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Homotypic and Heterotypic Antibody Response in Infants to Adenovirus Vaccine

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With 4 Figures

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It has been estimated that 8 to 9% of the total respiratory illnesses seen in a children’s hospital may be caused by adenoviruses; the illnesses include upper as well as lower respiratory infection (Chanock and Parrott, 1965). Certain members of the adenovirus group, particularly types 3 and 7, may produce serious and sometimes fatal pneumonia in young children (cf. review by Sohier, Chardonnet and Prunieras, 1965). For these reasons, it seems important to direct efforts toward control of adenovirus infection in young children by vaccination.

Several studies conducted in the years 1956—1960 demonstrated that inactivated adenovirus vaccines containing types 4 and 7 or types 3, 4 and 7 were highly effective in preventing adenovirus disease in military recruit populations (cf. review by Hilleman, 1966). Reports on the effect of inactivated adenovirus vaccine in children have been far less numerous. Kozinn, Wiener and Burchall (1961) inoculated 104 children over one year of age with two doses of a hexavalent vaccine containing types 1, 2, 3, 4, 5 and 7. They found only a moderate increase in titers for types 3, 4 and 7 and no reduction in the incidence of respiratory illness. Laxdal et al. (1964) studied the effectiveness of a polyvalent vaccine containing influenza A, A1, A2 and B viruses, adenovirus types 3, 4 and 7, and para-influenza 1 and 3 viruses in a group of 516 children 7 months to 15 years of age. Serologic studies in 92 of these children revealed a moderate response to types 3 and 7 two weeks after the second injection. No protection against illness was conferred by the vaccine.

In contrast to the highly favourable results of adenovirus immunization of military recruits found in early studies, inactivated adenovirus
vaccines employed in later studies appeared to be less effective (cf. review by Hilleman, 1966). Presumably, this was related to a lowered antigenic potency of the vaccines, especially with regard to the type 4 component. Moreover, it was found that the oncogenic simian virus 40 (SV40) might be present as an adventitious contaminant of adenovirus vaccines (Sweet and Hilleman, 1960). The problem of vaccine safety was further complicated by the discovery of the oncogenic capacity in newborn hamsters of certain serotypes of the adenovirus group (Trentin, Yabe and Taylor, 1962) and of the phenomenon of "hybridization" of adenovirus type 7 with SV40 virus (Huebner et al., 1964; Rowe and Baum, 1964; Rapp et al., 1964). Because of the difficulties encountered in preparing adequate inactivated whole adenovirus vaccines, other approaches to adenovirus immunization, namely, application of live type 4 adenovirus enclosed in enteric-coated capsules by the oral route (Chanock et al., 1966; Edmondson et al., 1966) and use of noninfectious adenovirus soluble antigens (Kasel et al., 1964; Kasel et al., 1966), are now being explored.

In the present study, which was initiated early in 1962, inactivated whole adenovirus vaccine prepared in monkey kidney cell cultures and controlled according to the contemporary regulations was used. The antibody response of infants under one year of age to successive doses of vaccine was measured. Infants were chosen for this study, since protection against adenoviruses is needed at an early age. In addition, data are lacking on the efficacy of adenovirus vaccine in eliciting antibody in individuals with little or no prior experience with adenoviruses. Although alternate methods of adenovirus immunization are now being explored, it seemed of interest to present the results of the present study, since the novel data obtained are of potential value for future studies with other types of vaccine.

Materials and Methods

Vaccine. Trivalent vaccine, containing adenovirus types 3, 4 and 7, and placebo fluid were kindly supplied by Parke, Davis and Company. The adenoviruses employed in the preparation of the vaccine were propagated in monkey kidney tissue cultures. Inactivation of the viruses was accomplished by treatment with formaldehyde and supplemental treatment with ultraviolet irradiation and beta-propiolactone (Dr. Lease, personal communication).

Study population and immunization schedule. The study population consisted of 311 infants aged 3 to 12 months who where admitted to the hospital between March, 1962, and December, 1965. Infants from families living in Tilburg were selected for study with parental consent. No selection regarding the type of illness for which admission was sought was made. Immunization began on the third or second day before discharge. Infants were assigned to one of 3 groups in consecutive order to achieve randomization. Infants of the first group received two doses of vaccine with an interval of 6 months, those of the second group three doses of vaccine with intervals of 1 and 5