Journal of Tropical Medicine and Hygiene 1994, 97, 231–235

Prevalence of measles antibodies before and after vaccination in previously unvaccinated children of the Cordillera Province (Santa Cruz Department, Bolivia)

P. GUGLIELMETTI[1], M. L. BIANCHI BANDINELLI[2], A. BARTOLONI[3], H. GAMBOA[4], M. ROSELLI[3] & P.E. VALENSIN[2]

[1]Institute of Infectious Diseases, University of Siena, Siena, Italy
[2]Department of Molecular Biology, Division of Microbiology, University of Siena, Siena, Italy
[3]Chair of Infectious Diseases, University of Florence, Florence, Italy
[4]Cordillera Health District, Health Unit, Santa Cruz, Bolivia

SUMMARY

A study was carried out in the Cordillera Health District (Santa Cruz Department, Bolivia) from October 1988 to April 1989 to determine the seroprevalence of measles antibodies and the seroconversion rates among a group of previously unvaccinated children (9–36 months of age) from the urban and rural area of the province, before and after immunization with a standard dose of Schwarz measles vaccine. Among 265 previously unvaccinated children, 77 (29%) had measles IgG antibodies prior to immunization; 141 out of 147 (96%) seronegative children at the time of vaccination seroconverted. No difference in seroprevalence and in seroconversion rates was found between the urban and rural groups.

Keywords: measles, vaccination, Bolivia

INTRODUCTION

From 1981 the Bolivian Expanded Programme on Immunization (EPI) recommended a single dose of measles vaccine to all children aged over 9 months and under the age of 3 years (MPSSP 1988). The only data available for measles immunization in this country reported a national vaccination coverage, estimated by cluster survey, of approximately 65% (children aged 9 months–24 months) (MPSSP 1988). No measles vaccine efficacy studies nor serological evaluations are as yet available for this country. Precise data on measles vaccine coverage in Cordillera Province are not known. The anecdotal reports from the local health authorities of recent measles outbreaks among presumed vaccinated children stimulated the interest in evaluating seroconversion rates after a standard dose of Schwarz measles vaccine among previously unimmunized children in this area.

Correspondence: P. GUGLIELMETTI, Institute of Infectious Diseases, University of Siena, Via Mattioli 10, I-53100 Siena, Italy.

BACKGROUND, MATERIALS AND METHODS

The study was carried out in Cordillera Province, situated about 200 km south of Santa Cruz, in the south-eastern part of Bolivia, in agreement with the Ministry of Social Welfare and Public Health and the local district health authorities. The study was part of a cooperative programme conducted with the Department of Santa Cruz. Camiri is the main town of

Cordillera Province, with about 30 000 inhabitants. When the study was carried out the Cordillera Province was administratively divided into five rural areas: Heyti, Lagunillas, Cuevo, Gutierrez and Boyuibe, with about 2000–4500 inhabitants each.

A District Hospital exists in Camiri and in each area the population had access to rural hospitals and health facilities. Each rural area was organized with village health workers but the primary health care activities were particularly difficult because of the scattered population. The area hospitals are situated between 40 and 80 km from Camiri with very poor road conditions. The climate is described as sub-humid–dry (Sanabria 1977).

There are no gross social differences among the population of the Province, and health services are equally distributed. The birth rate is 4.5%, whilst the infantile mortality rate may reach 20% (Cordecruz-Cipca 1987).

In Cordillera Province, measles vaccination is administered as a mass campaign three times a year as part of the EPI. Children aged 9–36 months are the target group and each subject has a personal vaccination card. At the Camiri District Hospital vaccination is always available from the local health staff. In the adjacent rural areas vaccinations are provided by mobile teams in campaigns carried out three times a year (MPSSP 1988).

Information about coverage data, age distribution of measles cases and incidence of measles during the study period were not available. The only data available on measles vaccination coverage were for the Department of Santa Cruz, where Cordillera Province is located, which reported by cluster survey in 1987 a card-documented coverage of 66% among children aged 12–24 months (MPSSP 1988).

The study covered the period October 1988–April 1989. All the previously unvaccinated children aged 9–36 months attending for immunization in the mass campaign of October 1988 were enrolled in the study, from urban and rural areas of the province. All the children without age data and previously vaccinated against measles were excluded on the basis of the information reported on their vaccination cards. Two hundred and sixty-five children entered the study: 162 from the urban area of Camiri and 103 from the five rural areas of the Province. Each child had a personal report chart with data on time and place of vaccination, age, sex, weight and height. All the children were examined by the same physicians at ten and 30 days after vaccination to collect information about adverse reactions. Information on previous measles histories was not collected.

Heel-prick blood samples were obtained on filter paper immediately before vaccination (Time zero: T0), and after ten days (Time one: T1), one (Time two: T2) and 6 months (Time three: T3). Measles IgG were measured by haemagglutination inhibition test (HI) and the results were expressed as HI titres (Nakano *et al.* 1983).

A change from undetectable antibody to seropositivity (>1:8) between the first sample (T0) and T1 or T2 specimens was taken to indicate a significant titre rise. Among infants who were seropositive at T0 a fourfold increase in antibody titre between T0 and T1 or T2 samples was taken to indicate a seroconversion. All the blood samples were analysed in the same test run. An antibody titre <1:8 was considered to be negative.

The vaccine used was the Schwarz strain of measles virus distributed by the Government EPI, which was delivered to the Camiri District Hospital and to the rural areas by the existing cold chain. The vaccines were transported to the rural area hospitals in vaccine carriers, and prepared and administered according to the manufacturer's instructions by the members of the local Health Team. The batches of vaccine used in the study were tested by in-vitro culture on 37, MRC-5 and HEp-2 cells, before and after the immunization procedure. The serological evaluation and the infectivity tests were performed at the Division of Microbiology, Department of Molecular Biology, University of Siena. All the specimens were stored in Bolivia at $-20°C$ and transported in Italy in dry ice.

The purpose and the procedure of the survey were explained to the parents and written consent was obtained from them.

RESULTS

All the batches of the vaccine employed in the study, before and after vaccination, and assayed *in vitro* were potent with a TCID 50 $\geqslant 1000$ 0.5 ml^{-1}.

Of the 265 children studied, 77 (29%) had measles antibodies with HI titre of 1:8 or more at the time of vaccination (T0). Among the 77 seropositive subjects at T0, 45 out of 162 (27.8%) were from the urban area

Table 1. Measles antibody prevalence and geometric mean titre by age and urban or rural provenance in 265 previously unvaccinated children at the beginning of the study (time 0)

Age (months)	Children from urban area				Children from rural area			
	Number in group	+ve at T0		GMT of +ve	Number in group	+ve at T0		GMT of +ve
		n	(%)			*n*	(%)	
9	26	4	(15.4)	250	15	1	(6.7)	128
10	19	0	—	—	9	0	—	—
11	21	1	(4.8)	512	17	1	(5.9)	64
12–15	28	5	(17.8)	83	22	11	(50)	88
16–22	32	13	(40.6)	57	14	4	(28.6)	53
23–29	23	16	(69.6)	66	18	10	(55.5)	42
30–36	13	6	(46.1)	32	8	5	(62.5)	27
Total	162	45	(27.7)	96	103	32	(31)	59

+ve, Seropositive children.
T0, Time 0.
GMT of +ve, Geometric mean titres of seropositives.

Table 2. Increase in antibody titre in 54 children seropositive at time 0 and evaluated one month after vaccination with Schwarz vaccine (T2)

Age (months)	Number in group	+ve at T0[1]		⩾4-fold titre rise at T2	
		n	(%)	*n*	(%)
9	33	2	(6.1)	0	—
10	21	0	—	0	—
11	29	1	(3.4)	0	—
12–15	36	12	(33.3)	4	(33.3)
16–22	33	11	(33.3)	0	—
23–29	29	18	(62.1)	1	(5.5)
30–36	20	10	(50.0)	2	(20)
Total	201	54	(26.9)	7	(13.0)

+ve, Seropositive children.
T0, Time 0; T2, time 2.
[1]Children seropositive at T0 who had one or more blood samples taken to be evaluated for measles antibody levels following vaccination.

and 32 out of 103 (31%) were from rural areas ($P=0.7$).

Table 1 shows the prevalence data and the geometric mean titre (GMT) of the seropositive children at T0 by age and residential area. Fifty-four among the 77 seropositive children at T0 had one or more blood samples taken to be evaluated for measles antibody levels following vaccination. The GMT of the seropositive children was 1:59 at T0, 1:76 at T1, 1:67 at T2 and 1:47 at T3. Seven of the 54 children (13.0%) evaluable for seroconversion or boosting had a fourfold rise in antibody titres one month (T2) after vaccination (Table 2). One hundred and forty-seven seronegative children at T0 (HI titres <1:8 at T0; 83 urban and 64 rural) had two or more blood samples taken to be evaluated for seroconversion. Considering as significant a titre rise from undetectable antibody to seropositivity (⩾1:8) between the T0 and T1 or T2 specimens, 141 (96%) out of 147 evaluable children seroconverted. Seven children out of 141 (5.0%) seroconverted 10 days after vaccination (T1); all the other 134 children (95%) seroconverted after 30 days (T2). Among the six non-responders, five were aged 9–15 months and one was 16 months old (Table 3). The GMT at T2 and T3 of the children who seroconverted, by age and residence area, are reported in Table 4. Geometric mean titres fell between 1 month and 6 months post-vaccination in all age groups.

In the 9 and 11-months age group, 83 out of 107 children, including the seropositive and the seronegative at T0, had one or more blood samples taken to be evaluated for seroconversion. Seventy-five children out of 83 seroconverted; five were non-responders among children seronegative before vaccination and three seropositive at T0 showed no change in their titre following vaccination; the overall seroconversion rate in this age group was 90.3%.

No relevant adverse reaction was reported during the month following the vaccination.

Table 3. Seroconversion rate by age among 147 children seronegative prior to vaccination

Age (months)	Number in group	−ve at T0[1]		Responders	
		n	(%)	*n*	(%)
9	33	31	(93.9)	29	(93.5)
10	21	21	(100)	20	(95.2)
11	29	28	(96.5)	26	(92.8)
12–15	36	24	(66.7)	24	(100)
16–22	33	22	(66.7)	21	(95.4)
23–29	29	11	(37.9)	11	(100)
30–36	20	10	(50.0)	10	(100)
Total	201	147	(73.1)	141	(95.9)

−ve, Seronegative children.

[1]Children seronegative at T0 with one or more blood samples taken to be evaluated for measles antibody levels following vaccination.

DISCUSSION

The success of a measles vaccination campaign should be analysed in relation to vaccination coverage and deficient immune responses in vaccinated individuals, inadequate vaccine preservation, particularly with regard to refrigeration during distribution in remote rural areas, and defective vaccination technique (Walsh 1986). The titration of the vaccine batches used in our study and the demonstration that a seroconversion rate close to 95% can be attained, in urban and rural areas, among those children seronegative prior to vaccination, indicate the adequacy of the cold chain and the effectiveness of the vaccination technique. Furthermore, in our study all the children were vaccinated by the same team from the local Public Health Service, frequently in very difficult working conditions, particularly in rural areas.

The overall seroconversion rate of 90% among the 9–11-month-old children supports the feasibility of vaccine programmes in children before their first birthday (Henderson *et al.* 1988).

The decrease in the post-vaccination titre after 6 months is consistent with the specific antibody decline that normally occurs in the year following vaccination (Ministries of Health PAHO 1982). Further studies will be needed to monitor the titres in the future and to carry out a clinical evaluation as to whether or not these children are protected.

Because our study cannot distinguish between the persistence of maternal antibody and natural infection, it may be possible that the seropositivity in 9-month-old children at T0 could be of maternal origin, though some could also be acquired from undisclosed infection with measles virus. The finding of 16% seropositivity among 9-month-old children, no seropositives among 10-month-olds, and a subsequent steady increase in the proportion of seropositives is consistent with the pre-vaccination antibody being of mainly maternal origin in 9-month-olds and from infection with wild virus in older children.

The high prevalence of seropositivity in the 16–36-month-old children prior to vaccination confirms the frequency of early natural infection in this area of Bolivia, as in many other developing countries (Aaby &

Table 4. Geometric mean titre among responders from urban and rural areas after 1 (T2) and 6 (T3) months from the vaccination

Age (months)	Number in group	GMT of responders from urban area		GMT of responders from rural area	
		T2	T3	T2	T3
9	29	113	28	183	46
10	20	83	46	163	54
11	26	168	50	158	39
12–15	24	214	48	254	54
16–22	21	173	32	316	16
23–29	11	126	63	100	13
30–36	10	158	48	251	16
Total	141	147	45	203	34

T2, Time 2; T3, time 3.

Clements 1989). Among the group seropositive at T0 who could be evaluated for a serological response, the increase in antibody titre in seven children is difficult to evaluate. If the pre-vaccination antibodies were maternal we could consider these children as seroconverters to the vaccine: a small proportion of children with maternal antibody are expected to seroconvert after vaccination with standard titre Schwarz vaccine. Further studies have already been planned to obtain more information on the persistence of maternal antibody in children before their first birthday, with the aim of selecting the appropriate age of vaccination. Our findings suggest that the vaccination coverage reached in this population, although the vaccine is effective, does not prevent the virus from spreading. In this area efforts should be made to raise the vaccine coverage so as to obtain sufficient mass immunity to limit virus diffusion.

ACKNOWLEDGEMENTS

The authors are grateful to Dr R. Vargas, Director of the Epidemiology Department of the Ministry of Social Welfare and Public Health, La Paz, Bolivia, and to Dr R. Rivero, Director of the Health Department of Santa Cruz, for authorization and encouragement to carry out this work. Thanks are also due to Father T. Ciabatti, Coordinator of the Provincia Cordillera Health District, for making their facilities available to us, and to the field team, particularly to Dr L. Pereira, Mr A. Pinto, Mr J. Changaray, Mrs E. Flores, and Sister M. de Pablo, for their helpful assistance. Finally, we wish to thank Mr T. Amato for his skilful technical assistance in serology determinations.

REFERENCES

Aaby P. & Clements C.J. (1989) Measles immunization research: a review. *Bulletin of the World Health Organization* **67**, 443.

Cordecruz-Cipca (1987) Proyecto de salud rural. In *Programa de desarrollo Campesino de Cordillera. PDCC.* Volume 6. (ed. Cordecruz & Cipca), Camiri, Santa Cruz, Bolivia.

Henderson R.M., Keja J., Hayden G. *et al.* (1988) Immunizing the children of the world: progress and prospects. *Bulletin of the World Health Organization* **66**, 535.

Ministerio de Prevision Social y Salud Publica. Direccion Nacional de Epidemiologia (1988) *Plan Operativo del Programa Ampliado de Immunizaciones. Gestion 1989.* La Paz, Bolivia.

Ministries of Health of Brazil, Chile, Costa Rica, Ecuador, and the Pan American Health Organization (1982) Seroconversion rates and measles antibody titers induced by measles vaccine in Latin American children 6-12 months of age. *Bulletin of the Pan American Health Organization* **16**, 272.

Nakano J.H., Miller D.L., Foster S.O. & Brink E.W. (1983) Microtiter determination of measles hemagglutination inhibition antibody with filter papers. *Journal of Clinical Microbiology* **17**, 86.

Sanabria H. (1977) Monografia del Departamento de Santa Cruz. *Boletin de la Sociedad de Estudios Geograficos e Historicos* **30**, 60–77.

Walsh J.A. (1986) Measles. In *Strategies for Primary Health Care. Technologies Appropriate for the Control of Disease in the Developing World* (ed. J.A. Walsh & K.S. Warren). The University of Chicago Press, Chicago, p. 60.