Reactions Among Infants Immunized Intramuscularly with Typhoid Vaccine in Adjuvant

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In a region of high endemicity of trachoma and typhoid in Eastern Saudi Arabia, a vaccination program was undertaken to determine whether the administration of chemically inactivated trachoma viruses to children under 3 years of age would reduce the incidence of trachoma among the vaccinees. For several reasons, the decision was reached that trachoma vaccines should be contrasted with typhoid vaccines. It was also decided to compare the efficacy of these vaccines as aqueous versus adjuvant preparations.

This note records our observation that at least 87 of 1,189 children, aged 3 weeks to 3 years at the time of vaccination with typhoid in adjuvant, had developed local reactions at the end of 1 year. At that time, 29 of the reacting children showed healed sinus tracts, 27 had draining sinuses, and the remaining 31 had palpable masses at the vaccination site. Probably more reactions occurred than those recorded, but it was not possible to examine every child in the study 1 year after vaccination.

The trachoma vaccines were prepared as described by Bell and Theobald (Ann. N.Y. Acad. Sci. 98:337, 1962). The typhoid vaccine was the standard product obtained from the Massachusetts Public Health Biologic Laboratories (lot no. T301).

Both trachoma and typhoid adjuvant vaccines contained equal parts of Drakeol-Arlacel A (in a proportion of nine parts to one) and fluid antigen, either trachoma grown in chick embryo yolk sacs or the sediment from a centrifuged lot of monovalent typhoid vaccine incorporated into a suspension of normal yolk sac which had been prepared by exactly the same procedure used for the trachoma virus vaccine.

The typhoid adjuvant contained only *Salmonella typhosa*, in an amount approximating one-fourth the recommended adult dose of fluid vaccine. Both adjuvant vaccines were administered into the buttock, deep intramuscularly.

A commercial biologicals manufacturer emulsified and packaged the adjuvants at our request, releasing it to us for use only after the final product had passed the standard sterility and safety tests.

Table 1 summarizes the reactions according to type of vaccine. An analysis of the infants who developed reactions to typhoid in adjuvant showed that sexes were equally affected and that lesions occurred by age at time of vaccination as follows: under 6 months, 18; 6 to 12 months, 14; 13 to 24 months, 36; over 24 months, 19. The fluctuant masses of four infants were cultured at the time of incision, and were all sterile bacteriologically. Histological examination of tissues excised from the sinus tracts leading to the lesions of 10 infants showed changes interpreted as chronic granuloma by the pathologist.

In the experiments described, the local reactions were clearly associated with the adjuvant preparation containing bacterial products, and not with the preparation containing killed *Bedsonia*. Reactions of this type to bacterial products incorporated in oil-adjuvant have recently been reported for cholera vaccines (Philippines Cholera Committee, Bull. World Health Organ. 32:603, 1965) and for tetanus toxoid (MacLennan et al., Bull. World Health Organ. 32:683, 1965).

Data are not available to determine whether the reacting infants had already had typhoid fever before receiving the typhoid adjuvant. A further report will be made when a longer period of observation has ensued.

TABLE 1. Number of children showing local reactions 1 year after vaccination

Vaccine*	Total vaccinated	Healed lesions	Palpable lumps	Draining sinuses	Total reactions
Adjuvant-trachoma	1,393	0	0	0	0
Adjuvant-typhoid	1,189	29	31	27	87
Fluid-trachoma	487	0	0	0	0
Fluid-typhoid	482	0	0	0	0

* The adjuvant vaccines were prepared from the same batches of oil and emulsifiers. Fluid and adjuvant typhoid vaccines were prepared from the same batch of typhoid vaccine. Storage conditions were identical for all four vaccines.