Extrameningeal Complications of *Neisseria meningitidis* Serogroup W135 Infection

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(See the article by Faye et al. on pages 1635–7)

*Neisseria meningitidis* serogroup W135 has gone from a rarely implicated cause of invasive meningococcal diseases to being involved in outbreaks on infection with a world-wide distribution. The incidence of meningococcal disease due to the W135 serogroup has gradually increased over the past 15 years in Europe and the United States. Meningococcal epidemics associated with the annual pilgrimage to Mecca have occurred in the past and may have been a factor in the spread of infection in Africa, Asia, and the Middle East in the past [1]. The combination of >1 million individuals living in crowded conditions during the Hajj is a unique setting for acquisition and spread of invasive meningococcal disease. In 1987, an epidemic caused by *N. meningitidis* serogroup A prompted the Saudi Arabian government to mandate vaccination with the meningococcal A polysaccharide vaccine by all pilgrims entering the country for the Hajj. A subsequent serogroup A outbreak occurred in 1992 during Ramadan and Umra. The vaccination was subsequently made mandatory for all Umra visitors [2].

This program worked quite well until 2000 and 2001, when an epidemic caused by *N. meningitidis* serogroup W135 occurred in pilgrims and their contacts. Because of the immigration of Muslim populations over the past fifty years to western Europe and the United States, cases caused by W135 were reported with a worldwide distribution involving Saudi Arabia, western Europe, Africa, the United States, Asia, and the Middle East after the Hajj [3–5]. The W135 strain causing these outbreaks belonged to the electrophoretic type 37 (ET-37) clonal complex. This clonal complex is known to cause hyperendemic disease [3–5]. After the 2001 outbreak, the Saudi Arabian government changed the vaccination recommendation to mandate vaccination with the tetravalent (A, C, Y, and W135) vaccine. This has halted the spread of infection in the pilgrims themselves, but in Singapore, an outbreak was reported in nonvaccinated contacts of pilgrims returning from the Hajj [6, 7]. The risk of invasive disease developing in such nonvaccinated carriers has been estimated to be as high as 1 case in 70 acquisitions. It had been previously shown that W135 can attain high carriage rates, and recent data suggest that the duration of carriage can persist for long periods. Fifty-five percent of vaccinated pilgrims were still carriers 6 months after their return to Singapore. Transmission to 8% of their unvaccinated household contacts occurred within the first few weeks of their return.

The report by Faye et al. [8] in this issue of *Clinical Infectious Diseases* indicates that there may be a high incidence of extrameningeal complications associated with W135 ET-37 invasive infection. Several previous reports also suggest that this clonotype may be associated with extrameningeal complications. Vienne et al. [9] analyzed data from 2019 strains of *N. meningitidis* isolated in France from 1999 to 2001. Their data indicate that the complications of pericarditis, arthritis, and pneumonia occur at much higher rates with W135 infection than with serogroup B or C infection. During this same period, 54% of all cases of meningococcal pneumonia occurred in patients with serogroup W135 infection, which accounted for only 8.2% of all meningococcal infections documented. Similarly, arthritis occurred in 0.7% of all serogroup B infections, 1.4% of serogroup C infections, and 4.8% of serogroup W135 infections. Pericarditis was also much more common among patients with W135 infections, with rates 4 times higher than occurred with serogroup C infections. The reasons for this higher incidence of extrameningeal manifestations of disease with this serogroup are unknown. There is no evidence that serogroup W135 has evolved special virulence factors allowing it to infect extrameningeal sites. The capsular an-
tigen is a polymer of 4-O-α-D-galactopyranosyl-β-D-N-acetylneuraminic acid [10] and has not been linked in any way to this clinical phenomena. The widespread use of the tetravalent vaccine without side-effects strongly suggests that this is not the case. The recent respite in Hajj-related meningococcal disease due to use of the tetravalent vaccine may be temporary. There is no vaccine currently available for the prevention of meningococcal epidemics caused by serogroup B. This is one of the most prevalent serogroups infecting individuals in the developed world and is a cause of infection in developing countries. The serogroup B outer-membrane complex vaccine that is used to abort epidemics has to be designed on the basis of the strain infecting the population at risk. Thus, an outbreak must be in progress, with the serogroup B strain identified, for this vaccine to be designed and then applied. There is an urgent need for a broadly effective serogroup B vaccine that is not serotype based. Until this occurs, all efforts should be made to ameliorate the conditions related to the Hajj that contribute to these outbreaks of meningococcal infection, and international public health personnel should continue to monitor for outbreaks as soon as they occur so that appropriate chemoprophylaxis can be administered to affected individuals.

References