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Carriage of *Neisseria meningitidis* in the Hajj and Umrah mass gatherings

Saber Yezli [a,*], Annelies Wilder-Smith [b], Abdulaziz A. Bin Saeed [a,c]

[a] The Global Centre for Mass Gatherings Medicine, Public Health Directorate, Ministry of Health, Riyadh, Saudi Arabia
[b] Lee Kong Chain School of Medicine, Nanyang Technological University, Singapore
[c] Department of Family and Community Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia

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SUMMARY

Meningococcal disease is a serious public health threat, especially during mass gatherings such as Hajj and Umrah which provide optimal conditions for disease transmission. The disease is caused by *Neisseria meningitidis* and transmitted mainly via asymptomatic carriers. A review of the literature on asymptomatic *N. meningitidis* carriage among Hajj and Umrah pilgrims and their household contacts was performed. Carriage studies reported carriage rates to be higher in Hajj pilgrims compared to Umrah pilgrims and that these events promote acquisition of carriage among pilgrims. With some outliers, most studies found carriage rates among pilgrims to be comparable to those in populations under non-epidemic settings. However, these results should be interpreted with caution, taking into account the limitations within the studies identified. A wide variety of *N. meningitidis* serogroups appear to be circulating among Hajj and Umrah pilgrims, with serogroups W135 and B being most prominent. Current Hajj and Umrah meningococcal disease preventative measures do not necessarily prevent carriage and transmission, which may result in local and international outbreaks among susceptible populations. Monitoring carriage states of visitors and local inhabitants in the Kingdom of Saudi Arabia, as well as the implementation of preventive measures that impact carriage, are warranted to reduce the risk of Hajj and Umrah-related meningococcal disease outbreaks.

1. Introduction

Neisseria meningitidis is one of the leading causes of bacterial meningitis globally and can also cause sepsis, pneumonia, and other localized infections.[1] Invasive meningococcal disease remains a serious public health problem affecting up to 1.2 million people annually and leading to between 50 000 and 135 000 deaths worldwide.[2] Even with appropriate treatment, the case fatality rate is high, and the risk of long-term disabling sequelae of meningococcal infection adds to the disease burden, especially in developing countries.[1] In total, 13 serogroups of *N. meningitidis* have been reported, but only six (A, B, C, W135, X, and Y) cause almost all life-threatening disease worldwide.[3,4]

The Kingdom of Saudi Arabia (KSA) hosts over two million Muslim pilgrims annually from all over the world during the Hajj period and several million pilgrims throughout the year for the Umrah religious mass gatherings in the holy cities of Mecca and Medina. The Hajj pilgrimage is held on every 12th month of the Islamic calendar, while the Umrah pilgrimage may be undertaken at any time of the year. These mass gathering events create conditions of overcrowding that are conducive to human-to-human disease transmission, such as meningococcal disease.[5] Hajj and Umrah have been associated with a number of local and international meningococcal disease outbreaks, including a large serogroup A outbreak in 1987 and major serogroup W135 outbreaks in 2000 and 2001.[6–9] Returning international pilgrims carrying *N. meningitidis* were the vehicle for the exportation of the disease outside KSA and also the introduction of new serogroups into other regions of the world, affecting the global epidemiology of the disease.[3,10,11]

A review of the literature on *N. meningitidis* carriage among Hajj and Umrah pilgrims and their household contacts was performed. The rate of carriage of the organism at these mass gatherings and the serogroups circulating among pilgrims and their contacts is reported here. A PubMed search of the relevant literature (up to 2015) was performed with a combination of the following terms:

* Corresponding author. Tel.: +96611401555 ext 1863.
E-mail address: saber.yezli@gmail.com (S. Yezli).

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'*Neisseria meningitidis*', 'meningococcal', 'carriage', 'Hajj', 'Umrah', 'pilgrims', and 'pilgrimage'. Reference lists of relevant articles were also hand-searched to identify further material.

2. Asymptomatic carriage of *N. meningitidis*

Asymptomatic carriage of *N. meningitidis* was first described in Europe in 1896[12] and occurs in 8–25% of the human population, with adolescents being the major reservoir.[2] Meningococci are spread from person to person through direct contact with oropharyngeal secretions, and asymptomatic carriers are the primary source of *N. meningitidis* transmission under both epidemic and endemic conditions.[1,13] Although asymptomatic carriage of both pathogenic and non-pathogenic strains is common, few carriers develop invasive disease. For the majority of people, carriage is an immunizing process that results in a systemic, serogroup-specific protective antibody response.[1] Vaccination with the polysaccharide vaccines does not prevent the acquisition of carriage, but there is evidence that conjugate vaccines do impact the carriage state.[1,13–15] For instance, the use of monovalent meningococcal conjugate vaccines in routine universal vaccination programs were associated with reductions in carriage and a consequent herd effect, such as reductions of invasive meningococcal disease in unvaccinated age cohorts.[15]

The prevalence of meningococcal carriage differs within and between countries, varying across age groups, serogroup distribution, and over time. The rate is also influenced by contact with cases and the epidemic/endemic situation. For example, the reported prevalence of meningococcal carriage in the USA is 5–10% under non-epidemic conditions.[16] In comparison, a carriage prevalence of between 3% and 30% has been documented for the African meningitis belt.[17] In closed populations, such as among military recruits, carriage can reach levels of 40–80%.[18]

3. Carriage of *N. meningitidis* at the Hajj and Umrah mass gatherings

There are several risk factors associated with meningococcal carriage. These include crowded conditions (e.g., military barracks, dormitories, events), travel to endemic areas, personal behaviors (e.g. kissing, coughing, smoking), and respiratory viruses and Mycoplasma.[6,13,19] In this context, mass gatherings such as the Hajj and Umrah are very relevant. These events are characterized by heavily overcrowded conditions of a pilgrim population originating from diverse geographical areas. These pilgrims all live for extended periods of time in close proximity to each other, with shared facilities, and perform exhausting religious rites. These are optimal conditions for meningococcal exposure and colonization of susceptible individuals and carrier-to-carrier acquisition of strains, as well as increased rate of new carrier acquisition.[6] It is not surprising that a very high prevalence of asymptomatic *N. meningitidis* carriage has been reported at such events, with a rate of up to 86% documented for Mecca pilgrims in 1992.[7]

Local data show that the carriage rate of *N. meningitidis* among the population is higher in cities hosting the Hajj and Umrah mass gatherings compared to other regions of KSA. Two such studies, one performed by Ashoor and Turkestani[20] and the other by Kholeidi et al.,[21] both outside the Hajj pilgrimage season, showed the carriage rate among locals from Mecca to be higher than that in those from Medina (the second most holy city for Muslims) and also higher than that among local inhabitants from the city of Riyadh, where there is no contact with pilgrims; rates were 1.1%, 0.1%, and 0%, respectively. Another study conducted during the 2001 pilgrimage found the carriage rate among the local population of Jeddah and Mecca to be 4.7%.[22] Serogroup W135 accounted for 40% of the meningococci isolated, while only 6.5% were serogroup A and 13% were serogroup B. This is not surprising given that serogroup W135 was the outbreak strain in the 2000 and 2001 Hajj seasons.[6,23]

3.1. *Rate of* N. meningitidis *carriage among Hajj pilgrims*

A number of *N. meningitidis* carriage studies have been conducted on Hajj pilgrims (Table 1). Most of these studies have reported an overall carriage rate of 5–10%, which is comparable to those found in populations in non-epidemic settings.[16] However, there are some outliers. For example, studies among pilgrims from the USA in 2001[24] and Singapore in 2002[25] found significantly lower carriage rates of only 1.9% and 1.7%, respectively. More recently, Benkouiten and colleagues did not detect *N. meningitidis* carriage among 298 French pilgrims sampled before and after the 2013 Hajj,[26] while Ceyhan et al. reported a high (18.7%) overall carriage rate among Turkish pilgrims attending the 2010 Hajj.[27] Several studies have also documented the effect of Hajj on the acquisition of carriage (Table 1), the majority of which found that the pilgrimage increased *N. meningitidis* carriage. However a number of studies have found carriage rates among pilgrims post-Hajj to be lower than those pre-Hajj, even among the same cohorts of pilgrims.[25,28,29]

The above findings however need to be put into context considering a number of important factors. First, most of these carriage studies were conducted in small cohorts of country-specific pilgrim populations.

Second, given the demographics of Hajj pilgrims, carriage studies during the event were conducted on a mostly adult population. The *N. meningitidis* carriage rate differs with age, with a rate of <3% in children younger than 4 years, increasing to 24–37% in the age group 15–24 years, and decreasing to <10% in older age groups.[13]

Third, most of these carriage studies were conducted during, or soon after, the 2000 and 2001 international Hajj-related meningococcal disease outbreaks. Hence, they were performed at a time when a number of meningococcal disease prevention measures had been introduced, both in Saudi Arabia and internationally, to prevent future outbreaks. Of note is the introduction of compulsory meningococcal vaccination with the quadrivalent (A/C/W/Y) vaccine by 2002 for all pilgrims before attending Hajj.[6] The Saudi recommendations do not yet specify which vaccine technology should be used. Although licensed since 2005, the quadrivalent conjugate meningococcal vaccine is still not used universally by all countries participating in Hajj.[30] In most of the Hajj carriage studies the majority of pilgrims, if not all of them, received meningococcal vaccination (Table 1). Vaccination using the polysaccharide quadrivalent vaccine does not prevent carriage, nor does it eradicate existing meningococcal carriage.[1,27] The effect of the polysaccharide vaccines on colonization and the transmission of the organisms are transient or negligible.[13] However, vaccination protects pilgrims from invasive disease and has been linked to a significant reduction in cases of disease during Hajj.[8] The effect of vaccinating the entire Hajj population led to a reduction in invasive disease, which would have impacted carriage rates.[31,32]

Fourth, antibiotic use among pilgrims was found to vary between studies, ranging from 13% to 59% (Table 1). This factor is partially relevant for studies reporting carriage rates in pilgrims post-Hajj. Antibiotic use is common during Hajj and can lead to a reduction or elimination of *N. meningitidis* carriage. In one study, a single dose of ciprofloxacin (500 mg) given to a cohort of Iranian pilgrims 24 h before leaving Hajj reduced the carriage rate from 8.1% before Hajj to 0% post-Hajj.[29] In another study, *N. meningitidis* carriage was not detected post-Hajj among 177 Kuwaiti pilgrims, 83% of whom received one dose of ciprofloxacin before leaving Hajj.[33]

Table 1
Rate of *Neisseria meningitidis* carriage among Hajj pilgrims and their household contacts

Study population	Study year	Overall carriage (%)	Carriage pre-Hajj (%)	Carriage post-Hajj (%)		Notes	Ref.
		Pilgrims	Pilgrims	Pilgrims	Household contacts		
USA[a]	1987	-	-	37/318 (11.6)	-	17% of 192 travelers received meningococcal vaccination. 15% of 186 travelers used rifampicin during their stay in Saudi Arabia.	18
Singapore	2001	30/375 (8)	1/204 (0.5)	29/171[b] (17)	19/233 (8.2)	Rate of antibiotic use in returning pilgrims was 41%.	35
8 countries	2001	134/1458 (9.2)	57/715 (8)	77/743 (10.4)	-	Some pilgrims had received meningococcal vaccination.	49
USA	2001	22/1153 (1.9)	4/452 (0.9)	18/701 (2.6)	-	Carriage rate among returning non-pilgrims was 2.7% (3/112). Rate of antibiotic use was 15% and 44.8% in the pre-Hajj and post-Hajj groups, respectively. Over 97% of pilgrims were vaccinated with the quadrivalent polysaccharide vaccine.	24
Thailand	2001	-	-	0/374 (0)	-	77.8% of pilgrims were vaccinated against meningococcal infection.	50
Singapore	2001	-	-	61/373 (16.4)	13/117 (11.1)	55% of carriers remained positive after 5–6 months. All pilgrims were vaccinated with the quadrivalent polysaccharide vaccine. Some pilgrims took antibiotics during Hajj.	31
Singapore	2002	6/346 (1.7)	4/193 (2.6)	2/153[b] (1.3)	-	All pilgrims were vaccinated with the quadrivalent polysaccharide meningococcal vaccine. Rate of antibiotic use in returning pilgrims was 53%.	25
UK	2002	32/427 (7.5)	21/253 (8.3)	11/174 (6.3)	9/70[c] (12.9)	All pilgrims were vaccinated with the quadrivalent polysaccharide vaccine. Rate of antibiotic use in returning pilgrims was 21%.	28
29 countries	2003	11/344 (3.2)				At least 44% of pilgrims were vaccinated against meningitis in the previous 4 years (92% with the quadrivalent vaccine and 8% with the bivalent vaccine). 12.8% of 163 pilgrims took antibiotics during Hajj.	42
Iran	2003	66/1348 (4.9)	35/674 (5.2)	31/674[b] (4.6)	-	3 new serogroups identified in returning pilgrims (Z, Z′, and A). All pilgrims received the quadrivalent polysaccharide vaccine. At least 58.2% of post-Hajj pilgrims took antibiotics during Hajj.	29
Iran	2003	-	10/123 (8.1)	0/123[b] (0)	-	All pilgrims were given one dose of 500 mg ciprofloxacin 24 h before leaving Hajj. All pilgrims received the quadrivalent polysaccharide vaccine.	29
Kuwait	2005	-	-	0/177[b] (0)	-	92% of the pilgrims were vaccinated with the meningococcal quadrivalent vaccine. 83% of pilgrims received one dose of ciprofloxacin before leaving Hajj.	33
14 countries	2009	152/2046 (7.3)	84/1433 (6)	68/613[d] (11)	-	-	36
Turkey	2010	144/768 (18.7)	63/472 (13)	81/296[b] (27)	10/39[c] (25.6)	All pilgrims were vaccinated using the quadrivalent polysaccharide vaccine.	27
Iran	2012	6/844 (0.7)	0/422 (0)	6/422[b] (1.4)	-	58.5% of pilgrims took antibiotics during Hajj. All pilgrims received the quadrivalent polysaccharide vaccine.	51
France	2012–13	0/596 (0)	0/298 (0)	0/298[b] (0)	-	-	26

[a] High-risk travelers (including pilgrims and non-pilgrims) who visited Mecca and Medina during the Hajj season.
[b] The same pilgrims sampled pre-Hajj.
[c] Contacts of carrier pilgrims.
[d] The same pilgrims or pilgrims from the same Hajj group.

Fifth, other factors could have influenced the reported carriage rates, including poor sampling techniques, differences in laboratory methods, and the rapid autolytic rate of meningococcus, as well as differences in living conditions, degree of overcrowding, or social activities during the Hajj in the populations studied.[22,31]

3.2. *Rate of* N. meningitidis *carriage among Umrah pilgrims*

Few studies have reported meningococcal carriage during Umrah. Wilder-Smith and colleagues investigated 160 Singaporean pilgrims returning from Umrah pilgrimage in 2001.[34] The carriage rate was 1.3%, which was significantly lower than that found in returning Singaporean Hajj pilgrims (17%; $p < 0.001$) in the same year.[35] None of the Umrah pilgrims carried serogroup W135, whereas 90% of the isolates from retuning Hajj pilgrims were serogroup W135.[34,35] A similar statistically significant difference in results was noted by Ashgar et al., who reported an overall carriage rate of *N. meningitidis* of 4% among Umrah visitors and pilgrims compared to 7.3% ($p < 0.0001$) among Hajj pilgrims in 2009.[36] The carriage rate increased from 2.4% before Umrah to 5.7% after Umrah. These differences may be explained by the fact that the length and intensity of interaction among the pilgrims during the Hajj is far greater than during the Umrah.

3.3. N. meningitidis *serogroups carried by pilgrims*

Carriage studies conducted on Hajj and Umrah pilgrims have shown a wide variety of *N. meningitidis* serogroups to be circulating during these mass gatherings (Table 2). Serogroups W135 and B appear to be dominant, which mirrors the epidemiology of serogroups causing disease in Saudi Arabia and in countries of the populations investigated.[8,37] Other serogroups were also identified, including serogroups A, C, D, E, Y, X, Z, and Z′. Hence, the six serogroups causing almost all life-threatening disease worldwide (A, B, C, W135, and Y)[37] were all found to be circulating among pilgrims.

In reviewing the literature on *N. meningitidis* carriage among pilgrims it is clear that serogroup W135 has become the predominant serogroup since the 2000 outbreak. Carriage of W135 was first reported in one US traveler returning from Saudi Arabia during the 1987 Hajj season.[18] High levels of asymptomatic carriage of W135 meningococcus strains belonging to the ET-37 clonal complex (involved in Hajj outbreaks) were found during a vaccine trial in children in Gambia in 1996.[38] This serogroup has been recovered regularly from pilgrims since the 2000 outbreak (Table 2), sometimes with an overwhelming prevalence among *N. meningitidis* isolates. With few exceptions,[28,29] serogroup W135 has accounted for 44–100% of isolates from returning pilgrims and 42–100% of their household contacts. In a recent study, W135 accounted for 82.5% of isolates from Turkish pilgrims sampled pre-Hajj, 91.3% of those from pilgrims sampled post-Hajj, and all isolates recovered from household contacts of carrier pilgrims.[27]

Serogroup B *N. meningitidis* has also been isolated regularly from pilgrims both pre- and post-Hajj, at a rate of 9–25% among isolates (Table 2). In one study, the prevalence of serogroup B among isolates from UK pilgrims was 24% pre-Hajj and 27% post-Hajj, and comprised 22% of isolates recovered from household contacts of returning carrier pilgrims.[28] In general, serogroup B appears to have been the dominant isolated serogroup among pre-Hajj pilgrims, probably reflecting the epidemiology of meningococcal disease in the countries from where the studied pilgrims originated.[37] The regular isolation of serogroup B *N. meningitidis* from pilgrims is concerning. The current compulsory meningococcal vaccination for Hajj and Umrah pilgrims with the quadrivalent ACYW135 vaccine does not protect against disease caused by serogroup B. In addition, many counties with large Muslim populations have been experiencing trends of increased serogroup B meningococcal disease.[39] There is thus the threat of a sudden change in the etiology of meningococcal disease during these mass gatherings.

3.4. *Carriage of non-serogroupable* N. meningitidis *among pilgrims*

A stable feature of carriage studies performed during Hajj and Umrah is the high proportion of non-serogroupable *N. meningitidis* among pilgrims and household contacts. Capsular polysaccharides are the outermost antigens on the meningococcal surface and the prime target for mucosal and humoral immunity.[4,13] Patient strains are encapsulated. In contrast, approximately 50% of the strains isolated from carriers lack the capsule and are therefore serologically not groupable.[13] The carriage rate of such isolates in pilgrims was found to range between 28% and 75% (Table 2). The significance of these isolates is not clear. Non-serogroupable meningococci were formerly assumed to be non-pathogenic, but it was found that capsule production in meningococcal strains can

Table 2
Prevalence of various serogroups among *Neisseria meningitidis* isolates from pilgrim carriers and their household contacts

Study population	Study year	Prevalence of serogroup in pre-Hajj isolates (%)		Prevalence of serogroup in post-Hajj isolates (%)				Ref.
		n	Pilgrims	*n*	Pilgrims	*n*	Household contacts	
USA[a]	1987		-	37	A (91.9)		-	18
Singapore	2001	1	X (100)	29	W135 (89.6)	19	W135 (42.1)	35
8 countries	2001	57	W135 (5.3), A (5.3), B (15.8), X (14), Y (7), NS (50.8)	77	W135 (44.2), B (3.9), X (3.9), NS (46.7)		-	49
USA	2001	4	B (50), Y (50)	18	W135 (50), B (16.6), NS (27.7)		-	24
Singapore	2001		-	61	W135 (91.8)	13	W135 (69.2)	31
Singapore	2002	4	B (25), NS (75)	2	W135 (100)		-	25
UK	2002	21	W135 (9.5), B (23.8), NS (66.6)	11	W135 (9.1), B (27.3), E (9.1), NS (54.5)	9	W135 (22.2), B (22.2), NS (55.6)	28
Iran	2003	35	W135 (2.8), B (25.7), C (14.2), D (14.2), Y (14.2), NS (28.5)	31	W135 (3.2), A (3.2),B (6.4), C (3.2), Y (6.4), Z (3.2), Z′ (6.4), NS (67.7)		-	29
Turkey	2010	63	W135 (82.5), A (14.3), B (1.6), Y (1.6)	81	W135 (91.3), A (6.2), B (1.2), Y (1.2)	10	W135 (100)	27

n, total number of isolates; NS, non-serogroupable.
[a] High-risk travelers (including pilgrims and non-pilgrims) who visited Mecca and Medina during the Hajj season.

switch on and off at a high frequency and that phase variation in the expression of virulence factors that include the capsule is common.[13,40] The loss of the capsule may enhance the capability of meningococci to colonize the human nasopharynx and avoid the human defense systems.[13] There is accumulating evidence of the pathogenic potential of strains that are not groupable by standard slide agglutination (SASG).[41]

Many carriage studies performed on pilgrims and their contacts have used SASG methods to serogroup isolates.[22,25,31,42] Hence data from such studies should be interpreted with caution as they may have underreported the carriage of potentially pathogenic strains. An example of this comes from the work by Dull et al., who evaluated the carriage of *N. meningitidis* among US travelers to the 2001 Hajj.[24] Of the 25 *N. meningitidis* isolates obtained, 15 (60%) were non-serogroupable when tested by SASG techniques. However, using PCR, nine (60%) of the non-serogroupable isolates were characterized as serogroups W135 ($n = 2$), B ($n = 4$), and Y ($n = 3$). In one instance, an *N. meningitidis* serogroup W135 isolate was recovered from an elderly male pilgrim. His wife was also a carrier, but her isolate was not groupable by SASG. When the two strains were further evaluated by molecular and phenotypic techniques, they were found to be identical except for capsule expression.[24]

3.5. *Carriage of* N. meningitidis *among household contacts of returning pilgrims*

Carriage studies have also indicated that household contacts of returning pilgrims are colonized by meningococci carried by pilgrims. Although vaccination may protect the pilgrims from invasive disease, carriage data show that returning pilgrims represent a sizeable reservoir of transmissible and sometimes persistent meningococcal clones, which places their unvaccinated family contacts (and possibly the community at large) at risk of invasive disease. This is all the more relevant given that carriage of *N. meningitidis* can persist for prolonged periods of time both among returning pilgrims and their household contacts.[31,43] Wilder-Smith et al.[31] reported that 55% of carrier pilgrims and 50% of their contacts carriers remained positive for up to 6 months. This long duration of carriage indicates that returning pilgrims may represent an ongoing threat to the community. For instance cases of W135 disease were identified in the UK several months after the end of the Hajj, but most of these case-patients had had no identifiable direct contact with Hajj pilgrims.[44]

Household contacts of returning pilgrims have been implicated in international Hajj-related meningococcal disease outbreaks.[45–47] The estimated attack rate of the W135 disease for household contacts of returning Singaporean pilgrims was 18 cases per 100 000 contacts for the outbreak year of 2000 and 28 cases per 100 000 contacts for the outbreak year of 2001.[11] On the basis of rates of transmission of W135 carriage and epidemiological data, the calculated risk that an unvaccinated household contact who has acquired W135 carriage will develop invasive meningococcal disease was estimated to be 1 case per 70 acquisitions.[11]

The reported rate of meningococcal carriage among household contacts of returning pilgrims was found to vary between studies, ranging from 8% to 25% (Table 1). Household contacts are generally colonized by the same clones carried by the returning pilgrims. Ceyhan et al. reported that 25.6% of household contacts of pilgrims (all carrying the meningococcal serogroup W135) were also carriers of the same serogroup, and that the clonal structure of the bacteria was the same as the source cases.[27] The rate of transmission to household contacts in the study was similar to that observed among household contacts of patients with meningococcal disease (20.5%).[48] Wilder-Smith et al.[35] reported a lower rate of transmission of 8.2% among household contacts of returning pilgrims. This may be explained by the fact that only 29% of the returning pilgrims were carriers. Nevertheless, 42% of the contacts carried the W135 clone, which was prevalent in 90% of the isolates from returning pilgrims. All but one of the contacts carrying the W135 clone were contacts of returning pilgrims colonized with W135. These results are in line with rates of acquisition of the same strain by contacts of patients with meningococcal diseases (50%).[48]

4. Concluding remarks

Due to the potential for contact and epidemic spread, rapid onset, high case-fatality rate, and neurological sequelae of meningococcal disease, a single case is of immediate public health importance, especially during mass gathering events such as Hajj and Umrah. These events create optimal conditions for disease transmission, including that of meningococcal disease. Several Hajj-related meningococcal disease outbreaks have been documented, including international outbreaks of serogroups A and W135. These outbreaks were exported outside KSA via returning pilgrims carrying the organism who transmitted this to their contacts.

We reviewed the literature on *N. meningitidis* carriage among Hajj and Umrah pilgrims and their household contacts. Carriage studies have reported the rate of *N. meningitidis* colonization among the population to be higher in cities hosting the Hajj and Umrah mass gatherings compared to other regions of KSA. Also, carriage rates have been higher in Hajj pilgrims compared to Umrah pilgrims and both of these events promote the acquisition of the carriage state. With some outliers, most studies have found carriage rates among pilgrims to be comparable to those in populations in non-epidemic settings. A considerable variation in reported carriage rates was found, which may be a reflection of the impact of a number of factors including the year of pilgrimage, the population investigated, antibiotic use, and vaccination status, as well as the sampling and laboratory techniques used.

A wide verity of *N. meningitidis* serogroups appear to be circulating among Hajj and Umrah pilgrims, with serogroups W135 and B being dominant. This is of concern, given that the current meningococcal disease preventive measures for Hajj and Umrah do not protect against serogroup B. The current preventive measures of KSA include compulsory vaccination with the quadrivalent vaccine (ACYW135) issued no more than 3 years and no less than 10 days before arrival in Saudi Arabia. For visitors arriving from countries in the African meningitis belt, chemoprophylaxis is also administered at the port of entry to lower the rate of carriers. Available preventive measures against meningococcal disease caused by serogroup B should be considered in preparation for a sudden change in the etiology of meningococcal disease during the Hajj and Umrah.

The current Hajj and Umrah health requirements have been effective in reducing meningococcal cases during these mass gatherings and in preventing outbreaks related to these events in the last few years. However, as vaccination does not prevent carriage and transmission of the organism, returning pilgrims carrying *N. meningitidis* after Hajj or Umrah represent a sizeable reservoir of transmissible and persistent clones, which places their unvaccinated family contacts, and potentially the community at large, at risk of invasive disease. This issue needs to be addressed by an appropriate public health intervention which may include prophylaxis at the point of departure, vaccination of the pilgrims' contacts, and reinforcement of the current preventive measures. A move towards the use of conjugate quadrivalent vaccine for pilgrims will be most beneficial because of the potential for reducing transmission by preventing/clearing carriage. Such public health interventions need to be evidence-based and take into consideration the potential for the development of antibiotic resistance, rate of uptake of the vaccine by pilgrims and their contacts, and the cost and effectiveness of the preventive measure.

Surveillance and tracking the occurrence of invasive meningococcal disease is ultimately more informative to guide interventions for disease prevention than investigating carriage of the organism. However, continued surveillance of the characteristics of the *N. meningitidis* carrier state in the population in Saudi Arabia and among Hajj and Umrah pilgrims will assist in understanding the changing epidemiology and pathogenesis of the organism and in predicting and possibly preventing epidemic outbreaks during future Hajj and Umrah pilgrimages. Such outbreaks could be caused by the emergence of new serogroups in KSA, such as serogroup B or X, or new meningococcal clones resulting from genetic exchange with other bacteria during the carriage state. Carriage investigations including during outbreaks should include the molecular characterization of isolates to avoid underestimation of true carriage and genotype-specific attack rates. Finally, investigation of the carrier state may contribute significantly to our understanding of the main mechanisms involved in the establishment of a commensal relationship between the bacterium and the host, and the link between meningococcal carriage and disease, which has been a fundamental question in meningococcal biology and pathogenesis.

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