Persistence of Antibodies Induced by Measles-Mumps-Rubella Vaccine in Children in India

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Antibody levels in 41 Indian girls were measured 6 years after measles-mumps-rubella (MMR) vaccination. Rates of seropositivity were 88% (measles antibodies), 95% (mumps antibodies), and 100% (rubella antibodies). The MMR vaccine induces long-term immunity in a majority of vaccinees; however, due to the observation of some seronegative vaccinees, the policy of administering a second dose of the MMR vaccine seems appropriate.

Measles outbreaks in immunized populations have been reported previously (7, 13). Similarly, mumps outbreaks in highly vaccinated populations (4, 10), including the recent large epidemic in the United States (5), have occurred. Both primary vaccine failure and waning immunity are responsible for the outbreaks in vaccinated populations. The infective dose and the vaccine strain are important factors for long-lasting immunity (6).

In India, the measles-mumps-rubella (MMR) vaccine is manufactured by the Serum Institute of India Ltd. at Pune. The vaccine contains Edmonston-Zagreb measles virus, Leningrad-Zagreb mumps virus, and RA 27/2 rubella virus. Studies of Indian children using this vaccine have shown over 95% seroconversion against measles and rubella and 90% seroconversion against mumps (2, 12). The antibody persistence study would indicate the likely duration of protection afforded by the vaccine. Therefore, the present study was undertaken to assess the antibody titers persisting in a previously vaccinated pediatric population.

In November and December 1999, 99 healthy children aged 1 to 10 years from Kusumbai Motichand Mahila Seva Gram, Karve Road, Pune, an organization for the rescue and rehabilitation of women and children, were given a single dose of an MMR vaccine (Serum Institute of India Ltd.) for the first time. The present study was conducted between April and August 2005 to assess the persistence of antibodies. The serological tests were conducted in the quality control department of the Serum Institute of India Ltd.

The study was approved by the ethics committee of the Serum Institute of India Research Foundation. Informed written consent from the legal guardian of each child or the warden of the institute and signed assent from the subjects were obtained. Forty-one children from this group were available for follow-up in 2005. Acute febrile illness, any other infection, conditions associated with immunosuppression, the receipt of immunosuppressive therapy, and participation in any other clinical trial within 1 month before and during the course of the study were criteria for exclusion.

In 1999, the batch number of the vaccine used was 320-V (expiration date, August 2001). A 0.5-ml dose of reconstituted vaccine was given subcutaneously. In 2005, measles and rubella immunoglobulin G (IgG) antibodies were assayed by the enzyme-linked immunosorbent assay technique using Trinity Biotech kits. Mumps IgG antibodies were assayed by using a Calbiotech Inc. kit. For measles and rubella antibodies, immune status ratios of >1.1 were interpreted as seropositive. For data analysis, values below 1.1 were considered negative. For mumps antibodies, antibody indices of >1.1 were seropositive. For data analysis, values of ≤1.1 were considered negative.

The proportion of seropositive vaccinees and the geometric mean of IgG antibody levels were calculated, along with 95% confidence intervals (95% CI). For geometric mean titer calculations, exact titers were used even for equivocal and seronegative results.

Of 99 original vaccinated subjects, 19 were males and 66 were females. Forty-one of the 99 subjects were available for follow-up analysis. All 41 subjects met the inclusion criteria, and none were excluded from study. The mean age of the subjects was 14.04 years (standard deviation, 1.80 years; range, 8 to 16 years). All the subjects were females. None of the males were available for follow-up.

The number of children seropositive for measles IgG was 36 (88%; 95% CI, 74 to 96%); 39 were seropositive for mumps IgG (95%; 95% CI, 83 to 99%), and 41 were seropositive for rubella IgG (100%; 91 to 100%). The geometric means of antibody titers are given in Table 1.

A study by Boullanne et al. (3) found that 5 to 6 years after the immunization of children with MMR II (Merck Sharp and
TABLE 1. Geometric means of immune status ratios (measles and rubella antibodies) and antibody indices (mumps antibodies)a

| Antibody type | Geometric mean ratio or antibody index | 95% CI for geometric mean | GSD |
|---------------|--------------------------------------|--------------------------|-----|
| Measles       | 1.8612                               | 1.6158–2.1444            | 1.5653 |
| Mumps         | 1.4484                               | 1.3508–1.5535            | 1.2482 |
| Rubella       | 2.2746                               | 2.1662–2.3884            | 1.1671 |

a Forty-one subjects were included in the study. GSD, geometric standard deviation (antilog of standard deviation of log titer values).

Dohme) and Trivirix (SmithKline Beecham) vaccines, the proportions of children seronegative for antibodies were as follows: measles, 3.6% (Trivirix) and 12% (MMR II); mumps, 7% (Trivirix) and 14.9% (MMR II); and rubella, 3.1% (Trivirix) and 3.3% (MMR II). For measles and mumps, the proportions were significantly higher with MMR II than with Trivirix. The proportions of seronegative vaccinees in our study were as follows: measles, 12.5%; mumps, 4.82%; and rubella, 0. Trivirix is no longer in use.

Usonis et al. (9) compared mumps antibody titers detected by enzyme-linked immunosorbent assays 18 months after the vaccination of 12- to 24-month-old infants with either Priorix (SmithKline Beecham) or M-M-R II. Seropositivity rates were 80 to 81% with both vaccines, suggesting that the two vaccines provided equivalent protection against mumps over this 18-month period.

Though statistical comparison was not possible, for the measles component, our results seem to be comparable to those with MMR II in the Boullanne study (3). For mumps and rubella antibodies, our results seem to be better than those with MMR II. Similarly, the degree of persistence of mumps antibodies in our study was higher than those reported by Usonis et al. (9).

We conclude that a single dose of the MMR vaccine from the Serum Institute of India Ltd. gives long-term seropersistence of antibodies against all three individual diseases in a majority of vaccinees. However, some of the vaccinees may be still at risk for measles and mumps infections. It is for this reason that the World Health Organization (1) and the Advisory Committee on Immunization Practices (11) have recommended two doses of an MMR vaccine. The Indian Academy of Pediatrics (8) also recently updated their position to include two doses of an MMR vaccine in the immunization schedule. In fact, by December 2005, two-dose schedules had been implemented in >80% of the 110 countries that have included a mumps vaccine in their national immunization programs (1). The results of the present study further reinforce this policy.

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