A vaccination campaign in Iran demonstrates the feasibility of smallpox eradication in foci with adverse climatic, topographic, and socioeconomic conditions. In these rugged conditions, mobile teams administered dried vaccine to the population along travel routes. The techniques can be integrated with malaria eradication work.

Smallpox Control by Mass Vaccination With Dried Vaccine

By HARALD FREDERIKSEN, M.D., M.P.H., D.T.M.& H.
and JAMES P. SHEEHY, B.C.E. in S.E.

A SMALLPOX VACCINATION campaign testing the efficacy of selective mass vaccination with dried vaccine has been under way in Isfahan Province in Iran since June 1955. At that time, Isfahan was confronted by a wave of smallpox epidemics which had arisen in the northwestern provinces and was spreading southward and eastward along the major travel routes (fig. 1). It seemed that without extraordinary preventive measures massive invasion of Isfahan was only a matter of time.

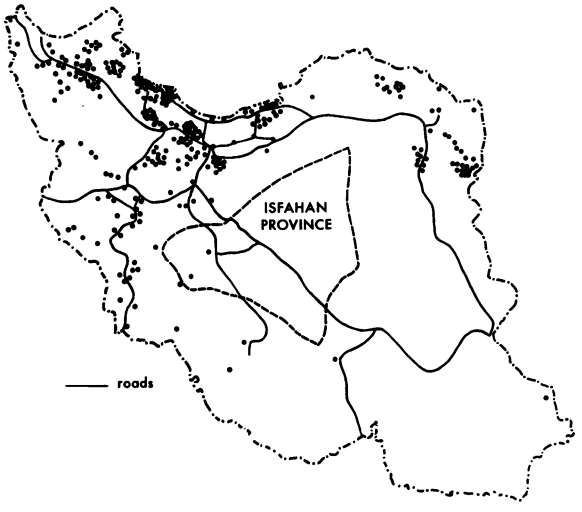
Dr. Frederiksen, a Public Health Service officer, was assigned to the United States Operations Mission to Iran, International Cooperation Administration, Department of State, from April 1954 through June 1956. He was, in succession, co-director of the Public Health Cooperative Organization in Azerbaijan Province, co-director of the Public Health Cooperative Organization in Isfahan Province, and deputy chief of the health division of the United States mission. He is now assigned to the United States Operations Mission to Bolivia as chief of the health and sanitation division. Mr. Sheehy, also a Public Health Service officer, was assigned to the United States Operations Mission to Iran from February 1954 through May 1956. He was acting co-director of the Public Health Cooperative Organization in Isfahan Province.

Prevention of smallpox in Isfahan is beset with many difficulties. The population is dispersed over 90,000 square miles. Of an estimated 1,300,000 population, about 750,000 live in some 2,000 villages, 350,000 in 10 urban centers, and 200,000 in migrating tribes. The eastern two-thirds of the province is largely desert, with small villages along the roads, trails, and caravan routes. The western third is traversed by the Zagros Mountains, impenetrable to vehicles in the winter and difficult of access at any time of the year. The villages in the more habitable areas are served by unsurfaced roads and trails.

Vaccination of infants and revaccination of school children and military conscripts is compulsory in Iran, but shortage of medical facilities and personnel and other factors combine to reduce the effectiveness of the law. Iran has only about 1 physician for every 10,000 persons, and most of the physicians are in the larger cities. More than 40,000 villages, comprising most of the country's 20 million population, are without permanent medical facilities or personnel. The nomadic tribes have never been reached by medical or public health programs.

In past years, the Ministry of Health of Iran has conducted the vaccination program, using itinerant or stationary vaccinators and glycer-

Figure 1. Smallpox epidemics in Iran, January–December 1955.



inated vaccine. Such limitations as lack of public understanding of the disease, inadequate reporting of cases, lack of isolation facilities for patients, improperly qualified and supervised vaccinators, and inadequate transportation and refrigeration facilities explain the persistence of endemic and epidemic smallpox.

When the routine vaccinations failed to check the occurrence and spread of smallpox in 1955, an anti-epidemic program was undertaken by the Public Health Cooperative Organization (a department of the Iranian Ministry of Health established with the cooperation of the United States Technical Cooperation Mission to Iran in 1953). When an epidemic was reported, the PHCO dispatched teams to vaccinate the people of the infected villages or cities and of the neighboring villages. During 1955, 3 million persons were vaccinated in the epidemic areas, but because of incomplete or delayed reporting of the outbreaks, the anti-epidemic measures were usually too late to prevent further spread of the disease.

In view of these circumstances, the PHCO decided to undertake systematic mass vaccinations in Isfahan Province, where as yet no smallpox epidemics had been reported. The campaign was designed to test the efficacy of dried vaccine under adverse field conditions and to evaluate the degree of protection afforded by mass vaccination of selected population groups. The groups were selected because of their population density, their location with reference to potential exposure, or their high mobility.

Plan of the Campaign

The first step in the mass campaign was to seal the travel routes to the spread of smallpox (fig. 2). During the summer and fall of 1955, people in all villages within about 10 kilometers of the roads and trails were vaccinated with dried vaccine. During the winter of 1955-56, the provincial capital and the nine municipalities were protected by mass vaccination with glycerinated vaccine. Glycerinated vaccine was used in the cities because of the limited supply of dried vaccine.

The second step was to prevent infection among the Bakhtiari tribes returning from their winter quarters in Khuzistan Province in the southwest to their summer quarters in Isfahan. During May and June 1956, more than 100,000 tribal people were vaccinated with dried vaccine as they moved through the mountain passes into Isfahan. Not only has a desired service been provided the tribes, but the spread of smallpox from Khuzistan with the mass migration has been prevented.

Figure 2. Villages and cities vaccinated in Isfahan Province, June 1955–June 1956.

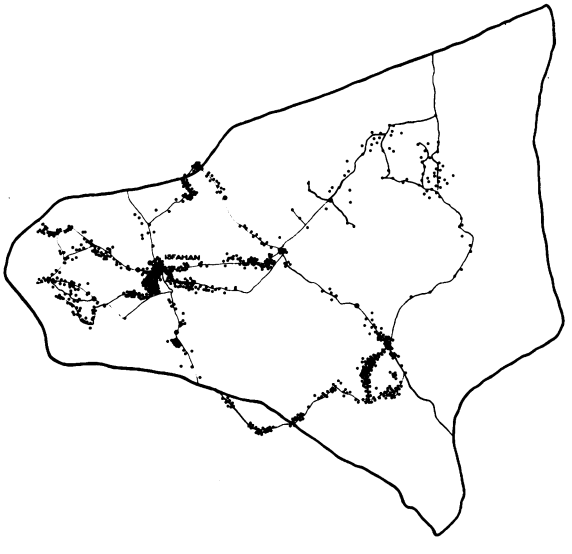
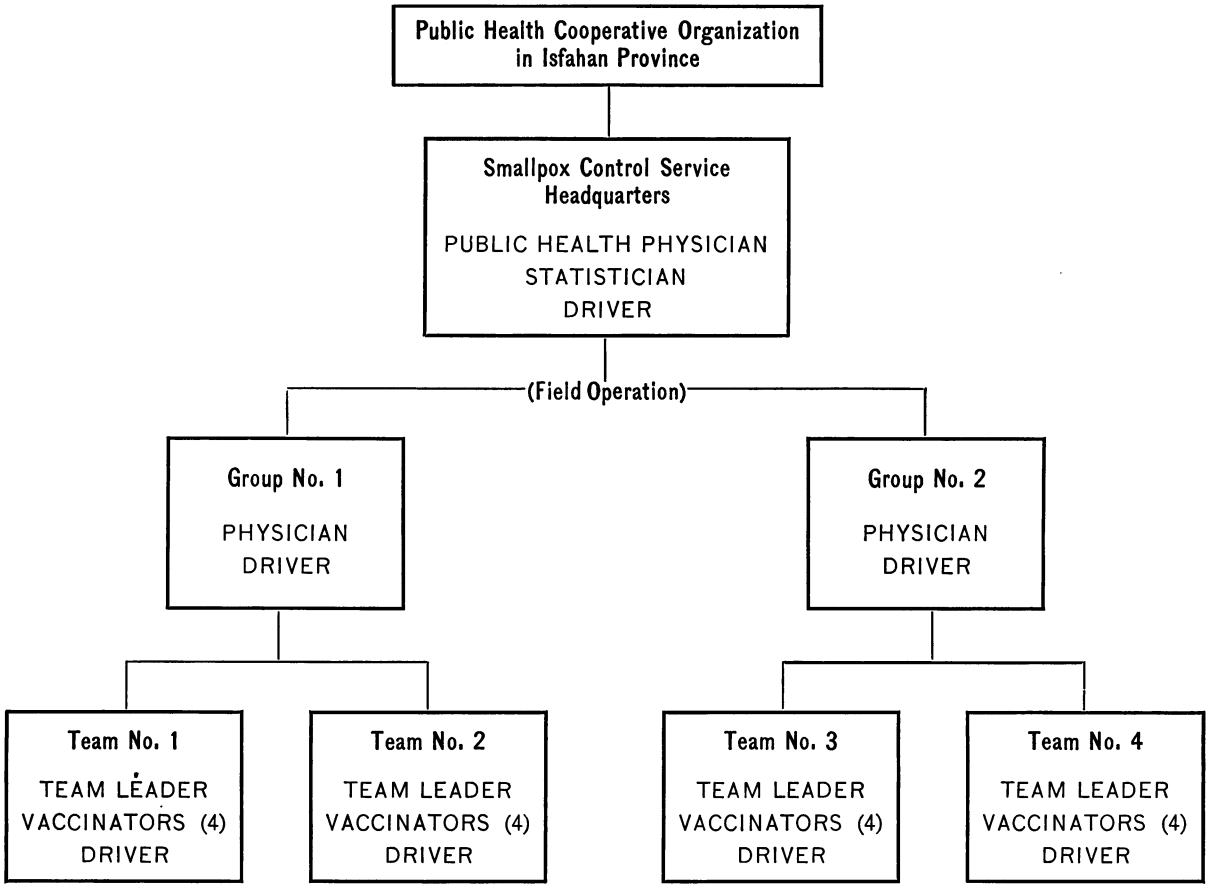


Figure 3. Organization of smallpox control service in Isfahan Province, Iran.



With these measures, we believe smallpox will be little if any threat to Isfahan in the near future. The isolated and rather inaccessible villages not reached by the campaign will be kept under surveillance.

Smallpox Control Service

For the campaign, a smallpox control service was established within the Isfahan office of the PHCO. A physician was placed in charge of all administrative and technical aspects of the program. He was assisted by a clerk in tabulation of technical data, preparation of maps, and administrative routine. So that he could make frequent unannounced inspections of the field operations, the physician was provided with a jeep and driver.

In June 1955, control operations were initiated with a pilot campaign of 1 month's duration for the development of methods and training of supervisory personnel. During the pilot phase, a second physician was added to the staff to supervise the field team of four vaccinators and to inspect vaccination reactions in sample villages. The four vaccinators were formerly sanitary aides of the PHCO. After 4 weeks as vaccinators, they had demonstrated the ability to perform an adequate quantity and quality of vaccinations and were appointed supervisors of 4 teams of 4 vaccinators each. The 16 new vaccinators, formerly leaders of malaria spray teams, received theoretical and field training for 2 weeks.

The four vaccination teams were dispatched into the field about the end of July. Once the campaign was in full swing, 2 physicians were assigned to the inspection of vaccination reactions in sample villages, 1 physician to 2 teams (fig. 3).

Table 1. Reactions to glycerinated vaccine in Tabriz, Iran, 1954

Years since previous vaccination	Total	Primary reaction		Accelerated reaction		Immune reaction		No reaction	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
More than 10	91	31	34. 0	30	32. 9	28	30. 7	2	2. 2
Less than 10	453	73	16. 1	214	47. 2	161	35. 5	5	1. 1

The Village Schedule

The physician in charge of the campaign outlined on a map the work schedule for each vaccination team. The day before a team was to vaccinate, the team leader went to the designated villages and arranged for suitable centers for the vaccinations. He also announced that vaccinations would be given the next day.

When the team arrived in a village, the team leader announced by loudspeaker that vaccinations were being given and urged the people to come. "Smallpox either kills, blinds, or disfigures, attacking young and old," he explained. "Vaccinations should be repeated; an effective vaccine is being used. Everyone should come for vaccination and should wash the left upper arm beforehand." He also supervised the mixing of the vaccine and the vaccinations, seeing that the prescribed techniques were followed. To protect the vaccine from the heat, vaccinations were done only in the early morning, 7 to 11 a. m., and in the late afternoon, 3 to 7 p. m. These hours also gave persons working in the fields an opportunity to be vaccinated.

The teams remained in the field for about 2 weeks and then returned to headquarters for 2 or 3 days of briefing and reporting. At headquarters, the vehicles received maintenance, and the teams obtained new supplies.

Each team was carried by a jeep personnel cargo carrier equipped with four-wheel drive and a battery-operated loudspeaker. The vehicles were modified to carry the team leader and the four vaccinators in addition to the driver and equipment. Supplies included folding work tables and chairs, cots, blankets, tents, and kerosene lamps, as well as vaccination kits.

Selection of the Vaccine

Earlier experiences in Azerbaijan Province with glycerinated vaccine had suggested the use of dried vaccine in the rural areas of Isfahan. In a mass campaign in the city of Tabriz, glycerinated vaccine, produced by the Pasteur Institute in Teheran and applied by vaccinators of the PHCO, had given takes comparable to the takes obtained with this type of vaccine at the induction centers of the United States Armed Forces in 1951 (tables 1 and 2). However, in the rural areas of the province, where the vaccine could not be kept under refrigeration, glycerinated vaccine had proved unsatisfactory. This is illustrated by events in Andab village. In the spring of 1955, the people of this village were vaccinated with glycerinated vaccine by an itinerant vaccinator. An epidemic of smallpox in the following

Table 2. Reactions to glycerinated vaccine at induction centers of the United States Armed Forces, 1951

Years since previous vaccination	Total	Primary reaction		Accelerated reaction		Immune reaction	
		Number	Percent	Number	Percent	Number	Percent
More than 10	1, 297	163	12. 6	727	56. 0	407	31. 4
Less than 10	760	76	10. 0	343	45. 1	341	44. 9

SOURCE: Liao, S. J.: Responses to smallpox vaccination in military recruits. Pub. Health Rep. 70 : 723–728, August 1955.

Nomadic tribes stop at the vaccination post at Dopolan Pass in southwestern Iran.

months affected equally those never vaccinated and those recently vaccinated (table 3).

As illustrated by the following reports, dried vaccine has a long and favorable history; yet it has been systematically produced and used on a large scale only in one country, Indonesia. Why it has not been applied widely throughout the tropics is difficult to understand.

In 1927, Otten reported that dried vaccine maintained under vacuum retains its potency at 36° C. for months and at the usual temperatures of the tropics for years (*1*). In a later study, by comparing the takes of 16,000 infants vaccinated on the left arm with dried vaccine and on the right arm with glycerinated vaccine, Otten found that the local reactions of the two vaccines did not differ in any respect (*2*).

More recently, Hornibrook and Gebhard reported that smallpox vaccine can be dried with only slight loss of potency (*3*). Simple equipment can be used in the drying process.

In 1955, L. H. Collier reported a study of the preservative influence of suspending media on purified vaccinia virus (*4*). None was effective in the liquid state, but all protected the virus against the lethal influence of freeze drying. Virus dried in 5 percent peptone still gave a full quota of successful primary reactions after storage for 12 months at 22° C. or for 4 months at 37° C. Using partially purified sheep virus dried in 5 percent peptone, Collier produced a vaccine which showed a high degree of resistance to heat, was relatively free from bacterial contamination, and was easy to reconstitute after prolonged storage.

Earlier W. A. Collier had declared that dried vaccine can be produced in practically unlimited quantities at no greater cost than that of glycerinated vaccine for the mass vaccination of populations in tropical areas (*5*). He pointed out that prolonged storage without loss of potency obviates the need constantly to replace lots of vaccine, as is necessary with glyc-

Table 3. Smallpox incidence, mortality, and case fatality, among children under 7 years of age in the village of Andab, Iran, during an epidemic in 1955

Vaccination status	Population	Number cases	Number deaths	Incidence (percent)	Mortality (percent)	Case fatality (percent)
Vaccinated [1]	18	9	1	50.0	5.5	11.1
Never vaccinated	33	14	3	42.4	9.1	21.4
Total	51	23	4	45.1	7.8	17.4

[1] Vaccinated shortly before the epidemic by itinerant vaccinators using glycerinated vaccine without refrigeration.

erinated vaccine. In 1949, the Pasteur Institute of Bandoeng, Indonesia, prepared 26 million doses of dried vaccine for the vaccination program in Indonesia.

In 1955, Baltazard, at the Pasteur Institute in Teheran, had freeze-dried calf lymph for experimental purposes. This type of dried vaccine is easily and safely reconstituted by inserting a double needle first into a vial containing glycerine and then into the vial of vaccine containing about 100 doses under vacuum. We decided to give it a trial in the rural areas of Isfahan. Confirmation of its effectiveness would permit extension of the vaccination campaign to the rest of the country.

Vaccination Techniques

The dried vaccine was stored in a refrigerator until issued to the field team, which received a 2 weeks' supply. In the field the vaccine was kept without refrigeration. It was not mixed with glycerine until immediately before vaccination, and then only one vial at a time. Mixing was done indoors, and, once reconstituted, the vaccine was not removed from the room or shelter. The vial of reconstituted vaccine was placed in a fitted cloth sack which was wetted to reduce the temperature through evaporation. Any reconstituted vaccine not used in the morning was discarded, and a new vial was reconstituted in the afternoon.

Vaccinations, either with dried or glycerinated vaccine, were performed on the left upper arm at the insertion of the deltoid muscle, with a vaccinostyle. A single scratch about 4 mm. in length was made through the drop of vaccine without drawing blood. After each vaccination, the style was sterilized in the blue portion of a flame and allowed to cool. Another style was used for the next patient. For the vaccination of the nomadic tribes, disposable straight pins were used instead of vaccinostyles.

Persons with eczema or any febrile illness were not vaccinated. The patients were told not to place a bandage over the site of a vaccination.

To facilitate inspection of the vaccination, the tip of the little finger of the left hand of

Table 4. Reactions to dried vaccine among 1,094 people in 20 villages of Isfahan Province, Iran, 1955

Years since previous vaccination	Total	Primary reaction		Accelerated reaction		Immune or no reaction [1]	
		Number	Percent	Number	Percent	Number	Percent
More than 10	423	95	22.5	187	44.2	141	33.3
Less than 10	671	81	12.1	293	43.7	297	44.2

[1] No reaction on day of inspection, usually the 8th or 9th day after vaccination.

A Bakhtiari child is vaccinated with dried vaccine. In the tribal vaccinations, a disposable pin was used to make the scratch.

each person vaccinated was marked with an indelible dye.

Efficacy of the Vaccine

In a mass campaign under field conditions, it is impractical to inspect the vaccination reaction more than once. A reading on the ninth day permits the differentiation of primary and accelerated reactions, which suffices for the evaluation of the vaccine. No emphasis need be placed on the differentiation of immune reactions and no reactions, either of which may be the result of deteriorated vaccine.

The reactions among members of sample households in sample villages were inspected by a physician usually the eighth or ninth day after vaccination. The age, sex, and history of smallpox and of previous vaccination for all members of the household were recorded, along with the size and type of reaction of those currently vaccinated.

To evaluate the efficacy of the dried vaccine, the reactions of 1,094 individuals with previous vaccination in 20 consecutive villages along the major north-south road of Isfahan were analyzed. The results, shown in table 4, compare favorably with the results obtained with glycerinated vaccine in Tabriz (table 1) and at the induction centers of the United States Armed Forces (table 2). Whereas glycerinated vaccine used under field conditions without refrigeration apparently failed to provide protection from smallpox (table 3), the dried vaccine used under such conditions gave satisfactory results.

Data from these villages also provided an estimate of the prevalence of smallpox in past years. Of 1,520 individuals in the sample households, 12.5 percent displayed the typical scars of smallpox, and almost all of these gave a history of the disease sometime during childhood. Although these individuals usually could not state either the exact year of birth or of the smallpox attack, tabulation by estimated age suggests a decline in the incidence of smallpox over the past years (table 5).

Table 5. Number and percentage of persons with smallpox scars in 20 villages of Isfahan Province, Iran, 1955

Age group	Number examined	Number scarred	Percent scarred
0–9	726	2	0.3
10–19	293	10	3.4
20–29	172	27	15.7
30–39	160	64	40.0
40–49	66	35	53.0
50 and over	85	50	58.8
Total	1,502	188	12.5

At the time of the mass campaign, the level of immunity in these villages was inadequate to prevent smallpox epidemics. In addition to the 12.5 percent who had had smallpox, 72.8 percent had previously been vaccinated but had not had smallpox, and 14.6 percent had had neither a previous vaccination nor smallpox. Sixty percent of those who had previously been vaccinated and 42 percent of those who had had smallpox had primary or accelerated reactions.

Evaluation of the Campaign

By the end of June 1956, more than 750,000 people in Isfahan had been vaccinated in the mass campaign (fig. 2). Those vaccinated included 270,354 in the provincial capital and the 9 municipalities (about 75 percent of the urban population), more than 380,000 villagers (about 50 percent of the rural population), and about 100,000 tribesmen, the latter virtually all for the first time. An average of about 250 vaccinations were done per man-day.

The campaign reached 797 villages located near roads or trails and accessible by motor vehicle. In about half of these (359), 76 to 100 percent of the population were vaccinated on one visit of the team. In 223 villages, 51 to 75 percent were vaccinated on one visit; in 150 villages, 26 to 50 percent; and in 65 villages, 25 percent or less. The villages in which 25 percent or less were vaccinated on the first visit were visited a second time. Invariably, the villagers were more receptive on the second visit.

The number of villages in the province is unknown, but it has been estimated to be as high as 2,000. Some of these, however, comprise only a few households and others only abandoned huts. We believe that most of the villages not reached by the campaign are of little significance to the potential spread of smallpox because of their isolation.

The mass vaccination of the capital of Isfahan, with a population of about 200,000, was accomplished without the threat of a single case of smallpox in the city. Posters, films, newspaper articles, loudspeaker announcements, and leaflets dropped from the air were effective in stimulating participation. In a sample of 12,770 persons, 72 percent were vaccinated during a 3-week period. Tabulation of these individuals by age showed that 80 percent of those under 15 years, the most susceptible group, were vaccinated.

The centrifugal distribution of smallpox epidemics in Iran during the 20 months from January 1955 through August 1956 suggests that the mass campaign in Isfahan was successful in protecting the province (figs. 1 and 4). During 1955, Isfahan had only two isolated outbreaks, both preceding vaccination in those areas. The first occurred in a village of the mountainous southwest as a result of the practice of variolation with smallpox. A team of vaccinators was immediately dispatched to this village. The second outbreak occurred in the municipality of Sedeh. A sample of 1,018 individuals in that city indicated that 95 percent of the 30,000 population was subsequently vaccinated. Both outbreaks were abruptly terminated, and the infection did not spread to any other areas of the province. During the first 8 months of 1956, the only outbreak in Isfahan occurred in a nomadic tribe that had

been infected in a neighboring province. On arrival in Isfahan, the entire tribe was vaccinated, and only one case of smallpox developed after vaccination. In this case, the disease was apparently in incubation when the vaccination was done.

In the surrounding provinces, 297 epidemics were reported during 1955, and 198 were reported during the first 8 months of 1956 despite extensive peri-epidemic vaccinations with glycerinated vaccine.

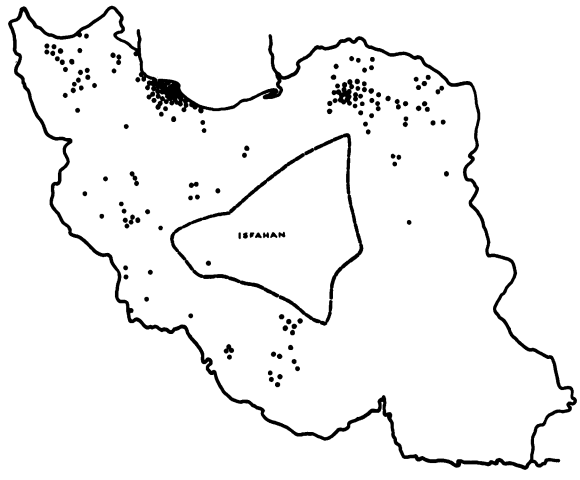
Comparison of the distribution of smallpox in 1955 with that in 1956 shows the gradual encirclement of Isfahan Province. The pincer movement of the epidemics, which arose in the northwestern province, is now threatening to close in on the southeastern province. The absence of smallpox epidemics in the southeastern province up to this time, if not the result of poor reporting, might well be attributed, at least in part, to the barriers provided by the mass vaccinations in Isfahan.

An estimate of the cost of the campaign in the rural areas is based on operations during August 1955, the month of peak activity. Operational costs for this month totaled $3,030 and 126,229 villagers were vaccinated, an average of 2.4 cents per person. This sum covered salaries, per diem payments, expendable supplies, and maintenance and operation of vehicles, but not the depreciation of vehicles or the cost of the vaccine.

Integration with Malaria Control

In the summer of 1955, the mass campaign techniques applied in the province of Isfahan were modified to permit smallpox control to be combined with malaria control in the province of Azerbaijan. One vaccinator was assigned to each malaria spray team. The malaria control organization provided lines of communication and supply and supervision and transportation for the vaccinators, with consequent reductions in operational costs to about 2 cents per person. Each sprayman served as health educator for smallpox control while he was spraying a house. As far as possible, the organization and techniques developed in the campaign in Isfahan were retained, in particular the use of dried vaccine and personnel

Figure 4. Smallpox epidemics in Iran, January–August 1956.



of the PHCO, the method of vaccination, and the system of inspection of reactions.

There were 30 spray teams in the field in Azerbaijan, but a shortage of dried vaccine limited the number of vaccinators to about 15. During a period of 3 months, more than 220,000 inhabitants of 1,745 villages, with a total population of about 500,000, were vaccinated.

On the basis of this experience, we conclude that smallpox control can be effectively and economically associated with malaria control without sacrificing efficiency in either program. The association stimulated the receptiveness of the villagers toward both programs.

It is expected that in a combined smallpox-malaria program, the percentage of population protected from smallpox can be increased, with further reductions in per capita cost of vaccination. Now that an adequate supply of dried vaccine is assured, the mass vaccinations can be extended to the critical proportion of the rural inhabitants of Azerbaijan. Since spray operations are repeated each year for 4 to 5 years, there are repeated opportunities for vaccination.

The National Program

The Minister of Health of Iran has appointed a commission to study the problem of smallpox and to formulate a national control program. With the Isfahan campaign an apparent success, it has been decided to extend the techniques

nationwide. Similar smallpox control services are being established in all provinces, within the PHCO. Priority will be given to the mass vaccination of cities and villages along the network of major travel routes. Where feasible, the vaccination teams will be integrated with the malaria control teams. The Pasteur Institute of Teheran will produce dried vaccine in amounts sufficient for mass vaccination in rural areas. The Government of Iran (Plan Organization) has allocated vehicles and funds.

Iran hopes that this program will encourage its neighbors to participate in a collective effort to eradicate endemic smallpox from the Near East. The Pasteur Institute could provide dried vaccine for other countries at cost.

Summary

1. Dried vaccine used without refrigeration under adverse climatic and topographic conditions proved to be a satisfactory immunizing agent in Isfahan, Iran. The percentages and types of reactions in a sample of 1,094 individuals were comparable to those obtained with glycerinated vaccine kept under refrigeration.

2. The protection of Isfahan, the central province of Iran, from invasion by the smallpox epidemics occurring in surrounding provinces supports the concept of smallpox control by mass vaccination of population groups selected because of their density, mobility, or potential exposure.

3. The mass campaign techniques developed in Isfahan were modified to permit integration of mass vaccination with malaria spray operations in Azerbaijan. The results suggest the feasibility of integrating mass vaccination campaigns with malaria control work for the simultaneous eradication of both diseases.

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Environment and Venereal Disease

Venereal disease is unique among the communicable infections in that it is not wholly a clinical problem. Its roots lie in the socially unacceptable environment, in social maladjustment. The venereal disease control program deals with the dilemma that is apparent, that is, the presence of a venereal disease. Our services are specific; we treat the infected individual and try to give him enough information so that he will not become reinfected or, if he does, that he will know what to do about it. However, we only skirt the edges when we look at the clinical aspects of the disease, and do not deal with the deeper social causes or remote origin of the person's present difficulties.

—C. A. SMITH, M.D., *chief of the Venereal Disease Program, Public Health Service, addressing the 1956 meeting of the Cincinnati Social Hygiene Society.*