

Persistence of Antibody in Human Subjects for 7 to 10 Years following Administration of Combined Live Attenuated Measles, Mumps, and Rubella Virus Vaccines (40967)

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Abstract. Antibody persistence was measured in children in the open community 10.5 years after combined measles-mumps-rubella (14 children), 9 years after measles-rubella (17 children), 10.5 years after mumps-rubella (9 children), and 7 years after measles-mumps (20 children) vaccines were given. There were increases, declines, and stationary titers among the children in the serum samples taken 6 weeks after vaccination compared with those taken at later time periods. This reflected a decline in antibody in some children and subclinical natural reinfection in others. Importantly, all the children still retained detectable antibody, indicating long-term persistence of immunity by vaccination with combined virus vaccines.

An outstanding attribute of live attenuated virus vaccines is the long-term persistence of antibody and of immunity following administration to susceptible persons. The presence of circulating antibodies against measles, mumps, and rubella virus is the basis for protection against the natural disease.

Combined live measles-mumps-rubella (M-M-R), measles-mumps (M-M-VAX), measles-rubella (M-R-VAX), and mumps-rubella (BIAVAX), were licensed for general use between 1970 and 1973. These vaccines make possible immunization against more than one virus by means of a single injection of vaccine. The Moraten measles, Jeryl Lynn mumps, and HPV-77 duck embryo vaccine virus strains were used in the vaccines. This report presents follow-up studies to measure levels of antibodies 7 to 10.5 years following vaccination in field trials that were initiated between 1968 and 1972.

Materials and methods. The vaccines and clinical trials in which they were investigated were described previously (1-7). The methods for surveillance were given in earlier reports (1-4). The late bleedings required to carry out the present investigations were obtained during March-June 1979, with informed written consent, and in

compliance with the Investigative New Drug Laws. The preceding blood samples were obtained 6 weeks after vaccination and at 2- to 3-year intervals thereafter. The serum samples were tested for antibodies using procedures described previously (8-10). In the tests, the next previous serum sample was reassayed in the same test together with the new serum sample and the same test procedure was employed throughout. The close agreement in the values obtained provided assurance that differences in serum titer were not being introduced by the test itself. The parents, guardians, or children were queried at the time of the late bleedings as to whether they had been revaccinated or had experienced measles, mumps, or rubella in the intervening period following vaccination. None of the children was revaccinated and none developed any of the corresponding illnesses since the time of vaccination.

Results. Combined measles-mumps-rubella vaccine. A total of 30 initially seronegative children were given combined measles-mumps-rubella vaccine in a study in suburban Philadelphia between September 26 and October 10, 1968 (2). A sample of 14 children was bled 10.5 years after vaccination. Measles and rubella hemagglutination-inhibiting (HI)

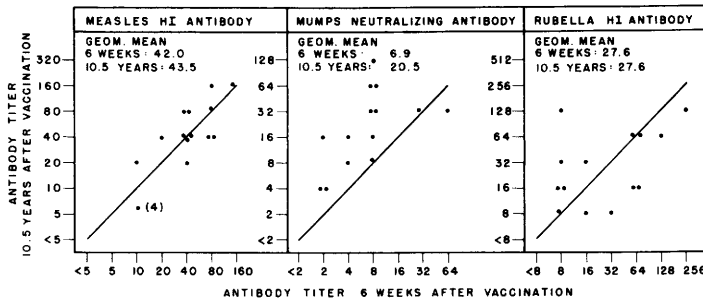


Fig. 1. Retention of measles, mumps, and rubella antibodies 10.5 years after vaccination with combined live measles (Moraten)-mumps (Jeryl Lynn)-rubella (HPV 77-DE) virus vaccine (Study 212).

antibodies and mumps-neutralizing antibody titers were compared with those found 6 weeks after vaccination. The findings shown in Fig. 1 revealed that all children retained antibody against all the viruses. Decreases and increases in antibody were evident. The geometric mean titers of measles and rubella antibodies were roughly the same after 10.5 years as they were 6 weeks after vaccination. By contrast, the mean neutralizing antibody titer against mumps had increased markedly, probably as the result of subclinical mumps virus reinfection in some of the subjects.

Combined measles-rubella vaccine. Of 128 initially seronegative children in the greater Philadelphia community 17 were given combined measles-rubella vaccine between April 9 and June 11, 1970, and were bled 6 weeks and 9 years after vac-

ination (3). The findings in the tests for homologous antibodies are shown in Fig. 2. The geometric mean antibody titers declined somewhat over the 9-year period. However, all children still had detectable measles and rubella antibody.

Combined mumps-rubella vaccine. The combined mumps-rubella vaccine was administered in September and October 1968 in suburban Philadelphia (1). Serum samples taken from nine initially seronegative children 6 weeks and 10.5 years after vaccination were tested for homologous antibodies. As seen in Fig. 3, the geometric mean mumps-neutralizing antibody titers at 6 weeks and 10.5 years were essentially the same. The mean rubella antibody titers declined to slightly less than half the 6-week value. All children had detectable antibody against both viruses.

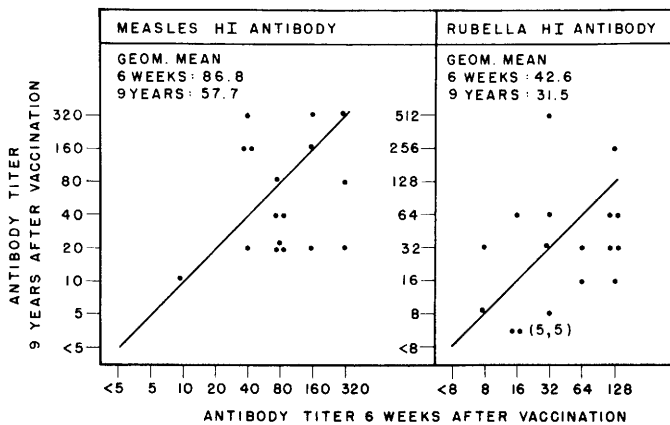


Fig. 2. Retention of measles and rubella antibodies 9 years after vaccination with combined measles (Moraten)-rubella (HPV 77-DE) vaccine (Study 244).

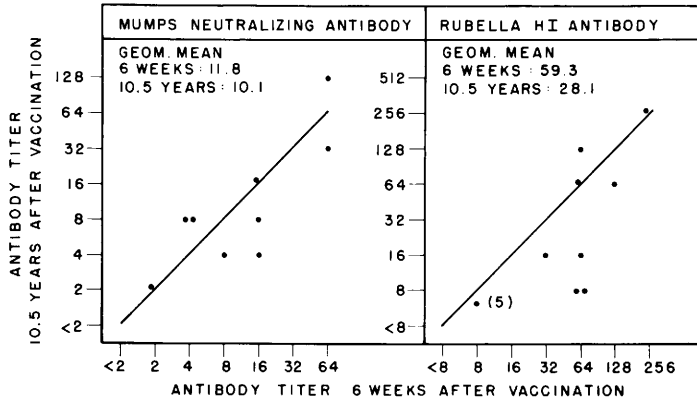


FIG. 3. Retention of mumps and rubella antibodies 10.5 years after vaccination with combined live mumps (Jeryl Lynn)–rubella (HPV 77-DE) virus vaccine (Study 212).

Combined measles–mumps vaccine. Twenty initially seronegative children who were given combined measles–mumps vaccine between January 19 and April 19, 1972, in suburban Philadelphia were bled 6 weeks and 7 years after vaccination (4). The results of the tests for homologous antibodies are shown in Fig. 4. There were individual declines and increases in antibody levels, probably reflecting a decrease in titer or subclinical reinfection in some persons. Measles hemagglutination-inhibiting antibody was not detectable in the serum of one of the children but serum-neutralizing antibody was shown to be present. There was an approximate three-fold decline in the mean measles antibody titer, but the mumps mean titer was about the same as at 6 weeks.

Discussion. The use of monovalent and combined measles, mumps, and rubella virus vaccines in the United States has been followed by dramatic declines in the incidence of these diseases (11, 12). Homologous circulating antibody following these combined vaccines persisted up to 10.5 years in the sera from all of the recipients. The height of antibody needed to protect is very small and is probably smaller in amount than detectable in laboratory tests.

The occurrence, in recent years, of clinical measles among persons who had been vaccinated (11, 13–19) has been explained on several bases: (1) use of killed virus vaccine that affords only short-term immunity, (2) the usual and expected failure of serologic response in 2 to 5% of persons who were given vaccine under proper con-

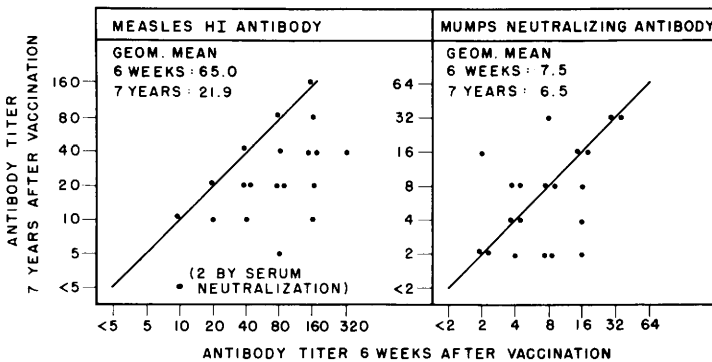


FIG. 4. Retention of measles and mumps antibodies 7 years after vaccination with combined measles (Moraten)–mumps (Jeryl Lynn) vaccine (Study 296).

ditions, (3) the use of live measles vaccine of low or no potency owing to improper handling, storage temperature, overexposure to light, etc., (4) administration of the vaccine concomitantly with human immunoglobulin as originally carried out routinely with Enders' original vaccine or was improperly done with more attenuated measles virus vaccine, and (5) neutralization of live virus in the vaccine by maternal measles antibody.

Live attenuated measles, mumps, and rubella virus vaccines have performed exceptionally well and continue to provide long-lasting and possibly lifelong protection against clinical disease, similar to natural immunity, despite lower initial antibody titers and frequent subclinical infection following vaccination. This acceptable performance has been found with the combined vaccines as well, and antibody stimulated with combined vaccine shows the same high frequency of persistence as that following the single vaccines. Antibody, in some individuals, may fall to low titer values but any detectable amount of antibody, in all but rare instances, is protective against measles, mumps, and rubella (20-23). It is of little consequence that subclinical reinfection followed by antibody production may occur in nature in vaccinated persons since protection against the disease is afforded.

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