine then in universal use. Vaccine was produced in 77 different national laboratories, primarily by growth on the flank of a cow, sheep or water buffalo. Taking into account local production, there appeared to be ample vaccine, assuming the pledge of 25 million doses annually from the USSR and the U.S. intent to supply all vaccine needed for Western and Central Africa plus possible additional contributions from other industrialized countries.

It was decided, as a first step, to insist that all vaccine for the program be subjected to independent quality control for potency, purity and stability. The Director General's Office advised that WHO had no authority to do this and no enforcement mechanisms should changes be needed. Nevertheless, plans for testing proceeded and laboratories in the Netherlands (Rijks Institute) and Canada (Connaught Laboratories) agreed to perform such tests. Local producers were often reluctantly cooperative and sometimes special pressures were needed to assure compliance.

It was soon apparent that vaccine supply had to be a top priority. In the 50 or so countries that were endemic or bordering endemic areas, not more than 10% of the vaccine then in use met international standards and much of it was in the heat-labile liquid form. In some vaccines, no virus whatsoever could be detected. Meanwhile, it was discovered that most smallpox vaccine laboratories in the industrialized countries had a production capacity of only a few million doses per year and, consequently, few donations could be expected.

Under Dr. Isao Arita's leadership, an urgent consultation was convened in Geneva bringing together principal production staff from the U.K., USSR, Netherlands, Canada and the U.S. to develop an agreed upon step-by-step production and testing manual. The participants then undertook visits to the larger production laboratories and, using the manual, worked with them to improve vaccine quality. Equipment to permit production of the stable, freeze-dried vaccine was provided by UNICEF. Countries with small laboratories and those with facilities in need of extensive renovation were advised to close down but with the promise that WHO would supply national needs, primarily using the USSR vaccine.

Five years were required to fully solve the problems but, by 1973, all vaccine in use in the program fully met international standards and more than 80% of it was being produced in the endemic or recently endemic countries.

The jet gun and alternative vaccination methods

With large-scale vaccination programs anticipated, simpler methods for application of the vaccine were sought. The customary vaccination technique at the inception of the program was to cleanse the vaccination site with alcohol and to let it dry before placing a small drop of vaccine on the skin using some sort of dropper. A lancet was used to scratch through the drop, thus implanting virus in the superficial layers of the skin.

In the U.S. a jet injector gun had been developed in the early 1960's which permitted vaccine under high pressure to be injected intradermally. The vaccine was contained in a 500 dose vial attached to the gun and the gun was powered by a hydraulic pump operated by foot pedal. As many as 1000 persons per hour could be vaccinated with more than 95% of the vaccinations being successful. The gun was introduced for use

throughout Western and Central Africa and later in some areas of Latin America and Asia. Logistically, however, it proved difficult to assemble sufficient people in one place to permit full use of the gun's potential. Moreover, the guns had a major drawback in that they required daily, skilled maintenance. For every gun in use, there was a need for at least one back-up gun and a mechanic.

Within a few years, however, use of the gun was abandoned because of a simple, ingenious invention, the bifurcated needle, a creation of Dr. Benjamin Ruben of Wyeth Laboratories. The needle is two inches long and has a tiny fork at the end. Ruben developed the needle in the early 1960's as a convenient instrument for transferring vaccine from a multi-dose vaccine vial to the skin surface where it could be pressed into the skin using multiple pressures, a method then in common use in the U.S. When the needle is dipped in the vaccine, a small amount of vaccine adheres to the tines by capillarity, much less being required than when a dropper is used. With the new needle, the usual 0.25 ml vial of vaccine was found to be sufficient to vaccinate 100 persons instead of only 25 by customary methods. At WHO, we developed a new technique for inserting the vaccine. The needle was held perpendicular to the skin and 15 rapid strokes were made (it is called the multiple puncture method). Satisfactory technique could be learned by the average villager with 15 to 20 minutes instruction. Successful vaccinations with this method approached 100%. Moreover, the needles were only US $5 per 1000 and, with sterilization, could be reused hundreds of times.

A final step in simplifying the vaccination technique was to abolish cleansing of the skin with an alcohol sponge. Studies showed that normal cleansing of the skin with alcohol did little more than rearrange bacteria. Observations in the field indicated that the very low frequency of secondary infections was no different whether the skin was cleansed or not.

The goals of simplicity and speed were achieved. In the African programs, vaccinators were able to routinely vaccinate an average of 500 or more persons per day. The only pieces of equipment required were the 100 dose vials of freeze-dried vaccine, a vial of diluent for each vaccine vial, a tube containing bifurcated needles and a pot for boiling and sterilizing the needles each night.

The duration of protection provided by vaccination

At the inception of the program, it was generally believed that revaccination at intervals of several years was required to sustain immunity. However, reliable data regarding the duration of protection were not available. Laboratory workers were revaccinated annually; countries required international travelers to be vaccinated every three years; and a number of industrialized countries recommended revaccination every five to ten years. In the endemic countries, however, few persons received more than a single primary vaccination, if they were vaccinated at all. In planning program operations, it was assumed that to reach a satisfactory level of vaccination immunity, it would be necessary to vaccinate all ages in the population.

However, early surveillance data from Africa and Asia provided puzzling findings. Among adult smallpox patients, in particular, we had expected to see some with a vaccination scar indicating previous successful vaccination but whose immunity had waned. Almost none were found. The explanation for this mystery was discovered by a research team in Pakistan. It found that in households with smallpox, previously vaccinated children had a dramatic increase in smallpox antibodies such as one would expect after a clinical smallpox infection but they showed no symptoms. It was clear that they had experienced sub-clinical smallpox which, like clinical smallpox, provided life-time protection. In endemic areas, many would have been so protected whether or not they were revaccinated.

These findings let to a change in vaccination strategy to emphasize getting a vaccine scar on every arm rather than endeavoring to vaccinate the entire population.

The rapidity of spread of smallpox

Classic textbooks emphasized the ease and rapidity of spread of smallpox, likening it to a prairie fire and, thus, we expected to find cases widely dispersed geographically in the endemic countries. These beliefs proved wrong—smallpox did not spread readily such as do measles and influenza and, with an average incubation period between infection and onset of illness of 10-12 days, it did not spread rapidly.

Only patients with a rash could transmit infection and this was from the time of onset of rash until some two weeks later when scabs had formed. Because the rash developed some two to three days after the patient had become very ill and had usually taken to bed, most contact cases were among susceptible household members and

visitors. Significant spread did not occur at such as schools or work sites. This made it easier for surveillance teams to trace the spread of smallpox from person to person as it progressed in a continuing chain of infection.

Cases tended to be concentrated in a country rather than being widely dispersed because of the nature of the spread of disease. This concentration permitted teams to selectively focus their efforts on the most heavily infected areas.

Evolution of the Program

Because of the paucity of available resources, it was necessary at the beginning to set priorities for the program. It was decided to utilize WHO funds preferentially in Brazil and Indonesia as these two populous countries did not abut any other endemic countries and, once they had interrupted transmission, it was thought that funds would be able to be shifted to other countries in Asia and Africa. Meanwhile, the U.S. had made a commitment to support eradication programs in 18 (later 20) countries of Western and Central Africa, programs to be directed by CDC and its program director, Don Millar. WHO encouraged the initiation of programs in other endemic countries but few advisors and only limited additional resources could be made available. The last of the endemic countries, Ethiopia, began its program in late 1971.

Details regarding each of the country and regional programs from January 1967 until the occurrence of the last case in October 1977 are set forth in detail in the book, *Smallpox and its Eradication.* A brief summary is here included to offer continuity between the events leading up to eradication and to the critical events that threatened to thwart the achievement of eradication during its concluding years, 1975-77.

Progress during the program's first six years was dramatic and exceeded expectations. The 20 countries of Central and Western Africa interrupted smallpox transmission in 1970, Brazil in 1971 and Indonesia in 1972. By the summer of 1973, the only endemic countries were Ethiopia and four countries of Asia – India, Pakistan, Bangladesh and Nepal. Importations of cases into other countries were diminishing in number and were quickly being controlled.

Despite growing optimism regarding the possibility of achieving eradication by the end of 1976, well within the 10 year goal, finances continued to be severely constrained. Voluntary contributions were far less than had been hoped; the Region of

the Americas, despite being free of smallpox, refused to permit its allocation of funds to be transferred; and from the WHO Director-General's Office, there was a growing disparagement of "vertical" programs, citing smallpox eradication as an example, as contrasted to "horizontal programs" (i,e, development of Basic Health Services).

On the positive side, strong support was being provided by CDC in the form of experienced epidemiologists and managers; young volunteers from the U.S., Austria and Japan were making important contributions in Ethiopia and a growing cadre of dedicated, international staff were dealing ever more effectively with a host of challenges. Their efforts were materially aided by WHO's administrative staff who had overall responsibility for budget, personnel, internal audit, etc and who went to considerable efforts to provide support to the program.

By the summer of 1973, India, with its 600 million population, was reporting more than three-fourths of the world's cases. It was recognized to be the ultimate and most problematic challenge to the achievement of eradication. There were armies of vaccinators, albeit performing poorly, and large numbers of Indian supervisory staff but the methods for surveillance and containment that had worked well in other countries, were not interrupting transmission. Some argued that India and the Ganges River Basin must possess unusual ecological characteristics that served to make this area a natural "home" of smallpox, such as was thought to be the case with cholera.

Epidemiological studies, however, revealed that failures to detect outbreaks rapidly and to contain them were primarily responsible. Frequent travel throughout India appeared to be an important factor. India was served by a surprisingly extensive rail and bus system which was inexpensive and heavily used. Religious festivals drawing hundreds of thousands were common; commuter traffic was heavy in urban areas; and it was discovered that entire families often traveled from urban areas to their home villages when one of the family members became ill.

It was decided that more rapid case detection and containment was needed. Thus, in the summer of 1973, it was decided to utilize a proportion of the veritable army of public health staff to search for smallpox in every village in India over a 7 to 10 day period and to take immediate measures to contain the outbreaks that were found. The first searches began in October of that year utilizing some 120,000 health workers. The

completeness of the initial searches left much to be desired but tens of thousands of unreported cases were found, many times more than anyone had expected. The sudden surge of reported cases alarmed WHO staff, as well as high levels of government, and served to generate a substantial increase in political support for the program. The searches were repeated every 2 to 3 months thereafter, with a focus on the areas with continuing transmission. Containment measures were made increasingly stringent. As performance improved, the objective was altered to that of contacting every house in India during the search.

Little more than 18 months after the special program began, the last outbreaks were discovered and contained. Meanwhile, Pakistan and Nepal, adopting similar methods, became free of smallpox and by May, 1975, smallpox in Asia was confined to limited areas in neighboring Bangladesh. There, it was the beginning of the summer season, a time when smallpox spreads slowly and can reasonably readily be contained.

Meanwhile, in Africa, programs had progressed well and by May, 1975, smallpox was restricted to limited areas of just one country, Ethiopia.

Concluding chapters: on the brink of defeat

In May 1975, the global eradication of smallpox appeared to be all but a certainty and perhaps achievable within a year. In Bangladesh, experienced WHO and national staffs were working well. By August, there were less than 20 infected villages (i.e. those that had experienced a case within the preceding 6 weeks) and effective national searches were being conducted utilizing some 24,000 health staff. Ethiopia appeared to be in a less favorable situation; civil war had broken out the year before but Ethiopian and national advisers continued working actively although at considerable personal risk. With smallpox limited to only two countries substantially more resources could be made available as well as experienced staff from other countries. For Ethiopia, contributions of two helicopters, as well as a fixed-wing aircraft, eased the difficult transport problems and neighboring countries assisted by undertaking surveillance and containment measures near their borders but within Ethiopia.

Beginning in August 1975, however, two major problems arose that seriously threatened the possible achievement of eradication.

Bangladesh

In August, the Director General and I were scheduled to travel to Dacca to meet Bangladesh national leaders to encourage them and their staff in the apparent final phase of the eradication of variola major. We had been in India to celebrate its annual Independence Day and, Prime Minister Ghandi's proclamation of India's freedom from smallpox for the first time in its recorded history.

En route to the airport after the ceremonies, we were informed that Sheik Mujibur Rahman, the first President of Bangladesh and revered father of the newly independent country, had been assassinated along with his family in a military coup. All flights were cancelled; the borders were sealed; communications were suspended; and Indian troops began mobilizing to deal with what was expected to be a mass exodus of refugees. We knew from experience that civil war and refugees were a certain prelude to rapidly spreading epidemic smallpox.

The veteran national and international staff had endured four difficult years contending with smallpox during major floods, civil unrest, and famine and were well accustomed to adversity. Wisely, they dispersed all their vehicles from a motor pool to rural areas so as to preclude their being seized by military or rebels. They suspended most operations for some two weeks but gradually resumed activities. Surprisingly, the country remained relatively calm and on 16 October, a 3 year old girl, Rahima Banu, developed smallpox, the last case in Asia and the last case of variola major, the severe form of the disease.

Ethiopia

Smallpox eradication in Ethiopia was an especially daunting task. It was the last infected country and the challenges were awesome. The population of 25 million was widely dispersed in small villages across a vast highland area and in nomadic groups that roamed across the Danakil and Ogaden Desert crossing unmarked borders into Somalia and Djibouti. It was said that half the population lived more than three days walk away from any accessible road. The health infrastructure was at an early stage of development and there were few professional staff.

The program did not start until late 1971, almost 5 years after the global smallpox program had been decided. Until then national and international malaria program staff had persuaded the Minister of Health of the need to focus all efforts on malaria

eradication which was heavily supported by bilateral funds. The malaria program was the dominant health program with a staff of some 8000 workers, more than twice the number of all other health staff personnel. Reluctantly, the government agreed to a smallpox eradication effort and provided 21 Ethiopian sanitarians to assist. Gradually, the international staff grew with U.S., Japanese and Austrian Peace Corps-type volunteers being added and, later, additional WHO staff but the numbers of national and international staff were not large and much of the transport was on foot and by mule.

In addition to the many logistical problems, security problems became increasingly serious late in 1974 as a major revolution occurred, the Emperor was deposed and a new government undertook a number of radical changes. Pockets of armed rebellion emerged throughout the country, open warfare began with neighboring Somalia, and Eritrea declared itself independent. The problems persisted throughout 1975 and 1976; the volunteers were withdrawn; and international staff, except for those in the smallpox program, were not permitted to venture outside of the capital. An intrepid group of Ethiopians and international staff continued work despite all but impossible obstacles. Finally, in June 1976, they detected an outbreak in a small village in the Ogaden Desert. They contained the outbreak and searched everywhere for other cases. To their surprise, they found none.

Seven weeks elapsed and celebrations were cautiously being planned in hopes of being able to celebrate the global eradication of smallpox. These were rudely interrupted by a report from neighboring Somalia of 5 cases in Mogadishu, the capital. Immediate consultation by WHO staff confirmed that the cases were indeed smallpox but where, specifically, they had been infected could not be ascertained. Somalia had been conducting a special surveillance and vaccination program since 1969 and reported that 85% of its population was vaccinated. Between 1972 and 1975, the country reported only 38 cases, all importations from Ethiopia.

WHO epidemiologists worked with Somali staff to search suspected areas in Mogadishu but the government would not permit them to travel outside of the city. Through December 1976, 34 cases were officially admitted to the Mogadishu hospital and containment measures were taken for these cases. However, staff were suspicious that the government might be suppressing reports but the magnitude of this deception

only was realized some two years later when confidential records were discovered showing that more than 500 patients had actually been admitted to the hospital in Mogadishu but were sequestered in a different section of the building.

Not until March 1977 did the government agree to travel of staff outside of Mogadishu and for the assignment of additional WHO staff to cope with a steadily increasing number of cases with apparent sources of infection in other parts of Somalia. The staff grew steadily through June, eventually to comprise some 40 WHO and Somali epidemiologists and more than 2500 Somali surveillance agents. Many of the cases were among the nomads but simply finding these roving nomads in the high brush of the vast desert areas was a real challenge. A disturbing discovery was the fact that continuing chain of infection was possible in groups as small as 35 to 55 people and for up to 5 months. The numbers of cases reached a peak of 1388 in June and there were some 3229 cases in all before transmission was stopped.

On October 26, 1977, fully 12 months after the first alert that smallpox was present in Somalia, the last case was diagnosed and containment measures taken. As problematic as this last epidemic was, a concurrent threat was that the disease might be carried to Mecca at the time of the annual pilgrimage and from there spread to pilgrims coming from all parts of the world. In Ethiopia and Somalia, the milder variola minor had been prevalent and, even when ill, patients could move about reasonably readily. With Somalia being so near to Mecca, there are, every year, tens of thousands of Somalis who make the overland trek to the holy city. To forestall problems, special vaccinators were assigned to pilgrimage groups to assure that all were vaccinated, to vaccinate others who might later join the group and to report possible cases. None occurred.

A legacy of the smallpox eradication program

During the evolution of the smallpox eradication program, two important developments were fostered that are serving to help transform the practice of public health in much of the developing world. One was to build on the experience and methodology of the smallpox vaccination program to incorporate the use of other vaccines. The second was to begin to utilize a surveillance network for the purposes of planning and monitoring other vaccine preventable disease efforts.

Early in the smallpox eradication program, it became clear that an effective large-scale vaccination effort could be implemented utilizing surprisingly small numbers of vaccinators and attaining good coverage of the population. By deploying vaccinators in teams, close supervision was possible to assure proper vaccination technique and preservation of the vaccine. Quality control was possible by revisiting a sample of the villages 7 to 10 days later to assure that coverage was at least 80% and that more than 90% of the vaccinations had been successful.

It seemed only logical to consider expanding the efforts of the smallpox vaccination teams to administer a number of vaccines. By the mid 1970s few developing countries were utilizing diphtheria-pertussis-tetanus (DPT) vaccine or poliovaccine at all and none outside of the West and Central African program used measles vaccine. To further discuss the possibilities, an international meeting of senior health staff from a number of countries was convened in 1970 at PAHO headquarters in Washington. From this came the recommendation to the World Health Assembly that it approve an "Expanded Program on Immunization" which, for the developing countries would include six antigens (smallpox, diphtheria, pertussis, tetanus, measles and polio). In 1974, this was approved by the World Health Assembly.

At the inception of that program, it was estimated that less than 5% of children in the developing world were receiving DPT, polio or measles vaccines. Gradually, the initiative gained momentum, finally meeting its target of reaching 80% of children throughout the developing world by 1990. In the course of the program, the polio eradication program emerged.

In the developing world, the concept of surveillance as an active instrument for program implementation and monitoring was effectively unknown. What was established for smallpox was an innovation for most countries and for WHO itself but more readily established than had been expected. It was critical for our understanding of the epidemiological behavior of the disease, for prioritizing program operations and for monitoring progress. It involved receiving each week a report from every health center and hospital regarding numbers of cases of smallpox as well as basic data on each patient (age, sex, village, date of onset, vaccination status). Data were analyzed concurrently at each administrative level and by WHO program staff in Geneva.

Such reports are now being gathered on poliomyelitis and, in the Americas and some other countries, for measles and rubella cases. Other diseases are being added to the list.

The future of eradication

In 1980, only months after smallpox was declared to have been eradicated, the first of many conferences was convened to explore what next should be eradicated. Many different diseases were proposed and considered at the different meetings but only two were eventually agreed upon by the World Health Assembly – poliomyelitis and Guinea Worm disease. Programs for each of these diseases have now been in progress for more than 20 years. Their expected target dates for eradication passed many years ago. They each continue to face formidable obstacles as prospects for eradication stretch into a distant and uncertain future.

My views regarding the feasibility of other public health eradication programs were tempered in the fires of smallpox eradication. It never occurred to me to contemplate the possibility of another disease being eradicated, at least for the foreseeable future and I don't recall such an initiative ever having been discussed among our senior staff. However, only months after the World Health Assembly declared that smallpox had been eradicated, all manner of enthusiasts emerged to advocate for adoption of other global eradication targets such as polio, measles, urban rabies, hunger, road accidents and many more.

For those of us who had lived the smallpox eradication experience, who knew the sacrifices that were necessary and who knew how narrowly it had succeeded, it was difficult to understand how anyone could take the proposals seriously. In 1982, at a meeting of the American Philosophical Society I stated:

> "*Many have proposed that another disease should be targeted for eradication and another global campaign launched. In my opinion, there is no other disease which possesses so many characteristics favorable to an eradication effort or for which we now have available, effective, simple and inexpensive measures for prevention or treatment. 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 events as an unexpected change in government, a cessation of hostilities or a heroic exhibition of dedication, courage and leadership by WHO and national staff. There were a multitude of miraculous and timely events…Even with these, eradication just barely succeeded"

I suggested that, for now, the most appropriate goal was to eradicate the word "eradication" as applied to a global program. I have seen nothing since 1982 that would warrant altering that conclusion. (*Read at the American Philosophical Society Annual Meeting, 23 April 1982. Proceedings of the American Philosophical Society 126:461-471, 198)2*

Rational for decisions on mitigation measures

- Epidemiological field observations
- Historical data
- Models
- Intuitive good sense

Basis for decisions –Models and epidemiological data

- Epidemiological data - very limited
  - Contagiousness of patients during illness?
  - Aerosol or droplet spread?
  - Role of fomites?
- Historical data from 1918
- Modeling predictions -- potentially misleading
- Secondary effects can be serious

Evaluation of mitigation measures

- Logistical assessment: Is the disease mitigation measure feasible?
  - Implications of duration of enforcement
  - Manpower needed for mandatory or voluntary measures
  - Economic impact

Evaluation of mitigation measures

- Unintended adverse social, economic, and political effects
  - School closure
    - Increased absenteeism of work force
    - Should malls, fast-food sites, churches, etc be closed?
    - School feeding programs (30 million children)
    - Cessation of payments for school employees
  - Home quarantine
    - Increased work-force absenteeism
  - Potential for catastrophic economic disaster

Disease control measures

recommended

- Vaccination
  - Most important measure to be taken
  - Vaccine will not be available until 6 months after disease begins human-to-human spread
  - No vaccine available until after first wave
- Isolation of sick in hospital or at home
  - The sick are the most contagious
  - Isolation throughout symptomatic phase
    - Mandatory isolation – not feasible and counter-productive

Disease control measures

recommended

- Some use of anti-viral medications
  - Potential for epidemic "quenching" -- low to nil
  - Supply is limited
    Amount needed for prevention for epidemic period requires 5-7 times amount needed for treatment
  - Priorities for use and method for distribution -- ?
- Hand-washing and respiratory etiquette

Disease control measures

not recommended

- Quarantine
  - "forced isolation and quarantine are ineffective and impractical" (WHO)
- Home quarantine
  - Secondary problems
    - Absentee rates in essential and commercial services
    - Provision of supplies to those in quarantine
    - Loss of wages for hourly workers
    - What to do for such as college students

Disease control measures

not recommended

- Travel restrictions
  - "screening and quarantining entering travelers at international borders did not substantially delay virus introductions in past pandemics...and will likely be even less effective in the modern era" (WHO)

Disease control measures

selective use

- Prohibition of social gatherings
  - Widespread prohibition not advisable
    - Potentially, many possible sites --e.g. theaters, churches, restaurants, bars, athletic events, malls, stores.
    - Selective for large, crowded events
- School closure
  - 7 to 10 day closure early in epidemic is common
  - Longer closure has serious secondary effects

Disease control measures

selective use

- Masks and personal protective equipment
  - Hospital
    - Staff – N95 masks or PAPRs if possible
    - Patients – surgical masks
  - Community
    - Masks are not recommended

Community response to a pandemic

an overriding principle

Experience has shown that communities faced with serious adverse events respond best and with the least anxiety when the normal social functioning of the community is least disrupted.

Community response to a pandemic

summary

1) Community-wide vaccination
2) Provision for medical care and isolation of patients
   - Regional Health Care Operations Committee
   - Community-wide plan for caring for large numbers of patients
   - Stockpiling of masks, antibiotics, etc
   - Plan for added staff for medical care facilities
   - Control center to monitor beds, supplies, personnel

Community response to a pandemic
summary

3) Planned communications strategy
- Communication contact with medical care personnel
- Frequent communication with public thro press and civic leaders
- Request those who are ill to remain isolated
- Encouragement of employees to come to work so as to assure continuity in essential services

4) Hand washing and respiratory hygiene

Community response to a pandemic
summary

5) Possible early closure of schools for 10-14 days
6) Selective canceling or postponing of large meetings or events to be held in crowded halls

Not recommended
1) Mandatory isolation of patients
2) Quarantine of anyone – including families or groups
3) Closure of air or rail hubs or transportation systems
4) Screening of travelers at borders

Fundamental realities

- Pandemic flu spreads very rapidly – locally, nationally and internationally
- A variety of non-vaccine mitigation measures have been used to try to deter influenza spread. None have been shown to be effective
- Applications of deterrent measures involving large numbers have the potential to cause serious adverse secondary effects that are difficult to anticipate and impossible to model

Long-term

- Problems we are now addressing will be with us indefinitely
- Need for better global knowledge of disease
  - International surveillance
  - Intelligence
- Sustained medical and public health preparedness
- Expanded relevant research programs
- Rapidly responsive biotech industry

Reeves,
Bhattacharya.

As time has passed and others have struggled, so far unsuccessfully, with other eradication programs 'myths' have grown about the [illegible] of Spx [illegible]

- Spx – major prob. – WHA [illegible] approved.
- 'Smallpox army' was rapidly recruited [illegible] with rigid controls by the Army [illegible] staff in GVA
- Everybody [illegible] – voila – 10 yrs. no smallpox

The Global Eradication of Smallpox:

historical perspectives and future prospects

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University of Pittsburgh Medical Center

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Wellcome Trust Centre

London

30 May 2007

The lecture series

- Eradication in India
  The largest and most problematic of all programs
  "Experience of Spx"
- Eradication in Brazil Amaral
  An early success provides an important impetus
- Eradication from the Horn of Africa
  The last stronghold poses new challenges
- Prospects for 21st century eradication efforts Brennan
- An historical perspective on smallpox eradication

A tale of a program that almost wasn't initiated, was forecast to fail, and barely succeeded

Outline

- Eradication -- the concept
- Targeting smallpox - 1950-1967
- Strategies and the unexpected
- Progress and, at the end, near disaster
- The "Expanded Programme on Immunization"
- What next should we eradicate?

Eradication – the concept

- 1800 -- Jenner
  - *"Cowpox...capable of extirpating (smallpox) from the earth"*
- 1884 – Eradication as a realistic program
  - *Bovine contagious pleuropneumonia in U.S.*
  - *Eradication of other zoonoses*
- 1888 – Charles Chapin, health officer in R.I.
  - *"Any disease that can be prevented in part, can be prevented in its entirety". Proposal – tuberculosis.*

Efforts to eradicate a human disease

- Hookworm - 1909-23 14 years
  - Rockefeller philanthropy
  - Screening and treatment; latrines
  - USA (11 states); 52 countries on 6 continents
- Yellow fever – 1915-32 17 years
  - Rockefeller Foundation
  - Control *A. aegypti* breeding in towns >50,000
  - Latin America; research center in Africa

Efforts to eradicate a human disease

- Yaws – 1948-66 18 years
  - World Health Organization
  - Screening and treatment with penicillin
  - 49 countries
- Malaria – 1955-73 18 years
  - World Health Organization
  - DDT, treatment
  - All endemic countries except Africa
  - More than $2 billion dollars expended

Smallpox as a target

- 1950 -- Regional eradication in the Americas
  - PAHO approves eradication programs for malaria, yaws and smallpox
  - Focus -- freeze-dried smallpox vaccine production
- 1953 – Director General proposal to the Assembly
  "...a practical world program, of importance and value to every country...demonstrating the importance of WHO to every Member State"

  Rejected as being uneconomical and unfeasible
  Prominent in opposition – U.K. and U.S.

Global eradication program approved

- 1958 USSR Vice-Minister Victor Zhdanov

  Soviet Union returns to participate in WHO

  Formal report with proposed global eradication program of 4-5 years
- 1959 Adopted by World Health Assembly
- 1959 -1967
  - Budget of $60,000 to 100,000 per year
  - One staff member in HQ and 5 in the field
    Bolivia, Mali, Kenya, Liberia, Afghanistan

8 year Soviet ... Khatkov

A program in West Africa 1962-66

- U.S. measles vaccine evaluation – 1962-64
  - Trial in Upper Volta › national vaccination
  - Extension of program to 6 countries, later 9
- CDC proposal to USAID -- 1965
  - Smallpox eradication and measles control in 18 countries

Rejected by USAID
Accepted for International Cooperation Year – 1965

"(It is) useless to discuss the theoretical flaws and technical difficulties of eradication programs, because more earthy factors will certainly bring them soon to a gentle and silent death... Eradication programs will eventually become a curiosity item on library shelves, just as have all social utopias."

Dr. René Dubos, in *Man Adapting,* 1965

WHO's "intensified" program - 1967

- Assembly requires Director-General to submit in 1966, a plan for an "intensified" program
- Plan calls for a 10 year program and a special budget of $US 2.4 million/year
- Objections by delegates
  - Not feasible
  - Demand for no further increases in WHO budget
- 58 votes needed for acceptance of the proposal; 60 votes received

Program leadership

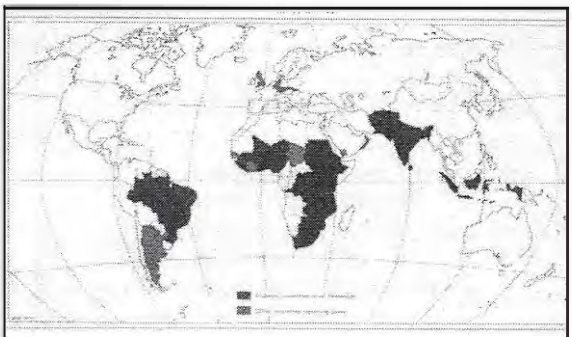
- Director General stated his belief that program will fail with resulting loss of confidence in WHO and loss of credibility
- He demanded an American serve as Director
  - The identified candidate declines:
    - Major responsibilities for new CDC African program
    - Problems of coordination over 6 Regional Offices
    - Limited resources of <$50,000 each for 50 countries
  - The appointment

Characteristics of Smallpox Favoring Eradication

- Man -- the only host
- Virus spread -- only during rash
- Permanent immunity after recovery
- Spread of virus -- face-to-face contact
- A highly stable vaccine requiring one dose
- Vaccination success measurable by skin reaction
- Scars of smallpox provide historical record

The Challenge

- Global status of smallpox – 1967
  - 10,000,000 – 15,000,000 cases
  - 2,000,000 deaths
  - 43 countries reported cases
- Program staff
  - Headquarters – 4 medical, 2 admin, 3 secretaries
  - Regions – one each in 4 WHO Regions
  - International staff – never more than 100



■ = Endemic countries
■ = Others with cases

Smallpox 1967

The Strategy

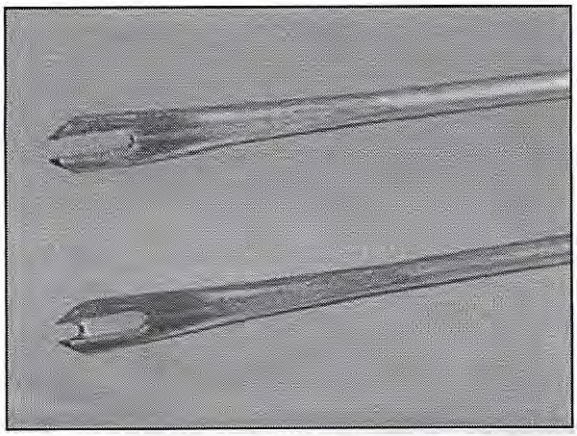
- Vaccination
  - Target – 80% of population
  - Quality control
- Surveillance-containment
  - Surveillance – weekly report from every health center and hospital
  - Teams to investigate and do containment vaccination ("ring vaccination")

Wrong assumptions - vaccine

- Available supplies would be adequate
  - All countries were doing some vaccination
  - USA providing vaccine for 18 African countries
  - USSR providing 25 million doses each year
- Quality would be generally acceptable
  - Control labs (Canada and Netherlands) prove otherwise
  - Less than 10% met accepted standards
  - Budget is too small to permit vaccine purchase

Solutions for the vaccine problem

- Development of vaccine production
  - Manual and training
- Change vaccination procedures to use less vaccine
  - Jet injector gun
  - Bifurcated needle
    - Only one-fourth as much vaccine required
    - Training time of no more than 15 to 20 minutes
    - Vaccination successful in 95%+
    - Needles can be easily sterilized and reused
    - Cost of $5 per thousand



Wrong assumptions

- Revaccination required every 5 to 10 years
  - Surveillance shows almost all cases are unvaccinated but few revaccinations were being performed
  - West Pakistan studies reveal sub-clinical infections
- Smallpox spreads "like a prairie fire"
  - Case tracing shows that a patient usually infects very few others
  - From onset of prodrome, most patients are very sick and go to bed

Innovative administrative steps

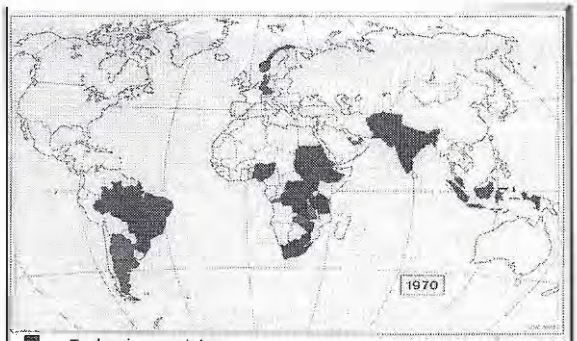
- All personnel must spend not less than one-third of their time in the field
- Direct communications with field established Originals of memos, etc. to be sent to the WHO Regional Offices with copies directly to field staff
- All communications from the field to be answered within 3 days

Reports – new departures

- Surveillance reports for all smallpox managers
  - First reports are stopped by senior administration
  - Weekly Epidemiological Record becomes the answer
    - Data, advisories and field observations included
- Consolidation of data at WHO and countries
  - Reports required by quarantine regulations
  - Annual national statistical reports
  - Smallpox program staff data

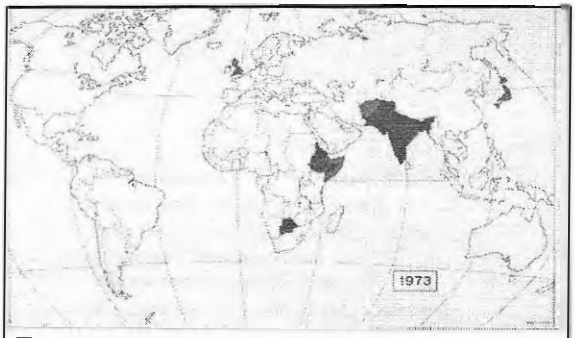
= Endemic countries
= Others with cases

Smallpox 1967



= Endemic countries
= Others with cases

Smallpox 1970



= Endemic countries
= Others with cases

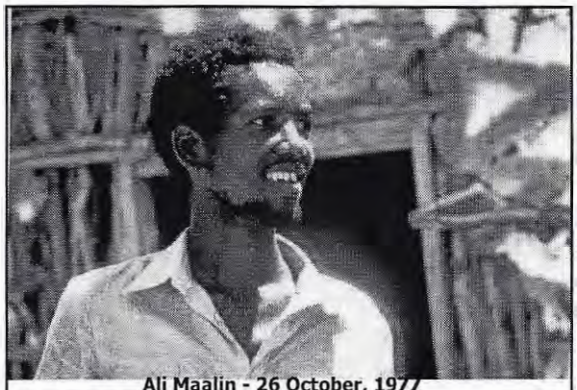
Smallpox 1973

Critical final challenges

- India
  - National leadership; searches; reward system
- Bangladesh – August 1975
  - The only remaining endemic area for variola major
  - President and family are assassinated
  - Martial law declared; borders are closed
- Somalia – Summer 1977
  - The only remaining endemic country
  - Nomadic, minimal health infrastructure
  - Variola minor patients readily able to move about
  - The time of the Hajj is coincident with outbreak

= Endemic countries
= Others with cases

Smallpox 1976



Ali Maalin - 26 October, 1977

After smallpox – the EPI

- Pertinent observations
  - Wards full of children with vaccine-preventable diseases – Basic health units without supervision or refrigeration
  - High productivity of smallpox vaccination teams --quality control and supervision possible
- WHO international conference at PAHO—1970
  - Report approved recommending 7 antigens for all children
- Expanded Program on Immunization adopted by World Health Assembly in 1974
- Special support by UNICEF and Rotary
  - *Target: 80% coverage by 1990 (~5 % in 1975)*

After smallpox – what next?

- The first conference on eradication
  - Fogarty Center, August 1980
    - The logical – polio, measles, dracunculiasis, yaws
    - The illogical – hunger, poverty, urban rabies, traffic accidents
- Eradication programs
  - Poliomyelitis
    - Americas – 1985
    - Global – 1988
  - Dracunculiasis (Guinea worm) -- 1986

Poliomyelitis eradication

- Increasingly a separate, independent program
- Status at the end of its 19th year
  - 2000 cases (400,000 infections) -- 2006
  - 4 "endemic" countries
    - India, Pakistan, Afghanistan, Nigeria
  - 4 "non-endemic" countries with continuing transmission for more than two years
    - Somalia, Ethiopia, Angola, Congo Dem. Rep.
- Cost to date
  - $4.5 billion in international assistance
  - >$4.5 billion in national costs

- *...there is no disease other than smallpox which possesses so many characteristics favorable to an eradication effort or for which we now have available, effective, simple and inexpensive measures for prevention... Even with these many advantages, smallpox eradication just barely succeeded."*

D.A.Henderson, April 1982
Proc.Amer.Phil Soc 126:461, 1982

The next eradication program that needs to be undertaken is to eradicate the word "eradication"