The Risk of Meningococcal Disease in Travelers and Current Recommendations for Prevention

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With the economic recovery gaining momentum, travel experts predict that tourism in all regions will increase in 2010 by an estimated 3% to 4%. This increase in travel is forecasted to exceed 5% in Africa, Asia, and the Middle East, where the risk of acquiring meningococcal disease or becoming a carrier is higher.

When evaluating the need for vaccination in travelers, particularly for those traveling to developing world countries, it is important to consider not only the incidence rate but also the impact of the respective infection. As an example, meningococcal disease is rarely reported in travelers, but the impact of this infection can be as devastating for travelers as for any other individual. With its rapid clinical course and narrow window for diagnosis, the potential for negative outcomes from meningococcal disease may be increased particularly in travelers to remote locations where access to adequate health care facilities and antibiotics is limited. There is an additional public health concern with meningococcal infection, as travelers who are carriers may spread the infection in the society back home.

Travelers’ Risk of Meningococcal Disease

Outbreaks of meningococcal disease frequently occurred among Hajj pilgrims, their contacts, and thereafter even in persons without known contacts prior to 2002, when authorities of the Kingdom of Saudi Arabia issued a quadrivalent meningococcal vaccination requirement to obtain a Hajj visa. Otherwise meningococcal disease usually has been considered to be rare among travelers (Figure 2). A single retrospective survey has attempted to quantify the risk of meningococcal disease among international travelers originating in industrialized countries. Health authorities in 56 of 108 contacted countries (51.9%) completed questionnaires concerning reported cases of meningococcal disease, and tourism data were derived from statistics provided by the World Tourism Organization and national tourism authorities for the study period (1986–1989). On the basis of 13 cases imported to 56 countries, a monthly incidence rate of 0.4 per million was extrapolated, which corresponds to approximately 0.4 per 100,000 population per year. When this rate is compared with the commonly quoted annual incidence rate of 0.5 to 10 cases per 100,000 population in industrialized countries, it appears that ordinary travel does not result in an increased risk for meningococcal disease.

As in the general population, infections in travelers can occur in healthy persons without any apparent risk factors and regardless of the type of traveling or the travel destination. In the past few years, a number of anecdotal reports of meningococcal disease among travelers have been published (Table 1). Additional six cases, which so far are unpublished, have been detected in the GeoSentinel, a worldwide communication and data collection network for the surveillance of travel-related morbidity. Among them, two occurred after a visit to Disney World (Pat Schlagenhauf, personal communication). This demonstrates that, among travelers, meningococcal disease may occur in all parts of the world and in various types of travelers—trekkers, leisure and business travelers, students, and pilgrims—and in all age groups. As in the population affected at home, children and young travelers were most frequently affected. Some of the cases of meningococcal disease in travelers reported in recent years confirm what we know from data in other populations: environmental risk is increased by staying in dormitories, educational or military institutions, and refugee camps and by attending sporting events and discotheques. Clusters of meningococcal disease caused by the same strain have occurred in children whose connection was riding the same school bus, which indicates there could be potential for transmission aboard tour buses. Almost 30 years ago during an outbreak situation, six trekkers fell ill in Nepal. The sum of these examples illustrates that the risk of meningococcal disease in travelers can vary based on destination, mode of transport, type of accommodation, and reason for travel/destination activities. While high-risk groups can be determined primarily on theoretical and general
Figure 1 Impact and incidence of vaccine-preventable diseases in travelers to developing countries.\(^3\) PPD = purified protein derivative, a tuberculin test.

Figure 2 Incidence rate per month of vaccine-preventable diseases in developing countries—2010.\(^3\) CFR = case fatality rate.

epidemiological considerations, there is no zero risk in any traveler.

International travelers can also facilitate the global spread of meningococcal disease. Until 2002, this occurred almost annually after the Hajj. However, potentially risks may still occur, as illustrated by a 2009 case of an individual aged 43 years who contracted a fluoroquinolone-resistant strain of *Neisseria meningitidis* serogroup A.\(^1\) The patient developed symptoms within 24 hours of returning to Italy after traveling to Delhi and Chennai in India, with a stopover of a few hours in Frankfurt, Germany. Although the patient had no known contact with anyone in India with previous or current meningococcal disease, testing revealed the strain was the same that had caused epidemics in the area in 2005 to 2006. Fortunately, no known secondary cases have been reported in Italy.\(^1\)
Table 1  Anecdotal cases of meningococcal disease in travelers, 1996 to 2008

<table>
<thead>
<tr>
<th>Traveler Type</th>
<th>Origin</th>
<th>Location</th>
<th>Infection</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>UK, Germany</td>
<td>Majorca, Spain</td>
<td>2 children died in same hotel</td>
<td>2 died, 2 recovered</td>
</tr>
<tr>
<td>Student Athlete</td>
<td>Swiss/French</td>
<td>Germany, Jaca, Spain</td>
<td>1 died, 1 recovered</td>
<td>Recovered</td>
</tr>
<tr>
<td>Tourist</td>
<td>Swiss</td>
<td>Tirol, Austria</td>
<td></td>
<td>Died</td>
</tr>
<tr>
<td>Business</td>
<td>Italy</td>
<td>India</td>
<td>Recovered from serogroup A disease</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3  Predicted probability of epidemic experience of meningococcal meningitis.

The African Meningitis Belt

During epidemics of meningococcal disease in sub-Saharan Africa, the so-called African meningitis belt that stretches from Senegal to Ethiopia, as many as 1,000 per 100,000 population may be affected. Recently, the epidemic-susceptible area has been expanded to Guinea-Bissau, Guinea, the Ivory Coast, Togo, the Central African Republic, and Eritrea. Countries around the Rift Valley and Great Lakes regions are also now considered to be at risk (Figure 3).

The Hajj

During the annual Hajj pilgrimage, >2 million Muslims from across the globe travel to Mecca and Medina. The congregation of such a large population of individuals from such a wide variety of regions, as well as the crowded conditions at the destination, creates a good environment for meningococcal disease transmission, and the international spread of meningococcal disease resulting in outbreaks and epidemics in several countries has been linked to pilgrims returning from the Hajj prior to the institution of current vaccination protocols. In 1987, outbreaks in the United States and a large epidemic in Africa of meningococcal serogroup A disease were associated with returning pilgrims. More recently, in 2001 to 2002, outbreaks of serogroup W-135 disease in Europe, the United States, the Middle East, and Asia, as well as a large epidemic in Burkina Faso in Africa, were linked to returning pilgrims. One study assessing the risk for meningococcal disease spread as a result of the Hajj-evaluated N meningitidis carriage in US pilgrims traveling through John F. Kennedy Airport in New York, NY, in February 2001. The prevalence of N meningitidis carriage was higher in those returning from the Hajj (2.6% of 844) than in departing pilgrims (0.9% of 425). Although none of the outbound study participants tested were carriers of serogroup W-135, nine of those tested inbound were positive for the serogroup (1.3%; p = 0.01). After the 2001 Hajj, a 15% serogroup W-135 carriage rate also was observed in 171 pilgrims returning to Singapore, with evidence of spread to household contacts. In comparison, data from 2001 indicate that the risk of the international spread variability, risk exists somewhat all year. Population displacements, such as when nomads and farmers congregate in traditional market areas, and overcrowded living conditions can increase the risk of transmission and contribute to epidemics of disease. According to the World Health Organization (WHO), in the 2009 epidemic season, 78,416 suspected cases of meningococcal disease, including 4,053 deaths, were reported in 14 African countries implementing enhanced surveillance techniques. This represents the largest number of cases and deaths since the previous large meningococcal disease epidemic in this region in 1996 to 1997, during which >25,000 people died. However, to our knowledge, there has not been a single case published about a traveler having been affected in the African meningitis belt. At the least, to some extent, this may be due to the fact that, following essentially congruent vaccination recommendations, a fair proportion of high-risk travelers may have been protected appropriately. This may also be, in part, because active surveillance is limited in Africa, Latin America, and Asia, which may result in an underestimation of burden. Finally, an important proportion of travelers has a different behavior and far more social distancing as compared to the local population.

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of meningococcal disease is much lower for Umrah pilgrimage, which is shorter, occurs all year, and involves much smaller groups of travelers. Fortunately, as a consequence of enforced implementation of the meningococcal vaccine requirements issued by the Kingdom of Saudi Arabia health authorities, no exportation of meningococcal disease by Hajj pilgrims has been reported since 2004. There is, however, some concern about serogroup B meningococcal disease for the future.

**Air Travel**

Approximately every 6 weeks, the CDC investigates an incident of possible transmission of meningococcal disease on an aircraft. Many other national institutions have similar queries, and passengers have been diagnosed with meningococcal disease after arrival, such as a journalist with serogroup W-135 in Singapore and an Israeli student in the United States. On the other hand, to our knowledge, only two reports of in-flight transmission have been published. The first occurred on a 14.5-hour flight from Los Angeles to Sydney. Two individuals who had been sitting 12 rows apart were diagnosed with serogroup B meningococcal disease of the same allelic profile. Both patients were women aged >65 years, and both recovered after treatment with antibiotics. One patient reported walking around the plane with some frequency, whereas the other, seated in an aisle seat, only got up a few times to use the rest room. It remains unknown whether transmission occurred from one passenger to the other or whether a third carrier infected them both. In the second report, one passenger and one crew member were infected on an 11-hour military charter flight from the Southwestern United States to Frankfurt. One of the individuals had serogroup B disease; the serogroup in the other individual was undetermined.

**Meningococcal Disease Vaccination Travel Requirements and Recommendations**

**Countries Requiring Meningococal Vaccination for Entry**

Vaccination against meningococcal disease is not required for individuals traveling into any country except for Hajj and Umrah pilgrims to Saudi Arabia. This visa requirement for Saudi Arabia has been extended to all nationals of many countries in tropical Africa arriving by air. Proof of immunization is needed for all Hajj and Umrah visa applicants of all ages; depending on the age group and origin, other vaccinations may also be required (yellow fever, poliomyelitis, and influenza). Applicants must have been immunized more than 10 days and less than 3 years before entering Saudi Arabia.

Because of this requirement for periodic vaccination, waning immunity due to immunologic hyporesponsiveness after repeat administration of meningococcal polysaccharide vaccines can be a concern. A study on residents of Mecca and Jeddah, Saudi Arabia, aged 10 to 29 years found that repeated administration of the AC polysaccharide vaccine resulted in immunologic hyporesponsiveness to serogroup C. Hyporesponsiveness is not a factor with conjugate quadrivalent meningococcal vaccines, and they should therefore be preferred for use for instance in Hajj pilgrims.

**Meningococcal Vaccination Recommendations for Travelers**

Several national health authorities as well as the WHO have issued guidance on vaccinating travelers against meningococcal disease based on environmental factors, such as travel destination, time of year, and type of contact with the local population (Table 2). Although not all the recommendations are consistent—especially in terms of the strength of the recommendation—many overlap to some degree, and all recommend vaccination for all travelers visiting destinations with current outbreaks or epidemic situations.

In its 2010 edition of *International Travel and Health*, the WHO lists meningococcal disease vaccination as being of selective use in travelers, along with hepatitis A vaccine, for example. For travelers to industrialized nations, where they may be exposed to sporadic cases of meningococcal disease, WHO cautions that risk is increased in locations where large groups of adolescents and young adults congregate, such as in schools and college dormitories, and recommends considering vaccination for college students. Vaccination should also be considered in “all travelers to countries in the sub-Saharan meningitis belt.” The risk of infection may be greater in those traveling during the dry season or those staying in the area for longer periods and living with or being in close contact with the local population. Vaccination is also to be considered in “all travelers … to areas with current epidemics.”

The WHO, US, UK, and German/Swiss recommendations are very similar (Table 2). Essentially, vaccination is considered or recommended in similar at-risk groups as those mentioned in the WHO guidance, including travelers to the African meningitis belt and those with prolonged contact with indigenous populations. The UK recommendations also specify meningococcal vaccination for health care workers and travelers visiting friends and relatives due to the close contact these activities involve. The US Centers for Disease Control and Prevention (CDC) and the German/Swiss guidelines explicitly recommend vaccination with a quadrivalent meningococcal vaccine.

The preferred vaccine in the United States for individuals aged 2 to 55 years is a glycoconjugate vaccine, with the polysaccharide quadrivalent meningococcal vaccine currently still recommended for those aged >55 years. Children who received either vaccine at age 2 to 6 years who remain at risk should be revaccinated 3 years later with the indicated glycoconjugate quadrivalent meningococcal vaccine, and then
 Synopsis of meningococcal vaccine recommendations in travelers

<table>
<thead>
<tr>
<th>Travel to:</th>
<th>WHO</th>
<th>CDC (United States)</th>
<th>CATMAT (Canada)</th>
<th>NaTHNac (UK)</th>
<th>ECTM Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hajj/Umrah</td>
<td>Mandatory</td>
<td>Mandatory</td>
<td>Mandatory</td>
<td>Mandatory</td>
<td>Mandatory</td>
</tr>
<tr>
<td>Occupation KSA</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Mandatory</td>
<td>Not specified</td>
<td>Some required</td>
</tr>
<tr>
<td>College US/UK</td>
<td>Consider</td>
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<td>Not specified</td>
<td>Not specified</td>
<td>Some required</td>
</tr>
<tr>
<td>Military</td>
<td>At risk</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td>Sub-Saharan MB</td>
<td>All</td>
<td>Consider</td>
<td>Consider</td>
<td>Risk groups</td>
<td>Consider</td>
</tr>
<tr>
<td></td>
<td>Dry season</td>
<td>—</td>
<td>Recommend</td>
<td>—</td>
<td>Recommend</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>Epidemic</td>
<td>Consider</td>
<td>Consider</td>
<td>—</td>
<td>Recommend</td>
</tr>
<tr>
<td></td>
<td>Hyperendemic</td>
<td>Not specified</td>
<td>Recommend</td>
<td>Consider</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Prolonged contact with local population</td>
<td>At risk</td>
<td>Recommend</td>
<td>Consider</td>
<td>—</td>
</tr>
<tr>
<td>Other</td>
<td>Young children</td>
<td>Not specified</td>
<td>At risk</td>
<td>Not specified</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Health care work</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Visit friends/relatives</td>
<td>—</td>
<td>—</td>
<td>Indicated</td>
<td>—</td>
</tr>
</tbody>
</table>

WHO = World Health Organization; CDC = Centers for Disease Control and Prevention; CATMAT = Canadian Committee to Advise on Tropical Medicine and Travel; NaTHNac = National Travel Health Network and Centre; ECTM = Expert Committee for Travel Medicine.

every 5 years thereafter. Recommendations are similar for those aged 7 to 55 years who remain at increased risk, except that the period from the initial vaccination to the first revaccination is 5 instead of 3 years.8 Travelers to or residents of countries where meningococcal disease is hyperendemic or epidemic are one of the groups considered to have prolonged increased risk for meningococcal disease (along with those with increased susceptibility to infection and those with anatomic or functional asplenia).45 Although the CDC travelers’ guidelines do not include a recommendation for college students studying abroad in endemic areas (eg, Europe), general guidelines from the Advisory Committee on Immunization Practices recommend all college freshman living in dormitories in the United States who were vaccinated with the quadrivalent polysaccharide vaccine more than 5 years ago be revaccinated with a glycoconjugate quadrivalent meningococcal vaccine.45 According to the American College Health Association adolescents and young adults account for nearly 30% of all cases of meningitis in the United States. Some 100 to 125 cases of meningococcal disease occur on college campuses each year, and 5 to 15 students will die as a result. Evidence shows 70% to 80% of cases in the college age group are caused by serogroup C, W-135, or Y, which are potentially vaccine preventable.46 One could extrapolate that this recommendation would hold whether the student was entering college in the United States or abroad. However, national recommendations differ according to the specific indicated age groups and availability of the vaccine. Thus, as new vaccines are developed, country recommendations should be revised accordingly.

Recently, the Canadian Committee to Advise on Tropical Medicine and Travel (CATMAT) issued extensive guidance on the rationale and recommendations for meningococcal disease vaccination in travelers.47 In general, the guidelines recommend a risk-based approach to the decision to vaccinate. Vaccination should be considered for any individuals traveling to a region of “increased meningococcal disease caused by one of the serogroups represented in the vaccine.”47 These include not only the African meningitis belt countries (the guidelines note that the dry season varies from country to country and extends the time frame to 9 months—from October to June) but also those countries in sub-Saharan Africa outside the traditional meningitis belt where recent epidemics have occurred, including the Congo and Tanzania.47 The guidelines also recommend vaccination for the usual groups of travelers who may have prolonged close contact with the local population in these areas, but specify this may include medical personnel and those using public transportation. In addition to areas with active epidemics, vaccination may also be warranted for travelers to areas with “heightened disease activity,” including industrialized nations where sporadic cases of disease have been reported in the previous 6 months. In developed countries, travelers should follow the recommendations of the destination country.47

Although vaccination against serogroup C with a monovalent vaccine is required for all Canadian children, CATMAT notes that this routine vaccination does not provide sufficient protection to individuals traveling to destinations where disease due to other serogroups is reported. Broad serogroup protection is warranted due to this risk, and the preferred vaccine is a glycoconjugate quadrivalent meningococcal vaccine due to its “significant advantages over polysaccharide vaccines including better immune memory, longer
duration of efficacy, lack of hyporesponsiveness with booster doses, and possible reduction of bacterial carriage rates." \(^{47}\)

**Applying a Risk-Based Approach to Assess Travelers’ Need for Meningococcal Vaccination**

For the vast majority of travelers, ie, those not making pilgrimages to Saudi Arabia or those not entering college where vaccination is required (chiefly in the United States), the decision to vaccinate is based essentially on an assessment of the risk to the individual of developing disease and/or of becoming a carrier of infection. This assessment must account for destination, nature and duration of potential exposure, age, and overall background health of the traveler (ie, host factors) (Figure 4). Because meningococcal vaccines are associated with relatively few adverse events and contraindications, these aspects hardly ever need to be considered.

**Destination**

Obviously, vaccination should be recommended for all travelers visiting destinations with outbreaks or epidemic situations, wherever that might be, except those who have been vaccinated within the past 3 years. There are Web sites that can advise clinicians on active areas, such as http://www.meningvax.org/epidemic-updates.php, developed by a WHO/PATH partnership. As noted above, most expert groups recommend vaccination against meningococcal disease for at least some travelers with destinations in the African meningitis belt. There is disagreement over whether this recommendation should be limited to the dry season, defined by various bodies as occurring from October to June \(^{47}\) or only December to June,\(^{8}\) or whether, in view of the recently changing meteorological patterns, no seasonal limitation ought to be imposed (as in the WHO and German recommendations).\(^{44}\) Increasingly, experts also consider parts of the Rift Valley in Africa, including Darfur, Western Kenya, parts of Western Tanzania, Rwanda, Burundi, and Malawi, to pose as many risks as the traditional meningitis belt,\(^{47}\) but not the usual safari tourist destinations in East Africa.

Recommendations may also slightly differ based on risk of exposure to meningococcal disease in the high-risk destination countries as described in the paragraph below. A meningococcal vaccine that covers all four serogroups (ACWY) is necessary for travelers to the African meningitis belt due to the need to protect against multiple serogroups that cause disease in the area.\(^{41}\)

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**Figure 4** Meningococcal vaccination decision algorithm for travelers. 4V = quadrivalent; KSA = Kingdom of Saudi Arabia; UK = United Kingdom; US = United States; VFRs = visiting friends and relatives.

\[^{4V}\] = quadrivalent; KSA = Kingdom of Saudi Arabia; UK = United Kingdom; US = United States; VFRs = visiting friends and relatives.
Meningococcal Disease in Travelers: Risks and Recommendations

Behavior at Destination
Besides the general destination-specific factors, we must also consider that personal exposure, living conditions, and professional and social behavior play a decisive role. Disaster relief personnel or staff for humanitarian aid (eg, in refugee camps) may be at higher risk. In the African meningitis belt, any health professional should consider not only the duration of exposure, but also whether there will be close contact to the local population in the activity, the accommodations, and type of public transportation. Globally, exposure in dormitories or similar accommodations may pose an increased risk of transmission, and meningococcal vaccination ought at least to be considered.

Host Factors
Finally, host factors need to be taken into account. There is consensus that, for instance, persons with splenectomy and some with immune or complement deficiencies should receive meningococcal vaccination regardless of travel.45,47 This factor is often neglected, and thus a pretravel consultation is an opportunity for catch-up vaccination in such patients; however, HIV infection is not an indication for meningococcal vaccination, although such patients “may elect vaccination.”46 Possibly these patients may only have received a vaccine against serogroup C and may request quadrivalent protection. Some health care professionals will also consider that children are at higher risk of exposure and/or that senior travelers may be immunosenescent and thus at higher risk of serious illness.

Conclusions and Future Prospects
As with many other immunization programs in the general population, the goal of vaccinating travelers is to both protect the individual from meningococcal disease and protect society from its spread. In view of the large variety of geographical distribution worldwide, broad coverage against all vaccine-preventable serogroups is warranted and therefore multivalent meningococcal vaccines are to be preferred over monovalent vaccines for travelers. Moreover, wherever possible, meningococcal glycoconjugate vaccines should be preferred over polysaccharide vaccines due to their advantages in terms of improved immunogenicity in infants, stimulation of immunologic memory, longer duration of efficacy, apparent lack of hyporesponsiveness with repeat administration, and efficacy in reducing asymptomatic carriage of N meningitidis.45 Glycoconjugate vaccines are particularly beneficial considering that the aim of immunization in travelers is to reduce the risk of disease in the individual as well as reduce the likelihood of transmission to others and the international spread of infection. At present, there are two glycoconjugate multivalent meningococcal vaccines available that protect against disease caused by serogroups A, C, W-135, and Y for use in individuals aged 11 to 55 years; one also includes 2- to 10-year-olds. Although these vaccines are effective and well tolerated, gaps remain in our arsenal against meningococcal disease. There currently is no vaccine available that offers broad protection against multiple strains of N meningitidis serogroup B, which is a major cause of meningococcal disease outbreaks and epidemics in many regions in the world. Moreover, the emergence of the new serogroup X in recent years, mainly in Niger, must be closely monitored, as there is no vaccine available for it.49 Finally, there is no vaccine currently indicated for protection against meningococcal disease in infants under 2 years of age. However, there is hope for the future. A glycoconjugate meningococcal ACWY-CRM vaccine is now licensed in various countries that can be used from the age of 2 months. Vaccines against serogroup B are in advanced development. Furthermore, updated national travel recommendations may provide travel medicine providers with an effective tool to evaluate meningococcal vaccination as a means to help prevent contagion and spread of infectious disease globally.

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