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Clinical and Serological Evaluation of Purified Polysaccharide Vaccines Prepared from *Neisseria meningitidis* Group Y (39828)

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Highly purified capsular polysaccharide vaccines prepared with groups A and C *Neisseria meningitidis* have been developed (1, 2). Groups A and C vaccines have been shown to be antigenic and free of significant side effects (3-5). These vaccines have been licensed for limited distribution and use by the Bureau of Biologics, Food and Drug Administration.

Other sero groups of meningococci represent potential medical problems; among these are the group Y meningococci. Epidemiological surveillance has identified carriers of group Y meningococci in several populations (6-8), and meningococcemia and meningococcal meningitis due to the group Y strain have been observed in military populations (9, 10).

This report summarizes the clinical and serological findings in studies of adult individuals given purified polysaccharide vaccines derived from group Y meningococci.

Materials and methods. Vaccines. The three vaccines used in this study were prepared in the Merrell-National Research Laboratories using a culture of group Y meningococci, designated 6306Y, obtained from M. S. Artenstein, Walter Reed Army Institute of Research. The cold phenol method of Gotschlich *et al.* (11) was used to purify the polysaccharide. Chemically, the polysaccharide met the criteria established by Bhattacharjee *et al.* (12) for serogroup Y polysaccharides. In addition, the vaccines met the general requirements of the Bureau of Biologics, Food and Drug Administration, for the release of groups A and C meningococcal polysaccharide (13) and other existing standards pertinent to the use of vaccines (14). Using a Sepharose 4B column, the three vaccines employed exhibited molecular sizing characteristics of 95.3, 91.5, and 95% recoveries at a K_d of 0.4.

A placebo consisting of isotonic sodium chloride with 0.01% thimerosal was used in this study.

Clinical studies. The study population consisted of healthy adult volunteers, employees, and staff of a university hospital who had given their informed consent. Both men and women, 18 to 56 years of age (mean age of 28 years), were included in the study population. Each vaccine was administered to 30 individuals, each of whom received 50 μg of purified polysaccharide (in 0.5 ml) subcutaneously in the upper arm in the region of the deltoid muscle. A total of 20 additional individuals received 0.5 ml of the placebo. Blood specimens were obtained by venipuncture (antecubital vein) prior to the immunizations and 3 weeks after. Sera were collected and stored frozen at $-20°$ until serological testing was conducted.

Pharyngeal cultures for determining the presence of meningococci were taken (preimmunization and 3 weeks postimmunization) by passing a sterile cotton swab across the posterior wall of the pharynx. The swabs were placed in transport media consisting of growth media (2), supplemented with 5% sterile horse sera (Grand Island Biological Co.), Vancomycin (3 μg/ml), and nystatin (12.5 unit/ml; Baltimore Biological Laboratories). These specimens were transported and stored frozen until subcultures to Thayer Martin media (15) were made.

Clinical observations were made and recorded for each individual at 4-hr intervals until bedtime on the day of immunization,

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TABLE 1. SERUM BACTERICIDAL ANTIBODY RESPONSES IN HUMAN SUBJECTS MEASURED 3 WEEKS AFTER A SINGLE DOSE OF ONE OF THREE LOTS OF MENINGOCOCCAL POLYSACCHARIDE VACCINE, GROUP Y.

Lot No.	No. of subjects in study	Initial seronegatives			Initial seropositive		
		≥fourfold rise			≥fourfold rise		
		No./total[a]	(%)	G.M.[b]	No./total	(%)	G.M.
				<2			64
2306	30	26/28	93	416	2/2	100	1024
				<2			49
2307	30	26/27	96	388	2/3	66	724
				<2			49
2308	26	21/21	100	274	3/5	60	446

[a] Number showing rise/total number tested
[b] Geometric mean titer

then daily for the next 3 weeks. Oral temperatures were taken for the first 3 days regularly and were continued if the volunteer had any symptoms. Any adverse local or systemic reactions were recorded on individual case report forms.

Bactericidal tests were performed on pre- and postimmunization sera (inactivated at 56° for 30 min) using a procedure developed by the Bureau of Biologics (13).

Results. A total of 90 subjects received one of the purified polysaccharide vaccines. No systemic reactions were observed by any volunteer in the study population; no temperatures above 37.5° were observed. Individuals receiving the vaccine reported mild local reactions ranging from tenderness to erythema and slight swelling at the injection site. None of the vaccinees reported any local reaction persisting longer than 48 hr. Reactions were observed by 2 of the 20 volunteers who received the placebo.

Neisseria were not isolated from the pharynx of any individual in the study population, either immediately before immunization or when cultured 3 weeks later.

Bactericidal tests were performed in duplicate on paired preimmunization and postimmunization sera. Eighty out of eighty-six individuals for whom paired sera were available had significant antibody rises, i.e., a fourfold or greater difference between pre- and postimmunization sera. The results are summarized in Table 1. One of the individuals in the placebo group had an antibody rise. The geometric mean titers (G.M.) of the individuals receiving the vaccine were 3.0 prior to immunization and 416 at 3 weeks postimmunization.

Discussion. This study indicates that the group Y meningococcal polysaccharide vaccine is antigenic and produces only mild local reactions that are clinically acceptable. No systemic reactions were noted. These results are quite similar to the laboratory and clinical results observed with groups A and C polysaccharide vaccines manufactured by this laboratory.

Of greater significance were the serological conversions induced as a result of the immunizations. Ninety-three percent of the individuals immunized responded with significant levels of group Y bactericidal antibody. A correlation has been made between the presence of bactericidal antibodies and resistance to meningococcal disease (16). Since clinical efficacy has been shown with polysaccharide vaccines of groups A and C meningococci (3, 4, 5) which induce antibody levels comparable to those observed in this study, it seems probable that the group Y polysaccharide vaccine also would be clinically efficacious.

Summary. The clinical and serological testing of a group Y meningococcal polysaccharide vaccine is described. Only minor local reactions at the injection site were observed. High levels of bactericidal antibody were observed in 93% of the individuals 3 weeks after receiving the vaccine.

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