A pilot program in Bolivia demonstrates the feasibility of smallpox eradication by mass vaccination at the sources of the disease.

Smallpox Eradication

HARALD FREDERIKSEN, M.D., M.P.H., D.T.M.&H.
NEMESIO TORRES MUÑOZ, M.D.
ALFREDO JAUREGUI MOLINA, M.D., M.P.H.

NATIONS freed of smallpox are confronted by a continuous threat of reinvasion from the endemic foci remaining in the world. The concept of control, limited to the protection of a national population and resigned to the existence of endemic foci in other nations, requires a perpetual and elaborate system of defense: education, general vaccination in infancy, routine revaccination, reporting, isolation, disinfection, quarantine, investigation, contact vaccination, general revaccination, international notification, certification, and medical inspection. However, the frequent movement of the disease across international boundaries shows that, even with elaborate control measures, no nation can permanently prevent reinfection.

Dr. Frederiksen, who is now program officer, Division of International Health, Public Health Service, served in 1957 and 1958 as director of the Servicio Cooperativo Interamericano de Salud Pública, a joint agency of the Republic of Bolivia and the United States. Dr. Torres Muñoz was associate director of the agency, and Dr. Jauregui Molina, director of SCISP's vaccination service.

Only the eradication of smallpox would end the threat of the disease, as well as the otherwise unending efforts and costs of control. What are the prospects for eradication once all nations join in an unrelenting attack on smallpox wherever transmission persists?

Rather than evaluate hypothetical obstacles to eradication it seems appropriate to cite the circumstances, methods, and results of the pilot program in Bolivia undertaken by the Servicio Cooperativo Interamericano de Salud Pública. With one of the highest attack rates for smallpox, Bolivia was one of the principal endemic foci in the American Hemisphere (*1*). Because of a unique combination of adverse factors, Bolivia was a testing ground for the feasibility of smallpox eradication through the progressive elimination of the endemic foci remaining in the world.

The Setting

Landlocked in the heart of the South American continent, Boliva has climate and scenery that range from steaming tropical to Alpine. Most of its 1 million square kilometers is tropi-

cal lowland along the cayman-infested headwaters of the Amazon. The majority of the 3.3 million people of Bolivia live on the highland plateau, the Altiplano, at an elevation of 3,500 meters, where La Paz, the seat of government, is located.

Bolivia is thinly populated, with a density of 3.3 persons per square kilometer. Means of communication are limited. Much of the country is inaccessible by road, and most of the existing roads are unsurfaced and frequently are blocked by floods and landslides. Bolivia is one of the few countries of the world with areas still awaiting exploration.

While ethnic distinctions are blurred, the population can be divided sociologically into a literate minority, largely of Spanish descent, and an illiterate majority of Indian stock. The Indians usually have only a little knowledge of the official language, Spanish.

A number of devastating wars and revolutions have impeded development. The country, while potentially rich, remains undeveloped, and the per capita income is low. The combination of adverse factors has limited health services to a minority.

Past Control Efforts

Data indicated that vaccinations in Bolivia were deficient in quantity and and quality. In 115 samples totaling 47,742 persons from the highland plateau, the valleys, and lowlands, the proportion of those previously vaccinated fluctuated between 11.1 percent and 94 percent, with a median of 69.3 percent. While this percentage may seem fairly satisfactory, a closer examination reveals a less reassuring situation. In Sucre, the legal capital, which had one of the highest percentages of previous vaccinations, 93.1 percent, only 32.5 percent were found to be vaccinated in the 0–4 age group. In other provinces fewer persons have been vaccinated during infancy and childhood.

The lack of vaccination during infancy and childhood is reflected by the high proportion of the smallpox deaths which are reported in the 0–4 age group. In a recent sample, 95 of 136 consecutive deaths reported were in this age group.

The low percentage of vaccinations, particularly during early childhood, is complicated by the poor quality of vaccinations in the past, largely attributable to the use of glycerinated vaccine without adequate refrigeration facilities. A potent glycerinated vaccine has been successfully produced and applied in Sucre, but this vaccine has not produced reliable results in other parts of the country, as a result of difficulties in maintaining the potency of the glycerinated vaccine. A sample of 463 individuals from a highland province with a temperate

Table 1. Prevalence of pockmarked persons in Bolivia by age group and department, 1958

Department	Age group (years)														
	0–4			5–9			10–19			20–39			40 and over		
	Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked	
		Number	Percent		Number	Percent		Number	Percent		Number	Percent		Number	Percent
La Paz	1,526	13	0.9	3,279	120	3.7	4,390	292	6.7	2,600	687	26.4	1,500	613	40.9
Oruro	598	1	.2	834	9	1.1	798	25	3.1	792	117	14.8	258	58	22.5
Potosí	907	14	1.5	2,031	41	2.0	1,579	77	4.2	1,086	182	16.8	544	171	31.4
Cochabamba	2,959	60	2.0	3,193	102	3.2	3,134	212	6.8	3,070	406	13.2	2,048	478	23.3
Chuquisaca	759	0	0	1,682	2	.1	1,427	19	1.3	1,144	97	8.5	846	173	20.4
Tarija	128	0	0	156	0	0	229	0	0	184	2	1.1	146	14	9.6
Beni	36	0	0	48	1	2.1	39	1	2.6	48	3	6.3	25	3	12.0
Santa Cruz	1,372	2	.1	1,295	18	1.4	1,612	39	2.4	1,488	110	7.4	828	76	9.2

Table 2. Correlation between population density and the prevalence of pockmarked persons by age groups in five provinces of the highland plateau of Bolivia, 1958

Province	Population density per square kilometer	Age group (years)														
		0–4			5–9			10–19			20–29			40 and over		
		Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked		Number in sample	Pockmarked	
			Number	Percent		Number	Percent		Number	Percent		Number	Percent		Number	Percent
Manco Kapac	60. 3	20	1	5	47	4	8. 5	46	10	21. 7	36	18	50	30	23	76. 6
Camacho	32. 5	252	4	1. 6	282	30	10. 6	344	81	23. 5	449	206	45. 9	310	173	55. 8
Omasuyos	31. 4	171	1	0. 6	245	17	6. 9	196	33	16. 8	218	81	37. 1	167	82	49. 1
Los Andes	30. 9	231	1	0. 4	300	8	2. 6	408	21	5. 1	363	89	24. 5	223	103	46. 1
Ingavi	12. 2	222	0	0	254	7	2. 7	401	24	5. 9	360	101	28	147	57	38. 7

climate revealed that only 37.6 percent of those vaccinated within the past 10 years were immune, and of those vaccinated 10–40 years previously, only 3 percent were immune. The low percentages cannot solely be attributed to a loss of immunity and lack of revaccination.

The prevalence of pockmarked persons by age groups and department gives an indication of the previous incidence of smallpox (table 1). It might be recalled that for every three pocked individuals there has been one death from smallpox with the assumption of a fatality rate of 25 percent.

The highest prevalence of pockmarked persons is in the La Paz Department, particularly among those over 40 years of age with 40.9 percent pockmarked. The greatest prevalence of pockmarked individuals in this department may be attributed to the cool dry climate and the relative density of the population and the means of communication, as compared with the remainder of Bolivia.

The correlation of smallpox with cool dry climate is supported by the seasonal peak observed in Bolivia during the dry winter months.

The percentages of pockmarked persons in five provinces of the La Paz Department along the shores of Lake Titicaca, quite identical in respect to topographic, climatic, socioeconomic, and racial factors, confirm the correlation between population density and the prevalence of pockmarked individuals (table 2).

It is interesting to note that immunity following smallpox, at least to vaccination, is not absolute. In a sample of 434 pockmarked persons over 10 years of age, only 56.5 percent displayed immune reactions. Nevertheless, a second attack in the same individual seems to be a rare occurrence, which is attributed to the longer duration of immunity to smallpox than to vaccination.

The assessment of the consequences of the disease must also include blindness. In Bolivia smallpox ranks as the principal cause of blindness, with more than one-third of the inmates of institutions for the blind dating their history of disability from an attack of smallpox.

The Campaign

Cochabamba, the central department of Bolivia, was the epicenter of an epidemic wave with 87 outbreaks of smallpox reported during 1957. Emergency efforts were undertaken during the latter half of that year. Simultaneously, preparations were made for a nationwide campaign. The preparations included a successful request for a budget of $125,000 and supporting legislation, importation of equipment and vaccine, development of methods, preparation of a plan of operations, and selection and training of personnel. The emergency efforts to combat the epidemic in Cochabamba, undertaken with personnel and equipment borrowed from other programs, provided a test for the methods and plan of operations.

Methods first developed and successfully applied in Iran were refined and reapplied in Bolivia (*2*). The campaign was conducted by the Servicio Cooperativo Interamericano de Salud Pública under the auspices of the Ministry of Public Health of Bolivia and the International Cooperation Administration of the United States.

We hoped that approximately 2.5 million of the estimated 3.3 million people of Bolivia in areas with incidence of smallpox or with relative density of population would be vaccinated during the attack phase of the campaign in 1958.

Personnel and Equipment

During the attack phase the smallpox vaccination service of the Servicio, full strength, consisted of 11 teams of vaccinators and supervisory and supportive personnel, a total of 83 persons. Each team of four vaccinators was headed by a team leader who was responsible for quantity and quality of the vaccinations, discipline of the vaccinators, and maintenance of equipment. A physician and two inspectors were assigned to direct and inspect the operations of each of the five teams. A director of the service, an administrative assistant, 17 drivers, and 3 boatmen completed the organization. In addition, the vaccination service had the full support of the administration, health education, and statistics divisions of SCISP, as well as substantial support from other agencies and the public.

Each vaccinator carried a portable vaccination kit which contained all necessary materials for vaccination house to house. The kit included disposable sterile pins, lyophilized vaccine, diluent (50 percent glycerine), and an indelible dye (10 percent silver nitrate).

The motorized teams, inspectors, and physicians were provided with four-wheel drive vehicles equipped with winches and loudspeakers. Three launches powered by 12-hp. outboard motors transported a fluvial team.

The teams were also supplied with portable battery-operated loudspeakers. The staff received two sets of uniforms and boots. Adequate campaign equipment and supplementary rations were issued.

Vaccination Techniques

Only lyophilized vaccine was used in the campaign. The vaccine was supplied by the Institut de Vaccine, Paris, and the Instituto Nacional de Salud Pública, Lima. At no time was the vaccine refrigerated. Some of the vaccine had been stored for as long as 1 year prior to use. Routinely, the potency of the vaccine was retested prior to issuance. The minimal standard for potency required confluency at 1:1,000 dilution with the method of Force and Leak; all lots from Lima and Paris produced confluency at greater dilutions.

The vaccine was reconstituted with a 50 percent solution of glycerine and distilled water by the team leader in the field. Any reconstituted vaccine remaining unused at the end of the day was discarded.

The vaccination procedure was simplified by eliminating the prior application of alcohol or other virucide and by using a sterile, disposable pin for each inoculation. A drop of vaccine was placed over the insertion of the deltoid of the left arm and a single scratch of about 5 mm. in length was made through the drop without drawing blood.

Using the single scratch, which provides visible evidence of vaccination, facilitated uniformity of technique. Consequently, standards could be maintained. The little finger of the vaccinee's left hand was dipped in indelible ink to expedite subsequent inspection of the quantity and quality of the vaccinations. No vaccination certificates were issued, and the vaccinators kept no records other than noting in an itinerary the number of vaccinations and the lot number of the vaccine.

Inspection

The inspectors followed the vaccinators, reading the takes on the ninth day and checking the work of a different vaccinator each day. With 1 inspector for every 8 to 12 vaccinators, the work of every man was reviewed at least once every 2 weeks. The samples inspected consisted of a sufficient number of households to obtain, whenever possible, a total of at least 100 individuals in each locality or subdivision covered by a vaccinator during 1 day. The inspectors recorded the name, age, evidence of previous smallpox, and previous and current

vaccination with type of take of each person in the samples.

The data of the vaccinators and inspectors were routinely tabulated to provide a variety of information including the number vaccinated by month, province, and vaccinator; average number vaccinated per man-day; percentage vaccinated in the campaign; percentage pockmarked by age group and province; percentage with prior vaccination; and percentage of primary takes by vaccinator and lot of vaccine. In addition, tables and maps were maintained for the cases and deaths reported.

Public Information

In the rural areas advance notification of the day of vaccination was given, and at that time the cooperation of the community leaders was obtained. Prior to and during the vaccinations loudspeakers were employed to arouse and inform the public. Possibly of greatest importance was the personal contact of the vaccinator with the individual at the time of vaccination. Everyone vaccinated was considered a potential health educator who could inform family, friends, and neighbors of the harmless but important procedure.

Additional means of informing the public in urban areas included newspapers, radio, pamphlets, and posters. In epidemic situations in two of the largest cities the public cooperated with a more or less spontaneous boycott of those not vaccinated. When the majority of the population had been vaccinated, permission was obtained from the officials of certain public facilities to announce that no one unvaccinated would receive service, effective the following week. Immediately, bus drivers, elevator operators, and most everyone who had taken the trouble to get vaccinated spontaneously supported the boycott. Instead of creating bad feelings, it led to a new form of salute, the raised little finger. The epidemics were abruptly terminated.

Operations

The operations of the vaccination campaign were outlined in specific intineraries for the vaccinators covering periods of about 25 days, including Sundays and holidays, and followed by commensurate days of compensatory leave when preparations were made for the next itinerary. The vaccinators received individual assignments of specific areas to facilitate the evaluation of the quantity and quality of work. To maintain discipline and aid morale, whenever possible the teams of four vaccinators were given assignments sufficiently close together to permit them to share eating facilities and billeting.

Vaccinations were performed house to house and, when appropriate, were followed by a vaccination session at a temporary center for those who had been missed in the house-to-house vaccinations. Everyone was vaccinated, regardless of age, sex, or previous history of vaccination and smallpox. Those less than 4 weeks old, the acutely ill, and those with eczema were the only exceptions.

The teams proceeded along the main or secondary roads and the rivers and their branches, reaching on foot population concentrations up to 20 kilometers distant from road or river. In instances of reported outbreaks, the teams rented mules and traveled up to 100 kilometers distance from the roads.

Evaluation and Results

With the vaccination of 2,432,186 persons, about three-fourths of the estimated population of Bolivia, the attack phase of the campaign was completed on schedule by the end of 1958.

In the target areas samples totaling 42,075, widely distributed in time and place, showed 91 percent of the population had been vaccinated. The high percentage vaccinated is attributed to the house-to-house visits, followed by a vaccination session at a temporary center, and the use of loudspeakers to attract the people.

The inspection of primary vaccinations of 3,662 infants in samples, widely distributed in time and place, yielded 96.3 percent primary takes.

An average of 210 vaccinations were performed per man-day, excluding the performance in major cities from the calculation. This high average is attributed to advance planning of itineraries, simplicity of the vaccination technique, and paucity of recording required of the vaccinator, permitting exclusive

dedication to vaccination. The indelible dye not only saved time but provided a more reliable record for inspection purposes than histories or vaccination certificates.

As a result of the high average of vaccinations per man-day, the costs of the campaign, including personnel, vehicle, equipment, vaccine, and all other expenses, were held to 5 cents per vaccination.

The dramatic reduction in reports of smallpox best illustrates the results of the attack phase. In 1957 Bolivia suffered the highest attack rate for smallpox in the Americas. By the end of 1958 Bolivia enjoyed one of the highest levels of immunity and experienced an apparent cessation of transmission (table 3). Since November 1958, no smallpox has been reported in the Weekly Epidemiological Reports of the Pan American Sanitary Bureau.

The efficiency of the methods and the efficacy of the lyophilized vaccine are confirmed.

Consolidation and Followup

During the consolidation phase, to be completed by four mobile teams in 1959, vaccinations will be extended to those in sparsely populated and rather inaccessible areas not reached during the attack phase.

With the completion of this phase the Servicio will have discharged the mandate of the bilateral project agreement. Unless the agreement is amended and extended, maintenance of vigilance and a high level of immunity will be a function of the Ministry of Public Health.

Now that smallpox is no longer endemic in Bolivia the occurrence of a single case must be considered as an emergency and treated accordingly. The prevention of rapid recurrence of widespread infection will require the maintenance of a complete and efficient system of defense including a network of centers and mobile teams for vaccination and revaccination, early recognition of any residual focus and imported cases, reporting, laboratory confirmation, casefinding, and contact and ring vaccination in remote rural as well as urban areas. Arrangements for the continued importation or the national production and testing of lyophilized vaccine will also be necessary.

The high level of vigilance and immunity will have to be maintained even after the completion of campaigns in other South American nations removes the source of this disease from the American Hemisphere until global eradication is achieved.

Global Eradication

Abrupt elimination of one of the principal foci in the American Hemisphere by a mass campaign in the face of a unique combination of factors adverse to control through routine services illustrates the feasibility of smallpox eradication by a systematic attack on the sources of the disease.

The campaign in Bolivia, assisted by the International Cooperation Administration, formed an integral part of a hemispheric campaign. In 1950 the governing bodies of the Pan American Sanitary Organization recommended that the member governments undertake systematic programs of smallpox vaccination and revaccination in their respective territories with the aim of eliminating the disease from all parts of the Western Hemisphere. The Pan American Sanitary Bureau drew up a program designed to stimulate the efforts of the Americas (*3*).

Table 3. Cases of smallpox reported by the Ministry of Public Health, Bolivia, to the Pan American Sanitary Bureau, by 4-week periods, 1955–59

Year	Total	4-week periods												
		1st	2d	3d	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th
1955	356	15	7	58	38	35	16	36	8	16	30	42	17	38
1956	417	29	11	7	22	38	28	41	77	38	23	43	49	11
1957	1,310	36	31	38	56	94	276	189	141	148	106	121	53	21
1958	183	14	16	11	4	13	11	27	45	32	8	1	1	0
1959	-------	0	0	0	0	0	0	0	------	------	------	------	------	------

Smallpox has been eliminated from North and Central America. In 1958 smallpox eradication programs, assisted by the Pan American Sanitary Bureau, were being undertaken in eight American countries. Intensification of efforts in three countries with residual foci would rapidly eliminate smallpox from the Western Hemisphere.

Endemic smallpox has been banished from Europe, U.S.S.R., Australia, and certain areas of Africa. However, the Eastern Hemisphere still contains major endemic foci. Asian countries provide about four-fifths of the smallpox cases reported worldwide and a major proportion of exportations of smallpox to other countries (*4*). The African Continent contains the second most important focus.

The establishment of the priority for smallpox control and, likewise for eradication, involves consideration of the relative importance of the disease in the light of mortality, morbidity, and sequelae, and cannot be limited to the magnitude of the problem remaining, with existing control efforts being taken for granted. Rather, future as well as current action is justified by the potential of smallpox in the hypothetical absence of existing control efforts.

Smallpox is one of the most contagious diseases. There is no specific treatment. Prior to the advent of vaccination, susceptibility was universal, and almost all persons were attacked. Those who recovered from the disease were disfigured, if not blind. Fatal in one in every three or four cases, smallpox depopulated cities and nations. During an epidemic in Iceland in 1707 smallpox killed 36 percent of the total population in 1 year.

Despite the prevailing policies of control, smallpox is still only too prevalent in many areas of the globe. With reporting very incomplete, an annual average of 178,000 cases was notified to WHO in the 5 years 1951–55 (*4*). This situation requires either an extension of complex and continuing systems of control to all areas of the globe or short-term campaigns so placed and timed as to lead to the worldwide eradication of smallpox.

A policy of eradication is favored by the relative amenability of smallpox to eradication. From the point of view of the individual, vaccination is a specific and reliable protection against smallpox, involving minimal inconvenience. From the point of view of health authorities, no other preventive measure can be extended with such ease, economy, and effect.

Vaccination is unquestionably the most effective of all preventive procedures, having been credited with saving as many lives as all the rest of preventive and curative medicine since Jenner's discovery in the 18th century (*5*). Now that lyophilized vaccine exists, only the ultimate utility of a thermostabile vaccine remains to be exploited. Full utilization of the vaccine would break the chain of infectious cases on which the smallpox virus depends for its continued existence, carrying disease prevention to a logical conclusion—eradication. Thus smallpox is an anachronism. Thomas Jefferson, an early active supporter of vaccination, wrote to Jenner in 1806, "future nations will know by history only, that the loathsome smallpox has existed."

There is a growing awareness of the national obligation to eliminate endemic smallpox in recognition of the right of other countries to be protected against the reinfection of areas freed of smallpox. Thus the intensified national efforts represent contributions to international health. If it is accepted that the whole world benefits from national campaigns which are an integral part of worldwide eradication of smallpox and that the costs of the campaigns exceed by far the costs of technical assistance, then the more prosperous countries, already freed of smallpox, cannot expect to share the benefits without sharing the cost of the national operations. The alternative is for the countries with endemic smallpox, large populations, and little surplus for investment to assume the major financial burden of eradication.

Mass vaccinations probably can be limited to the endemic foci. Costs, globally distributed, should not be a major obstacle when total costs of vaccination by mobile teams in sparsely populated areas are in the order of 5 cents per capita.

The Eleventh World Health Assembly noted that the funds devoted to smallpox control and vaccination throughout the world exceed those necessary to eradicate sources of the infection. Moreover, eradication represents a capital investment that makes the recurrent costs of con-

trol redundant. The Assembly recommended to all governments that the population be vaccinated where principal endemic foci exist and subsequently where the disease persists. The Assembly also recommended that all countries in which smallpox vaccination is compulsory continue to give smallpox vaccinations during the eradication of this disease throughout the world.

At the Twelfth World Health Assembly in May 1959 the arguments in favor of smallpox eradication were reiterated, and the urgency of worldwide eradication was emphasized. It remains for the governments to initiate timely cooperative action.

REFERENCES

(*1*) Pan American Sanitary Bureau: Summary of 4-year reports on health conditions in the Americas. Scientific Publication No. 40. Washington, D.C., June 1958.

(*2*) Frederiksen, H., and Sheehy, J. P.: Smallpox control by mass vaccination with dried vaccine. Pub. Health Rep. 72: 163–172, February 1957.

(*3*) Pan American Sanitary Bureau: Quadrennial report of the Director, January 1954–December 1957, and 1957 annual report. Washington, D.C., May 1958.

(*4*) World Health Organization: The first ten years of the World Health Organization. Geneva, 1958.

(*5*) Ingraham, H. S.: Statistics and medical knowledge. Am. J. Pub. Health 48: 1449–1459, November 1958.

H. Trendley Dean Retires

Dr. H. Trendley Dean retired July 19, 1959, as secretary of the Council on Dental Research of the American Dental Association.

His pioneer research and continuing study on the effects of adding fluoride to city water supplies established Dr. Dean as an international authority.

One measure of his contribution is that a population of 35.6 million persons in 1,800 cities throughout the United States use public water supplies to which fluoride has been added to inhibit dental caries.

Before joining the association in 1953, Dr. Dean was associated for more than 30 years with the Public Health Service.

Dr. Dean's research into fluoridation dates back to the 1930's. During a study of mottling of teeth in communities where there was a high concentration of fluorides in the water, Dr. Dean and his associates observed also that the tooth enamel was unusually well preserved.

This observation led to a long-term study to determine the level that would avoid staining of the enamel and still check tooth decay.

In 1942, following a study of 21 cities in which more than 7,000 children were examined, Dr. Dean and his fellow scientists concluded that: "Where the fluoride level is about one part per million, there are about 60 percent fewer decayed teeth than in nonfluoride areas."

In 1945, Grand Rapids, Mich., became the first city to add fluorides to its water supply. The measure has been employed since then in communities in Brazil, Chile, Colombia, England, Germany, Holland, Japan, Sweden, and elsewhere.

Dr. Dean expects to continue his efforts in support of fluoridation. He feels more strongly than ever that: "The time is past when fluoridation could be considered a 'progressive' step. It is an integral and routine part of any complete public health program. Cities thus far which have failed to adopt the measure are simply failing in their responsibility to the public."