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"The Saga of Smallpox Eradication
An End and A Beginning"

by

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Your kind invitation to me to participate in this meeting was thrice welcome: first, as an opportunity to pay special tribute to Drs. Bob Wilson and Paul Fenje of Connaught Laboratories which as one of WHO's two International Smallpox Vaccine Reference Centers played a vital role in the development of smallpox vaccine production throughout the Americas; second, to express my thanks to Dr. Arnold Duvilliers and CIDA for both moral and substantive support to the program during some of its darkest hours; and, lastly, as an opportunity to return to the country which my family called home beginning in 1798, when they discovered Canada and Edward Jenner discovered smallpox vaccine.

Development of the Smallpox Eradication Program

Today, I will try to sketch for you from a personal vantage point the saga of smallpox eradication as it developed over the past 11 years, to provide to you some sense of its dimensions, of reasons for the program being undertaken, of some of the difficulties we faced and, lastly, an indication of what this program might mean for the future.

The decisive point in time was May, 1966, when the World Health Assembly decided to undertake a coordinated intensified program to eradicate smallpox from the globe within a 10-year period. The program was to commence on January 1, 1967 and the hope was expressed that the last case would be discovered and isolated by December 31, 1976. The rhetoric at that 1966 Assembly was optimistic and confident. Privately, I believe it is fair to say that very few believed the project to be a practical objective, even if theoretically possible. In fact, no disease had ever before been eradicated. Moreover, and realistically, experienced international staff could well foresee the practical difficulties of achieving any workable degree of cooperation among the 50 or so nations which would be required to undertake special programs. Not to be dealt with lightly were the technical and logistical difficulties of executing a program which would inevitably have to be conducted in some of the most inhospitable places on earth. Better control of smallpox was envisaged but eradication was another dimension.

The 10 year time limit proposed was not grounded in an elaborate operations research process or, for that matter, in any other planning process. Quite simply, Kennedy, as you will recall, had said some years before "we will land a man on the moon in 10 years". The delegates reasoned that if one could land a man on the moon in 10 years, surely one could eradicate smallpox on earth in 10 years.

The then Director-General of WHO, Dr. Marcelino Candau, a Brazilian, expressed certainty that eradication in the Amazon basin, let alone elsewhere, was impossible. And being Brazilian, he knew the Amazon basin well. With WHO's only other eradication program - that for malaria - foundering at that time, the Director-General understandably did not want to be charged with the responsibility for yet another eradication program which he knew would fail. He asked, in effect, that the United States share in the onus of failure by making available an American, myself, to develop and direct the program.

I had been working at CDC as Chief of the Surveillance Section and had been directing programs of infectious disease surveillance, vaccine evaluation and vaccination campaigns against a variety of diseases. In the early 1960's, as one of a number of programs, a smallpox unit was created to assess smallpox vaccine complication rates; to assess the jet injector as a possible tool for administering the vaccine; and to prepare staff to cope with smallpox cases should they be imported into the USA.

Meanwhile, USAID, in the early 60's, had promoted a series of measles vaccination programs in Francophone Western Africa which were beset with all manner of problems. In 1965, CDC was asked to help. Not wanting to refuse to assist but concerned about the basic assumptions of the program, we countered with a vastly more extensive plan for smallpox eradication throughout a bloc of 18 west and central African states with a proposal that measles vaccination be given simultaneously in countries where it was desired. Although technically sound, the proposal was far more ambitious than the limited measles control program under consideration. To our surprise, President Johnson on November 23, 1965, announced the decision of the United States to undertake this program and I was asked to assume responsibility for its implementation. This program was only in its initial phases of planning, recruitment, securing of intergovernmental agreements and the like when the World Health Assembly made its historic decision to undertake global smallpox eradication. Abruptly, I was dispatched to Geneva as the global director. I had seen only 12 cases of smallpox in Argentina in 1957 and one in Toronto in 1962. It was understood, however, that my assignment would only be for perhaps 9 to 18 months to initiate development of the program. Accordingly, we left half of our household goods in storage and so, inauspiciously, began an incredible 10 year adventure.

I recount this to dispel any notion that this - no less than so many other memorable enterprises - developed logically and coherently within the political-planning process.

The Rationale for Smallpox Eradication

Why eradicate smallpox? Why, among all the afflictions besetting mankind, select this disease? As McNeill has so well described in his recent history, "Plagues and People", smallpox, throughout written history, has been preeminent as the most devastating disease known to mankind - the disease which more than any other has again and again altered the course of history. Diseases such as plague or cholera or yellow fever have been, overall, of lesser consequence. Smallpox once was a disease, like measles, which was prevalent worldwide, eventually infecting almost everyone and killing 20% to 30%. In some areas of central Europe, a child was not given a name until after surviving smallpox. It was smallpox which decimated the indigenous Indian population of America's East Coast and so facilitated settlement. It was this disease, not the Conquistadores, which defeated the Aztecs and Incas. Although an effective vaccine had been discovered by Jenner in 1798 and steadily became widely available, health officials throughout the world continued to fear this disease as no other.

Until 1971 in the United States, some 14 million people were vaccinated annually to protect against importation and spread of smallpox despite the fact that the last known case had occurred more than 20 years before. Not only was this costly, but complications following vaccination caused between 6 and 12 deaths annually. In the United Kingdom, there were 8 smallpox hospitals maintained on a stand-by basis to admit cases should smallpox be imported. I suspect that few of you are aware of the fact that following importation of the single case of smallpox into Canada from Brazil in 1962, it was all but decided to: (1) vaccinate everyone from New York City, the boy's point of entry, to Buffalo and (2) to close the Canadian border. Fortunately, reason prevailed - although just barely - but these events speak for themselves of the fear which smallpox engendered.

Smallpox - The Disease and Its Epidemiology

Smallpox is caused by a virus which is transmitted from person to person through minute droplets expelled from the nose and mouth. The susceptible contact inhales these and after a period of 10 to 12 days, experiences high fever and aching pains similar to the symptoms of influenza. After 2 to 4 days of fever, a rash appears on the face and rapidly spreads over the rest of the body, the lesions being most dense on the face, arms and legs. The vesicles which first appear become pustular by about the fifth day of rash. Subsequently, scabs form which separate during the third and fourth week of rash. Approximately 20% to 30% of those afflicted with variola major, the severe Asian form of smallpox, died from the disease. There is no treatment for smallpox; importations into Europe were no less serious than those in Asia. Two-thirds of those who experienced the disease were left permanently scarred and some were blinded. The form of smallpox which was found throughout most of Africa was milder and resulted in death among 5% to 15% of those afflicted. The least serious form of smallpox, variola minor, was present in South America, South Africa and in Ethiopia - Somalia, and caused death in less than 1%.

Although the disease was serious and widespread, it had certain characteristics which facilitated eradication. In contrast to such as yellow fever, man is the only known reservoir of the disease and for the virus to persist, it must pass from person to person in a continuing chain of transmission. Each individual, each link, in the chain of transmission experiences rash and a large proportion of those who survive bear permanent scars of the disease. In effect, the disease was visibly apparent wherever it was and left its "footprints" wherever it had been. Thus, one could readily ascertain whether or not smallpox was present or had been present in any geographic area. The disease itself was recognized by even illiterate populations and thus it was possible through surveys in markets or by house to house survey to detect smallpox in any given area. Sometimes, cases of chicken pox were mistaken for smallpox, particularly by recently graduated physicians. However, the grandmothers in the villages generally were quite accurate in their diagnosis.

Epidemiological studies conducted early in the program confirmed that the disease almost inevitably spread as a result of close face to face contact, usually within the confines of a house. In major part, this accounted for the occurrence of the disease in clusters of villages within a district or in sections of a town rather than being randomly dispersed over an extensive area. This feature enabled outbreak containment teams to focus their efforts in particular geographic areas. Moreover, the infected individual is able to transmit the virus for only 3 to 4 weeks, that is, from the time the rash first appears until the last scabs separate. Asymptomatic carriers thus played no role in transmission as they do in malaria. In the more remote areas, the disease, continued to spread for only a finite period of time - until the susceptibles had acquired the disease and had died or survived. Logistically, this permitted us to focus our efforts on the more densely populated, more accessible areas with expectations that the disease would spontaneously die out in many remote areas, such as mountain valleys or the further reaches of the Amazon. In fact, this is precisely what occurred. Lastly, the smallpox vaccine is an excellent one, providing a high level of protection against the disease for a decade or more and protection against death for an even longer period.

Smallpox Eradication - 1958-66

When I indicate that the program started in 1967, I am slightly misstating the fact. Eight years before this, the World Health Assembly had decided that a global eradication program should be undertaken on a voluntary basis. It was voluntary in the sense that endemic countries were asked to undertake systematic mass vaccinations and non-endemic countries were asked to provide donations to the campaign. In fact, however, annual contributions to the program over this 8 year period averaged only \$100,000 in cash and in kind. The strategy consisted simply of mass vaccination to create herd immunity. It had been anticipated that when 80% of the population was vaccinated that transmission would cease. However, New Delhi, in an intensified Indian campaign, reached a level of "140%" vaccinated and found that smallpox was still spreading. The figure of 140% relates to the number of vaccinations

performed divided by the population. Obviously, many were being repeatedly vaccinated and others not at all. A WHO Expert Committee was convened in 1965 and proposed that the target for vaccination be increased to 100%. Practically, of course, vaccination of 100% of any population is impossible.

Underlying many of the events of the period was the fact that few believed eradication to be possible. However, in the 1966 resolution, a special budget of \$2.5 million was approved as a last gesture to the effort before abandoning it. In all, it was expected that programs would need to be conducted in some 50 countries which were either endemic for the disease or adjacent to them. The total budgeted was thus an average of \$50,000 per country.

The Intensified Smallpox Eradication Program - Developmental Approach

The program commenced on 1 January 1967 - the objective was the occurrence of the last case by 31 December 1976.

As the program commenced, we immediately faced two major problems:

1. Provision of adequate quantities of suitable vaccine and appropriate vaccination devices - the guns and bullets of the campaign, if you will; and
2. The selection of a suitable strategy - mass vaccination obviously was not the answer but what was?

Supply of Vaccine

The endemic countries, as the program began, were all conducting some sort of vaccination program to control the disease. Vaccine was being obtained from diverse sources. Two laboratories, Connaught Laboratories and the Rijks Institute in the Netherlands, agreed to test batches of vaccine in use or donated to the program. The initial results were appalling. Not more than 10% of the vaccine in use in the endemic countries met accepted standards. Some batches of vaccine, in fact, were found to contain no detectable virus whatsoever. We estimated the total need for vaccine to be approximately 250 million doses each year. At a cost of 1 cent per dose, this was equivalent to our total budget. There was no choice but to encourage the development of production in the endemic countries and, in the interim, to solicit contributions of vaccine from countries who were producing it. A group of consultants were convened and a step-by-step manual of production procedures was developed. Selected consultants traveled from laboratory to laboratory in the endemic areas to assess their potential for vaccine production, to determine what their needs were in the way of equipment and training and to participate in the training of local staff. Drs. Bob Wilson and Paul Fenje were two key consultants. As the laboratories commenced production, each batch was tested by one of the international testing laboratories. As the laboratories gained confidence and the quality of the vaccine improved, an ever smaller proportion of the batches of

vaccine produced were tested. However, throughout the program, efforts were made to test at least three batches of vaccine from each laboratory every three months.

During the first few years, the principal contributors of vaccine were the Soviet Union, which contributed some 140 million doses each year, and the United States, which provided some 40 million doses of vaccine each year for countries in western and central Africa. Smaller amounts of vaccine were donated by some 20 other countries, including Canada. By 1970, essentially all vaccine met accepted standards and these standards were rigorous. The freeze-dried vaccine had to meet minimum potency requirements after incubation at 37°C for 30 days. By 1973, 80% of the vaccine being used was produced in the developing countries and certain of these countries were contributing vaccine for the use of others.

Vaccination Technique

Since Jenner's time, vaccine had been applied by some sort of scratch technique in most parts of the world. The multiple pressure technique was preferred but was difficult to teach to vaccinators. A better approach appeared to be the jet injector. With this gun, vaccine is expelled under high pressure through a very small opening into the superficial layers of the skin. Vaccination of as many as 1,000 persons per hour is possible. The gun was introduced for use in Brazil and countries of central and western Africa. Although theoretically, as many as 1,000 persons per hour could be vaccinated with this device, logistically, it was impossible to realize this potential. In fact, most teams in western and central Africa averaged no more than 1,000 to 2,000 vaccinations per day. With dispersed populations, difficulties of travel and problems in organization, greater numbers simply could not be vaccinated. A major drawback in use of the jet injector was the need for maintenance and repair and provision of a continuing supply of spare parts. In the developing countries, the establishment of an effective maintenance and repair scheme, let alone a satisfactory storage and distribution system for spare parts, is a formidable task.

The ultimate solution proved to be the very simple bifurcated needle, which had been developed by Wyeth Laboratories. The needle, approximately 2 inches in length, has two small sharpened tines at one end. In 1967 it was being tested for possible application for multiple pressure vaccination. We reasoned that the needle might be equally effective if held at right angles to the skin and multiple punctures made. The design of the needle was such that only superficial penetration of the skin was possible, a desirable attribute since the vaccinia virus proliferates only in the superficial layers of the skin. Tests of multiple puncture vaccination proved most successful with a higher proportion of successful vaccinations registered than was obtained by scratch vaccination. Training of the vaccinator could be accomplished within a matter of minutes. The needle offered another important advantage in that much less vaccine was required for vaccination. When the needle was dipped into a vaccine vial, a very small amount of vaccine adhered between the

two times, an amount sufficient for vaccination. A vial of vaccine previously designed to vaccinate 25 people could now be used to vaccinate up to 100 persons. Wyeth Laboratories had envisaged that the needle would be disposable but with the limited budget available to us in WHO, we felt we had to have a needle which could be sterilized and reused many times. Accordingly, it was fabricated using a harder steel alloy. Tests showed that the needle could be used hundreds of times.

A final refinement of vaccination technique related to the use of alcohol or soap and cotton sponges to "sterilize" the skin. Earlier studies in England had showed that use of a 70% alcohol solution did little more than redistribute the bacteria on the skin surface. Accordingly, studies were conducted in which complication rates were compared for children vaccinated without cleansing the skin and those vaccinated following cleansing of the skin with alcohol or soap. There was no difference in the frequency of septic complications. In some areas, the savings in alcohol, soap and cotton sponges paid a substantial proportion of the petrol costs.

Finally, a simple plastic container was developed which permitted one needle at a time to be dispensed and which was resistant to high temperatures. A vaccinator was issued two such plastic holders, one containing approximately 100 needles and the other empty. As each needle was used, it was placed in the originally empty container. At the end of the day, the vaccine holder containing used needles could be boiled for 20 minutes, shaken once or twice and the vaccinator was ready for the next day's work. Thus, the vaccinator's equipment consisted only of these two containers plus a few vials of vaccine. All of this could be placed in a shirt pocket. Since the dried vaccine remained potent for a period of one month at 98°F, a vaccinator could work in tropical areas over long periods far from refrigeration.

Strategy

Previous to the intensified eradication program, progress in any smallpox campaign had been measured in terms of millions of vaccinations performed. Unquestionably, a program of vaccination was important but the real objective was "zero" cases of smallpox. Thus, a two-prong strategy was developed: (1) vaccination; (2) surveillance.

Vaccination

In most of the endemic countries, vaccination immunity was low. Thus, systematic campaigns were developed with the objective of reaching 80% of the population. The figure of 80% was not based on epidemiological principles, but rather on a feasible operational goal. Vaccination campaigns in the different countries developed in different ways, depending on the health structure and the particular circumstances of the country. This we encouraged. Illustrative is the program in Afghanistan. When the program began there, available maps of the country were obsolete and sometimes erroneous. Over the years, new villages had been built and old ones had disappeared.

Accordingly, each vaccination team was assigned an "advance man" whose responsibilities included preparation of an updated map which showed each village, school and health facility. To do this, he traveled ahead of the team to a known village and inquired there about other villages in the area. Each of these was specifically identified on the map and visited and information in regard to other villages sought. While visiting the villages, he discussed the nature of the program with the village leaders to explain what vaccination could achieve and to solicit their support and help. Later, a vaccination team progressed house by house in each village, vaccinating each person. The team carried no records from house to house but, rather, when work in a village was completed, they counted the number of needles which had been used and recorded this number. By proceeding in this manner, fewer records needed to be prepared and they were able to move more rapidly. Ten to fourteen days later, an assessment team visited a 10% to 20% sample of the villages. The villages were selected by the simple expedient of listing each village name on a piece of paper, placing the pieces of paper in a box and drawing at random the villages to be assessed. Although statistically, objections could be raised to this technique, it was a method which was readily comprehended by assessment team leaders and operationally, it proved to be workable and effective. If the assessment team found on inspection that less than 80% of individuals bore marks of recent or past vaccination, the vaccination team was required to return to the area without per diem to revaccinate the area. This technique served to increase the motivation of the vaccination teams.

Surveillance

Regular reporting of all known cases was essential if outbreaks were to be identified and contained. However, in 1967, the reporting of smallpox cases was a shambles. At the national level, some countries reported to the World Health Organization not at all, some sporadically, and some suppressed reports of smallpox. Reporting from national levels was actively encouraged through frequent repetitive contact with the respective governments and through persuasion that it was better to report known cases than to suppress them.

The problems at state, district and local levels were no less serious. Frequently, it was found that perhaps 200 cases were known to exist at the local level but, due to casual recording practices or sometimes deliberately, no more than perhaps 100 cases would be reported to district level. At district level, the same procedure was repeated so that perhaps 20 cases would eventually be reported at national level. Various approaches were employed to improve reporting. In Africa, the most effective was to assign a mobile team of 2 to 4 persons for each 2 to 5 million population. The team visited each health unit on a regular basis to encourage them to report each week whether or not cases had been reported. On discovery of cases, the containment team participated with local

health staff in the containment of the outbreak. By repeated visits and by working with the local health staff in containment of outbreaks, reporting steadily improved as it became clear to the local health staff that there was a real concern that cases be reported. In some countries, the fact that any higher level health staff visited a health center was itself a unique event; that anyone took action on a report which had been sent to higher levels was viewed as something of a miracle.

In 1967, 131,000 cases were officially reported but later studies revealed that not more than 1% of all cases which actually occurred that year were recorded. Thus, the total number of cases which occurred in 1967, during the first year of the program, is estimated to have been between 10 and 15 million cases.

In brief, then, the strategy consisted of two components: (1) a vaccination program designed to assure that 80% of the population bore a mark of vaccination and (2) a program to improve reporting and containment measures so that those outbreaks which were present could be identified and could be contained.

Progress in the Program

In 1967, 34 countries were considered to be endemic and 11 others experienced importations. By 1970, the number of endemic countries had decreased to 17 and by 1973, to 6. However, these 6 included India, Pakistan, Bangladesh and Nepal which together had a total population of 700 million persons. In these countries, traditional vaccination programs had been in progress for many years. However, reporting of cases was poor; the containment of outbreaks was all but ignored; and throughout the subcontinent, there prevailed a sense of profound pessimism.

Techniques successfully employed in Africa were not effective. Thus, in the summer of 1973, the strategy was changed. A plan was developed for India and later extended to the other countries, which called for the utilization for one week each month all health workers in a village by village, later house by house, search for cases. Special containment teams (called firefighting units) were organized which would move in promptly to stop the outbreaks. As was done with the vaccination program, special assessment teams were formed which visited a sample of the villages to determine whether, in fact, the search had been properly performed. To facilitate the discovery of cases, a reward was offered to anyone who reported a case. The reward initially was very small, but as the number of cases declined, the reward was steadily increased. The result of these measures was a veritable explosion in recorded cases. The experience in one Indian state, Uttar Pradesh, illustrates this. Considerable work to improve reporting had been in progress for almost two years, but the state was large and had a population of 100 million persons. During September, 1973, between 100 and 300 cases had been reported weekly. During the first search week, some 7,000 cases were discovered. Later we were to learn that during that first search, only

50% of the villages had, in fact, been searched and thus the true number of cases at that time was even greater. Once cases were discovered, however, they could be contained. The system of search and containment was steadily improved as time passed and, eventually, assessments showed that in every state of India, more than 90% knew that there was a reward for reporting a case of smallpox and knew where to report a case. Between searches, special surveillance teams moved from market to market inquiring about cases. Knowledge of the reward and the interest generated resulted in literally hundreds of thousands of cases of rash of all types being reported to health authorities. Each was individually screened and assessed. However, as the smallpox incidence fell and smallpox cases disappeared, the fact that so many cases with rash were being reported provided increasing confidence that if a case were present, it would be discovered. The experience in Bangladesh, Nepal and Pakistan paralleled that in India.

To appreciate the magnitude of the undertaking of the search operation in India, some data are useful. In all, some 120,000 health staff searched 120 million households in more than 500,000 villages in India on repeated occasions. For each search, more than 8 tons of forms were required. Assessment of the search was performed at three levels - district, state and national - the separate assessments serving to cross-check each other.

In October 1974, the last known case of smallpox occurred in Pakistan; in April 1975, in Nepal; in May 1975, in India. The last known case of smallpox in Asia and the last known case of the severe form of smallpox, variola major, occurred in a three-year old girl, Rahima Banu, on Bhola Island, Bangladesh. The date was 16 October 1975, two years ago.

The Final Phases

The last battleground of the smallpox eradication campaign proved to be Ethiopia where the least severe form of smallpox, variola minor, was prevalent. Death rates due to this form of smallpox were less than 1%. Several factors account for the persistence of smallpox in Ethiopia after it had disappeared from all other countries. The program there, for various political reasons, started three years later than in any other country. Political stability was a real problem; the road system was very limited; the terrain was perhaps the most difficult of any country in which the program was conducted. Local rebel groups sometimes shot at the teams and, on repeated occasions, WHO advisors as well as national staff were kidnapped and held hostage for varying periods of time by rebel groups. Each week was another chapter in the "Perils of Pauline". Every conceivable approach had to be used to overcome the problems. Because of the size of the country, the all but impossible road conditions, and the limited number of supervisory staff available, helicopters were employed. Gradually, smallpox incidence diminished and in August, 1976, the last known case occurred. More than 2,000 Ethiopian staff and WHO advisors searched the country. For seven weeks, no cases could be found anywhere. We thought that the last case had been discovered and contained.

However, in late September, cases were discovered in Mogadishu, the capital of Somalia, which lies adjacent to Ethiopia. Subsequent investigation revealed that cases had been imported into Somalia as early as April or May of 1976 and although discovered by lower level government health officials, reports of these cases had not reached higher authority. Parenthetically, smallpox transmission in Somalia had been interrupted in 1963 but in 1968 a WHO-sponsored program had been inaugurated because of the high risk of importation of cases into Somalia from Ethiopia. The objective of the program was to strengthen surveillance and to conduct systematic vaccinations. Almost 700,000 of 3 million persons were vaccinated annually. Until 1976, importations had been rapidly identified and contained.

When the cases were discovered in Mogadishu, the necessary containment measures were greatly delayed and poorly conducted. Not until late in the year were satisfactory measures able to be applied. In mid-January, 1977, transmission appeared to have been stopped in Mogadishu. Limited search conducted among nomads in the vast Ogaden desert area surrounding the capital revealed no cases. Again, we thought that perhaps the last case had been detected. However, as later information revealed, at least 3 to 4 infected nomadic camps remained in the desert. Again, some of these were known to lower level government health authorities but were not reported. In March and April, as the rainy season began, the nomadic groups began moving to agricultural development areas. With this movement, the disease spread rapidly. Increasing numbers of Somali staff were deputed to the program, the government declared a state of national emergency and additional WHO veteran smallpox eradication workers were brought into the country. By June, a major effort was underway. In all, somewhat more than 3,000 cases occurred during 1977. Meanwhile, in adjacent areas of Kenya, search operations detected one importation but it was rapidly contained. In adjacent areas of Ethiopia, serious civil disturbances since August hampered surveillance but by various devices surveillance was able to be continued. No further cases were discovered following those in August 1976. As of today, 24 November, 28 days have elapsed since the world's last known case of smallpox occurred - on 26 October 1977. It may or may not prove to have been the last but, as of today, there is no known active case of smallpox.

Our 10 year time target expired on 31 December 1976. Thus, regrettably, eradication has not been achieved within the allotted 10-year period. At most, however, I believe it will not have been missed by more than one year.

Confirmation of Eradication

To confirm that eradication has been achieved, two full years of intensive search will have to be conducted to be certain that transmission of smallpox is not still occurring. Only then can a WHO International Commission be convened to determine through inspection of records and field visits that they are satisfied that smallpox is no longer present. So far, WHO Commissions have certified smallpox eradication in South America and in all of western and central Africa. On December 14, we

expect that the last international commission for endemic Asian countries will certify the eradication of variola major. Hopefully, the last areas will be able to be certified in December, 1979.

Meanwhile, a number of research studies have been conducted to determine if naturally-occurring smallpox transmission could be detected in nature. None has been found. The fact that during the past 10 years, every focus of smallpox in non-endemic areas has been able to be traced to known endemic regions is the most persuasive evidence that no natural reservoir of smallpox exists.

With the cessation of smallpox transmission, variola virus will be confined to research laboratories. Since 1975, WHO has been engaged in a special program to identify and register all laboratories retaining stocks of variola virus. All governments have been officially queried; all laboratories registered as being able to conduct variola virus diagnosis have been contacted; and all laboratories which since 1950 have reported in the literature having done research with variola virus have been questioned. At present, only 17 laboratories in 10 countries are registered as retaining stocks of variola virus; more than 60 have destroyed their stocks. By 1979, it is expected that no more than 4 laboratories will retain variola virus under high security precautions.

Cost

We have endeavored to tabulate all international assistance made available to this program in whatever form. Through 1979, when we believe that final certification of eradication will be possible, approximately 100 million dollars will have been spent, only two-thirds as much as the United States alone spent in a single year for smallpox vaccination and quarantine measures. The developing countries themselves will have spent perhaps twice this amount but few will have spent much more than what they were spending in smallpox control programs. With final confirmation of eradication, vaccination everywhere will be able to be stopped. The savings worldwide are estimated to be in excess of \$1000 million dollars annually.

The Future

Is this then the end of a program or the beginning of some greater effort?

Many of the same individuals who were scathing of the prospects of eradication only 10 years ago now argue that its achievement was some sort of fluke, an aberration in the health system, that no disease could be dealt with in the same manner, that such "prodigious" sums of money could not possibly be mobilized for other health problems, and so on. In brief, many have effectively made a plea to return to business as usual.

But can it ever be the same again? In many of the developing countries, where health ministries have often been held in low esteem, there is a

perceptible new sense of confidence in their own ability to deal with the overwhelming health problems they face. Moreover, there is respect within their own governments that given modest support, well-conceived plans, involvement of the community and an element of management that the impossible is within reach. Specifically, a global WHO immunization program embracing six antigens is now gaining momentum.

More than 700 international staff from 52 countries served WHO in this campaign and, in the process, acquired an expertise, a point of view and a sense of the possible. The majority were under 40 years of age, far younger than the average WHO consultant. Many were not physicians. Several are now already serving in directorate general positions in their own governments; one is Assistant Director General of WHO; and two of the U.S. Public Health Service's six agencies are headed by former smallpox staff.

More than this, one senses that there is an increased perception that in this one world, better health per se is important and important to all countries. That prevention rather than sickness care can be far more effective at far less cost. It is my hope, and I know the hope of the thousands with whom I have worked in this program that we have helped to do much more than eradicate smallpox - that this achievement, unique though it may be, represents but a very small beginning in a very much greater and more complex effort to prevent disease at the source rather than to treat sickness after it occurs. It is this hope which brought me to the country's oldest and the world's largest school of public health - at Johns Hopkins - in hopes that I might participate even more actively in accelerating the necessary process of change.