Meningococcal ACYW135 polysaccharide vaccine merited the continuation of its use in this age group. However, the immunogenicity of the tetravalent ACYW135 polysaccharide vaccine in these age groups was unknown. A follow-up study was performed to assess the serologic responses of children <5 years old to meningococcal tetravalent ACYW135 polysaccharide vaccine (2). Children less than 18 months old received two doses 2 to 3 months apart, and those ≥24 months old received one dose. Poor serum bactericidal antibody (SBA) responses were observed to the serogroup C, W135, and Y components of the vaccine in children ≤18 months old, whereas 42% of children had SBA titers of ≥8 for serogroup A. In children ≥2 years old, ≥80% had SBA titers of ≥8 for serogroup A, with a similar number observed for serogroup Y for children 4 years of age. However, poor responses to serogroup C and W135 were still observed for children 4 years of age. As a result of this study, the use of the tetravalent polysaccharide vaccine in children ≤2 years old has been discontinued in Saudi Arabia.

The study also demonstrated that responses to meningococcal polysaccharides are both age and polysaccharide dependent, with serogroup A polysaccharide being more immunogenic in younger children, confirming previous reports (5, 8, 12). It is well known that the immune systems of young children cannot process polysaccharide antigens in a manner appropriate for stimulating an effective response, but it is unclear at what age the immune system is mature enough to provide the correct environment for this process. Hence, a study was performed with Saudi children 5 to 9 years of age to ensure that the responses to the tetravalent ACYW135 polysaccharide vaccine merited the continuation of its use in this age group.

Two hundred forty-one children were recruited to the study from Qassim Province and were split into the following age groups: 5 years old (n = 47), 6 years old (n = 45), 7 years old (n = 49), 8 years old (n = 50), and 9 years old (n = 50). Each group received one dose of Mencevac ACWY (GSK, Rixensart, Belgium), and blood samples were obtained from each child prior to and 1 month after vaccination following agreement to participate by the child's guardian. Serogroup-specific antibody responses were determined by SBA assays as previously described (11) by using the same meningococcal strains as those in the previous study of Saudi children <5 years old (2). Serogroup-specific immunoglobulin G (IgG) levels were determined using a tetraplex bead assay as previously described (9).

Unlike the previous report of responses in Saudi children <5 years old (2), there was no age-dependent trend observed for either the SBA responses or the IgG concentrations, and hence all age groups have been combined and results presented for each individual serogroup. The numbers of individuals with SBA titers of ≥8 for before and after vaccination and ≥4-fold increases in SBA titers from before vaccination to after vaccination are given in Table 1. Forty percent of children had SBA titers of ≥8 for serogroup A, and 55% had similar titers for serogroup Y before vaccination. Significant increases in the numbers of individuals with SBA titers of ≥8 from before vaccination to after vaccination for all serogroups were observed (McNemar's test; P < 0.001). The proportions of individuals with SBA titers of ≥8 ranged from 77% for serogroup C to 97% for serogroup Y. The number of children who demonstrated ≥4-fold increases from before to after vaccination was high, ranging from 65% for serogroup C to 88% for A.
serogroup W135. Analysis of the SBA titers with respect to a more conservative threshold of 128 (Fig. 1) illustrates the magnitude of the response to each of the individual serogroups. For serogroups A, W135, and Y, 84% of children had titers of 128, whereas only 54% achieved this titer level after vaccination for serogroup C.

The geometric mean concentrations (GMCs) and 95% confidence intervals (CIs) for serogroup-specific IgG levels before and after vaccination are given in Table 2. Low GMCs were observed prior to vaccination for serogroups C, W135, and Y; however, serogroup A had a GMC significantly higher than those of the other three serogroups (paired t test; \( P < 0.001 \)). All serogroups showed significant increases in IgG GMCs after vaccination (paired t test; \( P < 0.001 \)), with that of serogroup A again significantly higher than those of the other serogroups (paired t test; \( P < 0.001 \)). It is interesting that for serogroup A high numbers of individuals had prevaccination SBA titers of \( \geq 8 \), corresponding to high anticapsular IgG GMCs, whereas for serogroup Y the high numbers of individuals with prevaccination SBA titers of \( \geq 8 \) corresponded with low GMCs of anticapsular IgG. Inhibition studies indicated that the SBA prevaccination titers observed for serogroup Y were directed mainly towards the capsule, because 100% of samples tested (n = 16) with a range of positive titers (32 to 512) had SBA titers of 2 upon the addition of serogroup Y polysaccharide (data not shown). It is unclear why such high prevaccination SBA titers against serogroup Y were evident, because there are few cases of serogroup Y disease in Saudi Arabia. Furthermore, the carriage of serogroup Y meningococci is unlikely to contribute greatly in inducing high levels of SBA, because the carriage rate of serogroup Y is low, approximately 1%, as illustrated in the United Kingdom (10). One possible explanation may be exposure to cross-reactive epitopes, as has been described for other meningococcal polysaccharides (6, 13, 14).

In conclusion, tetravalent polysaccharide vaccines are immunogenic and elicit functional antibodies in greater than 90% of 5- to 9-year-old children for serogroups A, W135, and Y; however, for the serogroup C portion, only 77% of children reached putative protective levels after vaccination.

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REFERENCES


