Measles antibody prevalence after mass immunization in São Paulo, Brazil

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In 1987, a mass immunization campaign against measles was carried out in the greater metropolitan region of São Paulo, Brazil. During a ten-day period, 4 194 174 children from 9 months to 14 years old, representing 86% of the target population, were vaccinated regardless of their previous vaccination status. Four months later, the prevalence of measles antibodies was evaluated through a random seroepidemiological survey. The survey included all children in greater São Paulo between one month and 14 years old, irrespective of campaign participation. Blood samples were collected on filter-paper and tested for measles antibody by indirect immunofluorescence. Negative or doubtful cases were tested again using an immunoenzymatic assay (ELISA). Of the 8661 samples included in the study, 8146 (94.1%) were positive for measles antibody. In children aged one year or more a significant difference in antibody prevalence was observed when comparing those who were vaccinated during the mass immunization (98.0%) with those who did not participate in the campaign (91.3%). In addition, after the immunization, a marked and immediate decrease was observed in incidence rates for measles cases notified to the State Secretary of Health, falling from 222/100 000 inhabitants in 1987 to 2.7/100 000 in 1988. These data suggest that mass immunization can serve as an additional strategy for the rapid control of measles in developing countries.

Introduction

Although measles vaccines have been available since 1963, the infection continues in many parts of the world, causing more than 2 million deaths every year (*1*). In Brazil, measles represents a serious public health problem. In 1986, 129 126 measles cases were reported nationally with an incidence rate of 94.5 per 100 000 inhabitants. The number of unreported cases is not known so that the true number of cases must be higher than this figure.

The metropolitan region of São Paulo, also known as greater São Paulo, is the largest urban centre in Brazil, including the capital of the state of São Paulo and 37 neighbouring municipalities. In 1987, greater São Paulo had a population of 15 990 850 inhabitants. In this region, despite an immunization programme against measles since 1973, epidemics of measles have occurred every 2 to 4 years. In 1986, when 84% of 9-month-olds had received measles vaccine, household inquiries dis-

closed an incidence of 1636 cases per 100 000 inhabitants aged 15 years or less. The use of a single dose of measles vaccine before 10 months of age has been shown to be one of the factors contributing to these findings since, in this age group, the serological efficacy of the vaccine in São Paulo does not exceed 80% (*2, 3*). After some years this results in a significant clustering of susceptible individuals who can maintain the virus circulation within the population. A second dose of measles vaccine after 1 year of age was recommended, but measles control has not been achieved owing to frequent logistical difficulties in contacting children for the second dose.

Based on the above, the Center for Epidemiological Surveillance, a branch of the State Department of Health of São Paulo, initiated a statewide immunization campaign against measles. From 11 to 22 May 1987, measles vaccine was given to 4 194 174 children aged from 9 months to 14 years regardless of their previous vaccination status. It is estimated that this mass immunization reached 86% of the target population.

The present study evaluated the prevalence of measles antibody within this population at four months after the immunization.

Materials and methods

Population. The population in the survey was composed of the residents of greater São Paulo, born between 10 September 1973 and 31 August 1987. In addition to the target group for immunization

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during the campaign, which included children from 9 months to 14 years old, the sample also included children who were between 1 and 8 months old during the campaign. This latter group was included in order to examine the time of waning of measles antibodies of maternal origin.

Sampling. The sampling plan was based on probability sampling, with 2-stage selection, applied independently in each municipality of the metropolitan region of greater São Paulo. Census sectors were adopted as primary sampling units and secondary sampling units were private households or family units in collective households within each census sector.

First-stage selection was made with a probability that was proportional to the number of households within the sector, 444 sectors being selected. For the second stage all households within the drawn sectors were listed, and a random selection of these was made, an average of 11 households per sector being selected. There was no screening for previous vaccination or natural measles in the past.

Interview. Data were collected by means of a questionnaire completed in each household unit. Informants were the mothers or other adults responsible for the children in the study. Interviews and blood sample collection on filter-paper were performed by auxiliary nurses.

Analysis. Regarding the precision of the estimates, 95% confidence intervals were constructed for antibody prevalence against measles, taking into account the characteristics of the sampling process (5). For the analysis of the results the χ^2-test was used.

Blood sample collection for serology. Blood samples for serology were collected on filter-paper by finger or heel punctures employing techniques previously described (6). In brief, the filter-paper rectangles (Whatman, No. 1) were marked with two circles 2 cm in diameter. Both delimited areas were completely filled with blood from each patient. After drying, the samples were maintained at 4 °C until elution, which was performed within 24–48 hours of collection. For elution, the two blood-filled circles were sliced out of the filter-paper and placed in a tube containing 0.5 ml buffered saline, pH 7.2. Tubes were held at an angle for 24 hours at 4 °C. The resultant eluate was considered to be serum diluted 1:5.

Serology. Initially each sample was tested by indirect immunofluorescence (IFA). Negative or doubtful cases were tested again using an enzyme-linked immunosorbent assay (ELISA). For the purpose of the present study, seronegativity was defined as the absence of specific antibody in both the IFA and the ELISA, while seropositivity was defined by presence of antibody in either the IFA or the ELISA. The IFA reaction and the ELISA test were performed as described elsewhere (7–9).

Results

Of 8699 samples tested for specific antibodies to measles virus by indirect immunofluorescence 7434 (85.5%) were positive and 766 (8.80%) were negative. An additional 499 samples (5.7%) showed doubtful results, even after repeating the reaction, and were therefore classified as indeterminate. Of the 1265 sera with negative or indeterminate results by IFA, 1227 were tested again using the more sensitive immunoenzymatic assay (ELISA) and 712 (58.0%) were positive; 38 samples (0.44%), which could not be tested by ELISA due to the lack of eluate, were excluded from further analysis, resulting in a final sample number of 8661.

Using both IFA and ELISA the total specific antibody prevalence increased from 85.5% to 94.1% (8146/8661). Analysis of seropositivity according to different age groups revealed that for the children aged between 4 and 8 months 77.5% (158/204) of the samples were negative, while for those between 1 and 14 years of age only 3.4% (275/8163) were negative. Confidence intervals were calculated taking into account the design of this study (Table 1).

Measles antibodies were found in 97.3% (36/37) of newborns, reflecting indirectly the immune status of the adult population. Thereafter, a progressive decrease in antibody prevalence was observed. At 7–8 months of age only 6.8% of infants had detectable antibodies using both IFA and ELISA. However, at 9 months of age, when measles immunization begins, a marked increase in antibody prevalence was observed (Table 1).

Children presenting written evidence of participation in the mass immunization and who were aged one year or more at that time were found to have an antibody prevalence of 98.0% (4804/4901). In contrast, antibody prevalence in a similar group of children one year or older who did not participate in the campaign was 91.3% (861/943).

A striking difference was observed in children 1 to 4 years old. In this age group, 96.9% (1567/1617) of the children immunized during the mass campaign had measles antibody, as compared with 83.3% (165/198) of their age-matched controls who did not receive the vaccine.

Comparison of antibody prevalence by age groups with their respective confidence intervals,

Table 1: **Antibody prevalence against measles, four months after mass immunization, as detected by IFA and ELISA, according to age, in greater São Paulo, 1987**

Age	Serology	
	No. positive/total	Confidence interval (%)
<1 month	36/37 (97.3)[a]	91.25–103.35
1–3 months	97/112 (86.6)	79.31–93.91
4–6 months	41/130 (31.5)	22.29–40.79
7–8 months	5/74 (6.8)	0.14–13.38
9 months	11/46 (23.9)	9.64–38.18
10–11 months	68/99 (68.7)	58.11–79.26
1–4 years	2234/2370 (94.3)	93.18–95.35
5–6 years	1265/1307 (96.8)	95.68–97.89
7–9 years	1807/1858 (97.3)	96.40–98.12
10–14 years	2582/2628 (98.3)	97.67–98.83
Total	8146/8661 (94.1)	93.67–94.62

[a] Figures in parentheses are percentages.

shows that participation in the mass immunization campaign was associated with a significant rise in prevalence of specific antibodies for measles in all age groups (Table 2).

Discussion

Our data show that four months after a mass immunization campaign against measles in greater São Paulo, 96.6% (7888/8163) of children aged from 1 to 14 years had detectable measles antibodies. This suggests that virus circulation would be very low in this sector of the population. It has been suggested that for permanent control of measles within a population collective immunization levels of at least 94% would be required (10, 11). On the other hand, for the age group from 4 to 8 months, 77.5% (158/204) of the children studied did not have antibodies against measles and could therefore serve as a susceptible population in which virus circulation could be maintained. During an outbreak of measles in Brazil, in 1983, it was shown that in 93.3% of

measles cases in children aged less than one year the source of infection was a child older than one year. Children between 1 and 4 years old accounted for 60% of the sources (12). Therefore, the high prevalence of measles antibodies following mass immunization of children between 1 and 14 years old in greater São Paulo, as observed in this study, is likely to be an important factor in the control of intra-familial transmission of measles to this pool of susceptibles. This is particularly true in the group of 1–4-year-olds whose antibody prevalence was 96.9% following the mass immunization campaign. The prevalence rate for children between 1 and 4 years old who did not participate in the immunization campaign was 83.3% ($P = 0.05$) and this difference can represent an indirect measurement of the impact of mass immunization in this important age group.

In a population which has an antibody prevalence above 80% the costs and benefits of indiscriminate vaccination are difficult to evaluate. Nevertheless, in greater São Paulo, although routine two-dose vaccination has been used since 1979 for the age group of 7 to 15 months, and vaccine coverage is over 80%, the incidence rates for measles have remained high in recent years. After the mass immunization campaign here described, a rapid decrease was observed in incidence rate for measles cases notified to the State Department of Health among under-14-year-olds, with 222 cases per 100 000 inhabitants reported in 1987 but only 2.7/100 000 in 1988. These data show that in the metropolitan region of São Paulo mass immunization for measles control has succeeded and can be proposed as an additional strategy for a rapid increase of vaccine coverage and control of measles in developing countries.

Acknowledgements

Table 2: **Antibody prevalence against measles, four months after mass immunization, as detected by IFA and ELISA, according to age and whether present at the mass immunization, in São Paulo, 1987**

Age group (years)	Not present		Present	
	No. positive/total	Confidence interval (%)	No. positive/total	Confidence interval (%)
1–4	165/198 (83.3)[a]	77.65–89.02	1567/1617 (96.9)	96.06–97.75
5–6	92/102 (90.2)	84.12–96.27	791/808 (97.9)	96.91–98.89
7–9	183/202 (90.6)	86.36–94.82	1096/1113 (98.5)	97.75–99.19
10–14	421/441 (95.5)	93.48–97.45	1350/1363 (99.1)	98.53–99.56
Total	861/943 (91.3)	89.28–93.38	4804/4901 (98.0)	97.57–98.47

[a] Figures in parentheses are percentages.

Résumé

Prévalence des anticorps antirougeoleux à São Paulo, Brésil, après vaccination de masse

En 1987, on a mené une campagne de vaccination antirougeoleuse de masse dans le grand São Paulo, le plus grand centre urbain du Brésil englobant la capitale de l'Etat (ville de São Paulo) et 37 municipalités avoisinantes, soit une population totale de 15 990 850 habitants. Malgré le programme classique de vaccination antirougeoleuse instauré dès 1973, des épidémies de rougeole ont continué à se déclarer tous les 2 à 4 ans. En 1986, alors que 84% des enfants de 9 mois avaient été vaccinés, des enquêtes à domicile ont révélé une incidence de 1636 cas de rougeole pour 100 000 habitants chez les 0 à 15 ans. C'est sur la base de ces données qu'une campagne de vaccination de masse a été menée en mai 1987. Pendant 10 jours, 4 194 174 enfants ayant entre 9 mois et 14 ans, représentant 86% de la population cible, ont été vaccinés quels que soient leurs antécédents vaccinaux. Quatre mois plus tard, on a évalué la prévalence des anticorps antirougeoleux dans cette population au moyen d'une enquête séro-épidémiologique, fondée sur un échantillonnage probabiliste, avec sélection en 2 temps, auquel on a procédé séparément dans chaque municipalité de la région du grand São Paulo. On a adopté les secteurs du recensement comme unités primaires d'échantillonnage, et les foyers privés ou les cellules familiales des habitations collectives comme unités secondaires. Dans un premier temps, 444 secteurs ont été choisis, la probabilité pour l'un d'entre eux d'être choisi étant proportionnelle au nombre de foyers dans ce secteur. Dans un second temps, on a établi la liste de tous les foyers des secteurs choisis et on a opéré une sélection au hasard, en retenant en moyenne 11 foyers par secteur.

Les prélèvements sanguins ont été recueillis sur papier filtre et passés en immunofluorescence indirecte, à la recherche d'anticorps. Les cas négatifs ou douteux ont été retestés par titrage immuno-enzymatique (ELISA). Sur les 8661 échantillons testés, 8146 (94,1%) ont montré la présence d'anticorps antirougeoleux. On a observé une différence significative de prévalence des anticorps entre les enfants ayant au moins un an et qui avaient été vaccinés pendant la campagne de masse (98,0%), et les enfants du même groupe d'âge qui n'avaient pas participé à cette campagne (91,3%). Après la campagne de vaccination de masse, il y a eu une diminution rapide du nombre de cas de rougeole notifiés au Département d'Etat à la Santé chez les moins de 14 ans, qui est passé de 222 pour 100 000 en 1987 à 2,7 pour 100 000 en 1988. Dans l'ensemble, ces données laissent à penser que la vaccination antirougeoleuse de masse a bien été une réussite dans la région urbaine de São Paulo, et que c'est une stratégie qui peut être proposée pour éliminer rapidement la rougeole dans les pays en développement.

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