

A Review of Meningococcal Disease and Vaccination Recommendations for Travelers

Lidia C. Serra · Laura J. York · Amgad Gamil · Paul Balmer · Chris Webber

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ABSTRACT

Abstract: International travel has been steadily increasing since the middle of the twentieth century, including travel to regions with high levels of endemic meningococcal disease and areas with sporadic or sustained meningococcal outbreaks. Although invasive meningococcal disease (IMD) is relatively rare in travelers since the advent of quadrivalent meningococcal vaccines, it remains a serious concern because of its rapid progression, poor prognosis and outcomes, associated treatment delays, and the potential to precipitate outbreaks. Moreover, fatality occurs in up to 22% of those infected. This review will focus on IMD in travelers, with an emphasis on IMD epidemiology and the geographic regions of potential concern for

international travelers. As vaccination is the best approach for preventing IMD among travelers, currently available meningococcal vaccines and corresponding country-specific national meningococcal vaccination recommendations, where available, will be summarized by age and type of vaccine recommended. The use of the quadrivalent meningococcal vaccines, specifically the tetanus toxoid conjugate vaccine (including MenACWY-TT; Nimenrix[®]), as a protective measure against IMD in travelers will be emphasized.

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L. C. Serra (✉) · L. J. York · P. Balmer
Pfizer Vaccines, Medical Development, Scientific and Clinical Affairs, Collegeville, PA, USA
e-mail: Lidia.Oliveira@pfizer.com

A. Gamil
Pfizer Vaccines, Global Medical Development, Scientific and Clinical Affairs, Dubai, United Arab Emirates

C. Webber
Pfizer Vaccines, Clinical Research and Development, Pearl River, NY, USA

INTRODUCTION

Rates of global travel have been increasing since the 1950s. In 2000, 674 million individuals traveled internationally, with the number of travelers in 2010 and 2015 increasing even further to 950 and 1186 million, respectively [1]. Although invasive meningococcal disease (IMD) is relatively rare in travelers, it remains a serious concern because of its rapid clinical course, short time frame for diagnosis, difficulty in obtaining timely antibiotic treatment, potentially poor outcomes, and the ability of infection to spread rapidly among a population [2, 3]. Even with appropriate medical care, the

case-fatality rate remains high and can reach 22% [4], with approximately 20% of survivors experiencing debilitating long-term sequelae that include neurologic impairment, hearing loss, chronic pain, amputation, and skin scarring [5–7].

Although at least 12 serogroups of *N. meningitidis* have been reported, most cases of IMD are caused by serogroups A, B, C, W, X, and Y [8]. Currently, vaccination is the recommended approach for preventing IMD, with available vaccines targeting single serogroups or a combination of multiple serogroups; together, these vaccines can provide protection against 5 of the 6 major disease-causing meningococcal serogroups (i.e., A, B, C, W, and Y) [9]. Specifically, various formulations of conjugated quadrivalent ACWY vaccines are commonly used to target serogroups A, C, W, and, Y and recombinant protein vaccines target serogroup B.

This review will focus on IMD in international travelers, with an emphasis on the geographic regions of potential concern and the importance of vaccination with quadrivalent conjugate vaccines as a preventative strategy for IMD. Country-specific national vaccination recommendations based on the traveler's country of origin will be discussed. Emphasis will be given to the quadrivalent vaccines, including the recently approved tetanus toxoid conjugate vaccine (MenACWY-TT, Nimenrix®; Pfizer, Sandwich, UK), which is indicated for use in individuals ≥ 6 weeks of age [10]. This review is based on previously conducted studies and information obtained from online databases and did not recruit human participants or utilize animals.

GLOBAL EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN TRAVELERS

Regional IMD incidence at the traveler's destination is an important consideration when evaluating the overall risk of contracting IMD and should be taken into account when considering preventative strategies. Although travel to the African meningitis belt and the annual Hajj pilgrimage in Saudi Arabia currently pose

two of the greatest risks for contracting IMD, there are other regions of particular concern to the global traveler; these are discussed in more detail below. Importantly, the prevalence of disease-causing serogroups can vary widely by region and year, so, from a preventative standpoint, it is important to understand the predominant disease-causing serogroups at the time of travel [11]. For instance, the recent emergence of serogroup W in a number of countries, coupled with its often atypical presentation, has made this a serious concern for international travelers; therefore, more detail regarding the emergence of serogroup W by region is also discussed briefly in the following sections.

The African Meningitis Belt

Although endemic in various regions across the globe, the IMD burden is greatest in the 22 countries comprising the “meningitis belt” of sub-Saharan Africa, which stretches from Senegal in the west to Ethiopia in the east [12]. In this region, IMD is hyperendemic, with the number of cases approaching 1000 per 100,000 population during the dry season. Epidemics in this region can occur annually and are characterized by a broad distribution across age groups. Outside of epidemic situations, the highest incidence of IMD in this region typically occurs in young children [13].

Between 1993 and 2012, the majority of IMD in the meningitis belt was due to serogroup A, which was the etiologic agent identified in 80% of the epidemics with approximately 1 million cases and 100,000 deaths [12]. In response to the medical need, a monovalent meningococcal A conjugate vaccine, MenAfriVac (PsA-TT; Serum Institute of India, Pune, India) was developed and prequalified for use in children and adults aged 1–29 years [14, 15]. In 2010, MenAfriVac was used in prophylactic vaccination campaigns in three African countries (Burkina Faso, Mali, and Niger) [16], and by 2014, no cases caused by serogroup A were identified in these countries [17]. In the face of declining serogroup A disease, serogroup W emerged as a predominant pathogen and, by

2012, was responsible for 55% of confirmed IMD in the region [18]. Cases of serogroup C were also increasing in the region. From December 2016 to June 2017, Nigeria experienced a large outbreak of IMD, and, of the 433 confirmed cases, 358 (82.7%) were attributable to serogroup C [19]. This outbreak may represent the largest global outbreak of serogroup C to date, and a number of factors likely contributed to the large number of cases, including procedural and resource allocation inadequacies pertaining to specimen collection and identification, and delayed access to vaccines [19].

Hajj

A number of travel-related meningococcal outbreaks have been reported in the literature, and, of these, the largest and the most notable are those associated with the annual Hajj pilgrimage in Saudi Arabia. The Hajj is the largest annual mass gathering on Earth and attracts more than 2 million pilgrims annually [20]. Hajj pilgrims are geographically diverse, representing > 180 different countries, with many elderly participants who commonly have underlying medical conditions that would predispose them to IMD [20–22]. During the 1987 Hajj, an outbreak of serogroup A resulted in an incidence rate of 640 cases per 100,000 pilgrims. During the 2000 and 2001 Hajj, the majority of cases of IMD were not attributable to serogroup A, as expected, but to a hypervirulent strain of serogroup W, which before that time was of little epidemiologic concern [21].

In 2000, a total of 253 laboratory-confirmed IMD cases occurred in Mecca, Medina, and Jeddah, and, among these, 56% of cases occurred in travelers [23]. Of the 161 cases for which the serogroup was identified, 58% were serogroup W and 37% were serogroup A [23]. This outbreak resulted in 70 deaths (case-fatality rate, 28%) and the subsequent spread of serogroup W disease to at least 16 countries from the pilgrims returning from the Hajj [21, 23]. A retrospective study conducted in Saudi Arabia between 1999 and 2002 (encompassing the 2000 and 2001 epidemic years) identified 729 cases of IMD that

were reported within the country, and, of these, 42% occurred in travelers and 58% occurred in the local population [24]. The majority of these cases were identified in children, with 59 and 39% occurring in children < 5 and < 2 years of age, respectively [24]. Together, this suggests that the Hajj pilgrimages of 2000 and 2001 featured an epidemiologic shift from serogroup A to W. Information on case-fatality rates among pilgrims, many of whom are diagnosed upon returning to their native countries, is not consistently reported; however, data available from the 2000 Hajj epidemic suggest a high case-fatality rate associated with that outbreak, with reported rates ranging from 21% among pilgrims from Oman to 60% among pilgrims hospitalized in Mecca [25].

Other Regions

Transient and sporadic increases in IMD have also been noted globally in countries outside of the African meningitis belt and Saudi Arabia. Therefore, travelers should be aware of the local IMD epidemiology at any travel destination where increases in IMD cases have been documented. Some of these regions are discussed briefly below.

Europe

Although the IMD incidence in Europe is generally low, increases have been observed over the past decade. In 2015, the incidence of IMD in the European Union was 0.6 cases per 100,000 population, slightly down from the 0.7 cases per 100,000 population in 2010. Countries with the highest number of cases per 100,000 population in 2015 were Lithuania (1.9), Ireland (1.5), the United Kingdom (1.4), and Malta (1.2) [26]. Despite low IMD incidence overall, certain serogroups are emerging as a concern in localized areas.

For example, since 2009, a clonal complex variant of serogroup W (cc11) has been causing increases in IMD in the United Kingdom [27]. During the 2013–2014 epidemiologic year, serogroup W accounted for 15% of IMD compared with 1.8% in 2008–2009. This increase was due to the expansion of a single strain that

primarily affected adults ≥ 45 years of age in 2009–2010; however, by 2011–2012, cases were distributed across all age groups.

Serogroup C also emerged as a concern in Italy in 2015 and 2016, when 43 cases were reported in Tuscany within the span of 13 months; this was a substantial increase compared with the 12 and 16 cases reported in 2013 and 2014, respectively [28]. Ten of the 43 cases in Tuscany were fatal, and those infected ranged in age from 9 to 82 years. The molecular classification of the isolates obtained from these patients is ongoing [28].

Central and South America

In Central and South America, the annual incidence of IMD varies considerably, ranging from < 0.1 cases per 100,000 population in Bolivia, Cuba, Paraguay, and Peru to almost 2 cases per 100,000 population in Brazil. However, it should be noted that surveillance and reporting are not uniform across countries, which may account for the wide range in incidence [11].

Serogroups B, C, Y, and W are all known to cause disease in this region. Although serogroups B and C are responsible for most cases of IMD, serogroup W is emerging as a cause of outbreaks in several countries [11, 29].

The prevalence of disease-causing serogroups varies widely by region and by year [11]. Between 2006 and 2011, serogroups B and C predominated across Central America, the Caribbean, and Mexico; however, in 2012, most IMD cases were caused by serogroups B and Y [11]. In the Andean region (Bolivia, Colombia, Ecuador, and Venezuela), the proportions of serogroup B and C cases increased between 2006 and 2012 as the relative proportion of serogroup Y declined [11]. In Brazil between 2006 and 2012, serogroup C caused most cases [11]. In the Southern Cone (Argentina, Chile, Paraguay, and Uruguay), serogroup B caused the majority of IMD in 2006; however, cases caused by serogroup W increased over time so that, by 2012, it was the predominant serogroup leading to IMD [11].

Middle East

In the Middle East, IMD incidence rates were highest in Sudan (2006) and Yemen (2005) with 13.26 and 4.74 cases per 100,000 population, respectively [25]. In countries that reported outbreaks, most were caused by serogroups A or W, with the exception of Israel, where outbreaks were due to serogroups B or C [25]. Recent surveillance data from Kuwait cited a mean incidence rate of 0.5 per 100,000 population; the dominant serogroups were W and B, accounting for 80 cases (32% each). Serogroup B accounted for 34% of all cases in children ≤ 14 years, and serogroup A accounted for 40% of all adult cases. Three outbreaks in Kuwait in 1987, 1989, and 2002 were caused by serogroups A, W, and B, respectively [30].

Australia

In Australia in 2013, the incidence of IMD was relatively low at 0.6 cases per 100,000 population, but beginning in 2014, the number of cases began to increase, and, by 2016, an incidence rate of 1.1 cases per 100,000 population was reported [31]. In 2015, serogroup B was responsible for 64% of IMD cases, decreasing from previous years when serogroup B accounted for 75–88% of cases [32]. The proportion of cases due to serogroups W and Y have been rising in recent years, reaching 21% and 13%, respectively, in 2015 [32]. Although IMD has been decreasing in New Zealand since 2002, the most recent surveillance data in 2013 reports an incidence rate of 1.5 cases per 100,000 population, which, although still relatively high, is the lowest annual IMD incidence rate in the last 20 years [33]. The average annual incidence rate in New Zealand between 2009 and 2012 was 2.5 cases per 100,000 population.

North America

In North America, Canada had a peak in IMD incidence in 2001 with 1.18 cases per 100,000 population, but, thereafter, incidence rates have leveled off and, from 2002 to 2011, IMD incidence ranged between 0.45 and 0.75 cases per 100,000 population [34]. In the United States, the incidence of IMD decreased from 0.61 to 0.18 cases per 100,000 population over the

10-year period from 2003 to 2013 [35]. In 2016, the IMD incidence rate was 0.12 cases per 100,000 population, with serogroup B being the most predominant (0.04 cases per 100,000 population) [36].

Emergence of Serogroup W: a Concern for International Travelers

Although vaccination against serogroup W is not broadly recommended for travelers outside of Saudi Arabia and the African meningitis belt [37], serogroup W, as noted above, is emerging as a global concern. Before 2000, serogroup W cases were sporadic [38]; however, increasing incidence rates since the 2000 Hajj have been observed in a number of countries, including England [39], South America [40, 41], Africa [42, 43], Australia [44], Canada [45, 46], and the United States [47]. Therefore, vaccination to prevent serogroup W infection should be an important consideration for international travelers.

In England, the number of serogroup W cases began to increase in 2009 and almost doubled in a single epidemiologic year, as evidenced by 95 cases in 2013–2014 compared with 176 cases in 2014–2015 [39]. More recently, serogroup W has been responsible for several IMD cases in teenagers, which have been characterized by an atypical gastrointestinal presentation that included nausea, vomiting, and diarrhea [40]. Among 15 cases diagnosed in teenagers aged 15–19 years between July 2015 and January 2016, 7 had mainly gastrointestinal symptoms, and of these, 5 died within 24 h of hospitalization [40]. This marked and notable increase in serogroup W cases in England was due to a single strain (ST11) that was also responsible for an increased IMD incidence in South America [40, 41].

Serogroup W has also been implicated in large meningococcal epidemics in Africa [42, 43]. In one epidemic in The Gambia in 2012, an incidence rate of 1470 cases per 100,000 population (all serogroup W) was observed in children < 12 months of age, and a 13% fatality rate was reported in this age group [43].

In Australia, the percentage of meningitis cases due to serogroup W increased from 4 to 30% during the 2-year interval between 2013 and 2015 [44]. Of the 22 cases that were reported, 9 cases occurred in adults > 70 years of age, and the majority of isolates represented a single strain (ST11). An increased prevalence of IMD due to serogroup W has been noted in Canada between 2009 and 2016, with 18.8% of all cases attributable to serogroup W in 2016; the average percentage of serogroup W cases over the time period was 7.1% [46]. In the United States, where an outbreak of serogroup W in 2008–2009 was linked to 14 cases of IMD in Florida, 4 of these were fatal [47].

Clinically, serogroup W has not only been associated with atypical gastrointestinal presentation but subtle differences in sequelae that differentiate it from other IMD-causing serogroups have also been observed, although data are currently limited [38]. These atypical sequelae associated with serogroup W disease include septic arthritis, pericarditis, bacteremia and sepsis, neonatal sepsis, chronic meningococcemia, pneumonia, and peritonitis. Serogroup W has also been associated with a high case-fatality rate (16.3%) and infection of older adults (mean age, 53 years) at a higher rate [38].

Other Considerations for Travelers

Although regional IMD incidence is an important consideration when determining overall risk for international travelers, travelers should also consider a number of additional factors. For example, the traveler's occupation, length of stay, and activities undertaken during travel, particularly those that involve intensive interaction with indigenous populations and large groups, are also likely to influence the traveler's potential for contracting or spreading IMD. Some travelers may also be at higher risk for IMD due to certain medical conditions, such as inherited deficiencies in the complement pathway, asplenia, previous viral infections, and chronic underlying illness; smoking and crowded living conditions also pose a risk for IMD [48]. Therefore, in addition to regional IMD epidemiology at the traveler's destination, these

items should be considered when evaluating the need for preventative vaccination strategies.

AVAILABLE MENINGOCOCCAL VACCINES AND RECOMMENDATIONS FOR TRAVELERS

Quadrivalent Polysaccharide Conjugate Vaccines

Currently, three different quadrivalent meningococcal vaccines—each containing capsular polysaccharides conjugated to a carrier protein—are available in various regions for the prevention of IMD caused by serogroups A, C, W, and Y (Table 1) [49]. MenACWY-DT (Menactra[®], conjugated to diphtheria toxin; Sanofi Pasteur, Swiftwater, PA, USA) and MenACWY-CRM (Menveo[®], conjugated to C reactive protein; Novartis Vaccines and Diagnostics, Savigliano, Italy) were initially licensed in the United States in 2005 and 2010, respectively [49]. The third quadrivalent vaccine, MenACWY-TT (Nimenrix[®], conjugated to tetanus toxoid; Pfizer), was first licensed in Europe in 2010 [50]. All vaccines have been approved for use in multiple countries and are well tolerated and immunogenic [49].

Recombinant Protein Vaccines

Unlike serogroups A, C, W, and Y, the serogroup B polysaccharide is structurally similar to molecules found on human neuronal cells, and thus can be considered a human self-antigen [51]. Therefore, serogroup B vaccine development has focused on targeting surface-exposed proteins. Using this approach, two recombinant-protein vaccines are currently available for the prevention of IMD due to serogroup B. MenB-FHbp (Trumenba[®], bivalent rLP2086; Pfizer, Philadelphia, PA) [52], targeting both subfamily A and subfamily B variants of the conserved factor H binding protein (FHbp), was first licensed in the United States in 2014 [53], and, more recently, in Europe [54], Canada [55], and Australia [56]. A second serogroup B vaccine, MenB-4C (Bexsero[®],

4CMenB; GlaxoSmithKline Vaccines, Siena, Italy) [57], which includes three recombinant bacterial proteins (including subfamily B FHbp) and an outer membrane vesicle containing PorA [58], was first licensed in Europe in 2013 and is now licensed in several geographic regions [59, 60].

National Meningococcal Vaccination Recommendations for Travelers from Their Country of Origin

Vaccination is the best method for preventing meningococcal infection [9]. Currently, six countries including Australia [61], Bahrain [62], Canada [63], Saudi Arabia [64], the United Kingdom [65], and the United States [66] have national recommendations for meningococcal vaccination in travelers. Although there is some variability in country-specific guidance, specifically pertaining to the age of the vaccinees and the type of conjugate vaccine that is recommended (Table 2), there is general consistency across these guidelines regarding vaccination for travelers entering high-risk areas. For instance, all six of these countries recommend vaccination with a quadrivalent conjugate vaccine for travelers entering areas associated with an increased incidence of endemic or epidemic meningococcal disease that is caused by serogroups contained in the vaccine. Particular emphasis is given to vaccination for those traveling to the African meningitis belt and to Saudi Arabia for the Hajj and/or Umrah [61–64, 66, 67]. The United Kingdom also recommends vaccination for backpackers who are traveling in the “rough” and for those who are working with, or spending an extended period with, indigenous populations [65]. In addition to quadrivalent ACWY vaccination, the Public Health Agency of Canada recommends vaccination with a serogroup B vaccine for those entering areas with an increased incidence of serogroup B infection [63].

There are a number of resources available online for travelers documenting global and country-specific meningococcal disease epidemiology and vaccination recommendations (Table 3). For example, the World Health

Table 1 Available MenACWY conjugate vaccines

		Quadrivalent conjugate vaccines		
		MenACWY-TT	MenACWY-CRM	MenACWY-DT
Name		Nimenrix	Menveo	Menactra
Company		Pfizer	GSK	Sanofi Pasteur
Availability		European Union [77]	International [78, 79]	European Union [80]
Age indication, lower limit		≥ 6 weeks	≥ 12 months	≥ 9 months
Age indication, upper limit		None	55 years ^a	55 years
Dose schedule		≥ 6 to 12 weeks, 2 + 1	1 dose ^c	≥ 9 to 23 months, 1 dose
		≥ 12 months, 1 dose ^d		≥ 2 to 6 months, 3 + 1
				≥ 7 to 23 months, 2 doses
				≥ 2 to 55 years, 1 dose
				≥ 15 to 55 years, booster dose
Safety		Well tolerated	Well tolerated	Well tolerated
				Well tolerated

Table 1 continued

Quadrivalent conjugate vaccines			
	MenACWY-TT	MenACWY-CRM	MenACWY-DT
Co-administration with other vaccines ^{b,f}	6 weeks to < 1 year: DTaP-HBV-IPV/Hib, PCV10	Monovalent and combined HAV and HBV, yellow fever, typhoid fever, Japanese encephalitis, and rabies	DTaP, TT, Hib, polio, HAV, HBV, PCV7, PCV13, rotavirus, HAV/HBV
	1 to < 2 years: HAV, HBV, MMR, MMTV, PCV10, seasonal influenza		MMRV, MMR, V, PCV7, DT, Typhim, HAV, Daptacel
	1 to < 2 years: HAV, HBV, MMR, MMRV, seasonal influenza, PCV10		MMRV
	2nd year: DTaP, polio, HBV, Hib		AU: DT, Typhim

CRM cross-reactive material, *DT* diphtheria and tetanus toxoid, *DTaP* diphtheria and tetanus toxoid with acellular pertussis, *HAV* hepatitis A virus, *HBV* hepatitis B vaccine, *Hib Haemophilus influenzae* type b, *MMR* measles, mumps, and rubella, *MMRV* measles, mumps, rubella, and varicella, *PCV7* 7-valent pneumococcal conjugate vaccine, *PCV10* 10-valent pneumococcal conjugate vaccine, *PCV13* 13-valent pneumococcal conjugate vaccine, *TT* tetanus toxoid, *Typhim* typhoid Vi polysaccharide 16 vaccine, *V* varicella

^a The upper age limit for vaccination in Canada and Australia is 55 years

^b The upper age limit for vaccination in Canada is 55 years

^c In Canada and Australia, booster doses may be administered to those previously vaccinated with an unconjugated polysaccharide meningococcal vaccine

^d A booster dose may be recommended in some individuals

^e In Australia, vaccine may be administered until 55 years of age

^f Concomitant use in clinical vaccines studies

Table 2 Country-specific meningococcal vaccination recommendations for travelers

Age/population group	Recommended meningococcal vaccines
Australia [61]	
2–6 months	MenACWY-CRM
7–11 months	MenACWY-CRM
12–23 months	MenACWY-CRM or MenACWY-TT
2–6 years	MenACWY-DT MenACWY-CRM, or MenACWY-TT
≥ 7 years	MenACWY-DT MenACWY-CRM, or MenACWY-TT ^a
Bahrain [62]	
≥ 2 years ^b	MenACWY quadrivalent conjugate vaccine
Canada [63]	
≥ 2 months ^c	MenACWY-CRM; 4CMenB
Saudi Arabia [86]	
> 2 years ^d	MenACWY quadrivalent conjugate or polysaccharide vaccine
United Kingdom [65]	
Birth to < 9 months	MenACWY-CRM
9 to < 12 months	MenACWY-CRM or MenACWY-TT
12 months–2 years	MenACWY-TT
2–4 years	MenACWY-CRM or MenACWY-TT
≥ 5 years	MenACWY-CRM or MenACWY-TT preferred; MenACWY polysaccharide vaccine may be considered
United States [66]	
2 months	MenACWY-CRM
7–23 months	MenACWY-CRM or MenACWY-DT

Table 2 continued

Age/population group	Recommended meningococcal vaccines
2–55 years	MenACWY-CRM or MenACWY-D ^c
≥ 56 years (previously vaccinated)	MenACWY-CRM or MenACWY-D ^c
≥ 56 years (unvaccinated)	MPSV4

CRM cross-reactive material, DT diphtheria toxin, TT tetanus toxoid

^a Quadrivalent conjugate vaccine is preferred; however, the quadrivalent polysaccharide vaccine is a suitable alternative for travelers aged ≥ 7 years when the need for repeat doses is not anticipated

^b A single-dose quadrivalent conjugate meningococcal vaccine is recommended to citizens at 2 years of age and is recommended for Hajj pilgrims and for travelers to certain countries; 1 – 2 doses are recommended for individuals with certain hemoglobinopathies, congenital or acquired asplenia, presplenectomy, terminal complement deficiency, post bone marrow transplant, or certain cancers after the completion of treatment

^c For those not previously vaccinated with MenACWY-CRM or 4CMenB

^d Vaccination with quadrivalent vaccine is required for all citizens and residents of Medina and Mecca who have not been vaccinated during the past 3 years with a polysaccharide vaccine or during the past 5 years with a conjugate vaccine; all citizens and residents undertaking the Hajj who have not been vaccinated during the past 3 years with a polysaccharide vaccine or during the past 5 years with a conjugate vaccine; all Hajj workers, including individuals working at entry points or in direct contact with pilgrims, who have not been vaccinated in the past 3 years with a polysaccharide vaccine or in the past 5 years with a conjugate vaccine. Visitors from all countries arriving for the purpose of Umrah, pilgrimage (Hajj), or seasonal work must have proof of vaccination ≥ 10 days and < 3 years (polysaccharide vaccine) or ≥ 10 days and < 5 years (conjugate vaccine) before date of entry to Saudi Arabia

^e Even if vaccinated with Hib-MenCY-TT during infancy or childhood

Table 3 Links to information pertaining to current meningococcal disease epidemiology and travel-related vaccination recommendations

Source	Website
World Health Organization	http://www.who.int/csr/don/archive/disease/meningococcal_disease/en/
International Association for Medical Assistance to Travelers	https://www.iamat.org/elibrary/view/id/1359
European Centre for Disease Prevention and Control	https://ecdc.europa.eu/en/meningococcal-disease
US Centers for Disease Control and Prevention	https://www.cdc.gov/abcs/reports-findings/surv-reports.html
New Zealand Ministry of Health	https://surv.esr.cri.nz/surveillance/Meningococcal_disease.php
Australian Ministry of Health	http://www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-annlrpt-menganrep.htm

Organization maintains a database of meningococcal outbreaks and cases listed by the date of the most recent occurrence and the country of origin [68]. Another useful resource for travelers is the World Immunization Chart developed by the International Association for Medical Assistance to Travelers, which is continually updated and summarizes all global vaccination recommendations [37].

In addition, a number of societies have made similar recommendations for quadrivalent meningococcal vaccination for travelers entering high-risk areas, with the African meningitis belt and Saudi Arabia delineated as areas of potential concern. For example, the Malaysian Society of Infectious Diseases and Chemotherapy recommends vaccination with a conjugate meningococcal vaccine for pilgrims attending Hajj or Umrah, all travelers to high-risk areas, and adults with medical conditions that put them at high risk for infection (e.g., those with complement disorders or functional or anatomic asplenia) [69]. Because numerous societies put forth recommendations and there is no central repository for information, a summary of recommendations from societies is beyond the scope of the current review; however, it is advisable for travelers to check all recommendations in their country of origin when planning an itinerary.

Recommendations at the Traveler's Destination for Those Entering High-Risk Areas, Primarily Saudi Arabia

Since 2010, the Ministry of Health of Saudi Arabia and the Global Center for Mass Gathering Medicine has recommended that a quadrivalent conjugate meningococcal vaccination be administered to individuals 2–55 years of age residing in Saudi Arabia, and in 2013, a routine childhood vaccination program was implemented in that country [21]. However, due to the high cost, quadrivalent conjugate vaccines were initially recommended but not mandatory for international pilgrims [21]. Despite a lack of mandatory recommendations, overall vaccine coverage during the 2015 Hajj was high, with 91% of all pilgrims having received a quadrivalent vaccination, although vaccine coverage was < 70% in some countries [21]. In 2017, the Saudi Arabia Ministry of Health required quadrivalent meningococcal vaccination for all Hajj and Umrah pilgrims and for local pilgrims and seasonal workers [70].

Importance of Recommending Vaccines that Protect Against Multiple Meningococcal Serogroups

Considering the broad distribution of IMD serogroups worldwide and the presence and/or

emergence of multiple serogroups within geographical regions, meningococcal vaccines that protect against multiple serogroups provide the best preventative option for travelers. Currently available quadrivalent ACWY conjugate vaccines would therefore not only confer protection to those traveling globally but would also be expected to reduce the risk of transmission, thus reducing the spread of disease at home and abroad. However, as noted previously, multiple formulations of quadrivalent ACWY polysaccharide conjugate vaccines are currently available in different regions around the globe. The availability, indication, dosing, co-administration with other vaccines, and safety/immunogenicity of the conjugate quadrivalent vaccines is set out in Table 1. The text below will summarize the clinical data for the most recently approved vaccine, MenACWY-TT.

Summary of Clinical Data for MenACWY-TT

As evident from the information presented above, it is imperative that national meningococcal vaccination programs for travelers adapt to the variable nature of meningococcal disease at the traveler's destination; however, it is equally important that the recommending body make informed decisions regarding which vaccine to recommend when multiple formulations are available. To help inform these decisions, a brief summary of data available for MenACWY-TT is described.

The quadrivalent conjugated MenACWY-TT is licensed in the European Union and 43 additional countries, including Africa (18 countries), Asia (7 countries), Eastern Europe (3 countries), the Middle East (8 countries), North America (2 countries), Oceania (2 countries), and South America (3 countries). In some countries, including Europe, a 2-dose infant series of MenACWY-TT is indicated for infants beginning at 6 and 12 weeks followed by a booster dose, whereas a single dose is indicated for children aged > 12 months, adolescents, and adults [71]. In Canada and Australia, MenACWY-TT is indicated for individuals aged

12 months to 55 years [72, 73]. MenACWY-TT is not currently licensed in the United States.

The immunogenicity and safety of MenACWY-TT have been established in clinical studies in individuals across all ages compared with other meningococcal vaccines, using an established correlate of protection [74]. Among toddlers, the percentage of subjects achieving seroprotection after 1 dose of MenACWY-TT can reach 100% [75], but 2 doses may be required to achieve adequate protection in younger children [76]. In adolescents and adults, 80–97% of individuals achieve protective titers against the four serogroups in MenACWY at 1 month post-vaccination after a single dose [74]. Persistence of antibody responses up to 5 years after administration of the MenACWY-TT primary series has also been demonstrated across age groups [74]. It has also been demonstrated that MenACWY-TT can be given concomitantly with other commonly administered vaccines, including the hepatitis A and B vaccines, the mumps/measles/rubella vaccine, the 10-valent and 13-valent pneumococcal conjugate vaccines, the diphtheria/tetanus/acellular pertussis vaccine, and the combined diphtheria, tetanus, acellular pertussis/hepatitis B/inactivated polio virus/haemophilus influenzae type B vaccine.

MenACWY-TT is generally safe and well tolerated across age groups and has demonstrated an acceptable and consistent safety and reactogenicity profile in a pooled clinical study population that included 3079 toddlers (aged 12–23 months), 1899 children (aged 2–10 years), 2317 adolescents (11–17 years old), 2326 adults (18–55 years old), and 274 older adults (≥ 56 years old) [74]. Common local reactions included pain, redness, and swelling at the injection site, while common systemic events included drowsiness, fatigue, fever, headache, irritability, and loss of appetite. Safety was also demonstrated in 1052 infants receiving ≥ 1 MenACWY-TT dose beginning at 6–12 weeks of age and in 1008 toddlers (aged 12–14 months) who received a booster dose [74].

CONCLUSION

Outside of Saudi Arabia, the decision of travelers to vaccinate against meningococcal disease rests on country-based recommendations and perceived risks. Recent changes in the global epidemiology of IMD, particularly a global increase in serogroup W, have raised concerns in several countries worldwide and resulted in updated meningococcal vaccination recommendations, specifically the addition of conjugated MenACWY vaccine to existing recommendations. A quadrivalent conjugate vaccine, such as MenACWY-TT, can provide protection for travelers, especially those traveling to areas where the local meningococcal epidemiology involves multiple predominant serogroups or where the likelihood of epidemic outbreaks is high.

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