ANTIPOLIOMYELITIS PROGRAM IN BRAZIL: A SEROLOGIC STUDY OF IMMUNITY LEVELS[1]

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In connection with plans for a major drive against poliomyelitis, Brazil conducted a pilot survey of vaccination trials in Espirito Santo in 1971. This article reports the results of that survey and recommends the establishment of a nationwide surveillance system to monitor the effects of vaccination campaigns.

Poliomyelitis in Brazil, previously limited for practical purposes to major urban centers, has substantially extended its area of incidence in recent years, causing repeated outbreaks in many places (see Table 1).

Infants and young children between 3 months and 4 years old constitute the age group most susceptible to this disease. The virus most frequently involved is type I poliovirus, according to studies made in the states of Guanabara and Pará, and in the Federal District.

Along with other important factors, the availability of preventive techniques that have been proven safe, effective, low in cost, easy to administer, and suitable for mass application has led the Brazilian Government to undertake a national vaccination program for the control of poliomyelitis.

The aim of the program is to vaccinate 85 per cent of those in the 3-month to 4-year age group over a period of two years. Available demographic data indicates that countrywide the number of infants and children to be vaccinated totals about 15.7 million. For epidemiologic and administrative considerations the vaccination campaign will start in population centers with over 2,000 inhabitants; this portion of the program will require vaccination of approximately 6.5 million infants and young children.

The country's size, the necessary complexity of such a large campaign, problems in assuring adequate vaccine distribution and maintenance, possible enterovirus interference, and resulting uncertainty as to whether useful seroconversion levels will be obtained, made it essential to carry out preliminary field trials. The goal of these has been to verify the technical and operational feasibility of the program to be undertaken on a national scale.

Trial Area

The coastal state of Espírito Santo was selected as the area for the experimental trial. Although the state's incidence of poliomyelitis is relatively low, it possesses features that to some extent represent the differing demographic, geophysical, and communications situations that the poliomyelitis control program will have to deal with when nationwide coverage begins.

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[1]Also published in Spanish in *Boletín de la Oficina Sanitaria Panamericana*, Vol. LXXV, No. 6, pp. 511-522.

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TABLE 1–Poliomyelitis cases in Brazil, 1968-1971.[a]

Regions and federal units	1968	1969	1970	1971
North	**224**	**86**	**19**	**65**
Rondônia	–	–	...	...
Acre	–	...	...	...
Amazonas	1	20	1	2
Roraima	–	...	...	...
Pará	219	60	18	63
Amapá	4	6	...	...
Northeast	**155**	**202**	**637**	**619**
Maranhão	5	2	13	17
Piauí	19	27	16	3
Ceará	57	38	250	120
Rio Grande do Norte	6	9	15	23
Paraíba	13	11	13	23
Pernambuco	35	49	124	32
Alagôas	10[b]	2	142	40
F. Noronha	–	–	–	–
Sergipe	1	–	22	11
Bahia	9	64	42	350
Southeast	**649**	**357**	**1,043**	**950**
Minas Gerais	184	116	451	245
Espírito Santo	6	47	26	145
Rio de Janeiro	189	72	316	198
Guanabara	134	22	163	71
São Paulo	136	100[b]	87	291
South	**469**	**311**	**235**	**172**
Paraná	158	114	81	108[b]
Sta. Catarina	25	33	56	...
Rio Grande do Sul	286	164	98	64
West-Central	**88**	**199**	**322**	**210**
Mato Grosso	6	17	7	...
Goiás	48	98	191	169
Distrito Federal	34	84	124	41
Total	**1,585**	**1,155**	**2,256**	**2,016**

Sources: Boletín Epidemiológico da Fundaçao do Serviço Especial de Saúde Pública, Diretoria da Estatística, Department of Health and Welfare of the State of Espírito Santo.

[a] Subject to revision.

[b] Capital only.

– No data.

... Data unknown.

Aims

The objectives of the pilot project were as follows:

(a) With respect to various types of poliovirus, to determine the levels of immunity among the 3-month to 4-year age group that have either been acquired naturally through infection or as a result of prior vaccination;

(b) to identify the type(s) of poliovirus circulating in the area;

(c) to evaluate the effectiveness of the Sabin oral vaccine in the Brazilian context, on the basis of levels of seroconversion obtained;

(d) to demonstrate on a small scale the methodology, logistics, kinds of surveillance, and methods of appraisal that are to be used in the National Poliomyelitis Control Plan; and

(e) to establish a system of epidemiologic surveillance and polio vaccine maintenance directed at the control and ultimate eradication of poliomyelitis in the area under study.

Materials and Methods

To help achieve these objectives, the pilot program was divided into two parts—a serologic survey and a mass vaccination program.

1) The serologic survey was aimed at finding the immunity levels of the group studied, identifying the types of poliovirus in circulation, and judging the effectiveness of the oral vaccine to be used in the nationwide program in the light of special climatic conditions and possible factors that could interfere with the introduction of attenuated polioviruses.

2) The goal of the mass vaccination program was to vaccinate all those between 3 months and 4 years of age residing in the urban portion of localities with more than 2,000 inhabitants, in order to test the methodology to be adopted on a national scale under field conditions.

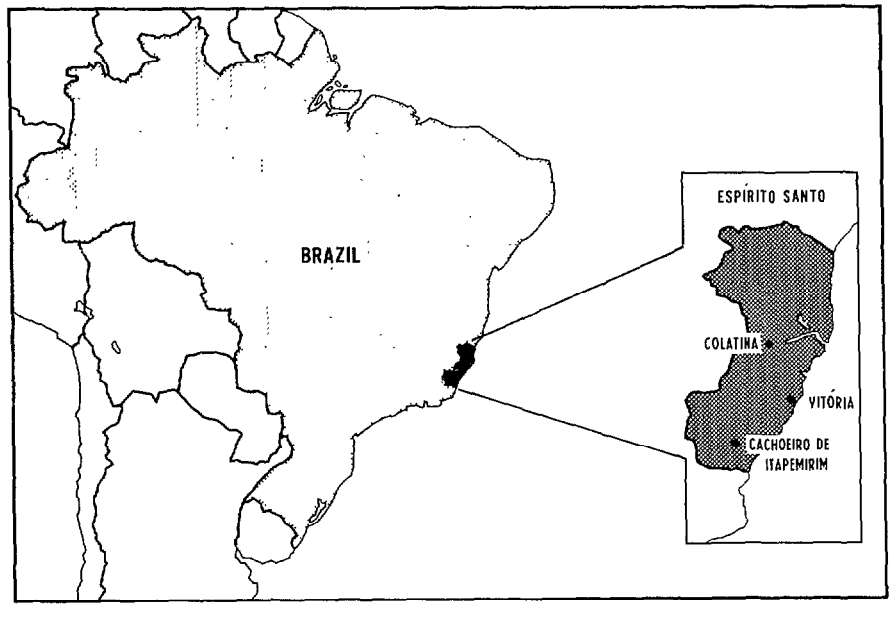
The present study will confine its attention to the serologic survey.

The Population Sample

It had previously been found that some 600 blood samples from infants and children between 3 months and 4 years of age would be needed. In view of limited laboratory operating capacity, this was the number of samples sought. These were collected in three localities —Colatina, Vitória, and Cachoeiro de Itapemirim—which were chosen partly because of existing difficulties with the supply and training of collection personnel. (The three towns are located in the north, central, and southern parts of the state, respectively.) The total numbers of subjects sampled in the three places were 300 in Vitória (the state capital) and 150 in each of the other two towns.

It was stipulated that 60 per cent of the total number of subjects be less than one year old, since this age group should contain the largest number of children without poliovirus

FIGURE 1—A map showing the State of Espírito Santo and the three population centers surveyed.



antibodies. This would help in obtaining an accurate evaluation of the conversion percentages achieved following administration of three doses of vaccine.

The subjects for the survey were selected at random, using areas marked off on the cadastral survey of each of the three towns, in an effort to obtain as representative a sample as possible.

Collection of Materials

Two blood samples were obtained by the digital puncture method—the first on 13 September 1971 when the first dose of vaccine was administered, and the second on 5 January 1972, three weeks after administration of the third dose.

Vaccine

Oral trivalent poliovaccine was used which contained 1,000,000, 100,000, and 300,000 $TCID_{50}$[7] of attenuated virus types 1, 2, and 3, respectively, in each 0.2 ml dose. The titers of the vaccines were tested initially and found to agree with those specified by the manufacturers.[8]

Special care was exercised in vaccine storage, shipping, and maintenance; each vaccination and serum collection team was provided with insulated containers for transporting material in the field.

Neutralizing Antibodies

The tissue culture microtechnique described by Schatzmayr and Homma in 1969 (*21*) was used in conducting neutralizing antibody tests. However, to increase reaction specificity, a serum dilution of 1:8 rather than 1:4 was employed.

[7] $TCID_{50}$: Tissue Culture Infective Dose, 50 per cent—the smallest quantity of a virus suspension that will infect 50 per cent of a particular type of cell culture.

[8] Vaccine from the Connaught Laboratory, Toronto, Canada.

Results Obtained

Dissemination of poliovirus in the communities surveyed was revealed by the immunity pattern of the population, the presence of antibodies in unvaccinated infants (Table 2), and clearcut evidence of diminished susceptibility with age. This gradual reduction in susceptibility with age suggests endemic virus circulation with a uniform effect on different age groups. Therefore, special attention should be paid to the presence in the three towns of subjects, even above two years of age, whose sera showed no antibodies for any of the three types of poliovirus.

Tables 3, 4, and 5 show the percentages, in each town, of sera that reacted positively against each type of poliovirus; they also record the antibody levels found among infants and young children previously immunized with oral vaccine. A review of this data reveals that type 3 vaccine prompted a lower rate of antibody formation than did the type 1 and 2 vaccines; this was true in all three towns studied. This same pattern also emerged from a similar study carried out in the State of Rio de Janeiro (*21*).

It was also observed that vaccinations undertaken earlier in the region produced low indices of seroconversion. Reports on prior vaccinations, including the number of doses, were obtained from families by the collection teams. These data, although incomplete, failed to show any significant relationship between the number of doses given and the presence of antibodies in the sera of previously vaccinated infants and young children. However, those previously vaccinated did show a uniform tendency to have higher rates of antibody formation than those not vaccinated before, especially in the town of Vitória. We do not feel that the limited number of subjects tested permits any broader conclusions, although an anamnestic reaction to the vaccine appears possible.

Tables 6, 7, and 8 show the subjects' ages and the conversion rates obtained in each town. There is no evidence that age had any definite

TABLE 2–Immune status of the 3 month-4 year age group in the towns of Vitória, Cachoeiro de Itapemirim, and Colatina for the three types of poliovirus, before vaccination. (First blood sample collected.)

Locality	Age group (months)	Polio 1			Polio 2			Polio 3		
		<1:8[a]	1:8	% susceptible[b]	<1:8	1:8	% susceptible	<1:8	1:8	% susceptible
Vitória	< 6	82	17	82.8	75	23	76.5	74	23	75.5
	6–12	77	29	72.6	81	29	73.6	72	24	75.0
	12–24	26	16	61.9	34	9	79.0	35	9	79.5
	>24	36	28	56.2	40	24	62.5	34	29	53.9
Cachoeiro de Itapemirim	< 6	35	5	87.5	26	12	68.2	32	7	82.0
	6–12	36	11	76.6	20	26	43.4	28	22	56.0
	12–24	9	6	60.0	7	10	41.2	12	4	75.0
	>24	22	5	81.5	11	21	34.4	22	9	70.9
Colatina	< 6	34	10	77.3	32	12	72.7	30	14	68.2
	6–12	23	7	76.6	19	10	65.5	19	11	63.3
	12–24	7	2	77.7	3	5	37.5	6	3	66.6
	>24	13	12	52.0	15	10	60.0	11	13	45.8

[a] Blood sample dilution.
[b] Percentage susceptible to virus.

TABLE 3–Vitória: Poliomyelitis antibodies in previously vaccinated and previously unvaccinated members of the 3 month-4 year age group, and results obtained from vaccination during the survey.

Poliovirus type	Vaccination status	Before survey vaccination			After survey vaccination		
		<1:8[a]	1:8	% immune[b]	<1:8	1:8	% immune
1	Previously vaccinated	79	28	26.1	16	91	79.7
	Unvaccinated	111	25	18.3	42	94	62.2
2	Previously vaccinated	74	28	25.9	13	89	82.5
	Unvaccinated	118	16	11.9	31	103	54.4
3	Previously vaccinated	68	32	32.0	31	69	54.4
	Unvaccinated	119	15	11.4	65	69	45.4

[a] Blood sample dilution.
[b] Percentage immune before survey vaccination.

influence on conversion rates, although the group over twelve months old generally experienced higher rates.

What seems important to us in connection with age and serologic conversion is the fact that infants less than six months old, who are the primary targets of the maintenance vaccination programs, showed adequate antibody formation rates.

A special study was made of infants in the

TABLE 4–Cachoeiro de Itapemirim: Poliomyelitis antibodies in previously vaccinated and previously unvaccinated members of the 3 month-4 year age group, and results obtained from vaccination during the survey.

Poliovirus type	Vaccination status	Before survey vaccination			After survey vaccination		
		<1:8[a]	1:8	% immune[b]	<1:8	1:8	% conversion
1	Previously vaccinated	51	12	19.0	6	57	88.3
	Unvaccinated	12	–	–	2	10	83.3
2	Previously vaccinated	37	24	39.3	5	56	86.4
	Unvaccinated	12	–	–	1	11	91.7
3	Previously vaccinated	39	19	32.7	10	48	74.4
	Unvaccinated	13	–	–	6	7	53.9

[a] Blood sample dilution.
[b] Percentage immune before survey vaccination.

TABLE 5–Colatina: Poliomyelitis antibodies in previously vaccinated and previously unvaccinated members of the 3 month-4 year age group, and results obtained after vaccination during the survey.

Poliovirus type	Vaccination status	Before survey vaccination			After survey vaccination		
		<1:8[a]	1:8	% immune[b]	<1:8	1:8	% conversion
1	Previously vaccinated	43	6	12.2	12	37	72.1
	Unvaccinated	28	6	17.6	11	23	60.7
2	Previously vaccinated	36	12	25.0	10	38	72.3
	Unvaccinated	29	4	12.1	7	26	75.9
3	Previously vaccinated	32	14	30.4	14	32	56.3
	Unvaccinated	30	2	6.6	14	18	53.4

[a] Blood sample dilution.
[b] Percentage immune before survey vaccination.

TABLE 6–Vitória: Percentage conversion among survey population members who showed no poliovirus antibodies before receiving their survey vaccination.

Poliovirus type	Age (months)	Before survey vaccination	After survey vaccination		% conversion
			<1:8[a]	1:8	
1	⩽ 6	68	19	49	72.0
	7–11	62	23	39	62.9
	⩾12	55	9	46	83.6
2	⩽ 6	64	17	47	73.4
	7–11	58	14	44	75.8
	⩾12	63	15	48	76.8
3	⩽ 6	65	27	38	58.4
	7–11	59	36	23	39.0
	⩾12	57	27	30	52.6

[a]Blood sample dilution.

TABLE 7–Cachoeiro de Itapemirim: Percentage conversion among members of the survey population who showed no poliovirus antibodies before receiving their survey vaccination.

Poliovirus type	Age (months)	Before survey vaccination	After survey vaccination		% conversion
			<1:8[a]	1:8	
1	⩽ 6	23	3	19	86.3
	7–11	23	4	19	82.6
	⩾12	20	1	19	95.0
2	⩽ 6	17	1	16	94.1
	7–11	19	3	16	84.2
	⩾12	16	3	13	81.2
3	⩽ 6	18	5	13	72.2
	7–11	17	6	11	64.7
	⩾12	16	4	12	75.0

[a]Blood sample dilution.

TABLE 8–Colatina: Percentage conversion among survey population members who showed no poliovirus antibodies before receiving their survey vaccination.

Poliovirus type	Age (months)	Before survey vaccination	After survey vaccination		% conversion
			<1:8[a]	1:8	
1	⩽ 6	30	13	17	56.6
	7–11	20	6	14	70.0
	⩾12	19	4	15	78.9
2	⩽ 6	27	6	21	77.7
	7–11	19	7	12	63.1
	⩾12	17	4	13	76.5
3	⩽ 6	24	10	14	58.3
	7–11	18	9	9	50.0
	⩾12	18	8	10	55.5

[a]Blood sample dilution.

survey population between 3 and 4 months of age (see Table 9) in order to find out more about their response to vaccination. With respect to type 1 poliovirus, the results showed a relatively low rate of antibody formation. The significance of this finding is difficult to analyze, since the infants in the study came from different socioeconomic backgrounds and no supplementary data about them was available. The neutralizing influence of breast-feeding on attenuated poliomyelitis virus has previously been noted (*7, 17*), and for this reason a six-hour break in feeding both before and after taking the vaccine is recommended (*8*). The possible effect of this factor on rates of conversion for type 1 vaccine could not be determined.

TABLE 9–Poliovirus antibodies in all infants between 3 and 4 months old included in the survey, before and after receiving their survey vaccination.

Poliovirus type	Before the survey		After the survey		% conversion
	<1:8	1:8	<1:8	1:8	
1	31	1	14	18	54.8
2	28	3	8	23	71.4
3	26	4	9	21	65.3

Table 10 shows the immune status of the survey population before the vaccination campaign in the three towns, indicating high rates of susceptibility to infection and high risk that paralytic cases would appear. The rates obtained were similar in the three towns, with the exception of the previously mentioned type 2 conversion rates in Cachoeiro de Itapemirim which suggest circulation of non-vaccinal virus.

Table 11 shows the immunization status of the populations in the study after immunization. These data indicate that Cachoeiro de Itapemirim had the highest immunization rates, though the rates in other cities should be considered within acceptable limits.

Discussion of Results

It is important to determine what minimum conversion rates are needed in order to consider that a population is protected against poliomyelitis. Initial oral vaccination results in some countries have indicated a conversion rate of 100 per cent. However, this optimum rate has not been obtained under tropical conditions, and lower figures have been reported by various authors, including Fossaert (1970–*3*).

The current consensus of epidemiologic opinion appears to accept the idea that at least

TABLE 10–Before the pilot vaccination program: Immune status of the infants and young children studied in Vitória, Cachoeiro de Itapemirim, and Colatina, for each poliovirus type.

Locality	Poliovirus type	Total No. included	Antibodies shown for a dilution of:		% immune
			<1:8	1:8	
Vitória	1	243	190	53	21.8
	2	236	192	44	18.6
	3	234	187	47	20.1
Cachoeiro de Itapemirim	1	75	63	12	16.0
	2	73	49	24	32.9
	3	71	52	19	27.0
Colatina	1	83	71	12	14.5
	2	81	65	16	19.8
	3	78	62	16	20.5

TABLE 11–After the pilot vaccination program: Immune status of the infants and young children studied in Vitória, Cachoeiro de Itapemirim, and Colatina during the period September-December 1971, for each poliovirus type.

Locality	Poliovirus type	Total No. included	Antibodies shown for a dilution of:		% immune
			<1:8	1:8	
Vitória	1	243	58	185	76.1
	2	236	44	192	81.3
	3	234	96	138	58.9
Cachoeiro de Itapemirim	1	75	8	67	89.3
	2	73	6	,67	91.7
	3	71	16	55	77.5
Colatina	1	83	23	60	72.3
	2	81	17	64	79.0
	3	78	28	40	64.1

80 per cent immunity must be achieved in a community before virus transmission can be reduced. We know that poliomyelitis immunity is probably linked to antibodies or local immunity at the point of implantation in the intestine. It is this local immunity, conditioned by immunoglobulin A, interferon, or other established serum mechanisms, that impedes circulation of the virus, while the antibodies in the blood control clinical manifestations of the disease and viral invasion of the central nervous system.

The level of blood serum antibodies should reflect the level of local immunity as well. Assuming this to be the case, the pilot immunization program can be said to have resulted in adequate antibody levels with regard to poliovirus types 1 and 2. However, blood antibody for type 3 were unsatisfactory (the type 3 attenuated virus strain is being re-evaluated throughout the world.)

Data on the immune status of the populations studied showed children two years of age and over with insufficient antibody levels,

indicating potential susceptibility of these populations to poliovirus. Furthermore, the presence of a large number of susceptible infants over one year old reveals the potential for an epidemic outbreak of the disease. At the same time, the decline in the proportion of susceptible subjects as age increases reflects circulation of poliovirus in the communities studied. With respect to type 1 virus in Cachoeiro de Itapemirim, a high degree of susceptibility (indicated by the lack of antibodies) was observed among subjects over 24 months old.

The poor conversion rates obtained with vaccinations administered before the campaign began emphasizes the need to evaluate the potency of a vaccine (i.e., the number of virus particles present per dose) before use. It is also vital to keep in mind the key roles played by preservation, transportation, and application methods, and by the time elapsed after thawing, in achieving successful immunization.

The low serologic conversion rates achieved by the attenuated type 3 vaccine virus has already been noted in other regions of the world, and the selection of a different type 3 strain for use in vaccination (as suggested by Melnick in 1970–*14*) is being studied.

Different conversion rates were achieved during the campaign in each of the three towns studied, clearly indicating a need for continued evaluation of vaccination campaigns. Because of differences in poliovirus circulation patterns, epidemiologic conditions in a given population vary with the seasons, the virulence of circulating viruses, the number of susceptible individuals, and other factors that are less well understood. Oral vaccine will therefore require different parameters of evaluation for each region in which it is employed, parameters that should be defined, analyzed, and used as the basis for future antipoliomyelitis campaigns.

Conclusions

1) The results obtained by the serologic survey in Espírito Santo showed satisfactory conversion rates resulting from vaccination against poliovirus types 1 and 2, but type 3 conversion rates were lower.

2) Among the children and infants who had been vaccinated previously (according to their families), many showed no circulating antibodies against poliovirus. This situation illustrates the need for rigorous efforts to eliminate the many factors that can negatively influence vaccination results.

3) With one exception, we observed no clear-cut evidence that the ages of the children and infants tested had any effect on their conversion indices. The exception occurred in the 3-month age group, which showed a conversion rate of 54.8 per cent for type 1 poliovirus. The reasons for this latter occurrence are not clear. Since it is not possible, after the fact, to analyze all the factors that might have produced this result, it is felt that the problem should be more fully examined in the course of subsequent surveys that are to be made in other parts of the country.

4) The information obtained shows a very clear and pressing need for poliomyelitis vaccination in communities such as those studied (which may enjoy a satisfactory level of health in other respects), that present a serious risk of poliomyelitis.

5) The survey results also show that complete immunization (100 per cent conversion) was not achieved among the children and infants tested. It would thus appear necessary to establish an epidemiologic poliomyelitis surveillance system, so as to obtain a true and accurate assessment of any vaccination effort, and in order to convincingly demonstrate reduction or elimination of the disease in the community. Such epidemiologic surveillance should be supported by a central laboratory capable of isolating and identifying the types of virus involved in suspected cases, so as to permit that countermeasures be directed against any foci discovered. It would also seem highly desirable to analyze vaccine at the various stages of distribution preceding actual use, to ensure that it has retained an acceptable level of potency.

SUMMARY

In 1971 the Brazilian Government conducted a serologic survey of poliomyelitis antibody levels in three towns of Espírito Santo State. Accordingly, serum samples were taken from 600 subjects in the 3-month to 4-year age group before and after they received three doses of Sabin oral vaccine.

This survey was part of a large vaccination program in Espírito Santo, which in turn was designed to pave the way for a nationwide vaccination campaign.

The study showed that there were large numbers of susceptible infants over one year old in all three towns. This circumstance, together with circulation of poliovirus in the communities studied, revealed the potential for an epidemic outbreak of disease. Failure of previous vaccinations to produce effective results also illustrated the importance of proper care in transporting, maintaining, and administering vaccine—as well as the advisability of evaluating vaccine potency before use.

Administration of three doses of oral vaccine during the survey produced satisfactory conversion rates against poliovirus types 1 and 2, but rates against poliovirus type 3 were lower. None of the three seroconversion rates approached the 100 per cent level of success sometimes reported in temperate climates; the authors have therefore recommended establishment of a nationwide surveillance system in order to obtain an accurate assessment of the effects of any vaccination efforts, and to convincingly demonstrate reduction or elimination of the disease.

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