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Long-Term Persistence of Antibody following Enders' Original and More Attenuated Live Measles Virus Vaccine (39564)

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Enders' original live attenuated measles virus vaccine (1-3) was first licensed for general use in 1963. Because of febrile and other reactions, human immune globulin containing measles virus antibody was most often coadministered with the vaccine (4). More attenuated measles virus vaccine (Moraten line, Attenuvax) (5) was introduced in 1968. This vaccine is made of highly attenuated virus and is given without immune globulin.

Concern has been expressed (6-9) in recent years for the increased incidence of measles in children, some of whom were previously vaccinated. These real and purported vaccine failures have been found to be of various causes, as will be discussed below. The present report describes the persistence of measles antibody for 15 years in children who received Enders' original measles vaccine with human immune globulin and for 8 years following Moraten line vaccine or Enders' original vaccine given without immune globulin.

Materials and methods. Study 17 (2-4). Initially seronegative children, 1 to 7 years of age, who resided in open populations in the Philadelphia area, were given at the same time but in opposite arms Enders' original live attenuated measles virus vaccine and 0.02 ml/lb body weight of human immune globulin. The vaccine was given between December 7, 1960, and October 11, 1961. A sample of subjects were bled prior to, 4 weeks, and aproximately 15 years following vaccination. Sera for comparative purpose were also collected from unvaccinated children who experienced natural measles about the same time or within a few months following the time when the vaccine was given.

Study 97 (5). Groups of 258 to 273 initially seronegative children, residing in open populations in the Philadelphia suburbs, were given Enders' original Edmonston vaccine or the Moraten (Attenuvax) more attenuated measles vaccine during May and June of 1967. These children have been under continuing surveillance for persistence of antibody since that time. The present report concerns the findings with sera from a representative sample of children taken 1 month and 8 years after vaccination. All sera were stored frozen at $-20°$ until tested. All selections of children in both studies were at random.

Antibody assay. The sera were titrated for content of measles hemagglutination-inhibiting (HI) antibody by a standardized procedure (10) employed here. Both serum samples for each subject were tested together in the same test.

Results. Figure 1 shows the persistence of measles antibody in persons who received the Enders' vaccine with human immune globulin. The geometric mean titers were 1:25, 1 month after vaccination, and 1:28, 15 years after vaccination. Decline or increase in antibody titers was shown in more than half of the individuals. Importantly, none of the subjects had become seronegative within the 15-year period. The pattern for antibody persistence was not remarkably different from that following natural measles, except that increase in antibody was more frequent in vaccinees, suggesting a higher rate for reinfection with measles virus in nature. The mean antibody titers following the natural disease were about 3.5 times higher than following vaccination.

The persistence of measles HI antibody 8

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years following vaccination with Enders' original and Moraten measles vaccines is shown in Fig. 2. Decreases and increases in antibody titer were evident in both groups due, probably in part, to loss of antibody and to reinfection with measles virus in nature. Only one of the antibody levels fell to zero value and this was in a recipient of Enders' original vaccine. The mean titers were retained remarkably well.

Discussion. The occurrence of measles in children who had been vaccinated has been recorded in several studies (6-9). Failures of vaccination have been found due to a number of contributory factors including (a) use of killed measles virus vaccine that affords only short-term immunity; (b) the usual and expected failure of serologic response in 2 to 5% of persons who were given the vaccine under proper conditions; (c) the use of live measles vaccine of low or no potency owing to improper handling, storage temperature, overexposure to light, etc.; and (d) neutralization of the live virus in the vaccine by maternal measles antibody in infants and by administration of the vaccine concomitantly with human immune globulin in children less than 1 year of age.

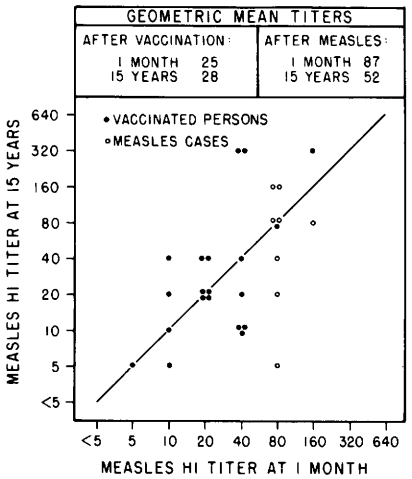

FIG. 1. Persistence of measles HI antibody for 15 years following administration of Enders' original measles vaccine coadministered with human immune globulin or following natural measles.

The present studies show remarkable persistence of measles antibody for at least 15 years in all children who received Enders' original vaccine along with gamma globulin. All the children were at least 1 year of age when vaccinated and all had responded initially to vaccination.

Similarly, there was excellent retention of measles antibody for at least 8 years after Enders' original vaccine given alone or after Moraten live measles vaccine. Higher antibody levels were achieved initially following Enders' original vaccine, but this difference was small 8 years after the vaccine was given.

The sum of the evidence indicates that antibody against measles persists for long time periods, perhaps lifelong, following administration of vaccine of proper potency given to subjects at proper age. It would appear that the attributes of live vaccine itself are far less important in producing and maintaining immunity against the disease than the matters of proper handling and administration of the vaccine and in achiev-

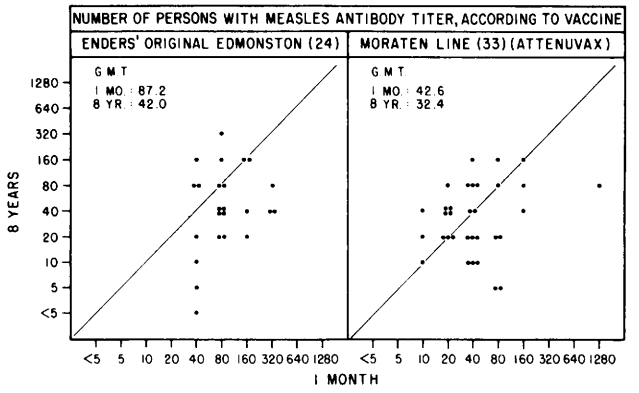

FIG. 2. Retention of measles HI antibody 8 years after vaccination with Enders' Edmonston or Moraten line measles virus vaccine.

ing maximal coverage of the susceptible population.

Summary. All of 20 children sampled who had received Enders' original measles vaccine, together with human immune globulin, retained measles antibody for 15 years with essentially no decline in antibody titer. All but one of 24 children who received Enders' original measles vaccine and all of 33 children who received more attenuated measles virus vaccine (Moraten line, Attenuvax) retained their antibody for 8 years, the longest time period tested. These data support the concept that the problems with efficacy of measles virus vaccine are more related to handling and administration of the vaccine itself than with the attributes of the vaccine.

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