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Immunity to Poliomyelitis in Guatemala

A Serological and Virological Survey*

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A mass poliomyelitis vaccination campaign, such as that under consideration in Guatemala, inevitably changes the immunological picture of a population by the artificial stimulation of antibodies in large numbers of individuals. It was therefore decided that before carrying out such a campaign, and to provide basic information for its conduct, a survey should be made to determine the degree of natural immunity to poliomyelitis and the amount of poliovirus and other enterovirus infection in the population, and to compare the poliovirus antibody titres of a small group of children who had already received Salk vaccine with those in unvaccinated children living in this area of probable high endemicity. The results of the survey show that both poliovirus and other enterovirus infections are common at an early age in Guatemala, and it is concluded that vaccination is most indicated for the 0-4-year-old group.

In planning programmes for vaccination against poliomyelitis, a knowledge of the immune status of the population to be vaccinated provides a helpful guide. This is true whether killed—i.e., Salk-type formalinized virus vaccine—or live, attenuated strains of poliovirus are to be used for the production of immunity. The present survey was undertaken in Guatemala in October-November 1957 at the request of local authorities and at a time when a large-scale vaccination programme (with formalinized vaccine to be purchased from the USA) was being considered by the Ministry of Health. The objectives of the survey were: (1) to determine the degree of "natural" immunity to poliomyelitis in normal Guatemalan children and adults, as reflected by the antibody patterns in different age-groups; (2) to determine how much poliovirus and other enterovirus infection was occurring in the population by screening the young children for excretion of these agents; and (3) to compare the poliovirus antibody titres of a small group of children who had already received Salk vaccine with the titres in unvaccinated children of comparable age living in this area of probable high endemicity.

HISTORY OF POLIOMYELITIS IN GUATEMALA

The first recorded cases occurred in the 1940's, and until 1949, fewer than 20 were listed each year. However, many of the 3 350 000 inhabitants live in remote areas and under-reporting is therefore likely. Since 1952, over 100 cases per year have been reported, and because of the increasing problem, a poliomyelitis rehabilitation centre was established in Guatemala City. Gradually, this centre has taken over most of the problems associated with poliomyelitis in Guatemala, including the diagnosis of acute cases referred from other hospitals and clinics, the hospitalization of acute and chronic cases, and the rehabilitation of patients with residual deformities.

Table 1 indicates the poliomyelitis case rate per 100 000 population since 1940, and the annual infant mortality for the same period.[3] As has been noted by Payne (1955) and Paul (1958) there may be

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[3] We are indebted to the Pan American Sanitary Bureau for these data.

TABLE 1

POLIOMYELITIS CASE RATES AND INFANT MORTALITY, GUATEMALA, 1940-56 [a]

Year	Infant mortality rate [b]		Poliomyelitis cases		
	Annual	5-year average	Number	Rate [c]	5-year average
1940	108.9		—	0.0	
1941	108.2		—	0.0	
1942	143.9		4	0.2	
1943	120.0		7	0.3	
1944	117.1	118.6	1	0.0	0.2
1945	103.5		8	0.3	
1946	114.5		3	0.1	
1947	109.5		18	0.7	
1948	117.4		5	0.2	
1949	101.7	105.4	45	1.7	0.5
1950	106.8		13	0.5	
1951	92.0		39	1.3	
1952	112.2		112	3.8	
1953	102.8		140	4.6	
1954	87.9	100.3	139	4.4	2.8
1955	101.4		86	2.6	
1956			146	4.4	

[a] Data kindly supplied by the Pan American Sanitary Bureau, Washington, D.C.
[b] Number of deaths under 1 year per 1000 live-births
[c] Case rate per 100 000 population

an inverse relationship between these two rates in many parts of the world, poliomyelitis case rates rising as infant mortality falls. In general, a shift from endemic to epidemic poliomyelitis in a given country has occurred when the infant mortality falls to below 75 per 1000 live-births. This may have occurred in Argentina (Paul, 1958) and British Guiana (Melnick, 1958). Furthermore, in areas of recurrent epidemics, the age-group attacked tends to shift from the very young—true infantile paralysis—to include older and older individuals. In Guatemala, as shown in Tables 1 and 2, the infant mortality rate is still high, 100 per 1000 live-births; poliomyelitis remains endemic, with an annual attack rate of less than 5 per 100 000; and the age-group involved is the youngest, 80%-90% of cases occurring in children less than 5 years old (Table 2).

TABLE 2

PARALYTIC POLIOMYELITIS CASES BY AGE, GUATEMALA, 1952-56 [a]

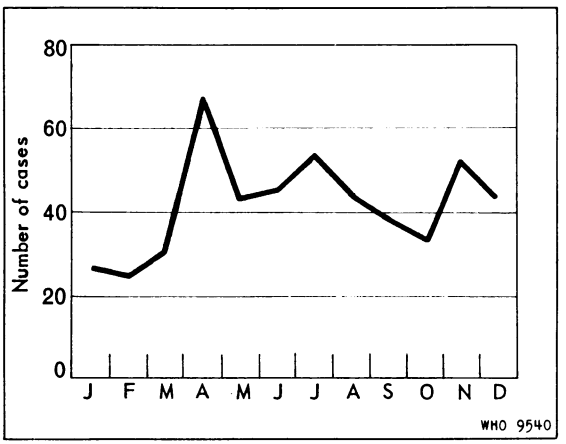
Year	Total cases	Percentage by age-group (years)				
		0-2	3-4	0-4	5-9	10 and over
1952	112	61.5	18.8	80.3	9.8	9.8
1953	140	70.0	16.4	86.4	12.1	1.5
1954	139	75.5	15.0	90.5	6.5	3.0
1955	86	63.0	17.5	80.5	11.5	8.0
1956	146	59.5	18.0	77.5	17.0	5.5

[a] Data kindly supplied by the Statistical Section, Ministry of Public Health, Guatemala

No marked *seasonal incidence* of cases has been noted. Fig. 1, based on 500 paralytic cases over an eight-year period,[1] indicates a peak incidence in spring (April), remaining high throughout the summer and fall, and reaching lowest levels between January and March.

FIG. 1

SEASONAL DISTRIBUTION OF 500 PARALYTIC CASES OF POLIOMYELITIS IN GUATEMALA, 1949-56



No information is available on *racial incidence*, although poliomyelitis is said to be rare in the Indians, who form about 50% of the 3 350 000

[1] We are indebted to Dr M. A. Aguilera, director of the Instituto de Rehabilitación Infantil y Clinica de Poliomielitis for these data.

population of the country. Since many of the Indians live in remote areas, it is probable that cases which occur among them are rarely seen or reported.

MATERIALS AND METHODS

Type of population

Persons included in both the serum and virus survey were from the lower socio-economic group, which includes a large percentage of the population. These people live in crowded urban areas, or in semi-rural types of surroundings. In either case most of their houses do not have running water, and the general level of sanitation is low. The climate is mild so that no heating is necessary; many of the semi-rural houses are made of thatch, others of adobe. Dirt floors are not uncommon. Large families are the rule.

Collection of blood specimens

The children from whom blood specimens were collected were largely those attending well-baby clinics or out-patient departments for minor complaints. The adults included some mothers of the children, and young men coming to the health department for VDRL tests in order to obtain "work cards". In addition a certain number of hospitalized patients were bled. These were children admitted for tonsillectomy, herniorrhaphy, eye operations, etc., or young adults convalescing from recent surgery. Most of the specimens were collected in Guatemala City, and were therefore of urban origin. Thirty-five bloods from the age-group 6 months to 5 years were obtained from Amatitlán, a small semi-rural settlement 20 km from Guatemala.

Thirty-two bloods were also collected from children 3-6 years old who had received Salk vaccine. These children, who were from the same socio-economic group as the non-vaccinated, attended a day orphanage—where they had all their meals, received their clothes, baths, etc.,—but returned to their homes at night. Almost all had received two doses of Salk vaccine 6-9 months earlier, and a few had received a third dose one week before the bleeding.

Vacuum syringes, 20-ml size, were used for all blood collections. With few exceptions the bloods were collected in the mornings, allowed to clot and separated in the afternoons; a few were allowed to stand (refrigerated) overnight before separation. The sera were stored in rubber-lined, screw-capped vials in a refrigerator at 4°C, and transported in iced containers at approximately this temperature to the base laboratory in New Haven, Conn., USA.

Collection of rectal swabs

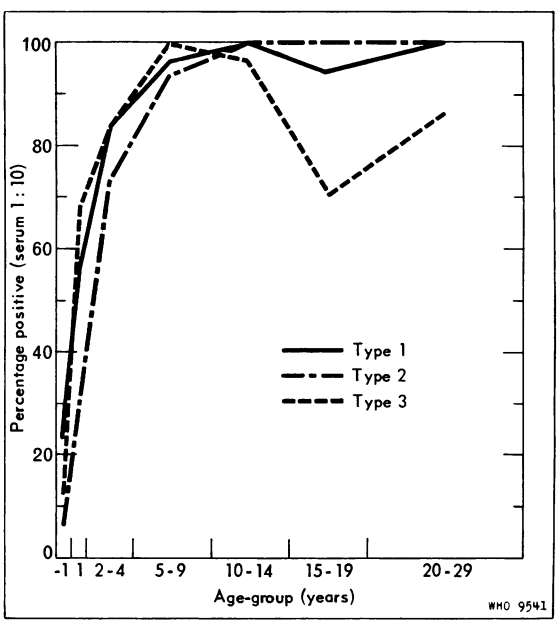
Only from children attending the well-baby or out-patient clinics were rectal swabs collected. The swabs used were larger than those commonly employed for throat swabs. They were dipped in 50% glycerol (in sterile H_2O) before insertion into the rectum, and the swab plus faecal material was stored at 4°C in vials containing 1 ml of 50% glycerol. For comparison, rectal swabs were also obtained from 44 mothers of children who were being similarly tested.

Serological tests

Neutralizing antibodies were determined by means of the colorimetric test using disposable plastic panels (Melnick & Opton, 1956). At least two tests at different times were performed on each specimen.

Complement-fixing (CF) antibodies were tested by using the lucite plate technique (Black & Melnick, 1954).

FIG. 2
AGE DISTRIBUTION OF NEUTRALIZING ANTIBODIES TO POLIOVIRUS, GUATEMALA



Virus isolations

Monkey kidney monolayer tissue cultures were used throughout. The eluates extracted from rectal swabs were inoculated in 0.2-ml amounts into three tubes, which were then followed for development of cytopathogenic effect (CPE). Agents isolated were typed by neutralization tests, using first serum pools against the three polioviruses and other enteroviruses (including ECHO types 1-19, Coxsackie B 1-5, and Coxsackie A 9) and then specific components of the pool which inhibited CPE.

RESULTS

Neutralizing antibodies

As shown in Table 3 and Fig. 2, neutralizing antibodies to all three types of poliovirus are acquired early in life in Guatemala. Since the results were similar for Guatemala City and the smaller city of Amatitlán, the two have been combined. At 5-11 months, maternal antibody presumably having been lost, the percentage of children who had had time to acquire infection was small—12%, 6% and

TABLE 3

AGE DISTRIBUTION OF ANTIBODIES AGAINST POLIOVIRUSES IN GUATEMALA

Age	Neutralizing					Complement-fixing				
	Number tested	Titre	Percentage positive			Number tested	Titre	Percentage positive		
			Type 1	Type 2	Type 3			Type 1	Type 2	Type 3
5-11 months	17	10+	12	6	24	16	8+	6	0	0
		50+	12	0	24		16+	6	0	0
		250+	6	0						
1 year	16	10+	69	31	56	15	8+	33	0	27
		50+	63	25	50		16+	20	0	13
		250+	31	13	25					
2-4 years	45	10+	84	73	84	43	8+	21	19	23
		50+	78	64	69		16+	19	12	21
		250+	51	42	36					
5-9 years	31	10+	97	94	100	30	8+	10	3	20
		50+	94	87	94		16+	7	0	3
		250+	65	45	48					
10-14 years	34	10+	100	100	97	27	8+	15	15	19
		50+	65	91	62		16+	4	4	4
		250+	41	50	35					
15-19 years	20	10+	95	100	70	18	8+	0	0	0
		50+	75	70	40		16+	0	0	0
		250+	20	20	10					
20-29 years	36	10+	100	100	86	32	8+	3	3	3
		50+	64	72	39		16+	0	0	3
		250+	19	19	6					
Total	199					181				

24%, respectively for the three types. Some of the low-level reactions at this age might well be due to heterotypic responses. During the age period 12-23 months, the greatest shift from negative to positive occurred, so that 69%, 31%, and 56% of children had acquired type 1, 2 and 3 neutralizing antibodies respectively. Over the age of 5 years, however, close to 100% of those studied had antibodies to all three types of poliovirus.

The relation of age to titre of neutralizing antibody is shown in Fig. 3. The majority of higher titres (250 and greater) were in the younger age-groups, while the lower titres (10 and 50) were found chiefly in those 15 years and over. A comparison of the neutralizing antibody titres of vaccinated and non-vaccinated children aged 3-6 years is shown in Fig. 4. No significant differences in titres were detected in the two groups for any of the three types.

FIG. 3
NEUTRALIZING ANTIBODY TITRES BY AGE-GROUP, GUATEMALA

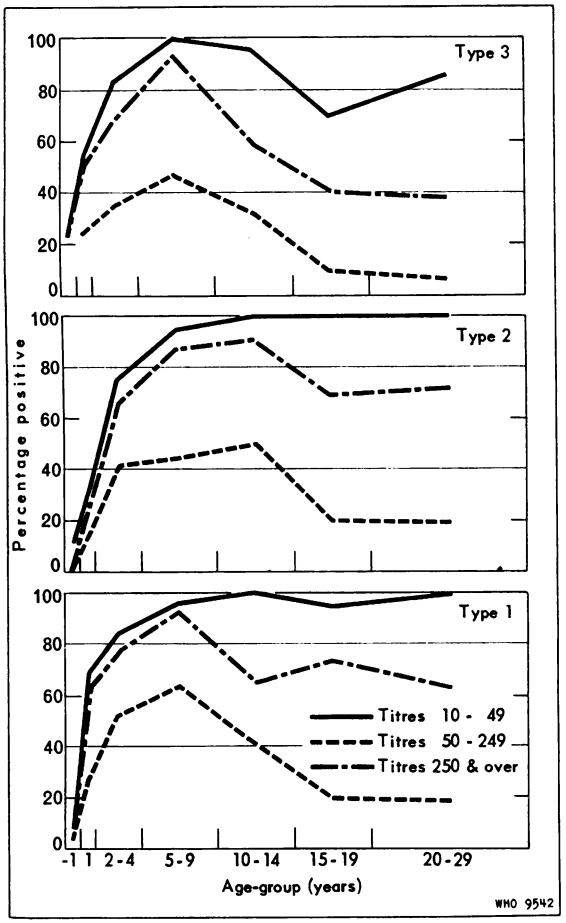
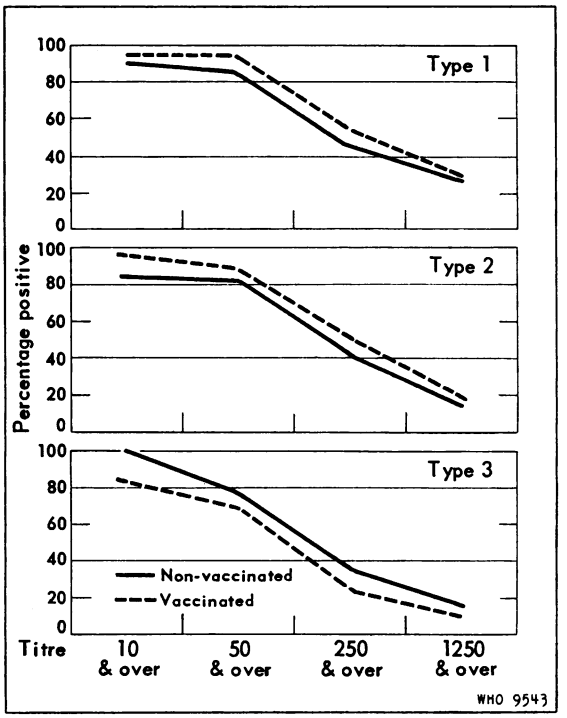


FIG. 4
COMPARISON OF NEUTRALIZING ANTIBODY TITRES IN 32 VACCINATED AND 27 NON-VACCINATED CHILDREN AGED 3-6 YEARS



Complement-fixing antibodies

High CF antibody titres more or less paralleled rises in neutralizing antibody (Table 3 and Fig. 5),

FIG. 5
COMPLEMENT-FIXING ANTIBODY TITRES (≥ 1 : 16) BY AGE-GROUP

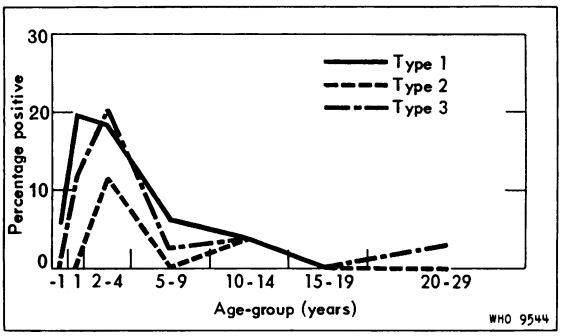


TABLE 4
ENTEROVIRUS EXCRETION BY 163 NORMAL PERSONS IN GUATEMALA

Age	Number tested	Percentage positive	Numbers of viruses isolated									Untypable
			Polio			Coxsackie		ECHO				
			1	2	3	A9	B3	6	7	14	15	
Children												
5-11 months	41	42		3			1	1	1	3	1	7
12-23 months	51	24	1	3	1	1	1	1	2			2
2-3 years	27	33	1	1					1	1	1	4
Total	119	33	10 (8.5%)			3 (2.5%)		12 (10%)				13 (11%)
Adults												
17-29 years	27	7							1		1	
30-42 years	17	12								1		1
Total	44	9						3 (7%)				1 (2%)

but the positive reactors fell off sharply in children over 5-9.

Virus isolations from rectal swabs

Approximately one-third of the children tested were found to be excreting some enterovirus (Table 4), either a poliovirus, Coxsackie, or ECHO virus. There was no striking difference in the percentage positive among children less than 1 year old and those 1-3 years of age, but the highest figure (42%) was actually for those 5-11 months. In each group 7%-10% were excreting polioviruses. Fewer Coxsackie viruses were isolated than either ECHO or polioviruses, perhaps owing to the fact that only monkey kidney tissue cultures were used in the test system, and many Coxsackie A viruses may therefore have been missed.

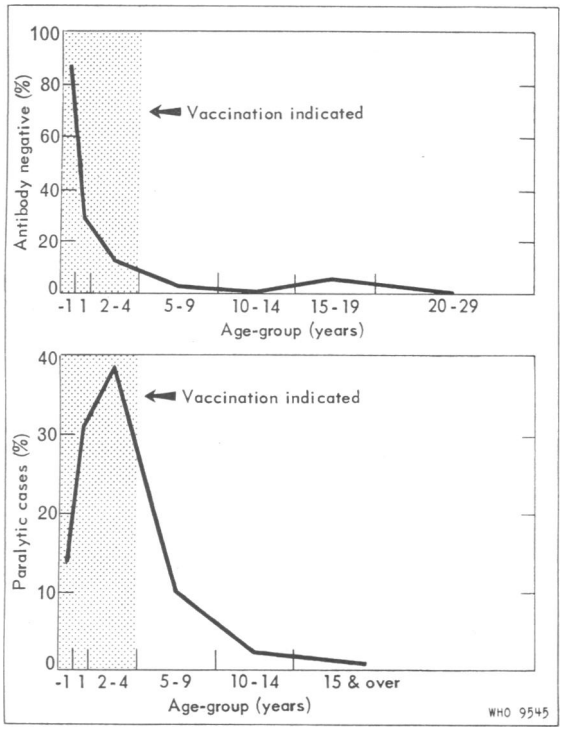
Four of the 44 mothers tested were also positive for ECHO viruses; the children of three of them were negative, but one mother and child were both excreting ECHO 15. No adults were found to be excreting polioviruses (Table 4).

COMMENT

The serological results indicate that poliovirus infections are common in Guatemala and are acquired early in life. This is a pattern which has been observed in other parts of the world with similar living conditions (Gear, 1948; Hammon et al., 1950; Paul et al., 1952; Paul & Horstmann, 1955). Thus in Egypt, Paul et al. (1952) found that poliovirus infections were prevalent among young children, and by the age of 4 or 5 years virtually all had acquired antibodies to all three types. Similarly in Morocco, exposure and infection were shown to occur early, and antibodies were detected in 90%-100% of children over 5 years (Paul & Horstmann, 1955). As in Guatemala, the infant mortality in these countries is high, and poliomyelitis has remained an endemic disease, with paralytic cases occurring only in young children.

The relationship of the pattern of neutralizing antibodies against polioviruses in Guatemala and the age distribution of the paralytic disease is illustrated in Fig. 6. Here, the lack of antibodies, i.e., susceptibility to infection by age, is compared with the percentage of paralytic cases in each age-group. It is evident that the majority of cases occur in the youngest children, who make up the most susceptible age-group. Thus vaccination—whether with a killed or with a live virus vaccine—would be especially indicated for the 0-4-year olds. As Fig. 4 indicates, vaccinating children of the 3-6-year-old group with formalinized vaccine offered little advantage, for no significant differences were noted between the antibody titres of children who had received several doses of vaccine and those of non-vaccinated children of the same age. This result may be explained in part on the basis of the immunological principle that if a child already has a high—or

FIG. 6
SUSCEPTIBILITY BY AGE TO POLIOMYELITIS IN GUATEMALA, AS MEASURED BY LACK OF NEUTRALIZING ANTIBODY TO TYPE 1 POLIOVIRUS AND PERCENTAGE OF PARALYTIC CASES



ceiling—antibody titre, vaccine administration does not provoke a further rise. However, it is unlikely that all of the children had high antibody levels, and the results may well be due in part to the use of a low potency vaccine.

The evidence provided by the enterovirus survey in Guatemala supports the serological evidence that polioviruses and other enteric agents infect this population early in life. Thus, on a single spot sampling, roughly one-third of the children 5 months to 3 years of age were excreting some enterovirus, and 10% of the 119 normal children tested were excreting one of the three types of poliovirus. This high prevalence of enteric virus infection in the young children who are the chief candidates for vaccination brings up the possibility that such natural infections might seriously hamper the efficiency of a vaccination programme which depends upon infection with attenuated poliovirus strains orally administered. Interference between polioviruses in man has been demonstrated (Sabin, 1958), and there is some evidence that this same mechanism may operate *in vivo* with other virus systems, such as poliovirus and ECHO or Coxsackie viruses (Gelfand et al., 1959). This is an aspect of large-scale oral vaccination programmes which cannot be ignored. The problem arises particularly in connexion with underdeveloped areas where living conditions are similar to those of Guatemala, areas to which to the oral method of vaccination is otherwise well suited because of its simplicity and modest cost.

ACKNOWLEDGEMENTS

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RÉSUMÉ

Avant d'entreprendre la vaccination antipoliomyélitique de larges secteurs de la population du Guatemala, il parut nécessaire d'avoir une idée de l'immunité naturelle de cette population, que la vaccination allait modifier. Une enquête fut donc organisée avec l'aide de l'OMS, en 1957. Elle devait porter sur *a*) le degré d'immunité naturelle d'enfants et d'adultes en bonne santé, tel que le révèle le schéma des anticorps dans divers groupes d'âge; *b*) la présence éventuelle du virus poliomyélitique et d'autres entérovirus dans les excrétions

des enfants; *c*) la comparison du taux des anticorps neutralisants dans un petit groupe d'enfants vaccinés par le vaccin inactivé de Salk, et un groupe du même âge non vacciné, vivant dans un milieu considéré comme fortement endémique.

Après avoir établi un parallèle entre le nombre annuel des cas de poliomyélite — dont la plus forte proportion se produit encore dans les groupes d'âge les plus bas — et le taux de mortalité infantile, qui reste élevé au Guatemala (100 décès pour 100 000 naissances vivantes), les auteurs décrivent les grandes lignes de l'enquête et en donnent les principaux résultats:

L'examen sérologique pratiqué sur des personnes en bonne santé appartenant au groupe socio-économique le moins favorisé a révélé que l'infection poliomyélitique se produit à un stade précoce de la vie. En effet, plus de 90% des sujets âgés de plus de 5 ans possédaient déjà des anticorps des trois types. D'après l'analyse d'un prélèvement effectué sur 119 enfants vivant au même endroit, un tiers de ceux-ci excrétaient des virus poliomyélitiques et d'autres entérovirus. Quatre mères sur 44 excrétaient des virus ECHO, tandis que trois de leurs enfants étaient négatifs. Dans un seul cas, la mère et l'enfant étaient porteurs tous deux du virus ECHO 15.

Chez un certain nombre d'enfants de trois à six ans, deux à trois doses de vaccin phénolé, dont l'administration avait débuté 7-9 mois plus tôt, n'ont provoqué aucune augmentation significative des anticorps neutralisants, par rapport à un groupe comparable d'enfants non vaccinés.

Il apparaît ainsi qu'au Guatemala, le groupe d'âge le mieux indiqué pour la vaccination antipoliomyélitique est le groupe le plus jeune, celui de 0-3 (ou 4) ans. Dans le groupe d'âge de 3-6 ans, la vaccination semble moins opportune, puisque l'on n'a pas observé de différence significative du niveau des anticorps chez les enfants non vaccinés et les enfants vaccinés.

D'autre part, si l'on organise une campagne de vaccination par voie orale, avec du virus atténué, il y a lieu de garder présente à l'esprit l'éventualité d'une interférence entre les virus poliomyélitiques du vaccin et les entérovirus naturels (polio, ECHO, Coxsackie) dont les enfants peuvent être porteurs. Cette interférence a déjà été relevée au sein du groupe des virus poliomyélitiques. On ne peut ignorer ce problème dans les campagnes projetées au sein de populations de pays dont les conditions de vie rappellent celles du Guatemala, et où la vaccination orale, simple et peu coûteuse, est la méthode de choix.

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