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EDITORIAL

Do we need revision in vaccination strategy against meningococcal disease in Haj pilgrims in Iran?

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Meningococcal disease is a global health problem. The World Health Organization estimates that there are 1.2 million cases of invasive meningococcal disease and 135,000 related deaths annually (1). Although the disease occurs sporadically in industrialized countries, the major disease burden is in the non-industrialized countries. A recent epidemic in Nigeria resulted in 4164 cases and 171 deaths in 1 week alone (2).

In the past, vaccines against meningococcal disease have failed to provide immunogenicity and long-term protection in infants who are at greatest risk. Although recent vaccines have improved coverage for this age group, there is still no broadly effective vaccine against *N. meningitidis* group B (NMB), which is now the predominant disease-causing isolate in industrialized countries (2). Meanwhile, Haj pilgrims are also high risk population.

In the 1960s, the first successful vaccines were developed against groups A and C and were based on capsular polysaccharide. Subsequently, polysaccharide vaccines were introduced against groups W-135 and Y; a meningococcal quadrivalent A, C, W-135, and Y polysaccharide vaccine, which has been licensed in the United States since 1981 on the basis of its safety and immunogenicity, has over 85% efficacy against the A and C components in older children and adults (3). However, apart from the group A component, these vaccines are poorly immunogenic in children younger than 2 years of age (3). Furthermore, polysaccharides are T-cell–independent antigens that result in short-lived immunity with no memory response. Thus, dosing is required every 3 to 5 years, but this may cause a reduced antibody response (hyporesponsiveness) as compared with the response to initial vaccination, owing to a depleted memory B-cell pool (3).

To overcome the problem of short-lived protection against the meningococcus, covalent binding (conjugation) of polysaccharides to a protein carrier has been used, resulting in T-cell–dependent immunity and a memory response (3). In 1999, the United Kingdom became the first country to introduce the meningococcal group C polysaccharide–protein conjugate vaccine (MenC) into schedules for routine infant immunization, with an initial catch-up campaign for children and adolescents up to 18 years of age (4). After the introduction of this vaccine, there was a marked decline in group C carriage and disease (5). MenC provides significant herd immunity, with a decline in disease even among unvaccinated persons; this effect is the result of reduced carriage among

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teenagers, who constitute the main reservoir for meningococcal transmission (6).

MenC is safe (4), and surveillance in all age groups has suggested an effectiveness of 95% at 1 year, with significant waning over a period of 4 years (7). Although protection was maintained in the catch-up group (overall effectiveness, 90%), the immunization of infants at 2, 3, and 4 months of age resulted in an overall effectiveness of only 66%. Vaccine effectiveness was 93% for up to 1 year in this group, but there was no evidence of protection after this time, with an effectiveness of –81% (7). Bacterial invasion can occur within hours, so the memory response that has been primed by conjugate vaccines cannot be initiated in time (8). Instead, protection requires circulating bactericidal antibodies, but their levels are not sustained after immunization in infancy (8), possibly owing to limited plasma-cell survival.

Because of its devastating effects, meningococcal infection continues to be a global threat to human health. Although conjugate vaccines have been shown to be effective and safe, it is unclear whether recent advances in vaccine development will lead to a universal NMB vaccine in the foreseeable future. Several challenges remain: First, we must improve the immunogenicity of meningococcal vaccines in infants, since this age group is still the most vulnerable to meningococcal infection. This is especially true in the United States, where MenC does not provide adequate coverage; although multivalent conjugate vaccines are licensed for use, they currently do not provide protection for infants. Second, we must ensure that variations of any newly identified antigens do not limit future vaccine efficacy. Finally, we must select vaccines that induce herd immunity to provide the dramatic disease reduction seen with MenC. Only then will it be possible to provide the broad-ranging vaccine against *N. meningitidis* group B that has so far remained elusive (2).

Although meningococcal vaccination has not been included in Extended Program of Immunization in Iran, polysaccharide meningococcal vaccine is mandatory for Haj pilgrims in Iran during the recent years. Nevertheless, new outbreaks have been reported among those Haj pilgrims who have been returned from Saudi Arabia, a fact that put Iranian health policy makers in a big challenge. Additionally, lack of herd immunity following the injection of polysaccharide variant of meningococcal vaccine is associated with fewer declines in group C carriage and disease. Therefore, a careful revision should be applied for meningococcal vaccination of Haj pilgrims in Iran, possibly polysaccharide variant of meningococcal vaccine should be substituted with conjugate vaccines, however, future studies are required to draw a firm conclusion in this regard.

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