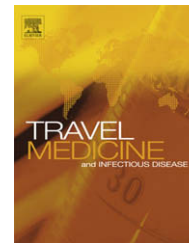




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GUEST EDITORIAL

Meningococcal disease and prevention at the Hajj

KEYWORDS

Meningococcal;
Hajj;
Vaccine;
Travel;
Pilgrimage

Summary The Islamic Hajj pilgrimage to Mecca, Kingdom of Saudi Arabia (KSA) has historically been associated with outbreaks of *Neisseria meningitidis* serogroup A. The main means of prevention against meningococcal disease was the bivalent serogroup A/C polysaccharide vaccine. During the Hajj pilgrimages of 2000 and 2001, there was an epidemiological shift from serogroup A disease to serogroup W135 disease together with an increase in incidence in younger age groups. This prompted the Ministry of Health to introduce quadrivalent ACYW135 polysaccharide vaccines. These interventions have quelled meningococcal disease since 2002. Trials on meningococcal quadrivalent conjugate vaccines are now underway in the KSA.

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Introduction

The Kingdom of Saudi Arabia (KSA) is the largest country of the Arabian Peninsula with an estimated population of 27.6 million. It is bordered by Jordan on the northwest, Iraq on the north and northeast, Kuwait, Qatar, Bahrain, and the United Arab Emirates on the east, Oman on the southeast, and Yemen on the south. The Persian Gulf lies to the northeast and the Red Sea to the west. The KSA faces extraordinary domestic demands on infection control policies during each Hajj season (once a year), when pilgrims visit the holy City of Makkah. In 2009, over 2.5 million pilgrims visited Makkah and the vast majority was international travellers with the remainder travelling to Makkah from within the kingdom. Hajj occurs once a year for a period of five days though pilgrims begin to arrive two months before and may remain for a further month. Camps, consisting of flats and tents, are provided by the Ministry of Hajj and are grouped by nationality with up to 4000 pilgrims inhabiting the same area in large tents which are adjacent to each other.

The Ministry of Health is the key department in ensuring the well-being of all pilgrims and their Infection Control and Preventive Medicines policies are updated annually taking into account outbreaks of infectious diseases that

have occurred in other parts of the world and which may pose a threat during the Hajj. Infectious hazards at the Hajj include respiratory tract infections, meningococcal disease, blood-borne diseases, skin infections and zoonotic diseases, all of which have implications when pilgrims travel home. This editorial summarises the published literature on prevention of meningococcal disease at the Hajj.

Clinical description and presentation of meningococcal disease

The major clinical features of meningococcal disease are fever, rash, and meningitis, but the initial signs and symptoms may be indistinguishable from those of other bacterial or viral infections. Many patients with serious meningococcal disease are initially misdiagnosed as having a benign viral illness. Over half of those with meningococcal disease will have experienced symptoms for less than 24 h when they present to the hospital. Patients typically present with abrupt onset of fever, headache, photophobia, myalgias, and malaise. A common sign is Nuchal rigidity except in infants for whom a more gradual onset of fever, poor feeding, and lethargy are more typical. A bulging fontanel is also a clear indication. A rash is present in the majority of

cases of meningococcal disease consisting of typical petechiae or larger purpuric lesions. Maculopapular rashes also are common and can occur in the absence of petechiae. Progression of disease may be rapid, with onset of hypotension and signs of multiple organ failure. Less common manifestations of meningococcal disease include pneumonia, myocarditis, endocarditis, or pericarditis, arthritis, conjunctivitis, urethritis and pharyngitis. Approximately 10–20% of patients who survive meningococcal disease develop permanent sequelae such as limb or digit loss, extensive skin scarring, cerebral infarction, neurosensory hearing loss, mild to moderate cognitive deficits or seizure disorders.

Classification of meningococci

Meningococci are aerobic, gram negative, oxidase positive, encapsulated diplococci.¹ There are 13 capsular groups that have been identified based on the immunochemistry of the capsular polysaccharide.^{2,3} Serogroups A, B, C, W135 and Y are responsible for the majority of meningococcal disease observed. Further classification of *Neisseria meningitidis* is based on the expression of outer membrane proteins (PorA and PorB),^{4–8} lipooligosaccharide (LOS) structure⁹ and sequence polymorphisms in housekeeping genes which provides a multilocus sequence type (MLST), often abbreviated to sequence type (ST).¹⁰

Risk factors

The meningococcus only colonises the nasopharynx of humans and has no other known environmental niche. It is transmitted from person to person by aerosol droplets or contact with respiratory secretions. Respiratory viruses and *Mycoplasma*,^{11–13} exposure to tobacco smoke^{14,15} or indoor firewood stoves,¹⁶ bar and disco patronage^{17,18} and intimate kissing¹⁵ have all been associated with increased rates of meningococcal carriage or disease.

Antibiotics

There are a number of antimicrobial agents available for the treatment of meningococcal disease, however, penicillin

remains the therapy of choice. Early initiation of antibiotic therapy and presentation to hospital have been associated with reduced mortality and morbidity.¹⁹ For the treatment of non-confirmed cases of meningococcal disease, antibiotics with a broader spectrum of action should be considered such as cefotaxime or ceftriaxone.²⁰ In adults, ciprofloxacin is utilised for the elimination of carriage and is used for all arrivals travelling to the Hajj from countries of the African meningitis belt²¹ (see Table 1). Children receive rifampicin tablets and pregnant women ceftriaxone injections. Ceftriaxone has been shown to be effective and can be used in pregnant women and infants.²² Of note, although antibiotic resistance in meningococci remains at a low level though serogroup A strains resistant to penicillin and non-susceptible to cefotaxime and ceftriaxone have been reported from Delhi, India.²³

Vaccines

Vaccines against meningococcal disease were first developed over 30 years ago but there is still no vaccine available that provides broad protection against all serogroups. Polysaccharide vaccines have existed in monovalent form for serogroup A, bivalent for serogroup A and C, trivalent for A, C and W135 and quadrivalent for A, C, Y and W135. These polysaccharide vaccines together with the new generation of polysaccharide protein conjugate vaccines are described below. Various approaches for vaccines against serogroup B disease have been developed and are not included in this editorial but have been extensively reviewed elsewhere.²⁴

Polysaccharide vaccines

Polysaccharide vaccines are regarded as T cell independent antigens and elicit serum bactericidal antibody (SBA) responses in the absence of T cell involvement. Hence these vaccines tend to be immunogenic in older children and adults, but fail to be as immunogenic in young children. Immunisation of infants with polysaccharide vaccine can induce anticapsular antibody but often this is not bactericidal.²⁵ Antibody titres elicited by polysaccharide immunisation in older children and adults tend to be greater than

Table 1 Health conditions issued by the Minister of Health of the Kingdom of Saudi Arabia for travellers to Saudi Arabia for the pilgrimage to the Hajj and/or Umra in 2008.²¹

For all arrivals	For arrivals from countries of the African meningitis belt ^a	Interior pilgrims and the Hajj workers
Adults and children over 2 years must be given the quadrivalent (ACYW135) polysaccharide vaccine. ^b	In addition to quadrivalent vaccine, chemoprophylaxis must be administered at the port of entry to lower carriage rates. Adults receive ciprofloxacin tablets (500 mg), children rifampicin tablets and pregnant women ceftriaxone injections.	Vaccination with quadrivalent vaccine is required for: <ol style="list-style-type: none"> All citizens and residents of Mecca and Medina who have not been vaccinated during the past 3 years. All citizens and residents undertaking the Hajj. All Hajj workers who have not been vaccinated in the past 3 years. Any individual working at entry points in Saudi Arabia.

^a Benin, Burkino Faso, Cameroon, Central African Republic, Chad, Côte d'Ivoire, Eritrea, Ethiopia, Gambia, Guinea, Guinea-Bassau, Mali, Niger, Nigeria, Senegal and Sudan.

^b Administered not more than 3 years previously and at least 10 days before arrival in the Kingdom of Saudi Arabia.

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