Meningococcal Control in the United States and Africa

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(See the articles by Mueller et al. and by Vu et al., on pages 812–20 and 821–8, respectively.)

It is estimated that there are 1400–2800 cases of invasive meningococcal infections each year in the United States, and serogroups B, C, and Y cause approximately one-third of the cases each [1]. The highest age-specific incidence occurs in young children, but a secondary peak is seen in adolescents [2]. Furthermore, morbidity and mortality caused by meningococcus are higher in older children than in younger children [3, 4].

College freshmen, especially those living in dormitories, have an increased incidence of systemic meningococcal infections, most of which are caused by serogroup C [5]. The Centers for Disease Control and Prevention and the American Academy of Pediatrics recommend that the quadrivalent meningococcal polysaccharide vaccine (MPSV-4) be provided for these college students, to decrease their risk of developing meningococcal disease [6]. The length of protection after MPSV-4 administration has been debated, but 3–5 years is the general estimate.

The first meningococcal conjugate vaccine (meningococcal polysaccharide–diphtheria toxoid conjugate vaccine [containing serogroup A, C, W-135, and Y polysaccharides]; MCV-4) was licensed in the United States in January 2005, on the basis of serum bactericidal antibody (SBA) titers for recipients of MCV-4 that were not inferior to those for recipients of the previously licensed MPSV-4 vaccine. Subsequently, MCV-4 was recommended for routine administration to children starting at age 11–12 years, and a catch-up strategy was suggested for 15-year-olds or those entering high school [1, 7].

How long protection will persist after MCV-4 administration is also unknown, but in this issue of the Journal of Infectious Diseases, Vu et al. [8] have extended the findings previously reported from a 3-year follow-up study of adolescents who received MCV-4, MPSV-4, or no meningococcal vaccine [9]. These investigators used a convenience sample of adolescents who were an average of 14 years old at the time of vaccination and for whom adequate serum samples were available 3 years later. Vu et al. confirmed that the concentrations of antibodies to the capsules of serogroups C, W-135, and Y were equivalent in children vaccinated with either MCV-4 or MPSV-4, and both were significantly higher than those in unvaccinated adolescents of the same age. Furthermore, when an SBA assay with human complement (as opposed to rabbit complement) was used, a significantly greater proportion of adolescents vaccinated with either MCV-4 or MPSV-4 had an SBA titer $\geq 1:4$—a titer that was considered to be protective—than was observed in unvaccinated adolescents. Taking the evaluation a step further, Vu et al. used an infant rat model of serogroup C Nesseria meningitidis bacteremia to assess passive protection. Serum samples from MCV-4 recipients were more protective than were those from either MPSV-4 recipients or controls, regardless of the SBA activity of the serum samples. Finally, when they focused on serum samples containing 0.3–0.99 μg/mL of antibodies—a concentration that was associated with borderline passive protection in the infant rat model—they found that serum samples from MVC-4 recipients were significantly more likely to be protective (77%) than were serum samples from MPSV-4 recipients (25%).

Greater serogroup antigens and antibodies avidity in the MCV-4 group may explain these differences.

Thus, 3 years after vaccination, the concentrations of antibodies measured with a radioantigen binding assay, an SBA assay using human or rabbit complement, or a passive antibody assay in an infant rat model of serogroup C meningococcal bacteremia in the MCV-4 group were either equivalent to or greater than those in the MPSV-4 group. These findings support the notion that, in adolescents, protective antibody levels conferred after MCV-4 vaccination will likely persist as long and probably longer than those conferred after MPSV-4 vaccination. In addition, Vu et al. have shown how a passive protection model can be used to assess the activity of antibodies during in vivo infection. Because new meningococcal vaccines for serogroup A, C, W-135, and Y will be licensed in the
United States on the basis of in vitro measurements, rather than on efficacy in the field, data from the infant rat model may help to refine the licensing process.

Although meningococcal disease in the United States can be deadly, and even isolated cases cause significant social disruption, its incidence is much higher in Africa, which has historically been associated with epidemics of serogroup A infections. The African meningitis belt described by Lapayssonnie [10] was thought to be almost exclusively related to serogroup A infections. World Health Organization recommendations have focused on responding with serogroup A polysaccharide vaccine to meningitis outbreaks. More recently, occasional cases of serogroup C infection have led to the use of vaccines containing both A and C capsular polysaccharides. Meanwhile, a consortium is attempting to license a serogroup A conjugated polysaccharide vaccine for use in Africa [11].

Now a new dimension has been added to the epidemiological aspects of meningococcal disease in Africa. Studies performed by the Agence de Médecine Préventive (a nongovernmental organization) and laboratories in Africa and the United Kingdom have brought to light the endemic presence of serogroup W-135. Circulation of strains from this serogroup in Africa may have begun when pilgrims brought back such strains during the outbreak at the Hajj in 2000 [12], but serogroup W-135 now seems to be established in Africa as an indigenous group of bacteria [13, 14]. The study by Mueller et al. in this issue of the Journal [15] shows carriage of serogroup W-135 strains in the pharynx of 18% of children 4–14 years old in Burkina Faso.

Curiously, carriage did not elicit a persistent bactericidal antibody response, and even when there was a response, it did not appear to influence carriage. On the contrary, bactericidal antibodies against serogroup A strains were prevalent, but carriage was rare, presumably because sufficient humoral or secretory antibodies were present in the pharyngeal secretions. In other words, prior serogroup A infection or vaccination limits subsequent carriage, whereas serogroup W-135 carriage does not elicit protective serologic responses. The former finding is encouraging for the development of a herd immunity effect by serogroup A conjugate vaccination, assuming that vaccine coverage is reasonably good.

Mueller et al. argue for the future use in Africa of a vaccine that includes serogroup W-135 antigens. Although MPSV-4 is already available, in view of the loss of antibodies after natural infection that these researchers found, a conjugated polysaccharide vaccine would be preferable, if it produces persistent protection. However, the efficacy of antibodies against invasive disease caused by serogroup W-135 needs to be confirmed, in view of their apparent inefficacy against the establishment of pharyngeal carriage.

The evidence from these studies introduces a complication into the selection of prophylactic measures against meningococcal disease in Africa. Is a vaccine against only serogroup A sufficient? It would appear that, whereas a serogroup A vaccine might substantially reduce the incidence of meningitis, a multivalent vaccine would be needed for optimal efficacy. Can a multivalent vaccine be made inexpensively enough so that it could be widely used in Africa? Only tiered pricing, which would be dependent on successful commercialization in developed countries, will allow this to happen.

As we learn more about the epidemiological aspects of meningococcal disease in ensuing years, from field investigations such as that conducted by Mueller et al., it should be possible to answer these questions with greater assurance. Nevertheless, an MPSV-4 for use in developed countries also provides a tool for potentially better control of meningitis in Africa and elsewhere, as will be indicated more precisely in the light of future information.

References