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# SEROLOGIC RESPONSE TO SEROGROUP C MENINGOCOCCAL VACCINE IN BRAZILIAN PRESCHOOL CHILDREN

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## SUMMARY

One hundred thirty-three children, 6 months to 6 years old, given 50 μg of a serogroup C meningococcal polysaccharide vaccine during a vaccine trial in the city and suburbs of São Paulo, were studied prior to and 1 month after vaccination; a radioactive immunoprecipitin test was used to measure the antibody response. Almost all children responded with a measurable rise in antibody titer; older children had a slightly higher post-vaccination titer. The effectiveness of the serogroup C meningococcal polysaccharide vaccine in preventing disease will be determined by the field trial of the same vaccine.

## INTRODUCTION

In 1972 the City of São Paulo experienced a large outbreak of meningococcal meningitis due to sulfonamide-resistant serogroup C *Neisseria meningitidis*. There were 1,447 cases, with the highest attack rates in preschool children [10]. In association with studies of the effectiveness of chemoprophylaxis in household contacts of cases [11], the Federal Ministry of Health and the Secretary of Health of São Paulo initiated a program to study the effect of a serogroup C meningococcal polysaccharide vaccine in preventing disease in children. Vaccine was available for only a limited number of children in the preschool age groups, and was distributed at 23 vaccination centers over a period of 2 weeks in late December 1972.

The meningococcal serogroup C polysaccharide vaccine prevents meningitis in adults [1, 3, 4, 6], but it had not been studied for its ability to prevent disease in children. The vaccine was found to be safe and to stimulate antibody in a small number of infants and children [2, 7].

This report concerns the serologic response to a 50 μg dose of meningococcal polysaccharide vaccine given to children between 6 months and 6 years of age, as part of a larger trial to measure the efficacy of the polysaccharide vaccine in preventing meningococcal disease in preschool children in São Paulo.

## MATERIALS AND METHODS

The serogroup C meningococcal polysaccharide vaccine was obtained from a lot pre-

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pared by Merck Sharp and Dohme for the United States Army. The lyophilized vaccine had been stored until 4 days before the study, when it was diluted to a concentration of 100 μg/ml. The diluted vaccine was stored in 50-dose vials at 4°C until used in doses of 0.5 ml containing 50 μg of polysaccharide. A diphtheria-tetanus toxoid was prepared in 50-dose vials at the Instituto Butantan, and given in doses of 0.5 ml. Vials of meningococcal polysaccharide and diphtheria-tetanus toxoid were wrapped in aluminum foil so that the bottles were indistinguishable.

Children 6 months to 6 years old who came to the vaccination center at the Hospital do Servidor Público Estadual "Francisco Morato de Oliveira" (HSPE) on December 15 and 16, 1972, were bled from the antecubital vein and then given by pedojet an intramuscular injection of 0.5 ml of either meningococcal polysaccharide vaccine or diphtheria-tetanus toxoid. Twenty-eight days later the children were bled again, and those who had been given diphtheria-tetanus toxoid were given meningococcal polysaccharide. The collected blood specimens were allowed to clot, and the serum was separated and stored in a −70° freezer in aliquots.

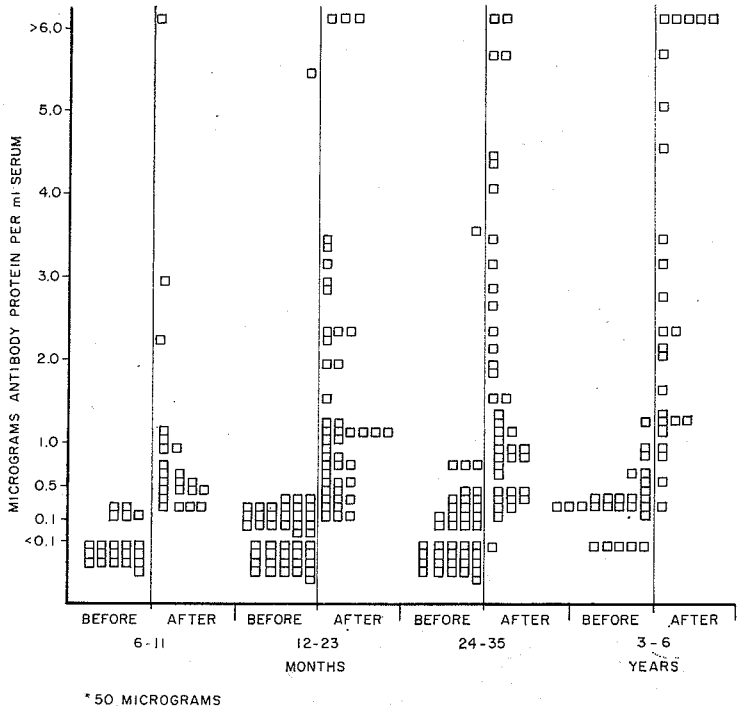
Serologic responses were measured with the radioactive immunoprecipitin test of Farr as modified by GOTSCHLICH [8]. All serum samples were tested in duplicate and the results expressed as μg of antibody protein per ml of serum.

Paired sera were available on 133 children given only meningococcal vaccine and on 33 children who received toxoid first.

## RESULTS

One of 33 children who received diphtheria-tetanus toxoid showed an antibody res-

SEROGROUP C MENINGOCOCCAL ANTIBODY BEFORE AND 4 WEEKS AFTER RECEIVING SEROGROUP C MENINGOCOCCAL POLYSACCHARIDE* IN CHILDREN 6 MONTHS - 6 YEARS, SAO PAULO, BRAZIL, DECEMBER 1972




*50 MICROGRAMS

ponse to the polysaccharide of serogroup C *N. meningitidis* during the month of study. Only 3 of these 33 children had antibody levels greater than 0.38 μg/ml. The prevaccination levels and serologic response to the 50 μg of serogroup C meningococcal polysaccharide in 133 children are shown in Fig. 1.

The prevaccination geometric mean values increased with increasing age (Table I).

TABLE I

Prevaccination serogroup C meningococcal antibody values in relation to age, São Paulo, December 1972

| Age | Number of children | Geometric mean(*) antibody values (± 2 SE) |
|---|---|---|
| 6-11 mo. | 22 | .11 (.10-.13) |
| 1 year | 45 | .14 (.12-.17) |
| 2 year | 40 | .18 (.14-.23) |
| 3-6 year | 26 | .21 (.16-.28) |

(*) Micrograms/ml

The post-vaccination sera showed a similar change with age (Table II).

TABLE II

Post-vaccination serogroup C meningococcal antibody values in relation to age, São Paulo, December 1972

| Age | Number of children | Geometric mean(*) antibody values (± 2 SE) |
|---|---|---|
| 6-11 mo. | 22 | .69 ( .48-1.01) |
| 1 year | 45 | 1.11 ( .81-1.53) |
| 2 year | 40 | 1.19 ( .85-1.69) |
| 3-6 year | 26 | 2.29 (1.47-3.58) |

(*) Micrograms/ml

When serum pairs were analyzed separately by age and antibody prior to vaccination, children with the low prevaccination values (less than 0.1 μg/ml) had lower post-vaccination values although only in the 2 year age group were the differences significant below the 5 percent level.

TABLE III

Comparison of post-vaccination serogroup C antibody responses in relation to prevaccination levels and age, São Paulo, 1972

| Age | Prevaccination value < 0.1 μg/ml | | Prevaccination value 0.1 μg/ml or greater | |
|---|---|---|---|---|
| | Number of children | Geometric mean (*) (± 2 SE) | Number of children | Geometric mean (*) (± 2 SE) |
| 6-11 mo. | 17 | .67 (0.48-0.92) | 5 | .79 (0.21-3.04) |
| 1 year | 21 | 1.00 (0.65-1.54) | 24 | 1.22 (0.76-1.95) |
| 2 year | 19 | .68 (0.45-1.04) | 21 | 1.99 (1.28-3.10) |
| 3-6 year | 5 | 1.14 (0.76-1.72) | 21 | 2.71 (1.61-4.56) |

(*) Micrograms/ml

## DISCUSSION

The prevaccination titers to serogroup C meningococcal polysaccharide in children in São Paulo were similar to those found in preschool children in the United States [5] and in Africa [8], with no indication that children in São Paulo had a higher percentage

of prevaccination immunity to the polysaccharide of serogroup C *N. meningitidis*, even though meningococcal disease had been epidemic in the city since July 1971 [10].

The older the age group of children, the higher the post-vaccination antibody level in response to the injection of 50 μg of meningococcal polysaccharide. This age-related response has been described in earlier studies of meningococcal vaccine in children in the United States using serogroup C and serogroup A meningococcal vaccines [5, 9].

This children in this study came from many parts of the city and suburbs of São Paulo but were not representative of children in the meningococcal polysaccharide vaccine trial in São Paulo. The children came to the HSPE center because their parents were employees of the São Paulo State Government. Many of the other vaccine centers in the city were used by persons from lower socioeconomic groups, which were not well represented in the HSPE center.

The results of the field trial to evaluate the effectiveness of the serogroup C meningococcal vaccine in preventing disease will show if the antibody induced by the vaccine was sufficient to prevent disease.

RESUMO

*Resposta sorológica à vacina meningocócica do sorogrupo C, em crianças brasileiras de idade pré-escolar*

A 163 crianças, com idades de 6 meses a 6 anos, foi administrada, durante campanha que teve lugar na cidade de São Paulo e em áreas suburbanas da mesma, uma dose de 50 μg de vacina antimeningocócica, elaborada com polissacáride de germes do sorogrupo C. Em amostras de soro obtidas antes da vacinação e um mês após foram determinados os teores de anticorpos, por meio de teste radioativo de imunoprecipitação, a fim de ser avaliada a resposta conseqüente ao uso de recurso preventivo citado.

A eficácia da vacina em questão, no sentido de evitar a ocorrência de doença, depende das observações em curso nas regiões onde ela foi empregada.

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