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Meningococcal disease during the Hajj and Umrah mass gatherings

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SUMMARY

The Hajj and Umrah religious mass gatherings hosted by the Kingdom of Saudi Arabia can facilitate the transmission of infectious diseases. The pilgrimages have been associated with a number of local and international outbreaks of meningococcal disease. These include serogroup A disease outbreaks in 1987 and throughout the 1990s and two international serogroup W135 outbreaks in 2000 and 2001. The implementation of strict preventative measures including mandatory quadrivalent meningococcal vaccination and antibiotic chemoprophylaxis for pilgrims from the African meningitis belt has prevented pilgrimage-associated meningococcal outbreaks since 2001. However, the fluid epidemiology of the disease and the possibility of outbreaks caused by serogroups not covered by the vaccine or emerging hyper-virulent strains, mean that the disease remains a serious public health threat during these events. Continuous surveillance of carriage state and the epidemiology of the disease in the Kingdom and globally and the introduction of preventative measures that provide broad and long-lasting immunity and impact carriage are warranted.

1. Introduction

Neisseria meningitidis is a Gram-negative, oxidase-positive, aerobic diplococcus of the family *Neisseriaceae*. It is an exclusive human pathogen, carried asymptomatically in the nasopharynx by about 10% of the general population in non-epidemic periods.[1] The bacterium can be either structurally encapsulated or not encapsulated. Capsule polysaccharide expression plays a key role in meningococcal pathogenesis and is the basis for the major serogrouping. In total, 13 serogroups of *N. meningitidis* have been reported, but only six serogroups (A, B, C, W135, X, and Y) cause almost all invasive meningococcal disease worldwide.[2,3] *N. meningitidis* strains that cause invasive disease are almost always encapsulated, which helps the survival of the bacteria during invasive disease and promotes transmission, as well as protection from antibodies and phagocytic cells.[3]

Meningococci are spread from person to person through direct contact with oropharyngeal secretions, and asymptomatic carriers are the primary source of *N. meningitidis* transmissions.[1] However, less than 1% of individuals who acquire carriage go on to develop meningococcal disease.[4] The balance between carriage of the organism and the development of the disease after acquisition is affected by *N. meningitidis* characteristics such as bacterial virulence factors and host and environmental factors including age, functional or anatomic asplenia, and host immune defense mechanisms.[4,5]

Human infections with *N. meningitidis* remain a serious health problem; 500 000 to 1.2 million people are infected and between 50 000 and 135 000 die per year worldwide.[6] Infections present as a spectrum of clinical illness, with meningitis (in 80–85% of cases) and septicemia being the most common. Less common presentations include pneumonia, septic arthritis, pericarditis, conjunctivitis, and urethritis.[4,7] Even with appropriate treatment, the case fatality rate is high: 10–40% depending on manifestation, age, and serogroup.[3,8] Among survivors, up to 20% suffer from complications and sequelae of meningococcal infection, including cognitive deficits, bilateral hearing loss, motor deficits, seizures, visual impairment, hydrocephalus, and loss of limbs due to tissue necrosis.[4]

2. The global epidemiology of meningococcal disease

A notable feature of the meningococcus is its fluid epidemiology. There are substantial cyclical fluctuations in meningococcal disease

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incidence and the occurrence of outbreaks and epidemics worldwide. Disease patterns and incidence vary in populations geographically and over time, among the different invasive meningococcal serogroups and sequence type clonal complexes.[2] The majority of countries in the high-incidence group are found in the African meningitis belt, while many moderate-incidence countries are found in the European and African regions and Australia; low-incidence countries include many from Europe and the Americas.[9]

By far the highest incidence of meningococcal disease occurs in the meningitis belt of Sub-Saharan Africa, extending from Senegal in the west to Ethiopia in the east. During epidemics, the incidence can reach 1000 cases per 100 000, or 1% of the population.[2] Serogroup A has been the most important serogroup in this region.[2,3] However, serogroup W135 has also been an important cause of more recent outbreaks. Serogroup C is responsible for smaller more historical outbreaks and there is recent evidence that serogroup X may now be emerging in the region.[9–11] The introduction of the newly developed meningococcal A conjugate vaccine in countries of the African meningitis belt since 2010 is thought to be responsible for a reduced case load and epidemic activity in the region in recent years, with expected elimination of epidemics caused by serogroup A.[12,13] However, recent outbreaks of the disease in the region, including the outbreak in Niger in 2015, the largest meningitis outbreak caused by serogroup C in the African meningitis belt, show that the disease remains a serious public health threat in the region.[13] In the Americas, the reported incidence of meningococcal disease is in the range of 0.3–4 cases per 100 000 population, with some countries such as the USA currently having incidence at a historical low.[2] Most of the disease in the Americas is caused by serogroups C and B, although serogroup Y causes a substantial proportion of infections in some countries and W135 is emerging.[9]

In European countries, the incidence of the disease ranges from 0.2 to 14 cases per 100 000, mainly caused by serogroup B strains, particularly in countries that have introduced serogroup C meningococcal conjugate vaccines.[2,9] The incidence of meningococcal disease decreased by one half from 1999 to 2006 in Europe (following the introduction of serogroup C conjugate vaccines), but has subsequently stabilized.[3] The burden of meningococcal disease in Asia is much less well defined, but based on limited data, most disease in Asia is caused by serogroup A and C strains.[9] Serogroup B predominates in Australia and New Zealand, with incidence rates ranging between 1.4 and 7.9 cases per 100 000 and between 2.6 and 17.4 cases per 100 000, respectively, spanning the pre- and post-vaccination eras in the two regions.[2,9]

Limited data are available on the epidemiology of meningococcal disease in the Middle East and North Africa.[10] Epidemiology in this region is affected by its proximity to the African meningitis belt and by the Hajj and Umrah mass gatherings as key factors influencing outbreaks and transmission. Whilst serogroup A remains the main cause of meningococcal disease in the region, cases of serogroup B, W135, and Y infections have increasingly been reported over the last two decades in some countries.[9,10] In the Gulf Cooperation Council States, the limited available data show reported incidence rates of below 2 cases per 100 000 in Bahrain, Oman, UAE, Kuwait, and Qatar, with the exception of a few higher rates in the 1980s.[10,14] In Kuwait there were 157 cases of the disease between 1997 and 2009, most of which were caused by serogroups B and W135 (43.0% and 22.1%, respectively), but also serogroups A, C, X, Y, and Z.[10,14] A total of 47 cases of meningococcal disease were reported in Qatar between 2008 and 2010, mostly caused by serogroup W135 (38%), while 48 cases were reported in the UAE in 2008.[14] Between 2001 and 2008, 45 cases of meningococcal disease were reported in Oman, a quarter of which were caused by serogroup W135. Serogroups A, B, C, and Y caused 21%, 2%, 16%, and 9% of the cases, respectively.[14,15]

In Saudi Arabia, the incidence of the disease has fluctuated over time, affected by the large numbers of Muslim pilgrims from the African meningitis belt participating in Hajj and Umrah and the various outbreaks and disease preventative measures introduced in the Kingdom over the years. In 1987 the incidence rate in Saudi Arabia was 12.83 cases per 100 000,[10] but following that peak it has remained relatively low. Between 1995 and 1999, the mean annual incidence was 0.20 cases per 100 000, ranging from 0.25 cases per 100 000 in 1995 to 0.06 cases per 100 000 in 1999. In the two outbreak years of 2000 and 2001, the annual incidence increased to 1.42 and 1.32 cases per 100 000, respectively. In the post-epidemic period between 2002 and 2010, the mean annual incidence did not exceed 0.06 cases per 100 000, ranging from 0.21 cases per 100 000 in 2002 to 0.01 cases per 100 000 in 2010.[16] Serogroups A, B, C, and W135 have been documented as causing disease in Saudi Arabia, where serogroups A and W135 are the most commonly reported.[9,10,16]

3. Meningococcal disease during Hajj and Umrah

Hajj, the annual pilgrimage to Mecca, Kingdom of Saudi Arabia, is one of the largest and most geographically and ethnically diverse mass gatherings in the world.[17] Every able-bodied adult Muslim who can afford to do so is required to make Hajj at least once in his or her lifetime. Hajj is performed in the 12th month of the Islamic (lunar) calendar over a few days and attracts over two million Muslims from more than 183 countries to the Kingdom each year.[18] Mecca is also the setting for a relatively smaller ritual called Umrah, performed year-round. It involves different rituals to Hajj and is performed in a shorter period of time. Improved international travel has rendered Umrah very congested, especially in the 3 months preceding the Hajj when the number of pilgrims rivals that of Hajj.[17] Although not an essential part of the Hajj or Umrah, many pilgrims also travel to Medina, north of Mecca, as part of their pilgrimage. Extended stays at holy sites, especially during Hajj, along with physical exhaustion, extreme heat, and crowded accommodation, facilitates disease transmission during these mass gatherings, including meningococcal disease.[17,18]

4. Meningococcal disease before 1990

Before 1990, meningococcal disease cases during Hajj and Umrah were not uncommon given the demographics of pilgrims and their interaction during these events. However, given the global nature of these mass gatherings, they can be the scene of large outbreaks of the disease with significant national and international repercussions. The first reported international meningococcal disease outbreak following the Hajj was caused by *N. meningitidis* serogroup A and occurred in 1987.[19] The epidemic emphasized the potentially high risk of transmission of *N. meningitidis* during the event. Pilgrimage-associated outbreaks of meningococcal disease also occurred in earlier years, but were less well documented.[20]

It is believed that *N. meningitidis* belonging to the III-1 clonal complex responsible for epidemics in Nepal, China, Europe, and possibly India in the 1980s, was introduced into Mecca by South Asian pilgrims attending the Hajj in 1987.[19] Hajjis who became meningococcal carriers during their stay in Mecca further disseminated this strain to both developed and developing countries around the world on their return home.[19,21] Outbreaks were first noted among South Asian pilgrims (from Pakistan, India, Nepal, and Bangladesh), who comprised approximately 10% of the pilgrims that year and had the highest attack rate during the epidemic.[19,21,22] The disease rapidly spread among pilgrims of other nationalities and the indigenous Saudi population. The attack rate was lowest among pilgrims from the meningitis belt of